

**THE UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL**

Department of Pathology

ANNUAL REPORT



1 JULY 2004 - 30 JUNE 2005

THE UNIVERSITY OF MICHIGAN

MEDICAL SCHOOL

Department of Pathology

ANNUAL REPORT



1 JULY 2004 - 30 JUNE 2005

LIST OF FACULTY

LIST OF FACULTY

<u>Name</u>	<u>Rank</u>	<u>Institutional Affiliation</u>
Abrams, Gerald D.	Professor Emeritus	The University of Michigan
Annesley, Thomas M.	Professor	The University of Michigan
Appelman, Henry, D.	M.R. Abell Professor	The University of Michigan
Baker, James R.	Associate Professor	The University of Michigan
Barr Jr., Mason	Professor ⁺	The University of Michigan
Blaivas, Mila	Associate Professor	The University of Michigan
Capps, Rodney D.	Assistant Professor	The University of Michigan
Chamberlain, Priscilla	Instructor II	Veterans Affairs Medical Center
Chensue, Stephen W.	Associate Professor	Veterans Affairs Medical Center
Chinnaiyan, Arul	S.P. Hicks Collegiate Professor of Pathology, Associate Professor of Pathology**	The University of Michigan
Cho, Kathleen R.	Professor*	The University of Michigan
Cooling, Laura	Assistant Professor	The University of Michigan
D'Amato, Constance J.	Assistant Professor Emeritus	The University of Michigan
Dai, Yiran	Assistant Professor	The University of Michigan
Davenport, Robertson	Associate Professor	The University of Michigan
de la Iglesia, Felix	Adjunct Research Scientist***	Pfizer
Dressler, Gregory R.	Associate Professor	The University of Michigan
Duckett, Colin	Assistant Professor	The University of Michigan
Elnor, Victor M.	Associate Professor ⁺⁺	The University of Michigan
England, Barry G.	Associate Professor	The University of Michigan
Fantone, Joseph C.	Godfrey D. Stobbe Professor in Pathology Education and Director, Anatomic Pathology	The University of Michigan
Fearon, Eric R.	Professor*	The University of Michigan
Ferguson, David	Assistant Professor	The University of Michigan
Finn, William	Associate Professor	The University of Michigan
Flint, Andrew	Professor	The University of Michigan
Friedman, Bruce A.	Professor	The University of Michigan
Fullen, Douglas R.	Associate Professor	The University of Michigan
Giacherio, Donald	Associate Professor	The University of Michigan
Gikas, Paul W.	Professor Emeritus	The University of Michigan
Giordano, Thomas J.	Associate Professor	The University of Michigan
Gordon, David	Professor	The University of Michigan
Greenson, Joel	Professor	The University of Michigan
Guo, Renfeng	Reseach Assistant Professor	The University of Michigan

Department of Pathology Annual Report

<u>Name</u>	<u>Rank</u>	<u>Institutional Affiliation</u>
Headington, John T.	Professor Emeritus	The University of Michigan
Heidelberger, Kathleen P.	Professor Emeritus	The University of Michigan
Hogaboam, Cory	Associate Professor	The University of Michigan
Inohara, Naohiro	Research Associate Professort	The University of Michigan
Johnson, Kent J.	Professor	The University of Michigan
Judd, W. John	Professor	The University of Michigan
Keller, Evan	Assistant Professor##	The University of Michigan
Killen, Paul D.	Associate Professor	The University of Michigan
Kleer, Celina	Associate Professor	The University of Michigan
Krueger, Cynthia	Lecturer	The University of Michigan
Kunju, Lakshmi (Priya)	Assistant Professor	The University of Michigan
Kunkel, Steven L.	Endowed Professor of Pathology Research and Co-Director, Division of General Pathology	The University of Michigan
Lieberman, Andrew P.	Assistant Professor	The University of Michigan
Lieberman, Richard W.	Assistant Professor+++	The University of Michigan
Lowe, Lori	Professor	The University of Michigan
Lucas, David	Associate Professor	The University of Michigan
Lucas, Peter	Assistant Professor	The University of Michigan
Lukacs, Nicholas	Associate Professor	The University of Michigan
Mandell, Stephen	Assistant Professor and Director, MLabs Program	The University of Michigan
McKeever, Paul E.	Professor	The University of Michigan
McKenna, Barbara J.	Associate Professor	The University of Michigan
Mellerick-Dressler, Dervla	Assistant Professor	The University of Michigan
Michael, Claire W.	Associate Professor	The University of Michigan
Midgley, A. Rees	Professor Emeritus	The University of Michigan
Miller, Richard A.	Professor	The University of Michigan
Murphy, Hedwig S.	Assistant Professor	The University of Michigan
Naylor, Bernard	Professor Emeritus	The University of Michigan
Newton, Duane	Assistant Professor	The University of Michigan
Nunez, Gabriel	Professor	The University of Michigan
Phan, Sem H.	Professor	The University of Michigan
Pu, Robert	Assistant Professor	The University of Michigan
Ramsburgh, Stephen R.	Assistant Professor	The University of Michigan
Rasche, Rodolfo	Assistant Professor	The University of Michigan
Remick, Daniel G.	Professor	The University of Michigan
Ross, Charles W.	Associate Professor	The University of Michigan

<u>Name</u>	<u>Rank</u>	<u>Institutional Affiliation</u>
Roulston, Diane	Associate Professor	The University of Michigan
Ruiz, Robert	Assistant Professor	The University of Michigan
Sarma, J. Vidya	Research Assistant Professor	The University of Michigan
Schmaier, Alvin	Professor	The University of Michigan
Schmidt, Robert W.	Professor Emeritus	The University of Michigan
Schnitzer, Bertram	Professor	The University of Michigan
Shah, Rajal B.	Assistant Professor	The University of Michigan
Silverman, Eugene M.	Associate Professor Emeritus	The University of Michigan
Smith, Lisa	Assistant Professor	The University of Michigan
Stoolman, Lloyd M.	Professor	The University of Michigan
Su, Lyndon	Assistant Professor	The University of Michigan
Thorson, John	Assistant Professor	The University of Michigan
Till, Gerd O.	Professor	The University of Michigan
Utiger, Cheryl	Lecturer	The University of Michigan
Valdez, Riccardo	Assistant Professor	The University of Michigan
Varani, James	Professor	The University of Michigan
Ward, Peter A.	Godfrey D. Stobbe Professor	The University of Michigan
Warner, Roscoe L.	Research Assistant Professor	The University of Michigan
Warren, Jeffrey S.	Aldred S. Warthin Professor and Director, Clinical Pathology	The University of Michigan
Wilson, Thomas	Assistant Professor	The University of Michigan
Zochowska, Anuska	Assistant Professor#	The University of Michigan

- * Joint Appointment, Department of Internal Medicine
- ** Joint Appointment in Urology
- *** Clinical Appointment, Pfizer
- + Joint Appointment, Department of Pediatrics and Communicable Diseases
- ++ Joint Appointment, Department of Ophthalmology
- +++ Joint Appointment, Department of Obstetrics and Gynecology
- # Joint Appointment, Department of Surgery
- ## Joint Appointment, ULAM and Institute of Gerontology



**FACULTY, RESIDENTS AND FELLOWS
DEPARTMENT OF PATHOLOGY
2004-2005**

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DEPARTMENTAL OVERVIEW



Department of Pathology
University of Michigan

**UNIVERSITY OF MICHIGAN MEDICAL SCHOOL
DEPARTMENT OF PATHOLOGY**

**DEPARTMENTAL OVERVIEW
ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

Introduction and Overview

The transition process for change in governance was in “high gear” by the spring of 2005, as Dr. Jay Hess gradually assumed leadership responsibilities as my replacement. Working closely with me, Dr. Hess began meeting with departmental faculty and staff as well as with institutional leaders. He has instituted a search process for a Director of Surgical Pathology as well as an informatics faculty member who will replace Dr. Bruce Friedman. The department has, with the Life Science Institute, recruited from Stanford University Dr. Jason Gestwicki whose interests focus on novel ways to block intracellular signaling pathways. There is also intense activity with consultants to develop plans for a Replacement Clinical Laboratory Building. Planning efforts are underway to define incremental research space that can be used for additional faculty members whose interests are significantly related to research. The Department remains in a very strong position, in teaching, service and research activities.

Teaching

Faculty members continue to fill leadership roles in the medical curriculum as course directors, sequence coordinators, and as Associate Dean for Medical Education, Assistant Dean for Admissions and Assistant Dean for Diversity and Career Development in the Medical School. Several faculty members continue to be recognized as recipients of outstanding teaching awards and selection as graduation class marshals. Pathology faculty and pathology laboratories continue to be a strength within the re-structured first year normal organ system and second year abnormal organ system sequences. Fourth year clerkships in Pathology and Laboratory Medicine are elected by approximately 20% of the Medical School class each year and receive excellent evaluations. The Department faculty have been active in working with the Dental School in re-structuring teaching of the biomedical sciences, including pathology within an organ system model focusing on the specific educational needs of these students and engaging them in more inter-active learning activities, including the implementation of Web-based instruction. The Pathology graduate program was successful in recruiting three new students. Four students received the Ph.D. degree. The Department faculty are actively involved in the Medical Scientist Training Program (MD/PhD) and combined graduate student recruitment activities associated with the Program in Biomedical Sciences (PIBS). The Pathology residency and fellowship programs continue to recruit outstanding residents especially as we realize increased interest in Pathology by U.S. medical school graduates over the past three years. Our program consists of 30 residents and fellows. Last year all graduates of the house officer program found desirable positions, in both academia and private practice, including fellowships at University of Michigan and Northwestern University and faculty positions at Case Western Reserve University.

Service

The volumes of clinical services in the Division of Anatomic Pathology continue to grow at an annual rate of approximately 4%. Two new faculty were added with area of dermatopathology and cytopathology. During the past year surgical pathology implemented sub-specialty sign-out services in gastro-intestinal pathology and breast pathology in addition to the established services in genito-urinary pathology, gynecologic pathology, renal pathology, neuropathology and dermatopathology. The dermatopathology service moved into newly renovated space in Medical Science Building 1. Renovations to accommodate expansion of the cytology and histology labs are planned, with completion scheduled for spring 2006. Faculty research programs and extramural support continues to increase especially in programmatic areas associated with the Cancer Center, GI pathology, Breast pathology and the SPORE in Urologic Disease.

The Clinical Laboratories continued to provide excellent, full-spectrum service (more than 850 different laboratory analyses) as the Health System continued to expand both its clinical volume and scope. The Molecular Diagnostics, Tissue Typing, and Immunopathology Laboratories were successfully relocated in December-January to incremental, new laboratory space at Traverwood. Substantial effort has again been directed towards aggressive laboratory utilization control, the improvement of test ordering, laboratory logistics, and achievement of compliance with CMS-mandated rules on documentation of test-ordering indications. Department of Pathology personnel are critically involved at many levels of the "\$74 million UMHS Orders Management Project" which promises to streamline patient care in the Hospitals and in so-called "Inpatient-like Venues". Superimposed upon

these efforts has been further development of computer links with M-Labs clients. In 2004-05 the Clinical Laboratories performed more than 3.5 million billable analyses (10 million individual measurements), supported a wide array of clinical and research programs, and added or replaced more than 50 testing methods. The maintenance of high quality services by the Clinical Laboratories, in the face of increasing complexity of demands, is testimony to the professionalism of the staff and the management capabilities of the laboratory directors and senior laboratory personnel. The Clinical Laboratories successfully completed the biennial College of American Pathologists on-site inspection in May 2005. Maintenance of the delicate balance among quality service, cost effective testing, utilization control, and the research and development that characterizes an academic institution will be a continuing challenge.

A major achievement was the continuing pursuit of an aggressive utilization management program. More than \$1.1M in direct laboratory cost avoidance and test utilization control were realized in 2004-05. This was made possible through educational meetings with selected clinical program directors and the support of the Clinical Decision Support Service.

Finally, the Clinical Laboratories have continued to respond to the change in scope and organization of UMHS patient care activities. In contrast to the early 1990s when 70% of laboratory testing volume came from inpatient services and 30% from ambulatory patients, the split is now 40:60 in the opposite direction. The laboratories currently support more than 30 UMHS-owned regional satellite facilities as well as many more patients who are M-Care subscribers. The Department was successful in the recruitment of a new M-Labs Program Director, Dr. Steven Mandell. In addition to excellence as a pathologist, Dr. Mandell brings great energy and expertise in outreach, informatics, management, and logistics.

Faculty and laboratory staff participated in a wide variety of intramural and extramural educational programs during 2004-05. For instance, the AIMCL (informatics) course in Las Vegas was again well attended, making it the most visible courses of its kind in the United States. The May AIMCL course brought together leaders from a variety of institutions and laboratory information technology fields to discuss the future of clinical pathology practice. These programs, along with the M-Labs educational programs, are prominent examples of educational outreach activities. The recently revised clinical pathology residency training format, which organizes pathology residents into teams that rotated through four blocks of clinical laboratories grouped according to "relatedness of discipline", was again updated in 2004-05. In keeping with a thematic approach, the 2005-06 version has established five rotation blocks and places greater emphasis on molecular diagnostics. The continued high quality of trainees in the Hematopathology Fellowship program has enhanced the service, educational, and academic missions of the Hematopathology group and the Department.

The academic achievements of faculty members within the Clinical Pathology Division have been outstanding. As a group, the CP faculty had approximately 80 articles published in peer-reviewed journals. Most faculty members played highly visible leadership roles in national organizations, courses, symposia, as well as on editorial boards, examining committees, and research review study sections; an illustration of their high levels of recognition throughout the United States. Numerous faculty members received extramural funding that supported a variety of scholarly activities.

Research

The Department of Pathology's research activities continue to be one of the many strengths of our academic mission. The Department's faculty members successfully compete for extramural research support, attract outstanding graduate students and fellows from both the national and international scene, publish in highly visible, peer-reviewed scientific journals, and serve on numerous national and international scientific committees. During the past year, the Department's research efforts increased as reflected by approximately 2 million dollars more spent when compared to the previous year's expenditures. The total research expenditures for FY2005 were \$21,716,554; this included \$16,049,685 in direct expenditures and \$5,666,869 in indirect expenditures. Faculty members in the Department of Pathology hold 99 individual grants from the National Institutes of Health (an increase of 13 funded applications over 03-04), 2 Program Projects, 2 MERIT Awards, and 2 training grants. In addition, other support originates from a variety of external non-federal sources including, the American Heart Association, American Lung Association, Kennedy's Disease Fund, The American Cancer Society, The American Federation for Aging Research, the MEDC Life Science Corridor Fund, Muscular Dystrophy Association, National Blood Foundation, Sandler Family Foundation and contract grants from nearly a dozen pharmaceutical companies. Many of the Departmental faculty actively participate in the support of institutional initiatives, including the University of Michigan Cancer Center, Urology SPORE Program, Breast Cancer Program, Interstitial Lung Disease SCOR, and the acute lung injury SCCOR. This blend of activity underscores the role of Pathology faculty in translational research, especially where DNA-based microarrays and tissue arrays are involved. These studies have resulted in publications dealing with tumors and inflammatory diseases. The faculty actively publish in both the clinical and experimental journals and cover very diverse scientific interests, including clinical pathology, anatomical pathology, and basic cellular and molecular mechanisms of disease. Our faculty members participate in peer review of both the intramural and extramural NIH Programs, and peer review of submitted scientific articles for diverse journals. Another index of the healthy academic research environment in the Pathology Department is the large number of post-doctoral fellows in the different laboratories, as over 40 post-doctoral fellows from many different countries are engaged in research activities and clinical fellowship. These post-doctoral scholars have actively sought positions in the Department of Pathology to enhance their research and clinical careers. Our faculty continue to provide expertise for both internal and external program review, which include serving as ad hoc and permanent members of NIH study sections, serving as committee members for site visit teams, providing expertise on government sponsored special emphasis panels, and organizing or chairing clinical and experimental scientific conferences.

Other Comments

It has been an honor and a pleasure to serve as Departmental Chair for the past 25 years. Especially rewarding has been the recruitment and development of young faculty in all spheres of departmental activity. Pathology at the University of Michigan has earned an international reputation as a first tier academic Department of Pathology. With new leadership in the Department, one can expect these standings to move to newer heights.

Respectfully submitted,

Peter A. Ward, M.D.

INDIVIDUAL FACULTY REPORTS

**GERALD D. ABRAMS, M.D.
PROFESSOR EMERITUS OF PATHOLOGY**

**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Pathologist, Cardiac Transplant Team. Transplant biopsies – 2 weeks.

II. TEACHING ACTIVITIES:

- A. Freshman Medical Class:
1. Course Director, Lecturer, General Pathology-Basic Concepts of Disease, in Patients and Populations Sequence and Normal Cell Sequence-14 lecture hours
2. Multidisciplinary Conferences - 2 contact hours.
3. Histopathology Sequence, Sequence Director, Lecturer, Lab Instructor-32 contact hours (8 lectures, 24 lab hours).
- B. Sophomore Medical Class:
1. Pathology Lab Instructor-all sequences. 50 contact hours.
- C. Undergraduate LS&A/Graduate:
1. Biology 224 - 1.5 lecture hours.
2. Pathology 585 – 2 contact hours
- D. Hospital Conferences:
1. Cardiovascular Pathology Case Conference – monthly.
- E. Community:
1. Organizer and director of “Mini-Med. School”, a six-week course for the public, Spring 2005..
- F. Invited Lectures:
1. Keynote Address-UM Medical School White Coat Ceremony, August 2004.
- G. Production of Teaching Materials:
1. Production of CD-Rom and syllabus for Histopathology Lab sequence for M-1.
2. Production of website to accompany M-1 Pathology Lectures.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Pathology of lesions produced by high intensity ultrasound, with Bioengineering staff and students.
- B. Protection afforded by tetrathiomolybdate in toxic and immunologic injury, with G.J. Brewer, Human Genetics
- C. COX-2 and myocardial infarction, with B.R. Lucchesi, Pharmacology

PUBLICATIONS:

- A. Seo J, Tran BC, Hall TC, Fowlkes JB, Abrams GD, O'Donnell M, Cain CA. Evaluation of Ultrasound Tissue Damage Based on Changes in Image Echogenicity in Canine Kidney. Transact Ultrasonics, Ferroelectrics, Freq Control 2005, in press
- B. Hou G, Dick, R, Abrams GD, Brewer GJ Tetrathiomolybdate Protects Against Cardiac Damage by Doxorubicin. J Lab & Clin Med 2005, in press.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL/UNIVERSITY:

- B. Member, Component I Committee.
- C. Ombudsperson, Medical Faculty.

REGIONAL AND NATIONAL:

- A. Editorial Board, Modern Pathology.
- B. Ad hoc reviewer- Journal of Neuro-ophthalmology - Cancer

**THOMAS M. ANNESLEY, PH.D.
PROFESSOR OF CLINICAL CHEMISTRY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Biochemistry Section, Clinical Pathology Laboratories.
- B. Laboratory Director, Chelsea Family Practice, M-Care Facility.
- C. Laboratory Director, Briarwood Medical Group, M-Care Facility.
- D. Laboratory Director, Briarwood Family Practice Facility.
- E. Laboratory Director, West Ann Arbor Health Care Facility.

II. TEACHING ACTIVITIES:

- A. House Officers:
 - 1. Lecturer, Clinical Pathology Grand Rounds.
 - 2. Lecturer, Clinical Pathology Didactic Lecture Series.
 - 3. Sign-out and Interpretation of Laboratory Results.

III. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Biochemistry Section, Clinical Pathology Laboratories.
- B. Coordinator, Clinical Pathology Laboratory CME Program.

REGIONAL AND NATIONAL:

- A. Board of Directors, American Association for Clinical Chemistry.
- B. Chair, Clinical Consulting Task Force, American Association for Clinical Chemistry.
- C. Board of Directors, National Academy of Clinical Biochemistry.
- D. Chair, NACB/AACC Distinguished Abstracts Program.
- E. House of Delegates, American Association for Clinical Chemistry.
- F. Executive Committee/Journal Management Group, Clinical Chemistry Journal.
- G. Organizing Committee, 9th International Congress on Therapeutic Drug Monitoring and Clinical Toxicology.
- H. Member, Academy of Clinical Laboratory Physicians and Scientists.
- I. Member, National Academy of Clinical Biochemistry.
- J. Member, Association of Clinical Scientists.
- K. Member, American Society for Mass Spectrometry.
- L. Member International Association of Therapeutic Drug Monitoring and Clinical Toxicology.

V. **OTHER RELEVANT ACTIVITIES:**

INVITED LECTURES:

- A. "Immunosuppressant Drug Analysis Using LC/MS", LC/MS Forum, American Association for Clinical Chemistry Annual Meeting, Los Angeles, California, July 2004.
- B. "Calibration and QC Standards for LC/MS", LC/MS Forum, American Association for Clinical Chemistry Annual Meeting, Los Angeles, California, July 2004.
- C. "Ionization Sources and Detectors for Mass Spectrometric Analyses", University of Virginia, Charlottesville, Virginia, September 2004.
- D. "Aspects of Sample Preparation for Clinical Mass Spectrometry Assays", Applications of Mass Spectrometry and Separation Strategies for Clinical Chemistry, Boston, Massachusetts, March 2005.
- E. "LC-MS Assay Development and Validation", 9th International Congress of Therapeutic Drug Monitoring and Clinical Toxicology, Louisville, Kentucky, April 2005.
- F. "LC-MS Costs and Requirements", 9th International Congress of Therapeutic Drug Monitoring and Clinical Toxicology, Louisville, Kentucky, April 2005.
- G. "Applications of Mass Spectrometry in the Clinical Laboratory", Keynote Speaker, Association of Clinical Scientists Annual Meeting, Troy, Michigan, May 2005.

JOURNAL EDITORSHIPS:

- A. Associate Editor, Clinical Chemistry.

EDITORIAL BOARDS:

- A. Clinical Chemistry, Editorial Board.
- B. Therapeutic Drug Monitoring, Editorial Board.
- C. Biomedical Chromatography, Editorial Board.
- D. Clinical Biochemistry, Editorial Board.

EDITORIAL REVIEW ACTIVITIES:

- A. Clinical Chemistry, Reviewer.
- B. Biomedical Chromatography, Reviewer.
- C. Therapeutic Drug Monitoring, Reviewer.
- D. Clinical Biochemistry, Reviewer.

AWARDS:

- A. 2004 Outstanding Speaker Award Winner, American Association for Clinical Chemistry.
- B. Clinical Chemist's Recognition Award, American Association for Clinical Chemistry.
- C. Awardee, Marquis Who's Who in America.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Annesley, T.M., and Clayton, L.T.: A simple, novel extraction protocol for the analysis of immunosuppressants in whole blood. *Clin. Chem.*, 2004;50:1845-1848.
2. Annesley, T.M.: Application of Commercial Calibrators for the Analysis of Immunosuppressant Drugs in Whole Blood. *Clin. Chem.* 2005;51:457-460.
3. Annesley, T.M., and Clayton, L.T.: Quantification of Mycophenolic Acid and Glucuronide Metabolite in Human Serum by HPLC-Tandem Mass Spectrometry. *Clin. Chem.* 2005;51:872-877.

ABSTRACTS:

1. Annesley, T.M.: Applications of mass spectrometry in the clinical laboratory. *Ann. Clin. Lab. Sci.* 2005;35:209.

CHAPTERS IN BOOKS:

1. Annesley, T.M., Rockwood, A., and Sherwood, N.: Mass Spectrometry. *Tietz Textbook of Clinical Chemistry, Third Edition*, C. Burtis, E. Ashwood, D. Bruns, eds. 2005.

**HENRY D. APPELMAN, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. General surgical and gynecologic pathology – 2 months.
- B. Gastrointestinal and hepatic pathology services - 7 months.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

- A. Medical Students:
 - 1. Pathology 600 - 2 full class lectures and laboratory 2-4 hours per week
 - 2. Pathology 630 (dental) - one full class lectures.
 - 3. Senior Elective in Pathology: supervising during diagnostic signout
- B. House Officers:
 - 1. Surgical pathology diagnosing room instruction for assigned house officer - 4 months
 - 2. Gastrointestinal and hepatic pathology tutoring - full time.
 - 3. Lectures in gastrointestinal and liver pathology, 2 hours
 - 4. Consult conferences, 4-5 hours
- C. Interdepartmental:
 - 1. G-I Tumor Conference - (2-3 hours per month).
 - 2. Liver Biopsy Conference – 4 hours per year.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Clinical trial of difluoromethylornithine in Barrett's esophagus, with Dean Brenner of the U of Mich, Gary Stoner of Ohio State Univ, Stuart Spechler, and Edward Lee of University of Texas-Southwestern, and Anil Rustgi of Pennsylvania.
- B. Anaplastic, lymphoma-like carcinoma arising in Barrett's mucosa, with BJ McKenna
- C. Is hyperplasia of the interstitial cells of Cajal a common reaction to intramural masses in the gut? With Meryem Koker
- D. The apoptotic form of microscopic colitis, with BJ McKenna
- E. Are juvenile-like polyps in adults the same as in children? With Meryem Koker

- F. What is the yield of significant microscopic disease in colorectal biopsies of adult patients with chronic diarrhea and normal endoscopic findings? With BJ McKenna
- G. G cells in the duodenal bulb and their response to therapy. With Wei Xin and Barbara McKenna
- H. Marginal collagenous colitis: does it exist? With BJ McKenna, W Xin, M Anderson and L Evans
- I. The effects of loss of IL-10 and Familial adenomatosis polyposis-like genetic changes on the development of colorectal carcinomas in knock-out mouse models. With Emina Huang.
- J. The prevalence of unsuspected invasive carcinomas in specimens resected for high-grade dysplasia in Barrett's mucosa and the gastric cardia. With Weijian Zhu, Barbara McKenna, Steven Ramsburgh, Joel Greenson and members of the Section of Thoracic surgery
- K. The yield of significant microscopic findings in terminal ileal biopsies and their relation to indications for endoscopy and endoscopic findings, with Jon McHugh and Barbara McKenna
- L. Calcium sensing receptors in colorectal carcinoma, with James Varani and colleagues
- M. CDX2 in colorectal carcinoma, with Duyan Dang, Long Dang, and colleagues

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Chairman, Advisory Committee on Appointments, Promotions and Tenure.

MEDICAL SCHOOL/HOSPITAL:

- A. Member, Cancer Work Group, University Hospital.
- B. Co-Coordinator, Gastrointestinal Sequence for 2nd year medical students.

REGIONAL AND NATIONAL:

- A. Member, Scientific Advisory Committee, and Board of Directors and President-Elect, International Organization for Statistical Studies of Diseases of the Esophagus, Paris, France.
- B. Member, Editorial Board, Human Pathology.
- C. Member, Editorial Board, Modern Pathology.
- D. Member, Editorial Board, American Journal of Surgical Pathology.
- E. President Elect, United States and Canadian Academy of Pathology.
- F. Member, Lung and Esophagus Task Force, American Joint Committee on Cancer, 2001-Present.

V. **OTHER RELEVANT ACTIVITIES:**

INVITED LECTURES/SEMINARS:

1. Gastrointestinal Pathology topics: "What in the hell is dysplasia?", "Neoplastic and non-neoplastic lesions of the gastroesophageal junction", "The role of the pathologist in the diagnosis and management of colitides". Pathology Update for Practicing Pathologists, American Society for Clinical Pathology, Montreal, Que, Canada, July, 2004
2. "What in the hell is dysplasia of the GI tract?" Visiting professor lecture, University of Illinois, Chicago, IL, July 27, 2004
3. "Just Another Day on the GI Biopsy Service", with B.J McKenna, Annual Meeting, American Society for Clinical Pathology, San Antonio, TX, October 9, 2004; Kansas City Society of Pathologists/The Kansas Society of Pathologists, Kansas City, MO, Oct 23, 2004; 24th Annual Current Issues in Surgical Pathology, Southwestern Medical School, Dallas, TX, May 12, 2005;
4. "Mundane Cases in GI Pathology--Even the Non-Interesting Can Be Exciting". Microscopic tutorial, Annual Fall Meeting, American Society of Clinical Pathologists, San Antonio, TX, October, 2004;
5. "Polyps with No Names", Oregon Association of Pathologists, Portland, OR, November 19, 2004
6. "Gastrointestinal Biopsies that have New Twists and/or New Information". Annual Seminar, Oregon Association of Pathologists, Portland, OR, November 20, 2004
7. "Gastrointestinal Stromal Tumors are as Annoying in 2004 as they were in 2003, 2002, etc." Visiting professor lecture, Einstein Medical College, Yeshiva University, New York NY, December 9, 2004
8. "The Differential Diagnosis of Artifacts in Gastrointestinal Biopsies", American Society for Clinical Pathology companion meeting at the annual meeting of the United States and Canadian Academy of Pathology, San Antonio, TX, February 28, 2005
9. "Neoplastic diseases of the intestine", sponsored by the American Society of Clinical Pathologists, Palm Springs, CA, April 21, 2005
10. "Gastrointestinal Polyps with No Names or with Obscure Names", Department of Pathology, University of Illinois, Chicago, IL, April 27, 2005
11. "What is Dysplasia in the Gut?", "The Differential Diagnosis of Artifacts in GI Biopsies", "Neoplasms of the Appendix and Anus: From One End of the Colon to the Other", Cleveland Clinic, Cleveland, OH, June 3, 2005
12. "Pathologic Features of Ischemic Colitis: How do Pathologists Use the Term", Ischemic Colitis Advisory Board, sponsored by GlaxoSmithKline, Hollywood, FL, June 4, 2005
13. "Why Is the GI Junction Such a Big Deal When it is so Small?", "Whatever Happened to the Old Ulcerative Colitis We Knew and Loved?", "What in the Hell is Dysplasia in the Gut?", "Gastrointestinal Stromal Tumors; The Counters Vs. the Lookers", "Neoplasms of the Appendix and Anus: Little Things Mean a Lot", Presented at the course: Pathology of the Gastrointestinal Tract, Liver and Pancreas, Sponsored by Scientific Symposia, Maui, Hawaii, June 27-30, 2005

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Appelman HD. What is dysplasia in the gut? Arch Path Lab Med. 129:170-173, 2005.
2. Chakrabarty S, Wang H, Canaff L, Hendy GN, Appelman H, Varani J. Calcium sensing receptor in human colon carcinoma: interaction with CA2+ and 1,25-dihydroxyvitamin D3. Accepted for Publication, Cancer Res. Jan, 15, 2005

CHAPTERS and BOOKS:

1. McKenna BJ, Appelman HD, Neoplasms of the small intestine, in Quigley EE and Marsh MN, eds.: The Small Intestine, Blackwell Scientific, Cambridge, MA, in press

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Evans LT, Xin W, McKenna BJ, Appelman HD, Anderson MA. Microscopic colitis with minimal collagen: is this lymphocytic colitis or collagenous colitis? Am J Gastroenterol. 99 (Supplement):S265, 2004
2. Xin W, Evans LT, Appelman HD, Anderson MA, McKenna BJ. Minimal collagenous colitis: microscopic colitis with minimal subsurface collagen is appropriately diagnosed as collagenous colitis. Mod Pathol. 18(Supplement 1):123A, 2005
3. McHugh JB, Appelman HD, McKenna BJ. What is the value of endoscopic terminal ileal biopsies? Mod Pathol. 18(Supplement 1):112A, 2005
4. McKenna BJ, Greenson JK, Appelman HD. Which Barrett's mucosal biopsies should be reviewed by expert pathologists. Gastroenterol. 128(Supplement 4):A-238, 2005
5. McKenna BJ, Greenson JK, Appelman HD. The diagnosis of Barrett's biopsies sent for expert pathologic consultation depend o the expert: All experts are not alike. Gastroenterol. 128(Supplement 4):A-239, 2005

**PRISCILLA CHAMBERLIN, M.D.
CLINICAL INSTRUCTOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Surgical Pathology sign out and consultations– 12 months - 25% of SP cases
- B. Cytology sign out and consultation – 12 months
 - 50% of Pap Smears
 - 50% of non-gynecological cases

II. TEACHING ACTIVITIES:

- A. Pathology residents, SP – 500 hours
- B. Pathology residents Cytology – 100 hours
- C. M2 pathology lab – 50 hours
- D. Lecture series for ENT residents – 25 hours
- E. Cytology lectures to pathology and surgical residents as needed – 10 hours
- F. Pathology Graduate Course – 30 hours

III. RESEARCH ACTIVITIES:

None.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director of Cytopathology for VA Hospital
- B. Medical Director of Microbiology, Immunology, Ancillary Testing, Accessioning and Chemistry labs at VA Hospital
- C. Anatomical Pathology Imaging at VA Hospital
- D. Laboratory Director for Toledo VA Out Patient Clinic
- E. Pathologists' Scheduling

MEDICAL SCHOOL/HOSPITAL:

- A. Medical School Admissions Committee
- B. VA Hospital Tumor Board
- C. VA Hospital Cancer Committee
- D. VA Hospital Safety Case Management Committee

UNIVERSITY OF MICHIGAN:

None.

REGIONAL AND NATIONAL:

None.

V. OTHER RELEVANT ACTIVITIES:

None.

VI. PUBLICATIONS:

None.

**STEPHEN W. CHENSUE, M.D., PH.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENT REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES

- A. Chief, Pathology and Laboratory Medicine Service, VA Ann Arbor Healthcare System, responsibilities include, overall laboratory supervision and administration, equipment and methodology evaluation, review and consultation regarding quality management programs, personnel evaluation, counseling and grievance procedures.
- B. Hematology, daily evaluation of pathologist referred blood smears, lymph nodes, bone marrow smears, VA Ann Arbor Healthcare System (6 months/year).
- C. Surgical/Frozen Section Diagnosis (2.5 months/year).
- D. Surgical Case Diagnosis VA Ann Arbor Healthcare System (2.5 months/year).
- E. Autopsy Service, rotational basis, on call 13 weeks/year.
- F. Special Chemistry/Immunology, daily interpretation of protein electrophoreses and problem ligand studies (6/months/year), VA Ann Arbor Healthcare System.
- G. Blood Bank, consults and investigations, full time as needed, VA Ann Arbor Healthcare System.

II. TEACHING ACTIVITIES

- A. Pathology house officers, Surgical Pathology/Autopsy supervision and instruction.
- B. Medical students, Pathology 600 laboratory.
- C. Graduate students, Pathology 585 lecture and laboratory
- D. Technologists, technicians and hospital staff, ongoing continuing medical education instruction on clinical laboratory topics.
- E. Research mentoring for post-doctoral, graduate, undergraduate, and high school trainees.

**III. RESEARCH ACTIVITIES
SPONSORED SUPPORT:**

- A. Principal Investigator, Chemokine Determinants of Th1 and Th2 Immune Responses, VA Merit Review Grant, (\$135,000 direct costs annually, 2000-2005).
- B. Principal Investigator, Chemokine Receptor Dynamics in Granuloma Formation, NIH AI43460 (\$150,000 direct costs annually, 2003-2007)
- C. Coinvestigator, Molecular Mechanisms of Lung Host Defense, VA REAP Grant (250,000 annually, 1998-2003)

PROJECTS UNDER STUDY:

- A. Regulation and participations of chemokine receptors during Th1 and Th2 immune and inflammatory responses.
- B. Role of chemotactic cytokines in granulomatous inflammation and Th1 and Th2 cell expression.
- C. Role of inducible costimulatory molecule (ICOS) in Th1 and Th2 cell-mediated responses in the lung.
- D. Role of chemokine receptors in dendritic cell recruitment and activation and in vivo migration during innate stages of granuloma formation and Mycobacteria infection.
- E. Role of chemokine receptors (CCR4, CCR6 and CXCR4) in Th1 and Th2 cell-mediated responses in the lung.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Pathology Graduate Program Preliminary Exam Committee.
- B. Member of graduate student thesis committees.
- C. Interviewing and evaluation of residents and faculty.

MEDICAL SCHOOL/HOSPITAL:

- A. Dean's Committee, University of Michigan Medical School and VA Ann Arbor Healthcare System, voting member.
- B. Clinical Executive Board, VA Ann Arbor Healthcare System, voting member.
- C. Professional Standards Board, VA Ann Arbor Healthcare System, voting member.
- D. Invasive Procedures Committee, VA Ann Arbor Healthcare System, voting member.
- E. Residency Review Board, VA Ann Arbor Healthcare System, voting member.
- F. VHA VISN 11 Laboratory Equipment Standardization Committee.
- G. Chief of Staff Advisory Committee, VA Ann Arbor Healthcare System, voting member.
- H. Personnel employment and annual performance evaluations.
- I. Anatomic Pathology Quality Assurance evaluation and reporting.
- J. Editor, VALabs Newsletter and webmaster for VA Laboratory webpage.

REGIONAL AND NATIONAL:

- A. Editorial Review:
 - 1. American Journal of Pathology
 - 2. Journal of Immunology
 - 3. Inflammation Research, Section Editor
 - 4. American Journal of Respiratory Cell and Molecular Biology
 - 5. Journal of Clinical Investigation
 - 6. Chest
 - 7. Journal of Leukocyte Biology
 - 8. Infection and Immunity

V. OTHER RELEVANT ACTIVITIES:

- A. Case presentations at Tumor Board and Morbidity and Mortality Conferences.
- B. Tissue evaluation for clinical and basic researchers.
- C. Team leader for College of American Pathologists (CAP), Laboratory Inspection Program

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Chiu, B., Freeman, C.M., Stolberg, V.R., Hu J.S., Zeibecoglou, K., Lu, B., Gerard, C., Charo, I.F., Lira, S. A. and Chensue, S.W. Impaired lung dendritic cell activation in CCR2 knockout mice. *Am. J. Pathol.* 2004, 165:1199-1209.
- 2. Murphy, H.S., Sun Q., Murphy, B.A., Mo, R., Huo, J., Chen, J., Chensue, S.W., Adams, M., Richardson, B.C., Yung, R. Tissue-specific effect of estradiol on endothelial cell-dependent lymphocyte recruitment. *Microvasc. Res.* 2004, 68:273-85.
- 3. Freeman, C.M, Chiu, B., Stolberg, V.R., Hu, J., Zeibecoglou, K., Lukacs, N.K., Lira, S.A., Kunkel, S. L., and Chensue, S.W. CCR8 is expressed by antigen-elicited, IL-10 producing CD4+CD25+ T cells which regulate Th2-mediated granuloma formation in mice. *J. Immunol.* 2005, 174:1962-1970.
- 4. Piotrowski, M.M., Bessette, R.L., Chensue, S. W., Cutler, D., Kachalia, A., Roseborough J.W., Saint, S., Underwood, W., Murphy, H.S. Learning to improve safety: False-positive pathology report results in wrongful surgery. *Joint Commission Journal on Quality & Safety* 2005, 31:123-131.
- 5. Menees SB, Anderson MA, Chensue SW, Moseley RH. Hepatic injury in a patient taking rosiglitazone. *J Clin Gastroenterol.* 2005, 39:638-40.
- 6. Osterholzer JJ, Ames T, Polak T, Sonstein J, Moore BB, Chensue SW, Toews GB, Curtis JL. CCR2 and CCR6, but not endothelial selectins, mediate the accumulation of immature dendritic cells within the lungs of mice in response to particulate antigen. *J Immunol.* 2005, 175:874-883.

BOOKS AND CHAPTERS IN BOOKS:

1. Chensue, S.W. Chemometrics: CXC: CXCL-1, 2 and 3 (GRO α , GRO β and GRO γ). In, Encyclopedia of Respiratory Medicine, Mark Knowles ed., Elsevier Limited: Oxford, UK, 2005 in press.

**ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR,
MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:**

1. Absood, A., Freeman, C., Chensue, S., and Dawes, L. Vasoactive Intestinal Polypeptide (VIP) Induces Cholesterol 7 α Hydroxylase Gene Expression in HepG2 Cells. AVAS, Richmond, VA, April 2004.
2. Freeman, C.M., Chiu, B-C., Stolberg, V.R., Hu, J.S. and Chensue, S. W. Chemokine receptor 4 knockout impairs cytokine production and inflammation during type-1 pulmonary granuloma formation FASEB J. 2005 19(4) Abstract# 854.3.
3. Dawes, L., Absood, A., Freeman C., and Chensue S. CCK Increase in CYP7A1 Expression in HepG2cells Is Blocked By the CCK2 Receptor Antagonist YF476. Digestive Disease Week (DDW) Scientific Sessions., Chicago, IL. May 14-19, 2005.
4. Chiu, B-C., Freeman, C.M., Stolberg, V.R. and Chensue, S. W. Respiratory Exposure to OVA Induces Functional Effector CD4 T Cells. Federation of Clinical Immunology Societies (FOCIS) Annual Meeting, Boston, MA., May 12-16, 2005. Abstract# F1.42.

**ARUL M. CHINNAIYAN, M.D., Ph.D.
ASSOCIATE PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Board-Certified in Clinical Pathology (2002), Diplomate of the American Board of Pathology

II. TEACHING ACTIVITIES:

- A. Mentor, Postdoctoral Fellows: Jindan Yu, Bharathi Laxman, Adaikkalam Vellaichamy, George Wang, Saravana Dhanasekaran
- B. Mentor, Clinical Fellows: Tim Bradford, MD (Urology), Rohit Mehra, MD (Pathology), Manish Bhandari, MD (Hematology-Oncology), Kajal Sitwala, MD, PhD (Pathology), David Hanauer, MD, MS (Pediatrics, Instructor)
- C. Mentor, Graduate/Medical Students: Scott Tomlins (MSTP, Pathology), Qi Cao (Pathology), Jianjun Yu (Bioinformatics), Daniel Rhodes (MSTP, Pathology), Julie Kim (Bioinformatics), Ronglai Shen (Biostatistics Masters Student), Barry Taylor (Bioinformatics), Chad Creighton (Bioinformatics), Woojin Yu (M4)
- C. Mentor, Undergraduate Students: Shilpa Murthy, CMB Honors Research, Jeff Fielhauer, Biology, Nicole Kaper, CMB Student, Benjamin Briggs, Honors Math Major, Zubair Sarmast, Biology
- D. Mentor, High School Students (Research Rotation): Pavan Ravipati (Novi High School), Sashir Reddy (Thomas Washington High School, Ohio)
- E. Pre-lim Committees:
Chair of graduate pre-lim committee for Bioinformatics Graduate Student, Chad Creighton
Chair of graduate pre-lim committee for Bioinformatics Graduate Student, Yili Chen.
Pre-lim committee for Bioinformatics Graduate Student, Viktoriya Strumba
Pre-lim committee for Bioinformatics Graduate Student, Daniel Rhodes
Pre-lim committee for Pathology Graduate Student, Scott Tomlins
Pre-lim committee for Pathology Graduate Student, Meghan Brennan
Pre-lim committee for Physiology Graduate Student, Greg Gurda
- F. Thesis Committees:
Daniel Rhodes, Bioinformatics Graduate Program, (Chair)
Chad Creighton, Bioinformatics Graduate Program (Chair)
Scott Tomlins, Pathology Graduate Program (Chair)
Qi Cao, Pathology Graduate Program (Chair)
Julie Kim, Bioinformatics Graduate Program (Chair)
Jianjun Yu, Bioinformatics Graduate Program (Chair)

- Meghan Brennan, Pathology Graduate Program
Lei Wang, Biochemistry Graduate Program
Dawei Liu, Biostatistics Graduate Program
- G. Co-Director, Bioinformatics 511
 - H. Instructor, Cancer Biology 553
 - I. Course Director and Instructor, Short Course in Cancer Bioinformatics
 - J. Instructor, Physiol/Pharmacol/HumGen 555
 - K. Instructor, SBUR Science Course, AUA Meeting, “Discovery and Clinical Application of Novel Molecular Markers of Urologic Tumors”
 - L. Interviewed prospective MSTP, PIBS, and Bioinformatics students

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, “Molecular Classification of Prostate Cancer”, American Cancer Society, RSG-02-179-01-MGO, 07/01/02 – 06/30/06, 15%, \$180,000/yr
- B. Principal Investigator, “The Role of Polycomb Group Proteins in Prostate Cancer”, National Institute of Health, R01 CA97063, 07/01/02 – 06/30/07, 20%, \$178,000/yr
- C. Principal Investigator, “Dysregulation of the Corepressor CtBP in Prostate Cancer”, Department of Defense, PC020322, 1/2/03- 12/31/05, 10%, \$125,000/yr
- D. Principal Investigator, “A Functional Genomics Approach to Cancer”, PEW Charitable Trust, 07/01/02 – 06/30/06, 0%, \$55,556/yr
- E. Co-Investigator, “Protective Effects of Anti-C5a in Sepsis”, National Institute of Health, GM61656 (PI: Ward), 12/01/01-11/30/06, 5%, \$225,000/yr
- F. Co-Investigator, “Functional Genomics Approach to Lethal Metastatic Prostate Cancer”, P50 CA69568 (PI: Pienta), 5/01/03 - 05/31/08, 10%, \$144,578/yr, S.P.O.R.E. in Prostate Cancer, Project 3 (PI Chinnaiyan)
- G. Co-Investigator, Tissue/Informatics Core of the UM Prostate SPORE, NCI, SPORE in Prostate Cancer, A69568 (PI: Pienta), 05/01/03- 05/30/08, 2.5%, \$253,643/yr
- H. Co-Investigator, “Molecular of Dissection of Benign Prostatic Hyperplasia”, U01 AG 22312 (PI: Rubin), Brigham and Women’s Hospital (NIH), 9/30/02-6/30/05, 5%, \$120,494/yr
- I. Co-Investigator, DAMD17-03-2-0033 (PI: Simons, M.D.), Brigham and Women’s Hospital (DOD), 04/01/03-03/31/06, 2.5%, \$36,410/yr
- J. Co-Investigator, “Molecular Changes Associated with Prostate Carcinoma (PCa) Bone Metastases”, R01 CA102872-01, NIH, (PI: Pienta), 09/24/03-08/31/07, 10%, \$173,280/yr
- K. Co-Investigator, “Prostate Cancer Harbinger Genes”, RO1 AG0214104-01 (PI: Rubin), 09/30/02–08/31/05, 2.5%, Brigham & Women’s Hospital (NIH Prime), \$53,595/yr
- L. Principal Investigator, “Epitomic Biomarkers of Prostate Cancer, U01 CA111275, 09/30/04-09/29/09, NIH, 10%, \$312,871/yr

- M. Co-Investigator, "Protein Microarrays for the Humoral Response of Cancer", R01 CA106402 (PI: Lubman), NIH/NCI, 06/15/04-05/31/09, 2.5%, \$83,694/yr
- N. Co-Investigator, "Pancreas-Specific Primary Regulatory Targets of Nkx2.2", NIH, R21 Dk065308 (Mellerick-Dressler), 2.5%, 08/01/03-03/01/05
- O. Principal Investigator, "Discovery of Cancer Biomarkers using High Throughput Multi-Blotting", GMP Companies, Inc., 12/01/02-03/05, 0% effort, \$168, 827/yr direct costs.

PENDING:

- A. Principal Investigator, "Integrative Proteomic and Genomic Analysis of Prostate Cancer Progression", Department of Defense, 08/01/05-07/31/08. Fundable Score of 1.2
- B. Principal Investigator, Era of Hope Scholar Award, Department of Defense
- C. "Autoantibody Profiles for Cancer Diagnosis, Prognosis, and Therapy", Burroughs Wellcome Award, Clinical Scientist Awards in Translational Research
- D. Co-investigator, Cancer Center Support Grant (PI, M. Wicha), P30 CA46592, \$3,434,955 direct costs, UMCCC Bioinformatics Core, \$250K/direct costs/ yr

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Co-Director, Division of Research Informatics
- B. Co-Director, Prostate SPORE Tissue-Informatics Core
- C. Director of the Pathology Microarray Research Lab
- D. Director, Pathology Proteomics Initiative
- E. Search Committee for Director of Clinical Informatics

MEDICAL SCHOOL/HOSPITAL:

- A. Member, MSTP Career Advisory Panel
- B. Bioinformatics student interviews
- C. Faculty Candidate Interviews for the Department of Urology and the Cancer Center
- D. MSTP student interviews
- E. Bioinformatics Faculty Search Committee
- F. Director of the U of M Bioinformatics, Proteomics, and Functional Genomics Seminar Series.
- G. Director of Cancer Bioinformatics, Comprehensive Cancer Center
- H. Bioinformatics Program Executive Committee, Member
- I. Biomedical Informatics Design Team, Dean's Office
- J. Proteomics Design Team, Dean's Office
- K. University of Michigan Medical School Conflict of Interest Board, Member
- L. Career Development Committee, Dr. Sami Malek, Physician-Scientist, Assistant Professor
- M. Tissue Usage Committee, Prostate SPORE

REGIONAL AND NATIONAL:

- A. Ad hoc reviewer for the following Journals: *Nature*, *PNAS*, *Nature Genetics*, *Nature Cancer Reviews*, *Nature Medicine*, *American Journal of Pathology*, *Journal of Biomedical Informatics*, *Cancer Research*, *Oncogene*, *Neoplasia*, *Cell Death & Differentiation*, *Cytokine*, *Clinical Cancer Research*, *Molecular Diagnosis*, *BMC Cancer*, *Urology*, *Cancer Cell*, and the *Journal of Biological Chemistry*.
- B. Ad-hoc Member, Modeling and Analysis of Biological Systems (MABS) Study Section, NIH, March 2005.
- C. Scientific Review Board, 2005 Genome Canada
- D. American Cancer Society Canary Fund Peer-Review Committee, 2005
- E. National Cancer Institute, EDRN Associate Membership Review Committee, 2005
- F. Integration Panel, 2004, Department of Defense Prostate Cancer Research Program

V. **OTHER RELEVANT ACTIVITIES:**

- A. Affiliated Faculty of the Bioinformatics Program
- B. Pew Scholars Program in the Biomedical Sciences, Pew Charitable Trusts
- C. Member, Michigan Comprehensive Cancer Center
- D. Joint Appointment in the Department of Urology
- E. Member of the Faculty Search Committee for the Bioinformatics Program
- F. MSTP Career Advisory Panel, University of Michigan
- G. Member, Michigan Urology Center

EDITORIAL BOARDS:

- A. Cancer Genomics and Proteomics
- B. Cancer Informatics
- C. Cancer Research

PATENTS:

- A. U.S. Provisional Application Serial no. 60/309,581 filed 8/02/01 and U.S. Provisional Application Serial no. 60/334,468 filed 11/15/01, "Prostate Cancer Biomarkers"
- B. U.S. Patent Application No. 09/734,628 COMPOSITIONS AND METHODS FOR IN SITU AND IN VIVO IMAGING OF CELLS AND TISSUES; Filing Date: December 11, 2000; Attorney Docket No.: UM 07825, University of Michigan Filing No.: 1850
- C. U.S. Patent Application. University of Michigan, Phage microarray profiling of the humoral response to disease. Filed June 9, 2004.

INVITED LECTURES/SEMINARS:

1. Henry Ford Health System, Invited Speaker, "Integrative Approaches to Cancer: Biology, Biomarkers, and Bioinformatics", Detroit, MI, July 1, 2004.
2. 12th SPORE Investigator's Workshop, Co-chair, Tumor Progression, Invasion and Metastases Thematic Poster Discussion Session, Baltimore, MD, July 11, 2004.
3. BioArrays-2004 New York Meeting on "Biochips in Diagnostics, Industrial Genomics & Proteomics: SystemomicsTM Approaches", Invited Speaker, New York, New York, July 26, 2004.
4. EDNRN GU Collaborative Group Meeting, Invited Speaker, "Genomic and Proteomic approaches in identification and development of markers for prostate cancer", Houston, Texas, September 14, 2004.
5. The Advancing Practice, Instruction, and Innovation through Informatics Conference (APIII 2004), Invited Speaker, "ONCOMINE: A Cancer Microarray Compendium and Data-Mining Platform", Pittsburgh, Pennsylvania, October 6-8, 2004.
6. Genentech, Invited Speaker, "Integrative Molecular Oncology: From Biomarkers to Biology", San Francisco, CA, October 28, 2004.
7. American Association for Cancer Research, Invited Speaker, "Genomic and Proteomic Approaches to Study Prostate Cancer", Bonita Springs, FL, November 17-21, 2004.
8. Breast Cancer Think Tank, Invited Speaker, "Integrative Molecular Oncology: From Biomarkers to Biology", Curacao, January 16-22, 2005.
9. InterProstate SPORE Meeting, Chair: "Laboratory Correlates in Translational Research", Houston, TX, January 30-31, 2005.
10. Mayo Clinic, Invited Speaker, Clinical talk: "Mining Molecular Profiles for Cancer Biomarkers", Research Talk: "Integrative Approaches to Molecular Oncology", Rochester, Minnesota, February 3, 2005.
11. American Society of Clinical Oncology, 2005 Multidisciplinary Prostate Cancer Symposium, Invited Speaker, Faculty Member, "Screening and Diagnosis Session: Proteomics/Genomics", Orlando, Florida, February 17-19, 2005.
12. EDNRN Annual Meeting, Presentation of the University of Michigan Biomarker Developmental Lab, March 21-23, 2005.
13. American Society of Investigative Pathologists Annual Meeting, Invited Speaker, Amgen Outstanding Investigator Award Lecture, "The future of pathology: genomics, Proteomics and bioinformatics", San Diego, California, April 2-6, 2005.
14. American Association for Cancer Research Annual Meeting, Minisymposium Co-Chairperson, "Molecular Profiling, Diagnosis, Prognosis, and New Target", Anaheim, California, April 16-20, 2005.
15. Society for Basic Urologic Research (SBUR) 2005 Spring Meeting, Invited Speaker, "Integrative Approaches to Prostate Cancer: Biomarkers, Biology, and Bioinformatics", San Antonio, TX, May 21, 2005
16. Society of Urologic Oncology, Invited Speaker, "RNA/Primary Tumor Expression Analysis-Unique Signatures to Predict Local Recurrence versus Bone Metastasis, San Antonio, TX, May 21, 2005.
17. Society for Basic Urologic Research (SBUR) 2005 Spring Meeting, Invited Speaker, "Discovery and Clinical Application of Novel Molecular Markers of Urologic Tumors", San Antonio, TX, May 25, 2005.

MEMBERSHIPS AND OFFICES IN PROFESSIONAL SOCIETIES:

1992 – present	Member, American Medical Association
1999 – present	Associate Member, American Association of Cancer Research
1999 – present	Member, College of American Pathologists
1999 – present	Member, American Society of Clinical Pathologists
1999 – present	Member, American Society of Investigative Pathologists (ASIP)
2004 – present	Member, Society of Basic Urological Research (SBUR)
2004 – present	Member, United States and Canadian Academy of Pathology (USCAP)
2004 – present	Member, Michigan Society of Pathologists (MSP)
2005 – present	Member, Association for Pathology Informatics (API)
2005 – present	Affiliate Member, American Urological Association (AUA)

HONORS AND AWARDS:

- A. April 2005, AMGEN Outstanding Investigator Award, American Society for Investigative Pathology (ASIP)

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION:

*Articles of special interest or of high-impact.

1. Paris PL, Andaya A, Fridlyand J, Jain AN, Weinberg V, Kowbel D, Brebner JH, Simko J, Watson JE, Volik S, Albertson DG, Pinkel D, Alers JC, Van Der Kwast TH, Vissers KJ, Schroder FH, Wildhagen MF, Febbo PG, **Chinnaiyan AM**, Pienta KJ, Carroll PR, Rubin MA, Collins C, Van Dekken H. (2004) Whole genome scanning identifies genotypes associated with recurrence and metastasis in prostate tumors. *Hum Mol Genet*. Jul 1;13(13):1303-13.
2. Nyati MK, Maheshwari D, Hanasoge S, Sreekumar A, Rynkiewicz, SD, **Chinnaiyan AM**, Leopold WR, Ethier SP, Lawrence TS. (2004) Radiosensitization by pan ErbB inhibitor CI-1033 in vitro and in vivo. *Clin Cancer Res*, 10(2): 691-700.
3. *Sreekumar A., Laxman B., Rhodes DR. Bhagavathula S, Harwood J, Giacherio D, Ghosh D, Sanda MG, Rubin MA, **Chinnaiyan AM**. (2004) Humoral Immune Response to alpha-Methyl-CoA Racemase and Prostate Cancer *Journal of the National Cancer Institute*, 96(11):834-43.
4. *Rhodes DR, Yu J, Shanker K, Deshpande N, Varambally R, Ghosh D, Barrette T, Pandey A, **Chinnaiyan AM**. (2004) Large scale meta-analysis of cancer microarray data identifies common transcriptional profiles of neoplastic transformation and progression. *Proceedings of the National Academy of Sciences*, 101(25):9309-14.
5. Ghosh DR, **Chinnaiyan AM**. (2004) Classification and selection of biomarkers in genomic data using LASSO. *The University of Michigan Department of Biostatistics Working Paper Series*. <http://www.bepress.com/umichbiostat/paper42>
6. Rhodes DR, **Chinnaiyan AM**. (2004) Bioinformatics strategies for translating genome-wide expression analyses into clinically useful cancer markers. *Ann N Y Acad Sci*, 1020:32-40.

7. *Rhodes DR, Yu J, Shanker K, Deshpande N, Varambally R, Ghosh D, Barrette T, Pandey A, **Chinnaiyan AM**. (2004) ONCOMINE: a cancer microarray database and integrated data-mining platform. *Neoplasia*, Jan-Feb;6(1):1-6.
8. *Shah RB, Mehra R, **Chinnaiyan AM**, Shen R, Ghosh D, Zhou M, Macvicar GR, Varambally S, Harwood J, Bismar TA, Kim R, Rubin MA, Pienta KJ. (2004) Androgen-independent prostate cancer is a heterogeneous group of diseases: lessons from a rapid autopsy program. *Cancer Res*. Dec 15;64(24):9209-16.
9. Shen R, Ghosh D, **Chinnaiyan AM**. Prognostic meta-signature of breast cancer developed by two-stage mixture modeling of microarray data. (2004) *BMC Genomics*. Dec 14;5(1):94.
10. Hofer MD, Fecko A, Shen R, Setlur SR, Pienta KG, Tomlins SA, **Chinnaiyan AM**, Rubin MA. (2004) Expression of the platelet-derived growth factor receptor in prostate cancer and treatment implications with tyrosine kinase inhibitors. *Neoplasia*. Sept-Oct;6(5):503-12.
11. Santagata S, Demichelis F, Riva A, Varambally S, Hofer MD, Kutok JL, Kim R, Tang J, Montie JE, **Chinnaiyan AM**, Rubin MA, Aster JC. (2004) JAGGED1 expression is associated with prostate cancer metastasis and recurrence. *Cancer Res*. Oct 1;64(19):6854-7.
12. Liu T, Dhanasekaran SM, Jin H, Tomlins SA, **Chinnaiyan AM**, Phan SH. (2004) Induction of FIZZ1 Expression in Lung Injury and Fibrosis. *American Journal of Pathology* 164:1315-26.
13. Dhanasekaran SM, Dash A, Yu J, Maine IP, Laxman B, Tomlins SA, Creighton CJ, Menon A, Rubin MA, **Chinnaiyan AM**. (2005) Molecular profiling of human prostate tissues: insights into gene expression patterns of prostate development during puberty. *FASEB J*. Feb;19(2):243-5.
14. Ghosh D, **Chinnaiyan AM**. (2005) Covariate adjustment in the analysis of microarray data from clinical studies. *Funct Integr Genomics*, Jan 5(1):18-27.
15. Narla G, Difeo A, Reeves HL, Schaid DJ, Hirshfeld J, Hod E, Katz A, Isaacs WB, Hebring S, Komiya A, McDonnell SK, Wiley KE, Jacobsen SJ, Isaacs SD, Walsh PC, Zheng SL, Chang BL, Friedrichsen DM, Stanford JL, Ostrander E, **Chinnaiyan AM**, Rubin MA, Xu J, Thibodeau, SN, Friedman SL, Martignetti JA (2005) A germline DNA polymorphism enhances alternative splicing of the KLF6 tumor suppressor gene and is associated with increased prostate cancer risk. *Cancer Res*. Feb 15;65(4):1213-22.
16. Lippman ME, Benz C, **Chinnaiyan AM**, Flockhart D, Harris A, Hudis C, Osborne CK, Press MF, Rae J, Sledge GW, Veer LV, Wicha M. (2005) Consensus statement: Expedition Inspiration 2004 Breast Cancer Symposium 'Breast Cancer - the Development and Validation of New Therapeutics'. *Breast Cancer Res. Treat.* 90(1):1-3.
17. Chinnaiyan P, Huang S, Vallabhaneni G, Armstrong E, Varambally S, Tomlins SA, **Chinnaiyan AM**, Harari PM. (2005) Mechanisms of enhanced radiation response following epidermal growth factor receptor signaling inhibition by erlotinib (Tarceva). *Cancer Res* Apr 15;65(8):3328-35.
18. Thomas M, Yu Z, Dadgar N, Varambally S, Yu J, **Chinnaiyan AM**, Lieberman, AP. (2005) The unfolded protein response modulates toxicity of the expanded glutamine androgen receptor. *J Biol Chem*. Jun 3; 280 (22): 21264-71.
19. **Chinnaiyan AM**. (2005) ONCOMINE and caBIG Advance Cancer Bioinformatics. *The Scientist* 19 (7): 22-4.
20. Bradley SV, Oravec-Wilson KI, Bougeard G, Mizukami I, Li L, Munaco AJ, Sreekumar A, Corradetti MN, **Chinnaiyan AM**, Sanda MG, Ross TS. (2005) Serum antibodies to huntingtin interacting protein-1: a new blood test for prostate cancer. *Cancer Res*. 2005 May 15;65(10):4126-33.
21. *Rhodes DR, Kalyana-Sundaram S, Mahavisno V, Barrette T, Ghosh D, **Chinnaiyan AM**.

- (2005) Mining for Regulatory Programs in the Cancer Transcriptome. *Nature Genetics* 2005 Jun; 37 (6): 579-583.
22. *Rhodes DR, **Chinnaiyan AM**. (2005) Integrative Analysis of the Cancer Transcriptome. *Nature Genetics* 2005, Jun; 37, Suppl: S31-S37.
23. Lakshmi PK, **Chinnaiyan AM**, Shah RB. (2005) Comparison of monoclonal antibody (P504S) and polyclonal antibody to AMACR in the work-up of Prostate Cancer. *Histopathology* (In press).
24. *Rhodes, DR, Tomlins, SA, Varambally, S. Kalyana-Sundaram, S. Ghosh, D., Pandey, A. and **Chinnaiyan A.M.** (2005) Integrative Prediction of the Human Protein Interaction Network and Application to Cancer Biology, *Nature Biotechnology*, In Press.
25. *Wang X. Yu J., Sreekumar A., Varambally S., Ghosh D, Shen R, Giacherio D, Mehra R, Montie JE, Pienta KJ, Sanda MG, Kantoff PW, Rubin MA, Wei JT, **Chinnaiyan AM** (2005) Autoantibody Signatures in Prostate Cancer. *New England Journal of Medicine*, In Press.
26. Witkiewicz AK, Varambally S, Shen R, Mehra R, Sabel MS, Ghosh D, **Chinnaiyan AM**, Rubin MA, Kleer CG. (2005). Alpha-methylacyl-CoA racemase protein expression is associated with the degree of differentiation in breast cancer using quantitative image analysis. *Cancer Epidemiol Biomarkers Prev.* 2005 Jun; 14(6):1418-23.
27. Rubin MA, Bismar TA, Andren O, Mucci L, Kim R, Shen R, Ghosh D, Wei JT, **Chinnaiyan AM**, Adami HO, Kantoff PW, Johansson JE. (2005) Decreased alpha-methylacyl CoA racemase expression in localized prostate cancer is associated with an increased rate of biochemical recurrence and cancer-specific death. *Cancer Epidemiol Biomarkers Prev.* 2005 Jun; 14(6):1424-32.
28. Finn WA, **Chinnaiyan AM**, Utiger C, Sreekumar A. (2005) Trisomy 12-Associated, t(11;14)-Negative Mature B-Cell Leukemia With Gene Expression Profile Resembling Mantle Cell Lymphoma. *Leukemia and Lymphoma*, In Press.
29. **Chinnaiyan P**, Varambally S, Tomlins SA, Huang S, **Chinnaiyan AM** and Harari PM. (2005) Enhancing the anti-tumor activity of ErbB blockade with histone deacetylase (HDAC) inhibition. *International Journal of Cancer*, In Press.
30. Ghosh D, **Chinnaiyan AM**. (2005) Classification and Selection of Biomarkers in Genomic Data Using LASSO *J Biomed Biotechnol.*(2):147-54.
31. Olle EW, Sreekumar A, Warner RL, McClintock SD, **Chinnaiyan AM**, Bleavins MR, Anderson TD, Johnson KJ. (2005) Development of an internally controlled antibody microarray. *Mol Cell Proteomics*, In Press.

BOOKS/CHAPTERS IN BOOKS:

BOOK CHAPTERS:

1. Creighton C, **Chinnaiyan AM**. DNA Microarrays in Cancer. (2005) In Signal Transduction: A SystemsBiology Approach. Editor, Pandey A. 1st Ed. In Press.
2. *Tomlins, SA, Rubin, MA., **Chinnaiyan, AM**. Integrative Biology of Prostate Cancer Progression Annual Review of Pathology: Mechanisms of Disease Volume 1, January 2006, In Press.
3. Tomlins, SA, **Chinnaiyan, AM**. Expression Profiling of Prostate Cancer Progression Prostate Cancer: Novel Biology, Genetics and Therapy. 2nd edition (2006), In Press.
4. Tomlins, SA, Laxman, Bharati, Yu, Jianjun, **Chinnaiyan, AM**. Biomarkers Identified by Differential Gene Expression Analysis and Their Application: (2005), In Press.

ABSTRACTS:

1. Several abstracts have been submitted from the Chinnaiyan Lab (during this period) to various national meetings including USCAP, American Association for Cancer Research (AACR), NCI S.P.O.R.E. meeting, and the Fall Research Symposium of the U of Michigan Cancer Center. Please refer to the published manuscripts that have resulted from these abstracts.

**KATHLEEN CHO, M.D.
PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Gynecological pathology consultation services (six months) and “Room G”/Gynecological Pathology sign out in surgical pathology – 14 weeks.

II. TEACHING ACTIVITIES:

- A. Postdoctoral Fellows:
Responsible during the academic year for the following:
1. Hongfeng Yu, Ph.D. (1 month)
 2. Navneet Sangha, Ph.D. (5 months)
- B. Graduate students:
1. Neali Hendrix (Dept. of Pathology), faculty mentor, doctoral candidate, PIBS program
 2. Albert Levin (Dept. of Epidemiology, School of Public Health), thesis committee member, Ph.D. candidate
 3. Course Faculty, Pathology 581 – two lecture hours
Course Faculty, IMS-I (new curriculum, Dental School) – two lecture hours
- C. Undergraduate students:
Jonathan Dunker
- D. House Officers:
Room G sign-out of gynecologic pathology cases; two staff consultation conferences
- E. Interdepartmental:
Multidisciplinary Gynecologic Oncology tumor board – one hour twice per month
- F. National:
Course Faculty and Co-organizer: Molecular Biology in Clinical Oncology Workshop, American Association for Cancer Research, The Given Institute, Aspen, Colorado.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, “Molecular Pathogenesis of Ovarian Endometrioid Adenocarcinomas”, NIH RO1 CA94172 (30% effort), February 1, 2002 – January 31, 2007.
- B. Principal Investigator (20% effort), “Molecular Markers of Invasion in Cervical Cancer Progression” NIH 1P50CA98252-01 (SPORE in Cervical Cancer, Program PI: T.C. Wu), September 30 2003 – August 31 2008.
- C. Co-Investigator (5% effort), “Markers of Progression to Cervical Cancer in Rural India” NIH 1P50CA98252-01 (SPORE in Cervical Cancer, Program PI: T.C. Wu), September 30 2003 – August 31 2008.

- D. Co-Investigator (10% effort), "The Role of β -Catenin/Tcf Pathway Defects in Cancer." NIH R01 CA85463 (Fearon), June 1 2000 – May 31, 2005.
- E. Co-Investigator (10% effort), "CDX2 Tumor Suppressor Pathway Defects in Colon Cancer", NIH R01 CA82223 (Fearon), August 1, 2004 – July 31, 2009.
- F. Co-Investigator (4% effort), "Liquid Proteomics for Marker Screening of Ovarian Cancer", NIH RO1 CA100104 (Lubman), April 15 2003 – April 14, 2008
- G. Co-Investigator and mentor for New Investigator (2.5% effort), "Development and Characterization of a Murine Model of Ovarian Endometrioid Adenocarcinoma Induced by Tissue Specific Expression of Oncogenic β -Catenin", Department of Defense, Ovarian Cancer Research Program: DAMD17-OC030117 (R. Wu), February 1 2004 – January 31 2007.

PENDING:

- A. Co-Investigator (10% effort), "The Role of β -catenin/Tcf Pathway Defects in Cancer", NIH RO1 CA85463 (Fearon)

PROJECTS UNDER STUDY:

- A. Molecular profiling of ovarian epithelial tumors using liquid proteomics and Affymetrix gene chip technologies.
- B. Identification and characterization of molecular markers of ovarian carcinomas.
- C. Identification of novel genes amplified in ovarian carcinomas.
- D. Evaluation of the role of Wnt/ β -catenin/Tcf pathway defects in the pathogenesis of ovarian endometrioid adenocarcinomas.
- E. Development of a murine model of ovarian endometrioid adenocarcinomas
- F. Identification of genes involved in cervical cancer progression

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Department of Pathology, internal Advisory Committee on Appointments, Promotions and Tenure, 2002 – present
- B. Department of Pathology Graduate Student Admissions Committee, 2002 – present
- C. Department of Pathology Director of Anatomic Pathology Search Committee, 2005

INSTITUTIONAL:

- A. Institutional Review Board, University of Michigan School of Medicine (IRB-MED), appointment from Feb 2001 – present

REGIONAL AND NATIONAL:

- A. Subcommittee A – Cancer Centers IRG (NCI-A RTRB-R), Ad hoc member for review of the Dana Farber/Harvard Cancer Center 2P30CA006516-43, Boston, MA, June 2005.
- B. Integration Panel, Department of Defense, Ovarian Cancer Research Program
- C. Member, Publications Committee, American Association for Cancer Research, 2002-present
- D. Co-Organizer and course faculty member, Molecular Biology in Clinical Oncology Workshop, American Association for Cancer Research, 2000-present
- E. Member, National Comprehensive Cancer Center Panel for establishment of endometrial and cervical cancer treatment guidelines, 1997-present
- F. Member, 2004 Dorothy P. Landon AACR Prize for Translational Cancer Research Selection Committee
- G. Secretary, International Society of Gynecological Pathologists, elected to two year term beginning 2004, renewable for two additional terms, not to exceed six years
- H. Member, Organizing Committee, 10th Biennial International Forum on Ovarian Cancer, Helene Harris Memorial Trust
- I. Co-Chairperson, New Concepts in Organ Site Research, Session Ovarian Cancer for 2005 AACR Annual Meeting, Anaheim CA
- J. Benjamin Castleman Award Committee, United States and Canadian Academy of Pathology (3 year appointment beginning 2005)

V. **OTHER RELEVANT ACTIVITIES:**

EDITORIAL BOARDS:

- A. Associate Editor, *Cancer Research*
- B. Associate Editor, *Clinical Cancer Research*
- C. Member, Editorial Board, *Human Pathology*
- D. Member, Editorial Board, *International Journal of Gynecological Pathology*
- E. Member, Editorial Board, *Diagnostic Molecular Pathology*
- F. Member, Editorial Board, *The Women's Oncology Review*
- G. Ad hoc reviewer for several additional journals

INVITED LECTURES/SEMINARS 2004-2005:

- 1. Role of Wnt Signaling Pathway Defects in Ovarian Cancer Pathogenesis. Invited Seminar, Department of Molecular Pharmacology/Experimental Therapeutics and Tumor Biology Program, Mayo Clinic, Rochester, Minnesota, 2004.
- 2. Molecular Pathology in Oncology: Overview and Selected Applications. Molecular Biology in Clinical Oncology Workshop, American Association for Cancer Research, The Given Institute, Aspen, Colorado, 2004.
- 3. Gynecological Cancers: Clues to Pathogenesis from Molecular Profiling. Molecular Pathology Seminar Series, Department of Pathology, The Johns Hopkins University School of Medicine, Baltimore, Maryland, 2005.

4. Ovarian Cancer: Updates from Bench and Bedside, session co-chair and invited speaker, "Ovarian Cancer: Insights from RNA and DNA profiling", Annual Meeting of the American Association for Cancer Research, Anaheim, California, 2005.
5. First Annual Conference for Dual-Degree Osteopathic Medical Students: "How to Develop a Career as a Physician Scientist", Michigan State University, East Lansing, Michigan, 2005.

VI. PUBLICATIONS (2004-2005):

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Wang, H., Kachman, M.T., Schwartz, D.R., Cho, K.R., and Lubman, D.M. Comprehensive Proteome Analysis of Ovarian Cancers Using Liquid Phase Separation, Mass Mapping and Tandem Mass Spectrometry: A Strategy for Identification of Candidate Cancer Biomarkers. Proteomics 4:2476-95, 2004.
2. Sherman ME, Berman J, Birrer MJ, Cho KR, Ellenson LH, Gorstein F, Seidman JD, Current challenges and opportunities for research on borderline ovarian tumors. Human Pathology, 35:961-70, 2004.
3. Chamorro MN, Schwartz DR, Vonica A, Brivanlou AH, Cho KR, and Varmus HE. FGF20 and DKK1 are transcriptional targets of β -catenin and FGF20 is implicated in cancer and development. EMBO J 24:73-84, 2005.
4. Shedden K, Chen W, Kuick R, Ghosh D, Macdonald J, Cho KR, Giordano TJ, Gruber SB, Fearon ER, Taylor JM, Hanash S. Comparison of seven methods for producing Affymetrix expression scores based on False Discovery Rates in disease profiling data. BMC Bioinformatics 6:26, 2005.
5. Shedden KA, Kshirsagar MP, Schwartz DR, Wu R, Yu H, Misek DE, Hanash S, Katabuchi H, Ellenson LH, and Cho KR. Histological type, organ of origin, and Wnt pathway status: Impact on gene expression profile in ovarian and uterine carcinomas. Clinical Cancer Research 11:2123-31, 2005.
6. Levin AM, Ghosh D, Cho KR, Kardia SLR. A model-based scan statistic for identifying extreme chromosomal regions of gene expression in human tumors. Bioinformatics, 21:2867-74, 2005.
7. Zhai Y, Hotary KB, Nan B, Bosch FX, Muñoz N, Weiss SJ, and Cho KR. Expression of membrane-type 1 matrix metalloproteinase is associated with cervical carcinoma progression and invasion. Cancer Research (in press), 2005.

INVITED REVIEWS

1. Fearon, E.R., and Cho, K.R. Cell survival guide. Nature, 431:35-36, 2004.

BOOKS/CHAPTERS IN BOOKS:

None

**LAURA COOLING, MD, MS
CLINICAL ASSISTANT PROFESSOR II
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENT REPORT
1 JULY 2004-30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Associate Medical Director, Transfusion Medicine
 - 1. Blood Bank, clinical coverage and administration
 - 2. Bone Marrow/Peripheral Stem Cell Collection and Processing
 - 3. Clinical Consultation/Management, Special Product Requests
 - 4. Clinical Coverage, Therapeutic Apheresis

II. TEACHING ACTIVITIES:

- A. Resident Education
 - 1. Responsible/Share didactic teaching activities for the following:
 - a. Blood Component Therapy
 - b. Transfusion Reaction Evaluation
 - c. Evaluation and Management of Platelet Refractoriness
 - d. Fundamentals of Clinical Apheresis (with nursing staff)
 - e. Evaluation and Management of Therapeutic Apheresis Requests
 - f. Administrative Issues on-call
 - 2. Clinical Teaching
 - Supervision Resident/ Visiting Fellow Activities (12 mo/yr)
 - a. Morning Report
 - b. Transfusion reaction sign-out
 - c. Clinical apheresis requests/patient management
 - d. Special product request evaluation and clinical follow-up
 - e. Case-based informal teaching
 - 3. Other Clinical Teaching
 - a. Hematology case conference.
 - 4. Resident Applicant Interviews.
- B. Medical Students
 - 1. Transfusion Medicine. Senior Therapeutics Course, Dept. of Pharmacology

RESEARCH ACTIVITIES:

- A. The Regulation and Biology of Globo-Series Glycosphingolipids
 - 1. Molecular basis and regulation of \square 1,3 galactosyltransferase V on globo- and lacto-antigen expression
 - 2. Globo/lacto antigens in infectious disease and cancer
 - 3. Molecular analysis of globo-glycotypes

- B. Clinical Research
 - 1. Factors effecting stem cell collection and engraftment
 - 2. Platelet immunology, role in transfusion therapy

SPONSORED RESEARCH:

CURRENT

- A. Molecular Analysis of Globo- and Lacto-Family Glycosyltransferases: Molecular Etiology of the LKE-negative and LKE-weak Phenotypes. National Blood Foundation. PI, Laura Cooling.

PENDING

- B. Globo-glycosphingolipids in disease and development. KO8 Mentored Clinical Scientist Development Award, National Institutes of Health. PI. Laura Cooling, mentor Dr. James Shayman, Dept. of Internal Medicine.

ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL

- A. Associate Director, Transfusion Medicine

HOSPITAL

- A. Transfusion Subcommittee
- B. Data Analysis Council

MEDICAL SCHOOL

- A. Admissions Committee

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

- 1. American Association of Blood Banks Annual Meeting, Baltimore, MD. Decreased H antigen and increased susceptibility to apoptosis by all-trans retinoic acid.
- 2. American Association of Blood Banks Annual Meeting, Baltimore, MD. Waldenstrom's macroglobulinemia with cryoglobulinemia: a challenge to apheresis.
- 3. Faculty, Pall Corporation Workshop, American Association of Blood Banks Annual Meeting, Baltimore, MD. Bacterial Testing of Platelet Concentrates.
- 4. McMaster University, Hamilton, Ontario. The Book of Luke (LKE): Is α 1,3 galactosyltransferase V a glycomic holy grail?

5. Blood Bank Association of New York 54th Annual Meeting, Vernona, New York. Extreme Makeover: Can we improve platelet concentrates?
6. Blood Bank Association of New York 54th Annual Meeting, Verona, New York. Transfusion reaction workshop.
7. Current Topics in Blood Banking, University of Michigan. Case Studies: H is for hemolysis.
8. Faculty, Current Topics in Blood Banking Workshop, University of Michigan. From ABO to GIL: an update on the human blood groups. Carbohydrate antigens, the sweet side of blood banking.
9. Internal Medicine Grand Rounds, Univ. of Michigan: Hemotherapy.
10. Clinical Pathology Grand Rounds, Univ. of Michigan: H is for Hemolysis.

REVIEWER

Blood

European Journal of Biochemistry

Journal of Lipid Research

Leukemia

Transfusion

Thrombosis and Hemostasis

Thrombosis Research

Vox Sanguinis

Scientific Abstracts, American Association Blood Bank 57th Annual Meeting

PROFESSIONAL MEMBERSHIPS

American Association of Blood Banks

Elected, Scientific Section Coordinating Committee (SSCC)

Secretary SSCC, 2005-2006

Michigan Association of Blood Banks

Education Committee

Board of Directors

Invitational Conference of Investigative Immunohematology

International Society for Blood Transfusion

American Society of Clinical Apheresis

Alpha Omega Alpha

VI. PUBLICATIONS:

JOURNALS:

1. Cooling LW, Kelly K, Barton J, Hwang D, Koerner TAW, Olson JD. Determinants of ABH expression on human blood platelets. *Blood* 2005, 105; 3356-3364.
2. Swanson JL, Cooling L. Pig RBCs express a polyagglutinable phenotype. *Transfusion* 2005; 45:1035-1036.

3. Cooling L, Hwang D. Monoclonal antibody B2, a marker of neuroendocrine sympathoadrenal precursors, recognizes the Luke (LKE) antigen. *Transfusion* 2005;45:709-716.
4. Hoffman S, Zhou L, Gu Y, Davenport R, Cooling L. Delayed platelet engraftment in group O patients after autologous progenitor cell transplantation. *Transfusion* 2005; 45:885-895.
5. Zhou L, Giacherio D, Cooling L, Davenport RD. Use of β -natriuretic peptide (BNP) as a diagnostic marker in the differential diagnosis of transfusion-associated circulatory overload (TACO). *Transfusion* 2005, in press.

BOOKS/CHAPTERS IN BOOKS:

1. Cooling LW. Thrombotic thrombocytopenia purpura. *Conn's Current Therapy*, In press.
2. Beading W, Cooling LW. Immunohematology. In *Henry's Clinical Diagnosis and Management by Laboratory Methods*, 21st Edition, ed. McPherson, Pinkus. WB Saunders, In Press.

PEER-REVIEWED ABSTRACTS:

1. Cooling L, Hwang D, Shayman JA. Decreased H expression and susceptibility to apoptosis by all-*trans* retinoic acid. *Transfusion* 2004;44:31A.
2. Zhou L, Giacherio DA, Cooling LLW, Davenport RD. BNP as a potential diagnostic marker in the differential diagnosis of transfusion-induced circulatory fluid overload. *Transfusion* 2004;44:17A.
3. Woloskie SA, Cooling L, Davenport RD. Waldenstrom's macroglobulinemia with cryoglobulinemia: a challenge to apheresis. *Transfusion* 2004;44:13A.
4. Cooling L. LKE expression on cord RBC. *Transfusion* 2004;44:177A.
5. Judd WJ, Cooling L. Novel application of the gel test: detection of microbial-induced hemagglutination. *Vox Sang* 2004; 87 (supplement) :S17.
6. Woloskie S, Cooling L. Plasmapheresis to prevent pigment nephropathy: two case studies. *J Clin Apheresis*, In press.
7. Judd JW, Cooling L, Dake LR, Davenport RD, Ellis S, Haverty D, Mullis N. Clinically significant anti-LKE-nonreactive in prewarmed tests. Submitted.
8. Cooling LW, Hwang D, Shayman JA. Co-regulation of Lewis^a, Lewis^b and galactosylgloboside by β 1,3 galactosyltransferase V. Submitted.
9. Cooling LW, Hwang D, Shayman JA. Upregulation of Luke (LKE) by β 1,3 galactosyltransferase V (β 3GalT5) and 5'azacytidine. Submitted.

OTHER PUBLICATIONS:

1. Cooling L. Q&A ABO and platelet transfusions. *AABB News*, 2006 in press.
2. Cooling L. Extreme Makeover: Can we improve platelet concentrates. *New York Association of Blood Banks Newsletter*, In press.

SUBMITTED MANUSCRIPTS:

1. Shu L, Murphy HS, Cooling L, Shayman JA. An in vitro model of Fabry disease.

**CONSTANCE J. D'AMATO, B.S.
PROFESSOR EMERITUS OF NEUROBIOLOGY, ACTIVE
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Occasionally work with house officers and staff in Pathology and other departments in the gross and microscopic examination of dementia brains from autopsies at University Hospital.
- B. Occasionally attend and instruct house officers in the removal and gross examination of brains from autopsies at University Hospital.
- C. Work with Neuropathology Staff on autopsy brain material sent for consultative study from University-associated hospitals, other hospitals, and institutions.
- D. Plan and present Dementia Brain Cutting Conference for house officers, students and faculty, for gross diagnosis and demonstrations of diagnostic methods, and teaching.
- E. Continuous review of quality control of diagnostic techniques, and autopsy neuropathology, and search for improved and new methods.

II. TEACHING ACTIVITIES:

- A. Neurology Sequence, Coordinator for the Neuropathology for Second Year Medical Students, four hours laboratory.
- B. Neuropathology 858. Intensive laboratory-lecture course for house officers and fellows, in Pathology and in the several clinical services concerned with the nervous system, and medical students, graduate students, and faculty; implement, plan, and teach the course. Annual, 8 hours. One credit hour elective.
- C. Occasionally help in the neuropathology teaching for house officers and fellows from the several clinical services concerned with the nervous system, and medical students who take an elective rotation in Neuropathology.
- D. Teach laboratory techniques and basic neuroanatomy and neuropathology to our laboratory technologist (MADRC).

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. The Pathologic Examination of Human Autopsy Brains From Patients With Clinical Diagnosis of Alzheimer's, Huntington's, Pick's, and Other Dementing Diseases is being done in collaboration with Andrew Lieberman, M.D., Ph.D. and the Michigan Alzheimer Disease Research Center.

IV. **ADMINISTRATIVE ACTIVITIES:**

DEPARTMENTAL:

- A. Anatomic Pathology Faculty Meeting.
- B. Organize and teach the Neuropathology 858 Course.
- C. Organize brain cutting conference and participate in the conference.

MEDICAL SCHOOL/HOSPITAL:

- A. Coordinator for Neuropathology, Neurology Sequence.
- B. Admissions Committee, the University of Michigan Medical School.

REGIONAL AND NATIONAL:

- A. American Association of Neuropathologists.
- B. American Academy of Neurology.
- C. International Society of Neuropathology.
- D. Society for Neuroscience.

V. **OTHER RELEVANT ACTIVITIES:**

- A. Coordinate lecture and participate in the brain cutting session annually for 24 students from Eastern Michigan (class for Care of Dementia Patients).

INVITED PRESENTATIONS:

None.

VI. **PUBLICATIONS:**

ARTICLES ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS, BOOK CHAPTERS:

None.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

None.

**ROBERTSON D. DAVENPORT, M. D.
ASSOCIATE PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Medical Director, Blood Bank and Transfusion Service.
- B. Cytopathology staff.

II. TEACHING ACTIVITIES:

- A. Introductory Course in Blood Banking/Transfusion Medicine for Pathology House Officers.
- C. Daily teaching rounds for Pathology House Officers assigned to the Blood Bank.
- D. Cytopathology sign-out with Pathology House Officers and Cytopathology Fellows.
- E. Current Topics in Blood Banking Conference, Towsley Center for Continuing Medical Education.
- F. M2 Hematology sequence, Blood Transfusion.
- G. Hematology fellows, blood transfusion.
- H. Director, Fellowship Program in Blood Banking/Transfusion Medicine

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Pathophysiology of transfusion reactions.
- B. Cefotetan induced immune hemolysis.
- C. Heparin-induced thrombocytopenia.
- D. Prediction of clinical significance of red cell antibodies

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

- A. Transfusion Committee.
- B. Blood Transfusion Process Improvement Team.

V. OTHER RELEVANT ACTIVITIES:

- A. Program Committee, Michigan Association of Blood Banks.
- B. Medical Advisory Committee, American Red Cross Southeastern Michigan Region.
- C. Editorial Board, Transfusion.
- D. National Institutes of Health, Erythrocyte and Leukocyte Biology Study Section, Ad hoc member
- E. AABB: Clinical Transfusion Medicine Committee

VI. PUBLICATIONS:

ARTICLES ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Davenport RD. Erythropoietic protoporphyria. *Transfusion*. 2004; 44:1401
2. Kleinman S, Caulfield T, Chan P, Davenport R, McFarland J, McPhedran S, Meade M, Morrison D, Pinsent T, Robillard P, Slinger P. Towards an Understanding of Transfusion Related Acute Lung Injury: Statement of a Consensus Panel. *Transfusion*. 2004; 44:1774-1789
3. Davenport RD. Blood components should be labeled for content. *Transfusion* 2005; 45:3-4.
4. Hoffmann S, Zhou L, Gu Y, Davenport R, Cooling L. Delayed Platelet Engraftment in Group O Patients After Autologous Progenitor Cell Transplantation. *Transfusion* 2005;45:885-9.
5. Srivastava N, Davenport RS, Burns MA. Nanoliter Viscometer for Analyzing Blood Plasma and Other Liquid Samples. *Anal Chem* 2005; 77:383 - 392
6. Zhou L, Giacherio D, Cooling L, Davenport RD: Use of B-natriuretic Peptide as a Diagnostic Marker in the Differential Diagnosis of Transfusion-Associated Circulatory Overload. *Transfusion* 2005; 45:1056-63.
7. Zhou L, Thorson JA, Nugent C, Davenport RD, Butch SH, Judd WJ. Non-Invasive Prenatal RHD Genotyping by Real-Time PCR Using Plasma from D-negative Pregnant Women. *Am J Obstet Gynecol* (in press).

ARTICLES SUBMITTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Judd WJ, Dake LR, Davenport RD. On a much higher than reported incidence of anti-c in R1R1 patients with anti-E. Submitted to *Immunohematology*.

CHAPTERS IN BOOKS:

1. Davenport RD: Management of transfusion reactions. In: Mintz PD (ed): *Transfusion Therapy: Clinical Principles and Practice*. 2nd ed. AABB Press, Bethesda, MD, 2005.
2. Davenport RD, Mintz PD. *Transfusion Medicine*. In: Hutchinson R (ed): *Henry's Clinical Diagnosis and Management by Laboratory Methods*, 21st Edition. Elsevier, Philadelphia, PA (in press).

ABSTRACTS AND PRELIMINARY COMMUNICATIONS:

1. Woloskie SA, Cooling L, Davenport RD. Waldenstrom's macroglobulinemia with cryoglobulinemia: a challenge to apheresis. *Transfusion* 2004; 44(9S):13A.
2. Zhou L, Giacherio DA, Cooling LW, Davenport RD. BNP as a potential diagnostic marker in the differential diagnosis of transfusion-induced circulatory fluid overload. *Transfusion* 2004; 44(9S):17A.
3. Dake LR, Judd WJ, Davenport RD. On a much higher than reported incidence of anti-C in R1R1 patients with anti-E. *Transfusion* 2004; 44(9S):115A.

**FELIX A. DE LA IGLESIA, M.D.
ADJUNCT PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004-30 JUNE 2005**

I. CLINICAL ACTIVITIES:

None

II. TEACHING ACTIVITIES:

None.

III. RESEARCH ACTIVITIES:

- A. In vitro live cell organelle toxicity research using multiple, simultaneous fluorescent probes.
- B. Study of internal fluorescent markers for drug uptake.
- C. Study of hemostatic proteins derived from Australian snake venom.

SPONSORED SUPPORT:

- A. Research activities with intramural support from Dr. Ward.
- B. Collaboration with K. Johnson in the development of morphometric models to evaluate pathologic tissue and cellular changes.
- C. NASA Grant – “Biosensors for real-time monitoring of radiation induced biologic effects in space.” (NAS-2-02069).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

None.

MEDICAL SCHOOL/HOSPITAL:

None.

REGIONAL AND NATIONAL:

Member, Scientific Advisory Committee, Center for Light Microscopy, Carnegie Mellon University, Pittsburgh, PA.

Member, Scientific Advisory Board, Cellomics Inc., Pittsburgh, PA.

Member, Scientific Advisory Board, QRx Pharma, Brisbane, Australia

Member, International Scientific Advisory Board, Center Internationale de Toxicologie, Paris, France

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

Editorial Board Member, Drug Metabolism Reviews.

INVITED LECTURES/SEMINARS:

Chairman, Genomics Session, International Scientific Symposium, Center Internationale de Toxicologie, Paris, France

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

ARTICLES SUBMITTED FOR PUBLICATION:

1. P B Sullivan , PJ Lewindon, C Cheng, PF Lenehan, K Bo-Sheng, JR Haskins, RA Goodlad , NA Wright, FA de la Iglesia. Intestinal mucosa remodeling by recombinant Human Epidermal Growth Factor $_{1-48}$ in neonates with severe necrotizing enterocolitis. (Submitted, 2005).
2. TM Sassanella, TP Thomas, A Kotlyar, B Keszler, IJ Majoros, NW Beeson, JR Baker Jr, FA de la Iglesia. Cellular Uptake of Folic Acid -targeted and Non-targeted Dendrimer-Fluorescent Dye Biosensing Nanodevices. (Submitted, 2005)

**GREGORY R. DRESSLER, Ph.D.
ASSOCIATE PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

- A. Pre-doctoral Students Supervised - Jing Mei Lin, Dept. of Pathology; Marc Prindle, CMB
- B. Post-doctoral Trainees Supervised - Yi Cai, M.D., Ph.D.; Sanj Patel, M.D., Doyeob Kim, Ph.D., Ming Feng, Ph.D.
- C. Ph. D. Thesis Committee Member - Brian Gummow, CMB; Collen Doyle, Dept. of Genetics, Ira Weiner, CMB; Rob Ward, CMB.
- D. Course Lectures - Path 581, 7.5 h; Path 582 course director; CDB 530, 3 h

MEDICAL SCHOOL/HOSPITALS:

- A. First year Medical Students – Renal Section 2 h, Endocrine Section 1h.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, “PAX2 Interacting Proteins in Development and Disease”, NIH/NIDDK 1 R01 DK54740-05 (30% effort), 7/1/02 – 6/30/03, Annual Direct Costs \$221,000.
- B. Principle Investigator, “Cell Signaling in Developing Epithelia”, (35% effort) NIH/NIDDK R01 DK62914-01, 9/20/03 – 6/30/07, \$224,000
- C. Collaborator “Novel SAPK activating kinase in renal epithelial stress”, Lawrence Holzman, PI (5% effort) NIH/NIDDK R01 DK52886, 8/1/98-7/31/07.
- D. Principle Investigator, “The Role of Groucho Corepressors in Development and Polycystic Kidney Disease”, (10% effort) The Polycystic kidney Disease Research Foundation, Grant-in-Aid.
- E. Principal Investigator, “Differentiation of ES cells into renal epithelia”, (20% effort) NIH/NIDDK 1R21 DK069689-01, 4/1/05 – 3/31/07, \$90,000

PROJECTS UNDER STUDY:

- A. The identification of co-factors required for Pax protein mediated transcription activation.
- B. The development of novel methods for identifying genes regulated by Pax proteins.
- C. The role of Pax-2 in the initiation and progression of polycystic kidney disease.
- D. The GDNF/RET signaling pathway in the developing kidney.
- E. The role of novel TGF-beta inhibitors in renal development and disease

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Dept. of Pathology - Preliminary Exam Committee, Curriculum Committee,
- B. Center for Organogenesis - Interim Co-Director, Steering Committee, Training Grant Review Committee, Advisory Committee, Seminar Committee (Chair)
- C. CMB preliminary Exams

REGIONAL AND NATIONAL:

NIDDK, MAGUD Advisory Board
NIDDK Special Emphasis Panel, PKD P30
Developmental Dynamics, Editorial Board

Reviewer for: *Developmental Cell*, *Nature Genetics*, *Science*, *Development*, *Proceedings of the National Academy of Sciences*, *Developmental Dynamics*, *Journal of Biological Chemistry*, *American J. of Physiology*, *Journal of Clinical Investigation*, *Molecular and Cellular Biology*, *Genes & Development*, *Kidney International*, *Journal of Cell Biology*, *Am. J. Pathology*.

V. OTHER RELEVANT ACTIVITIES:

Membership in the American Society of Nephrology
Membership in Society for Developmental Biology
Membership in University of Michigan Comprehensive Cancer Center
Membership in the Center for Organogenesis, University of Michigan

INVITED LECTURES/SEMINARS:

- 1. Dept. of Genetics, University of Nebraska School of Medicine, Omaha
- 2. 3rd Course on Genetics and Renal Disease, Genoa, Italy
- 3. Dept. of Biochemistry & Biophysics, Oregon State Univ., Corvallis

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Patel, S. and Dressler, G.R. (2004) Expression of Pax2 in the intermediate mesoderm is regulated by YY1. *Dev. Biol.*, 267, 505-516.
2. Lin, J., Patel, S.R., Cheng, X., Cho, E. A., Levitan, I., Ullenbruch, M., Phan, S.H., Park, J.M. and Dressler, G.R. (2005) Kielin/Chordin-like protein (KCP), a novel enhancer of BMP signaling attenuates renal fibrotic disease. *Nature Medicine*, 11, 387-393 (featured in news and views p.373)
3. Kim, D. and Dressler, G.R. (2005) Nephrogenic factors promote differentiation of mouse embryonic stem cells into renal epithelia. *J. Am. Soc. Nephrol.*, in press.
4. Patel, S. R. and Dressler, G. R. (2005) BMP signaling in renal development and disease. *Trends Mol. Medicine*, in press.

ARTICLES SUBMITTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Lin, J. and Dressler, G.R. (2005) The cysteine rich domain protein KCP is a suppressor of Activin/TGF- β signaling. submitted
2. Self, M., Lagutin, O., Bowling, B., Hendrix, J., Cai, Y., Dressler, G. R. and Oliver, G. (2005) The six2 gene is required for suppression of inductive signals and progenitor cell renewal in the developing kidney. submitted
3. Clarke J. C., Patel, S. R., Raymond, R. M., Andrew, S., Robinson, B. G., Dressler, G. R. and Brophy, P. D. (2005) Pax2 regulates the expression of c-Ret during branching morphogenesis in the mammalian kidney. submitted
4. Kim, D. and Dressler, G. R. (2005) Inhibition of epithelial cell migration and ureteric bud remodeling by the phosphatidylinositol phosphatase PTEN. submitted

BOOK CHAPTERS:

1. Dressler, G. R. (2004) Cell Lineages and Stem Cells in the Embryonic Kidney. in *Handbook of Embryonic Stem Cells* (R. Lanza, ed.) Elsevier Science, in press.
2. Dressler, G. R. (2005) Cell lineages and stem cells in the embryonic kidney. In: *Essentials of Stem Cell Biology* (R. Lanza, ed.) Elsevier Science, San Diego, CA

**COLIN S. DUCKETT, Ph.D.
ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
JULY 1 2004 – JUNE 30 2005**

I. CLINICAL ACTIVITIES:

None

II. TEACHING ACTIVITIES:

A. RESEARCH MENTOR:

1. John Wilkinson, Ph.D., Postdoctoral Fellow, 2002 - present.
2. Casey Wright, Ph.D., Postdoctoral Fellow, 2003 - present.
3. Arjmand Mufti, M.D., Fellow, Department of Internal Medicine 2003 - present.
4. Clara Hwang, M.D., Fellow, Department of Internal Medicine, 2004 – present.
5. Julie Rumble, Graduate Student, Immunology Program, 2004 - present
6. Rebecca Csomos, Graduate Student, Pathology Program, 2004 - present.
7. Karolyn Oetjen, MSTP Student, Pathology Program, 2004 – present

CO-MENTORING FACULTY MEMBER:

8. Jane Deng, M.D., Fellow, Department of Internal Medicine
9. Matthew Dimagno, M.D., Fellow, Department of Internal Medicine

B. THESIS COMMITTEE/EXAMINER:

1. Katie Johnson, Immunology Graduate Program
2. Brian Rudd, Pathology Graduate Program
3. Malinda Schaefer, Immunology Graduate Program
4. Michael Khodadoust, Cellular and Molecular Biology Program
5. Brendan Looyenga, Cellular and Molecular Biology Program
6. Cynthia Coffill, University of Ottawa Biochemistry Program

C. TEACHING:

1. Pathology 852
2. Pathology 581
3. Course Director, Immunology 815

III. **RESEARCH ACTIVITIES:**

PROJECTS UNDER STUDY:

- A. Role of X-linked IAP (XIAP) in TGF- β signal transduction pathways, in collaboration with Dr. Anita Roberts, National Cancer Institute.
- B. Analysis of the protective effects of XIAP in caspase-dependent and -independent cell death, in collaboration with Dr. Larry Boise, University of Miami.
- C. Characterization of VIAP, a novel IAP-associated factor, in collaboration with Dr. Pam Schwartzberg, Nation Human Genome Research Institute.
- D. Interaction of XIAP with Murr1, a factor whose gene is mutated in an inherited copper deficiency, in collaboration with Dr. Marty Mayo, University of Virginia, Drs. Cisca Wijmenga and Leo Klomp, University Medical Center, Utrecht, and Dr. George Brewer, University of Michigan..

SPONSORED SUPPORT:

- 2005 - 2010 "Control of Apoptosis and Signaling by XIAP," R01 GM067827-01 (NIGMS). (PI) (30%).
- 2004 - 2007 "XIAP as a molecular target for therapeutic intervention in prostate cancer." (15%). USARMC Prostate Cancer IDEA Award (PI).
- 2004 - 2005 "Role of XIAP and AIF in prostate cancer" (0%). NIH/NCI P50 pilot award (PI)
- 2004 - 2007 "Prostate cancer aggressiveness genes in hereditary prostate cancer," (15%). USARMC Prostate Cancer IDEA Award (Co-PI with K. Cooney)
- 2003 - 2008 "Prevention of Mammary Cancer in Her-2neu Transgenic Mice," (2.5%). R01 (Merajver PI).
- 2004 - 2009 "SCF in eosinophilic airway inflammation," "R01 (15%) (NIAID). (Lukacs PI).

FELLOWSHIP AWARDS SERVING AS MENTOR

- 2004 - 2006 "Role of the XIAP/AIF axis in the development and progression of prostate cancer." CDMRP Department of Defense Prostate Cancer Research Program, Postdoctoral Training Award to John Wilkinson, Ph.D.
- 2003 - 2006 "Characterization of a novel interacting partner of XIAP." American Gastroenterological Association Research Scholar Award to Ezra Burstein, M.D.
- 2004 - 2005 "CD30-mediated p100/NF-KB2 processing and activation." NHLBI Postdoctoral Training Grant to Casey Wright, Ph.D.
- 2005 - 2006 "Research Training in experimental immunopathology" NIAID Immunology Training Grant to Julie Rumble.
- 2005 - 2007 "Training for research in gastroenterology." NIDDK Postdoctoral Training Award to Arjmand Mufti, M.D.
- 2005 - 2007 "Understanding the roles of IAPs and TRAFs in CD30 malignancies" NCI Cancer Biology Predoctoral Training Grant to Rebecca Csomos.

PENDING

- 2005 – 2007 “The role of X-linked Inhibitor of Apoptosis in Breast Cancer.” DOD Breast Cancer Predoctoral Traineeship Award BC051269 Predoctoral Award to Karolyn Oetjen
- 2005 – 2010 “TLR3-mediated immune mechanisms in RSV infection.” R01 HL079944-01 (NHLBI). (Lukacs PI) (15%).
- 2005 – 2010 “Role of TLR9 in Lung Antibacterial Host Defense”. R01 HL57243 (NHLBI). (Standiford) (5%).

IV. ADMINISTRATIVE ACTIVITIES:

1. PIBS International Admissions Committee.
2. Immunology graduate program prelim committee
3. Pathology graduate program prelim committee
4. Scientific Advisory Board, Aegera Therapeutics, 2002
5. Permanent Reviewer, NIH Cellular and Molecular Immunology -B Study Section
6. Permanent Reviewer, American Cancer Society CCG Study Section, 2004
7. Program Committee Member, 96th AACR Annual Meeting

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL AND REVIEWING ACTIVITIES:

- A. Editorial Board: *Journal of Biological Chemistry*, 2002 – 2007
Associate Editor: *Biochemical Journal*, 2003 - 2006
- B. Reviewer (selected journals shown):
Cancer Cell,
Cell
Cell Death and Differentiation
Current Biology
EMBO Journal
EMBO Reports
Genes and Development
Immunity
Journal of Clinical Investigation
Molecular Cell
Nature Cell Biology
Nature Reviews Cancer
Nature Reviews Molecular Cell Biology
Oncogene
Proceedings of the National Academy of Sciences USA
Science

HONORS AND AWARDS:

- 2002 – Biomedical Scholar Award, University of Michigan
2005 University of Miami Sylvester Comprehensive Cancer Center Distinguished Lectureship
2006 – 2007 Selected Member of the 2004-2005 Defense Science Study Group (DSSG) administered by the Institute for Defense Analyses (IDA), sponsored by the Defense Advanced Research Projects Agency (DARPA).

INVITED LECTURES/SEMINARS:

1. University of Texas at Austin, TX (2004)
2. Gordon Research Conference on Toxicology, Colby College, ME (2004)
3. University of Miami Sylvester Comprehensive Cancer Center Distinguished Lectureship, MI (2004)
4. Albert Einstein College of Medicine, NY (2004)
5. Beatson Institute, Glasgow, UK (2004)
6. Gordon Research Conference on Toxicology (2004).

VI. PUBLICATIONS:

1. Beltrami, E., Plescia, J., Wilkinson, J.C., **Duckett, C.S.** and Altieri, D.C. Acute ablation of survivin uncovers p53-dependent mitotic checkpoint functions and control of mitochondrial apoptosis. *J. Biol. Chem.* **279**:2077-2084 (2004).
2. Burstein, E., Ganesh, L., Dick, R.D., van De Sluis, B., Wilkinson, J.C., Lewis, J., Klomp, L.W.J., Wijmenga, C., Brewer, G.J., Nabel, G.J. and **Duckett, C.S.** A novel role for XIAP in copper homeostasis through regulation of MURR1. *EMBO J.* **23**:244-254 (2004).
3. Jacob, J., Louis, J.M., Richter, B.W.M., **Duckett, C.S.** and Torchia, D.A. The C-terminal domain, of Viral IAP-associated factor (cVIAF) is a structural homolog of phosphatidylinositol 3-OH kinase: resonance assignments and secondary structure of the C-terminal domain of VIAF. *J. Biomol NMR* **82**:197-198 (2004).
4. Steinman, H.A., Burstein, E., Lengner, C., Gosselin, J., Pihan, G., **Duckett, C.S.** and Jones, S.N. An alternative splice form of Mdm2 induces p53-independent cell growth and tumorigenesis. *J. Biol. Chem.* **279**:4877-4886 (2004).
5. Lewis, J., Burstein, E., Birkey Reffey, S., Bratton, S.B., Roberts, A.B., and **Duckett, C. S.** Uncoupling of the signaling and caspase-inhibitory properties of XIAP. *J. Biol. Chem.* **279**:9023-9029 (2004).
6. Creagh, E.M, Murphy, B., **Duckett, C.S.** and Martin, S.J. SMAC/Diablo antagonizes XIAP ubiquitin ligase activity to potentiate apoptosis. *J. Biol. Chem.* **279**:29606-29614 (2004).
7. Wilkinson, J. C., Cepero, E., Boise, L.H. and **Duckett, C.S.** Upstream regulatory role for XIAP in receptor-mediated apoptosis. *Mol. Cell. Biol.* **24**:7003-7014 (2004).
8. Wilkinson, J.C, Wilkinson, A.S., Scott, F.L., Csomos, R.A., Salvesen, G.S. and **Duckett, C.S.** Neutralization of Smac/DIABLO by IAPs: a caspase-independent mechanism for apoptotic inhibition. *J. Biol. Chem.* **279**:51082-51090 (2004).
9. Wilkinson, J.C, Richter, B.W.M., Wilkinson, A.S., Burstein, E., Rumble, J.M., Balliu, B. and **Duckett, C.S.** VIAF: a conserved inhibitor of apoptosis (IAP) interacting factor that modulates caspase activation. *J. Biol. Chem.* **279**:51091-51099 (2004).
10. Rudd, B.D., Burstein, E., **Duckett, C.S.**, Li, X and Lukacs, N.W. A differential role for TLR3 in RSV induced chemokine expression. *J. Virol.* **79**:3350-3357.

11. Kamradt M.C., Lu, M., Werner, M.E., Kwan, T., Chen, F., Strohecker, A., Oshita, S., Wilkinson, J.C., Yu, C., Oliver, P.G., **Duckett, C.S.**, Buchsbaum, D.J., Lobuglio, A.F., Jordan, V.C. and Cryns, V.L. The small heat shock protein α B-crystallin is a novel inhibitor of TRAIL-induced apoptosis that suppresses the activation of caspase-3. *J. Biol. Chem* **280**:11059-11066 (2005).
12. Burstein, E., Hoberg, J.E., Wilkinson, A.S., Rumble, J.M., Csomos, R.A., Komarck, C.M., Maine, G.N., Wilkinson, J.C., Mayo, M.W. and **Duckett, C.S.** COMMD proteins: a novel family of structural and functional homologs of MURR1. *J Biol. Chem* **280**:22222-22232 (2005).
13. **Duckett, C.S.** IAP proteins: Sticking it to Smac. *Biochem. J.* 385:e1-e2 (2005).
14. Kucharczak, J.F., Simmons, M.J., Duckett, C.S. and Gélinas, C. Constitutive proteasome-mediated turnover of Bfl-1/A1 and its processing in response to TNF receptor activation in FL5.12 Pro- B cells convert it into a pro-death factor. *Cell Death Diff.*, in press.
15. Wright, C.W. and **Duckett, C.S.** Re-awakening the cellular death program in neoplasia through the therapeutic blockade of IAP function. *J. Clin. Invest.*, in press.

**VICTOR M. ELNER, MD, PHD
PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Surgical pathology of eye-related specimens
- B. Eye plastic and reconstructive surgery

II. TEACHING ACTIVITIES:

- A. Graduate students: N/A
- B. Undergraduate students: N/A
- C. Ophthalmology residents and medical students: biweekly ophthalmic pathology histopathologic review; ad hoc grossing of eye specimens; didactic pathology reviews (open sessions available to all interested)

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Department of Health and Human Services, Public Health Service, National Institutes of Health, National Eye Institute. "RPE-Mo Binding: Ca⁺⁺ - & O₂-Dependent AMD Responses." Victor M. Elner, MD, PhD, Principal Investigator, \$2,474,840, Project Period: 12/1/03-11/30/2008. 20% effort
- B. Department of Health and Human Services, Public Health Service, National Institutes of Health, National Eye Institute. "Expression Profile Approach to Glaucoma Gene Detection." Julia Richards, MD, Principal Investigator, Victor M. Elner, MD, PhD, Co-Investigator, \$3,105,653 total, 4/1/01-3/31/06. 5% effort
- C. University of Michigan (Internal funding). Improving trabeculectomy outcomes with amnion membrane grafts. \$100,000, Project period 2005-2006. 5% effort

PENDING:

- A. Research to Prevent Blindness, Senior Scientific Investigator Award.
- B. Department of Health and Human Services, Public Health Service, National Institutes of Health,
- C. National Eye Institute. Multicenter study to map genes for Fuchs' endothelial corneal dystrophy.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

None

OPHTHALMOLOGY DEPARTMENTAL:

- A. Physician Reimbursement Committee
- B. Space Committee, Department of Ophthalmology

MEDICAL SCHOOL/HOSPITAL:

None

UNIVERSITY OF MICHIGAN:

None

REGIONAL AND NATIONAL:

- A. National Eye Institute: Board of Scientific Counselors Ad Hoc Member; SBIR Study Section Grant Reviewer
- B. Board of Directors - American Association of Ophthalmic Pathologists (Elected 2002)

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

None

HONORS AND AWARDS

Consumers' Research Council of America - Top Ophthalmologists

PATENTS:

Method and Apparatus to Evaluate Metabolism in the Eye, University of Michigan, Ann Arbor, MI (Pending)

INVITED LECTURES/SEMINARS:

Edward W. Purnell, Lecturer, Case Western Reserve, Cleveland, OH

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Elner VM, Hassan AS, Frueh BR. Graded full thickness anterior blepharotomy for upper eyelid retraction. 2004. Arch Ophthalmol 122:55-60.
2. Mauffray RO, Hassan A, Elner VM. Double silicone intubation as treatment for persistent congenital nasolacrimal duct obstruction. 2004. Ophthalmic Plas Reconstr Surg 20:44-9.
3. Bian ZM, Elner SG, Yoshida A, Elner VM. Differential involvement of phosphoinositide 3-kinase/Akt pathway in human RPE MCP-1 and interleukin-8 gene expression. 2004. Invest Ophthalmol Vis Sci 45:1887-96.
4. Yoshizawa M, Feinberg SE, Marcelo CL, Elner VM. Ex vivo produced human conjunctiva and oral mucosa equivalents grown in a serum-free culture system. 2004. J Oral Maxillofac Surg 62:980-8.
5. Kindzelskii AL, Elner VM, Elner SG, Yang D, Hughes BA, Petty HR. Toll-like receptor 4 (TLR4) of retinal pigment epithelial cells participates in transmembrane signaling in response to photoreceptor outer segments. 2004. J Gen Physiol 124:139-49.
6. Kindzelskii AL, Elner VM, Elner SG, Yang D, Hughes BA, Petty HR. Human, but not bovine, photoreceptor outer segments prime HRPE cells for metabolic activation and massive oxidant release in response to lipopolysaccharide and interferon- γ . 2004. Exp Eye Res 79:431-5.
7. Elner VM, Flint A, Vine A. Histopathology of documented growth in small melanocytic choroidal tumors. 2004. Arch Ophthalmol 122:1876-8.
8. Hassan AS, Elner VM. Tarsus-grafted conjunctival flap for upper eyelid reconstruction. 2004. Techniques in Ophthalmol 2:162-5.
9. Elner SG, Elner VM, Yoshida A, Dick RD, Brewer GJ. Effects of tetrathiomolybdate in a mouse model of retinal neovascularization. 2005. Invest Ophthalmol Vis Sci 46:299-303.
10. Zareparsari S, Buraczynska M, Branham KE, Shah S, Eng D, Li M, Pawar H, Yashar BM, Moroi SE, Lichter PR, Petty HR, Richards JE, Abecasis GR, Elner VM, Swaroop A. Toll-like receptor 4 variant D299G is associated with susceptibility to age-related macular degeneration. Hum Mol Genet 2005 April 13; (e-publication ahead of print)

BOOKS/CHAPTERS IN BOOKS:

- A. Holmes LR, Munzenrider JE, Elner VM, Bardenstein DS, Lichter AS. Eye, Orbit, and Adnexal Structures. In: Abeloff MD, Armitage JO, Niederhuber JE, Kavanagh MB, McKenna WG (Eds). *Clinical Oncology*. 3rd Edition. Churchill-Livingstone, New York. 2004. Chap 70 pp.1433-1497.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

None

**BARRY G. ENGLAND
ASSOCIATE PROFESSOR OF REPRODUCTIVE BIOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

A. Director, Ligand Assay Laboratory.

II. TEACHING ACTIVITIES:

- A. Instructor for Pathology House Offices Laboratory Rotation.
- B. Participant, Clinical Pathology Grand Rounds.
- C. Graduate Student Advisor for Ph.D. Student Pablo Nepomnaschy

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

OTHER SUPPORT:

ACTIVE

U01 AG12495-11 (McConnell) 12/01/03 - 11/30/08 10%
NIH \$1,062,366 (YR-11)

Study of Women's Health Across the Nation-Endocrine Lab

The major purpose of the Central Ligand Assay Satellite Services (CLASS) laboratory is to continue supporting the Study of Women's Health Across the Nation (SWAN) through state-of-the-science, automated assays for all major reproductive axis hormones, adrenal markers of aging, other endocrine markers, and new ovarian markers which have the potential to allow us to hormonally define the menopausal transition and the postmenopause with greater precision.

5P60 DK20572 (WHHerman) 12/01/02 - 11/30/07 5%
NIH \$1,229,020 Total \$6,071,430

Michigan Diabetes Research and Training Center – Core Facility Lab.

I serve as a Co-Director of the Core Facility Laboratory of the MDRTC. This laboratory is charged with providing a variety of laboratory procedures for the measurement of analytes of interest in the investigator of diabetes and related diseases. These procedures include standard chemistry analyses and immunoassay techniques.

SCIENTIFIC COLLABORATIONS:

1. University of Michigan; Reproductive Science Program: Daniel S. McConnell, Ph.D.: The major purpose of the Central Ligand Assay Satellite Services (CLASS) laboratory at the University of Michigan is to support the Multicenter National Study of Women's Health Across the Nation (SWAN) through state-of-the-science, automated assays for all major reproductive axis hormones, selected markers of aging, other endocrine markers, and new ovarian markers which have the potential to define more accurately the menopausal transition and the characterize the postmenopause with greater precision.
2. University of Missouri: Mark Flinn, Ph.D.: We have monitored several biochemical markers of growth, puberty, stress and immunological function in the salivary excretions of children in a small isolated Caribbean village for approximately 8 years. We have examined several markers in saliva samples obtained from children between the ages of 2 and 21. Samples and a detailed history of relevant physical and emotional events are collected daily over a 2 - 3 month period each year throughout the multiyear study. Salivary levels of adrenal and gonadal steroid hormones provide good estimates of the concentration of biologically active hormone in the peripheral circulation on a twice-daily basis throughout the collection interval. This study has lead to a variety of new insights into the interaction between emotional and environmental stress and normal growth and development in human subjects.
3. University of Michigan: Paul Gauger, M.D.: The intra-operative determination of circulating levels of parathormone (PTH) allows for the on-site monitoring of PTH levels as an indicator of removal of hypersecreting parathyroid glands. We have developed a cart-mounted analytical system that permits rapid determination (15 min.) of PTH in the O.R. This procedure ensures that all hypersecreting glands are removed before the patient is released from the O.R., thereby greatly reducing the number of repeat surgeries.
4. University of Mississippi: Hamed Benguzzi, Ph.D. Long-term drug delivery is of considerable research and clinical interest, particularly if the rate and length of delivery time can be accurately controlled. This collaborative effort has focused on the use of immunologically inert biomaterial similar to bone in composition (ceramics) that has proven capable of delivering a wide variety of steroids, protein hormones, therapeutic drugs, vitamins, autocrine and paracrine factors, etc. collectively referred to as *drug*s. These delivery devices have proven capable of constant release of biological compounds into the circulation for as many as 12 months. These studies are continuing permitting increasingly tighter control in the rate and length of drug delivery.

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

- A. Director, Central Ligand Assay Laboratory.

MEDICAL SCHOOL/HOSPITAL:

- A. Co-Director, Standards and Reagents Core Facility, Reproductive Sciences Program.
- B. Co-Director, Michigan Diabetes Research and Teaching Center Core Facility Laboratory.
- C. Associate Director, CLASS laboratory in the SWAN study, Reproductive Science Program.
- D. Associate Research Investigator of Reproductive Biology, Reproductive Science Program.

V. PUBLICATIONS:

ARTICLES PUBLISHED AND IN PRESS IN SCIENTIFIC LITERATURE:

1. Adah F. Benghuzzi H. Tucci M. Russell G. Tsao A. Olivier J. England B. (2005) Evaluation of the male reproductive organs after treatment with continuous sustained delivery of statin for fracture healing. *Biomedical Sciences Instrumentation*. 41:54-61.
2. Woodrum DT. Saunders BD. England BG. Burney RE. Doherty GM. Gauger PG. (2004) The influence of sample site on intraoperative PTH monitoring during parathyroidectomy. *Surgery*. 136(6):1169-75.
3. Flinn, M.V. & England, B.G. (2004). *Are there critical periods in ontogeny of stress response and immune function?* *American Journal of Physical Anthropology Suppl.* 38, 95-96.
4. Flinn, M.V. & England, B.G. (2004). *Critical periods in ontogeny of stress response and immune function.* *American Journal of Human Biology* 16, 203.
5. Gauger PG, Mullan MH, Thompson NW, Doherty GM, Matz K, England BG. (2004) *An alternative analysis of intraoperative parathyroid hormone data may improve the ability to detect multiglandular disease.* *Archives of Surgery*. 139(2):164-9.
6. Benghuzzi H. Tucci M. Tsao A. Russell G. England B. Ragab A. (2004) *Stimulation of osteogenesis by means of sustained delivery of various natural androgenic hormones.* *Biomedical Sciences Instrumentation*. 40:99-104, 2004.
7. Nepomnaschy PA. Welch K. McConnell D. Strassmann BI. England BG.(2004) Stress and female reproductive function: a study of daily variations in cortisol, gonadotrophins, and gonadal steroids in a rural Mayan population. *American Journal of Human Biology*. 16(5):523-32.
8. Gangestad, S. W., Thornhill, R., Flinn, M. V., Dane, L. K., Falcon, R. G., Garver-Apgar, C. E., Franklin, M., & England, B. G. (2005). Men's Testosterone and Life History in a Caribbean Rural Village. *Proceedings of the Annual Meeting of the Human Behavior and Evolution Society* 2005, 37.

ABSTRACTS AND PAPERS AT SCIENTIFIC MEETINGS:

1. Nepomnaschy PA, and England BG (2004) *Reproductive suppression: The critical process of implantation*. LIFE Academy, The University of Michigan, Ann Arbor, Michigan.
2. Nepomnaschy PA, and England BG (2004) *Reproductive suppression: The critical process of implantation*. 73rd Annual Meeting, American Association of Physical Anthropologists, Tampa, Florida USA.
3. Nepomnaschy PA, Welch K , McConnell D, Low B., Barry England BG (2005) *Stress and Female Reproduction: Daily Stressors, Cortisol Levels, the Menstrual Cycle, and Early Pregnancy* . Annual Meeting of the Association of Human Biology, Milwaukee, Wisconsin.
4. Nepomnaschy PA, Welch K , McConnell D, Low B., Barry England BG (2005) *Stress and Female Reproduction: Daily Stressors, Cortisol Levels, the Menstrual Cycle, and Early Pregnancy*. LIFE Academy, Max Planck Institute, Berlin, Germany.
5. Nepomnaschy PA, England B. (2004) *Stress and female reproductive: Daily variations in urinary cortisol and its association with ovarian function and early pregnancy*. University of Trier, School of Psychobiology, Trier, Germany.
6. Leone D.V., Hayden, R., Stewart, J., Quinlan, R.J., England, B.G. & Flinn, M.V. (2004). *Effects of prenatal and early postnatal environment on growth*. MU Life Sciences Week #96.

**JOSEPH C. FANTONE, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Autopsy Service.

II. TEACHING ACTIVITIES:

- A. Director; Resident Training Program.
- B. Course Director; Pathology Teaching Laboratories.
- C. Laboratory Instructor; M1 Histopathology Sequence.
- D. Laboratory Instructor; M2 Pathology Labs.
- E. Lecturer and small group leader; M1 Immunology Course.
- F. Facilitator, M1 & M2 Longitudinal Cases
- G. Medical Student Advisor (3rd and 4th year).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Co-Investigator, "University of Michigan Integrative Curriculum for Medicine and Allied Health." National Institutes of Health. R25-AT00812-01 (2001-2006).
- B. Co-investigator, "Comprehensive Programs to Strengthen Physicians' Training in Geriatrics." The Donald Reynold's Foundation. (2001-2005).

PROJECTS UNDER STUDY:

- A. Outcomes measures of undergraduate medical education.
- B. Curriculum development in medical student education

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director, Anatomic Pathology.
- B. Director, Pathology Educational Programs.
- C. Director, Resident Training Program.
- D. Chairman's Advisory Committee.
- E. Department ACAPT Committee.
- F. Research Space Advisory Committee.
- G. Faculty Sexual Harassment Contact Person.

MEDICAL SCHOOL/HOSPITAL:

- A. Associate Dean for Medical Education.
- B. CD/ACD Education Committee (Chair).
- C. Curriculum Policy Committee (Chair).
- D. Medical Student Basic Science Academic Review Board (Chair).
- E. Medical Student Clinical Academic Review Board (Chair).
- F. Medical School Academic Hearing Committee (Chair).
- G. Faculty Group Practice, Finance Committee.

REGIONAL AND NATIONAL:

- A. USMLE, Step 1 IRC Test Committee.
- B. Pathology Residency Review Committee. ACGME.

V. INVITED LECTURES, CONSULTATIONS, PRESENTATIONS:

1. Invited Speaker, The Future of Pathology Education. Association of Pathology Chairs and PRODS Meeting, Mt. Tremblant, Quebec, Canada, 2004.
2. Consultant, University of Vermont College of Medicine, LCME Review, 2005

**ERIC R. FEARON, MD, PHD
PROFESSOR OF INT MED, HUMAN GENET, & PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Not applicable
- B. Not applicable

II. TEACHING ACTIVITIES:

- A. Graduate students:
 - 1. Responsible during the current academic year for teaching activities for the following:
 - a. Micro/Immun/Path 554 (Cancer Biol) – October 7, 2004 (1.5 hr/lecture)
 - b. Pathology 582 – November 8, 10, 15, 17, 2004 (1 hr/seminar)
 - c. Human Genetics 803 – November 17, December 1, 8, 2004 (2 hr/seminar)
 - d. Human Genetics 542 – February 16, 18, 23, 2005 (1 hr/lecture)
 - e. Mentor for Ira Winer – MD-PhD student in CMB Prog (Thesis)
 - f. Mentor for Grant Rowe – MD-PhD student in CMB (6-week rotation)
- B. Undergraduate students:
 - 1. Mentor for 2 undergraduate students pursuing honors research (Huseyin Kadikoy and Deanna Sikorsky – both LSA Cell and Mol Biol students)

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

ACTIVE

- A. 5 P30 CA46592-16; PI – Wicha, 6/1/01-5/31/06, 20%: NIH/NCI, \$3,434,995 (Fearon - salary support only) "University of Michigan Comprehensive Cancer Center Core Grant"; Basic Science Director.
- B. 5 P30 CA46592-16; PI – Wicha, 6/1/01-5/31/06, 5%: NIH/NC, \$3,434,995 (Fearon - salary support only) "University of Michigan Comprehensive Cancer Center Core Grant"; Program Co-Leader.
- C. 1RO1 CA82223-06; PI- Fearon, 08/15/99-07/31/09, 25%: NIH/NCI, Year 6 direct costs - \$202,500, "CDX-2 Tumor Suppressor Pathway Defects in Colon Cancer"
- D. 1 RO1 CA85463-05; PI – Fearon, 06/01/00-05/31/06 (no cost extension), 25%: NIH/NCI, Year 5 direct costs - \$180,000, "The Role of β -catenin/Tcf Pathway Defects in Cancer"
- E. R01 CA94172-04; PI – Cho, 02/01/02 – 01/31/07, 5%: NIH/NCI Year 3 direct costs - \$178,000 (Fearon – co-invest; salary support only), "Molecular Pathogenesis of Ovarian Endometrioid Adenocarcinomas (OEA's)"

- F. OC030117; Wu (PI), 02/01/04 - 01/31/07, 2.5%: Dept. of Defense OCRP, \$100,000 annual direct costs (Fearon – salary support only), “Development and Characterization of a Murine Model of Endometrioid Adenocarcinoma Induced by Tissue Specific Expression of β -Catenin”
- G. 1RO1 CAS1488-07; PI – Gruber, 01/01/99-03/31/09, 5%: NIH/NCI, \$772,892 (Fearon - co-invest; salary support only), "Molecular Epidemiology of Colorectal Cancer".

PENDING:

- A. 2 RO1 CA085463-06A1; PI - Fearon 04/01/06-03/31/11 20%
- B. NIH/NCI Year 5 direct costs - \$180,000
- C. "The Role of β -catenin/Tcf Pathway Defects in Cancer"

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. None

MEDICAL SCHOOL/HOSPITAL:

- A. Admissions Committee, University of Michigan School of Medicine
- B. Chair, University of Michigan Biological Sciences Program Search Committee

UNIVERSITY OF MICHIGAN:

- A. None

REGIONAL AND NATIONAL:

- A. President, American Society for Clinical Investigation

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

- A. Cancer Research, Associate Editor
- B. Molecular Cancer Research, Senior Editor
- C. Current Biology
- D. Journal of Clinical Investigation
- E. Genes, Chromosomes & Cancer
- F. Neoplasia
- G. Molecular Medicine, Deputy Editor

INVITED LECTURES/SEMINARS:

1. Fox Chase Cancer Center Symposium on "Cancer Genetics 2005: Focus of Colon and Ovarian Cancers Bridging Science and Practics"; Philadelphia, PA; "Insights into Somatic Defects in Colorectal Cancer Pathogenesis and Significance of the Findings for Clinical Management"
2. Molecular Medicine Seminar Series, University of Connecticut Health Science Center, Farmington, CT; "Molecular Pathogenesis of Gastrointestinal Cancer"
3. GlaxoSmithKline, Research and Development, Collegeville, PA; "Molecular pathogenesis of colorectal cancer: insights and clinical significance."

VI. PUBLICATIONS:**ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:**

1. Lipkin SM, Rozek LS, Rennert G, Yang W, Chen PC, Hacia J, Hunt N, Shin B, Fodor S, Kokoris M, Greenson JK, **Fearon E**, Lynch H, Collins F, Gruber SB. The MLH1 K132H variant is associated with susceptibility to sporadic colorectal cancer. *Nat Genet* 2004, 36:694-9.
2. Li W, Lee J., Vikis HG, Lee SH, Liu G, Aurandt J, Shen TL, **Fearon ER**, Guan UL, Han M, Rao Y, Hong K, Guan KL. Activation of FAK and Src are receptor-proximal events required for netrin signaling. *Nat Neurosci* 2004 7:1213-21.
3. Li CM, Kim CE, Margolin AA, Guo M, Zhu J, Mason JM, Hensle TW, Murty VV, Grundy PE, **Fearon ER**, D'Agati V, Licht JD, Tycko B. CTNNB1 Mutations and Overexpression of Wnt/ β -Catenin Target Genes in WT1-Mutant Wilms' Tumors. *Am J Pathol* 2004 165:1943-53.
4. Bommer GT, Jager C, Durr EM, Baehs S, Eichhorst ST, Brabletz T, Hu G, Frohlich T, Arnold G, Kress DC, Goke B, **Fearon ER**, Kolligs FT. DRO1, a gene down-regulated by oncogenes, mediates growth inhibition in colon and pancreatic cancer cells. *J Biol Chem* 2005, 280:7962-75.
5. Shedden K, Chen W, Kuick R, Ghosh, D, Macdonald J, Cho KR, Giordano TJ, Gruber SB, **Fearon ER**, Taylor JMG, Hanash S. Comparison of seven methods for producing Affymetrix expression scores based on false discovery rates in disease profiling data. *BMC Bioinformatics* 2005, 6:26.
6. Jong In Yook JI, Li XY, Ota I, **Fearon ER**, Weiss SJ. Wnt-Dependent Regulation of the E-cadherin Repressor Snail by a GSK3 β / β -TrCP Axis. *J Biol Chem* 2005, 280:11740-8.
7. Shedden KA, Kshirsagar MP, Schwartz DR, Wu R, Yu H, Misek DE, Hanash S, Katabuchi H, Ellenson LH, **Fearon ER**, Cho KR. Histologic type, organ of origin, and Wnt pathway status: effect on gene expression in ovarian and uterine carcinomas. *Clin Cancer Res* 2005, 11:2123-31.
8. Hinoi T, Gesina G, Akyol A, Kuick R, Hanash S, **Fearon ER**. CDX2 regulates expression of ceruloplasmin-related protein hephaestin in intestinal and colonic epithelium. *Gastroenterology* 2005, 128:946-61.

NON-PEER REVIEWED PUBLICATIONS - REVIEW ARTICLES AND EDITORIALS

1. Mehlen P, **Fearon ER**. Role of the dependence receptor DCC in colorectal cancer pathogenesis. *J Clin Onc* 2004, 22:3420-3428.
2. **Fearon ER**, Cho KR. Cancer: cell survival guide (News & Views). *Nature* 2004, 431:35-6.
3. **Fearon ER**, Cadigan KM. Wnt signaling glows with RNAi (Perspective). *Science* 2005, 308:801-3.

BOOKS/CHAPTERS IN BOOKS:

1. Bommer GT, Fearon ER. Developmental Signaling Networks, Wnt/ β -catenin Signaling in the Gastrointestinal Tract. In: Physiology of the Gastrointestinal Tract. 4th Edition. Elsevier, 2005 in press.

**ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR,
MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:**

None

**DAVID O. FERGUSON, MD, PHD
ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Board-Certified in Clinical Pathology (2002).

II. TEACHING ACTIVITIES:

- A. Graduate students:
Lecturer (2 hours total): Pathology 581 (1 hour), Human Genetics 542 (1 hour)
Doctoral committees (5 students): Yunfang Man (PIBS-Pathology), Phillip Palmbo (MSTP), Sandra Durkin (PIBS-Genetics), Fred Derheimer (PIBS-CMB), Kyunghee Burkitt (Toxicology)
Student laboratory rotations (3 months): Bin Zhao (Pathology)
Qualifying exam committee - 9 hours total (3 per student): Sarah Monroe (Pathology), Rebecca Csomos (Pathology), Karolyn Oetjen (Pathology)
Pathology graduate student seminar "feedback teaching" (2 contact hours total).
- B. Undergraduate students:
Mentor for 1 undergraduate research thesis for entire academic year: Brian Theissen (Univ. of Mich. - junior year)
- C. CME teaching
Pathology department seminar (1 hour).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Ferguson (PI), "Roles of Mre11 in lymphocyte development and DNA repair" R01 HL079118-01 (50% after 8/31/05). \$250,000/year direct (\$1,000,000/4 years direct), 4/1/2005 - 3/31/2009.
- B. Ferguson (PI), "Roles of Mre11 in lymphocyte development and DNA repair" (training grant) K08 HL067580-05 (75% until 8/31/2005) \$125,000/year direct, \$607,500/5 years direct 9/1/00 - 8/31/05.
- C. Ferguson (PI) "Genomic Instability in Cancer: Mechanisms of Gene Amplification and Roles of Mre11" SKF-04-089 Sidney Kimmel Cancer Research Foundation (0% - Lab support only). \$90,870/year direct, \$181,740/2 years direct. 7/1/04 - 6/29/06.
- D. Ferguson (PI) "Roles of the MRN complex in endoreduplication and breast cancer" (0% - Lab support only). John and Suzanne Munn Endowed Research Fund of the University of Michigan Comprehensive Cancer Center. \$25,000/year direct - one year. 3/1/05 - 2/28/06.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Pathology graduate program student qualifying exam committee.
- B. Pathology student recruitment activities (lunch, dinners, poster sessions, meetings).

MEDICAL SCHOOL/HOSPITAL:

- A. Member, MSTP Career Advisory Panel
- B. Faculty candidate interviews and recruitment (Pathology, Medicine, Cancer Center).

V. OTHER RELEVANT ACTIVITIES:

Member, Michigan Comprehensive Cancer Center, Division of Cancer Genetics

EDITORIAL BOARDS:

AD HOC REVIEWER:

- A. Nature
- B. Genes and Development

HONORS AND AWARDS

- A. Scholars award - Sidney Kimmel Cancer Research Foundation.

INVITED LECTURES/SEMINARS:

- A. Department of Pathology weekly research seminar. October 26, 2004.
University of Michigan Department of Pathology..

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Zhong H, Bryson A, Eckersdorff M, **Ferguson DO**. Rad50 depletion impacts upon ATR dependent DNA damage responses. Human Molecular Genetics. 2005 14(18); 1-9
2. Kang J, **Ferguson D**, Song H, Bassing C, Eckersdorff M, Alt FW, Xu Y. Functional interaction of H2AX, NBS1, and p53 in ATM-dependent DNA damage responses and tumor suppression. Mol Cell Biol. 2005 25(2):661-70.
3. Mills KD, **Ferguson DO**, Essers J, Eckersdorff M, Kanaar R, Alt FW. Rad54 and DNA Ligase IV cooperate to maintain mammalian chromatid stability. Genes Dev. 2004 18(11):1283-92.

BOOKS/CHAPTERS IN BOOKS:

**ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR,
MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:**

1. meeting abstract - The MRN complex exerts selective control over ATR dependent DNA damage responses. Hui Zhong, Alyson Bryson, Jennifer Leddon, Mark Eckersdorff, and **David O. Ferguson**. FASEB conference on Genetic Recombination and Genomic Rearrangements. Snowmass Village, Colorado, USA. July 23 - 28, 2005.
2. meeting abstract - The MRN complex is required for the cellular response to UV radiation in mammalian cells. Hui Zhong, Mark Eckersdorff, Alyson Bryson and **David O. Ferguson**. American Society of Microbiology conference on Mechanisms of DNA Repair. Bermuda. November 13 - 20, 2004.

**WILLIAM G. FINN, M.D.
CLINICAL ASSOCIATE PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004- 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Associate Director, Division of Clinical Pathology
- B. Director, Hematopathology Section.
- C. Diagnostic Hematopathology (Bone marrow biopsies, lymph nodes, blood smears, body fluids).
- D. Clinical Flow Cytometry Laboratory.
- E. Clinical Molecular Diagnostics Laboratory.
- F. Hematopathology Consultation Cases (including M-Labs).

II. TEACHING ACTIVITIES:

- A. House Officers:
 - 1. Sign-out of bone marrow biopsies, aspirates, blood smears, and body fluids in Hematology Laboratory.
 - 2. Sign-out of lymph node biopsies and review of hematopathology consultation material.
 - 3. Flow Cytometry sign-out.
- B. Hematopathology teaching:
 - 1. Leukemia conference/biweekly.
 - 2. Lymphoma conference/weekly.
 - 3. Hematology conference/biweekly.
 - 4. Clinical Pathology Grand Rounds.
 - 5. Clinical Pathology Case Conference/weekly.
- C. Medical Students:
 - 1. M-2 Hematology Sequence: Section leader for laboratory sessions (12 hours).
 - 2. M-2 Hematology sequence: "Pathology and Classification of Lymphoma" (Lecture) – 1 hour.
- D. Dental and Graduate Students: Pathology 580/630: "Pathology of White Blood Cells" (Lecture) – 1 hour.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

Unsupervised immunophenotypic profiling of lymphoma. Optimization of laboratory hematology practice

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

- A. Member, Pathology Chair Search Committee.
- B. Member, Hospital Credentialing Committee.

DEPARTMENTAL:

- A. Associate Director of Clinical Pathology
- B. Director, Hematopathology Section.
- C. Departmental Advisory Committee on appointment, promotion, and tenure (ACAPT) (pathology) (Henry Appelman, M.D., Chair.)
- D. Departmental Residency Selection Committee (Joseph Fantone, M.D., Chair).
- E. Pathology Quality Assurance Committee (Jeffrey Warren, M.D., Chair).
- F. A. James French Society of Pathologists – Member Board of Directors – Secretary/Treasurer 2004-2005.

REGIONAL/NATIONAL:

- A. Assistant Editor-in-Chief, Laboratory Hematology (Journal of the International Society for Laboratory Hematology).
- B. Associate Editor, Cytometry Part B: Clinical Cytometry.
- C. Ad hoc Editorial Reviewer: Blood, Human Pathology, Archives of Pathology & Laboratory Medicine, Leukemia & Lymphoma.
- D. American Society for Clinical Pathology, Check Path Planning Committee (Hematopathology).
- E. College of American Pathologists, Hematology and Clinical Microscopy Resource Committee.
- F. Society for Hematopathology, ASCP Companion Program Committee.
- G. American Society for Clinical Pathology, Hematology Resource Council.
- H. International Society for Laboratory Hematology Program Committee.
- I. International Society for Laboratory Hematology Board of Directors.
- J. American Society for Clinical Pathology Annual Meeting Committee. Michigan Society of Pathologists Board of Trustees.

V. **OTHER RELEVANT ACTIVITIES:**

INVITED LECTURES/SEMINARS:

1. "Elevating Patient Care Through Hematology and Related Technologies." Abbott Laboratories Hematology Expert Council, Chicago, IL, September 9, 2004.
2. "Challenges in Hematopathology." Moderator of Society for Hematopathology companion session, American Society for Clinical Pathology annual meeting. San Antonio, TX, October 6, 2004.
3. "Challenges in Diagnosing MPD/MDS Overlap Syndromes." Breakfast with the Experts. International Society for Laboratory Hematology Annual Meeting. San Francisco, CA, May 13, 2005.
4. "Diagnosis and Pathobiology of Common and Uncommon Lymphomas." Lymphoma at Mackinac. Mackinac Island, MI, June 2005.

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Bakshi NA, Ross CW, Finn WG, Valdez R, Ruiz R, Schnitzer B: Primary bone anaplastic large cell lymphoma in the pediatric age group. Am J Clin Pathol, in press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Finn WG, Sreekumar A, Chinnaiyan A: Trisomy 12-associated, t(11;14)-negative mature B-cell leukemia with gene expression profile resembling mantle cell lymphoma. Leuk Lymphoma (provisionally accepted pending revision).
2. Bakshi N, Finn WG, Ross CW, Valdez R, Schnitzer B: Fascin expression in diffuse large B-cell lymphoma, anaplastic large cell lymphoma and classical Hodgkin lymphoma.
3. Habib LK, Finn WG: Unsupervised immunophenotypic profiling of chronic lymphocytic leukemia.

BOOKS AND CHAPTERS IN BOOKS:

1. Finn WG: Mature T-Cell Leukemias. In: *Foundations in Diagnostic Pathology: Hematopathology*. Hsi ED (ed.). Churchill-Livingstone, in press

**ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR,
MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:**

1. Grant MR, Schnitzer B, Valdez R, Finn WG: Malignant lymphomas of the retroperitoneum. Poster presentation, United States and Canadian Academy of Pathology Annual Meeting, San Antonio, TX, 2005. *Mod Pathol* 2005; 18(suppl 1):232A.
2. Habib LK, Finn WG: Unsupervised immunophenotypic profiling of chronic lymphocytic leukemia (CLL). Poster presentation, United States and Canadian Academy of Pathology Annual Meeting, San Antonio, TX, 2005. *Mod Pathol* 2005; 18(suppl 1):233A.
3. Rawal A, Schnitzer B, Finn WG, Valdez R: Site-specific morphologic variations in extranodal marginal zone b-cell lymphoma (EMZL). Poster presentation, United States and Canadian Academy of Pathology Annual Meeting, San Antonio, TX, 2005. *Mod Pathol* 2005; 18(suppl 1): 248A.
4. Smith LB, Valdez R, Finn WG, Thorson JA: A rapid and comprehensive real time PCR assay for the detection and characterization of BCL2/IGH translocations in follicular lymphomas. Platform presentation, United States and Canadian Academy of Pathology Annual Meeting, San Antonio, TX, 2005. *Mod Pathol* 2005; 18(suppl 1): 251A.
5. Finn WG: Classification of refractory anemia (letter). *Leukemia Res* 28(2):213, 2004.

**ANDREW FLINT, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Surgical Pathology Rotations, July (1/4), August (2/4)
September (1/4); October (2/4), November (3/4), December (1/4); January (2/4)February
(2/4), March (1¹/₄); April (1/4); May (3/4), June (2/4)
- B. Ophthalmic Pathology Service, 52 weeks/year

II. TEACHING ACTIVITIES:

- A. Pathology 600 Lectures:
 - 1. Obstructive Lung Disease – September 2004
 - 2. Pulmonary Neoplasms – September 2004
 - 3. Pathology of ARDS - September 2004
 - 4. Tissue Reactions to Infectious Agents - September 2004
 - 5. Cardiovascular Pathology Review for Medical Students, September, 2004
 - 6. Pulmonary Pathology Review for Medical Students - September, 2004
 - 7. Gastrointestinal Pathology Review for Medical Students, January, 2005
 - 8. Endocrine Pathology Review for Medical Students, March, 2005
 - 9. Reproductive Pathology Review for Medical Students, March, 2005
 - 10. Musculoskeletal Pathology Review for Medical Students, November, 2004
 - 11. Introduction to Musculoskeletal Pathology, November, 2004
 - 12. Medical Students Question and Answer sessions, October, 2004 - April, 2005
 - 13. USMLE Pathology Review, March and April, 2005
 - 14. Laboratory Instructor, August, 2004 - March, 2005
- B. Residency Training:
 - 1. Diseases of the Chest I - January, 2005
 - 2. Diseases of the Chest II - January, 2005
 - 3. Diseases of the Chest III - January, 2005
 - 4. Consultant's Conferences - April, 2005

C. Other educational activities:

1. M4 student elective mentor, July 2004 - May, 2005
2. Participant, Teaching with Technology Institute, May, 2005
3. Provost's Seminar on Teaching, "New Bridges to New Knowledge: Instructional Technology and Collaboration", the University of Michigan, May, 2005
4. Radiology - Pathology Correlation elective for M4 students, Course Co-Director, April, 2005
5. Course Director, M-4 Student Pathology Clerkships, 2004-2005
6. Seminars, Center for Research on Teaching and Learning, the University of Michigan, May, 2005

III. **RESEARCH ACTIVITIES:**

SPONSORED SUPPORT:

- A. A Murine Model of Graft-Vs-Host Disease Lacrimal Gland Inflammation and Destruction: Histopathology, Immunopathology, and Intervention (Midwest Eye-Banks and Transplantation Center), Victor M. Elnor, MD, PhD (Principal Investigator), Andrew Flint, MD (Co-Investigator)
- B. Lung Image Database Consortium (IU01 CA91099-01). Chuck Meyer, PhD (Principal Investigator)
- C. Consultant, Fibroproliferation in Bronchiolitis Obliterans Syndrome, Vibha Lama, MD, Principal Investigator. National Institutes of Health/NHLBI; K23HL077719-01

PROJECTS UNDER STUDY:

- A. Histologic predictors of obliterative bronchiolitis in lung transplant patients
- B. "M2 Pathology", web-based learning of pathology for medical students in the context of cultural and social issues
- C. Clinico-pathologic correlations of interstitial lung diseases
- D. Ophthalmic manifestations of the systemic vasculitides
- E. "Pathology and the Patient", web-based learning and teaching for medical students.

IV. **ADMINISTRATIVE ACTIVITIES:**

DEPARTMENTAL:

None

V. **OTHER RELEVANT ACTIVITIES:**

Reviewer, Journal of Neuro-Ophthalmology 2004

EDITORIAL BOARDS:

None

INVITED LECTURES/SEMINARS:

1. "Concept Maps - application to Medical Student teaching", Teaching with Technology Institute, the University of Michigan, May, 2005

VI. PUBLICATIONS:

SUBMITTED PUBLICATIONS:

1. Elnor VM, Flint A, Vine AK: Histopathology of documented growth in small melanocytic choroidal tumors. Arch Ophth 122(12):1876-8, 2004

VII. ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Fraley C, Martinez FJ, Lama V, Colby T, Travis W, Toews GB, Flint A, Chang A, Flaherty KR. Distance Walking During a Six Minute Walk Test (6MWT) Relative to the Quantity of Desaturation Predicts Mortality in Patients with Idiopathic Pulmonary Fibrosis (IPF). *Proceedings of the American Thoracic Society* 2005; 2:A316. None
2. Flaherty K, Wells A, duBois R, Nicholson A, Lynch D, Wadenstorer F, Vyskocil J, Bassily N, Louvar E, Wilt J, Quick J, Knapp R, Raghu G, King T, Colby T, Travis W, Flint A, Thannickal V, Andrei A, Murray S, Fraley C, Gay S, Toews GB, Martinez FJ. Diagnostic Agreement Between Academic and Community Pulmonologists for Cases of Idiopathic Interstitial Pneumonia (IIP). *Proceedings of the American Thoracic Society* 2005; 2:A122.
3. Flaherty KR, Wells AU, duBois R, Nicholson A, Lynch D, Wadenstorer F, Vyskocil J, Bassily N, Louvar E, Wilt J, Quick J, Knapp R, Raghu G, King TE, Colby TV, Travis WD, Flint A, Thannickal VJ, Andrei A, Murray S, Fraley C, Gay SE, Toews GB, Martinez FJ. Diagnostic agreement between academic and community pathologists for cases of idiopathic interstitial pneumonia. *Proceedings of the American Thoracic Society* 2005; 2:A387.
4. Fraley C, Martinez FJ, Lama V, Colby T, Travis W, Toews GB, Flint A, Chang A, Flaherty KR. Distance Walking During a Six Minute Walk Test (6MWT) Relative to the Quantity of Desaturation Predicts Mortality in Patients with Idiopathic Pulmonary Fibrosis (IPF). *Proceedings of the American Thoracic Society* 2005; 2:A316.
5. Flaherty K, Wells A, duBois R, Nicholson, Brown K, Lynch D, Wadenstorer F, Vyskocil J, Bassily N, Louvar E, Wilt J, Quick J, Knapp R, Raghu G, King T, Colby T, Travis W, Flint A, Thannickal V, Andrei A, Murray S, Fraley C, Gay S, Toews GB, Martinez FJ. Diagnostic Agreement Between Academic and Community Radiologists for Cases of Idiopathic Interstitial Pneumonia. *Proceedings of the American Thoracic Society* 2005; 2:A122.

**BRUCE A. FRIEDMAN, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004- 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Director, Pathology Data Systems

II. TEACHING ACTIVITIES:

- A. House Officers:
1. Two week, 10-hour, lecture series for house officers in Pathology Informatics;
June, 2005

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. LIS architecture with special emphasis on the Virtual LIS (V-LIS)
B. XML standards for image exchange in pathology
C. "Middleware" software developed by in-vitro diagnostic companies

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

- A. Member, IRB-MED

DEPARTMENTAL:

- A. Clinical Pathology Director's Committee

REGIONAL/NATIONAL:

- A. Executive Council, Association for Pathology Informatics
B. Co-Chairman, Laboratory Digital Imaging Project, Association for Pathology Informatics

V. OTHER RELEVANT ACTIVITIES:

- A. Created a 501(c)(3) non-profit company, Pathology Education Consortium (PEC); PEC sponsors a yearly pathology informatics in Las Vegas called the Lab InfoTech Summit; this meeting last March attracted 28 exhibitors and 175 paid registrants.

INVITED LECTURES/SEMINARS:

- A. *Transforming the Classic LIS to a Web-Enabled Virtual LIS.* A lecture presented as part of a workshop at the annual meeting of the CAP, Phoenix, Arizona, September 19, 2004.
- B. *Current Status of Pathology Informatics in the United States.* A lecture presented at the 38th Brazilian Congress on Clinical Pathology and Laboratory Medicine, Florianopolis, Brazil, September 24, 2004
- C. *New Clinical Lab Products and Services Enabled by the Web.* A lecture presented at the first annual Lab InfoTech Summit, Las Vegas Nevada, March 10, 2004

**DOUGLAS R. FULLEN, M.D.
CLINICAL ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Dermatopathology Service – 12 months
- B. Dermatopathology Consultation Service – 12 months
- C. Immunofluorescence evaluation of skin biopsies

II. TEACHING ACTIVITIES:

- A. Medical Students:
 - 1. Dermatopathology laboratory instructor, MS II Dermatology Sequence
 - 1. Dermatopathology, Pathology Clerkship, MS IV
 - 2. Dermatopathology, Dermatology Clerkship, MS IV
- B. House Officers:
 - 1. Dermatopathology sign-out (dermatology and pathology sign-out)
 - 2. Review of dermatopathology consultation material
 - 3. Dermatopathology teaching conference (pathology residents – weekly)
 - 4. Dermatopathology teaching conference (dermatology residents – weekly)
 - 5. Anatomic Pathology Grand Rounds (two lectures)
 - 6. Review of immunofluorescence on skin biopsies (interesting cases)
- C. Diagnostic Conference, Department of Dermatology (weekly)

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. BRAF mutations and microsatellite instability in Spitz nevi, atypical Spitz tumors and Spitz-like melanoma (S. Gruber, M.D., J. Poynter, T. Johnson, M.D., J. Elder, M.D.)
- B. University of Michigan (UMMC 2000-0713): Molecular, biochemical and cellular basis of melanoma and other melanocytic lesions: Tissue Bank (T. Johnson, M.D., T. Wang, M.D., J. Schwartz, M.D., J. Voorhees, M.D., A. Dlugosz, M.D., L. Lowe, M.D., L. Su, M.D., C. Bradford, M.D., V. Cimmino, M.D.)
- C. Patient examination with Mela Find™ System developed by Electro-Optical Sciences, Inc., (EOS), 2001 (J. Schwartz, M.D., T. Johnson, M.D., T. Wang, M.D., D. Karimipour, M.D., J. Orringer, M.D., L. Lowe, M.D., L. Su, M.D., C. Bichakjian, M.D., M. Rabe, R.N.)
- D. Clusterin expression in CD30-positive lymphoproliferative processes of the skin (B. Schnitzer, M.D.)
- E. Telomerase expression in sebaceous lesions of the skin (L. Su, M.D.)
- F. CD13 and CD14 staining in fibrohistiocytic lesions (D. Lucas, M.D.)

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

Director of Histology Laboratory, Department of Pathology

REGIONAL AND NATIONAL:

1. Ad hoc manuscript reviewer, Journal of Cutaneous Pathology
2. Ad hoc manuscript reviewer, Journal of the American Academy of Dermatology
3. Ad hoc reviewer, Cancer
4. Ad hoc reviewer, Archives of Pathology and Laboratory Medicine

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. McHugh J, Fullen DR: "Atypical compound nevus arising in mature ovarian teratoma." Accepted for oral presentation at the American Society of Dermatopathology 41st annual meeting, October, 2004.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Bogner PN, Su LD, Fullen DR: Cluster Designation 5 (CD5) staining of normal and non-lymphoid neoplastic skin. J Cutan Pathol 32: 50-54, 2005.
2. Fullen DR, Zhu W, Thomas D, Su LD: HTERT expression in melanocytic lesions: an immunohistochemical study on paraffin-embedded tissues. J Cutan Pathol (accepted for publication).

BOOKS/CHAPTERS IN BOOKS:

1. Fullen DR: Cysts and Sinuses. In: Busam KJ, Goldblum JR (eds): Foundations in Diagnostic Pathology series (Dermatopathology) (Philadelphia, PA: Elsevier, Inc.) (in press).

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Zhu W, Su LD, Thomas D, Fullen DR: "HTERT expression in melanocytic lesions: an immunohistochemical study on paraffin-embedded tissues." Accepted for poster presentation at the American Society of Dermatopathology 41st annual meeting, October, 2004.
2. Fullen DR, Lowe L: "Epidermotropic mucinous adenocarcinoma arising at mucocutaneous stomal anastomosis site." Accepted for poster presentation at the American Society of Dermatopathology 41st annual meeting, October, 2004.

**DONALD A. GIACHERIO, Ph.D.
CLINICAL ASSOCIATE PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Director, Chemistry Laboratory
- B. Direct the operation of blood gas/electrolyte analyzers, coagulation testing meters, and hematology analyzers in the Emergency Department and the operating rooms of Main, Mott, and, Kellog Hospitals.
- C. Direct the workgroup overseeing the quality assurance programs for bedside blood glucose testing in the Medical Center.
- D. Planning group for the approval and establishment of alternate site testing programs.
- E. Technical Director for laboratories at U-M Health Center off-site clinics.
- F. Sign out of Quad Marker Prenatal Screen results from maternal serum testing
- G. Sign out and interpretation of lipoprotein electrophoresis results.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

- A. Pathology House Officers:
 - 1. Clinical Pathology Grand Rounds (3 lectures)
 - 2. Coordinator, Pathology House Officer rotation through Chemistry Lab
 - 3. Review sign-out and interpretation of electrophoresis results.
 - 4. Review of selected topics in Clinical Chemistry with Block B residents.
- B. Medical Technologists – 2 continuing education lectures

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- 1. 5P60 DK20572 (WH Herman, PI), 12/01/02 - 11/30/07, Lab. Director 5% Effort, NIH/NIDDK, \$1,229,020 :Total, \$6,071,430, Michigan Diabetes Research and Training Center – Core Facility Lab: This grant established a center within the University of Michigan Health System to promote and facilitate multidisciplinary research on diabetes and its related endocrine disorders. The Chemistry Core Lab in the MDRTC performs a variety of Chemistry tests and immunoassays at low cost to support diabetes related research studies.

PROJECTS UNDER STUDY

- A. Evaluation of EIA assays for extractable nuclear antigens.
- B. Automation of EIA assays for anti-CCP and anti beta-2-glycoprotein I
- C. Evaluation and implementation of testing for CA 19-9
- D. Implementation of chemistry / immunoassay automation system.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Incentive Committee
- B. Quality Assurance Committee
- C. Laboratory Reorganization / Automation Work Group
- D. Director, Chemistry Laboratory
- E. Director, Point of Care Testing

REGIONAL AND NATIONAL:

- A. Chair, Michigan Section AACC.
- B. Ad hoc reviewer, Clinical Chemistry.
- C. Ad hoc reviewer, Archives of Pathology and Laboratory Medicine
- D. Abstract review committee, AACC National Meeting 2005

V. OTHER RELEVANT ACTIVITIES:

- A. Consultant to Consultants in Laboratory Medicine, Toledo, OH
- B. Member Clinical Laboratory Advisory Council for Ortho-Clinical Diagnostics
- C. Member Clinical Laboratory Advisory Committee for Instrumentation Laboratories, Inc

INVITED LECTURES/SEMINARS:

1. "Urine Microalbumin Testing and Diabetic Nephropathy". Consultants in Laboratory Medicine and Promedica Health System, Toledo, OH. September 9, 2004.
2. "PSA Testing and Prostate Cancer." Michigan Allied Health Technologists Annual Meeting, Frankenmuth, MI. October 21, 2004.
3. "Intra-operative PTH testing: Current Issues and Options." Michigan Society for Clinical Laboratory Scientists Annual Meeting, April 21, 2005.

PUBLICATIONS:

ARTICLES PUBLISHED IN REFEREED JOURNALS:

1. Zhou L, Giacherio D, Cooling L, and Davenport RD: Use of B-natriuretic peptide (BNP) as a diagnostic marker in the differential diagnosis of transfusion-associated circulatory overload. *Transfusion* 2005; 45:1056-1063.
2. Wang x, Yu J, Sreekumar A, Varambally S, Shen R, Giacherio D, Mehra R, Montie JE, Pienta KJ, Sana MG, Kantoff PW, Rubin MA, Wei JT, Ghosh D, Chinnaiyan AM: Autoantibody signatures in prostate cancer. *NEJM* 2005 (in press)

ABSTRACTS, BOOK REVIEWS, LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Zhou L, Giacherio D, Cooling L, Davenport, RD: BNP as a potential diagnostic marker in the differential diagnosis of transfusion-induced circulatory fluid overload. *Transfusion* 2004; 44 S: 17A
2. Moyad M, Giacherio D, and Montie J: African-American men, high cholesterol, hsCRP, and alternative medicine use documented at a prostate cancer screening: A unique opportunity for a complete men's health intervention. *Journal of Clinical Oncology* 23:408s, 2005. Presented at American Society for Clinical Oncology annual meeting.

**PAUL W. GIKAS, M.D.
EMERITUS PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

- A. Histopathology Lab Section for M1 medical students – 14 hours.
- B. Urinary Sequence Lab for M2 medical students – 6 hours.

III. RESEARCH ACTIVITIES:

None.

PROJECTS UNDER STUDY:

None.

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

MEDICAL SCHOOL/HOSPITAL:

None.

REGIONAL AND NATIONAL:

None.

V. OTHER RELEVANT ACTIVITIES:

None.

**THOMAS J. GIORDANO, M.D., Ph.D.
ASSOCIATE PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. General, Breast and GYN Surgical Pathology - three months.
- B. Endocrine Surgical Pathology, Departmental and Outside Consultation - 12 months.
- C. Image Analysis Service for Breast Carcinoma - 12 months.
- D. M-Labs Surgical Pathology Consultation - 12 months.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

- A. Medical Students:
 - A. Sequence Co-Coordinator – Component II Endocrine Sequence.
 - 2. Component II Endocrine Sequence - 2 lectures on Endocrine Pathology.
 - 3. Endocrine Pathology Laboratories - preparation of course materials.
 - 4. Component IV Pathology Elective mentor – one month.
- B. House Officers:
 - B. General Surgical Pathology - 3 months.
 - C. Endocrine Surgical Pathology - 12 months as needed.
 - D. Consultation Conferences.
 - E. Molecular Pathology lectures.
 - F. Endocrine Pathology lectures.
- C. Interdepartmental:
 - 1. Endocrine Conference, Department of Surgery - monthly.
 - 2. Adrenal Cancer Conference - monthly.
 - 3. Lecture to Genetic Counseling Students, "Pathology of Cancer"
 - 4. Lecture to Molecular Biology Graduate Students, "Pathology of Cancer"

EXTERNAL:

- A. United States and Canadian Academy of Pathology, 94th Annual Meeting, 2005 Special Course, Introductory Molecular Pathology, "Introduction to Proteomics", San Antonio, TX

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Core Director, The University of Michigan Comprehensive Cancer Center, Histology/Immunohistochemistry Service, 9-02 to present, 10% effort
- B. Pathology Core Leader, "Proteomics Alliance for Cancer", Michigan Life Sciences Corridor, with G. Omenn (PI), 5% effort (\$2,605,490 direct cost/3 years)
- C. Principal Investigator, "Gene Expression Profiling Studies of Papillary Thyroid Carcinoma", The University of Michigan Comprehensive Cancer Center, Thyroid Cancer Program, 8/1/02 to 7/31/04 (\$50,000 direct costs).
- D. Co-Investigator, "Great-Lakes-New England Clinical and Epidemiology Center", NCI CA-99-007, 4/1/00 to 03/31/05 (\$4,987,159 total direct costs), with Dr. Dean Brenner, Department of Internal Medicine, 5% effort
- E. Co-Principal Investigator, "Proteomics Biomarker Development Laboratory", NCI U01-CA84982, 9/99 to 8/04 (\$304,900/yr direct costs for five years), with S. Hanash, Department of Pediatrics, 10% effort
- F. Director, "Tissue Procurement Collaboration", Genentech, Inc., 5/99 to 5/2005 (\$700,000 direct costs), 10% effort
- G. Core Director, The University of Michigan Comprehensive Cancer Center, Tissue Procurement Service, 7-98 to present, 10% effort
- H. Core Director, The University of Michigan Comprehensive Cancer Center, Laser Capture Microdissection Core, 1-99 to present
- I. Principal Investigator, "Pfizer Tissue Bank", Pfizer Inc., 1/1/04 to 12/31/06, (\$348,000/yr), 5% effort

PROJECTS UNDER STUDY:

- A. Principal Investigator, "Molecular Studies of Adrenal Cortical Neoplasms."
- B. Principal Investigator, "Molecular Studies of Thyroid Neoplasms."
- C. Principal Investigator, "Moleuclar Studies of Adrenomedullary Neoplasms."
- D. Co-Investigator with Dr. Jim Baker, "Molecular Studies of Thyroiditis."
- E. Co-Investigator with Dr. David Beer, "Molecular Studies of Lung and Esophageal Neoplasms"
- F. Co-Investigator with Drs. Steve Gruber, Eric Fearon, and Joel Greenson "Molecular Studies of Colorectal Carcinoma"
- G. Co-Investigator with Drs. Larry Baker and Dafydd Baker, "Molecular Studies of Soft Tissue Sarcomas."
- H. Co-Investigator with Drs. Frank Worden and Ron Keonig, "Clinical Trial of Gleevec for Anaplastic Thyroid Carcinoma"

IV. **ADMINISTRATIVE ACTIVITIES:**

DEPARTMENTAL and INSTITUTIONAL:

- A. House Officer Candidate Interviews
- B. Faculty Candidate Interviews
- C. Sequence Co-Coordinator – Component II Endocrine Sequence
- D. Director, Tissue Procurement Service
- E. Director, Frozen Tumor Bank
- F. Director, Laser Capture Microdissection Core
- G. Medical Institutional Review Board (IRB-Med), *ad hoc* member.
- H. MSTP Career Advisory Panel
- I. Director, Histology/Immunoperoxidase Service
- J. Department of Pathology Chairman Search Committee
- K. Department of Pathology, Director of Clinical Informatics Search Committee

NATIONAL:

- A. Editorial Board, *Endocrine Pathology*
- B. Grant Reviewer, National Institutes of Health, S-10 Shared Instrumentation Grants, Microscopes Subcommittee

V. **OTHER RELEVANT ACTIVITIES:**

- A. Program Committee, “Frontiers in Thyroid Cancer 2005: Clinical Care and Research for the Future”, held in Baltimore, Maryland
- B. External Advisory Board, Lung SPORE, Memorial Sloan Kettering Cancer Center

INVITED LECTURES/SEMINAR:

- A. Invited Speaker, “Expression Arrays in Thyroid Disease: Expression Arrays in the Analysis of Metabolism Abnormalities”, American Thyroid Association, Vancouver, Canada
- B. Invited Speaker, “Debates in endocrine pathology. Gene and protein arrays: an alternative to morphology for adrenal cortical lesions. The pro perspective”, XXV Congress of the International Academy of Pathology, Brisbane, Australia
- C. Invited Speaker, “Molecular profiling of thyroid carcinoma”, Kolling Institute of Medical Research, Royal North Shore Hospital, St. Leonards, Australia
- D. Invited Speaker, Pathology Grand Rounds, “Molecular profiling of thyroid tumors”, Department of Pathology, University of Minnesota, Minneapolis, Minnesota
- E. Invited Speaker, Pathology Grand Rounds, “Molecular profiling of thyroid tumors”, Department of Pathology, New York University School of Medicine, New York
- F. Invited Speaker, Pathology Seminar, “Molecular profiling studies of thyroid tumors”, Department of Pathology, Case Western Reserve School of Medicine, Cleveland, Ohio

- G. Invited Speaker, Frontiers in Thyroid Cancer 2005: Clinical Care and Research for the Future, Pathogenesis of Papillary Thyroid Cancer session, "Expression profiling of thyroid cancer", Baltimore, Maryland
- H. Invited Speaker, Texas Medical Center Endocrine Grand Rounds, "Molecular profiling studies of thyroid tumors", Baylor Medical College, Houston, TX
- I. Invited Speaker, Endocrine Research Seminar, "Expression profiling of thyroid cancer", University of Texas MD Anderson Cancer Center, Houston, TX

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Lin J, Lin L, Thomas DG, Greenson JK, **Giordano TJ**, Robinson GS, Barve RA, Wesihaa FA, Taylor JMG, Orringer MB, Beer DG. Melanoma-associated antigens in esophageal adenocarcinoma: identification of novel MAGE-A10 splice variants. Clin Cancer Res 2004;10:5708-5716.
2. Eisenhofer G, Bornstein SR, Brouwers FM, Cheung N-KV, Dahia PL, de Krijger RR, **Giordano TJ**, Greene LA, Goldstein DS, Lehnert H, Manger WM, Maris JM, Neumann HPH, Pacak K, Shulkin BL, Smith DI, Tishcler AS, Young WF. Malignant pheochromocytoma: current status and initiatives for future progress. Endocrine-Related Cancer 2004;11:1-14.
3. Richards ML, Gauger P, Thompson NW, **Giordano TJ**. Regression of type II carcinoids in multiple endocrine neoplasia type 1 patients with Zollinger-Ellison syndrome after surgical excision of all gastrinomas. World J Surg 2004;28:652-658.
4. Chen X, Wang S, Wu N, Sood S, Wang P, Jin Z, Beer DG, **Giordano TJ**, Lin Y, Shih WJ, Lubet RA, Yang CS. Overexpression of 5-lipoxygenase in rat and human esophageal adenocarcinoma and inhibitory effects of zileuton and celecoxib on carcinogenesis. Clin Cancer Res 2004;10:6703-6709.
5. Binkely CE, Zhang L, Greenson JK, **Giordano TJ**, Kuick R, Misek D, Hanash S, Logsdon CD, Simeone DM. The molecular basis of pancreatic fibrosis: common stromal gene expression in chronic pancreatitis and pancreatic adenocarcinoma. Pancreas 2004;29:254-263.
6. Lahn M, Su Chen, Li S, Chedid M, Hanna K, Graff JR, Sandusly GE, Ma D, Niyikiza C, Sundell KL, John WJ, **Giordano TJ**, Beer DG, Paterson BL, Su W, Bumol TF. Expression levels of protein kinase C-alpha in non-small cell lung carcinoma. Clin Lung Cancer 2004;6:184-189.
7. Thomas DG, **Giordano TJ**, Sanders D, Biermann S, Sondak VK, Tretn JC, Yu D, Pollock RE, Baker L. Expression of receptor tyrosine kinases epidermal growth factor receptor and HER-2/neu in synovial sarcoma. Cancer 2005;103:830-838.
8. Dobbin KK, Beer DG, Meyerson M, Yeatman TJ, Gerald WL, Jacobson JW, Conley B, Buetow KH, Heiskanen M, Simon RM, Minna JD, Girard L, Misek DE, Kuick R, Taylor JMG, Hanash S, Naoki K, Hayes DN, Ladd-Acosta C, Enkemann SA, Viale A, **Giordano TJ**. Inter-laboratory comparability study of cancer gene expression analysis using oligonucleotide microarrays. Clin Cancer Res 2005;11:565-572.

9. Shedden, K, Chen W, Kuick R, Ghosh D, Macdonald J, Cho KR, **Giordano TJ**, Gruber SB, Fearon ER, Taylor JMG, Hanash SM. Comparison of seven methods for producing Affymetrix expression scores based on false discovery rates in disease profiling data. BMC Bioinformatics 2005;6:26.
10. Creighton CJ, Bromberg-White JL, Misek DE, Monsma D, Brichory F, Kuick R, **Giordano TJ**, Gao W, Omenn GS, Webb CP, Hanash SM. Analysis of tumor-host interactions by gene expression profiling of lung adenocarcinoma xenografts identifies genes involved in tumor formation. Mol Cancer Res 2005;3;119-129.
11. Hinoi T, Gesina G, Akyol A, Kuick R, Hanash S, **Giordano TJ**, Gruber SB, Fearon ER. CDX2-regulated expression of iron transport protein hephaestin in intestinal and colonic epithelium. Gastroenterology 2005;128;946-961.
12. **Giordano TJ**, Kuick R, Thomas DG, Misek DE, Vinco M, Sanders D, Zhu Z, Ciampi R, Roh M, Shedden K, Gauger P, Doherty G, Thompson NW, Hanash S, Koenig RJ, Nikiforov YE. Molecular classification of papillary thyroid carcinoma: distinct *BRAF*, *RAS*, and *RET/PTC* mutation-specific gene expression profiles discovered by DNA microarray analysis. Oncogene 2005 (online).
13. Rozek LS, Lipkin SM, Fearon ER, Hanash S, **Giordano TJ**, Greenson JK, Kuick R, Misek DE, Taylor JMG, Douglas JA, Rennert G, Gruber SB. CDX2 polymorphisms, RNA expression, and risk of colorectal cancer. Cancer Res 2005;65;5488-92.
14. Stasik CN, **Giordano TJ**, Gauger PG. Ganglioneuroma presenting as an incidental adrenal mass in an adult with turner's syndrome. Endocrine Practice.
15. Schteingart DE, Doherty GM, Gauger PG, **Giordano TJ**, Hammer MT, Worden F. Management of patients with adrenal cancer: recommendations of an international consensus conference. Cancer
16. Hughes PM, Thomas DG, **Giordano TJ**, McDonagh, Baker LH. Essential *erbB* family phosphorylation in osteosarcoma as a target for CI 1033 Inhibition. Pediatric Blood and Cancer.
17. Connett JM, Badri L, **Giordano TJ**, Connett WC, Doherty GM. Interferon regulatory factor 1 (IRF-1) and interferon regulatory factor 2 (IRF-2) expression in breast cancer tissue microarrays. J Interferon Cytokine Res.
18. Adeniran AJ, Zhu Z, Gandhi M, Steward DL, Fidler JP, **Giordano TJ**, Biddinger PW, Nikiforov YE. Correlation between genetic alterations and microscopic features, clinical manifestations, and prognostic characteristics of thyroid papillary carcinoma. Am J Surg Path.

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Lin L, Wang Z, Albertson DG, van Dekken H, Thomas DG, **Giordano TJ**, Moran JV, Glover TW, Prescott MS, Orringer MB, Gruber SB, Beer DG. Sequential genomic instability and L1 5' induction of cellular transcripts in a 2 Mb 3q26.3-q27 segment during the development of Barrett's adenocarcinoma.
2. Cho R, Lobo N, **Giordano TJ**, Clarke MF. Identification and isolation of tumorigenic breast cancer cells in MMTV-Wnt1 transgenic mice.
3. Chen G, Wang X, Yu J, Varambally S, Yu J, Thomas DG, Wang Z, Fielhauer J, Ghosh D, **Giordano TJ**, Chang AC, Orringer MB, Beer DG, Chinnaiyan AM. Diagnosis and prognosis of lung adenocarcinoma based on autoantibody signatures.

**ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR,
MISCELLANEOUS PUBLICATIONS IN UNREFERRED JOURNALS:**

1. **Giordano TJ** (contributing author to thyroid and adrenal chapters). World Health Organization Classification of Tumors: Pathology and Genetics of Tumours of Endocrine Organs. IARC Press, Lyon, France, 2004.
2. **Giordano TJ**. Morphologic and molecular classification of human cancer. In: Cancer Epidemiology & Prevention (3rd edition), In press.
3. Nosowsky R, **Giordano TJ**. The Health Insurance Portability and Accountability Act of 1996 (HIPAA) Privacy Rule: Implications for Clinical Research. Annu Rev Med 2006.
4. Thomas D, Lizyness M, Kuick R, Sanders D, Misek D, Hanash S, Nikiforov Y, Koenig and **Giordano TJ**. Gene expression signature of oncocytic (Hurthle cell) thyroid carcinoma. Thyroid 2004;14;713.
5. Thomas D, Lizyness M, Sanders D, Koenig R, Misek D, MacDonald J, Kuick R, Nikiforov, Y, and **Giordano TJ**. Gene expression signature of PAX8-PPAR-g positive follicular thyroid carcinoma. Thyroid 2004;14;728.
6. **Giordano TJ**, Debates in endocrine pathology. Gene and protein arrays: an alternative to morphology for adrenal cortical lesions. Pathology International 2004;54(Suppl. 1);S111.
7. Bakshi N, Kunju LP, **Giordano TJ**, Shah RB. Expression of renal cell carcinoma antigen (RCC) in renal epithelial and non-renal tumors: diagnostic implications. Mod Pathol 2005;18:128A.
8. Thomas DG, **Giordano TJ**, Zalupski MM, Biermann S, Chugh R, Baker LH. P450 3A and MDR1 as mediators of chemotherapy resistance in patients with soft tissue sarcomas. Presented at 96th Annual Meeting of the AACR.
9. Chen G, Wang X, Yu J, Varambally S, Thomas DG, **Giordano TJ**, Chang AC, Chinnaiyan AM, Beer DG. Humoral immune response profiles associated with diagnosis and prognosis in lung adenocarcinomas. Presented at 96th Annual Meeting of the AACR.
10. Hughes DPM, Thomas DG, Lee KE, **Giordano TJ**, Baker LH. Nuclear and cell-surface expression of Her-4 is associated with constitutive phosphorylation in osteosarcoma. Presented at 96th Annual Meeting of the AACR.
11. Dobbin KK, Beer DG, Meyerson M, Yeatman TJ, Gerald WL, Jacobson JW, Conley B, Buetow KH, Heiskanen M, Simon RM, Minna JD, Girard L, Misek DE, Taylor JMG, Hanash S, Naoki K, Hayes DN, Ladd-Acosta C, Enkemann SA, Viale A, **Giordano TJ**. Inter-laboratory comparability study of cancer gene expression analysis using oligonucleotide microarrays. Presented at 96th Annual Meeting of the AACR.
12. Lin L, Miller CT, Caper AM, Lim J, Thomas DG, Orringer MB, Chang AC, Giordano TJ, Glover TW, Beer DG. Mapping of genomic amplification boundaries of the MET oncogene withing fragile site FRA7G and up-regulation of MET signaling pathways in esophageal adenocarcinoma. Presented at 96th Annual Meeting of the AACR.

**JOEL K. GREENSON, M.D.
ASSOCIATE PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Gastrointestinal and hepatic pathology – 17 weeks
- B. General surgical pathology – 3 weeks.
- C. Gastrointestinal and hepatic pathology consultation services - four months.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

- A. Medical Students:
 - 1. GI Pathology Sequence, assisted Dr. Appelman (ten contact hours).
 - 2. GI Pathology Sequence, 2 hours full class lecture, 2 hours of lab instruction
- B. Dental Students:
 - 1. Pathology 630-631 one full class lecture (one contact hour).
- C. House Officers:
 - 1. Surgical pathology diagnosing room instruction for house officers - four months.
 - 2. Two didactic lectures on gastrointestinal pathology - April, 2005.
 - 3. Gastrointestinal and hepatic pathology tutoring - four months.
 - 4. Four consultation conferences.
- D. Interdepartmental:
 - 1. Liver biopsy conference - one hour every 3 months.
 - 2. Multidisciplinary GI tumor board - 1hour every third week.
 - 3. GI pathology teaching sessions with GI fellows/residents - one hour/month.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Co-Investigator R01CA81488-01 (\$4,547,772) “Molecular Epidemiology of Colorectal Cancer”, 5% Salary Support, Stephen Gruber, M.D., Ph.D. Principal Investigator.
- B. Co-Investigator N01-DK-9-2323 (\$1,433,559) “Hepatitis C Clinical Trial”, 7% Salary Support, Anna Lok, M.D. Principal Investigator.
- C. Co-investigator with Hari Conjeevaram M.D., “Study of viral resistance to antiviral therapy of chronic hepatitis c (virahep-c) - clinical centers” (7.5% salary support year 2, 3% years 3 and 4), University of Michigan Grant NIH-NIDDK-01-007

PROJECTS UNDER STUDY:

- A. Study of fatty liver and steatohepatitis with Hari Conjeevaram in Division of Gastroenterology..
- B. NIH study of HCV with Anna Lok in Division of Gastroenterology.
- C. NIH study of the Molecular Epidemiology of Colon Cancer in Israel (grant renewed for 5 more years).
- D. Study of molecular classification of tumors with Stephen Gruber and Thomas Giordano
- E. Study of molecular genetic changes in pancreas and colon cancer in Egypt with Amr Soloman (New grant submitted)
- F. Study of Yersinia and Crohn's disease with Laura Lamps at the University of Arkansas.
- G. Study of UC dysplasia grading with GI Study Group.
- H. Study of small bowel biopsies with Barbara McKenna and Chris Golembeski
- I. Study of Barrett's dysplasia with Weijian Zhu.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director, Surgical Pathology Fellowship Program.
- B. Quality Assurance Officer for Surgical Pathology
- C. Member, Residency Selection Committee
- D. Member, Departmental Incentive Committee
- E. Member, University Hospital Tissue Committee

REGIONAL AND NATIONAL:

- A. Reviewer, Cancer.
- B. Reviewer, Archives of Pathology and Laboratory Medicine.
- C. Reviewer, Gastroenterology.
- D. Reviewer and Editorial Board member, Human Pathology.
- E. Reviewer and Editorial Board member, American Journal of Surgical Pathology.
- F. Reviewer, American Journal of Pathology.
- G. Reviewer, Modern Pathology
- H. Reviewer, Cancer Research
- I. Education Committee member, USCAP.
- J. Editorial Board member, Te Online Journal of Digestive Diseases
- K. American Board of Pathology, Test Question Committee
- L. Reviewer, American Journal of Gastroenterology
- M. Reviewer, British Journal of Cancer
- N. Reviewer, Journal of Clinical Oncology
- O. Vogel Award Committee Chairman, USCAP
- P. Reviewer and editorial board member, American Journal of Clinical Pathology
- Q. Chairperson, Program Committee of Arthur Purdy Stout Society

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Invited Speaker, GI Pathology short course, International Academy of Pathology, Birsbane, Australia Oct. 2004
2. Invited Speaker, GI Pathology slide seminar, International Academy of Pathology, Birsbane, Australia Oct. 2004
3. Speaker, USCAP short course on GI pathology, San Antonio, Texas, Feb 2005.
4. Moderator, GI Specialty Conference. USCAP Meeting, San Antonio, Texas, Feb 2005.
5. Invited Speaker, Gastrointestinal Pathology Society Companion Meeting, USCAP Meeting, San Antonio, Texas, Feb 2005.
6. Faculty Member, ASCP Workshop – Surgical Pathology of the Gastrointestinal Tract, Palm Springs, April 2005.
7. Invited speaker, Ohio State University CME course, Columbus Ohio, Sept. 2004
8. Invited Speaker, Harvard Medical School course “Surgical Pathology for the Practicing Pathologist. Ft. Myers, FL, March 2005.
9. Invited speaker, University of Geneva CME course, Geneva Switzerland, June 2005.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Hong SH, Misek DE, Wang H, Puravs E, Giordano TJ, **Greenson JK**, Brenner DE, Simeone DE, Logsdon CD, Hanash SM. An Autoantibody-Mediated Immune Response to Calreticulin Isoforms in Pancreatic Cancer. *Cancer Research* 64:5504-5510, 2004.
2. Lin J, Lin L, Thomas DG, **Greenson JK**, Giordano TJ, Robinson GS, Barve RA, Weishaar FA, Taylor JM, Orringer MB, Beer DG. Melanoma-Associated antigens in esophageal adenocarcinoma: Identification of novel MAGE-A10 splice variants. *Clinical Cancer Research* 10:5708-5716,2004.
3. Xin W, **Greenson JK**. The clinical significance of focally enhanced gastritis. *Am J Surg Pathol* 28:1347-1351, 2004.
4. Binkley CE, Zhang L, **Greenson JK**, Giordano TJ, Kuick R, Misek D, Hanash S, Logsdon CD, Simeone DM. The Molecular Basis for Pancreatic Fibrosis: Common Stromal Gene Expression in Chronic Pancreatitis and Pancreatic Adenocarcinoma. *Pancreas* 29:254-63, 2004.
5. Huang MA, **Greenson JK**, Chao C, Anderson L, Peterman D, Jacobson J, Emick D, Lok AS, Conjeevaram HS. One-year intense nutritional counseling results in histological improvement in patients with non-alcoholic steatohepatitis: a pilot study. *Am J Gastroenterol* 100:1072-81, 2005.
6. Poynter JN, Gruber SB, Higgins PD, Almog R, Bonner JD, Rennert HS, Low M, **Greenson JK**, Rennert G. Statins and the Risk of Colorectal Cancer. *N Engl J Med* 352:2184-92, 2005.
7. Hussain HK, Chenevert TL, Londy FJ, Gulani V, Swanson S, McKenna BJ, Appelman HD, Adusumilli S, Greenson JK, Conjeevaram H. MR Imaging for Quantitative Measurement and Display of Hepatic Fat Fraction – Early Experience. Accepted to *Radiology*.
8. Fryzek JP, Schenk M, Kinnard M, **Greenson JK**, Garabrant, DH. The association of body mass index and pancreatic cancer in residents of southeastern Michigan. Accepted to *Am J of Epidemiology*.

9. Rennert G, Almog R, Tomsho LP, Low M, Pinchev M, Chaitey Y, Bonner JD, Rennert HS, **Greenson JK**, Gruber SB. Colorectal polyps in carriers of the APC I1307K polymorphism. Accepted to Diseases of the colon and rectum.
10. Rozek LS, Lipkin SM, Fearon ER, Hanash S, Giordano TJ, Kuick R, Misek DE, Taylor JMG, **Greenson JK**, Rennert G, Gruber SB. CDX2 polymorphisms, RNA expression, and risk of colorectal cancer. Accepted to Cancer Research.
11. Robert ME, Washington MK, Lee JR, Goldenring JR, Bronner MP, Goldblum JR, **Greenson JK**, et al. Rab11a Immunohistochemistry Does Not Distinguish Between Indefinite, Low-, or High-Grade Dysplasia in Barrett Esophagus. Accepted to Am J Clin Pathol

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

BOOKS/CHAPTERS IN BOOKS:

1. **Greenson JK**. Inflammatory/Descriptive Colitides, In: Gastrointestinal and Liver Pathology. First Edition. Ed: Montgomery E, Iacobuzio-Donahue C. Elsevier, Philadelphia, PA. In Press.
2. Dahl J, **Greenson JK**. The Colon, In: Sternberg's Histology for Pathologists. Third edition. Ed: Stacey Mills. Lippincott, Williams & Wilkins, Philadelphia, PA. In Press.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Dahl J, Nostrant TT, **Greenson JK**. Eosinophils in the Esophagus: Reflux or eosinophilic esophagitis? Platform presentation at USCAP meeting 2005, Mod Pathol 18:100A, 2005.
2. Havens JM, Scott MA, Goldstein NS, **Greenson JK**, Bronner MP, Lamps LW. Yersinia DNA from gene that modulates macrophage response is detected in intestines of Crohn's disease patients. Poster presentation at USCAP meeting 2005, Mod Pathol 18:106A, 2005.
3. McKenna BJ, Greenson JK, Appelman HD. Which Barrett's mucosal biopsies should be reviewed by expert pathologists? Poster presentation at DDW 2005, Gastroenterol 128:A238-9, 2005
4. McKenna BJ, Greenson JK, Appelman HD. The diagnoses of Barrett's biopsies sent for expert pathologist consultation depend on the expert: All experts are not alike! Poster presentation at . DDW 2005, Gastroenterol 128:A239, 2005

**CORY M. HOGABOAM, PH.D.
ASSOCIATE PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Graduate Students:

1. Ph.D. Dissertation Committees, University of Michigan
 - b. Betsy Pierce (Graduate Immunology Program)
 - c. Tobias Rodriguez (Graduate Immunology Program)
 - d. Matt Schaller (Graduate Immunology Program)
 - e. Shikha Auora (Graduate Immunology Program)
 - f. Haitao Wen (Pathology Graduate Program)
2. Undergraduate Students
 - a. Jillian Ewing
3. PIBS Graduate Student Laboratory Rotations, University of Michigan
4. Preliminary Examiner for Ph.D. Program, Pathology and other Graduate Programs, University of Michigan
 - a. Sudha Natarajan
 - b. Rebecca Csomos
 - c. Haitao Wen
 - d. Sara Monroe
5. Formal Teaching, Dept. of Pathology
 - a. Pathology 581: Toll-like receptors in Innate Immunity

B. Postdoctoral Fellows:

1. Traci Ness, Ph.D.
2. Karen Buckland, Ph.D.
3. Alessia Meneghin, M.D.
4. Ana Coelho, Ph.D.
5. Amrita Joshi, Ph.D.
6. Tracy Raymond, Ph.D.

III. RESEARCH ACTIVITIES:
SPONSORED SUPPORT:

- A. Co-investigator, *Monokine gene expression/regulation in lung injury*. R01 HL31237 (5%), \$200,000 per annum, 4/01/00 - 3/31/05.
- B. Principal Investigator, *Specialized Centers of Research - Pathobiology of Fibrotic Lung Disease*. Project 1: Chemokines and chemokine receptors in IPF. P50 HL56402-08 (20%), \$186,210 per annum for Project 1, 12/01/01-11/30/06.
- C. Co-investigator, *Monocyte/Macrophage Signals in Lung Granuloma*. R01 HL35276 (5%), \$162,578 per annum, 07/01/01 - 06/30/06.
- D. Co-investigator, *SCF in Liver Repair after Hepatectomy or Toxic Injury*. R01 DK58106 (5%), \$225,000 per annum, 07/01/02-11/30/07.
- E. Co-investigator, *Role of chemokines in acute experimental acute hepatitis* Canadian Institutes of Health Proof of Principle Initiative Grant on Hepatitis C. \$100,000 (CAN) per annum, 07/01/02-06/30/05.
- F. Co-investigator, *The role of CC chemokines in eosinophil airway inflammation*. R01 AI3602-06 (5%). \$200,000 per annum, 07/01/02-06/30/07.
- G. Principal Investigator, *Therapeutic Targeting of RANTES/CCL5 during Chronic Fungal Asthma*. R01 HL69865 (25%), \$175,000 per annum, 08/15/03 - 07/31/07.
- H. Principal Investigator, *Pharmacological validation of a chronic fungal asthma model characterized by persistent airway hyperreactivity, inflammation, and remodeling*. Almirall Prodesfarma, S.A., \$59,000 per annum. 12/01/03-11/31/04.
- I. Co-investigator, *Specialized Center for Clinically Orientated Research (SCCOR)*
- K. *Project 1: Dynamic effects of chemokines on systemic inflammation*. P50 HL-074024-01 (5%) \$200,000 per annum. 10/01/03 - 09/30/08.
- L. Principal Investigator, *IL-13 fusion cytotoxin as a targeted therapeutic for IIP*.
- M. R01 HL073728-01 (25%), \$225,000 per annum, 10/01/03 - 09/30/07.
- N. Co-investigator, *Lung Tissue Research Consortium: Clinical Centers*.
- O. RFP-HR-04-08 (5%), Total amount of Contract: \$3,060,407.00. 01/30/04-01/29/09.
- P. Co-investigator, *Program Project - Inflammatory Cells and Lung Injury*.
- Q. P01HL31963-25 (5%), \$225,000 per annum. 12/01/04-11/30/09.
- R. Co-investigator, *Trial of Infant Probiotic Exposure on Developing Asthma*.
- S. R01 HL080074 (5%), \$306,069 per annum. 07/01/04-06/30/08.
- T. Principal Investigator, *Targeting IL-4 and IL-13 responsive cells in pulmonary silicosis*.
- U. Global REACH and the University of Michigan. \$10,000 per annum. 07/01/05-06/30/06.

PROJECTS UNDER STUDY:

- A. Role of chemokines in airway remodeling due to allergic airway disease and asthma.
- B. Role of chemokine receptors in airway remodeling due to allergic airway and asthma.
- C. Role of chemokines and chemokine receptors in human interstitial fibrotic disease.
- D. Novel approaches to targeting IL-4 and IL-13 in chronic allergic airway disease.
- E. Role of IL-4 and IL-13 in chronic interstitial fibrotic disease.
- F. Novel approaches to targeting IL-4 and IL-13 in human interstitial fibrotic disease.
- G. Regulation of fibroblast activities during idiopathic interstitial pneumonias.
- H. Role of chemokines and SCF in liver regeneration.
- I. Role of CC chemokines in acute and chronic pulmonary inflammation.
- J. Role of IL-4 and IL-13 in pulmonary silicosis.

IV. ADMINISTRATIVE ACTIVITIES:

REGIONAL AND NATIONAL:

- A. Membership in Professional Associations
 - 1. American Association of Immunologists (AAI)
 - 2. American Society for Investigative Pathology (ASIP)
 - 3. American Thoracic Society (ATS)
- B. Journal peer-review
 - 1. Journal of Immunology (Section Editor - July 1, 2004 – July 1, 2006)
 - 2. American Journal of Physiology
 - 3. American Journal of Pathology
 - 4. Journal of Clinical Investigation
 - 5. Journal of Leukocyte Biology
 - 6. Journal of Clinical Immunology
 - 7. American Journal of Respiratory Cell and Molecular Biology
 - 8. Infection and Immunity
 - 9. Blood
 - 10. Journal of Experimental Medicine
 - 11. Nature
 - 12. Trends in Microbiology
 - 13. Clinical Cancer Research
 - 14. Arthritis and Rheumatism
 - 15. Nature Medicine
 - 16. Critical Care Medicine
 - 17. Respiratory Research
 - 18. Editorial Board Member, Current Immunology Review (2004-present)
 - 19. Editorial Board Member, BMC Immunology (2004-present)
- C. Grant peer-review
 - 1. National Institutes of Health, National Heart, Lung and Blood Institute.
 - 2. Department of Veterans Affairs, Merit Review.
 - 3. University of Michigan. Office of the Vice President for Research.
 - 4. Canadian Institutes for Health Research.
 - 5. The Wellcome Trust.

V. OTHER RELEVANT ACTIVITIES:

- A. Center for Scientific Review, ZRG1 IMB (01)
- B. Fellowship (F32) and R15 Review.
- C. Member, Graduate Program in Immunology
- D. Member, Preliminary Examination Committee (Department of Pathology)
- E. Member, Committee on Student Biomedical Research (CSBR), University of Michigan Medical School.
- F. Course Organizer – Pathobiology of Inflammation. Oswaldo Cruz Institute, Rio de Janeiro, Brazil.

INVITED LECTURES/SEMINARS:

1. 'Aspergillus and asthma – any link? Advances against Aspergillus, San Francisco, CA.
2. 'Inflammation'. Symposium on Extracellular Matrix (SIMEC), Angra De Reis, Rio de Janeiro, Brazil
3. 'Enhanced CCL7 in Usual Interstitial Pneumonia.' 13th International Colloquium on Lung Fibrosis, Banff, Alberta, Canada.
4. 'CCR4 interfaces innate and acquired immune responses directed against Aspergillus fumigatus. Roswell Park Cancer Institute, Buffalo, NY.
5. 'Unique role of CCR4 in the linkage between innate and acquired immunity.' University of California, Irvine. Irvine, CA.
6. 'Chemokines in Bacterial Sepsis.' Wayne State University. Detroit, MI.
7. 'Following the chemokine link between pulmonary innate and acquired immune responses.' FeSBE, Sau Paulo, Brazil.

PATENTS

1. **IL-13 receptor-targeted immunotoxins ameliorates symptoms of asthma and of allergy.** Filed March 1, 2002. Docket Number 015280-448000.
2. **Method of treating allergen-induced airway disease.** Filed August 19, 2002. Docket Number 13235-012001.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICAITON IN REFERRED JOURNALS.

1. Choi E.S., Jakubzick C., Kunkel S.L., Evanoff H., Martinez F.J., Puri R.K., Flaherty K.R., Toews G.B., Colby T.V., Kazerooni E.A., Gross B.H., Travis W.D., **Hogaboam C.M.** *Enhanced Monocyte Chemoattractant Protein-3/CC chemokine Ligand-7 in Usual Interstitial Pneumonia.* **Am. J. Resp. Crit. Care Med.**, Sep 1; 170(5): 508-515, 2004. Epub Jun 10, 2004.
2. Profiled in: Year in Review. Bradley et al. *Interstitial lung disease, lung cancer, lung transplantation, pulmonary vascular disorders, and sleep-disordered breathing in AJRCCM in 2004.* **Am. J. Respir. Crit. Care Med.** 171: 675-85, 2005.
3. Ajuebor M.N., Swain M.G., **Hogaboam C.M.** *The role of CCL3/MIP-1 α in experimental colitis.* **Eur. J. Pharmacol.**, Aug 30;497(3):343-9, 2004.
4. Ajuebor M.N., **Hogaboam C.M.**, Le T., Proudfoot A.E.I., Swain M.G. *CCL3/MIP-1 α is pro-inflammatory in murine T cell-mediated hepatitis by recruiting CCR1-expressing IFN- γ producing CD4 (+) T cells to the liver.* **Eur. J. Immunol.**, 34(10): 2907-2918, 2004.
5. Jakubzick C., Matsukawa A., Wen H., Keller M., Kunkel S.L., **Hogaboam C.M.** *Role of CCR4 ligands, CCL17 and CCL22, during Schistosoma mansoni egg-induced pulmonary granuloma formation in mice.* **Am. J. Pathol.**, Oct;165(4):1211-21, 2004.
6. Jakubzick C., Kunkel S.L., Puri R.K., **Hogaboam C.M.** *Therapeutic Targeting of IL-4- and IL-13-Responsive Cells in Pulmonary Fibrosis.* **Immunol Res.** 30(3): 339-50, 2004.

7. Ness T.L., Carpenter K.J., Ewing J.L., Gerard C.J. **Hogaboam C.M.**, Kunkel S.L. *CCR1 and CCL5 interactions exacerbate innate immune responses during sepsis.* **J. Immunol.**, 173: 6938-6948, 2004.
8. Benjamim C.B., Lundy S., Lukacs N.W., **Hogaboam C.M.**, Kunkel S.L. *Reversal of long-term sepsis-induced immunosuppression through intrapulmonary dendritic cell therapy.* **Blood**, Epub December 16, 2004. 105: 3588-3595, 2005.
9. Moore B.B., Kolodsick, J.E., Thannickal V.J., Cooke K., Moore T.A., **Hogaboam C.M.**, Wilke C.A., Toews G.B. *CCR2-mediated recruitment of fibrocytes to the alveolar space following fibrotic injury.* **Am. J. Pathol.**, 166: 675 - 684, 2005.
10. Ramos C.D.L., Canetti C.A., Souto J.T., Silva J.S., **Hogaboam C.M.**, Ferreira S.H., Cunha F.Q. *MIP-1 α /CCL3 acting on the CCR1 receptor mediates neutrophil migration in immune inflammation via sequential release of TNF- α and LTB $_4$.* **J. Leukoc. Biol.**, Apr 14; Epub ahead of print, 2005.
11. Ajuebor M.N., Aspinall A.I., Zhou F., Le T., Yang Y., Sidobre S., Kronenberg M., **Hogaboam C.M.**, Swain M.G. *Lack of chemokine receptor CCR5 promotes murine fulminant liver failure by preventing the apoptosis of IL-4-producing CD1d-restricted NKT cells.* **J. Immunol.**, 174(12): 8027-8037, 2005.
12. Carpenter K.J., Ewing J.L., Schuh J.M., Ness T.L., Kunkel S.L., Aparaci M., Miralpeix M., **Hogaboam C.M.** *Therapeutic targeting of CCR1 during chronic fungal asthma.* **Br. J. Pharmacol.**, June 13 Epub ahead of print, 2005.
13. Coelho A.L., **Hogaboam C.M.**, Kunkel S.L. Chemokines provide the sustained inflammatory bridge between innate and acquired immunity. **Cytokine Growth Factor Rev.** June 17 Epub ahead of print, 2005.
14. **Hogaboam C.M.**, Carpenter K.J., Schuh J.M., Proudfoot A.E.I., Bridger G., Buckland K.F. *The Therapeutic Potential in Targeting CCR5 and CXCR4 Receptors in Infectious and Allergic Pulmonary Disease.* **Pharmacol. Therapeutics**, in press, 2005.
15. Ness, T.L., Kunkel S.L., **Hogaboam C.M.** *Chemokines: central mediators of the innate immune response to sepsis.* **Current Immunology Reviews**, in press, 2005.
16. Zhou F., Ajuebor M.N., Beck P., Le T., **Hogaboam C.M.**, Swain M.G. *CD154 expressing CD4+ T cells drive murine T cell mediated hepatitis via a novel cytokine-apoptotic cascade.* **Hepatology**, in press, 2005.
17. Choi E.S., Pierce E., Jakubzick C., Carpenter K.J., Kunkel S.L., Evanoff H., Martinez F.J., Puri R.K., Flaherty K.R., Moore B.B., Toews G.B., Colby T.V., Kazerooni E.A., Gross B.H., Travis W.D., **Hogaboam C.M.** *Focal interstitial CC chemokine receptor-7 (CCR7) expression in idiopathic interstitial pneumonia.* **J. Clin. Pathol.**, in press, 2005.
18. Carpenter K.J., Buckland K.F., Xing Z., **Hogaboam C.M.** *Intrapulmonary, adenovirus-mediated overexpression of KARAP/DAP-12 enhances fungal clearance during invasive Aspergillosis.* **Infect. Immun.**, in press, 2005.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Carpenter K.J., **Hogaboam C.M.** *Immunosuppressive effects of CCL17 on pulmonary anti-fungal responses during invasive pulmonary Aspergillosis.* **Infect. Immun.**, submitted, 2005.
2. Ajuebor M.N., Zhou F., Yang Y., **Hogaboam C.M.**, Kronenberg M., Swain M.G. *Ligand specific differential regulation of IFN- γ production in CD1d restricted NKT cells by TNF- α* **J. Immunol.**, submitted, 2005.

3. Denning D.W., O'Driscoll B.R., **Hogaboam C.M.**, Bowyer P., Niven R.M. *The link between fungi and asthma – a summary of the evidence.* **Eur. Respir. J.**, submitted, 2005.
4. Buckland K.F., Carpenter K.J., Xing Z., **Hogaboam C.M.** *Pulmonary triggering receptor expressed on myeloid cells (TREM-1) expression promotes A. fumigatus clearance from mice experiencing chronic fungal asthma.* **J. Immunol.**, in preparation, 2005.
5. Lin N.J., Schuh J.M., **Hogaboam C.M.** *Maintenance of airway hyperresponsiveness in chronic asthma may be mediated by Th2-independent mechanisms.* **J. Allergy Clin. Immunol.**, in preparation.
6. Buckland K.F., Carpenter K.J., **Hogaboam C.M.** *CCR8 modulates CCL24 and CCL26 generation during chronic fungal asthma in mice.* **J. Immunol.**, in preparation, 2005.
7. Ren X., Carpenter A., **Hogaboam C.M.**, Colletti L.M. *Stem cell factor restores hepatocyte proliferation in TNF-receptor-1 knockout mice following 70% hepatectomy.* In preparation.
8. Matsukawa A., Maeda T., Sano G., Lukacs N.W., **Hogaboam C.M.**, Kunkel S.L., Lira S.A. *Absence of CC chemokine receptor 8 enhances innate immunity during septic peritonitis.* In preparation.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

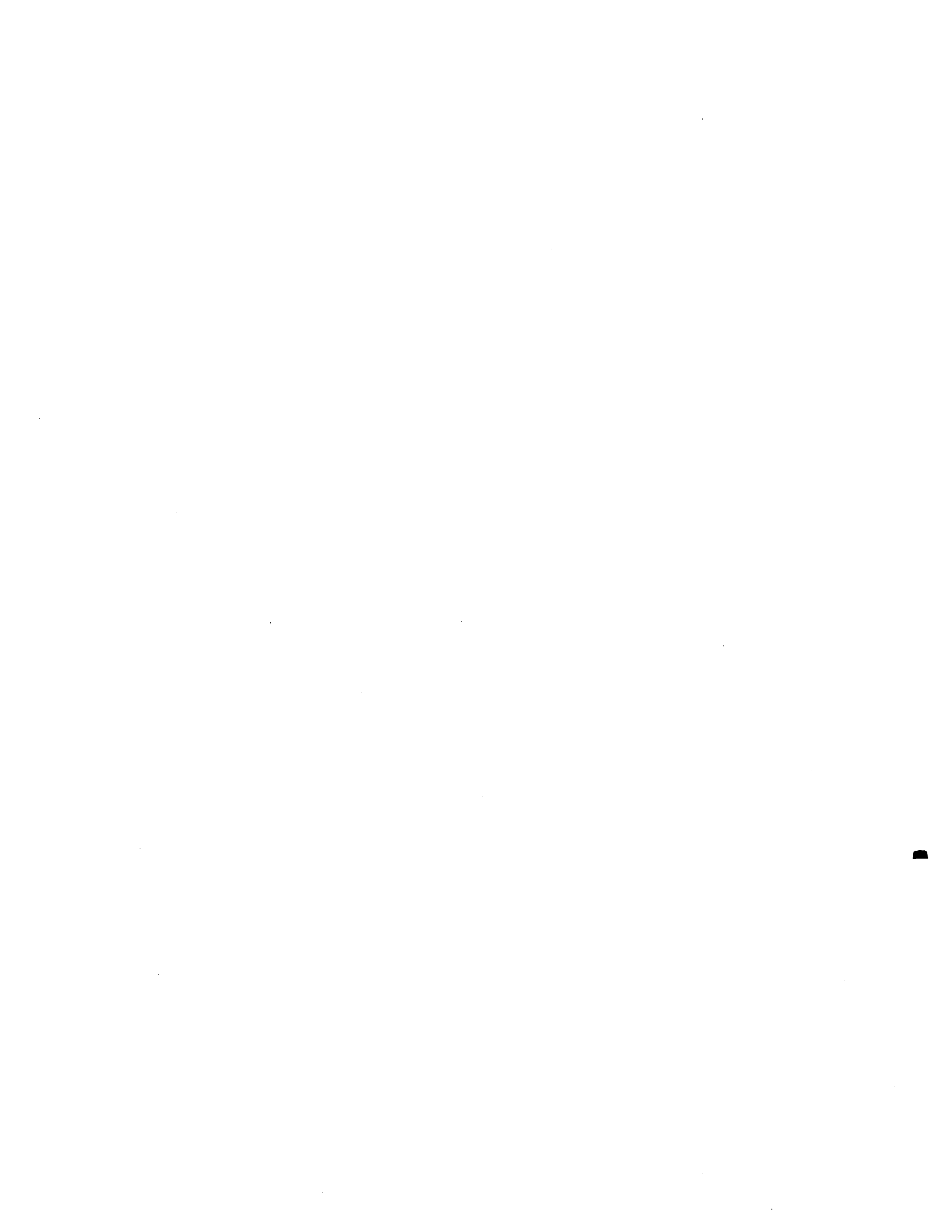
CHAPTERS:

1. **Hogaboam C.M.**, Carpenter K.J., Schuh J.M., Buckland, K.F. *Aspergillus and asthma – any link? In: Medical Mycology. Supplement 1. Ed: D. Denning. 43: S197-S202, 2005.*
2. Schuh J.M., **Hogaboam C.M.** *The innate and acquired pulmonary immune response to Aspergillus fumigatus. In: Fungal Immunology from an Organ Perspective. Ed: G. Huffnagel, P. Fidel. Chapter 11, pages 229-239, 2005.*
3. **Hogaboam C.M.**, Carpenter K.J., Evanoff H., Kunkel S.L. *Approaches to evaluation of fibrogenic pathways in surgical lung biopsy specimens. In: Methods in Molecular Medicine. Ed: J. Varga, D.A. Brenner, S.H. Phan. Chapter 12, Volume 117, pages 209-221, 2005.*
4. Buckland K.F., **Hogaboam C.M.** *Cytokine and chemokine responses in fungal allergy. In: Fungal Allergy. Ed: V. Kurup. In press, 2005.*

ABSTRACTS:

1. Zhou F., Ajuebor M.N., Le T., **Hogaboam C.M.**, Swain M.G. *CD40-CD40L interactions drive murine T cell-mediated hepatitis.* **CAG**, A53, 2004.
2. Ajuebor M.N., Aspinall A.I., Zhou F., Le T., Sidobre S., Kronenberg M., **Hogaboam C.M.**, Swain M.G. *Chemokine Receptor CCR5 Exerts a Novel Hepatoprotective Effect in Murine T Cell-Mediated Hepatitis by Promoting the Apoptosis of Activated NKT Cells and Suppressing IL-4 Production.* **CAG**, A44, 2004.
3. Ness T.L., Ewing J.L., **Hogaboam C.M.**, Kunkel S.L., *Critical role for CCR4 in TLR-mediated NF- κ B activation.* **FASEB J.** 19: A259.38, 2005.
4. Coelho A.L., Benjamim C.F., **Hogaboam C.M.**, Kunkel S.L., *Protective role of CCL6 during severe sepsis through interferon- γ generation.* **FASEB J.** 19: A826.10, 2005.
5. Wen H., **Hogaboam C.M.**, Kunkel S.L., *Severe sepsis impairs pulmonary dendritic cell IL-12 production: implications for the long-term pulmonary immune response.* **FASEB J.** 19: 856.10, 2005.

6. Peters-Golden M., Wettlaufer S.H., Moore B.B., Hogaboam C.M., Flaherty K.R., Martinez F.J., *Prostaglandin E2 production and responsiveness in lung fibroblasts from patients with usual and nonspecific interstitial pneumonia*. **Proceedings of the American Thoracic Society 2: A209, 2005.**
7. Choi E.S., Pierce E., Meneghin A., Carpenter K.J., Kunkel S.L., Evanoff H., Martinez F.J., Flaherty K.R., Moore B.B., Toews G.B., Colby T.V., Kazerooni E.A., Gross B.H., Travis W.D., Hogaboam C.M., *Enhanced CC chemokines receptor-7 (CCR&) transcript and protein expression in usual interstitial pneumonia (UIP)*. **Proceedings of the American Thoracic Society 2: A635, 2005.**
8. Carpenter K.J., Kunkel S.L., Hogaboam C.M., *CCR4 deficiency enhances the pulmonary innate immune response directed against Aspergillus fumigatus*. **Proceedings of the American Thoracic Society 2: A456, 2005.**
9. Buckland K.F., Carpenter K.J., Xing Z., Hogaboam C.M., *Pulmonary triggering receptor expressed on myeloid cells (TREM-1) expression promotes A. fumigatus clearance from mice experiencing chronic fungal asthma*. **Proceedings of the American Thoracic Society 2: A889, 2005.**



**JONATHON HOMEISTER, M.D., Ph.D.
CLINICAL LECTURER
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Autopsy Service, Attending Physician, 6 weeks

II. TEACHING ACTIVITIES:

- A. Dental Students: Instructor, Integrated Medical Sciences I and III.
1. 9/1/04, Renal Disease Laboratory
 2. 10/8/04, Female Reproductive System Pathology Laboratory
 3. 10/8/04, Male Reproductive System Pathology Laboratory
 4. 11/4/04, Hematopoietic Pathology Laboratory
 5. 1/7/05, Acute Inflammation Laboratory
 6. 1/12/05, Chronic Inflammation and Repair Laboratory
 7. 1/19/05, Neoplasia I Laboratory
 8. 4/6/05, Cardiovascular Pathology Laboratory
- B. Medical Students: M1 Histopathology Laboratory Instructor:
1. 1/19/05, Inflammation II
 2. 3/9/05, Circulatory Disturbances II

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "T cell-and monocyte-specific alpha (1,3)-fucosyltransferase-dependent selectin ligand contributions to atherogenesis." American Heart Association, Fellow to Faculty Transition Award 0275023N. \$593,000 7/1/2002-6/30/2007.
- B. Co-Director, morphology core, "Molecular Genetics of Coagulation Disorders." NIH-HLBI: P01-HL057346-06A1. \$602,180, 8/1/2003-7/31/2008.

IV. **ADMINISTRATIVE ACTIVITIES:**

UNIVERSITY OF MICHIGAN:

- A. Member, The Integrated Medical Science Series Curriculum Revision Team, University of Michigan Dental School

V. **OTHER RELEVANT ACTIVITIES:**

INVITED LECTURES/SEMINARS:

1. Invited Lecturer, "α(1,3)Fucosylation of selectin ligands regulates atherogenesis in ApoE(-/-) Mice." South East Lipid Research Conference. Callaway Gardens Resort, Pine Mountain, GA. September 23-26, 2004.
2. Invited Lecturer, "The α(1,3)fucosyltransferases FucT-IV and FucT-VII control selectin-dependent leukocyte recruitment, lymphocyte homing, and atherogenesis." Department of Pathology, University of North Carolina, Chapel Hill. December 10, 2004.

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Homeister JW, Daugherty A, Lowe JB. The α(1,3)fucosyltransferases FucT-IV and FucT-VII control susceptibility to atherosclerosis in ApoE(-/-) mice. *Arterioscler Thromb Vasc Biol.* 24: 1987-1903, 2004.
2. Hongmin S, Ringdah U, Homeister JW, Fay WP, Engleberg NC, Yang AY, Rozek LS, Wang X, Sjöbring U, Ginsburg D. Plasminogen Is a Critical Host Pathogenicity Factor for Group A Streptococcal Infection. *Science* 305(5688): 1283-1286, 2004.
3. Piccio L, Rossi B, Colantonio L, Grenningloh R, Gho A, Ottoboni L, Homeister JW, Scarpini E, Martinello M, Laudanna C, D'Ambrosio D, Lowe JB, Constantin G. Efficient recruitment of lymphocytes in inflamed brain venules requires expression of cutaneous lymphocyte antigen (CLA) and fucosyltransferase-VII. *J Immunol.* 174: 5805-5813, 2005.

**KENT J. JOHNSON, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Immunopathological evaluation of skin and renal biopsies.
- B. Director, Morphology Core.
- C. Renal pathology.
- D. Autopsy coverage.

II. TEACHING ACTIVITIES:

- A. Lecturer Genitourinary Pathology - Second Year Pathology Course.
- B. Lectures on Renal Pathology - Nephrology Fellows.
- C. Lectures on Renal and Skin Immunopathology - Pathology Residents.
- D. Lectures on Genitourinary Pathology - Dental Pathology Course.
- E. Laboratory Instructor - Second year Pathology Course.
- F. Lecturer Genitourinary Pathology – Second Year Pathology Course, Michigan State University Medical School

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Co-Principal Investigator, "Pathophysiology of Aspiration Pneumonitis", with Paul Knight, Anesthesia , R01, National Institutes of Health - Budget - \$720,866; \$187,518 annual, 08/96 - 07/04.
- B. Principal Investigator, "Inflammatory Cells and Lung Injury", Core C, National Institutes of Health, \$291,025.
- C. Co-Investigator, "A New Approach to Treat Lupus Nephritis", with Gary Glick, GMP Company
- D. Principal Investigator, "Mechanisms of Vasculitis", Pfizer, Inc., 5/02 – 5/07
- E. Co-Principal Investigator, "Mechanisms of MMP-Involvement in Acute Inflammatory Lung Injury" with Jim Varani, RO1, National Institutes of Health. Budget- \$775,000, \$225,000 annual, 6/01/03-6/01/06.
- F. Co-Investigator with James Baker, "Nanoemulsions for Decontamination". DOD. Budget \$3,100,000/year. 10/01/04.

PENDING SUPPORT:

- A. Co-Principal Investigator, "MMPs in Prostate Cancer" NIH
- B. Co-Principal Investigator, "Mechanisms of MMP Involvement in Acute Lung Injury" NIH

PROJECTS UNDER STUDY:

- A. Pathogenesis of IgG and IgA immune complex lung injury.
 - 1. Role of oxygen radicals.
 - 2. Role of proteases.
 - 3. Role of terminal components of the complement system.
- B. Oxidant and protease interaction in inflammation.
- C. Pathogenesis of vasculitis
- D. Pathogenesis of viral pneumonitis.
- E. Pathogenesis of pancreatitis and pancreatitis induced ARDS.
- F. Adhesion molecules and cytokines in inflammation.
- G. Cyclosporin-induced nephrotoxicity.
- H. Role of heme oxygenase in renal injury.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director, Immunopathology Fellowship Program.
- B. Director, Morphology Core.
- C. Renal Pathology Conference - Biweekly.
- D. Space Utilization Committee.
- E. Stobbe Funds Committee.

REGIONAL AND NATIONAL:

- A. Associate Editor - Laboratory Investigation.
- B. Reviewer for the following journals:
 - 1. American Journal of Pathology.
 - 2. American Review of Respiratory Diseases.
 - 3. American Journal of Respiratory Cell and Molecular Biology
- C. Consultant/Grant reviewer for the Veteran's Administration.
- D. NIH NHLBI Study Section.

V. INVITED LECTURES AND SEMINARS

1. Invited Speaker-Department of Pathology Seminal Series
2. Invited Speaker Pfizer Research and Development
3. Invited Speaker-Toxicology Forum

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Warner, R.L., Bhagavathula, N., Nerusu, K.C., Lateef, H.K., Younkin, E., Johnson, K.J., Varani, J.: Matrix metalloproteinases (MMP) in inflammatory tissue injury: Induction of MMP-3 and MMP-9 in fibroblasts by exposure to pro-inflammatory mediators *in vitro*. *Exp. Molec. Pathol.* 2004 76:189-195.
2. Jock, C.A., Paulauskis, J.D., Baker, D., Olle, E., Bleavins, M.R., Johnson, K.J., Heard, P.L. Influence of matrix application timing on spectral reproducibility and quality in SELDI-TOF-MS. *Biotechniques.* 2004 37(1):30-2, 34.
3. Warner, R.L., Lukacs, N.W., Shapiro, S.D., Bhagarvathula, N., Nerusu, K.C., Varani, J., Johnson, K.J. Role of metalloelastase in a model of allergic lung responses induced by cockroach allergen. *Am J Pathol.* 2004 165(6):1921-1930.
4. Glovsky, M.M., Ward, P.A., Johnson, K.J. Complement determinations in human disease. *Ann Allergy Asthma Immunol.* 2004 93(6):513-522.
5. McCune, W.J., Saluja, M., Johnson, K.J., Bhat, S., Lange, L.A., and Holzman, L.: Correlation of membranous glomerular ultrastructural changes with disease severity and outcome in lupus patients initiating cyclophosphamide therapy. *Lupus.* 2005 14:426-433.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Olle, E.W., Sreekumar, A., Warner, R.L., McClintock, S.D., Chinnaiyan, A.M., Bleavins, M.R., Anderson, T.D., and Johnson, K.J.: Development of an internally controlled antibody microarray. *Accepted.* *Molecular and Cellular Proteomics*, 2005.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. McClintock, S.D., Barron, A.G., Olle, E.W., Deogracias, M.P., Warner, R.L., Opp, M., Paulauskis, J., Johnson, K.J.: The role of interleukin-6 in IgG induced immune complex inflammatory lung injury. 2005 *Experimental Biology*, San Diego, CA, *FASEB J.* 19(4)865.7.
2. Barron, A., McClintock, S., Warner, R., Paulauskis, J., Johnson, K.: C5a levels in the sera of ANCA-positive Wegener's patients. 2005 *Experimental Biology*, San Diego, CA, *FASEB J.* 19(4)862.25.
3. Lasky, T., Olle, E., McClintock, S., Deogracia, M., Barron, A., Warner, R., Johnson K.J.: Tissue and organ pathobiology. 2005 *Experimental Biology*, San Diego, CA, *FASEB J.* 19(4)864.26.

4. Deogracia, M.P., Olle, E., McClintock, S., Anderson, T.D., Johnson, K.J.: Cytokine expression profiling of mouse dermal Arthus reaction in serum and tissues. 2005 Experimental Biology, San Diego, CA, FASEB J. 19(4)859.15.
5. Warner, R.L., Zaki, M., McClintock, S., Varani, J., Johnson, K.: Expression of stromelysin-1 in Type II epithelial cells, alveolar macrophages and interstitial fibroblasts following immune complex induced pulmonary injury. 2005 Experimental Biology, San Diego, CA, FASEB J. 19(4)614.8.
6. Olle, E., Deogracias, M., Messamore, J. Anderson, T.D., Johnson, K.J.: Development and optimization of small semi-quantitative antibody arrays. 2005 Experimental Biology, San Diego, CA, FASEB J. 19(4)857.8.
7. Bagnoli, P., Tredici, S., Bull, J.L., Brant, D.O., Johnson, K., Costantino, M.L., Hirschl, R.B.: Effect of repeated induced airway collapse during total liquid ventilation. 2005 Moses Gunn Research Conference.
8. LaFayette, N., Bagnoli, P., Tredici, S., Seetharamaiah, R., Bull, J.L., Brant, D.O., Johnson, K., Costantino, M.L., Hirschl, R.B.: Effects of repeated induced collapse on rabbit airways during total liquid ventilation. June, 2005 ASAIO Conference (American Society for Artificial Internal Organs).
9. Bagnoli, P., Tredici, S., Bull, J.L., Brant, D.O., Johnson, K., Costantino, M.L., Hirschl, R.B.: Effect of repeated induced airway collapse during total liquid ventilation. June, 2005 ASAIO Conference (American Society for Artificial Internal Organs).

**W. JOHN JUDD, F.I.B.M.S., M.I.BIOL.
PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004- 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Director, Blood Bank Reference Laboratory
- B. Consultant, Veteran's Administration Medical Center, Ann Arbor.

II. TEACHING ACTIVITIES:

RESIDENT TRAINING/CONTACT HOURS

- A. Clinical Pathology Grand Rounds:
 - 1. Program Director (CME Accredited Program 10016)
 - 2. Presented lecture on Special Methods in Antibody Identification
- B. Anatomical Pathology Conferences:
 - 1. Program Coordinator (CME Accredited Program 10004)
- C. Core-Lecture Series in Blood Banking for 1st-year Pathology House Officers:
 - 1. Program Coordinator
 - 2. Presented lectures on:
 - a) Pretransfusion testing 4 hours
 - b) Prenatal/perinatal testing 4 hours
 - c) Immune hemolysis 4 hours
 - d) Antibody identification 4 hours
- D. Clinical Pathology Case Study Conference (CME Accredited Program 10021)
 - 1. Program Coordinator
 - 2. Participant 40 hours
- E. Management Lecture Series
 - 1. Developed/coordinated series of 9 lectures on laboratory management issues relative to Pathology Residents
- F. Ethics
 - 1. Departmental liaison, GME ethics program
 - 2. Incorporated four 1-hour sessions on ethical issues into the Residency Training Program
- G. Transfusion Medicine Fellowship Program (inactive in 2004-5)
- H. Pathology Residents
 - 1. Provided instruction in immunohematology to six house-officers during their Blood Bank Rotation (over 200 contact hours)

- I Hematology Fellows
 - 1. Provided instruction in immunohematology to seven hematology/oncology fellows (21 hours).
- J. Current Topics in Blood Banking Conference, Towsley Center for Continuing Medical Education:
 - 1. Program Director – Planned and coordinated the June, 2005 Current Topics in Blood Banking Symposium and Preconference Workshops 11 hours
 - 2. Presented Workshop entitled: From ABO to GIL: An update on the human blood group systems
 - 3. Presented talk entitled: Cases and images in immunohematology

III. RESEARCH ACTIVITIES:

- 1. Yazer M, Judd WJ, Davenport RD, Dake LR, Lomas-Francis C, Hue-Roye K, Powell V, Reid M. Transient Inab Phenotype and an Agglutinating Anti-IFC in a Patient with a Gastro-Intestinal Problem. Abstract Submitted for the 2005 AABB Meeting.
- 2. Judd WJ, Cooling L, Dake LR, Davenport RD, Ellis S, Haverty D, Mullis N. Clinically Significant Anti-LKE - Nonreactive in Prewarmed Tests. Abstract Submitted for the 2005 AABB Meeting.
- 3. Judd WJ, Dake LR, Denomme GA. Confounding serological and molecular data in the investigation of Rh typing discrepancies. Abstract Submitted for the 2005 AABB Meeting.

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

- A. Blood Bank Daily Rounds.
- B. Weekly Blood Bank Communication Meetings.
- C. Monthly Clinical Pathology Faculty Meetings.

REGIONAL/NATIONAL/INTERNATIONAL:

- A. Michigan Association of Blood Banks:
 - 1. Member, Annual Meeting Program Committee.
- B. American Association of Blood Banks:
 - 1. Member, Editorial Board, Transfusion.
 - 2. Member, Editorial Board, Immunohematology
- C. Reviewer of articles submitted for publication in Transfusion, Immunohematology, Transfusion Medicine and Vox Sanguinis.
- D. International Society of Blood Transfusion
 - 1. Treasurer, Committee on Blood Group Nomenclature

V. **OTHER RELEVANT ACTIVITIES:**

INVITED LECTURES:

1. Validating your life away. Canadian Red Cross Blood Services, Toronto, ONT, September, 2004.
2. Top Ten Reasons Why Blood Group Serology is Fun. Canadian Red Cross Blood Services, Toronto, ONT, September, 2004.
3. Validating your life away. Michigan Association of Blood Banks, Detroit, MI, September 2004.
4. Top Ten Reasons Why Blood Group Serology is Fun. Michigan Association of Blood Banks, Detroit, MI, September 2004.
5. Top Ten Reasons Why Blood Group Serology is Fun. North Carolina Association of Blood Banks, Raleigh, NC, September 2004.
6. Why Gel Automation? DiaMed Au Symposium, Australian Society of Blood Transfusion, Melbourne, October 2004.
7. Antibody Identification by Gel. DiaMed Au Users Group Meeting, Australian Society of Blood Transfusion, Melbourne, October 2004.
8. Validating your life away. American Association of Blood Banks Annual Meeting, Baltimore, October, 2004.

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Davenport RD, Judd WJ, Dake LR. Persistence of cefotetan on red blood cells. *Transfusion* 2004;44:849-52.
2. Zhou L, Thorson J, Nugent C, Davenport RD, Butch S, Judd WJ. Non-Invasive Prenatal *RHD* Genotyping by Real-Time PCR Using Plasma from RhD-negative Pregnant Women. *Obstetr Gynecol*: Accepted.
3. Judd WJ, Dake LR, Davenport, RD On a much higher than reported incidence of anti-c in R1R1 patients with anti-E. *Immunohematology*. Submitted.

AWARDS:

1. The John Elliott Memorial Award of the American Association of Blood Banks, 2004.
2. The Pettaway-Sheppard Award of the North Carolina Association of Blood Banks, 2004.

**EVAN KELLER, PH.D.
ASSOCIATE PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 – 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

None.

VI. TEACHING ACTIVITIES:

Meghan Brennan, Dept. of Pathology, Graduate Student
Christopher Hall, Dept. of Urology, Post-Doctoral Fellow
Mary Valentine, Dept. of Urology Post-Doctoral Fellow
Kenine Comstock, Dept. of Urology, Assistant Research Scientist
Jinlu Dai, Dept. of Urology, Assistant Research Scientist
Kathy Ignatoski, Dept. of Urology, Assistant Research Scientist
Hui Song, Dept. of Urology, Assistant Research Scientist

VII. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Sponsor: National Institute of Aging, Role (PI, % effort): CoI, 3%, Title: Nathan Shock Center of Excellence in Basic Biology of Aging, Total Project Period: 7/1/05-6/30/10, Direct Annual Costs: \$579,759, Result (funded): Funded
- B. Sponsor: National Cancer Institute, Role (PI, % effort): PI, 40% effort, Title: The biology of prostate cancer skeletal metastases, Total Project Period: 6/1/04-5/30/09, Direct Annual Costs: \$1,004,000, Result (funded): Funded
- C. Sponsor: National Cancer Institute, Role (PI, % effort): PI, 20% effort, Title: Prostate cancer metastasis suppressor: Role of RKIP, Total Project Period: 3/1/04-2/28/09, Direct Annual Costs: \$162,000, Result (funded): Funded
- D. Sponsor: National Institutes of Health, Role (PI,NA): CoI, Title: PDGF-R expression and inhibition in skeletal metastases, Total Project Period: NA, Direct Annual Costs: \$175,000, Result (funded): Not Funded
- E. Sponsor: National Institutes of Health, Role (PI, % NA): PI, Title: Interleukin-6 and androgen refractory prostate cancer, Total Project Period: NA, Direct Annual Costs: \$200,000, Result (funded): Not funded
- F. Sponsor: National Institutes of Health, Role (PI, % effort): CoI, 5% effort, Title: IGF-I receptor is a therapeutic target in neuroblastoma. Total Project Period: 12/1/05-11/30/10, Direct Annual Costs: \$250,000, Result (funded): Pending

- G. Sponsor: American Kennel Club, Role (PI, % effort): CoI, 0% effort, Title: Mapping genes associated with osteosarcoma in large dog breeds. Total Project Period: 3/1/05-2/28/07, Direct Annual Costs: \$141,770, Result (funded): Funded
- H. Sponsor: Department of Defense, Role (PI, % effort): PI, 10% effort, Title: Defining mechanisms through which raf kinase inhibitor protein (RKIP), suppresses metastasis in prostate cancer. Total Project Period: 12/1/04-11/31/07, Direct Annual Costs: \$125,000, Result (funded): Not funded
- I. Sponsor: Centocor, Role PI 0% effort, Title: Targeting IL-6 in Prostate Cancer, Total Project Period: 2/01/04-12/01/05, Result: Funded
- J. Sponsor: Eisai Pharmaceuticals, Role PI: 0% Effort, Title: Targeting osteoclastogenesis in prostate cancer, Total Project Period: 06/01/04-12/01/05, Result: Funded

VIII. ADMINISTRATIVE ACTIVITIES:

GRANT REVIEWS:

- a. NIH, SIBR Cancer Therapy (2004)
- b. Standing Member of Tumor microenvironment (TME) study section of Center for Scientific Review (CSR)/NIH (2004-present)

MEDICAL SCHOOL/HOSPITAL:

- A. Department of Cariology Chairperson Search Committee, Dental School (2004-2005)
- B. Specific Teaching Responsibilities (e.g., Program or Assistant Program Director)

REGIONAL AND NATIONAL:

- A. Ad hoc reviewer, *Acta Pharmacologica Sinica* (2004)
- B. Ad hoc reviewer, *International Journal of Cancer* (2004-present)
- C. Ad hoc reviewer, *Journal of Urology* (2004-present)
- D. Ad hoc reviewer, *Peptide* (2005)

V. OTHER RELEVANT ACTIVITIES:

NATIONAL COMMITTEES:

- A. ACVIM Oncology Residency Training Committee (1996-present)
- B. National Scientific Advisory Council, American Federation Aging Research (1997-present)
- C. Scientific Advisory Board, Institute for Advanced Studies in Immunology and Aging (1998-present)

UM COMMITTEES:

- A. Colony for Aged Rodents Advisory Committee (1998-present)
- B. Member, Michigan Comprehensive Cancer Center (1999-present)
- C. Faculty, Graduate Program in Cellular and Molecular Biology (1999-present)
- D. Member, Multipurpose Arthritis and Musculoskeletal Disease Center (1999-present)
- E. Rackham Graduate Student Appeals Committee (1999-present)
- F. Director, NCCR Training Grant on Training Veterinarians as Biomedical Scientists (1999-2004)
- G. Co-Director, Program in Connective Tissue Oncology, U.M. Cancer Center (2000-present)
- H. Director, Nathan Shock Center Mutant & Transgenic Rodent Core (2000-present)

INVITED LECTURES/SEMINARS:

- 1. Invited speaker. "RKIP as a target for metastasis." Signal Transduction as a Therapeutic Target Annual Meeting. Luxembourg City, Luxembourg, January, 2004.
- 2. Invited speaker. "RKIP metastasis suppressor protein." The University of Michigan's Urologic Oncology Conference. Ann Arbor, Michigan, February, 2004.
- 3. Invited speaker. "RKIP, a prostate cancer metastasis suppressor gene." The Medical College of Ohio's Molecular Cancer Seminars, Toledo, Ohio, February, 2004.
- 4. Invited speaker. "Targeting bone metastases." Eisai Pharmaceuticals, Andover, Massachusetts, February, 2004.
- 5. Invited speaker. "The biology of skeletal metastases." Emory University, Atlanta, Georgia, April, 2004.
- 6. Invited speaker. "Prostate cancer metastasis." M.D. Anderson Cancer Center, Houston, Texas, September, 2004.
- 7. Invited speaker. "The biology of skeletal metastases." Amgen, Seattle, Washington, September, 2004.
- 8. Invited speaker. "RKIP a metastasis suppressor gene." The 9th World Congress on Advanced in Oncology, Crete, Greece, October, 2004.
- 9. Invited speaker. "Interleukin-6: In health and disease." Pfizer, Ann Arbor, Michigan, October, 2004.
- 10. Invited speaker. "RKIP: A metastasis suppressor gene." Prouts Neck Prostate Cancer Conference, Prouts Neck, ME, November, 2004.
- 11. Chair: Bone Metastasis Session: Prouts Neck Prostate Cancer Conference, Prouts Neck, ME, November, 2004.
- 12. Chair: Bone Metastasis Session: InterProstate SPORE meeting. Houston, TX, Jan 2005.
- 13. Invited Speaker. "Bone morphogenetic protein-6 and osteoblastic prostate cancer metastases. InterProstate SPORE meeting. Houston, TX, Jan 2005.
- 14. Invited speaker. "Targeting bone metastases." TEM study section. Washington DC, February, 2005.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Dai J, Kitagawa Y, Zhang J, Yao Z, Mizokami A, Cheng S, Nor J, McCauley LK, Taichman RS, Keller ET. Vascular endothelial growth factor contributes to the prostate cancer-induced osteoblast differentiation mediated by bone morphogenetic protein. *Cancer Res.* 64:994-999, 2004.
2. Keller ET, Brown J. Prostate cancer bone metastases promote both osteolytic and osteoblastic activity. *J Cell Biochem.* 91:718-729, 2004.
3. Zhang J, Lu Y, O'Brien CA, Dai J, Qi W, Hall DE, Manolagas SC, Ershler WB, Keller ET. In vivo visualization of aging-associated gene transcription: Evidence for free radical theory of aging. *Experimental Gerontology.* 39:239-247, 2004.
4. Artz AS, Fergusson D, Drinka PJ, Gerald M, Bidenbender R, Lechich A, Silverstone F, McCamish MA, Dai J, Keller E and Ershler WB, Mechanisms of Unexplained Anemia in the Nursing Home. *J Am Geriatr Soc* 52:423-427, 2004.
5. Keller ET, Fu Z. Defining RKIP as a protein that regulates prostate cancer metastasis. *Am J Urolog Rev* 2:72-80, 2004. Accompanying commentary on pp 81-83.
6. Keller ET. Signal transduction pathways as therapeutic targets. *IDrugs* 7:217-222, 2004.
7. Zhang J, Lu Y, Kitazawa R, Kitazawa S, Dai J, Zhao X, Yao Z, Pienta KJ, Keller ET. Role of TGF- β in Prostate Cancer Skeletal Metastases: In Vivo Real-time Imaging of TGF- β -induced RANK Ligand Transcriptional Activation in Prostate Cancer. *Prostate.* 59:360-369, 2004.
8. Chatterjee D, Bai Y, Wang Z, Beach S, Mott S, Roy R, Braastad C, Sun Y, Mukhopadhyay A, Aggarwal BB, Darnowski J, Pantazis P, Wyche J, Fu Z, Kitagawa Y, Keller ET, Sedivy JM, Yeung KC. RKIP sensitizes prostate and breast cancer cells to drug-induced apoptosis. *J Biol Chem* 279:17515-17523, 2004.
9. Keller, ET, Fu Z, Yeung K, Brennan M. Raf kinase inhibitor protein: A prostate cancer metastasis suppressor gene. *Cancer Letters* 207:131-137, 2004.
10. Mizokami A, Koh E, Fujita H, Maeda Y, Egawa M, Koshida K, Honma S, Keller ET, Namiki M. The adrenal androgen androstenediol is present in prostate cancer tissue after androgen deprivation therapy and activates mutated androgen receptor. *Cancer Res* 64:765-771, 2004.
11. Gandy S, DeMattos RB, Lemere CA, Heppner FL, Leverone JF, Aguzzi A, Ershler WB, Dai J, Fraser P, Hysloop PSG, Holtzman DM, Walker LC, Keller ET. Alzheimer A β Vaccination of Rhesus Monkeys (*Macaca mulatta*) *Mech Ageing Dev* 125:149-151, 2004.
12. Chen C, Koh AJ, Datta NS, Zhang J, Keller ET, Xiao G, Franceschi RT, D'Silva NJ, McCauley LK. Impact of Mitogen-activated Protein Kinase (MAPK) Pathway on Parathyroid Hormone Related Protein Actions in Osteoblasts. *J Biol Chem* 279:29121-29129, 2004.
13. Loberg RD, Fridman Y, Pienta B, Keller ET, McCauley L, Taichman R, Pienta KJ. Detection and isolation of circulating tumor cells in urologic cancer: A review. *Neoplasia* 6(4):302-9, 2004.
14. Keller ET, Fu Z, Brennan M. The role of Raf kinase inhibitor protein (RKIP) in health and disease. *Biochem Pharmacol* 68(6):1049-53, 2004.
15. Keller ET. Metastasis suppressor genes: A role for raf kinase inhibitor protein (RKIP). *Anti-cancer drugs* 15(7):663-9, 2004.

16. Gerhard GS, Malek RL, Cheng KC, Keller ET, Murtha J. Zebrafish, killifish, neither fish, both fish? (Letter) *J Exp Gerontol* 59(9):B873-B875, 2004.
17. Keller ET, Murtha JM. The use of mature zebrafish (*Danio rerio*) as a model for human aging and disease *Compar Biochem Physiol* 138(3): 335-341, 2004.
18. Keller ET, Fu Z, Brennan M. The biology of a prostate cancer metastasis suppressor protein: Raf kinase inhibitor protein. *J Cell Biochem* 94(2): 273-278, 2005.
19. Sun Y, Schneider A, Jung Y, Wang J, Dai J, Wang J, Cook K, Osman N, Liang Z, Koh-Paige A, Shim H, Pienta K, Keller E, McCauley L, and Taichman RS. Skeletal localization and neutralization of the SDF-1 (CXCL12)/CXCR4 axis blocks prostate cancer metastasis and growth in osseous sites in vivo. *J Bone Min Res* 20(2): 318-329, 2005.
20. Lu Y, Zhang J, Dai J, Dehne LA, Mizokami A, Yao Z, Keller ET. Osteoblasts induce prostate cancer proliferation and PSA expression through interleukin-6. *Clin Exp Met* (accepted)
21. Keller ET, Hall C, Dai J and Wallner L. Biomarkers of growth, differentiation and metastasis of prostate epithelium. *J Clin Ligand Assay*. (accepted)
22. Yung R, Keller ET, Zhang J. Aging and Immunity. In: Xi H-Z, ed. *Chinese Textbook of Geriatrics and Gerontology*, 2nd ed. Publisher of Peoples Public Health, China. In Press.
23. Brown JM, Zhang J, Keller ET. OPG, RANKL, and RANK in cancer metastasis: expression and regulation. In: Keller ET and Chung L, ed. *The Biology of Bone Metastases*. Kluwer Academic Publishers. In Press.
24. Keller ET. Mechanisms of bone resorption in prostate cancer skeletal metastases. In: F. Columbus, ed. *Progress in Prostate Cancer Research*. Nova Publishers. In Press.

BOOKS/CHAPTERS IN BOOKS

1. *The Biology of Bone Metastases*. Keller ET. Editor, Chung L. Associate Editor. Kluwer Academic Publishers. Boston, MA. 2004.

**PAUL D. KILLEN, M.D., PH.D.
ASSOCIATE PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Board Certification, Anatomic Pathology.
- B. Diagnostic Renal Biopsy Service (30 weeks).
- C. Chief Renal Consultant.

II. TEACHING ACTIVITIES:

- A. M2 Pathology Lecture - Renal Sequence (6 hours).
- B. M2 Pathology Laboratory- Renal Sequence (8 hours).
- C. Co-Coordinator - Renal Sequence (80 hours).
- D. Renal Pathology for Pathology Residents (5 hours).
- E. Renal Pathology for Nephrology Fellows Lectures (6 hours).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Core Director, Morphology Core, Biology of the Glomerular Podocyte , NIH-P50-DK39225, (5% Effort) \$129,949/year, 07/01/03-06/30/08.
- B. Co-Investigator, "The Glomerular Podocyte", NIH RO1-DK46073, (10% Effort) \$225,000 direct costs/year, 4/1/02-3/30/06.
- C. Co-Investigator, "Mouse Models of Diabetic Nephropathy and Neuropathy", RFA-DK-01-009, (5% Effort), \$545,421 direct costs/year, 9/30/01-9/30/06.
- D. Co-Investigator, Impact of an Expedited Allocation System and Pulsatile Preservation Upon the Transplantation of Kidneys from Extended Criteria Donors, 1H39 OT00123, (3% Effort) \$246,919, direct costs/year, 10/01/02-09/30/05.

PENDING SUPPORT:

None.

PROJECTS UNDER STUDY:

- A. Glomerular podocyte reaction to injury.
- B. Predictors of renal progression.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. AP Informatics
- B. Cerner V500 Core Committee

MEDICAL SCHOOL/HOSPITAL:

- A. Faculty recruitment, Departments of Internal Medicine, Pediatrics.
- B. Component II Curriculum development, M2 Urinary System.
- C. Director, Diagnostic Electron Microscopy Service.

REGIONAL AND NATIONAL:

- A. Planning Committee, Genetic Basis of Renal Disease. NIDDK, NIH.
- B. Ad hoc reviewer, Division of Extramural Activities, NIDDK, NIH.
- C. Ad hoc Reviewer, Juvenile Diabetes Foundation.

V. INVITED LECTURES AND SEMINARS:

None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Ohkita M, Wang Y, Nguyen, NDT, Tsai YH, Williams SC, Wiseman RC, Killen PD, Li S, Yanagisawa M, Garipey CE. Extrarenal ET_B Plays a Significant Role in Controlling Cardiovascular Responses to High Dietary Sodium in Rats. Hypertension, In Press, 2005.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Nakashima E, Pop-Busui R, Towns R, Thomas RP, Hosaka Y, Nakamura J, Greene DA, Killen PD, Schroeder J, Larkin DD, Stevens MJ. Differential suppression of endogenous osmoregulatory genes in human retinal pigment epithelial cells stably transformed to overexpress aldose reductase. Submitted.
2. Denny MF, Chandaroy P, Killen PD, Caricchio R, Lewis EE, Richardson BC, Lee KD, Gavalchin J, Kaplan MJ. Accelerated macrophage apoptosis induces autoantibody formation and organ damage in systemic lupus erythematosus. Submitted

**CELINA G. KLEER, M.D.
ASSOCIATE PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
JULY 1, 2004 - JUNE 30, 2005**

I. CLINICAL ACTIVITIES:

- A. Breast pathology sign out sessions 16 weeks per year. This session involves signing out in house and transfer cases from other institutions and teaching residents and fellows.
- B. Breast pathology consult cases, approximately 4 hours per week / year.
- C. Review of in house and transfer breast cancer cases to be presented in the Breast Care Multidisciplinary Conference – Every Monday for 18 weeks/year.

II. TEACHING ACTIVITIES:

- A. Mentor for six M4 students for 1 month
- B. Multi-disciplinary Conference, Mock Breast Tumor Board. Reproduction 611, M2 Reproduction Sequence 2005. University of Michigan.
- C. Mentor for Iris Wei, M1, who rotated in my laboratory for the summer. Iris was working on “Promoter methylation causes WISP3/CCN6 down-regulation in the development of inflammatory breast cancer” Iris will present her poster at the U of Michigan Year 2005 – Student Biomedical Research Forum
- D. Breast pathology diagnostic room instruction for house officers – 16 weeks
- E. Two slide conferences on interesting cases in breast pathology – 2 contact hours
- F. One didactic lecture on breast pathology – 2 contact hours
- G. Teaching Dr. David Sturtz, M.D., breast pathology fellow during diagnostic sign out, preparation for Breast Care Conference, and during sign out of consultation cases.
- H. Mentor for Sara Monroe during her second year as a pathology graduate student for 1 year. Sara was working on “Role of WISP3/CCN6 in the growth of inflammatory breast cancer”.
- I. Member of the Thesis Dissertation Committee for Neali Hendrix (Pathology Ph.D. candidate, mentor Dr. Kathleen Cho)
- J. Member of the Theses Dissertation Committee for Lisa Privette (Human Genetics Ph.D. candidate, mentor: Dr. Elizabeth Petty)
- K. Breast Care Clinic Multidisciplinary Conference (weekly)– 18 weeks/year
- L. Breast Oncology Program Conference (1 lecture/year)
- M. Breast Care Educational Forum (1 lecture/year)

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. **Principal Investigator**, *Detection of Metastatic Potential in Breast Cancer by RhoC-GTPase and WISP3 Proteins*, Department of Defense, Career Development Award, DAMD17-02-1-0490 (13%), \$355,152, 4/17/02 – 4/16/05
- B. **Principal Investigator**, *Detection of Metastatic Potential in Breast Cancer by RhoC-GTPase and WISP3 Proteins*, Department of Defense, Clinical Bridge Award, DAMD17-02-1-0491 (5%), \$451,531, 4/17/02 – 4/16/06.
- C. **Principal Investigator**, *Role of LIBC (WISP3) in the Development of the Inflammatory Breast Cancer Phenotype*, NIH/NCI, K08 CA090876-01A2 (80%), \$678,000 (total, direct plus indirect) - 9/30/03 - 8/31/08
- D. **Principal Investigator**, *Role of EZH2 in Breast Cancer Progression*, NIH/NCI, RO1 CA107469-01 (30%), \$1,296,876 (total, direct plus indirect) 02/01/2005 - 01/31/2010
- E. **Co-investigator**, *Breast cancer in african-american women*, PI: Lisa Newman, M.D., Susan G. Komen Breast Cancer Foundation (2%), \$79,948, 04/02/03 – 09/30/04

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director the Breast Pathology, involved in the planning and coordination of the breast pathology service, and quality assurance.
- B. Director, Breast Pathology Fellowship
- C. Supervision of the breast pathology fellow
- D. Member of the Breast Care Center Task Force to improve the care of patients with breast Cancer at the University of Michigan.
- E. Member of the Medical School Admissions Committee
- F. Member of the Pathology Graduate School Admissions Committee

REGIONAL AND NATIONAL:

- A. Ad hoc reviewer- Breast Cancer Research, Breast Cancer Research and Treatment, Modern Pathology, Cancer Research, Neoplasia, Experimental Cell research.
- B. Grant Reviewer for the Breast Alliance for Cancer Research.
- C. Grant Reviewer Department of Defense Breast Cancer Research Program, Cell Biology Study

INVITED LECTURES:

- 1. “Pathologic and Molecular Prognostic Factors in Breast Cancer” Breast Cancer Educational Forum, University of Michigan Cancer Center, February 4th, 2004.
- 2. “The Critical Role of the Pathologist in Delineating the Prognosis of Breast Cancer Patients” 2nd Annual Contemporary Issues in Multidisciplinary Breast Cancer Management. Ritz Carlton, Dearborn, MI, June 12th, 2004.
- 3. “Role of EZH2 in the Development of Breast Cancer” Breast Cancer Think Tank, Curacao, January 16-22nd, 2005.

4. "The Pathologist Role in Breast Cancer Decision Making Process", International Symposium on Breast Cancer, Tianjin, China, April 17-19, 2005.
5. "Characterizing Aggressive Breast Cancer Phenotypes: From Biology to Biomarkers" Elizabeth Copeland Hem/ONC Grand Rounds, Henry Ford Hospital, March 25th, 2005.
6. "Breast Pathology" American Society for Clinical Pathologists (ASCP), Resident Review Course. Chicago, IL, May 14th, 2005.
7. "Inflammatory Breast Cancer: from the lab to the clinic," Centennial Surgical Pathology Symposium, Mayo Clinic, October 1st - 2nd, 2005.
8. "Difficult Spindle Cell Tumors of the Breast" American Society for Clinical Pathologists (ASCP) teleconference, October 8, 2005.

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Kleer CG, Zhang Y, Pan Q, Wolf J, Wu M, Wu Z-F, Merajver SD. WISP3 and RhoC-GTPase Cooperate in the Development of Inflammatory Breast Cancer. *Breast Cancer Research* 6(1): R110-5, 2004.
2. Ray ME, Yang ZQ, Albertson D, Kleer CG, Washburn JG, Macoska JA, Ethier SP. Genomic and Expression Analysis of the 8p11-12 Amplicon in Human Breast Cancer Cell Lines. *Cancer Research* 64(1):40-47, 2004.
3. Van Den Eynden GG, Van Der Auwera I, Van Laere S, Colpaert CG, Van Dam P, Merajver S, Kleer CG, Harris AL, Van Marck EA, Dirix LY, Vermeulen PB. Validation of a tissue microarray to study differential protein expression in inflammatory and non-inflammatory breast cancer. *Breast Cancer Res Treat.* 85(1):13-22, 2004.
4. Kleer CG, Zhang Y, Pan Q, Merajver SD. WISP3 is a Secreted Tumor Suppressor Protein that Modulates IGF Signaling in Inflammatory Breast Cancer. *Neoplasia*, 6(2):179-85, 2004.
5. Koker M and Kleer CG. P63 Expression in Breast Cancer: A Highly Sensitive and Specific Marker of Metaplastic Carcinoma. *Am J Surg Pathol*, 28(11):1506-12, 2004.
6. Marcus B., Arenberg D., Kleer C.G., Chepeha D., Schmalbach C., Pan Q., Hanash S, Kuick R., Lee J., Merajver SD, Teknos TN. Prognostic Factors in Oral Cavity and Oropharyngeal Squamous Cell Carcinoma: The Impact of Tumor-Associated Macrophages. *Cancer*, 101(12):2779-87, 2004.
7. Roubidoux MA, Sabel MS, Bailey JE, Kleer CG, Klein KA, Helvie MA. Small (<2.0-cm) Breast Cancers: Mammographic and US Findings at US-guided Cryoablation – Initial Experience. *Radiology*, 233(3):857-67, 2004.
8. Stearns V, Gallagher MA, Kleer CG, Singh B, Freedman M, Haddad B, Isaacs C, Warren R, Brown M, Trock B and Hayes DF. A Pilot Study to Establish a Clinical Model to Perform Phase II Studies of Breast Cancer Chemopreventive Agents in Women at High Risk Using Biomarkers as Surrogate Endpoints for Activity. *Clin Cancer Res*, 10(24):8332-40, 2004.
9. Pu RT, Schott AF, Sturtz DE, Griffith KA, and Kleer CG. Pathologic Features of Breast Cancer Associated With Complete Response to Neoadjuvant Chemotherapy: Importance of Tumor Necrosis. *Am J Surg Pathol*, 29(3):354-58, 2005.

10. Witniewicz A, Shen R, Lnu S, Mehra, R, Chinnaiyan AM, Sabel MS, Rubin MA, and Kleer CG. Alpha Methylacyl-CoA Racemase (AMACR) Protein Expression is Associated with the Degree of Differentiation in Breast Cancer Using Quantitative Image Analysis. *Breast Cancer Biomarkers, Epidemiology and Prevention*, 14(6):1418-23, 2005. Cover Article.
11. Khan A, Sabel MS, Nees A, Diehl KM, Cimmino VM, Kleer CG, Schott AF, Hayes DF, Chang AE, Newman LA. Comprehensive Axillary Evaluation in Neoadjuvant Chemotherapy Patients with Ultrasonography and Sentinel Lymph Node Biopsy. *Ann Surg Oncol*, 12(9): 1-8, 2005.
12. Kleer CG, Griffith K, Sabel MS, vanGolen KL, Gallagher G, Wu, ZF, Merajver SD. RhoC-GTPase is a Novel Tissue Biomarker Associated with Biologically Aggressive Carcinomas of the Breast. *Breast Cancer Research and Treatment*, In Press.
13. Schott AF, Roubidoux MA, Helvie MA, Hayes DF, Kleer CG, Newman LA, Pierce LJ, Griffith KA, Murray S, Hunt KA, Paramagul C, Baker LH. Clinical and Radiologic Assessments to Predict Breast Cancer Pathologic Complete Response to Neoadjuvant Chemotherapy. *Breast Cancer Research and Treatment*, In Press.
14. Ben-David MA, Kleer CG., Paramagul C, Griffith KA, and Pierce LJ. Is LCIS a Component of Breast Cancer a Risk Factor For Local Failure Following Breast- Conserving Therapy? Results of a Matched Pair Analysis. *Cancer*, In Press.
15. Pan Q, Bao LW, Kleer CG, Sabel M., Merajver SD. Protein kinase C ϵ is elevated in high grade breast cancer and a novel target for RNA interference anticancer therapy. *Cancer Research*, In Press.
16. Zeidler M, Varambally S, Qi C, Chinnaiyan AM, Merajver SD and Kleer CG. The Polycomb Group Protein EZH2 Impairs DNA Repair in Human Mammary Epithelial Cells. Submitted to Neoplasia
17. O'Malley FP, Mohsin SK, Badve S, Bose S, Collins LC, Ennis M, Kleer CG, Pinder SE, and Schnitt SJ. Interobserver Reproducibility in the Diagnosis of Flat Epithelial Atypia of the Breast. Submitted to AJSP

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Koker M and Kleer CG. Metaplastic Carcinoma of the Breast: P63 is a highly sensitive and specific marker. Platform Presentation, USCAP Meeting, Vancouver, BC, 2004.
2. Koker M, and Kleer CG. Smooth muscle actin and p63 in the diagnosis of difficult lesions of the breast. Poster Presentation, USCAP Meeting, Vancouver, BC, 2004.
3. Koker, M., Griffith K, Newman L, Sabel M, Rubin MA and Kleer CG. Pathologic Factors Predictive of Sentinel Lymph Node Metastasis in Patients with Breast Cancer. Poster Presentation, USCAP Meeting, Vancouver, BC, 2004.
4. Witkiewicz A, Rubin MA and Kleer CG. AMACR Expression in Breast Adenocarcinomas. Poster Presentation, USCAP Meeting, Vancouver, BC, 2004.
5. Kleer CG, Cao Q, Varambally S, Shen R, Ota I, Tomlins SA, Ghosh D, Sewalt RG, Otte AP, Hayes DF, Sabel MS, Livant D, Weiss SJ, Rubin MA and Chinnaiyan AM. EZH2 is a Marker of Aggressive Breast Cancer and Promotes Neoplastic Transformation of Breast Epithelial Cells. Platform Presentation, USCAP Meeting, Vancouver, BC, 2004.

6. Kleer CG, Griffith K, Sabel S, Gallagher G, Merajver SD. RhoC GTPase is a New Tissue Biomarker Predictive of Local Recurrence in Patients with Breast Cancer. Poster Presentation, AACR meeting, Orlando, FL, 2004.
7. Kleer CG, Griffith K, Sabel MS, vanGolen KL, Gallagher G, Wu, ZF, Merajver SD. RhoC-GTPase is a Novel Tissue Biomarker Associated with Biologically Aggressive Carcinomas of the Breast. Poster Discussion Session, San Antonio Breast Cancer Symposium. December 8-11, 2004.
8. Mehra R, Chinnaiyan AM, and Kleer CG. GATA3 as a novel prognostic marker for breast cancer. Platform presentation, USCAP meeting, San Antonio, February 28- March 3, 2005.
9. Mehra R, Chinnaiyan AM, and Kleer CG. The role of Minichromosome maintenance protein 3 in breast cancer. Platform presentation, USCAP meeting, San Antonio, February 28- March 3, 2005.
10. Mohsin SK, Badve S, Bose S, Kleer CG, Pinder SE, O'Malley F. Assessment of Variability in Diagnosing 'Atypia' in Columnar Cell Lesions (CCL) of the Breast. Poster Session, USCAP meeting, San Antonio, February 28 – March 3, 2005.
11. Mehra R, Varambally S, Poisson LM, Rhodes DR, Ghosh D, Chinnaiyan AM, Kleer CG. Overexpression of Minichromosome Maintenance Protein 2 Is Associated with Tumor Aggressiveness and Outcome in Breast Cancer. Platform presentation, USCAP meeting, San Antonio, February 28- March 3, 2005.

**CYNTHIA HEGG KRUEGER, M.D.
LECTURER
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Cytopathology Diagnostic Service:
 - 1. Fine Needle Aspiration Service – 11 weeks
 - 2. Hospital Cytology Service (Gynecologic and Non-gynecologic specimens) - 11 weeks
- B. “Room C” Routine surgical pathology cases – 4 weeks
- C. “Room I” General surgical pathology afternoon frozen section coverage – 4 weeks
- D. Autopsy Service - 18 days

II. TEACHING ACTIVITIES:

- A. Pathology House Officers and Cytopathology Fellows:
 - 1. Fine Needle Aspiration Cytology – 11 weeks
 - 2. Hospital Cytology Service – 11 weeks
 - 3. Cytopathology Teaching Conferences – 3 contact hours
- B. Surgical Pathology Fellows:
 - 1. Frozen Section Interpretation (Room I, afternoons) – 4 weeks
- C. Pathology House Officers:
 - 1. Autopsy performance, documentation, and interpretation – 18 days
- D. Graduate Students:
 - 1. Pathology 585 Course, Dermatopathology Lecture and Lab – 2.5 contact hours
- E. Cytotechnologists:
 - 1. Cytopathology Teaching Conferences – 2 contact hours
- F. Interdepartmental:
 - 1. GI Pathology Conferences (GI Specialty Board Prep) for GI Fellows – 5 contact hours

III. RESEARCH ACTIVITIES:

None

IV. ADMINISTRATIVE ACTIVITIES:

LOCAL:

- A. Liaison from Michigan Society of Pathologists to MI State Medical Society Council of Specialty Societies

V. OTHER RELEVANT ACTIVITIES:

None

VI. PUBLICATIONS:

SUBMITTED PUBLICATIONS:

1. Rhode MR, Lucas DR, Krueger CH, and Pu RT. FNA of Spinal Osteoblastoma in a Patient with Lymphangiomatosis. (Submitted 7/05 to Diagnostic Cytopathology as a brief report)

**L PRIYA KUNJU, MD
LECTURER
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004-30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. General Surgical pathology (Room 1 and Room C): Six weeks
- B. Genito-Urinary Pathology Sub-specialty Service: Eighteen weeks
- C. Breast Sub-specialty Service: Two weeks
- D. Genito- Urinary Pathology Transfer (TS) cases: Twenty two weeks
- E. Genito-Urinary Pathology Consultation Service: Fourteen weeks
- F. On-call for intra-operative consultation: Five weeks
- G. Urology Tumor Board: Weekly, 12 months
- H. Rapid warm autopsies coverage for advanced prostate cancer: Back-up coverage, 24/7 availability, 12 months

II. TEACHING ACTIVITIES:

- A. Medical Students:
 - 1. M-2 GU Pathology Lab Sequence: 2 hours lab session
- B. Dental Students
 - 1. Didactic Lecture on Testis and Prostate Pathology: One/year
- C. House Officers and GU Fellow:
 - 1. Surgical Pathology Diagnostic Room Teaching for House Officers : Six weeks
 - 2. GU Pathology Diagnostic Room Teaching for HO & Fellow: Seventeen weeks
 - 3. GU Pathology TS/Consult cases Teaching for GU fellow : Twenty two weeks
 - 4. Didactic Lecture on Testicular tumors for House Officers : One, Sep'03
 - 5. Pathology Residents GU Path Slide (Consult) Conferences: Two/year

III. RESEARCH ACTIVITIES:

PENDING SUPPORT:

- A. Co-Investigator- R-21 Grant –NIH- 5% Effort- Characterization of Neoadjuvant Paclitaxel, Carboplatin and Gemcitabine Response in Locally Advanced Bladder Cancer. (P.I. Cheryl T Lee)

IV. PROJECTS UNDER STUDY:

- A. Papillary Renal Carcinoma: Morphologic Sub typing and correlation with Clinicopathologic and Immunohistochemical parameters. Focus on utility of CK 7 and P504S to distinguish Type 1 from Type 2.
- B. Significance of positive proximal urethral margin in radical prostatectomy: Does the presence of benign prostate glands make a difference?
- C. Significance of Flat Epithelial Atypia (FEA) in mammotome core breast biopsies: Should it be excised?
- D. Co-Investigator- Characterization of Neoadjuvant Paclitaxel, Carboplatin and Gemcitabine Response in locally advanced bladder cancer.
- E. Partial Atrophy in Prostate Needle Biopsies: Significance and Immunostaining characteristics
- F. Incidence and Significance of HGPIN and Atypical Small Acinar Proliferation (ASAP) in era of extended needle biopsies: Experience from a single high- volume institution.
- G. Assessment of Lympho-vascular invasion (LVI) in TURBT specimens: How do they compare with LVI status in Cystectomy specimens?

V. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Faculty Candidate Interviews
- B. Surgical Pathology Fellow Candidate Interviews
- C. Pathology Residency Program Candidate Interviews

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

- 1. Comparison of Monoclonal Antibody (P504S) and Polyclonal Antibody to α - Methylacyl-CoA-Racemase (AMACR) in the Work-up of Prostate Cancer. *LP Kunju*, A Chinnaiyan, RB Shah. Accepted at *Histopathology*, May 2005.
- 2. Utility of Cytokeratin 20 and Ki-67 as Markers of Urothelial Dysplasia. *LP Kunju*, CT Lee, J Montie and RB Shah. *Pathology International*, 2005;55:248-254.
- 3. Usefulness of Basal Cell Cocktail (p63+ 34 β E12) in Diagnosis of Atypical Prostatic Glandular Proliferations. RB Shah, *LP Kunju*, R Shen, M LeBlanc, M Zhou, MA Rubin. *Am J of Clin Pathol* 2004;122:517-523.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Role of Percutaneous Image-guided Renal Biopsy in the Management of Renal Masses in Contemporary Urologic Practice: Indications, Adequacy, Accuracy and Limitations of Pathologic Diagnosis. RB Shah, N Bakshi, D Wood, K Hafez and **LP Kunju**. Submitted to *Human Pathol*, June 2005.

PRESENTATIONS:

1. Role of Percutaneous Image-guided Renal Biopsy (IGRB) in management of Renal Masses: Adequacy, Accuracy and Limitations of Pathologic Diagnosis. **LP Kunju**, N Bakshi, D Wood, K Hafez and RB Shah. Platform presentation at 94th United States and Canadian Academy of Pathology Meeting, San Antonio, TX, Feb 2005.
2. Morphologic Subtyping of Papillary Renal Carcinoma: Clinico-pathologic and Immunohistochemical Analysis. **LP Kunju**, N Bakshi, L Poisson, K Hafez, K Wojno and RB Shah. Platform presentation at 94th United States and Canadian Academy of Pathology Meeting, San Antonio, TX, Feb 2005 and Poster Presentation at American Urological Association (AUA) Annual Meeting, San Antonio, May 2005.
3. Comparison of Utility of Polyclonal and Monoclonal Antibody to Alpha-Methyl Acyl Co A Racemase in Work-up of Prostate Cancer. **LP Kunju**, Arul Chinnaiyan and Rajal Shah. Poster presentation at 94th United States and Canadian Academy of Pathology Meeting, San Antonio, TX, Feb 2005.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO EDITOR:

1. Role of Percutaneous Image-guided Renal Biopsy (IGRB) in management of Renal Masses: Adequacy, Accuracy and Limitations of Pathologic Diagnosis. **LP Kunju**, N Bakshi, D Wood, K Hafez and RB Shah. *Mod Pathol* 2005; 18(1): 151A (695).
2. Morphologic Subtyping of Papillary Renal Carcinoma: Clinico-pathologic and Immunohistochemical Analysis. **LP Kunju**, N Bakshi, L Poisson, K Hafez, K Wojno and RB Shah. *Mod Pathol* 2005; 18(1): 150A (694).
3. Comparison of Utility of Polyclonal and Monoclonal Antibody to Alpha-Methyl Acyl Co A Racemase in Work-up of Prostate Cancer. **LP Kunju**, Arul Chinnaiyan and Rajal Shah. *Mod Pathol* 2005; 18(1): 150A (693).
4. Minimally Invasive Prostatectomy (Laparoscopic and Robot-assisted): Clinicopathological Characteristics of 82 cases from a Single Institution. N Bakshi, **LP Kunju**, D Wood and RB Shah. *Mod Pathol* 2005; 18(1): 128A (585).
5. Expression of Renal Cell Carcinoma Antigen (RCC) in Renal Epithelial and Non-renal Tumors: Diagnostic Implications. N Bakshi, **LP Kunju**, T Giordano and RB Shah. *Mod Pathol* 2005; 18(1): 128A (586).
6. Gleason Grading Multifocal Adenocarcinoma in Prostatectomy Specimens: Implications for Grading Needle Biopsies. MA Baig, **LP Kunju**, EW Schervish, RB Shah and KJ Wojno. *Mod Pathol* 2005; 18(1): 127A (584).

**STEVEN L. KUNKEL, PH.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

- A. Host Defense Sequence, First Year Medical School
- B. Case Reports First Year Medical Students
- C. Grand rounds: Rheumatology
- D. Academic Advisor, Immunology graduate program
- E. Operating committee Graduate Program in Immunology
- F. Member, Pathology graduate program committee
- G. Director, Research Training in Experimental Immunology Training Program (Pathology)
- H. Member, Lung Immunopathology Post-doctoral Training Program (Pathology)
- I. Member, Pulmonary Cellular and Molecular Biology Training Program
- J. Member, Pediatric Training Grant "Cellular and Molecular Biology in Pediatrics"
- K. Member, Systems and Integrative Biology Training Program (Physiology)
- L. Member, Hematology Training Grant
- M. Member, Multidisciplinary Training Program in Lung Disease
- N. Member, Graduate Teaching Award Review Committee
- O. Supervised/serve on thesis committee the following postdoctoral fellows, graduate students, medical Students and undergraduates:
- P. Fellows: Tracy Raymond, Traci Ness, Ana Lucia Coelho
- Q. Graduate Students; Hital Wen, Clauda Jakubzick
- R. Undergraduate Students: Ester Choi, Ted Martens, Jillian Ewing,
- S. Doctoral Thesis Committee Member/Orals Committee for the following graduate students: Haitao Wen (Pathology), Chinh Tran (Immunology), Andrea Waite (CMDB)), Tina Yee (Micro/Immunology)
- T. Oral preliminary examination committee

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. NIH - Macrophage/Monocyte Signals in Lung Granuloma Formation; HL-RO1-35276; Principal Investigator, MERIT Grant
- B. NIH - Monokine Gene Expression/Regulation in Lung Injury HL-RO1-31237; Principal Investigator
- C. NIH - Inflammatory Cells and Lung Injury; Program Project HL-31963; Principal Investigator
- D. SCOR Occupational and Immunological Lung Disease, P50HL-46487, Principal Investigator for Project 3
- E. SCCOR Acute Lung Injury, P50HL60289, Principal Investigator Project 3.
- F. Research Training in Experimental Immunology Training Grant Principal Investigator

PROJECTS UNDER STUDY:

- A. Role of cytokines in acute inflammation
- B. Regulation of chemokine gene expression
- C. Macrophage-lymphocyte interactions in the initiation, maintenance, and resolution of chronic inflammation

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Co-Director General Pathology
- B. Operating committee Pathology graduate program
- C. Space utilization and research committee
- D. Interview candidates for graduate program
- E. Member, Department of Pathology ACAPT committee
- F. Chair, Medical School Selection Tuition Selection Committee

MEDICAL SCHOOL/HOSPITAL/UNIVERSITY:

- A. Member, Committee on medical student research
- B. Medical school admission interview committee
- C. Medical scientist training program interviewer
- D. Member MMP Microbiology Molecular mechanisms in Microbial Pathogenesis Training Program
- E. Member, Research Council of the Office of the Vice President for Research
- F. Member, Michigan cancer center
- G. Grant reviewer, Biomedical Research Council
- H. Member, Advisory Committee Cancer Center Animal Core
- I. Associate Dean for Interdisciplinary Programs, Rackham Graduate School
- J. CMB Advisory Committee

- K. Dean's Research Advisory Board
- L. Medical School Space master Plan Steering Committee
- M. Medical School Communications Advisory Committee
- N. Member, Advisory committee on Medical School appointments, promotions, and tenure
- O. Member, Human Research Coordinating Council
- P. Member, Dean's Task Force on Rodent Populations
- Q. Committee of associate chairs for research
- R. Member, LCME Self-Study group
- S. Associate Dean, Rackham Graduate School
- T. Interim Dean Rackham Graduate School
- U. Interim Associate Provost for Academic Affairs
- V. Member, search committee Chair of Biomaterial Sciences (Dental School)
- W. Member, search committee for Chair of Pathology Department
- X. Member, search committee faculty recruit ULAM
- Y. Member PEERS accreditation team for OVPR

REGIONAL AND NATIONAL

- A. Associate Editor, Experimental and Molecular Pathology,
- B. Associate Editor, Shock
- C. Editorial board, Mediators of Inflammation
- D. Reviewer for the following journals: American Journal of Pathology, American Review of Respiratory Disease, Circulation, Infection and Immunity, Laboratory Investigation, Science, Journal of Immunology, American Journal of Respiratory Cell and Molecular Biology
- E. Grant Reviewer, The Arthritis Society
- F. Grant Reviewer, Veterans Administration
- G. National Institutes of Health Study Section, Lung Biology and Pathology (ad hoc)
- H. Chair, Publications Committee American society of Investigative Pathology

V. OTHER RELEVANT ACTIVITIES:

- A. Co-Chair, National Institute of Allergy and Infectious Diseases. Board of Scientific Counselors, Laboratory of Host Defense and Clinical Investigation. Ad hoc. Bethesda,

INVITED LECTURES AND SEMINARS:

1. Invited Speaker, Pharmacopeia Research Seminar, New Jersey, August 2004
2. Keynote Speaker, Second Annual Advances in Inflammation Research Symposium, Brown Medical School/Rhode Island Hospital, September 2004
3. Invited Speaker, Gordon Conference on Chemokines, Aussious, France, September 2004
4. Invited Speaker "Molecular Mechanisms of Inflammatory and Degenerative Processes, Lubeck, German September 2004
5. Invited Speaker, Brazilian Society of Immunology, Ouro Preto, Brazil, October 2004
6. Invited Speaker, International Cytokine Society meeting, Puerto Rico, October 2004
7. Invited Speaker, Novartis Inflammatory Group, Horsham, UK, October 2004
8. Invited Speaker, 4th International Congress on Autoimmunity, Budapest Hungary, November 2004
9. Session Chair, 4th International Congress on Autoimmunity, Budapest Hungary, November 2004
10. Invited Speaker, Immunology Center, University California, Irvine, January 2005
11. Invited Speaker (Grand Rounds) University of California Los Angeles, February 2005
12. Invited Speaker, Immunology Group, Proctor and Gamble, Ohio, March 2005.
13. Invited Speaker, Archemix Biotechnology, Cambridge, MA, May 2005.

VI. PUBLICATIONS

ARTICLES PUBLISHED IN REFEREED JOURNALS

1. Ajuebor, MN, Kunkel, Sl, Hogaboam, CM. The role of CCL3/macrophage inflammatory protein -1 alpha in experimental colitis. *Eur J Pharmacol* 2004, 497:343-349.
2. Varma, MR, Moaveni, DM, Dewyer, NA, Varga, AJ, Deatrick, KB, Kunkel, SL, Upchurch, GR, Wakefield, TW, Henke, PK. Deep vein thrombosis resolution is not accelerated with increased neovascularization. *J Vasc Surg* 2004, 40:536-542.
3. Jakubzick, C, Wen, H., Matsuskawa, A, Keller, M, Kunkel, SL, Hogaboam, CM. Role of CCR4 ligands, CCL17 and CCL22, during *Schistosoma mansoni* egg-induced pulmonary granuloma formation in mice. *Am J Pathol* 165:1211-1221.
4. Ehlert, JE, Addison, CA, Burdick, MD, Kunkel, SL, Strieter, RM. Identification and partial characterization of a variant of human CXCR3 generated by posttranscriptional exon skipping. *J Immunol* 2004 173:6234-6240.
5. Jakubzick, C, Kunkel, SL, Puri, RK, Hogaboam, CM. Therapeutic targeting of IL-4 and IL-13 responsive cells in pulmonary fibrosis. *Immunol Res* 2004, 30:339-350.
6. Ness TL, Carpenter KJ, Ewing JL, Gerard CJ, Hogaboam CM, Kunkel SL. CCR1 and CC chemokine ligand 5 interactions exacerbate innate immune responses during sepsis. *J Immunol*. 2004. 173(11):6938-48.
8. Benjamim CF, Lundy SK, Lukacs NW, Hogaboam CM, Kunkel SL. Reversal of long-term sepsis-induced immunosuppression by dendritic cell. *Blood*. 2005, 105(9): 3588-95. Epub 2004 Dec 16.

10. Benjamim CF, Kundy, SK, Lukacs, NW, Hogaboam, CM, Kunkel, SL. Opposing and hierarchical roles of leukotrienes in local innate immune versus vascular responses in a model of sepsis.. *J Immunol.* 2005.174(3):1616-20.
11. Stamatovic, SM, Shakui, P, Keep, RF, Moore, BB, Kunkel, SL, Van Rooijen, N, Anjelkovic, AV. Monocyte chemoattractant protein-1 regulation of blood-brain barrier permeability. *J Cereb Blood Flow Metab.* 2005 Feb 2; [Epub ahead of print]
12. Freeman CM, Chiu BC, Stolberg VR, Hu J, Zeibecoglou K, Lukacs NW, Lira SA, Kunkel SL, Chensue SW. CCR5 is expressed by antigen-elicited, IL-10-producing CD4+CD25+ T cells, which regulate Th2-mediated granuloma formation in mice. *J Immunol.* 2005.174(4):1962-70.
13. LaFleur, AM, Lukacs, NW, Kunkel, SL, Matsukawa, A. Mediators Role of CC chemokine CCL6/C10 as a monocyte chemoattractant in a murine acute peritonitis. *Inflamm.* 2004.13(5-6):349-55.
14. Hogaboam, CM, Carpenter, KJ, Evanoff, H, Kunkel, SL. Approaches to evaluation of fibrogenic pathways in surgical lung biopsy specimens. *Methods Mol Med.* 2005;117:209-21.
15. Lukacs NW, Hogaboam CM, Kunkel SL. Chemokines and their receptors in chronic pulmonary disease. *Curr Drug Targets Inflamm Allergy.* 20005; 4:313-7.
16. Kasama T, Miwa Y, Isozaki T, Odai T, Adachi M, Kunkel SL. Neutrophil-derived cytokines: potential therapeutic targets in inflammation. *Curr Drug Targets Inflamm Allergy.* 2005 Jun;4(3):273-9.
17. Coelho AL, Hogaboam CM, Kunkel SL. Chemokines provide the sustained inflammatory bridge between innate and acquired immunity. *Cytokine Growth Factor Rev.* 2005 Jun 17; [Epub ahead of print]
18. Carpenter KJ, Ewing JL, Schuh JM, Ness TL, Kunkel SL, Aparici M, Miralpeix M, Hogaboam CM. Therapeutic targeting of CCR1 attenuates established chronic fungal asthma in mice. *Br J Pharmacol.* 2005 Aug;145(8):1160-72.

**ANDREW LIEBERMAN, M.D., Ph.D.
ASSISTANT PROFESSOR
ANNUAL DEPARTMENTAL REPORT**

**DEPARTMENT OF PATHOLOGY
1 JULY 2004 – 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Diagnostic surgical neuropathology, 6 weeks
- B. Autopsy evaluation of brains submitted to the Michigan Alzheimer's Disease Research Center

II. TEACHING ACTIVITIES:

- A. Graduate students and postdoctoral fellows:
 - 1. Responsible during the current academic year for teaching activities for the following:
 - a. Monzy Thomas, Ph.D. (postdoctoral fellow)
 - b. Zhigang Yu, M.D. (postdoctoral fellow)
 - c. Christopher Pacheco (thesis student)
 - 2. Rotating graduate student
 - a. Dustin Gibson, Neuroscience Graduate Program
 - 3. Thesis committee member
 - a. Valerie Drews, Neuroscience Graduate Program
 - b. Mary Heng, Neuroscience Graduate Program
 - c. Yunfang Man, Pathology Graduate Program
 - d. Scott Tomlins, Pathology Graduate Program
 - 4. Preliminary examination committee member
 - a. Sudha Natarajan, Pathology Graduate Program
 - b. Rebecca Csomos, Pathology Graduate Program
 - c. Holly Brevig, Pharmacology Graduate Program
- B. Lecturer on neurodegenerative disease, pathology house officers
- C. Lecturer and laboratory instructor, M2 Pathology, Neuroscience Sequence
- D. Instructor, Pathology/Radiology elective for M4 students
- E. Course director and instructor, "Introduction to neuropathology", Pathology 858
- F. Lecturer and instructor, "Triplet repeat disorders", Pathology 582
- G. Lecturer and laboratory instructor, "Neuropathology", Pathology 585
- H. Member, Neuroscience Graduate Program
- I. Member, Pathology Graduate Program

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, Paul Beeson Career Development Award in Aging Research, NIH and American Federation for Aging Research, K08 AG024758, "Modifiers of polyglutamine toxicity", 75%, \$200,000/yr (\$600,000/5 yr), 8/1/04 – 5/31/07
- B. Principal Investigator, Muscular Dystrophy Association, "Altered androgen receptor function in Kennedy's disease", 5%, \$73,409/yr (\$219,000/3 yr), 7/1/02 – 6/30/05
- C. Principal Investigator, Kennedy's Disease Association, "A knock-in mouse model of Kennedy's disease", 0%, \$23,810/yr, 3/1/04 – 2/28/05
- D. Principal Investigator, Nathan Shock Center of Excellence in Aging Mutant and Transgenic Rodent Core, "A knock-in mouse model of Kennedy's disease", 0%, \$22,584/2 yr, 7/1/03 – 6/30/05
- E. Principal Investigator, Biomedical Research Council University of Michigan, "Early death of mutant males in a knock-in mouse model of Kennedy's disease", 0%, \$30,000/yr, 7/1/04 – 6/30/05
- F. Principal Investigator, Atorvastatin Research Award, Pfizer, "Understanding the neuropathology of Niemann-Pick C through mouse models", 0%, \$45,000/yr (\$90,000/2 yr), 7/1/04 – 6/30/06
- G. Core Principal Investigator, Michigan Alzheimer's Disease Research Center, NIH, P50 AG08671, 15%, "Neuropathology Core", \$47,034/yr, 6/1/99 – 5/31/10
- H. Principal Investigator, Muscular Dystrophy Association, "A knock-in mouse model of Kennedy's disease", 5%, \$90,000/yr (\$270,000/3yr), 7/1/04 – 6/30/07
- I. Sponsor/Mentor, (Christopher Pacheco, Principal Investigator), NIH, F31 NS51143, "Understanding Niemann-Pick C with cell and mouse models", 0%, \$35,248/yr (\$140,992/4yr)

PROJECTS UNDER STUDY

- A. Mechanism of neurodegeneration in Kennedy disease
- B. Mechanism of neurodegeneration in Niemann-Pick C

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Chair, Pathology Graduate Program Admissions Committee
- B. Member, Pathology Graduate Program Preliminary Examination Committee
- C. Pathology residency training program and faculty candidate interviews

MEDICAL SCHOOL/HOSPITAL:

- A. Director, Neuropathology Core, Michigan Alzheimer's Disease Research Center
- B. Member, Medical Scientist Training Program Advisory Committee
- C. PIBS student interviews
- D. Grant review, Biomedical Research Council

REGIONAL AND NATIONAL:

- A. Manuscript review for:
 - 1. Brain
 - 2. FEBS Letters
 - 3. Human Molecular Genetics
 - 4. Journal of Biological Chemistry
 - 5. Journal of Cell Science
 - 6. Journal of Neuro-ophthalmology
 - 7. Journal of Neuropathology and Experimental Neurology
- B. Grant review for:
 - 1. Alzheimer's Association
 - 2. Telethon Foundation of Italy

V. OTHER RELEVANT ACTIVITIES:

HONORS AND AWARDS:

- A. Paul Beeson Career Development Award in Aging Research, NIH and American Federation for Aging Research

VI. INVITED LECTURES/SEMINARS:

- 1. "Cellular and mouse models of inherited neurodegenerative diseases", Neuroscience Graduate Program retreat, August, 2004
- 2. Invited speaker and panel discussant, Kennedy's Disease Association Conference, San Diego, CA, October, 2004.
- 3. "Cellular and mouse models of inherited neurodegenerative disease", Program in Biological Sciences New Faculty Seminar Series, October, 2004
- 4. "Kennedy's Disease", Pathology Graduate Program retreat, November, 2004
- 5. "Androgen receptor toxicity in Kennedy's Disease", Department of Pathology Research Seminar Series, February, 2005
- 6. "Androgen receptor toxicity in Kennedy's Disease", Department of Neurology ground rounds, February, 2005
- 7. Invited speaker, Astra-Zeneca Ischemia Workshop, "Neuropathology of stroke and the blood brain barrier", Ann Arbor, MI, April, 2005.

8. Invited speaker and instructor, "Autopsy diagnosis of Alzheimer's disease and related dementias", Advanced Course in Dementia Care, Eastern Michigan University, Ann Arbor, MI, May, 2005.

VII. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Drews VL, Lieberman AP, Meisler MH. Multiple transcripts of sodium channel SCN8A (NaV1.6) with alternative 5' and 3' UTRs and initial characterization of the SCN8A promoter. *Genomics*, 85:245-257, 2005.
2. Rath TJ, PC Sundgren, Brahma B, Lieberman A, Chandler WF, Gebarski SS. Massive symptomatic subependymoma of the lateral ventricles: case report and review of the literature. *Neuroradiology*, 47:183-188, 2005.
3. Thomas M, Yu Z, Dadgar N, Varambally S, Yu J, Chinnaiyan AM, Lieberman AP. The unfolded protein response modulates toxicity of the expanded glutamine androgen receptor. *J Biol Chem*, 280:21264-21271, 2005

MANUSCRIPTS SUBMITTED FOR PUBLICATION:

1. Yu Z, Dadgar N, Albertelli M, Scheller A, Albin RL, Robins DM, Lieberman AP. Abnormalities of germ cell maturation and Sertoli cell cytoskeleton in androgen receptor 113 CAG knock-in mice reveal toxic effects of the mutant protein. Submitted for publication.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Foster NL, Koeppe RE, Giordani BJ, Nichols TE, Lieberman AP. Variations of the phenotype in frontotemporal dementias. In *Genotype - Proteotype - Phenotype Relationships in Neurodegenerative Diseases* (Cummings J, Hardy J, Poncet M, Christen Y, eds) Springer-Verlag, Berlin, pp 139-152.
2. Thomas M, Yu Z, Lieberman AP. The unfolded protein response modulates polyglutamine toxicity. Society for Neuroscience meeting, San Diego, CA, October, 2004.
3. Foster NL, Koeppe RE, Giordani BJ, Lieberman AP. Variations of the phenotype in frontotemporal dementias. *Genotype-Proteotype-Phenotype Relationships in Neurodegenerative Diseases*. Paris, France, September, 2004.
4. Thomas M, Harrell JM, Plane J, Peng H-M, Pratt WB, Lieberman AP. Expression of the hsp90 cochaperone p23 inhibits steroid hormone receptor trafficking and production of aggregates by the expanded glutamine androgen receptor of Kennedy disease. Annual meeting of Beeson Scholars, La Jolla, CA, June, 2005.
5. Yu Z, Dadgar N, Albertelli M, Scheller A, Robins DM, Lieberman AP. Abnormalities of germ cell maturation and Sertoli cell cytoskeleton in androgen receptor 113 CAG knock-in mice. Gordon Research Conference on CAG Triplet Repeat Disorders, South Hadley, Massachusetts, July, 2005.

6. Pacheco CD, Dadgar N, Lieberman AP. Generation of an *Npc1* conditional null allele in mice. Gordon Research Conference on the Molecular and Cellular Biology of Lipids, Waterville Valley, New Hampshire, July, 2005.
7. Thomas M, Harrell JM, Plane J, Peng H-M, Pratt WB, Lieberman AP. Expression of the hsp90 cochaperone p23 inhibits steroid hormone receptor trafficking and production of aggregates by the expanded glutamine androgen receptor of Kennedy disease. Society for Neuroscience meeting, Washington, DC, November, 2005.

**RICHARD W. LIEBERMAN, M.D.
CLINICAL ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Gynecologic Pathology Consultation - twelve months.
- B. Gynecologic Oncology Semimonthly Tumor Planning Conference - twelve months.
- C. Autopsy service – twelve months (14 weeks, 6 weekends).
- D. Gynecologic Oncology – Colposcopy Clinic, one half day/week, twelve months.
- E. Placental Pathology – twelve months.

II. TEACHING ACTIVITIES:

- A. Residents:
 - 1. Sign-out - Gynecologic Pathology, Placentas, and Autopsy cases.
 - 2. Review cases and supervise presentation of semimonthly Gynecologic Oncology Tumor Planning Conference – twelve months.
 - 3. Instruction in the Gross Examination, frozen section diagnosis, and processing of Gynecologic Surgical specimens and Placentas, July-September 2002.
 - 4. Instruction and supervision in the performance, presentation and sign-out of autopsy cases.
 - 5. Teaching Conferences- lecture in Gyn Pathology, Jan 2002.
 - 6. Consult Case Conference - two/year.
 - 7. Miscellaneous resident evening conferences in Gyn Path
 - 8. Resident resource web page in Gyn Pathology (<http://gynonc.path.med.umich.edu> – Web access to Gyn Pathology Grossing Manual, lecture slides, “Blue Book” Online guide to Gynecologic Oncology, and other resources
 - 9. Morbidity and Mortality Conferences – Internal Medicine, General Surgery, and Obstetrics & Gynecology
- B. University of Michigan Medical Students:
 - 1. M2, Obstetrics & Gynecology Sequence: Five hours Gynecologic Pathology lectures; preparation of examination questions.
 - 2. M2, Obstetrics & Gynecology Sequence: Laboratory instruction.
 - 3. M2 resource web page in Gyn Pathology (– Web access to Gyn Pathology laboratory, lecture slides, and other resources
 - 4. M3 – Teaching during weekly Colposcopy Clinic.
- C. Ob/Gyn Residents and Gynecologic Oncology Fellow:
 - 1. Semimonthly Tumor Planning Conference – twelve months.
 - 2. Colposcopy clinic staff – one-half day per week (twelve months).
 - 3. Operating Room Instruction – one-half day per week.
 - 4. Lectures in Gynecologic Pathology to Gyn Oncology Service – two/year.
 - 5. Gyn Pathology Rotation for 3rd year Gyn Oncology Fellow – one month.
 - 6. Placental Pathology Lectures – two hours.
- D. University of Michigan Dental School – D2:
 - 1. D2, Reproductive Sequence – two hours

III. RESEARCH ACTIVITIES:

SOFTWARE DEVELOPMENT:

- A. PathView Image Database – Software Disclosure (U of Michigan 2000)
- B. Profiler, Tissue Microarray & Genomics DB Module (under PathView) – Disclosure July 2002
- C. Placental Imaging Project – Imaging and Bar Code Schema for Image Capture

NON-SPONSORED SUPPORT:

- A. **Digital Imaging for Web-based Review of Tumor Histopathology for Rapid Confirmation Eligibility in a GOG Protocol; Addendum to GOG 207 and Subsequent GOG Studies** Direct Sponsor: The Gynecologic Oncology Group. \$10,000 for administrative support
- B. **Long-Term Outcomes from Irradiation of Advanced Stage Low-Malignant Potential Serous Ovarian Cancer with Noninvasive Implants.** Pathology review of cases for Dr. Sheila Krishnan, Dr. Joseph Herman, and Dr. Avraham Eisbruch, Department of Radiation Oncology, UMHS
- C. **Correlation of colposcopic stereoscopic photography (colpography) and Hyperspectral Diagnostic Imaging (HSDI, developed by STI-Medical: Science and Technology International) with the underlying cervical LEEP histopathology.** Pending IRB Approval (as of June 2005)

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Member, Pathology Bioinformatics, Department of Pathology.
- B. Director of Telepathology, Department of Pathology

MEDICAL SCHOOL/HOSPITAL:

Member of Picture Archiving and Communication System Committee (PACS).

REGIONAL AND NATIONAL:

- A. Member, College of American Pathologists, Informatics Committee.
- B. Member, Medical Informatics Committee, Gynecologic Oncology Group.
- C. Member, Pathology Committee, Gynecologic Oncology Group.
- D. Member, Tissue Utilization Committee, Gynecologic Oncology Group.
- E. Member, National Comprehensive Cancer Network (NCCN) Cervical/Endometrial Cancer Screening Panel.
- F. Editorial Reviewer, Obstetrics and Gynecology.
- G. Editorial Reviewer, Cancer.

V. **OTHER RELEVANT ACTIVITIES:**

INVITED LECTURES/SEMINARS:

1. HPV Panel Discussion -- Update on Women's Health Issues - Towsley Center, December 2004

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED IN REFEREED JOURNALS:

1. Feters MD, Lieberman RW, Abrahamse PH, Sanghvi RV, Sonnad SS. *Cost Effectiveness of Vaginal PAP Smear Screening After Total Hysterectomy for Benign Disease*. J Lower Gen Tract D (Journal of Lower Genital Tract Disease, Summer 2003).
2. Ayers AW, Carr DW, McConnell DS, Lieberman RW, Smith GD. *Expression and intracellular localization of protein phosphatases 2A and 2B, protein kinase A, A-kinase anchoring protein (AKAP79), and binding of the regulatory (RII) subunit of PKA to AKAP79 in human myometrium*. (Journal of the Society for Gynecologic Investigation: Fall 2003)

**ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR,
MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:**

PUBLICATIONS (non-peer reviewed):

1. Vulva: Benign and Inflammatory Conditions. Haefner, H (editor), Lieberman, R (Web Editor/developer), et al. <http://www.asccp.org/edu/practice/vulva.shtml>.
2. Vulva: HPV and VIN. Haefner, H (editor), Lieberman, R (Web Editor/developer), et al. http://gynonc.path.med.umich.edu/ASCCP/HPV_VIN/default.htm.
3. Vulva: HPV and VIN. Haefner, H (editor), Lieberman, R (Web Editor/developer), et al. http://gynonc.path.med.umich.edu/ASCCP/HPV_VIN/default.htm.
4. On-line Gynecologic Pathology Manual. GOG Pathology Committee: Benda J (Chair), Lieberman R (Web Editor) <http://www.gog.org>.

LORI LOWE, M.D.
CLINICAL PROFESSOR OF PATHOLOGY AND DERMATOLOGY
DEPARTMENTS OF PATHOLOGY AND DERMATOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005

I. CLINICAL ACTIVITIES:

- A. Dermatopathology Service – 12 months.
- B. Dermatopathology Consultation Service - 12 months.

II. TEACHING ACTIVITIES:

- A. Medical Students:
 - 1. Lecturer, MS II Dermatology Sequence (2 hours full class lecture)
 - 2. Dermatopathology laboratory director and instructor, MS II Dermatology Sequence (2 contact hours)
 - 3. Dermatopathology, Pathology Clerkship, MS I and MS IV students (4 students).
 - 4. Dermatopathology, Dermatology Clerkship, MS IV students (3 students)
- B. Dental Students:
 - 1. Lecturer, Skin Integument Model, "Introduction to Clinical Dermatology with Histopathologic Correlates, Parts I and II (2 hours full class lecture)
- C. House Officers:
 - 1. Dermatopathology sign-out (Pathology and Dermatology Residents).
 - 2. Review of dermatopathology consultation material.
 - 3. Dermatopathology teaching conference (weekly-twice monthly).
- D. Diagnostic Conference, Department of Dermatology (weekly).
- E. Director of Diagnostic Conference, Department of Dermatology – (2 hours/month)
- F. Hospital Conferences:
 - 1. Multidisciplinary Melanoma Conference (twice monthly).
- G. Honors:
 - 1. William B. Taylor Resident Teaching Award, Department of Dermatology, University of Michigan, 2004-2005.
 - 2. Listed in *America's Top Doctors for Cancer*, 2005 by Castle Connolly Medical Ltd.
 - 3. Listed in the *Guide to America's Top Physicians*, 2004-2005 edition by the Consumer's Research Council of America

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

Patient Examination with MelaFind™ system developed by Electro-Optical Sciences, Inc. (EOS). 2001 Jennifer L. Schwartz, M.D., Timothy M. Johnson, M.D., Timothy S. Wang, M.D., Darius J. Karimipour, M.D., Jeffrey S. Orringer, M.D., Lori Lowe, M.D., Lyndon Su, M.D., Doug Fullen, M.D., Christopher Bichakjian, M.D., Mitzi Rabe, R.N. (Study ongoing through 2005) \$5,750.

PROJECTS UNDER STUDY:

- A. University of Michigan (UMMC 2000-0713): Molecular, biochemical, and cellular basis of melanoma and other melanocytic lesions: Tissue Bank. Timothy M. Johnson, M.D., Timothy S. Wang, M.D., Jennifer L. Schwartz, M.D., John J. Voorhees, M.D., Anj Dlugosz, M.D., Lori Lowe, M.D., Lyndon Su, M.D., Doug Fullen, M.D., Carol Bradford, M.D., Vincent Cimmino, M.D.
- B. University of Michigan (UMCC 2-15): A phase III randomized double-blind pivotal trial of immunotherapy with BCG plus a polyvalent melanoma vaccine, CancerVax™ vaccine versus BCG plus a placebo as a post-surgical treatment for Stage III melanoma. Principal investigator: Michael Sabel, M.D.
- C. NIH/NIDDK Grant DK59169. Topical Retinoids for Diabetic Foot Ulcers. Member, NIDDK Data and Safety Monitoring Plan. Principal Investigator: James Varani, Ph.D. 2003-ongoing.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL AND INSTITUTIONAL:

- A. Director, Dermatopathology Service, Department of Pathology, University of Michigan
- B. Member, Advisory Committee on Appointments, Promotions, and Tenure (ACAPT), Department of Pathology, University of Michigan
- C. Member, Residency Review Committee, Department of Dermatology, University of Michigan
- D. Member, Melanoma Tissue Core Distribution Committee (IRBMED #2004-0618)
- E. Coordinator, QA/QC program (Mohs surgery slides), Cutaneous Surgery and Oncology Program, Department of Dermatology, University of Michigan
- F. Member, Multidisciplinary Melanoma Program, University of Michigan Comprehensive Cancer Center
- G. Interviewer, Pathology House Officer Candidates

REGIONAL AND NATIONAL:

- A. Member, North American Melanoma Pathology Study Group
- B. Member, American Medical Women's Association Mentorship Program
- C. Member, American Academy of Dermatology's Minority Medical Student Mentor Program
- D. Ad hoc manuscript reviewer, *Journal of Cutaneous Pathology*
- E. Ad hoc manuscript reviewer, *Dermatologic Surgery*
- F. Ad hoc manuscript reviewer, *Human Pathology*

IV. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

- A. Editorial Board, Skin Section Editor, *CANCER*
- B. Member, Editorial Board, Journal of the American Academy of Dermatology

INVITED LECTURES/SEMINARS:

1. Advanced Self-Assessment in Dermatopathology, faculty, American Academy of Dermatology Annual Meeting, New Orleans, February 2005.
2. Invited Lecturer, University of Michigan, Department of Internal Medicine, Division of Rheumatology, Rackham Arthritis Research Unit lecture series, "Cutaneous Manifestations of Rheumatologic Disease".

COMMUNITY SERVICE:

1. Lecture, "How to Prevent Skin Cancer," Emerson School, Ann Arbor, MI, May, 2005.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Sondak VK, Taylor JMG, Sabel MS, Wang Y, **Lowe L**, Grover AC, Chang AE, Yahanda AM, Moon J, Johnson TM: Mitotic rate and younger age are predictors of sentinel lymph node positivity: Lessons learned from the generation of a probabilistic model. *Ann Surg Oncol* 11: 247-258; 2004.
2. Wechter ME, Reynolds RK, Haefner HK, **Lowe L**, Gruber SB, Schwartz JL, Johnston CM, Johnson TM: Vulvar melanoma: Review of diagnosis, staging, and therapy. *J Low Genit Tract Dis* 8: 58-69; 2004.

3. Rosi YL, **Lowe L**, Kang S: Treatment of hidradenitis suppurativa with Infliximab in a patient with Crohn's disease. *Journal of Dermatologic Treatment* 16: 58-62; 2005.
4. Sabel MS, Griffith K, Sondak VK, **Lowe L**, Schwartz JL, Cimmino VM, Chang AE, Rees RS, Bradford CR, Johnson TM: Predictors of non-sentinel lymph node positivity in patients with a positive sentinel node for melanoma. *J Am Coll Surg* 201: 37-47; 2005.
5. Cho S, **Lowe L**, Hamilton TA, Fisher GJ, Voorhees JJ, Kang S: Long term treatment of photoaged human skin with topical retinoic acid improves epidermal cell atypia and thickens collagen band in the papillary dermis. *J Am Acad Dermatol* (in press).
6. Schmalbach CE, **Lowe L**, Teknos TN, Johnson TM, Bradford CR: Reliability of sentinel lymph node mapping with biopsy for identifying regional spread of head and neck Merkel cell carcinoma. *Arch Otolaryngol* (in press).
7. Arora A, **Lowe L**, Su L, Rees R, Bradford C, Cimmino VC, Chang AE, Johnson TM, Sabel MS: Wide local excision alone for desmoplastic melanoma. *Cancer* (in press).
8. Rosamilia LL, Schwartz JL, **Lowe L**, Gruber SB, Quint EH, Johnson TM, Reynolds RK, Haefner HK: Vulvar melanoma in a 10 year old child in association with lichen sclerosus. *J Am Acad Dermatol* (in press).

ARTICLES SUBMITTED FOR PUBLICATION:

1. Constantino D, **Lowe L**, Brown DL: Basosquamous carcinoma- An under-recognized, high risk cutaneous neoplasm: Case study and review of the literature. *British J of Plastic Surg* 2005.
2. Shors AR, Kim S, White E, Barnhill RL, **Lowe L** (member, North American Dysplastic Nevus Panel), Piepkorn, MW. Risk of melanoma associated with histologically dysplastic nevi. *Cancer* 2005.

ABSTRACTS, BOOK REVIEWS, PRELIMINARY COMMUNICATIONS, PANEL DISCUSSIONS:

1. Fullen, DR, **Lowe L**. Epidermotropic mucinous adenocarcinoma arising at mucocutaneous stomal anastomosis site. *American Society of Dermatopathology 41st Annual Meeting, Boston, MA, October 2004.*
2. Grachtchouk M, Wang A, Wei L, Liu J, Hutchin M, **Lowe L**, Glick A, Dlugosz AA. Deregulated hedgehog signaling in extracutaneous basaloid squamous cell carcinomas. *Society for Investigative Dermatology Annual Meeting, 2004.*

**DAVID R. LUCAS, M.D.
CLINICAL ASSOCIATE PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Surgical pathology - 26 weeks
- B. Bone and soft tissue pathology consultation – 12 months

II. TEACHING ACTIVITIES:

- A. Medical/Dental Students
 - 1. Pathophysiology 540- D1 dental students, 100 students, 3 class lecture hours
 - 2. M4 pathology mentorship- 8 students, 1 month rotations
- B. House Officers
 - 1. Surgical pathology sign-out – 26 weeks
 - 2. Bone and soft tissue pathology elective – 7 house officers, 1 month each
 - 3. Lectures in soft tissue pathology – 3 hours
 - 4. Consultant conferences – 3 hours
 - 5. Oral surgery slide conferences-10 hours

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. RTOG 0330, A pilot phase II study of pre-operative radiation therapy and thalidomide (IND 48832; NSC 66847) for low grade primary soft tissue sarcoma or pre-operative MAID/thalidomide/radiation therapy for high/intermediate grade primary soft tissue sarcoma of the extremity or body wall. Study chair: Burton L. Eisenberg, M.D.
- B. Randomized trial of neoadjuvant adriamycin/ifosfamide vs. gemcitabine/taxitotol in high grade soft tissue sarcoma (U of M trial). Principal investigator: Mark Zalupski, M.D.
- C. Sporadic vs. radiation-associated angiosarcoma: biologic and clinicopathologic correlations. First author: Jonathan McHugh, M.D. PGY 3
- D. Morphologic spectrum of myxoid liposarcoma with molecular correlations. First author: Christopher Przybycin, M.D. PGY 2
- E. Histologic response to neoadjuvant chemotherapy in soft tissue sarcoma: development of a grading system with clinical correlation. First author: Malti Kshirsagar, M.D. PGY 1

PENDING:

- A. S0346, Phase II study of trastuzumab (NSC-688097), celecoxib or the combination in treatment of recurrent synovial sarcoma (SWOG trial). Study coordinator: Laurence Baker, M.D.

IV. ADMINISTRATIVE ACTIVITIES:

REGIONAL AND NATIONAL:

- A. Abstract Review Board, Bone and soft tissue pathology, United States and Canadian Academy of Pathology
- B. Invited Reviewer, Archives of Pathology and Laboratory Medicine
- C. Invited Reviewer, Journal of Surgical Oncology

V. OTHER RELEVANT ACTIVITIES:

- A. Search Committee, Director of Anatomic Pathology, U of M

INVITED LECTURES/SEMINARS:

- 1. Lecture and Slide Seminar. "Soft tissue tumors for the general pathologist," 22nd Annual M-Labs Symposium (Ann Arbor).

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Mendelson S, Wooley P, Lucas D, Markel D, The effect of hyaluronic acid on a rabbit model of full-thickness cartilage repair. Clin Ortho 1(424), 266-271, 2004.
- 2. Zmurko MG, Mott MP, Lucas DR, Hamre MR, Miller PR. Multicentric Osteoid Osteoma. Orthopedics 27(12): 1294-6, 2004.
- 3. Chuba PJ, Hamre MR, Yap J, Severson RK, Shamsa F, Lucas D, Amr A. Bilateral risk for subsequent breast cancer after lobular carcinoma in situ: Analysis of SEER data. J Clin Oncol (In Press)
- 4. Al-Abbadi MA, Saleh HA, Lucas DR, Tabaczka PM. Differential expression of her-2/neu receptor of invasive mammary carcinoma between caucasian and african american patients in the detroit metropolitan area. correlation with overall survival and other prognostic factors. breast cancer research and treatment (In Press)
- 5. Kraybill W, Spiro I, Harris J, Ettinger D, Trotti A, Lucas D, Blum R, Eisenberg B, RTOG 95-14: Phase II study of neoadjuvant chemotherapy and radiation therapy compared with radiation therapy in the management of high-risk, high-grade soft tissue sarcomas of the extremities and body wall. J Clin Oncol (In Press)

ARTICLES SUBMITTED FOR PUBLICATION:

- 1. Chughtai A, Cronin P, Kelly AM, Pagani FD, Lucas DR. Cardiac pseudosarcomatous fibromyxoid tumor: a review of the literature.
- 2. Hamre MR, Chuba PJ, Severson R, Lucas DR, Aref A, and Mott M. Survival after limb sparing versus radical surgery for malignant fibrous histiocytoma (MFH) of the extremity.

3. McHugh JB, Thomas DG, Herman JM, Baker LH, Adsay NV, Rabah R, Lucas DR. Primary versus radiation-associated craniofacial osteosarcoma: biologic and clinicopathologic comparison. *Am J Surg Pathol*
4. Rhode MG, Lucas DR, Krueger CH, Pu RT. Fine needle aspiration of spinal osteoblastoma in a patient with lymphangiomatosis. *Diag. Cytopathol*

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. McHugh JB, Thomas DG, Herman JM, Adsay NV, Rabah R, Baker LH, Lucas DR. Primary versus radiation-associated craniofacial osteosarcoma: biologic and clinicopathologic comparison. *Mod Pathol* 18 (Sup 1), 18A, 2005
2. Olsen SH, Thomas DG, Lucas DR. Cluster analysis of immunohistochemical profiles in malignant peripheral nerve sheath tumor (MPNST), Ewing sarcoma (EWS) and synovial sarcoma (SS) segregates distinct tumor subpopulations. *Mod Pathol* 18 (Sup 1), 20A, 2005
3. Thorson JA, Ruiz RE, Weigelin HC, Howard JK, Lucas DR. Detection and genotypic identification of characteristic fusion gene transcripts from formalin-fixed soft tissue tumor specimens using multiplex RT-PCR/capillary electrophoresis. *Mod Pathol* 18 (Sup 1), 22A, 2005
4. Thorson JA, Ruiz RE, Weigelin HC, Howard JK, Lucas DR. Detection and genotypic classification of *SYT/SSX* transcripts from synovial sarcomas using multiplex RT-PCR/capillary electrophoresis. *Mod Pathol* 18 (Sup 1), 22A, 2005
5. Hamre MR, Chuba PJ, Severson RK, Lucas D, Mott M: Pediatric chondrosarcoma: analysis of SEER data. 37th Congress of the International Society of Paediatric Oncology. (SIOP) Vancouver, Canada September 21-24, 2004.
6. Hamre MR, Chuba PJ, Severson RK, Lucas D, Mott M: Overall survival after limb sparing or radical surgery for malignant fibrous histiocytoma (MFH) of the extremity: Analysis of prognostic factors by using SEER data. International Sarcoma Meeting. Stuttgart, Germany June 15-17, 2005
7. Chuba PJ, Hamre MR, Severson RK, Lucas D, Mott M: 3480 cases of dermatofibrosarcoma protuberans. International Sarcoma Meeting. Stuttgart, Germany June 15-17, 2005
8. Case of the Week: PathologyOutlines.com. Epithelioid fibrosarcoma. Case #3, 4/15/05
9. Case of the Week: PathologyOutlines.com. Myxoid/round cell liposarcoma. Case #10, 6/10/05



**PETER C. LUCAS, M.D., Ph.D.
ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Sign-out of breast pathology transfer cases and extramural breast pathology consultation cases; 13 weeks
- B. Sign-out of internal breast pathology material (Room BE); 8 weeks
- C. Review of breast pathology cases for multidisciplinary breast care clinic; 18 weeks
- D. Pathology representative, weekly interdisciplinary Breast Care Conference; 18 weeks
- E. Autopsy pathology; 5 days

II. TEACHING ACTIVITIES:

- A. Medical Students (M2):
M2 Pathology Laboratory Instructor (Respiratory, Bone/Soft Tissue sequences);
7 labs (approx 14 hours)
- B. Medical Students (M4):
M4 Pathology/Radiology Correlation Course Instructor;
1 lecture/workshop (3 hours)
- C. Dental School:
Integrated Medical Sciences-III Course Instructor,
1 lecture (1 hour)
- D. Pathology House Officers:
 - a. Mentoring of breast pathology fellow; 18 weeks
 - b. Room BE sign-out of breast pathology, with resident instruction; 8 weeks
 - c. Autopsy supervision and sign-out (5 call days)

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

CURRENT:

- A. Principal Investigator (70% effort), "NF- κ B Signaling and the Molecular Pathogenesis of MALT Lymphoma" (Mentored Career Development Award), K08 CA094920, National Institutes of Health (NCI), \$684,500 (total direct costs), 7/1/02 – 6/30/07.
- B. Collaborator (0% effort), "Aberrant NF- κ B Activation in MALT Lymphoma Pathogenesis", Doris Duke Clinical Scientist Development Award, Fellow to Faculty Transition (McAllister-Lucas), 7/01/05 – 6/30/06

PENDING:

- A. Principal Investigator (25% effort), “Angiotensin II Signaling Through a Novel NF- κ B Pathway”, NIH R01 HL082914, 12/01/05 – 11/30/10
- B. Principal Investigator (20% effort), “A Novel Signaling Pathway Mediating Hypertension- and Obesity-dependent Insulin Resistance”, Michigan Diabetes Research and Training Center (DRTC) Pilot/Feasibility Program, 1/01/06 – 12/31/06
- C. Principal Investigator (10% effort), “A Novel NF- κ B Signaling Pathway Mediating Angiotensin II-Dependent Cardiovascular Pathology”, American Heart Association Grant-in-Aid, 1/01/06 – 12/31/07
- D. Collaborator (0% effort), “The Role of Homo-oligomerization in API2-MALT1 Mediated Oncogenesis”, American Society of Hematology Junior Faculty Scholar Award (McAllister-Lucas), 7/01/06 – 6/30/08

PROJECTS UNDER STUDY:

- A. Characterization of signaling pathways involved in Angiotensin II dependent vascular inflammation.
- B. Characterization of signaling pathways mediating obesity and hypertension related insulin resistance.
- C. Molecular mechanisms responsible for MALT lymphoma tumorigenesis.
- D. Biochemical properties of the API2-MALT1 fusion protein, the product of a t(11;18) translocation in MALT lymphoma.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Quality assurance for the breast pathology service
- B. Pathology residency training program candidate interviews
- C. Surgical pathology fellow candidate interviews

MEDICAL SCHOOL/HOSPITAL:

- A. Career Advisory Panel, Medical Scientist Training Program

V. OTHER RELEVANT ACTIVITIES:

- A. Member, Michigan Comprehensive Cancer Center

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Longo, K.A., Wright, W.S., Kang, S., Gerin, I., Chiang, S-H., Lucas, P.C., Opp, M.R., and MacDougald, O.A. (2004) Wnt10b inhibits development of white and brown adipose tissues. **J. Biol. Chem.**, 279:35503-35509
2. Williams, J., Lucas, P.C., Griffith, K.A., Choi, M., Fogoros, S., Hu, Y.Y., and Liu, J.R. (2005) Expression of Bcl-xL in ovarian carcinoma is associated with chemoresistance and recurrent disease. **Gynecol. Oncol.** 96:287-295
3. Degnim, A.C., Reynolds, C., Pantvaitya, G., Zakaria, S., Hoskin, T., Barnes, S., Lucas, P.C., Oh, K., Koker, M., Sabel, M.S., and Newman, L.A. (2005) Measured size of sentinel node metastasis improves prediction of nonsentinel node metastasis in breast cancer. **American Journal of Surgery**, in press
4. Rivers, A.K., Griffith, K.A., Hunt, K.K., Degnim, A.C., Sabel, M.S., Diehl, K.M., Cimmino, V.M., Chang, A.E., Lucas, P.C., and Newman, L.A. (2005) Clinicopathologic features associated with having four or more metastatic axillary nodes in breast cancer patients with a positive sentinel lymph node. **Annals Surg. Oncol.**, in press

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. McAllister-Lucas, L.M, Kuffa, P., Siu, K., Inohara, N., Nunez, G., and Lucas, P.C. (2004) The Role of homo-oligomerization in API2-MALT1 fusion protein-mediated NF- κ B activation and oncogenesis. **15th Annual Pediatric Research Symposium**, University of Michigan.
2. McAllister-Lucas, L.M, Kuffa, P., Siu, K., Lucas, P.C., Inohara, N., and Nunez, G (2004) Purification of a Bimp3-binding complex: A novel method for identifying critical lymphocyte signaling proteins. **Doris Duke Charitable Foundation Clinical Research Symposium**, Cold Spring Harbor Laboratories.
3. McAllister-Lucas, L.M., Kuffa, P., MacDonald, C., Siu, K., Lucas, P.C., and Nunez, G. (2005) The role of homo-oligomerization in API2-MALT1 fusion protein-mediated NF- κ B activation and lymphomagenesis. **18th Annual Meeting of the American Society of Pediatric Hematology and Oncology**, Washington, D.C.

**NICHOLAS W. LUKACS, Ph.D.
ASSOCIATE PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENT REPORT
1 JULY 2004-30 JUNE 2005**

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

- A. Dental School. Lectures on Inflammation, cytokines and Chemokines
- B. Immunology 850, Course Director, Fall and Winter.
- C. Pathology 581, Graduate Students. Lectures on Inflammation and Immune responses.
- D. Pathology 643, Course Director, Immune mechanisms of Disease, Fall, 2005.
- E. Post-doctoral fellows- Allen Baptist, Barb Steffes, Jetse Smit, Dennis Lindell, Vladislav Dolgachev
- F. Graduate Students- Molly Thomas, Matt Schaller, Brian Rudd

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. RO1 AI36302-07 (Lukacs, N.W. PI), 8/1/96-7/30/06, 25%, "Role of chemokines in eosinophil airway inflammation" - The major goals of this project are to evaluate the cytokine-chemokine networks in the initiation of asthmatic responses by Respiratory syncytial virus (RSV) infections.
- B. RO1 HL59178-05 (Lukacs, N.W., PI), 5/1/98-4/30/08, 20%, "Role of SCF in airway eosinophil inflammation" - The major goals of this grant is the activation of eosinophil inflammation via Stem cell Factor (SCF) production within the airway during allergen introduction, leading to the activation of mucus overproduction via EGFR.
- C. PO1 HL (Lukacs, PI, Project IV), 3/1/99-2/28/10, 20%, "Cockroach allergen-induced airway inflammation" - NIH Program Project, Project IV; P.A. Ward, M.D., Program Director.
- D. R43-AI060202-01 (Lukacs, PI, consortium SBIR), 4/1/04-3/31/05, 5%, "NMSO3: A Novel therapy for Respiratory Syncytial Virus" - This proposal is in Collaboration with Microbiotex, Inc. in a Phase II SBIR grant to examine the effects of a specific anti-viral using our animal model of RSV infection.
- E. P50 HL 56402- (Galen Toews, PI), 12/1/96-11/30/06, 5%, Co-Investigator, "Fibrotic cytokine phenotypes in interstitial lung disease" Project 3, NIH Special Centers of Research (SCOR) grant, with Steven L. Kunkel, Ph.D. - The major goals of this project are to assess pathologic mechanisms involved in progressive and proliferative lung disease.

- F. P50 HL60289 (Theodore Standiford, PI), 12/01/98-11/30/08, 10%, Co-Investigator, "Acute Lung Injury", Project 2, NIH Special Centers of Research (SCOR) grant, Project 3 with Steven L. Kunkel, Ph.D. This project of the SCOR investigates the diverse effects of monocyte chemotactic protein-1 in systemic inflammation response syndromes, comparing animal models to patient specimens.
- G. RO1 HL69865 (Cory Hogaboam, P.I.), 8/15/03-7/30/07, 10%, "Targeting of RANTES/CCL5 during chronic fungal asthma" - The main goal of this grant is to determine the role of RANTES in chronic fungal asthma and whether a therapeutic strategy could help attenuate fibrotic airway disease.

TRAINING GRANTS (T32-FACULTY MENTOR):

- A. Pathology pulmonary training grant. Peter A. Ward, PI.
- B. Pediatric Training grant. Janet Gilsdorf, PI.
- C. Pulmonary and Critical Care Medicine Fellows Training grant. Galen Teows, PI.
- D. Immunologic Sciences Training Grant. Richard Miller, PI.

PROJECTS UNDER STUDY:

- A. Role of chemokines and their receptors in pulmonary immune responses (allergic and viral).
- B. Viral activation of TLR3 in determining the pulmonary immune environment
- C. The role of stem cell factor (SCF) and its receptor c-kit in the development of chronic pulmonary disease.
- D. The signal transduction of chemokine and toll-like receptors on immune and non-immune cell populations.

IV. ADMINISTRATIVE ACTIVITIES:

- A. Departmental representative- Curriculum Committee for Graduate program, PIBS.
- B. Admissions Committee- Immunology Graduate Program in PIBS.
- C. Curriculum Committee for Pathology Graduate Program.
- D. Director of Preliminary exam committee for Pathology Graduate Program.

UNIVERSITY AND MEDICAL SCHOOL:

- A. Immunology Training Grant T-32 (NIAID) Steering committee (2003-present)
- B. Institutional Biosafety Committee (IBC) (2004-present)
- C. Advisory committee on Appointments, Promotions, and Tenure (ACAPT). (2004-2007)
- D. Associate Chairs of Research Committee for the Medical School (2004-present)

REGIONAL AND NATIONAL:

- A. Editorial Boards:
 - 1. Section Editor - Journal of Interferon & Cytokine Research (January 1, 2003)
 - 2. Editorial Boards- Lab. Investigation (Jan, 2004)
 - 3. Amer. J. Pathology (Jan, 2004).
- B. Reviewer for the following Journals:
 - 1. Journal of Immunology
 - 2. American Journal of Pathology
 - 3. American Journal of Respiratory Cell and Molecular Biology
 - 4. Infection and Immunity
 - 5. Immunology Today
 - 6. European Respiratory Journal
 - 7. Journal of Experimental Medicine
 - 8. Hepatology
 - 9. Shock
 - 10. Journal of Leukocyte Biology
 - 11. Cellular Immunology
 - 12. BLOOD
 - 13. Journal of Clinical Investigation
 - 14. Journal of Allergy and Clinical Immunology
 - 15. Science
 - 16. Nature Journals
- C. Grant Review committees:
 - 1. NIAID, AITRC grant review committee, standing member until June, 2005.
 - 2. Special Emphasis –Hyper-ID- grant review panel, 6/04, 11/04, 12/04, 2/05, 4/05.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

- 1. Cytokines and chemokine targets in asthmatic lung disease. Pharmacopia, Princeton, NJ. August 18th, 2004.
- 2. Alteration of the pulmonary immune environment by RSV and asthmatic disease. NIEHS/NIH, Pulmonary Biology Section. RTP, NC. September 8th, 2004.
- 3. Chemokine receptors in Asthma. Symposium presentation. American Association of Allergy, Asthma and Immunology (AAAAI) Annual Meeting. San Antonio, TX. March 18th, 2005.
- 4. Inflammation and Immunopathology of Disease. Symposium. ASIP Annual meeting at Experimental Biology 2005. April 2, 2005.
- 5. The role of chemokines in Pulmonary disease. University College of Dublin, Institute for Scientific Research, Dublin, Ireland, April 19, 2005.

PATENTS AND DISCLOSURES:

- A. C-x-CR2 binding chemokines in treatment of acute liver damage. Cory Hogaboam, Steven Kunkel, Robert Strieter, Ken Simpson, and Nicholas Lukacs. 1998. #US 6,719,969 B1(patent issued 2004).

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERREED JOURNALS:

1. Liu, T., H. Jin, M. Ullenbruch, B. Hu, N. Hashimoto, B. Moore, A. McKenzie, NW Lukacs, and S.H. Phan. Regulation of FIZZ1 in bleomycin-induced lung fibrosis: Role of IL-4/IL-13 and mediation via STAT6. *J. Immunol.* 173(5):3425-31, 2004.
2. Alison John, Aaron A. Berlin and Nicholas W. Lukacs. The role of CCL28 in the development of allergic eosinophilic airway inflammation. *Am. J. Pathol.* 166(2):345-53.
3. Aaron A. Berlin and Nicholas W. Lukacs. Treatment of cockroach allergen asthma model with Gleevec attenuates airway responses. *AJRCCM* 171(1):35-9, 2005.
4. Alison E. John, Craig J. Gerard, Allison L. Miller, Aaron A. Berlin, Matthew A. Schaller, Allison A. Humbles, and Nicholas W. Lukacs. Respiratory syncytial virus induced exaggeration of allergic airway disease is dependent upon CCR1-associated immune responses. *Eur. J. Immunol.* 35(1):108-16, 2004.
5. Brian D. Rudd, Ezra Burstein, Colin Duckett, Xiaoxia Li, and Nicholas W. Lukacs. Differential role of TLR3 in RSV induced chemokine expression. *J. Virology* 79(6):3350-7.
6. Christine M. Freeman, Bo-Chin Bhiu, Valerie R. Stolberg, Jerry Hu, Kyriaki Zeibecoglou, Nicholas W. Lukacs, Sergio A. Lira, Steven L. Kunkel, and Stephan W. Chensue. CCR8 is expressed by antigen-elicited, IL-10 producing CD4+CD25+ T cells which regulate Th2-mediated granuloma formation. *J. Immunol.* 174(4):1962-70.
7. R.L. Warner, N.W. Lukacs, S.D. Shapiro, N. Bhagarvathula, K.C. Nerusu, J. Varani, and K.J. Johnson. Role of Metalloelastase in a model of allergic lung responses induced by cockroach allergen. *Am. J. Pathol.* 165:1921-1930, 2004.
8. Steven K. Lundy, Sergio A. Lira, Donald N. Cook, Aaron A. Berlin, and Nicholas W. Lukacs. Attenuation of allergen-induced responses in CCR6^{-/-} mice is dependent upon altered pulmonary T lymphocyte activation. *J. Immunol.* 174(4):2054-60.
9. Zeng X, Moore TA, Newstead MW, Deng JC, Lukacs NW, and Standiford TJ. IP-10 Mediates Selective Mononuclear Cell Accumulation and Activation in Response to Intrapulmonary Transgenic Expression and During Adenovirus-Induced Pulmonary Inflammation. *J Interferon Cytokine Res.* 2005 Feb;25(2):103-12.
10. Matthew A. Schaller, Steven K. Lundy, Gary B. Huffnagle¹, and Nicholas W. Lukacs. Tc2: CD8⁺ T cell contributions to type 2 mediated eosinophil response and airway hyperreactivity. *Eur. J. Immunol.*, June 10, 2005.
11. Ziegelbauer, K., F. Gantner, N. W. Lukacs, A. Berlin, K. Fuchikami, T. Niki, K. Sakai, H. Inbe, K. Takeshita, M. Ishimori, H. Komura, T. Murata, T. Lowinger, and K. B. Bacon. 2005. A selective novel low-molecular-weight inhibitor of IkappaB kinase-beta (IKK-beta) prevents pulmonary inflammation and shows broad anti-inflammatory activity. *Br J Pharmacol* 145:178.
12. LaFleur, A. M., N. W. Lukacs, S. L. Kunkel, and A. Matsukawa. 2004. Role of CC chemokine CCL6/C10 as a monocyte chemoattractant in a murine acute peritonitis. *Mediators Inflamm* 13:349.

13. Benjamim, C. F., S. K. Lundy, N. W. Lukacs, C. M. Hogaboam, and S. L. Kunkel. 2005. Reversal of long-term sepsis-induced immunosuppression by dendritic cells. *Blood* 105:3588.
14. Chen, G. H., R. A. McDonald, J. C. Wells, G. B. Huffnagle, N. W. Lukacs, and G. B. Toews. 2005. The gamma interferon receptor is required for the protective pulmonary inflammatory response to *Cryptococcus neoformans*. *Infect Immun* 73:1788.

BOOKS/CHAPTERS IN BOOKS

1. Miller AL, Lukacs NW. Chemokine receptors: understanding their role in asthmatic disease. *Immunol Allergy Clin North Am*. 2004 Nov;24(4):667.
2. MS Thomas, AL Miller, and NW Lukacs. 2005. Chemokines and chemokine receptors in pulmonary disease. *Current Topics in Membranes*. Volume 55 (In Press).

**STEVEN H. MANDELL, M.D.
ASSISTANT PROFESSOR
M-LABS PROGRAM DIRECTOR
SENDOUTS MEDICAL DIRECTOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL FACULTY REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. General surgical pathology and surgical consultation sign-out, MLabs (10% effort)
- B. Surgical pathology specialty coverage alternate, placental pathology (1 week) and breast pathology consultations (2 weeks).
- C. Clinical consultations for Sendouts (reference lab) and MLabs client inquiries

II. TEACHING ACTIVITIES (5% effort):

- A. Graduate students:
 - 1. Special project consultant for two graduate students in the school of engineering (Nimisha Srivastava and Rohit Pal) developing a miniaturized microfluidics viscometer regarding FDA approval of medical point of care testing devices, systems analysis, sales, pricing and marketing strategies, and technology transfer; their presentation won 3rd place at the 2005 Venture Challenge Competition in San Diego.
- B. Medical Students:
 - 1. M-1 Pathology Laboratory Coverage for Dr. Fantone and Dr. McKenna (4 hours).
- C. Medical Technology Students:
 - 1. Lunch and learn lecture, "Client Service Initiatives" (1 hour)
- D. Pathology Residents:
 - 1. Clinical Pathology Rotation B, monthly orientation: sendouts initiatives and make vs. buy analyses (2 hours/month)
- E. Nurses:
 - 1. Continuing education during nursing blitz, specimen processing

III. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Lab Handbook Committee
- B. Quality Assurance Committee
- C. Medical Director, MLabs (75% effort)
 - 1. Daily operational oversight, problem solving, planning and improvements
 - 2. Client site visits and communication meetings
 - 3. Team lab web portal RFP development, selection and implementation planning
 - 4. Automated QA program initiative using Risk Management Pro Software Product
 - 5. Implemented automated survey tool using Advisor-123.com
 - 6. Automated, web-based forms for M-Labs clients and internal projects initiated
 - 7. Joint marketing program for Botsford and MLabs

8. Strategic planning using Microsoft Visio implemented
9. New client recruitment and client retention efforts.
- D. Medical Director, Sendouts (10% effort)
 1. Daily operational oversight, problem solving, planning and improvements
- E. Professional Development and Process Improvement
 1. Attended Lab Infotech Summit, March 2005
 2. Visited Specialty Laboratories, March 2005
 3. Attended CLMA conference, March 2005
 4. Six Sigma Green Belt Certificate Program-Healthcare Industry Focus and QE Tools Course, June 2005
 5. Initiated Lean Six Sigma program education and implementation processes for department
 6. Dr. Michael Laposata's conference on "Diagnostic lab testing algorithms" at the Michigan Society of Pathologists' Annual Meeting
 7. Dr. David Grignon's lectures on "Current classification of renal epithelial neoplasms with emphasis on differential diagnosis and new entities" at the Michigan Society of Pathologists' Annual Meeting
 8. Attended audio conferences on point-of-care testing, billing compliance and outreach laboratory initiatives.

MEDICAL SCHOOL/HOSPITAL:

- A. Clinical Computing Advisory Committee
- B. Michigan Health Corporation representative to Joint Venture Hospital Labs (JVHL)

REGIONAL AND NATIONAL:

- A. Michigan Cancer Consortium – Basic Pathology Lexicon for Cancer – Steering Committee. Designing and implementing strategies to improve the reporting frequency, quality and character of cancer prognostic parameters for the state of Michigan
- B. Michigan Society of Pathologists' Representative to the Michigan Cancer Consortium Board of Directors Cross-organizational representative and communications liaison
- C. Michigan Cancer Consortium – Evaluations Subcommittee. Designing and implementing strategies to quantify and document the scope and effectiveness of MCC member organizations in forwarding MCC initiatives

IV. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "Point of Care Testing: Systems Analysis and Device Evaluation", invited Lecturer, in "Review of University of Michigan Technology: Microfluidics and Lab-on-a-chip for Medical Diagnostics." Michael Krihak, PhD - NASA Johnson Space Center's visit to Engineering Professor Mark Burn's Laboratory and U of M Engineering School, Lurie Engineering Center, Ann Arbor, October 7, 2005.
2. "Ethics – Coding and Reimbursement." University of Michigan Pathology Grand Rounds, March 15, 2005.
3. "Ethics – Results Reporting." University of Michigan Pathology Grand Rounds, April 19, 2005.

4. "MLabs Life Cycle – All in the Family." University of Michigan CP Faculty and Lab Communications Council Meetings, November 2005.
5. "Pathology Lab Orientation." Welcome and orientation for departmental Bring Your Child to Work Day 2005.

V. PUBLICATIONS:

**ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR,
MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:**

1. Mandell S, Sitwala K. "Laboratory Testing for Myasthenic and Paraneoplastic Syndromes." MLabs Spectrum featured article (submitted/accepted for publication June 20, 2005).

**PAUL E. McKEEVER, M.D., Ph.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 – 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Daily weekday and weekend 24 hour surgical neuropathology call. Individual case follow up, immunohistochemical and special stains. and electron microscopic neuropathology; weekly Brain Tumor Board, review of neurosurgical, neuroradiologic, neuropathologic and clinical-pathologic correlation, 28 weeks. Surgical neuropathology case load is four times the national average.
- B. Diagnostic neuropathology consultant, Veterans Administration Hospital.
- C. Examination of all University Hospital autopsy neuropathologic material – brain cutting, sampling, microscopic examination, and special stains.
- D. General autopsies, 12 days.

**II. TEACHING ACTIVITIES:
DEPARTMENTAL:**

- A. Medical Students:
 - 1. Neuroscience Sequence, Neuropathology for Second Year Medical Students. Prepared two laboratories and two lectures on brain tumors; toxic, metabolic, demyelinating and infectious diseases. Taught four laboratories.
 - 2. Senior medical student Neuropathology electives Bret Mobley, Leo Chen, Genevieve Kruger, Jonathan Morrow, - M4 mentoring.
 - 3. Three lectures per year to Dental students on Neuropathology.
- B. House Officers:
 - 1. Brain cutting, sampling, microscopic examination and special stain instruction of pathology and clinical House Officers.
 - 2. Individual instruction of Pathology, Neurology and other House Officers on neurosurgical biopsy material, 28 weeks.
 - 3. Review neurosurgically removed material in the hospital in CME-approved Thursday Special Conferences rotated with other faculty monthly conference, 27 weeks.
 - 4. Invited presentations of neuropathologic observations at various clinical conferences and CPC conferences.
 - 5. Pathology Resident's Tuesday AP Conference rotated with other faculty.
 - 6. One month House Officer Electives.
 - 7. Autopsy call, and Pathology Gross Conference.

- C. Review laboratory techniques with UMMC Histologists.
- D. Other Faculty: Brain Tumor Board, CPC, and other joint clinical conferences.

REGIONAL AND NATIONAL:

- A. Faculty, "New Methods of Brain Tumor Analysis": Annual AFIP Kenneth M. Earle Memorial Neuropathology Reviews, Armed Forces Institutes of Pathology, Rockville, Maryland, 2003, 2004, 2005.

III. RESEARCH ACTIVITIES:

- A. Study of pituitary adenoma hypophyseal stroma with Drs. Jason Jarzembowski and Ricardo V. Lloyd.
- B. Isolation and characterization of neural cancer stem cells with Dr. Sean Morrison, 5% effort on grant.
- C. Tumor proliferation and apoptosis in transgenic mice with Drs. Brian D. Ross and Thomas Chenevert, 10% effort on grant.
- D. Mechanisms of glioma and medulloblastoma formation in p53 genetically altered mice with Dr. Yuan Zhu.
- E. Correlation of MIB-1 and tumor progression of resected meningiomas with Dr. Byron Greg Thompson.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Chief, Section of Neuropathology.
- B. Director, Neuropathology Residency Training. Full accreditation from the Accreditation Council for Graduate Medical Education obtained in 1996, status inactive for lack of funds.
- C. Member, Photography Committee.
- D. Member, Immunoperoxidase Committee.

MEDICAL SCHOOL/HOSPITAL:

- A. Organization and scheduling of Pathology, Neurology, Neuroradiology and Neurosurgery House Officer Neuropathology teaching conferences, individual instruction and consultation review.
- B. Organization of call logistics, specimen handling, and schedules for coverage of diagnostic neuropathology by staff.
- C. Interaction with Chiefs and Staff of other clinical services, particularly Neurosurgery, Neurology, Nuclear Medicine, Radiation Oncology, Neuro-oncology and Neuroradiology.
- D. Quality control of microscopic, ultrastructural and immunodiagnostic neuropathology. This included various ad hoc reviews requested by faculty and staff.

REGIONAL AND NATIONAL:

- A. Editorial Board, Journal of Histochemistry and Cytochemistry.
- B. Primary Review Pathologist, Children's Cancer Study Group CCG 9897 nationwide study of childhood low grade gliomas.
- C. Reviewer for many journals including the following:
 - 1. Journal of Neuropathology and Experimental Neurology.
 - 2. Journal of Histochemistry and Cytochemistry.
 - 3. American Journal of Pathology.
 - 4. Archives of Pathology and Laboratory Medicine.
- D. Member, Brain Tumor/EMF Study Scientific Advisory Panel, National Cancer Institute, Jonathan Samet, Chairman.
- E. M-Labs Neuropathology Services.
- F. Program Project Site Visit Committee, National Cancer Institute, Berkeley, California.
- G. Subcommittee E – Cancer Epidemiology, Prevention and Control, National Cancer Institute, Bethesda, Maryland

V. OTHER RELEVANT ACTIVITIES:

PROFESSIONAL ORGANIZATIONS:

- A. Faculty of Graduate Program of Department of Pathology.
- B. Member, International followed by U.S. & Canadian Academy of Pathology, 1972 --.
- C. Member, Alpha Omega Alpha, Eta Chapter, 1972 --.
- D. Member, American Association of Neuropathologists, 1978 --.
- E. Member, Society of Neuroscience, 1983 --.
- F. Member, American Association of Pathologists, 1984 --.
- G. Member, Children's Cancer Study Group, 1985 --.
Pathology Committee, 1989 --.
- H. Member, Histochemical Society, 1989 --.
Constitution Advisor 1996 --.Make certain that Council functions in accord with constitution.
- I. Lieutenant Colonel, U.S. Army Reserve Medical Corps, 1997 --.
 - 1. Duty station AFIP, 1997-2005
 - 2. Duty station Pathology Dept., Walter Reed Army Medical Center, 2005 --

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Jain R, Mukherji SK, Garton H, Gujar S, **McKeever PE**, Robertson P.: Imaging findings of childhood primary intracranial squamous cell carcinoma. *Am. J. Neuroradiol* 24:109-111, 2003.
2. Hassan AS, Trobe JD, **McKeever PE**, Gebarski SS: Linear magnetic resonance enhancement and optic neuropathy in primary angitis of the central nervous system. *Journal of Neuro-Ophthalmology* 23: 127-31, 2003.
3. **McKeever PE**, Junck L, Li L, Mena H, Tkaczuk A, Yan M.: Block age affects MIB-1 proliferation indices. (in preparation).
4. Wechsler SB, Howrylak J, Jarzembowski JA, **McKeever PE**, Gordon D, and Petty E: Siblings with microencephaly, developmental delay and dilated cardiomyopathy. (submitted)
5. Mobley BC, Roulston D, Shah, GV, Bijwaard KE, and **McKeever PE**: Peripheral PNET/Ewing sarcoma in the craniospinal vault: case report and review. (submitted)
6. Jarzembowski JA, Lloyd RV, **McKeever PE**. Type IV collagen immunostaining provides a simple, reliable way to distinguish between adenoma and normal pituitary. *Modern Pathology* 18 Suppl 1:92A. Presented at the Annual Meeting, United States and Canadian Academy of Pathology, San Antonio, Texas, February 26-March 4, 2005.

BOOKS/CHAPTERS IN BOOKS:

1. **McKeever PE**: New Methods of Brain Tumor Analysis. In: *Kenneth M. Earle Memorial Neuropathology Review*. Armed Forces Institute of Pathology, Washington, D.C., 2005, pp.1-54.
2. **McKeever PE**: Glial cell pathology. In: *Encyclopedia of Neuroscience, Elsevier Science, 3rd edition*. Smith BH and Adelman A, eds., (in press).
3. **McKeever PE**: Laboratory methods of brain tumor analysis. In: *Principles and Practice of Neuropathology*. Nelson JS, Mena H, Parisi J, Schochet S (Eds). Oxford, New York 2003, pp. 272-297.
4. **McKeever PE**: Immunohistochemistry of the nervous system. In: *Diagnostic Immunohistochemistry, 2nd edition*. Dabbs DJ (Ed). (in press).
5. **McKeever PE**, Boyer P: The brain, spinal cord, and meninges. In: *Sternberg's Diagnostic Surgical Pathology, 4th edition*. Mills SE, Greenson JK, Carter, D, Reuter VE, Stoler MH, Oberman HA (Eds). Lippincott, Philadelphia 2004, pp. 399-503.

**BARBARA J. MCKENNA, M.D.
ASSOCIATE PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. General surgical pathology – 1 month.
- B. Gastrointestinal and hepatic pathology services - 6 months.
- C. Cytology Services—2.5 months.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

- A. Medical Students:
 - 1. Pathology 600 - laboratory 2-4 hours per 3 weeks
 - 2. Pathology 500—laboratory 4 hours
 - 3. Senior Elective in Pathology: supervising during diagnostic signout
- B. House Officers:
 - 1. Surgical pathology diagnosing room instruction for assigned house officer – 3 months
 - 2. Cytopathology service, cytopathology fellows and resident instruction—2.5 months
- C. Gastrointestinal and hepatic pathology tutoring - full time.
 - 1. Lectures in gastrointestinal and liver pathology, 2 hours
 - 2. Consult conferences, 4-5 hours
 - 3. Cytology conferences, 4 hours
- D. Interdepartmental:
 - 1. G-I Tumor Conference - (2-3 hours per month).
 - 2. Liver Biopsy Conference – 4 hours per year.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Anaplastic, lymphoma-like carcinoma arising in Barrett's mucosa, with HD Appelman
- B. The apoptotic form of microscopic colitis, with HD Appelman
- C. What is the yield of significant microscopic disease in colorectal biopsies of adult patients with chronic diarrhea and normal endoscopic findings? With HD Appelman

- D. G cells in the duodenal bulb and their response to therapy. With Wei Xin and HD Appelman
- E. Marginal collagenous colitis: does it exist? With HD Appelman, W Xin, M Anderson and L Evans
- F. The prevalence of unsuspected invasive carcinomas in specimens resected for high-grade dysplasia in Barrett's mucosa and the gastric cardia. With Weijian Zhu, HD Appelman, Steven Ramsburgh, Joel Greenson and members of the Section of Thoracic surgery
- G. The yield of significant microscopic findings in terminal ileal biopsies and their relation to indications for endoscopy and endoscopic findings, with Jon McHugh and HD Appelman
- H. The yield of significant microscopic findings in duodenal biopsies with the clinical suspicion of celiac diseases, with C Golembeski and J Greenson
- I. Comparison of routine cytologic evaluation and molecular analysis of pancreatic EUS-guided FNA, with Michelle Anderson
- J. A trial of fenofibrate therapy for nonalcoholic fatty liver disease, with H Conjeevaram
- K. The underlying pathophysiology of hepatitis C and hepatic steatosis, with C Burant, H Conjeevaram and H Hussain
- L. MRI evaluation of fatty liver, comparison with histology, with H Hussain

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Residency committee

MEDICAL SCHOOL/HOSPITAL:

REGIONAL AND NATIONAL:

- A. Ambassador, United States and Canadian Academy of Pathology
- B. Board of Directors, American Society for Clinical Pathology
- C. Chair, Commission on Assessment, American Society for Clinical Pathology
- D. Chair, ASCP Resident Inservice Examination (RISE) Committee
- E. Chair, ASCP Maintenance of Certification Committee
- F. Co-Director for AP and Lecturer, ASCP Resident Review Course
- G. Advisor, ASCP Resident Council

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

- A. Editorial Board, Human Pathology

HONORS AND AWARDS

- A. Fall 2003 Component I, Medical Student Award for Teaching Excellence (notified April 28, 2005)

INVITED LECTURES/SEMINARS:

1. Visiting Professor Lecture on Non-IBD Colitis and Slide Seminar for Residents and Faculty, Berkshire Medical Center Department of Pathology, Pittsfield, MA, August 17, 2004
2. "Dysplasia is a pain in the gut" Roger C. Haggitt Society of Gastrointestinal Pathology Companion meeting, at ASCP Annual Meeting, San Antonio, Texas, Oct. 6, 2004
3. "Surgical Pathology Reports—communication or obfuscation?" Roundtable discussion at ASCP Annual meeting, San Antonio, Texas, Oct. 9, 2004
4. "Dysplasia in the gastrointestinal tract: There's something for everyone" Flint Area Pathologists meeting, March 30, 2005.
5. "Just Another Day on the GI Biopsy Service", with HD Appelman, Annual Meeting, American Society for Clinical Pathology, San Antonio, TX, October 9, 2004; Kansas City Society of Pathologists/The Kansas Society of Pathologists, Kansas City, MO, Oct 23, 2004; 24th Annual Current Issues in Surgical Pathology, Southwestern Medical School, Dallas, TX, May 12, 2005;
6. "Troublesome Gastrointestinal Biopsies" Microscopic tutorial, Annual Fall Meeting, American Society of Clinical Pathologists, San Antonio, TX, October, 2004;
7. "RISE and be Counted", American Society for Clinical Pathology companion meeting at the annual meeting of the United States and Canadian Academy of Pathology, San Antonio, TX, February 28, 2005

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Hussain HK, Chenevert TL, Londy FJ, Gulani V, Swanson S, McKenna BJ, Appelman HD, Adusumilli S, Greenson J. MR imaging for quantitative measurement and display of hepatic fat fraction. Accepted for publication in Radiology, 2005
2. DiMagno MJ, Lee S-H, Hao Y, Zhou S, McKenna BJ, Owyang C. A proinflammatory, anti-apoptotic phenotype underlies the susceptibility to acute pancreatitis in UNC cfr (-/-) mice. Accepted for publication, Gastroenterol, 2005

CHAPTERS and BOOKS:

1. McKenna BJ, Appelman HD, Neoplasms of the small intestine, in Quigley EE and Marsh MN, eds.: The Small Intestine, Blackwell Scientific, Cambridge, MA, in press

**ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR,
MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:**

1. Evans LT, Xin W, McKenna BJ, Appelman HD, Anderson MA. Microscopic colitis with minimal collagen: is this lymphocytic colitis or collagenous colitis? *Am J Gastroenterol*. 99 (Supplement):S265, 2004
2. JB McHugh, HD Appelman, BJ McKenna. What is the value of endoscopic terminal ileal biopsies? *Mod Pathol* 2005;18:112A
3. W Xin, LT Evans, HD Appelman, MA Anderson, BJ McKenna. Minimal collagenous colitis: microscopic colitis with minimal subsurface collagen is appropriately diagnosed as collagenous colitis. *Mod Pathol* 2005;18:123A
4. BJ McKenna, MD and L Culver-Edgar, MBA, MT(ASCP). Pathology resident education in laboratory administration is less effective than other areas of pathology, as measured by the ASCP Resident Inservice Examination (RISE). Presented at the Institute for Quality in Laboratory Medicine Meeting, Atlanta, GA, April, 2005
5. M.J. DiMagno, S.H. Lee, Y. Hao, B. McKenna, J.A. Williams, C. Owyang. A proinflammatory, anti-apoptotic phenotype underlies the susceptibility to acute pancreatitis in UNC cfr (-/-) mice. Presented at 2005 ASCI/AAP Joint Meeting, Chicago, IL, April 2005
6. McKenna BJ, Greenson JK, Appelman HD. Which Barrett's biopsies should be reviewed by expert pathologists? *Gastroenterol* 2005;128:A-238-9
7. McKenna BJ, Greenson JK, Appelman HD. The Diagnosis of Barrett's biopsies sent for expert pathologist consultation depends on the expert: not all experts are alike! *Gastroenterol* 2005;128:A-239
8. Book review: McKenna BJ. Liver Biopsy Interpretation, by Stephen Geller and Lydia Petrovic. *Am J Surg Pathol* 2005;29:139-40

DERVLA MELLERICK-DRESSLER, PhD
ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005

I. **CLINICAL ACTIVITIES:**

None.

II. **TEACHING ACTIVITIES:**

A. Graduate students:

1. Course Lectures - Path 581, 3.0 hours Pharmacology 481, faculty group leader, 24.0 hours.
2. Fall rotation mentor for Zachary Gaber, doctoral candidate.

III **RESEARCH ACTIVITIES:**

SPONSORED SUPPORT:

- A. Principal Investigator, NIH R01 " How does the *Drosophila vnd* homeobox gene integrate positional information?" 35% effort.
- B. Co-investigator, NIH R01 "Cell Signaling in Developing Epithelia." 35% effort.
- C. Principal Investigator, NIH R21 "NKx2.2 pancreas specific targets." 35% effort.

PENDING:

- A. Principal Investigator, BBRC Interim Funding "Homeobox Genes and the Combinatorial CNS Code"
- B. Principal Investigator, OVPR grant "Vnd-specific target genes."
- C. Consultant NIH RO1 " Epigenetic Control of Kidney Development" G.Dressler, PI; 10% effort

PROJECTS UNDER STUDY:

- A. Development of the novel DAM ID profiling technique in *Drosophila* transgenic embryos to identify targets of the Vnd homeodomain protein.
- B. Identification of the mechanisms underlying the ability of the *vnd* and *ind* homeobox genes to specify neural stem cell identity in *Drosophila*.

- C. Determination of the function of the HLH protein, Olig, in *Drosophila* neurogenesis.
- D. Elucidation of the role of the extracellular BMP modulator, CV-2, in *Drosophila* epithelial patterning.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

- A. Organogenesis Center Seminar Committee member
- B. Prelim committee for Pathology graduate students, Kary Oetjen, Rebecca Csmos, and Haitao Wen.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

- 1. "Co-factor availability influences Vnd's capacity to regulate transcription." Neurofly. Goettingen, Germany, Oct 3, 2004.

VI. PUBLICATIONS:

- 1. Yu, Z. Syu, L-J. and Mellerick, D.M. (2005). Contextual interactions determine whether the homeodomain transcription factor Vnd acts as a repressor or an activator. *Nucleic Acids Res.* 33, 1-12.

ARTICLES SUBMITTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Uhler, J., Zhang, H. Syu L-J and Mellerick D.M. The NK-2 box of Vnd contributes to the repression activity of this homeodomain protein in a Groucho-dependent manner.
- 2. Syu L-J, Uhler, J., Zhang H., and Mellerick, D.M. Molecular mechanisms underlying the regulatory activity of *Drosophila Nkx6*.

**CLAIRE W. MICHAEL, M.D.
CLINICAL ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Cytopathology – Eighteen weeks.
- B. Thoracic Multidiscipline Conference – twelve months
- C. Breast Cancer Clinic, Cytopathology – twelve months
- D. Review all ductal lavage specimens – twelve months.
- E. Cytopathology Consultation Service, Department of Pathology - twelve months.
- F. Necropsy Service - one weekend.

II. TEACHING ACTIVITIES:

- A. Medical School Students:
 - 1. Mentor for medical students' senior clerkship – six weeks.
- B. Residents and Cytopathology Fellow:
 - 1. Sign out; Gynecologic and Non-Gynecologic Cytology cases.
 - 2. Instruction in the performance and interpretation of fine needle aspirates.
 - 3. Monthly Cytopathology Resident Conference.
 - 4. Weekly Cytopathology Fellowship Conference
 - 5. Consult Case Conference.
 - 6. Anatomic Pathology Conference: 2/year-Review of Cytopathology
- C. Other Education Activities:
 - 1. Developing slide and written test for competency evaluation of residents and fellows. (2002)
 - 2. Cytotechnologists - Cytopathology Slide Conferences. (2003)

III. **RESEARCH ACTIVITIES:**

SPONSORED SUPPORT:

- A. Co-Investigator (Principle Investigator: E-J Wamsteker, M.D.) ASGE Endoscopic Research Award (\$25,000) "Approaches to improve the cytologic diagnosis of pancreatico-biliary malignancy by ERCP", 0% effort, American Society for Gastrointestinal Endoscopy.
- B. Co-Investigator/Project Pathologist (Primary investigator: Daniel F. Hayes, M.D.), 0% effort, Daniel F. Hayes Breast Cancer Gift Fund, "A Pilot Study to Determine the Feasibility of Splitting Ductal Lavage Samples". (Phase I)
- C. Co-Investigator/Project Pathologist (Primary investigator: Daniel F. Hayes, M.D.), 0% effort, Daniel F. Hayes Breast Cancer Gift Fund, "Investigation of surrogate biomarkers of breast cancer risk and evidence of chemopreventive agent activity using ductal lavage samples."
- D. Co-Investigator/Project Pathologist (Primary investigator: Daniel F. Hayes, M.D.), 0% effort, Daniel F. Hayes Breast Cancer Gift Fund, "A pilot study to correlate change in mammographic density and to determine safety of tetratrismolyhdate chemoprevention in women at high risk for breast cancer."
- E. Co-Investigator/Project Pathologist (Primary Investigator: Lisa Newman, M.D.) "Feasibility Study of Evaluating Breast Cancer patients with Ductal Lavage" 0% effort
- F. Co-Investigator/Project Pathologist (Principle investigator: David Reisman, M.D.) American Lung Association, "Loss of BRG1 and BRM in non-small cell lung cancer-An alternate mechanism to disrupt the retinoblastoma pathway", 5% effort (\$35,000/year-direct cost).
- G. Co-Investigator/Project Pathologist. (Primary Investigator: Gustavo R. Rosania) Development of microanalysis methods for studying transport and secretory functions of mammary epithelia." (Pending)
- H. Co-Investigator/Project Pathologist. (Primary Investigator: Gustavo R. Rosania) "Develop laboratory analysis protocols to study shed vesicles originating from healthy and pathologic mammary epithelia." (Pending)
- I. Co-Investigator. (Primary Investigator: David Kurnit, M.D.) Sensitive and specific detection of human papilloma virus (HPV) associated with cervical malignancies and dysplasia determined by MASS Array Method. (Pending)
- J. Co-Investigator. (Primary Investigator: Daniel Hayes, M.D.) Spore in Breast Cancer. (Pending)

PROJECTS UNDER STUDY:

- A. Evaluation of common bile duct brushes by ploidy analysis.
- B. Establishing adequacy criteria for thyroid aspirates on ThinPrep slides.
- C. The utility of one versus two ThinPreps in fine needle aspirates.
- D. The utility of virtual imagining in producing reproducible cytological diagnosis.
- E. Evaluating the diagnostic ability of cytology in the work-up of malignant mesothelioma.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director, Cytopathology Laboratory.
- B. Director, Cytopathology Fellowship.
- C. Member, Residency Review Board.

MEDICAL SCHOOL/HOSPITAL:

None.

REGIONAL AND NATIONAL:

- A. Member, Editorial Board, Diagnostic Cytopathology
- B. Reviewer, Diagnostic Cytopathology.
- C. Reviewer, Cancer Cytopathology.
- D. Reviewer, Journal of Clinical Pathology
- E. Reviewer, Medical Science Monitor
- F. Reviewer, Archives of Laboratory Medicine
- G. Secretary, Papanicolaou Society of Cytopathology.
- H. Member, American Society of Clinical Pathologists, Non-Gynecologic Star Program
- I. Member, American Society of Cytopathology, Scientific Committee
- J. Chairperson, Educator of the Year Award Task Force, Papanicolaou Society of Cytopathology

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "The interpretation of cytologic specimens prepared by the ThinPrep technique". **Guest speaker**, McKee Cytology Seminar, Charleston, S.C. April 9, 2005.
2. "Pregnancy related changes on Pap smears". **Guest speaker**, McKee Cytology Seminar, Charleston, S.C. April 9, 2005.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Michael CW, Richardson PH, Boudreaux CW. Pulmonary lymphoma of the MALT type: report of a case with cytological, histological, immunophenotypical correlation, and review of the literature. *Annals of Diagnostic Pathology* 2005; 9:148-152.
2. Liu W, Michael CW. Malignant mesothelioma versus adenocarcinoma in serous fluids: The everlasting challenge. *Check Sample, American Society of Clinical pathology*, June 2005. Volume 33(7) No. C05-7(C-373).
3. Ruffin MT, Bailey BM, Normelle DP, Michael CW, Bjeniasz ME, Kmak DC, Unger ER, Brenner DE. Low dose topical delivery of All-Trans Retinoic acid for CINII and III. *Cancer Epidemiology: Biomarkers and prevention*. 2004; 13:2148-2152.
4. Afify A, Stern R, Michael CW. Differentiation of mesothelioma from adenocarcinoma in serous effusions: The role of hyaluronic acid on CD44 localization. *Diagn Cytopathol*, 2005; 32:145-150.
5. Dai Y, Bedrossian CWM, Michael CW. The expression pattern of Beta-Catenin in mesothelial proliferative lesions and its diagnostic utilities. (in press, *Diagn Cytopathol*).
6. Li Q, Bavikatty N, Michael CW. The role of Immunohistochemistry in distinguishing squamous cell carcinoma from mesothelioma and adenocarcinoma in pleural effusion (in press, *Diagn Cytopathol*.)

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Reiseman R, Georgina C, Michael CW, Johnson L. BRG1 is irreversibly altered while BRM is relatively silenced in cancer cell lines. (Submitted to *Cancer Research*).
2. Yang K, Yang H, Jin Y, Khafagi A, Li J, Tang Y, Opiari AW, Ruffin M, Patel D, Newton D, Michael CW, Oeth PA, Jia X-Y, and Kurnit DM. Sensitive and specific detection of the 13 types of human papillomavirus responsible for cervical dysplasia and cancer using multiplexed real competitive PCR and MassARRAY.
3. PuRT, Yang J, Wasserman PG, Bhuiya T, Griffith KA, and Michael CW. Does Hurthle cell lesion/neoplasm predict malignancy more than follicular lesion/neoplasm on thyroid fine needle aspiration? (submitted to *Diagn. Cytopathol*)
4. Siddiqui M, Su I, Michael C, Pu R. Synchronous ordinary lipoma and spindle cell lipoma diagnosed by FNA. (submitted to *Diagn. Cytopathol*)

**ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR,
MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:**

1. Zhu W, Michael CW. How important is on-site adequacy assessment for thyroid FNA? An evaluation of 883 cases. ASC, Nov 2004.
2. Pu, R, Bedrossian CW and Michael CW. Performance and cost analysis of immunohistochemistry stains on ThinPrep versus cellblock preparations in diagnosing adenocarcinoma in serous effusions. ASC, Nov, 2004.
3. W Zhu, Michael CW. WT1, Monoclonal CEA, TTF-1, and CA125 antibodies in the differential diagnosis of lung, breast and ovarian adenocarcinoma in serous effusions. Mod Path, 2005;18;365A.
4. Pu R, Michael CW. Does Hurthle cell lesion/neoplasm predict malignancy more than follicular lesion/neoplasm on thyroid fine needle aspiration? Presented at the 4th Asia-Pacific IAP Congress in Beijing 2005.
5. Pu R, Yang J, Wasserman PG, Bhuiva T, Griffith KA, and Michael CW. Outcomes of thyroid FNA diagnoses of follicular neoplasms/lesion vs Hurthle cell neoplasm/lesion : A two-institution experience (accepted for the American Society of Cytopathology 53rd Annual Scientific meeting, Nov 2005).
6. Bedrossian CWM, Michael CW, Risberg B, Schmitt F, Reis-Filho J, Davidson B. Novel techniques applied to effusion specimens: Bridging the gap between molecular biology and diagnostic pathology in malignant mesothelioma and mimics. Pulmonary Pathology Society, 4th Biennial Symposium, Annecy France, June 2005.

**RICHARD A. MILLER, M.D. PH.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Graduate students:

1. Responsible during the current academic year for teaching activities for the following:
 - a. Human Growth and Development Course "Biology of Aging", 1 hour.
 - b. Pathology 581, Cellular and Molecular Basis of Disease, 3 hour.
2. Immunology Program Prelim Exam Committee
3. Cellular and Molecular Biology Preliminary Examination Committee
4. Ph.D. Dissertation Committees, University of Michigan:
 - a. Lynn Kamen
 - b. Omer Yilmaz
5. Ph.D. Dissertation Advisor:
 - a. Tim Hale
 - b. Scott Berger
 - c. Adam Salmon
 - d. Scott Leiser

B. Postdoctoral Fellows:

- a. Amir Sadighi-Akha
- b. Shin Murakami
- c. Scott Maynard
- d. Kyoko Yasumura
- e. Oge Arum

C. In Lab:

1. Gonzalo Garcia, Ph.D., Research Investigator
2. James Harper, PhD. , Research Investigator
3. Ricky Malhotra, PhD, Research Assistant Professor

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, R. A. Miller, "Laboratory for Anti-Geric Testing, Evaluation and Research," NIH/NIA U01-AG022303-03, \$378,998 direct costs/year, 7/03-6/08.
- B. Principal Investigator, R. A. Miller, "Biomedical Research Training in the Biology of Aging," NIH/NIA T32 AG000114-21, \$378,495 direct costs/year, 5/05-4/10.
- C. Principal Investigator, S. Cummings, "A Consortium to Study the Genetics of Longevity," NIH/NIA U19-AG023122-01A1, \$200,420 direct costs/year, 10/1/04-6/30/09.
- D. Principal Investigator, R. A. Miller, "Wild Derived Mouse Stocks: New Models for Aging Research." NIH/NIA R01-AG13711-07, \$225,000 direct costs/year, 9/1/00 – 8/31/05.
- E. Principal Investigator, R. A. Miller, "Genetic Control of Longevity in Mice." NIH/NIA R01-AG11687-10, \$298,784 direct costs/year, 9/1/04 8/30/09.
- F. Principal Investigator, R. A. Miller, "Activation Defects in T Cells of Aged Mice," NIH/NIA R01-AG19619-04, \$250,000 direct costs/year, 9/30/00 – 8/31/05.
- G. Principal Investigator, R. A. Miller, "Genetics of Age-Sensitive Traits in Mice," NIH/NIA P01-16699-05 direct costs/year 5: \$637,739, 5/1/99–8/31/05. Core A (Administrative), R. A. Miller, \$31,575. Core C (Animal), R. A. Miller, \$26,671. Project 1 (Immunology), R. A. Miller, \$60,486.
- H. Program Director, R. A. Miller, "Research Training in Experimental Immunology," NIH T32-AI-07413-11, \$312,412 direct costs/year, 9/15/98 – 8/31/08.
- I. Principal Investigator, J. Halter, "Claude D. Pepper Older Americans Independence Center," NIH P30-AG08808-16, \$146,000 direct costs/year, 9/1/04-7/31/09. R. A. Miller serves as (a) Director, Core Facility for Aged Rodents, direct costs/year \$63,097; (b) Director, Research Development Core, \$60,154 direct costs/year; and (c) Project Director, "Weight Gain Trajectory and Life Span in Mice," \$103,510 direct costs/year.
- J. Principal Investigator, J. Faulkner, "Nathan Shock Center of Excellence in the Basic Biology of Aging," NIH P30-AG13283-10, \$139,000 direct costs/year, 9/1/95–6/30/05. R. A. Miller directs the Gene Expression Profiling Core and the Laboratory for Anti-Geric Testing.
- K. Principal Investigator, Andrzej Bartke, Southern Illinois University, "Gene expression and Biomarkers in Dwarf Mice," SIU Subcontract 02-17, component of R01-AG19899-03, \$32,894 direct costs/year, 9/1/01–8/31/06
- L. Principal Investigator, R. Buffenstein, "Mechanisms of Aging in the Long-Lived Naked Mole Rat." CCNY Subcontract., component of R01-AG022891-02, \$25,237 direct costs/year, 9/30/03-8/31/08. R. A. Miller subcontract for gene expression studies.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director, Experimental Immunology Training Program
- B. Director, Biomedical Research Training in Aging Program

MEDICAL SCHOOL/HOSPITAL:

- A. Director, Core Facility for Aging Rodents
- B. Member, Cancer Biology Training Program
- C. Member, Cell and Molecular Biology Training Program
- D. Member, Rheumatology Training Program
- E. Associate Director for Research, Geriatrics Center

REGIONAL AND NATIONAL:

- A. Board of Scientific Advisors, Buck Center for Research on Aging
- B. Chair, Research Committee, American Federation for Aging Research
- C. Vice-President, American Federation for Aging Research

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

- A. Journal of Gerontology: Biological Sciences.
- B. Aging: Clinical and Experimental Research
- C. Mechanisms of Ageing and Development
- D. Experimental Gerontology
- E. Aging Cell
- F. AAAS Science of Aging Knowledge Environment (SAGE-KE)

INVITED LECTURES/SEMINARS:

2004

1. Molecular Biology of Aging Course, Woods Hole, MA. "Not Your Father's Aging Rodent: New Models for the Biology of Aging." August 11.
2. Gordon Conference on Aging, Aussois, France. "How to Make a Really Old Mouse: Multiple Pathways to Super-Longevity." Sept 11 - 17.
3. Aging and Immunity Workshop, Trudeau Institute, Saranac Lake, NY. "Genetic Control of T Cell Maturation and Aging Rate." Oct 2 - 5.
4. Department of Nutritional Sciences, University of Alabama, Birmingham, AL. "Multiple Pathways to Mouse Longevity." October 19.
5. University of Michigan Darwinian Medicine Interest Group. "Are There Genes for Aging?" November 9.

6. National Institute of Environmental Health Sciences, Southern Pines, NC. "Not Your Father's Aging Rodent: New Models for the Biology of Aging." December 2 - 3.
7. University of Michigan Hematology/Oncology Fellows Training Course. "Aging and Cancer." December 8.

2005

1. Oregon Regional Primate Center, Portland, OR. "Immune and Genetic Analyses of Aging in Mice." February 25.
2. Department of Pathology, University of Washington, Seattle, WA. "Size, Stress, and Longevity." April 5.
3. Kronos Research Institute, Phoenix, AZ. "Early Life Predictors and Mid-Life Biomarkers of Aging in Mice and Humans." April 15.
4. Brown University, Providence, RI. "Size, Stress and Aging." May 24.
5. American Aging Association Annual Meeting, Oakland, CA. "Size, Stress and Aging." June 4.
6. University of Michigan, Ann Arbor. Summer Training Course in the Biology of Aging. "Introduction to the Biology of Aging" and "Mouse Models for Aging Research" June 12 – 16.
7. University of Michigan Geriatrics Center, Ann Arbor, MI. "Biology of Aging: Four Paths to Wisdom." June 23.
8. University of Texas Health Science Center, San Antonio, TX. "Comparative Biology of Aging." June 24.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Volkman, S. K., A. T. Galecki, D. T. Burke, R. A. Miller, and S. A. Goldstein. 2004. Quantitative trait loci that modulate femoral mechanical properties in a genetically heterogeneous mouse population. *J. Bone and Mineral Research* 19:1497-1505.
2. Wissler, K. C., J. A. Schauer, D. T. Burke, A. Galecki, S. Chen, R. A. Miller, and A. Gafni. 2004. Mapping tissue-specific genes correlated with age-dependent changes in protein stability and function. *Archives of Biochemistry and Biophysics* 432:58-70.
3. Lipman, R., A. Galecki, D. T. Burke, and R. A. Miller. 2004. Genetic loci that influence cause of death in a heterogeneous mouse stock. *J. Gerontol. Biol. Sci.* 59A: 977-983.
4. Vergara, M., M. Smith-Wheelock, J. M. Harper, R. Sigler, and R. A. Miller. 2004. Hormone-treated Snell dwarf mice regain fertility but remain long-lived and disease resistant. *J. Gerontol. Biol. Sci.* 12:1244-1250.
5. Miller, R. A. 2004. Accelerated aging: a primrose path to insight? *Aging Cell* 3:47-51.
6. Miller, R. A. 2004. Rebuttal to Hasty and Vijg, Accelerated aging by mouse reverse genetics: a rational approach to understand longevity. *Aging Cell* 3:53-54.
7. Miller, R. A. 2004. Roy Walford: a tribute. *Experimental Gerontology* 39:917-918.
8. Garcia, G. G., S. B. Berger, A. A. Sadighi Akha, and R. A. Miller. 2005. Age-associated changes in glycosylation of CD43 and CD45 on mouse CD4 T cells. *Eur. J. Immunol.* 35: 622-631.
9. Miller, R. A., G. Buehner, Y. Chang, J. M. Harper, R. Sigler, and M. Smith-Wheelock. 2005. Methionine-deficient diet extends mouse life span, slows immune and lens aging, alters glucose,

- T4, IGF-I and insulin levels, and increases hepatocyte MIF levels and stress resistance. *Aging Cell* 4:199-125.
10. Miller, R. A., S. B. Berger, D. T. Burke, A. Galecki, G. G. Garcia, J. M. Harper, and A. A. Sadighi-Akha. 2005. T cells in aging mice: genetic, developmental and biochemical analyses. *Immunological Reviews* 205: 94–103.
 11. Miller, R. A. 2005. The anti-aging sweepstakes: catalase runs for the ROSES. *Science* 308:1875-1876.
 12. Salmon, A. B., S. Murakami, A. Bartke, J. Kopchick, K. Yasumura, and R. A. Miller. 2005. Fibroblast cell lines from young adult mice of long-lived mutant strains are resistant to multiple forms of stress. *Am J Physiol Endocrinol Metab* 289:E23-E29.
 13. Berger, S. B., A. A. Sadighi Akha, and R. A. Miller. A glycoprotein endopeptidase enhances calcium influx and cytokine production by CD4+ T cells of old and young mice. *International Immunology*, in press.
 14. Harper, J. M., S. J. Durkee, M. Smith-Wheelock, and R. A. Miller. Hyperglycemia, impaired glucose tolerance and elevated glycated hemoglobin levels in a long-lived mouse stock. *Experimental Gerontology*, in press.
 15. Miller, R. A. Genetic approaches to the study of aging in mammals. *J. Amer. Geriatrics Soc.*, in press.
 16. Sadighi Akha, A. and R. A. Miller. Signal transduction in the aging immune system. *Current Opinion in Immunology*, in press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Hanlon, P., A. Lorenz, Z. Shao, J. Harper, S. Volkman, S. Goldstein, A. T. Galecki, R. A. Miller, and D. T. Burke. Identification of genetic interactions among mouse QTL using a random walk approach. Submitted
2. Labrie, J. E., III, D. T. Burke, A. T. Galecki, R. A. Miller, and R. M. Gerstein. Bone marrow B cell populations in aged mice are influenced by genetic polymorphisms and correlated with T cell subset variations. Submitted

BOOKS/CHAPTERS IN BOOKS:

1. Miller, R. A. and S. N. Austad. Growth and aging: why do big dogs die young? *Handbook of the Biology of Aging*, 6th Edition. E. J. Masoro and S. N. Austad, Eds. Academic Press, NY. In press.
2. Miller, R. A. Principles of animal use for gerontological research. In: *Handbook for Models of Human Aging*. M. Conn, ed. New York: Elsevier. In press.

**HEDWIG S. MURPHY, M.D., Ph.D.
ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Surgical Pathology and Frozen Section Diagnosis (17 weeks/year).
- B. Frozen section diagnosis (17 weeks/year).
- C. Autopsy Service, rotational basis, on call 13 weeks/year.
- D. Clinical Electron Microscopy (52 weeks/year).
- E. Case presentations at Urologic Pathology Conferences (bi-weekly).
- F. Coordinator, "Topics in Pathology", CME accredited lecture series.

II. TEACHING ACTIVITIES:

- A. Pathology House Officers
 - 1. Pathology house officers, Autopsy supervision and instruction (13 weeks /year)
 - 2. Pathology house officers, instruction in gross examination, processing and frozen section processing and diagnosis (17 weeks/ year)/
 - 3. Pathology house officers, Surgical Pathology supervision and instruction, (17 weeks/year).
- B. Urology House Officers
 - 1. Urologic Pathology Conferences: case presentation and discussion (27 hr/year)
 - 2. Urologic Pathology Lectures for Urology residents (~8/year)
- C. Medical Students
 - 1. Laboratory Instructor, pathology 600 (M2 pathology course)
- D. Graduate students:
 - 1. Course Director, Pathology 585, Lecture and Laboratory course for Graduate students (4 credits)
 - 2. Lecturer, Pathology 585, 20 classes, 50 contact hrs.
 - 3. Pathology graduate student Thesis Committee: Christine Freeman

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Co-Investigator, Department of Veterans Affairs Research Enhancement Award Program (REAP) (renewal years 05-10) "Pulmonary Innate Immunity in the Pathogenesis of Tobacco-induced Lung Diseases" PI, Jeffrey L. Curtis (\$1,125,000 total direct costs).
- B. Principal Investigator "Hormones and Dendritic cells" Veterans Education and Research Association of Michigan (VERAM). \$25,000. 07/2003-2005

PROJECTS UNDER STUDY:

- A. Gender-specific effects of hormones in autoimmunity: Hormone regulation of cytokine expression by microvascular endothelial cells.
- B. Hormones regulation of dendritic cell activation and T cell function.
- C. Reactive oxygen species in lung microvascular endothelial cells in inflammation.
- D. The role of endothelial cell derived oxidants in signaling and cell injury
- E. Repertoire of endothelial cell derived cytokines: role in inflammation.
- F. C11-Acetate imaging of Prostate and Renal tumors.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Member of graduate student thesis committee, Christine Freeman, Dept. of Pathology.

MEDICAL SCHOOL/HOSPITAL:

- A. Member, Admissions committee of the University of Michigan Medical School, 1999-present.
- B. 2001-present Chief, Histopathology, Pathology and Laboratory Medicine, VAAHS.
- C. Chief, Clinical Electron Microscopy, Pathology and Laboratory Medicine, VAAHS.

REGIONAL AND NATIONAL:

- A. Manuscript Review for
 - 1. Clinical Immunology and Immunopathology
 - 2. Biochemical pharmacology
 - 3. Shock
 - 4. Free Radical Biology and Medicine
 - 5. American Journal of Pathology
 - 6. Microvascular Research

- B. Membership in National organizations
1. American Association for the Advancement of Science (1991-present)
 2. New York Academy of Science (1991-present)
 3. American Society for Investigative Pathology (Fellow, 1995-present).
 4. American Society of Clinical Pathologists (Fellow, 1995-present)
 5. American Association of University Women (199-present)
 6. The A. James French Society of Pathologists (1996-present)
 7. Society for Experimental Biology and Medicine (2000-present)
 8. The Oxygen Society (2001-present)
 9. Society for Free Radical Research International (2001-present)
 10. The Nitric Oxide Society (2001v)
 11. American Heart Association (1997-present)

V. **OTHER RELEVANT ACTIVITIES:**

- A. Case presentations at Tumor Board
- B. Case presentations at Morbidity and Mortality Conferences.
- C. Case presentations at Urologic Pathology Conferences
- D. Tissue evaluation for clinical researchers.

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Murphy HS. Sun Q. Murphy BA. Mo R. Huo J. Chen J. Chensue SW. Adams M. Richardson BC. Yung R. Tissue-specific effect of estradiol on endothelial cell-dependent lymphocyte recruitment. *Microvascular Research*. 68(3):273-85, 2004.
2. Warner RL. Winter HC. Speyer CL. Varani J. Oldstein IJ. Murphy HS. Johnson KJ. Marasmus oreades lectin induces renal thrombotic microangiopathic lesions. *Experimental & Molecular Pathology*. 77(2):77-84, 2004
3. Montgomery, J. S., B. K. Hollenbeck, P. C. Fisher, H. S. Murphy, W. Underwood. Benign Paratesticular Schwannoma. *Canad. J. Urology* 11(5): 2322-4, 2004.
4. Grimmer, J.F. Gunnlaugsson, C.B. Alsberg, E, Murphy, H.S., Kong, H, Mooney, D.R., Weatherly, R.A. Tracheal Reconstruction Using Tissue-Engineered Cartilage. *Arch Otolaryngol Head Neck Surg*. 2004 Oct;130 (10):1191-6.
5. Park, P, Gala, V C, Choksi, V R, Murphy, H S, Ramnath, S. Well-circumscribed, Minimally Enhancing Glioblastoma Multiforme of the Trigone: Case Report and Review of the Literature. *American Journal of Neuroradiology*. 26(6):1475-8, 2005.
6. Chun TH. Sabeh F. Ota I. Murphy H. McDonagh KT. Holmbeck K. Birkedal-Hansen H. Allen ED. Weiss SJ. MT1-MMP-dependent neovessel formation within the confines of the three-dimensional extracellular matrix. *Journal of Cell Biology*. 167(4):757-67, 2004.

7. Mo, R., Chen, J., Grolleau-Julius, A., Murphy, H.S., Richardson, B.C., Yung, R.L. Estrogen Regulates CC Chemokine Receptor Gene Expression and Function in T Lymphocytes. *J. Immunol.* 174:6023-6029, 2005.
8. Piotrowski, M. Bessette, R., Chensue, S. Cutler, D., Kachalia, A., Roseborough, J. W., Saint, S., Underwood, W., Murphy, H.S. Learning to Improve Safety: False Positive Pathology Report Results in Wrongful Surgery. *Joint Comm J. Quality and Safety* 31:123-131, 2005.
9. Ray, D, A. Wu, J E Wilkinson, H S Murphy, Q Lu, B Kluve-Beckerman, J J Liepnieks, M Benson, R, Yung, B. Richardson. Aging in heterozygous Dnmt1 deficient mice: effects on survival, the DNA methylation genes and the development of amyloidosis. *J. Gerontology: Biological Sciences* (accepted for publication).
10. Liming S, H.S. Murphy, L. Cooling, J A. Shayman. An in vitro model of Fabry Disease. (accepted for Publication).

SUBMITTED PUBLICATIONS

1. Murphy, H. S., Q.Sun, B. A. Murphy, D. Ray, R. Yung, B.C. Richardson. Estrogen enhances spleen dendritic cell MHCII expression and antigen presentation. (submitted *Journal of Immunology*).

BOOKS AND CHAPTERS IN BOOKS

1. H.S. Murphy, J.Varani and P.A.Ward. Endothelial Cell Injury and Defense. In Perspectives in Lung Endothelial Cell Barrier Function. C. Patterson (ed). Elsevier. 2004.
2. H.S., Murphy, ., Ward, P.A. Inflammation. In Pathology. E. Rubin (ed) Lippincott-Raven New York in Press.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. HS Murphy, Q Sun, BA Murphy, D Ray, BC Richardson. Estradiol Upregulates MHCII and Enhances Antigen Presentation by Dendritic Cells. *FASEB Journal* 18:A427.2004.
2. HC Winter, C Speyer, J J Varani, I J Goldstein, H S Murphy, K J Johnson. Marasmius oreades lectin induces renal thrombotic microangiopathic lesions: A model of hemolytic uremic syndrome. *FASEB Journal* 18:A1188. 2004.
3. H.S. Murphy, Q. Sun, B.A. Murphy, D. Ray, B.C. Richardson. Estradiol Upregulates MHCII and Enhances Antigen Presentation by Dendritic Cells. *Keystone Symposium, Immune Evasion*. 2004.
4. Choksi, V.R., Park, P, Kaza, A, Murphy, HS, Ramnath, S. Minimally Enhancing Glioblastoma Multiforme of the Trigone *American Society of Neuroradiology*. 2004.
5. M E. Murphy, Sun, Q., Richardson, B.C., Murphy, H.S. Estrogen Enhances IL-4 Mediated MCP-1 Exoression in Endothelial Cells. *FASEB Summer Research Conference: Steroid Hormone Receptors: Integration of Plasma Membrane- and Nucelar-Initiated Signaling in Hormone Action*. 2004.
7. T-H. Chun, F. Sabeh, H. S. Murphy, K. McDonagh, E. D. Allen, S.J. Weiss. MTI-MMP-dependent Neovessel formation within the confines of the 3-dimensional extracellular matrix. *American Heart Association Scientific Sessions*. 2004.

**BERNARD NAYLOR, M.D.
PROFESSOR EMERITUS OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Consultation Service: Cytopathology: 12 months.
- B. Autopsy Service, 2 weeks coverage.

II. TEACHING ACTIVITIES:

- A. Pathology residents – Diagnostic consultations.

III. RESEARCH ACTIVITIES:

- A. Effect of pollution on zooplankton in the River Ganges.
- B. History of cytopathology.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

REGIONAL AND NATIONAL:

- A. Cytopathology, Editorial Advisory Board.
- B. Acta Cytologica
Associate Editor
Editorial Advisory Board
North American Review Board

V. OTHER RELEVANT ACTIVITIES:

None.

VI. PUBLICATIONS:

- 1. Omair M, Naylor B, Wiley MJ, et al: Biological and chemical characteristics of the River Ganga (Ganges). J International Inst 2005, 12, 16.

**DUANE W. NEWTON, PH.D.
ASSISTANT PROFESSOR, CLINICAL TRACK
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Director, Clinical Microbiology/Virology Laboratories.
- B. Co-Coordinator, Infectious Disease Microbiology Laboratory Rounds.
- C. Technical Consultant - M-Labs.
- D. New clinical test development, verification and implementation.
Selected current activities in progress or completed during this year:
 - 1. Evaluation of automated ID/AST systems (in progress)
 - 2. Evaluation of real-time PCR instrumentation (in progress)
 - 3. Implementation of automated sample processing and real-time quantification of HCV viral loads (completed)
 - 4. Implementation of HCV genotyping (completed)
 - 5. Implementation of automated sample processing and real-time quantification of HBV viral loads (in progress)
 - 6. Implementation of EBV viral load testing (in progress)
 - 7. Evaluation of Galactomannan assay for detection of invasive aspergillosis (in progress)

II. TEACHING ACTIVITIES:

- A. Instructor, Pathology House Officer Microbiology/Virology Program.
- B. Coordinator, Clinical Microbiology/Virology In-service Program.
- C. Instructor, Infectious Disease Laboratory Rounds.
- D. Coordinator, Clinical Microbiology Journal Club
- E. Preceptor for M-4 elective in Pathology.
- F. Preceptor for Pharmacy Resident rotation in Clinical Microbiology and Virology.
- G. Lecturer, Epidemiology 680, "Hospital Epidemiology," School of Public Health
- H. Assistant Professor, Department of Epidemiology, School of Public Health
- I. Faculty, EPID 525, Clinical and diagnostic microbiology, Winter term, 2005 (developed course, wrote lectures, presented lectures 2x/week for entire term)

- J. Clinical Pathology Grand Rounds, UM Dept. of Pathology.
 - 1. "HIV testing: antigens, antibodies, and nucleic acids." Grand Rounds presentation, Clinical Pathology Division, Department of Pathology, University of Michigan Medical Center. 10/19/04.
 - 2. "Antimicrobial susceptibility testing." Grand Rounds presentation, Clinical Pathology Division, Department of Pathology, University of Michigan Medical Center. 11/2/04.
- K. Continuing Education Lecturer, UM Dept. of Pathology.
 - 1. "Introduction to molecular methods in clinical microbiology." Brown-bag lunch seminar for Medical Technology students, Department of Pathology, University of Michigan Medical Center. 02/09/05.

III. **RESEARCH ACTIVITIES:**

SPONSORED SUPPORT:

- A. Co-investigator (20% effort), R01 NIH Grant AI057853-01A1, Principal Investigator: Arnold S. Monto, MD, Project Title: Comparative Study of Influenza Vaccines in Adult

PROJECTS UNDER STUDY:

- A. Providing support (sterility testing) for several clinical trials including Human Applications Lab, KeraCure, and Aastrom
- B. Risk factors for ESBL+ *Enterobacteriaceae* in hospitalized patients (DePestel/Chenoweth, Pis)
- C. Identification of factors affecting quorum sensing in *Enterobacteriaceae* isolated from blood and urine (Younger, PI)
- D. Molecular methods for detection of fungal pathogens in culture negative specimens (Rogers, PI)
- E. Use of the HandyLab bedside PCR device for detecting *Streptococcus agalactiae* during pregnancy (Wu, PI).
- F. Antimicrobial nanoemulsions as therapy for recurrent cold-sores (Peters, PI)

IV. **ADMINISTRATIVE ACTIVITIES:**

DEPARTMENTAL:

- A. Clinical Pathology Laboratory Directors Committee.
- B. Quality Assurance Committee
- C. Clinical Microbiology/Virology Senior Staff committee.
- D. Clinical Pathology Training Program Review Committee
- E. Laboratory Infection Control Committee, Chairman

MEDICAL SCHOOL/HOSPITAL:

- A. Hospital Infection Control Committee.
- B. Antimicrobial Use Subcommittee of the Pharmaceutical & Therapeutics Committee.
- C. Pediatric Virus Prevention Program Committee, Infection Control & Epidemiology
- D. SARS Preparedness Planning Working Group

REGIONAL/NATIONAL:

- A. Corporate Liaison Co-chair, South Central Association for Clinical Microbiology.
- B. Rabies Working Group, Michigan Department of Community Health
- C. Ad hoc reviewer, Journal of Clinical Microbiology
- D. Ad hoc reviewer, Morbidity and Mortality Weekly Report

V. OTHER RELEVANT ACTIVITIES:

PROFESSIONAL ORGANIZATIONS:

- A. American Society for Microbiology.
- B. Infectious Disease Society of America.
- C. South Central Association for Clinical Microbiology.
- D. Pan American Society for Clinical Virology.

INVITED LECTURES/ SEMINARS:

1. "It's not just a cold—clinical and laboratory diagnosis of Flu, RSV and SARS." Presentation at Dade-Behring Continuing Education conference, Ypsilant, MI. 9/14/04.
2. "Flu, RSV, and SARS—Are you ready for winter respiratory virus season?" Kentucky Branch Fall Meeting, South Central Association for Clinical Microbiology, Lexington, KY. 10/22/04.
3. "Introduction to Molecular Microbiology." Kentucky Branch Fall Meeting, South Central Association for Clinical Microbiology, Lexington, KY. 10/22/04.
4. "Hospital laboratories in the private/public health partnership." Association of Public Health Laboratories Infectious Diseases Conference, Orlando, FL. 03/04/05.
5. "Molecular methods in the diagnosis and management of Hepatitis C virus infections." South Central Association for Clinical Microbiology Audioconference Series. 03/15/05.
6. "Case presentations in molecular infectious disease testing." South Central Association for Clinical Microbiology Annual Meeting, Elizabeth, IN. 04/15/05.
7. "Molecular for Dummies the molecularly challenged." South Central Association for Clinical Microbiology Annual Meeting, Elizabeth, IN. 04/16/05.

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. A.M. Moormann, K. Chelimo, O.P. Sumba, M.L. Lutzke, R. Ploutz-Snyder, **D. Newton**, J. Kazura, and R. Rochford. 2005. Exposure to holoendemic malaria results in elevated Epstein-Barr virus loads in children. *Journal of Infectious Diseases* **191**:1233-8.

BOOKS/ CHAPTERS IN BOOKS:

1. **D.W. Newton**. 2005. West Nile virus. In R. Carrico, editor. *APIC Text of Infection Control and Epidemiology*, 2nd edition. Association for Professionals in Infection Control and Epidemiology (APIC), Washington, DC.
2. **D.W. Newton**. 2005. Rabies. In R. Carrico, editor. *APIC Text of Infection Control and Epidemiology*, 2nd edition. Association for Professionals in Infection Control and Epidemiology (APIC), Washington, DC.

ABSTRACTS, BOOK REVIEWS, LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. T. Ackley, R. Hankerd, and **D.W. Newton**. 2005. Evaluation of the Roche LightCycler EBV quantitative analyte specific reagent (ASR) assay. Poster presented at the 21st Annual Clinical Virology Symposium and Annual Meeting of the Pan American Society for Clinical Virology, Clearwater, FL.
2. **D.W. Newton**, N. Turner, J. Polomski, and R. Hankerd. 2005. Evaluation of Invader HCV genotyping assay using Roche COBAS Amplicor and TaqMan PCR products. Poster presented at the 21st Annual Clinical Virology Symposium and Annual Meeting of the Pan American Society for Clinical Virology, Clearwater, FL.
3. C. Brenke, C.L. Young, and **D.W. Newton**. 2005. Comparison of cefoxitin and oxacillin disk diffusion to *mecA* PCR for detection of *mecA*-mediated resistance in *Staphylococcus* sp. Poster presented at the 105th General Meeting of the American Society for Microbiology, Atlanta, GA.

**GABRIEL NUÑEZ, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 July 2004 30 June 2005**

I. CLINICAL ACTIVITIES:

- A. Autopsy Service (two weeks and one weekend on-call).

II. TEACHING ACTIVITIES:

- A. Supervised, Yasunori Ogura, Theresa Dowd, Cyrus Piraya, Peter Lucas, Linda Lucas-MacAllister, Yasumasa Nishito, Ruth Alvarez, Lech Czerski, Mathias Chamillard, Nesrin Ozoren, Christine McDonald, Luigi Franchi, Amal Amer M.D., Mathilde Body-Malapel, Thirumala-Devi Kanneganti and Jong-Hwan Park.
- B. Department of Pathology, Graduate Program Course 581, University of Michigan, Ann Arbor, Michigan, (2 lectures).
- C. Instructor, Microbiology and Immunology 553, Cancer Biology Training Program, University of Michigan, (1 lecture).
- D. Instructor, Cell Biology Course 530 for Graduate Students, University of Michigan (1 lecture).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Ciper: a novel NF-kappaB-activating gene involved in Cancer" National Institutes of Health, \$175,000, (total direct costs) 07/01/00-06/31/05.
- B. Principal Investigator, "Nod2: A Susceptibility Gene for Crohn's Disease" National Institutes of Health, \$200,000, (total direct costs) 07/01/02-06/30/07.
- C. Principal Investigator, "Role of Nod1 and Nod2 in the control of Paneth cell function and intestinal microflora" Broad Medical Research Program, \$120,000, (total direct costs) 06/01/04-05/31/06.
- D. Principal Investigator, "Cypopyrin Signaling in Inflammation and Innate Immunity", National Institutes of Health, \$212,500, (total direct costs) 05/01/05-01/31/10.
- E. Principal Investigator, "Peptidoglycan signaling in Crohn's disease", National Institutes of Health, \$250,000, (total direct costs) 08/01/04-07/30/09.

PROJECTS UNDER STUDY:

- A. Role of Ciper/Bcl10 Pathway in Signal transduction and lymphoma development.
- B. Role of Nod Family in Innate Immunity and Inflammatory Disease.
- C. IPAF

IV. DEPARTMENTAL:

- A. Member, Comprehensive Examination Committee, Pathology Graduate Program, University of Michigan, Ann Arbor, MI.
- B. Member, Admissions Committee, Molecular and Cellular Biology, Graduate Program, University of Michigan, Ann Arbor, MI.

MEDICAL SCHOOL/HOSPITAL:

- A. Co-Director, Cell Biology Program, University of Michigan Cancer Center.
- B. Member, Faculty Search Committee, Rheumatology Division, and Department of Microbiology/Immunology.
- C. Reviewer, Departmental Grants and Summer Student Scholarship Program.
- D. Member, Biomedical Research Core Facilities (BRCF), University of Michigan, Ann Arbor, Michigan.
- E. Member, Biomedical Research Council, University of Michigan, Ann Arbor, Michigan.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARD:

- A. Reviewer for the following journals: American Journal of Pathology; Cancer Research; Cell; Cell Death and Differentiation; Immunity; Journal of Biological Chemistry; Journal of Cell Death and Differentiation; Journal of Immunology; Oncogene; Journal of Cell Biology; Laboratory Investigation; Proceedings of National Academy of Science USA; Science, Nature Cell Biology.

INVITED LECTURES AND SEMINARS:

- 1. Invited Speaker "Role of NODs in Innate Immunity and Inflammatory Disease", Gastroenterology Conditional Medical Education Conferences, University of Florida, Gainesville, FL, June 3, 2004
- 2. Invited Speaker "Role of NODs in Innate Immunity and Inflammatory Disease", NIAMS IRP Retreat, Molecular Basis of Diseases, Gettysburg, PA, June 8, 2004
- 3. Invited Speaker "The NOD family of proteins: Role in innate immunity and inflammatory disease", Mechanisms of Cell Death, 5th Symposium of the International Cell Death Society, Maynooth, Ireland, June 28, 2004
- 4. Invited Speaker and minisymposium co-chair " Role of NOD Protein Family in Innate Immunity and Disease", 12th International Congress of Immunology, Montreal, Quebec, Canada, July 19, 2004

5. Invited Speaker and session co-chair: Role of NODs in Innate Immunity and Inflammatory Disease”, 16th International Federation of Associations of Anatomists, Kyoto, Japan, August 25, 2004
6. Invited Speaker “The Role of LRR-containing Protein in Innate Immunity, 1st AGA-BSG Research Meeting: Pathogenesis of Intestinal Inflammation, University of Oxford, England, September 2, 2004
7. Invited Speaker and Session Co-Chair “The NOD Protein Family: Role in Innate Immunity and Inflammatory Disease”, 12th International Conference of the Inflammation Research Association, Lake George, Bolton Landing, New York, October 5, 2004
8. Invited Speaker “NOD2 and Inflammatory Disease”, 68th American College of Rheumatology Meeting, San Antonio, Texas, October 17, 2004
9. Invited Speaker “Role of NOD protein family in Innate Immunity and Inflammatory Disease”, University of Michigan Life Sciences and the Weizmann Institute Collaborative Meeting, Tel-Aviv, Israel, November 1, 2004
10. Invited Speaker “Nod2 is expressed in Paneth cells and regulates innate immunity to intracellular bacteria in the intestinal tract”, Third Annual Broad Medical Research Investigator Meeting, Los Angeles, California, February 24, 2004
11. Invited Speaker “Nod Protein Family: Role in Innate Immunity and Disease” University of California San Francisco, San Francisco, California, April 11, 2004
12. Invited Speaker, “Nod Protein Family: Role in Innate Immunity and Disease” Genentech Inc., San Francisco, California, April 12, 2004
13. Invited Speaker “Nod Family Protein: Role in Innate Immunity and Disease”, Harvard Medical School Immunology Seminar, April 27, 2004
14. Invited Speaker, “Nod Protein Family: Role in Innate Immunity and Disease” Immunology Seminar Series, Stanford University, Palo Alto, California, May 6, 2004
15. Invited Speaker, “The NOD Protein Family: Role in Innate Immunity and Inflammatory Disease,” MSTP Annual Summer Retreat, Case Western Reserve, Ohio, July 29, 2004

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNAL:

1. Imaizumi K, Benito A, Kiryu-Seo S, Gonzalez V, Inohara N, Leiberman AP, Kiyama H, **Nuñez G**. Critical role for DP5/Harakiri, a Bcl-2 homology domain 3-only Bcl-2 family member, in axotomy-induced neuronal cell death. *J Neuroscience*. 24:3721-3725 (2004).
2. Tanabe T, Chamaillard M, Ogura Y, Zhu L, Qiu S, Masumoto J, Ghosh P, Moran A, Predergast MM, Tromp G, Williams CJ, Inohara N, **Nuñez G** . Regulatory regions and critical residues of NOD2 involved in muramyl dipeptide recognition. *EMBO J*. 7; 23:1587-1597 (2004).
3. Dowds TA, Masumoto J, Zhu L, Inohara N, **Nuñez G**. Cryopyrin-induced interleukin 1beta secretion in monocytic cells: enhanced activity of disease-associated mutants and requirement for ASC. *J Biol Chem*. 279:21924-21928 (2004).
4. Swanson PJ, Kuslak SL, Fang W, Tze L, Gaffney P, Selby S, Hippen KL, **Nuñez G** , Sidman CL, Behrens TW. Fatal acute lymphoblastic leukemia in mice transgenic for B cell-restricted bcl-xL and c-myc. *J Immunol*. 172:6684-6691 (2004).

5. Lucas PC, Mc-Allister-Lucas L, **Nuñez G**. NF-kappaB signaling in lymphocytes: a new cast of characters. *J Cell Sci.* 117:31-39 (2004).
6. Chamaillard M, Inohara N, **Nuñez G**. Battling enteroinvasive bacteria: Nod1 comes to the rescue. *Trends Microbiol.* 12:529-32 (2004).
7. Kobayashi KS, Chamaillard M, Ogura Y, Henegariu O, Inohara N, **Nuñez G**, Flavell RA. Nod2-dependent regulation of innate and adaptive immunity in the intestinal tract. *Science.* 307:731-4 (2005).
8. Song W, Sun Q, Dong Z, Spencer DM, **Nuñez G**, Nor JE. Antiangiogenic gene therapy: disruption of neovascular networks mediated by inducible caspase-9 delivered with a transcriptionally targeted adenoviral vector. *Gene Ther.* 4:320-9 (2005).
9. Suzuki T, Nakanishi K, Tsutsui H, Iwai H, Akira S, Inohara N, Chamaillard M, **Nuñez G**, Sasakawa C. A novel caspase-1/Toll-like receptor 4-independent pathway of cell death induced by cytosolic Shigella in infected macrophages. *J Biol Chem.* Feb 4; [Epub ahead of print] (2005).
10. Hysi P, Kabesch M, Moffatt MF, Schedel M, Carr D, Zhang Y, Boardman B, von Mutius E, Weiland SK, Leupold W, Fritzschn C, Klopp N, Musk AW, James A, **Nuñez G**, Inohara N, Cookson WO. NOD1 variation, Immunoglobulin E, and asthma. *Hum Mol Genet.* Feb 17; [Epub ahead of print] (2005).

**SEM H. PHAN, Ph.D., M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Autopsy Service.

II. TEACHING ACTIVITIES:

- A. Lecturer, Pathology 581
- B. Training of postdoctoral fellows
- C. Member, Pathology Graduate Program thesis committees
- D. House officer training in autopsy service
- E. Pathology graduate program student counseling
- F. Supervise Undergraduate Research Opportunities Program (UROP) student projects

III. RESEARCH ACTIVITIES:

- A. Principal Investigator, "Mechanisms of pulmonary fibrosis," NIH, R37, HL28737 MERIT Award.
- B. Principal Investigator, "Myofibroblasts in pulmonary fibrosis," NIH, R01, HL 52285.
- C. Principal Investigator, "A novel telomerase expressing lung fibroblast phenotype," NIH, R01, HL77297.
- D. Principal Investigator, "Bone marrow progenitor cells in airway remodeling," The Sandler Family Supporting Foundation.
- E. Project Leader, Project III, "Lung FIZZ1 expression and its regulation in fibrosis," NIH, PO-1, HL 31963.
- F. Co-investigator, SCOR in Human idiopathic pulmonary fibrosis, NIH, P-50 HL 56402.

PROJECTS UNDER STUDY:

- A. Mechanisms of lung injury and fibrosis.
- B. Bone marrow precursor cells as extrapulmonary sources of lung fibroblasts
- C. Molecular regulation of the α -smooth muscle actin, telomerase reverse transcriptase and FIZZ1 promoter and gene expression.
- D. Myofibroblast differentiation and its regulation by cytokines.
- E. Microarray analysis of lung gene expression in lung fibrosis.
- F. Induction and regulation of telomerase expression in lung fibrosis.

- G. Eosinophil recruitment, activation and role in pulmonary fibrosis.
- H. Characterization of FIZZ1 and its role in myofibroblast differentiation

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director, Pathology Graduate Program.
- B. Member, Graduate Program Committee.
- C. Member, Departmental Research and Space Advisory Committee.
- D. Member, Pathology House Officer Selection Committee.

MEDICAL SCHOOL/HOSPITAL:

- A. Member, Medical Scientist Training Program Operating Committee.
- B. Member, Program in Biomedical Sciences Admissions Committee.

REGIONAL AND NATIONAL:

- A. Associate Editor, American Journal of Pathology.
- B. Reviewer for the following journals:
 - 1. American Journal of Respiratory and Critical Care Medicine.
 - 2. American Journal of Pathology.
 - 3. Journal of Immunology.
 - 4. American Journal of Physiology.
 - 5. American Journal of Respiratory Cell and Molecular Biology.
 - 6. Journal of Clinical Investigation,
 - 7. Experimental Cell Research.
 - 8. Journal of Applied Physiology.
 - 9. Journal of Experimental Medicine
- C. Reviewer/site visitor for NIH Program Project/Study Sections and VA grant proposals.

INVITED LECTURES/SEMINARS:

- 1. Invited Speaker- "Insights from animal models of pulmonary fibrosis", 8th International Scleroderma Workshop, Cambridge, UK, 2004
- 2. Invited Speaker- "Mesenchymal stem cells in lung repair", Symposium on "Mechanisms of lung repair", European Respiratory Society 2004 Annual Meeting, Glasgow, UK, 2004
- 3. Invited Speaker- "Bone marrow-derived precursor cells in lung fibrosis", 4th Annual meeting on Mesenchymal Non-hematopoietic Stem Cells, New Orleans, LA, 2004
- 4. Invited Speaker- "FIZZY alveolar epithelial cells induce myofibroblast differentiation", European Tissue Repair Society Focus Meeting on "Tissue repair, contraction and the myofibroblast", Nyon, Switzerland, 2004
- 5. Invited Speaker- "Fibroblast ontology in lung fibrosis", University of Southern California, Pulmonary Division, Los Angeles, CA, 2005

6. Invited Speaker- "Origin of the myofibroblast in lung fibrosis", University of Maryland, Workshop on lung fibrosis, Baltimore, MD, 2005
7. Invited Speaker- "Bone marrow stem cells and pulmonary fibrosis", Post graduate course, American Thoracic Society Annual Meeting, San Diego, CA, 2005
8. Invited Speaker- "Enigma of the eosinophil in fibrosis", International Eosinophil Society Bi-annual Symposium, Berne Switzerland, 2005
9. Invited Speaker- "Origin of the myofibroblast in pulmonary fibrosis", Université Catholique de Louvain, Brussels, Belgium, 2005

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Liu, T., Jin, H., Ullenbruch, M., Hu, B., Hashimoto, N., Moore, B., McKenzie, A., and **Phan, S.H.** Regulation of FIZZ1 expression in bleomycin-induced lung fibrosis: role of IL-4/IL-13 and mediation via STAT-6. *J. Immunol.* 2004; 173: 3425-3431.
2. Brewer, G.J., Dick, R., Ullenbruch, M.R., Jin, H., and **Phan, S.H.**: Inhibition of key cytokines by tetrathiomolybdate in the bleomycin model of pulmonary fibrosis. *J. Inorg. Biochem.* 2004; 98:2160-2167.
3. Hu, B., Wu, Z., Jin, H., Hashimoto, N., Liu, T., and **Phan, S.H.**: C/EBP β isoforms and the regulation of α -smooth muscle actin expression by IL-1 β . *J. Immunol.* 2004; 173: 4661-4668.
4. Lin, J., Cho, E.A., Chen, X., Levitan, I., Patel, S.R., Ullenbruch, M., **Phan, S.H.**, Park, J.P., and Dressler, G.R.: Kielin/Chordin-Like Protein 1 (KCP1) a Novel Enhancer of BMP Signaling Mediates Renal Fibrotic Disease. *Nat. Med.* 2005; 11:387-393
5. Gharaee-Kermani, M., Hatano, K., Nozaki, Y., and **Phan, S.H.**: Gender-based differences in bleomycin-induced pulmonary fibrosis. *Am. J. Pathol.* 2005; 166:1593-1606

BOOKS/CHAPTERS IN BOOKS/REVIEWS:

1. Varga, J., Brenner, DA., **Phan, SH.**, eds *Methods in Molecular Medicine, Volume 117, "Fibrosis Research: Methods and Protocols"*, 2005, Humana Press, Totowa, NJ.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. White, ES, Atrasz RG, Thannickal VJ, Hu B, Phan SH: Regulation of myofibroblast differentiation by protein phosphatase activity of the tumor suppressor PTEN. *Proc. Am. Thoracic Soc.* 2005; 2:A210
2. Hashimoto N, Usui M, Matsuo M, Hashimoto I, Imaizumi K, Hasegawa Y, Shimokata K, Phan SH: Expression of α -smooth muscle actin in pulmonary veins. *Proc. Am. Thoracic Soc.* 2005; 2:A717

- 3.
4. Liu T, Jin H, Ullenbruch M, Lukacs N, Phan SH: Stat6 is essential for bleomycin-induced lung fibrosis. *Proc. Am. Thoracic Soc.* 2005; 2:A852
5. Hu B, Wu Z, Liu T, Ullenbruch MR, Hong J, Phan SH: Gut-enriched Kruppel-like factor represses TGF β signaling by inhibiting Smad3. *FASEB J.* 2005; 19:A296
6. Liu T, Ullenbruch M, Jin H, Phan SH: Over-expressed FIZZ1 promotes bleomycin-induced lung fibrosis. *FASEB J.* 2005; 19:A1092

**ROBERT T. PU, M.D., Ph.D.
ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Cytology sign out 20 weeks
- B. GU surgical pathology sign out 5 weeks
- C. Autopsy service: 5 days
- D. Cytology consultation for TC cases, M-lab cases, etc
- E. Fine needle Aspirations performance at Cancer Center Clinic and hospital wards
- F. On site evaluation for specimen adequacy at Taubman Endocrine Clinic, Medical Procedure Unit, Ultrasound and CT-guided aspirations performed by clinical colleagues
- G. Daily surgical pathology consensus conference participation.

II. TEACHING ACTIVITIES:

- A. Medical students, Residents, and Fellows:
 - 1. Responsible during the current academic year for teaching activities for the following:
 - a. At daily sign out sessions
 - b. Teaching of FNA at FNA clinic
 - c. Three 1-hour lectures on cytopathology
 - d. Weekly interesting cytology case conference
 - e. Monthly cytopathology conference
 - 2. Mentoring a Summer Research Program student from medical school, Iris Wei
- B. Cytotechnologist:
 - 1. Slide conference (1 hour each X 2)

III. RESEARCH ACTIVITIES:

- A. Methylation profile of mesothelioma vs. benign mesothelial cells in effusion fluid. **Pu, R., Shen, M., Michael, C., Rhode, M., and O'Leary, T.**
- B. Mechanism of WISP3 down-regulation in inflammatory breast cancer: promoter methylation? **Wie, I., Zhang, Y., Kleer, C. and Pu, R.**
- C. Comparison of outcome of FNA diagnoses of follicular neoplasm/lesion vs. Hurthle cell neoplasm/lesion.
- D. **Pu, R., Yang, J., Griffith, K., Wasserman P., and Michael, C.**
- E. Methylation profiling of urothelial carcinoma and potential application to urine cytopathology
- F. **Pu, R. Laitala, L. and Clark, D.**

IV. **ADMINISTRATIVE ACTIVITIES:**

CANCER CENTER:

- A. **Co-director**, Cancer Center Tissue Core

DEPARTMENTAL:

- A. Interviewing Resident, Fellow, and Faculty candidates (8-10)
B. Evaluation of Fellows and Residents.

OTHER:

- A. **CAP Inspector**, cytopathology laboratory inspection at University of Chicago Hospital (Oct. 6, 2004)

V. **OTHER RELEVANT ACTIVITIES:**

- A. Reviewer:
1. Archives of Pathology & Laboratory Medicine

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Pu, Robert; Schott, Anne; Sturtz, David; Griffith, Kent; Kleer, Celina. Pathologic Features of Breast Cancer Associated With Complete Response to Neoadjuvant Chemotherapy: Importance of Tumor Necrosis. **American Journal of Surgical Pathology**. 29(3): 354-358, March 2005.
2. Pu, Robert and Rosenthal, Dorothy (in press) Incidental Giardiasis diagnosed by FNA of a phantom cecal mass. **Diagnostic Cytopathology**.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. **Pu, R.** and Michael, CW. Does Hurthle Cell Lesion/Neoplasm Predict Malignancy More Than Follicular Lesion/Neoplasm on Thyroid Fine Needle Aspiration? (Presentation at 4th Asia-Pacific IAP congress in Beijing 2005).

ARTICLES SUBMITTED

1. Siddiqui, M; Su, L; Michael, C; and Pu, R. Synchronous ordinary lipoma and spindle cell lipoma diagnosed by FNA. (Submitted to diagnostic cytopathology).
2. Rhode, M., Lucas, D., Krueger, C., and Pu, R. FNA diagnosis of spinal osteoblastoma of a patient with lymphangiomatosis (Submitted to diagnostic cytopathology).
3. Does Hurthle Cell Lesion/Neoplasm Predict Malignancy More Than Follicular Lesion/Neoplasm on Thyroid Fine Needle Aspiration? Robert T. Pu, Jack Yang, Patricia G. Wasserman, Tawfiqul Bhuiya, Kent A. Griffith, and Claire W. Michael. (Submitted to diagnostic cytopathology).

**RODOLFO F.H. RASCHE, M.D.
CLINICAL ASSISTANT PROFESSOR II
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Surgical Pathology coverage of M-Labs cases, including most from the following hospitals/clinical practices:
 - 1. Forest Health Medical Center, Ypsilanti;
 - 2. University of Michigan Health Service;
 - 3. Livonia SurgiCenter and other University of Michigan Clinics and satellite sites;
 - 4. Other clients such as clinics outside of Washtenaw County.
- B. Cytopathology: provide coverage in gynecologic, non-gyn and FNA services (performance of aspirate/interpretation) at U of M Hospitals for 10-14 weeks.
- C. Autopsy coverage at the University Hospitals, for weekdays and weekends. Autopsy coverage is also provided to Forest Health Medical Center, Ypsilanti.
- D. Outside consults to a growing list of pathologists. These are stat consults and we provide fast turn around times. Most of these cases are shown in consultation to other faculty.
- E. Review peripheral smears at Forest Health Hospital and University of Michigan Health Service.
- F. Clinical Pathology consults for M-Labs client hospitals.

II. TEACHING ACTIVITIES:

- A. Supervise performing of autopsies by residents and sign out M-Labs and University of Michigan cases.
- B. Organize and lecture at the M-labs Symposium (23rd Symposium in April 2005), a one day-long event with lectures and case presentations for pathologists (most are M-Labs clients). CME credits are provided. Held twice a year (October/April).
- C. Sign-out in cytopathology, with residents, fellow and, occasionally with medical students.
- D. In-service teaching to laboratory staff at the University of Michigan Health Service (UHS).
- E. Monthly colposcopy meetings with the Gyn medical staff at UHS.

III. RESEARCH ACTIVITIES:

None

IV. ADMINISTRATIVE ACTIVITIES:

- A. Associate Director, M-Labs: (for more details, see M-Labs' Annual Report). Participate in planning, marketing and implementation of M-Labs programs.
- B. Medical Director of the University of Michigan Health Service Laboratory, and Forest Health Medical Center in Ypsilanti.

Department of Pathology Annual Report

- C. Active medical staff member at Forest Health Medical Center (FHMC) and Community Health Center of Branch Co (Coldwater). Attend FHMC medical staff meetings.
- D. Intra-departmental meetings (e.g., Cytopathology)

V. **OTHER:**

- A. Inspector, for the CAP Accreditation Program. Recent inspections outside the U.S.

**DANIEL G. REMICK, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Director, Autopsy Service.
- B. Supervision of Autopsies- 3 weeks.
- C. Coordinator, Trauma/burn autopsy conference monthly
- D. Coordinator of Senior Staff Autopsy Call Schedule.
- E. Deputy Medical Examiner, Washtenaw County.

II. TEACHING ACTIVITIES:

- A. Coordinator, Biweekly Pathology Gross Conference.
- B. Lectures to Pathology House Officers in Anatomic and Clinical Pathology.
- C. Longitudinal Case Studies, Provided written critiques of student autopsy write-ups (200).
- D. Laboratory Instructor, Pathology 600 (M2 pathology course), year long
- E. Thesis Committee - Yoko Kamotani, College of Engineering, Sudha Natarajan, Pathology, Devin Horton, Cell and Molecular Biology Program
- F. Mentored research of Stewart Wang, M.D., Ph.D. (Department of Surgery), Grace Su, M.D., (Department of Medicine), Jean Nemzek, D.V.M. (Unit for Lab Animal Medicine), Postdoctoral fellows, Hong Yan Xiao, M.D., Ekram El Laban, M.D., Michelle Law, Ph.D., and Marcin Osuchowski, D.V.M., Ph.D.
- G. Graduate Students – Laura McKinley, Department of Pathology, Devin Horton, Program in Cell and Molecular Biology, Sudha Natarajan, Department of Pathology
- H. Undergraduate Students – Lisa Abernathy, Alan Commet, and Julia Sun

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Regulation of gene expression of soluble mediators of inflammation using the following models:
 - 1. Endotoxin-stimulated human whole blood.
 - 2. Endotoxin injection in mice.
 - 3. Cecal ligation and puncture.
 - 4. 2 hit model of acid aspiration induced lung injury
- B. Toxic effects of immunomodulators.
- C. Pathophysiology of septic shock.
- D. Quantitation of mediators in septic shock.

- E. Cloning, sequencing, and expressing cytokines including mTNF, hTNF, mIL-6, hIL-8, mIL-18, mIL-1ra.
- F. Oxidant regulation of chemokine gene expression.
- G. Chemokines in the pathogenesis of murine asthma

SPONSORED SUPPORT

- A. Principal Investigator, "The Role of Cytokines in Sepsis and Trauma", GM44918 \$906,182, 1990-2004. 30% effort
- B. Principal Investigator, "Immunopathology of Sepsis" GM67189, 2005 – 2008 Project leader, Project #1 Role of Cytokines in Sepsis and Trauma, \$157,486 annual costs, 25% effort Core Director Cytokine Measurement Core, \$191,091 annual costs, 5% effort
- C. Principal Investigator, "Regulation of IL-8 gene expression: four years, GM50401 \$870,822, 1995- 2004. 20% effort
- D. Co-Investigator, "Inflammation and the Host Response to Injury", GM-99-007, Ronald Tompkins, M.D. Principal Investigator Mass. General Hospital. Protein Analysis and Cell Biology Core, \$613,115, 2001 – 2006, 5% effort.
- E. Co-Investigator, "Inflammation and the Host Response to Injury", GM-99-007, Ronald Tompkins, M.D. Principal Investigator Mass. General Hospital. Protein Analysis and Cell Biology Core, \$613,115, 2001 – 2006, 10% effort.

PENDING GRANTS:

- A. The following grant was reviewing in June and scored at the 3rd percentile Principal Investigator "Regulation of ongoing inflammation" GM50401, \$225,000 annual costs, 2005-2010, 20% effort.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director - Autopsy Service.
- B. Interviewer - Candidates for faculty, house officer, postdoctoral, and graduate student positions.
- C. Co-ordinator of call schedule, both weekend and weekday, autopsy service.

MEDICAL SCHOOL/HOSPITAL:

- A. Assistant Dean for Admissions, Medical School – 25% appointment
- B. Member, Biomedical Research Council Undergraduate Research Council
- C. Reviewer, Biomedical Research Council grants
- D. Representative for Pathology to Program in Biomedical Sciences (PIBS) Admissions Committee
- E. Member, Program in Cell and Molecular Biology

REGIONAL AND NATIONAL:

- A. Executive Committee, Michigan Association of Medical Examiners.
- B. Deputy Medical Examiner for Washtenaw County.
- C. Member, American Society of Investigative Pathology Education Committee
- D. Member, Michigan Coalition on Donation
- E. Publications Committee, International Cytokine Society
- F. Awards Committee, Shock Society
- G. Organizer, Shock Society Young Investigator's Research Forum 2001-04
- H. Organizer, Shock Society Fun Run 2004, 2005
- I. Member, Michigan Association of Medical Examiners, Shock Society, American Association of Immunologists, A. James French Society, American Society of Investigative Pathologists, United States-Canadian Academy of Pathology
- J. Program Chair, Shock Society Annual Meeting, 2006, Broomfield CO
- K. 2004 Feb, Chair, NIH Special Emphasis Panel
- L. 2004 Jun, Chair, NIH Special Emphasis Panel
- M. 2004 Dec, NIH Special Emphasis Panel
- N. 2005 Jan, Chair, NIH Special Emphasis Panel
- O. 2005 Jun, On Site Reviewer Oklahoma Medical Research Foundation NIH U19 grant

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL ACTIVITIES:

Associate Editor, Shock

Executive Editor, Cross Section (Official Newsletter of the Michigan Association of Medical Examiners)

Editorial Board, Journal of Investigative Surgery

- A. Editorial Board: Shock
- B. Reviewer:
 - 1. National Science Foundation, Veterans Administration Merit grants
 - 2. American Review of Respiratory Disease
 - 3. Laboratory Investigation
 - 4. Journal of Immunology
 - 5. Infection and Immunity
 - 6. Journal of Leukocyte Biology
 - 7. American Journal of Pathology
 - 8. American Journal of Physiology
 - 9. Journal of Clinical Investigation
 - 10. Circulation
 - 11. Annals of Internal Medicine
 - 12. Blood
 - 13. Hepatology
 - 14. Cytokine
 - 15. Critical Care Medicine

LECTURES/SEMINARS:

1. International Sepsis Forum, Oak Island Resort, Canada, *Acute Pancreatitis, Models, Markers, and Mediators*, 2004.
2. Member Panel Discussion, American Association of Medical College Annual Meeting, Boston, MA, *Michigan Affirmative Action, One Year Later*, 2004.
3. Invited Speaker, American Association of Medical College Annual Meeting, Boston, MA, *Admissions Decisions and Disabilities*, 2004.
4. Panel Member, Minority Student Recruitment Fair, University of Florida, Gainesville, FL, 2004.
5. Invited Speaker, Association of University Anesthesiologists, Baltimore, MD, *Making the Grant Reviewer Your Friend*, 2005.
6. Invited Speaker, Society for Critical Care Medicine, Phoenix, AZ, *Sepsis and Cytokines*, 2005.
7. Consultant, Blantyre Malaria Project, Blantyre, Malawi (Africa) *Pathogenesis of Human Cerebral Malaria*, 2005.

VI. PUBLICATIONS:

ARTICLES PUBLISHED

1. Xiao H, Kovics R, Jackson V, Remick DG: Effects of platelet inhibitors on propyl gallate-induced platelet aggregation, protein tyrosine phosphorylation, and platelet factor 3 activation. *Blood Coagul Fibrinolysis* 15: 199-206., 2004.
2. Woodford NL, Call DR, Remick DG, *et al.*: Model of angiogenesis in mice with severe combined immunodeficiency (SCID) and xenografted with Epstein-Barr virus-transformed B cells Endothelial barrier dysfunction caused by LPS correlates with phosphorylation of HSP27 in vivo. *Comp Med* 54: 209-15., 2004.
3. Nemzek JA, Xiao HY, Minard AE, Bolgos GL, Remick DG: Humane endpoints in shock research. *Shock* 21: 17-25., 2004.
4. McKinley L, Kim J, Bolgos GL, Siddiqui J, Remick DG: Reproducibility of a novel model of murine asthma-like pulmonary inflammation. *Clin Exp Immunol* 136: 224-31, 2004.
5. Knight PR, Sreekumar A, Siddiqui J, Laxman B, Copeland S, Chinnaiyan A, Remick DG: Development of a sensitive microarray immunoassay and comparison with standard enzyme-linked immunoassay for cytokine analysis. *Shock* 21: 26-30., 2004.
6. Hirano S, Rees RS, Yancy SL, Welsh MJ, Remick DG, Yamada T, Hata J, Gilmont RR: Endothelial barrier dysfunction caused by LPS correlates with phosphorylation of HSP27 in vivo. *Cell Biol Toxicol* 20: 1-14., 2004.
7. Copeland, S, Siddiqui J, **Remick D.** 2004. Direct comparison of traditional ELISAs and membrane protein arrays for detection and quantification of human cytokines. *J Immunol Methods* 284: 99-106.
8. McKinley, L, Kim J, Bolgos GL, Siddiqui J, **Remick DG.** 2004. Reproducibility of a novel model of murine asthma-like pulmonary inflammation. *Clin Exp Immunol* 136: 224-31.
9. Zeng, X. K., **D. G. Remick,** and X. Wang. 2004. Homocysteine induces production of monocyte chemoattractant protein-1 and interleukin-8 in cultured human whole blood. *Acta Pharmacol Sin* 25:1419-1425.

10. Kim, J., L. McKinley, J. Siddiqui, G. L. Bolgos, and **D. G. Remick**. 2004. Prevention and reversal of pulmonary inflammation and airway hyperresponsiveness by dexamethasone treatment in a murine model of asthma induced by house dust. *Am J Physiol Lung Cell Mol Physiol* **287**:L503-509.
11. **Remick, D. G.** 2004. Do not get sick when you are sick: the impact of comorbid conditions. *Crit Care Med* **32**:2147-2148
12. Xiao, H., and **D. G. Remick**. 2005. Correction of perioperative hypothermia decreases experimental sepsis mortality by modulating the inflammatory response. *Crit Care Med* **33**:161-167.
13. Su, G. L., K. Q. Gong, M. H. Fan, W. M. Kelley, J. Hsieh, J. M. Sun, M. R. Hemmila, S. Arbabi, **D. G. Remick**, and S. C. Wang. 2005. Lipopolysaccharide-binding protein modulates acetaminophen-induced liver injury in mice. *Hepatology* **41**:187-195
14. Cobb, J. P., M. N. Mindrinos, C. Miller-Graziano, S. E. Calvano, H. V. Baker, W. Xiao, K. Laudanski, B. H. Brownstein, C. M. Elson, D. L. Hayden, D. N. Herndon, S. F. Lowry, R. V. Maier, D. A. Schoenfeld, L. L. Moldawer, R. W. Davis, R. G. Tompkins, H. V. Baker, P. Bankey, T. Billiar, B. H. Brownstein, S. E. Calvano, D. Camp, I. Chaudry, J. P. Cobb, R. W. Davis, C. M. Elson, B. Freeman, R. Gamelli, N. Gibran, B. Harbrecht, D. L. Hayden, W. Heagy, D. Heimbach, D. N. Herndon, J. Horton, J. Hunt, K. Laudanski, J. Lederer, S. F. Lowry, R. V. Maier, J. Mannick, B. McKinley, C. Miller-Graziano, M. N. Mindrinos, J. Minei, L. L. Moldawer, E. Moore, F. Moore, R. Munford, A. Nathens, G. O'Keefe, G. Purdue, L. Rahme, **D. Remick**, M. Sailors, D. A. Schoenfeld, M. Shapiro, G. Silver, R. Smith, G. Stephanopoulos, G. Stormo, R. G. Tompkins, M. Toner, S. Warren, M. West, S. Wolfe, W. Xiao, and V. Young. 2005. Application of genome-wide expression analysis to human health and disease. *Proc Natl Acad Sci U S A* **102**:4801-4806.

**CHARLES W. ROSS, M.D.
ASSOCIATE PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004- 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Director, Clinical Flow Cytometry Laboratory.
- B. Diagnostic Surgical Pathology, Hematopathology.
- C. Clinical Hematology Laboratory.
- D. Clinical Molecular Diagnostics Laboratory.
- E. Hematopathology Consultation Cases (including M-Labs and Veterans Administration Hospital).
- F. Electron Microscopy (platelet ultrastructure).

II. TEACHING ACTIVITIES:

- A. Medical Students and Dental Students:
 - 1. Lecturer, M2 Hematology Sequence.
 - 2. Laboratory Instructor, M2 Hematology Sequence.
 - 3. Lecturer, Dental School Pathology 630.
 - 4. Laboratory Instructor, M1 Histopathology Course.
- B. House Officers:
 - 1. Sign-out of bone marrow biopsies, aspirates, blood smears, and body fluids in Hematology Laboratory.
 - 2. Sign-out of lymph node biopsies and review of hematopathology consultation material.
 - 3. Flow Cytometry sign-out.
 - 4. Hematopathology case conferences.
 - 5. Hematopathology lecturer.
- C. Hematopathology teaching:
 - 1. Leukemia conference/biweekly.
 - 2. Lymphoma conference/weekly.
 - 3. Hematology conference/biweekly.
 - 4. Pathology Grand Rounds (two lectures).
 - 5. Clinical Pathology Case Conference/weekly.
 - 6. Cutaneous Lymphoma Conference/monthly.
 - 7. Multiple myeloma conference/biweekly
 - 8. Hematology/Oncology Morbidity and Mortality Conference
 - 9. Pediatric Hematology/Oncology Fellows Teaching Conference – 1 hour.
 - 10. Adult Hematology/Oncology Fellows Teaching Conference – 1 hour.
 - 11. Continuing Medical Education for Clinical Laboratory Staff – 3 hours.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Immunophenotypic profiling of hematolymphoid neoplasms by flow cytometry and immunohistochemistry.
- B. Pathology reviewer for therapeutic trials in systemic mastocytosis (with Cem Akin, M.D.).
- C. Pathology reviewer for zebrafish model of mutational defects in hematopoiesis (with Susan Lyons, M.D.).
- D. Genomic aberrations in follicular low grade lymphoma (with Sami Malek, M.D.).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director, Clinical Flow Cytometry Laboratory.
- B. Clinical Pathology Incentive Distribution Committee.
- C. Interviewer of residency candidates.

REGIONAL/NATIONAL:

- A. Resident In-Service Examination (RISE) Committee, American Society for Clinical Pathology.
- B. American Society for Clinical Pathology, CheckPath Expert Review Panel, Hematopathology
- C. Manuscript reviewer, Clinical Cytometry.
- D. Manuscript reviewer, Human Pathology

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

- 1. "Applications of flow cytometry in diagnosis of hematolymphoid neoplasia", lecture to residents and fellows, Department of Radiation Oncology, April 2005.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Kaminski MS, Tuck M, Estes J, Kolstad A, Ross CW, et. al. : ¹³¹I-Tositumomab Therapy as Initial Treatment for Follicular Lymphoma. NEJM 352:441-449, 2005.
- 2. Bakshi NA, Ross CW, Finn WG, Valdez R, Ruiz R, Koujok K, Schnitzer B: ALK-Positive Anaplastic Large Cell Lymphoma (ALCL) with Primary Bone Involvement in Children. Am J Clin Pathol (accepted for publication).

ARTICLES SUBMITTED FOR PUBLICATION:

1. Bakshi N, Finn WG, Ross CW, Valdez R, Schnitzer B: Fascin expression in diffuse large B-cell lymphoma, anaplastic large cell lymphoma and classical Hodgkin lymphoma.

**ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR,
MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:**

1. Hepatosplenic T-cell lymphoma. Society for Hematopathology, Case of the Quarter (submitted for publication).



**DIANE ROULSTON, Ph.D.
CLINICAL ASSOCIATE PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Director, Clinical Cytogenetics Laboratory

II. TEACHING ACTIVITIES:

- A. House Officers and Fellows
1. Rotations in Cytogenetics
 - a. Pathology residents (N=5)
 - b. Hematopathology fellows (N=2)
- B. Clinical Cytogenetics teaching
1. Abnormal Cytogenetics Case Conference (Biweekly) for technologists, residents, fellows, and faculty
 2. Leukemia Conference (Biweekly)
 3. Medical Genetics Conference (Monthly)
 - a. "Microduplication of 15q11-13 associated with schizophrenia and mental retardation detected by interphase FISH analysis in two sisters"
 4. Clinical Pathology Grand Rounds: "Microduplications and genomic disorders"
 5. Invited speaker, HG641 Applied Clinical Genetics (for Genetic Counseling) "Clinical Cytogenetics"
 6. Rotations in Cytogenetics: Genetic Counseling graduate students (N=6)
 7. Invited speaker for Hematology/Oncology Fellow's Conference "Cancer Cytogenetics"
 8. Pediatric Neurology Conference "FISH testing for microduplications of 15q11-13"
 9. Invited speaker, Continuing Education for Clinical Laboratory Staff: "Medical Cytogenetics: An introduction to human chromosome pathology"

III. RESEARCH ACTIVITIES:

- A. Cytogenetic analysis of human embryonic stem cells for the U-M Center for HES Cell Research
- B. Cytogenetic analysis of mammary tumor cell line MCF10A for *EZH2* gene studies
- C. Identification of a novel t(2;22) in a Ewing sarcoma/PNET leading to the cloning and characterization of a new *EWS* partner gene, *SP3* and the *EWS/SP3* fusion gene.
- D. Characterization of double minutes using spectral karyotyping and FISH and demonstration of gene amplification of *MYC* in a diffuse large cell lymphoma

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director, Clinical Cytogenetics Laboratory
- B. Interviewer
 - 1. Hematopathology Fellow Candidates
 - 2. Hematopathology Faculty Candidates
- C. Clinical Pathology Planning Committee

UNIVERSITY OF MICHIGAN:

- A. Interviewer
 - 1. Clinical Genetics Residency/Fellowship Candidates

REGIONAL AND NATIONAL:

- A. American Board of Medical Genetics
 - 1. Maintenance of Certification: Clinical Cytogenetics Committee, Item Writer
 - 2. Fellow, American College of Medical Genetics
- B. Peer Review: *Blood*
- C. Children's Oncology Group (COG)
 - 1. Cytogenetics Committee member: review cases for national study group
 - 2. Director of an Approved Laboratory; submit clinical cases for review
 - 3. Cytogenetics Committee Workshop
- D. Southwest Oncology Group (SWOG)
 - 1. Director of an Approved Laboratory; submit cases for review

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES:

"Molecular cytogenetics of acute leukemia relevant to the Children's Oncology Group," COG Cytogenetics Workshop August 27, 2004, St. Louis, MO.

VI. PUBLICATIONS:

ARTICLES PUBLISHED IN REFEREED JOURNALS:

- 1. Choi SW, Boxer LA, Pulsipher MA, Roulston D, Hutchinson RJ, Yanik GA, Cooke KR, Ferrara JL, Levine JE. Stem cell transplantation in patients with severe congenital neutropenia with evidence of leukemic transformation. *Bone Marrow Transplant.* 35(5):473-7. 2005.
- 2. Thornburg CD, **Roulston D**, Castle VP. Burkitt lymphoma and Williams syndrome: a model for children with a multisystem disorder and malignancy. *J Pediatr Hematol Oncol.* 27(2):109-11. 2005.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Mobley BC, **Roulston D**, Shah GV, Bijwaard KE, McKeever PE. Peripheral PNET/Ewing sarcoma of the craniospinal vault: case reports and review.

ABSTRACTS:

1. Cox B, Lefebvre N, Mindell M, Martin DM, Smith LR, **Roulston D**. "Microduplication of 15q11-13 associated with schizophrenia and mental retardation detected by interphase FISH analysis in two sisters" Association of Genetic Technologists 30th Annual Meeting, June 16-19, Kansas City, MO.



**ROBERT E. RUIZ, M.D., PH.D.
CLINICAL ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 – 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Consultant, pediatric surgical pathology, full time
- B. Consultant, pediatric autopsy pathology, full time
- C. Consultant, Teratology histopathology, full time
- D. Surgical pathology signout, Room 1, 6 weeks
- E. Surgical pathology frozen section call, 5 weeks
- F. Medical Director, Special Studies Laboratory (see separate report)
- G. Pathology coordinator, Children's Oncology Group cases

II. TEACHING ACTIVITIES:

- A. Medical Students
 - 1. M2 Pathology Laboratory (~25 hours)
 - 2. M4 Pathology Elective (~8 hours)
- B. Pathology House Officers:
 - 1. Pathology Teaching Conferences (4 hours lecture, 4 slide conferences)
 - 2. Pediatric Pathology Case Review (2-3 hours per week)
 - 3. Pediatric Autopsy Pathology cases and signout (variable)
 - 4. Pediatric Surgical Pathology Cutting Manual Revision (ongoing)
- C. Interdepartmental:
 - 1. Teratology histopathology signout (1 hour per week)
 - 2. Pediatric GI Pathology Case Conference (2 hours per month)
 - 3. Pediatric GI Pathology Teaching Conference (2 hours per month)
 - 4. Pediatric Hematology Oncology Tumor Board (2 hours per month)
 - 5. Pediatric Surgery, Radiology, Pathology Conference (1.5 hours per month)
 - 6. Pathology contributor for Pediatric Surgery, Radiology, Pathology Conference teaching case web presentations, Pediatric Surgery internal website (www.surgery.med.umich.edu/i/peds/Internal_site.htm)
 - 7. Pediatric uroradiology Conference (1-2 hours per month)
 - 8. Pediatric Pulmonology Conference (1 hour per month)
 - 9. Pediatric Morbidity & Mortality Conference (1 hour per quarter)
 - 10. Pediatric Hematology Oncology Fellow Pathology Tutorials (variable)
 - 11. Pediatric Hematology Oncology Wednesday Morning Teaching Conference (variable)

III. RESEARCH ACTIVITIES:

- A. Development of new laboratory tests for diagnosis of pediatric tumors (ongoing, with Dr. John Thorson)
- B. Case study of intraosseous teratoma with Dr. Jason Jarzembowski (manuscript in preparation)

IV. ADMINISTRATIVE ACTIVITIES:

- A. Mott Executive Committee

V. ABSTRACTS

- 1. Weigelin HC, Lucas DR, Ruiz RE, Howard JK, Thorson JA. Multiplex RT-PCR/capillary electrophoresis to detect and genotype characteristic translocations from formalin fixed soft tissue tumor specimens. *Journal of Molecular Diagnostics* 6: 427, 2004.

VI. PUBLICATIONS:

- 1. Koujok K, Ruiz RE, Hernandez RJ. Myofibromatosis: imaging characteristics. *Pediatric Radiology* 35: 374, 2005.

**BERTRAM SCHNITZER, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Director, Hematopathology Fellowship Training Program
- B. Diagnostic Surgical Pathology, Hematopathology (12 months)
- C. Diagnostic Hematopathology Consultant, Veterans Administration Hospital
- D. Diagnostic Hematopathology of M-Labs clients
- E. Consultant for external and transfer Hematopathology cases
- F. Review of lymphoma cases entered into Children's Cancer Study Group protocols

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

- A. Daily sign-out of bone marrow biopsies and aspirates.
- B. Daily review of blood smears and body cavity and joint fluids in the Hematology Laboratory.
- C. Daily review of in-house and consultation hematopathology cases and correlation with flow cytometry data and immunoperoxidase studies.
- D. Daily review of outside consultation cases.
- E. House Officer Conferences in Hematopathology, Clinical Pathology Grand Rounds.
- F. Biweekly House Office Hematopathology Conference.
- G. Monthly lectures to house officers on acute leukemias, lymphomas, and benign lymphadenopathy.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

None.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Diagnostic Surgical Pathology, Hematopathology.
- B. Diagnostic Clinical Pathology, Hematology.

MEDICAL SCHOOL/HOSPITALS:

- A. Director of Hematopathology Fellowship Training Program

REGIONAL AND NATIONAL:

- A. Member, Hematology Workshop Review Committee, American Society of Clinical Pathologists.
- B. Hematology Planning Committee, American Society of Clinical Pathologists.
- C. Chair, Hematology Check-Path Committee, American Society of Clinical Pathologists.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARD:

- A. Human Pathology. Designated reviewer.
- B. American Journal Clinical Pathology. Designated reviewer.

INVITED LECTURES/SEMINARS:

- 1. "A Practical Approach to Diagnostic Hematological Problems," ASCP Educational Course, Lectures given included a) Classification of Non-Hodgkin's Lymphomas. b) Hodgkin's Disease; c) Extranodal Lymphomas. Vancouver, BC, November 2004.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

None.

BOOKS AND CHAPTERS IN BOOKS:

- 1. Hsi ED, Schnitzer B. Benign Lymphadenopathies. In Jaffe ES, Harris NL, Vardiman J (eds). Diagnostic Hematopathology. Harcourt Health Sciences, 2005.
- 2. Schnitzer, B. Hodgkin's Lymphoma – In Goldblum JR, Hsi ED (eds). Foundations in Diagnostic Pathology. Hematopathology. Churchill-Livingstone, 2006.

**ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR,
MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:**

1. Grant MR, Valdez R, Schnitzer B, Finn WG. Malignant lymphomas of the retroperitoneum. *Mod. Pathol.* 18:1076, 2005.
2. Rawal A, Schnitzer B, Finn WG, Valdez R. Site-specific morphologic variations in extranodal marginal zone B-cell lymphoma. *Mod. Pathol* 18:1151, 2005.
3. Gesk S, Gascoyne R, Schnitzer B, Bakshi N, et al: ALK-positive diffuse large B-cell lymphoma with ALK-Clathrin fusion belongs to the spectrum of pediatric lymphomas. Letter to the Editor. *Leukemia* (in press).

**RAJAL B. SHAH, M.D.
CLINICAL ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

A.	Room #1 General Surgical Pathology sign-out	4 weeks/year
B.	GU surgical subspecialty sign-out	17 weeks/year
C.	Genitourinary transfer cases (TS)	26 weeks/year
D.	GU consultation service, daily	12 months
E.	Participation in Urology Tumor Board and Grand Rounds, biweekly	12 months
F.	Rapid warm autopsies for men with advanced prostate cancers, 24/7 availability	12 months
G.	Backup coverage of Nephropathology service	1 week/year

II. TEACHING ACTIVITIES:

A.	Residents didactic Monday evening Anatomic Pathology Lectures	3/year
B.	Residents Wednesday Consultation Conferences	3/year
C.	GU clinical pathology resident teaching, daily	18 weeks
D.	General surgical pathology resident teaching	8 weeks
E.	GU fellow (Nasir Bakshi) teaching	12 months
F.	Post doctoral fellow (Rohit Mehra)	12 months
G.	Urology resident pathology lectures, monthly	12 months
H.	M2-Renal Sequence and Reproductive Sequence Lectures	3/year

III. RESEARCH ACTIVITIES:

A.	Director, Tissue core, Prostate SPORE	12 months
B.	Translational research/pathology consultant for Genitourinary research	12 months

IV. SPONSORED SUPPORT:

- A. University of Michigan Prostate SPORE (Specialized Program for Research Excellence) Tissue Core Grant (Director (from June, 2004), Co-director (7/03-5/04) tissue core, 20% salary support)- P50 CA69568 (PI, Pienta-07/01/03-05/31/08)
- B. Analysis of 8p loss in Human Prostate Cancer- Co Investigator, Ro1, 5RO1 CA 60948-08, (JA Macoska, PI), 4/01/01-3/31/05-5% salary support

- C. DAMD17-01-1-0076 (M.J. Imperiale) 7/1/01-6/30/04, Co-investigator, 5% salary support. Role of the Human Polyomavirus, BKV, in Prostate Cancer-Co-investigator Department of Defense/USAMRMC

V. **ADMINISTRATIVE ACTIVITIES:**

DEPARTMENTAL:

- A. Director, Prostate SPORE tissue core laboratory
- B. B) Section Chief, Urological Pathology
- C. GU fellowship coordination
- D. House officer, GU fellowship and faculty Candidate Interviews

HONORS AND AWARDS:

- A. Co-Chair, Proffered Papers: Genitourinary Pathology: United States and Canadian Academy of Pathology, March 1, San Antonio, Texas

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. **Shah RB**, Kunju L, Shen R, LeBlanc M and Rubin M. Usefulness of Basal Cell Cocktail (p63+34 β E12) in the Diagnosis of Atypical Prostate Glandular Proliferations. *Am J Clin Pathol*, 122:517-523, 2004
2. Das D, **Shah RB** and Imperiale M. Detection and Expression of Human BK Virus Sequences in Neoplastic Prostate Tissues. *Oncogene*, 1-16, 2004
3. **Shah RB**, Mehra R, Chinnaiyan A, Shen R, Ghosh D, Zhou M, MacVicar G, Varambally S, Harwood J, Bismar T, Kim R, Rubin M, and Pienta K. Androgen Independent Prostate Cancer is a Heterogeneous Group of Diseases: Lessons from a Rapid Autopsy Program. *Cancer Research*, 64:9209-9216, 2004
4. Kunju L, Lee C, Montie J and **Shah RB**. Cytokeratin 20 and Ki- 67 as Markers of Urothelial Dysplasia. *Pathol Int*, 55(5):248-54, 2005
5. Khaira H, **Shah RB** and Wolf S, Jr. Laproscopic and Open Surgical Nephrectomy for Xanthogranulomatous Pyelonephritis. In press, *Journal of Endourology*
6. Siu W, Dunn RL, **Shah RB**, and Wei JT. Use of Extended Pattern Technique for Initial Prostate Biopsy. In press, *J Urol*
7. Kunju L, Chinnaiyan A, **Shah RB**. Comparison of Utility of Polyclonal and Monoclonal Antibody to alpha Methyl Acyl Co A Racemase (AMACR) in Work-up of Prostate Cancer. In press, *Histopathology*

8. Caoili EM, Cohan RH, Inampudi P, Ellis JH, **Shah RB**, Faerber GJ and Montie JE. MDCT Urography of Upper Tract Urothelial Neoplasms. *AJR* 2005;184:1873-1881
9. Fu Z, Kitagawa Y, Shen R, **Shah RB**, Mehra R, Rhodes D, Keller P, Mizokami A, Dunn R, Chinnaiyan AM, Yao Z, Keller ET. The metastasis suppressor gene Raf Kinase inhibitor (RKIP) is a novel prognostic marker in prostate cancer. In press, *The Prostate*

VII. PRESENTATIONS:

1. "Phenotype and Immunophenotype of Androgen Independent Metastatic Prostate Cancer" - Guest Speaker, Prostate Breakout session, 12th SPORE National Cancer Institute Meeting, Baltimore, MD - July 12, 2004.
2. "Prostate Cancer: From a Pathologist's Perspective" - The Prostate Cancer Education and Support Network, The University of Michigan Comprehensive Cancer Center, January 6, 2005
3. "Interpretation of Prostate Needle Biopsies: Critical Issues" 23rd MLABS symposium, April 9, University of Michigan Hospitals
4. "University of Michigan Prostate SPORE tissue core: An update of new developments" The University of Michigan GU oncology conference, June 30, 2005.
5. "Epidermal Growth Factor Receptor (ErbB1) Expression in Prostate Cancer Progression: Correlation with Androgen Independence". United States and Canadian Academy of Pathology, March 1, San Antonio, Texas
6. "Heterogeneous Androgen Receptor (AR) Protein Expression in Metastatic Androgen-Independent Prostate Cancer: Implications for Complex AR Mechanisms in the Progression to Androgen Independent Prostate Cancer". United States and Canadian Academy of Pathology, March 1, San Antonio, Texas

VIII. ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Azabdaftari G, **Shah R**, Bismar T, Kim R, Zerkowski M, Rimm D, Pienta K, Rubin M. Androgen Receptor Expression in Hormone Refractory Prostate Cancer from a Rapid Autopsy Series: Quantitative Subcellular Localization Using AQUA. *Modern Pathol*, 18(1):5A, Jan 2005.
2. Baig M, Kunju L, Schervish E, **Shah R**, Wojno K. Gleason Grading Multifocal Adenocarcinoma in Prostatectomy Specimens: Implications for Grading Needle Biopsies. *Modern Pathol*, 18(1):127A, Jan 2005.
3. Bakshi N, Kunju L, Wood Jr D, **Shah R**. Minimally Invasive Prostatectomy (Laparoscopic and Robot-Assisted): Clinicopathological Characteristics of 82 Cases from a Single Institution. *Modern Pathol*, 18(1):128A, Jan 2005.
4. Bakshi N, Kunju L, Giordano T, **Shah R**. Expression of Renal Cell Carcinoma Antigen (RCC) in Renal Epithelial and Non-Renal Tumors: Diagnostic Implications. *Modern Pathol*, 18(1):128A, Jan 2005.

5. De Marzo A, Platz E, Epstein J, Billis A, Chan T, Cheng L, Datta M, Ertoy-Baydar D, Farre X, Fine S, Iczkowski K, Ittmann M, Knudsen B, Loda M, Lopez-Beltran A, Magi-Galluzzi C, Mikuz G, Montironi R, Rubin M, Sebo T, Sesterhenn I, **Shah R**, Signoretti S, Simko J, Troncoso P, Tsuzuki T, van Leenders G, Yang X, Zhou M, Figg W, Hoque A, Lucia M. Interobserver Reproducibility of a Proposed Classification of Focal Prostate Atrophy Lesions. *Modern Pathol*, 18(1):135A, Jan 2005.
6. Kunju L, Chinnaiyan A, **Shah R**. Comparison of Utility of Polyclonal and Monoclonal Antibody to alpha Methyl Acyl Co A Racemase (AMACR) in Work-up of Prostate Cancer. *Modern Pathol*, 18(1):150A, Jan 2005.
7. Kunju L, Bakshi N, Poisson L, Hafez K, Wojno K, **Shah R**. Morphologic Subtyping of Papillary Renal Cell Carcinoma: Clinicopathologic and Immunohistochemical Analysis. *Modern Pathol*, 18(1):150A, Jan 2005.
8. Kunju L, Bakshi N, Poisson L, Hafez K, Wojno K, **Shah R**. Morphologic Subtyping of Papillary Renal Cell Carcinoma: Clinicopathologic and Immunohistochemical Analysis. *J Urol*, 2005
9. Kunju L, Bakshi N, Wood D, Hafez K, **Shah R**. Role of Percutaneous Image-Guided Renal Biopsy (IGRB) in the Management of Renal Masses: Adequacy, Accuracy and Limitations of Pathologic Diagnosis. *Modern Pathol*, 18(1):151A, Jan 2005.
10. **Shah R**, Ghosh D, Pienta K, Elder J. Epidermal Growth Factor Receptor (ErbB1) Expression in Prostate Cancer Progression: Correlation with Androgen Independence. *Modern Pathol*, 18(1):163A, Jan 2005.
11. **Shah R**, Chinnaiyan A, Mehra R, Varambally S, Shen R, Harwood J, Bismar T, Kim R, Pienta K, Rubin M. Heterogeneous Androgen Receptor (AR) Protein Expression in Metastatic Androgen-Independent Prostate Cancer: Implications for Complex AR Mechanisms in the Progression to Androgen Independent Prostate Cancer. *Modern Pathol*, 18(1):163A, Jan 2005.

IX. WORKSHOPS, COURSES AND SLIDE SEMINARS:

1. Twenty-third MLABS Symposium. "Interpretation of Prostate Needle Biopsies". Case presentations and review. April 9, 2005.

X. PROJECTS SUBMITTED FOR PUBLICATION:

1. Development of a Non-T7 Based Whole Transcriptome Amplification Method for Gene Expression Profiling. Submitted for publication (2004)
2. Treatment of BK Nephropathy with Intravenous Immunglobulin. Submitted for the publication (2004)
3. Integrative Proteomic and Genomic Analysis of Prostate Cancer Progression (2005)
4. Role of image-guided biopsy in the evaluation of renal mass lesions in contemporary urologic practice: indications, adequacy, accuracy and limitations of the pathologic diagnosis (2005).

XI. PROJECTS UNDER STUDY

1. Use of tissue micro arrays to identify markers associated with response to interleukin-2 in renal cell carcinoma.
2. Papillary renal cell carcinoma: Emphasis on the histological typing and its correlation with clinicopathologic and immunohistochemical parameters.
3. Minimally invasive radical prostatectomy: Initial experience and evaluation of clinicopathologic parameters.
4. Significance of positive proximal urethral margin in staging radical prostatectomy: does the presence of benign prostate glands make a difference?
5. Erb signaling in the progression of prostate cancer.

**LISA R. SMITH, PH.D
CLINICAL ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Assistant Director, Cytogenetics Laboratory

II. TEACHING ACTIVITIES:

- A. House Officers and Fellows
1. Rotations in Cytogenetics
 - a. Pathology Residents (N=6)
 - b. Hematology/Oncology Fellows (N=3)
- B. Hematology/Cytogenetics Case Conference (monthly)
- C. Graduate Students
1. Rotations in Cytogenetics
 - a. Genetic Counseling Students (N=6)
- D. Invited Lectures
1. HG643: Reproductive Genetics
 - a. Clinical Cytogenetics
 2. Clinical Pathology Grand Rounds
 - a. "Cytogenetics II: Imprinting and Uniparental Disomy"
- E. Clinical Cytogenetics
1. Abnormal Cytogenetics Case Conference (Biweekly)--- technologists, residents, and fellows
 2. Leukemia Conference (Biweekly)
 3. Hematology Conference (Biweekly)
 4. Pediatric Genetics Post-clinic Conference (Weekly)
 5. Teratology Conference (Weekly)
 6. Joint Genetics Conference (Monthly)

III. RESEARCH ACTIVITIES:

- A. Paraffin-embedded tumor fluorescence in situ hybridization (PET FISH)

PROJECTS UNDER STUDY:

- A. "Study of pro-fibrotic milieu in cells and fluid obtained at bronchoalveolar lavage (BAL) in the development of Bronchiolitis Obliterans Syndrome in post-lung transplant patients" PI: Vibha Lama, MD; Dept of Pathology and Critical Care + 8 Co-Pi

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Assistant Director, Clinical Cytogenetics Laboratory
B. Interviewer for Pathology Residency Candidates
C. Interviewer Hematopathology Candidates

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Szymanska, J., Smith, L.R., Heiber, D., Cummings, O., Thurston, V., Einhorn, L., and Vance, G. *Submitted*. Comparative genomic hybridization of metastatic and non-metastatic teratomas reveals amplifications at 12p and Xq, and losses at 9p and 18q. *Genes, Chromosomes and Cancer*.

PEER-REVIEWED ABSTRACTS:

1. Lama V.N., Flint A., **Smith L.R.**, Martinez F.J., Peters-Golden M., Toews G.B., Thannickal V.J. Role and Origin of Myeloblasts in the Pathogenesis of Bronchiolitis Obliterans in Lung Transplant Recipients. *Am J Respir Crit Care Med*. 2004; 169:A504.

CASE REPORTS:

1. Lama, V.N., **Smith, L.R.**, Martinez, F.J., Peters-Golden, M., Toews, G.B., Thannickal, V.J. Presence of donor derived mesenchymal cells in bronchioalveolar lavage of lung transplants. 13th Annual Department of Internal Medicine Research Symposium, University of Michigan, April 29-30, 2005. Ann Arbor, MI
2. Lefebvre, N., Cox, B., Mindell, M., Martin, D.M., **Smith, L.R.**, Roulston, D. Microduplication of 15q11-q13 associated with schizophrenia and mental retardation detected by interphase FISH analysis in two sisters. Southern Michigan Cytogenetics Conference, May 13, 2005. Detroit, MI
3. Cox, B., Lefebvre, N., Mindell, M., Martin, D.M., **Smith, L.R.**, Roulston, D. Microduplication of 15q11-q13 associated with schizophrenia and mental retardation detected by interphase FISH analysis in two sisters. 30th Annual AGT Conference, June 16-19, 2005. Kansas City, MO

**LLOYD M. STOOLMAN, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. **Flow Cytometry Diagnostic Service (3 months):** interpretation of cell surface marker studies in the evaluation of hematologic disorders, primary and secondary immune deficiencies and autoimmune processes.
- B. **Autopsy Service (weekend coverage)**

II. TEACHING ACTIVITIES:

- A. **Research mentor (200+ contact hours)**
 - 1. **Rughi Okuyama, M.D., post-doctoral fellow (4/02-present) and Ronald Craig, PhD, Research Associate (1/91-present):** Mechanisms and clinical ramification of donor T-cell trafficking during adoptive cellular immunotherapy for metastatic cancer. Identified the vascular selectins as the principle vascular adhesion receptors required for effector T-cell entry into subcutaneous murine melanomas. Showed that selectin- and, to a minor extent, $\alpha 4$ -integrin-mediated trafficking of host and donor lymphocytes into tumors initiates anti-tumor activity. Showed that trafficking is inefficient due to limited expression of the vascular selectins on tumor-associated vessels (selectin+ venules concentrated at the invasive boarder). Preliminary data suggests that T-cells enter tumors primarily through co-opted normal vessels rather than the angiogenic vessels induced by the tumor. Therefore, adoptive cellular immunotherapy and anti-angiogenic therapy may target different tumor-associated vessels and the malignant cells that they support. NCI support obtained for conducting a pre-clinical trial combining an experimental anti-angiogenic agent with adoptive immunotherapy.
 - 2. **Randall Knibbs, Ph.D., Research Scientist (1/94-present):** Dr. Knibbs characterized the host's immunologic response to subcutaneous murine tumors as they enlarge using high-density oligonucleotide arrays. This approach revealed a complex immune response that initially resembled that seen in response to a contact sensitizing agent but rapidly diminished in intensity as the tumors enlarged. Multiplexed real-time quantitative PCR and ELISA based analyses are currently under development to confirm and extend these findings. In addition, viral transduction vectors were developed that encode T-cell adhesion and chemokine receptors that interact with the vascular receptors and chemokines found in the tumor microenvironment. These vectors will be used test the hypothesis that tumor-specific effector T-cells transduced immediately prior to

adoptive transfer will traffick more efficiently into tumors and improve the therapeutic response.

3. **Undergraduate and graduate research assistants:** Mentored three undergraduate students in the laboratory participating in work/study programs and one graduate student.
 4. **Thesis committee member:** participated in 5 thesis committees (Immunology Program) with two graduate students successfully completing degree requirements this year.
- B. **Co-director, lecturer and seminar leader, M2 Hematology Sequence** (16 contact hours+100 hours administration/development): Authored the 8th generation of The Virtual Microscope-Hematopathology Interactive Syllabus (<http://141.214.6.12/virtualheme99>). Unique software provides access to interactive case-presentations and high-resolution "virtual slides" covering the pathophysiology, diagnosis and treatment of the hematologic malignancies. This award-winning "active" learning experience captures the essentials of the in-class laboratory exercises thus provides students with a flexible tool for preview and review. Teaching performance metrics: lecture rating: 4-4.5/5 (mean for all faculty in sequence: 3.8-4.1); laboratory rating: 4.32/5 (mean for all faculty in sequence: 4); selected student comments (Class 2007):
1. *Dr. Stoolman is such an enthusiastic professor. He really cares that we learn it, and puts in so much extra time and effort (i.e., the additional resources such as the interactive PowerPoint and the various websites) to assist us in our learning. Those materials helped a ton, as I am filling this out after our final exam. Thank you!*
 2. *Stoolman has absolutely fantastic web-based resources for the pathology labs. They were extremely helpful. I really enjoyed Dr. Stoolman's interactive PowerPoint presentation! It was great of him to do the review and put together the Unknown PowerPoint as well.*
 3. *This man's websites are amazing! I was very impressed! Good use of technology on the PowerPoint slides (and overall throughout the course).*
 4. *Dr. Stoolman presented topics in a very understandable manner. It was nice to have this lecture before the whirlwind lectures that followed on lymphomas - which apparently seemed to focus on clinical trials, basic science research and a lot of random drug names that didn't mean much to us yet. Dr. Stoolman went through, very clearly, the lineages and development of each type of lymphoma, and provided great pictures that were very helpful. His online, web-based resources were also EXTREMELY helpful, especially when going back through things several times on my own. I can't speak highly enough of professors (especially those doing histo/histopath) who put resources online for our perusal in our own time. very very very helpful.*
 5. *Dr. Stoolman's was the best lecture in the sequence. He should be asked to teach more. He made things very clear. His websites are superb--a very valuable educational asset. Dr. Stoolman should get a raise! The review PowerPoint was very helpful.*
 6. *The lab instruction was excellent, and the website provided was very helpful in connecting information from the lab with the information from lecture.*

7. *Dr Stoolman definitely had his act together and was able to fire answers to anything students asked. I liked how he was constantly drawing comparisons between slides because it really helped when it was time to study for the final.*
 8. *Dr. Stoolman's website was absolutely outstanding. It really made the material make sense to me very much so enhanced my understanding of the appearance of leukemias.*
 9. *One of the best prepared lab sessions I've had this year. Also, the virtual microscope idea is fantastic and feel it should be used more in the curriculum. Dr. Stoolman, really helpful.*
 10. *I REALLY appreciated having all the lab information online that we did. There was an abundance of web-based information and things like this are extremely helpful for me. For one, it gives me the opportunity to go over everything as much as I need, in my own time, without having to purchase yet another book. Secondly, I have great difficulty with the microscope work done in labs (i usually only attend labs to hear the instructors, and don't even use the scope) because I get extremely motion sick when scanning through a microscope.*
- C. **Lecturer and Seminar leader M1 Host Defense Sequence** (4 contact+30 development):
Lectured and developed computer-based courseware for lecture syllabus and case presentations. Teaching performance metrics: Lecture rating: 4.5/5 (mean for all faculty in sequence: 4.31). Selected student comments (Class 2007):
1. *Dr. Stoolman's classroom presentation was the most technologically advanced of the series and that increased the effectiveness of his presentation.*
 2. *The visuals kept me awake. Also the visuals added to the lecture, reinforcing important points. It was also helpful to hear certain important points clearly re-emphasized.*
 3. *Dr. Stoolman made a real effort to keep students interested in the material. The time he spent preparing his presentation must have been enormous, and I appreciate the effort very much.*
 4. *The use of animation and movies in the PowerPoint presentation for his lecture made the material more relevant and understandable for the students. It provided a more comprehensive understanding of the material than would sheer words on a page that might describe the same processes. Moreover, the animation was so engrossing that it kept all the students' attention for the entire lecture. It was a lasting impression.*
 5. *Audiovisuals and presentation were immaculate. He seemed very lucid and clear. I enjoyed his presentation.*
 6. *The movies were excellent. The repetition was excellent (really driving home what we needed to know). I really appreciated Dr. Stoolman's lectures and the time he put into his presentation.*
 7. *Dr. Stoolman had excellent animated slides that really demonstrated his points well.*
 8. *Engaging and interesting presentations, with good audiovisuals.*
 9. *The movies that he used were very good and gave me another way to digest and understand the information that was presented.*
 10. *Best AV presentation I've likely ever seen. Kept the lecture interesting and helped us to really see how things happen.*

11. *I really liked how Dr. Stoolman used animations in his presentation. Not only did it lighten the mood and make it more fun to learn, but it also enabled us to grasp and visualize the material better. He also made sure to stress the key points so that we would know what is most important.*
 12. *Dr. Stoolman's animations were creative and clearly must have required much effort and time to produce. I appreciated his desire to put together a lecture that students would enjoy.*
 13. *Incredible audiovisuals and that helped liven things up. The movies really augmented the lecture.*
 14. *Dr. Stoolman did an OUTSTANDING job on his slides. The animation and sound effects made the lecture very interesting and made the material easier to understand.*
 15. *Excellent presentation. Needs to teach the other profs. how to use PowerPoint.*
- D. **Author, Pathology Laboratory Course for Dental Students:** 8th generation of The Virtual Microscope- Interactive web-based syllabus for General and Organ systems pathology for dental students. URL= <http://141.214.6.12/cyberscope631/>. This award-winning site incorporates several hundred, high resolution (1900 X 1300 pixel) photographs of gross and microscopic specimens into an interactive laboratory syllabus. The Virtual Microscope Website now serves as the primary histopathology teaching modality for Dental Students. The platform allowed the Department to meet the teaching requirements of the revised dental curriculum while reducing faculty effort by ~50%.
- E. **Resident Teaching:** (30 contact hours): Flow cytometry service, case sign-out (3 months); Autopsy service, weekend coverage.

III. RESEARCH ACTIVITIES:

- A. **Principal Investigator- T Cell Trafficking in Adoptive Cellular Immunotherapy;** NIH, R01CA73059, 27% effort, \$196,000 (annual, direct); April 2001 -Mar 2006
- B. **Principal Investigator- Lymphoma/leukemia therapies using dendritic cells engineered to overexpress lymph-node homing receptors.** The Leukemia & Lymphoma Society Translational Research Program. \$130,000 (direct + indirect, annual); Oct 2003-Sept 2006.
- C. **Principal Investigator- Research Training in Translational Tumor Immunology;** NIH/NCI, T32 CA 88784, 5% effort (no salary support), \$321,306 (annual, direct); supports 2 pre-doctoral students and 4 post-doctoral students; Feb 2001-Jan 2006.
- D. **Co-investigator on Project 2 and Co-director of the Immunology Core (with A.E. Chang and B. Redman, Surgical Oncology Division, University of Michigan)- Cellular Vaccines for Cancer Immunotherapy,** NIH P01CA59327, 13% effort, \$1,000,000 (annual, direct); June 2001-April 2006.
- E. **Co-investigator (with B. Redman and A. E. Chang, Surgical Oncology Division, University of Michigan)- T-Cell Therapy of Human Renal Cell Cancer;** NIH R01CA69102, \$250,000 (annual, direct), 10% effort, April 2001 -Mar 2006.
- F. **Co-investigator (with A. E. Chang, Surgical Oncology Division, University of Michigan)-“T-cell Activation for Cancer Immunotherapy”;** NIH R01CA82529, \$211,282 (annual, direct); 5% effort, Jul 2004-June 2008.

- G. **Trainer on four funded pre-/post-doctoral training grants: Translational Immunology (L. Stoolman, PI); Surgery Oncology Research (A.E. Chang, PI), Immunopathology (R. Miller, PI) and Vascular Biology Training Grant (T. Wakefield, PI).**

IV. ADMINISTRATIVE ACTIVITIES:

- A. **Director, Pathology High Resolution Slide Scanning Service** (200 hours administration/development): This Service generates diagnostic quality, high resolution (200-400X resolution) digital scans of tissue sections. The sections can be viewed, annotated and analyzed online. It is anticipated that digital scans will replace tissue sections/microscopes in teaching venues, complement traditional microscopic approaches in resident/fellow training and foster research collaborations that involve faculty at multiple centers. Dr. Stoolman supervised a team that installed, beta-tested and optimized the Aperio T2 robotic scanner and Imagescope server (<http://www.aperio.com/>). The laboratory began operations November of 2004 with installation of production servers and a 5-terabyte SANS completed in June 2005. 1000 200X scans completed to date including: (1) M1 Histopathology, (2) M2 Organ Systems Pathology, (3) Neuropathology and (4) M1 Histology collections (<http://scanscope.path.med.umich.edu:82>). Selected 400X scans of slides in these collections are currently underway. M1 students granted access to the Histopathology Web-based online collection Winter of 2005. Beta testing of Imagescope viewer conducted in LRC culminating in successful “virtual laboratory” for M1 pre-matriculation students (see comments below). Limited student access to full Histology, Histopathology and Organ Systems pathology collections planned for Fall 2005. Comments from pre-matriculation students on Histology Virtual Laboratory:
1. *I am part of the pre-matriculation program that tested the virtual microscopy software. My overall impression is that it is a powerful teaching and learning tool. It is easy to use and, as all students were viewing the exact same slides, we could readily identify and discuss common features. I would highly recommend having an additional data layer or annotated file to provide identification and labeling of examples of prominent features. This could be a layer that could be turned on and off as necessary. Making the images available to students would also be helpful. My only concerns with exclusively using this approach in place of having students using microscopes are that: 1) the amount of variability of structural appearance that students will be exposed to will be limited (variability from different sections and preparation techniques); and 2) the inability to focus on certain features that are out of the focal plane. Despite these concerns, I think that the benefits far outweigh these concerns.*
 2. *The ability to compare to slides at once side by side was invaluable. I got to see the inactive and active mammary glands next to one another and the differences were easy to see. I suspect that normal vs. diseased tissues could be viewed like this also in the pathology classes as well. VERY COOL. The interface was easy to understand and control. Can't wait to see it next year!*

3. *I thought that looking at the slides on the computer was much easier than using the microscope. It is very easy to navigate, zoom in and see the structures. It especially nice because we don't have to worry about focusing in. I think it would be best if we switched to the computer models.*
- B. **Director of Research Flow Cytometry Service and Co-Director of Clinical Flow Cytometry Laboratory** (100 hours administration): The research flow cytometry service is available to Department of Pathology investigators and their laboratory personnel currently at no cost to individual laboratories. Dr. Stoolman and his research staff maintain, provided training and access to a Coulter/Beckman FC 500, Dual Laser, 8-parameter instrument. A GroupWise-base scheduling system was implemented this year that enabled investigators to view instrument availability and schedule time from any computer workstation. In the first quarter of 2005, 27 undergraduates, graduate students, post-docs and research associates from 10 departmental laboratories were trained and used the instrument. During Q1 2005, the instrument was used a total of 500 hours or 85% of its available capacity.
- C. **Faculty Coordinator for Technology in the Medical Education** (50 hours administration): Faculty representative at all planning and management meetings concerning the use of the CTools platform for support of Medical School programs (<https://ctools.umich.edu/portal>). Current focus is on the adequacy and reliability of the CTools platform for the unique needs of Medical School educational programs. Member, CTools Faculty Advisory Committee (convened by Dr. James Hilton, Associate Provost for Academic, Information and Instructional Technology). Dr. Stoolman represents the Medical School on this committee.
- D. **Principal Investigator- Research Training in Translational Tumor Immunology**; NIH/NCI, T32 CA 88784, 5% effort (no salary support), \$321,306 (annual, direct); supports 2 pre-doctoral students and 4 post-doctoral students; Feb 2001-Jan 2006.
- E. **Member, Graduate Student Administrative Committee, Immunology Training Program**
- F. **Co-Director, M2 Hematology Sequence** - see educational activities.
- G. **Medical School Representative to Faculty Senate.**

V. PUBLICATIONS:

ARTICLES IN PEER REVIEWED PUBLICATIONS:

1. J Skitzki, RA Craig, R Okuyama, RN Knibbs, K McDonagh, AE Chang and **LM Stoolman**. Donor cell cycling, trafficking and accumulation during adoptive immunotherapy for murine lung metastases. 2004. Can. Research. 64: 2183.
2. Sabel MS, Skitzki J, **Stoolman** L, Egilmez NK, Mathiowitz E, Bailey N, Chang WJ, Chang AE. Intratumoral IL-12 and TNF-alpha-loaded microspheres lead to regression of breast cancer and systemic antitumor immunity. 2004. Annals of Surgical Oncology. 11(2):147.
3. Q. Li, A.L. Carr, E.J. Donald, J. Skitzki, R. Okuyama, **L.M. Stoolman**, A. E. Chang . Synergistic Effects of IL-12 and IL-18 in Skewing Tumor-reactive T Cell Responses Towards a Type 1 Pattern. 2005. Can. Research. 65(3): 1063.

ABSTRACTS, BOOK REVIEWS, LETTERS TO THE EDITOR, MISCELLANEOUS UNREFEREED PUBLICATIONS:

1. R. Okuyama, J. Skitzki, R. Craig, R. Knibbs and **L. M. Stoolman**. Vascular adhesive interactions control clinical responses during adoptive immunotherapy of murine cancer. Invited speaker. Keystone Symposium on Tumor Immunology. Keystone CO, March 2005.
2. **Lloyd M. Stoolman**, Ryuji Okuyama, Joseph Skitzki, Randall N. Knibbs, Ronald A. Craig. T-Cell Trafficking and the Therapeutic Response during Adoptive Immunotherapy. Poster and oral presentation. 12th International Congress of Immunology. Montreal, Canada, July 2004.
3. **LM Stoolman**. 1998-2005 (updated annually). The Virtual Microscope- Interactive web-based syllabus for medical student (M2) Hematopathology laboratory. URL=<http://141.214.6.12/virtualheme99/>.
4. **LM Stoolman**. 1998-2005 (updated annually). The Virtual Microscope- Interactive web-based syllabus for General and Organ systems pathology for dental students (D2). URL=<http://141.214.6.12/cyberscope631/>.
5. **LM Stoolman**. 1999-2005 (updated annually). Hematopathology Unknown Exercises. Powerpoint-based exercise containing high resolution, annotated images and imbedded questions used by Medical Students (Hematology Sequence, year 2).
6. **LM Stoolman**. 1999-2005 (updated annually). Leukocyte Pathophysiology and Leukocyte Trafficking. Powerpoint lecture outlines including high-resolution images, video clips and animations used by Medical Students (Host Defense Sequence, year 1), Dental Students (General Pathology Course, year 1) and Graduate Students (Pathology 581).

**LYNDON SU, M.D.
CLINICAL ASSOCIATE PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Dermatopathology Service – (University Hospital and Transfer cases) – 12 months
- B. Dermatopathology Consultation Service (including personal and M-Labs consultations) – 12 months

II. TEACHING ACTIVITIES:

- A. Medical Students:
 - 1. Medical students – (on elective rotation in dermatopathology)
 - 2. Instructor in medical student laboratories
- B. House Officers:
 - 1. Dermatopathology daily sign-out (dermatology and pathology residents, and medical students)
 - 2. Review of dermatopathology consultation material
 - 3. Dermatopathology Teaching conference – (dermatology residents-weekly)
 - 4. Dermatopathology Teaching conference – (pathology residents-3 per year)
 - 5. Anatomic Pathology Core Conference – (2 per year)
 - 6. Anatomic Pathology Consultation Conference – (2 per year)
- C. Diagnostic Conference, Department of Dermatology – (weekly)
- D. Cutaneous T-Cell Lymphoma Conference—(monthly)

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. EZ-H2 expression in melanocytic tumors. (D. Fullen.; L. Lowe; and C. Kleer)

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Co-director, Dermatopathology Service

REGIONAL AND NATIONAL:

- A. Ad hoc manuscript reviewer, Journal of Cutaneous Pathology
- B. Ad hoc manuscript reviewer, Journal of the Academy of Dermatology
- C. Ad hoc manuscript reviewer, Cancer
- D. Ad hoc manuscript reviewer, Journal of Pediatrics
- E. Ad hoc manuscript reviewer, American Journal of Dermatopathology
- F. Ad hoc manuscript reviewer, Applied Immunohistochemistry and Molecular Morphology

V. OTHER RELEVANT ACTIVITIES:

None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED, ACCEPTED OR SUBMITTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Avram AM, Gielczyk R, Su L, Vine AK, Sisson JC. Choroidal and skin metastases from papillary thyroid cancer: case and a review of the literature. *J Clin Endocrinol Metab.* 2004 Nov;89(11):5303-7
2. Bogner PN, Su LD, Fullen DR. Cluster designation 5 staining of normal and non-lymphoid neoplastic skin. *J Cutan Pathol.* 2005 Jan;32(1):50-4.
3. Fullen DF, Zhu W, Thomas D, Su LD. HTERT Expression in melanocytic lesions: An immunohistochemical study on paraffin-embedded tissue. Accepted for publication in *Journal of Cutaneous Pathology*
4. Arora A, Lowe L, Su L, Rees R, Bradford C, Cimmino VC, Chang AE, Johnson TM, Sabel MS. Wide excision alone provides excellent local control for desmoplastic melanoma. Accepted for publication in *Cancer*.
5. Siddiqui MA, Su L, Michael C, Pu RT. Synchronous ordinary lipoma and spindle-cell lipoma diagnosed by fine needle aspiration. In review.

**JOHN A. THORSON, M.D., PH.D.
CLINICAL ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 – 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Director, Molecular Diagnostics Laboratory
- B. Clinical Immunology Laboratory; sign out of cases (4 weeks/year)

II. TEACHING ACTIVITIES:

- A. House Officers:
 - 1. Coordinator, Pathology House Officer rotation through Clinical Molecular Diagnostics Laboratory
 - 2. Review of selected topics in Molecular Diagnostics with Block D residents
- B. Anatomic Pathology Conference:
 - 1. "Molecular Methods in Surgical Pathology I" (3/15/05)
 - 2. "Molecular Methods in Surgical Pathology II" (3/22/05)
- C. Lecturer, Advanced Clinical Concepts in Medical Genetics course (HG 649)

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Use of insertion/deletion polymorphisms to assess bone marrow transplant engraftment status
- B. High throughput multiplex PCR assays for detection of BCL2 and BCL1 translocations in formalin fixed tissue specimens
- C. Multiplex real time PCR assay for blood group antigen genotyping
- D. Fluorescent multiplex RT-PCR/capillary electrophoresis assays for the detection of tumor specific chimeric transcripts in soft tissue tumors

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL AND INSTITUTIONAL:

- A. Director, Molecular Diagnostics Laboratory
- B. House Officer Candidate interviews
- C. Faculty Candidate interviews
- D. MSTP Career Advisory Panel

V. **OTHER RELEVANT ACTIVITIES:**

- A. Consultant, Consultants in Laboratory Medicine, Toledo, OH
- B. College of American Pathologists, Clinical Laboratory Inspector

EDITORIAL BOARDS:

- A. Ad hoc manuscript reviewer, Thrombosis and Haemostasis

PROFESSIONAL MEMBERSHIPS:

- A. American Society of Clinical Pathologists
- B. College of American Pathologists
- C. United States and Canadian Academy of Pathology
- D. Academy of Clinical Laboratory Physicians and Scientists
- E. American Association for Clinical Chemistry
- F. Association for Molecular Pathology
- G. American Society of Human Genetics

INVITED LECTURES/SEMINARS:

- A. "Pharmacogenomics: The Genome Project Meets the Clinical Laboratory", invited presentation, American Association for Clinical Chemistry, Michigan Section Annual Dinner Meeting, November 3, 2004, Bloomfield Hills, MI.
- B. "Pharmacogenomics: Medicine Meets the Genome Project", Medical Grand Rounds, William Beaumont Hospital, Royal Oak, MI, April 20, 2005.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Si MW, **Thorson JA**, Lauwers GY, DalCin P, and Furman, J. 2004. Hepatocellular lymphoepithelioma-like carcinoma associated with Epstein Barr virus: a hitherto unrecognized entity. *Diag Mol Path* 13(3):183-189.
2. Zhou L, **Thorson JA**, Nugent C, Davenport RD, Butch SH, and Judd WJ. 2005. Non-invasive prenatal RHD genotyping by real time PCR using plasma from D-negative pregnant women. *Am J Obstet Gynecol* (in press).

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Multiplex RT-PCR/capillary electrophoresis to detect and genotype characteristic translocations from formalin-fixed soft tissue tumor specimens. Weigelin HC, Lucas DR, Ruiz RE, Howard JK and Thorson JA. Poster presentation, The Association for Molecular Pathology Annual Meeting, Los Angeles, CA, Nov 10-13, 2004. *J Mol Diag* 6(4) p. 426 Abs # ST1.
2. Detection and genotypic identification of characteristic fusion gene transcripts from formalin-fixed soft tissue tumor specimens using multiplex RT-PCR/capillary electrophoresis. Thorson JA, Ruiz RE, Weigelin HC, Howard JK, and Lucas DR. Poster presentation at the United States and Canadian Academy of Pathology Annual Meeting, San Antonio, TX, Feb 26 – Mar 4, 2005. *Mod Pathol* 18 suppl 1 p. 22A Abs # 87.
3. Non-Invasive prenatal RHD genotyping by real-time PCR using plasma from RHD-negative pregnant women. Zhou, L, Thorson, J, Nugent, CE, Davenport, RD, and Judd WJ. Poster presentation at the United States and Canadian Academy of Pathology Annual Meeting, San Antonio, TX, Feb 26 – Mar 4, 2005. *Mod Pathol* 18 suppl 1 p.337A Abs # 1564.
4. Detection and genotypic classification of *SYT/SSX* transcripts from synovial sarcomas using multiplex RT-PCR/capillary electrophoresis. Thorson JA, Ruiz RE, Weigelin HC, Howard JK, and Lucas DR. Poster presentation at the United States and Canadian Academy of Pathology Annual Meeting, San Antonio, TX, Feb 26 – Mar 4, 2005. *Mod Pathol* 18 suppl 1 p.22A Abs #88.
5. A rapid and comprehensive real time PCR assay for the detection and characterization of *BCL2/IGH* translocations in follicular lymphomas. Smith LB, Valdez R, Finn WG, and Thorson JA. Platform presentation at the United States and Canadian Academy of Pathology Annual Meeting, San Antonio, TX, Feb 26 – Mar 4, 2005. *Mod Pathol* 18 suppl 1 p. 251A Abs # 1162.



**GERD O. TILL, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

None

II. TEACHING ACTIVITIES:

- A. Instructor, General Pathology for Dental Students and Graduate Students (Pathology 630/580)
- B. Mentor, graduate student - Lai Ming Lee
- C. Mentor, NIH Training Grant in Trauma, Burn and Wound Healing Research (T32 GM08616)

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Co-Investigator, "Mechanisms and Prevention of Lung Injury Caused by Mustard Gas" (U.S. DOD)
- B. Co-Investigator, "Liquid Ventilation in ARDS" (NIH HL-54224)
- C. Co-Investigator, "Lung Injury Produced by Oxygen Metabolites", (NIH GM-29507).
- D. Senior Mentor, "Training Grant in Burn, Trauma and Wound Healing Research" (NIH)

PENDING SUPPORT:

None

PROJECTS UNDER STUDY:

- A. Lung injury caused by 2-chloroethyl ethyl sulfide.
- B. Pathomechanisms of ischemia-reperfusion injury.
- C. Pathophysiologic role of complement activation products in secondary lung injury

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Interviewed candidates for faculty and postdoctoral positions
- B. Participation in undergraduate research program

MEDICAL SCHOOL/HOSPITAL:

- A. Course Director, Pathology 580/630
- B. Member Medical School Committee on Student Biomedical Research Programs
- C. Member Doctoral Thesis Committee
- D. Interviewed candidates for faculty positions
- E. Consultant for clinical research programs
- F. Reviewer of intra-departmental grant proposals

REGIONAL AND NATIONAL:

None

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

- A. Member Editorial Board, International Immunopharmacology, 1998-present
- B. Member Editorial Advisory Board, Immunobiology, 1980- present
- C. Reviewer for the following scientific journals:
 - 1. American Journal of Pathology
 - 2. American Journal of Physiology
 - 3. Archives of Pathology and Laboratory Medicine
 - 4. International Immunopharmacology
 - 5. Journal of Applied Physiology
 - 6. Journal of Leukocyte Biology

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. McClintock SD, Hoesel M, Das SK, Till GO, Kunkel RG, Smith MG, Ward PA: Attenuation of CEES-induced acute lung injury in rats. *J. Appl. Toxicol.* (in press)
2. Smith MG, Stone W, Crawford K, Ward P, Till G, Das S: Are antioxidant liposomes (STIMAL) the universal antidote to several weapons of mass destruction? *Janes.com* (in press)
3. Till GO, McClintock SD, Elford HL, Ward PA. Protective effects of polyhydroxyphenyl compounds on 2-chloroethyl-ethyl-sulfide-induced lung injury (to be submitted)

ABSTRACTS, BOOK REVIEWS, LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Ward PA, McClintock S, Smith MG, Till GO: Protective effects of anti-oxidant liposomes in lung injury after exposure to mustard gas compound. In: *Proceedings of Bioscience 2004 Medical Defense Review*, p 258. Hunt Valley, Maryland, May 16-21, 2004

**RICCARDO VALDEZ, M.D.
CLINICAL ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004- 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Diagnostic Hematopathology (including peripheral blood and body fluid smears).
- B. Clinical Hematology Laboratory (including review and verification of CAP Survey results).
- C. Clinical Flow Cytometry Laboratory.
- D. Hematopathology Consultation Cases (including M-Labs and Veteran's Hospital).
- E. Tissue Typing/Histocompatibility Laboratory (medical director in training).
- F. Diagnostic Heart Transplant Biopsies (ad hoc, 24 cases).
- G. Blood Bank, attending coverage (ad hoc, 1 week).
- H. Dermatopathology service coverage (GVHD cases, 2 days)

II. TEACHING ACTIVITIES:

- A. Medical Students:
 - 1. Laboratory Instructor, M2 General Pathology Course (22 hours).
 - 2. Rotation Mentor, M4 Pathology Elective (1 month, 6 students).
 - 3. Faculty Mentor/Advisor, Latin American-Native American Medical Student Association (15 hours).
 - 4. Laboratory Instructor, M1 Introduction to Histopathology (ad hoc, 6 hours).
- B. House Officers:
 - 1. Review and signout of in-house bone marrow biopsies (including bone marrow aspirate smears and peripheral blood smears), body fluid smears, lymph nodes, and spleens (residents and fellows).
 - 2. Review and signout of hematopathology transfer case material (residents and fellows).
 - 3. Review and signout of hematopathology consultation material (fellows).
 - 4. Flow cytometry signout (residents and fellows).
 - 5. Hematopathology case conferences (three with residents).
- C. Hematopathology teaching:
 - 1. Leukemia conference/biweekly.
 - 2. Lymphoma conference/weekly.
 - 3. Hematology conference/biweekly.
 - 4. Multiple myeloma conference/biweekly.
 - 5. Hematology/Oncology Morbidity and Mortality Conference.
 - 6. Internal Medicine Morbidity and Mortality Conference.
 - 7. Clinical Pathology Case Conference/weekly.

- D. Laboratory Staff:
 - 1. Hematology and flow cytometry laboratory CME.
 - 2. Tissue typing laboratory CME.
- E. National teaching:
 - 1. American Society for Clinical Pathology (ASCP), Pathology Resident Review Course, Instructional Faculty: Lymph Node Pathology.
 - 2. American Association for Cancer Research, Edward A. Smuckler Workshop: Pathobiology of Cancer, Co-director for Hematopoietic Tissues Laboratory and Laboratory Instructor for General Pathology.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Evaluation of PTEN (tumor suppressor gene) loss on hematopoietic stem cells in knockout mice.
- B. Characterization of mouse hematopoiesis and hematomphoid tumors following stem cell transplantation (A and B with Dr. Sean Morrison and Omer Yilmaz, M.D., Ph.D. student).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Tissue Typing/Histocompatibility Laboratory (medical director in training).
- B. Clinical Pathology Resident Training Review Committee.
- C. Clinical Pathology Resident Training (CPA block and Hematopathology fellowship training coordinator).
- D. Interviewer for pathology residency program.

REGIONAL/NATIONAL:

- A. Histocompatibility Committee, Gift of Life Michigan.

V. OTHER RELEVANT ACTIVITIES:

None

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Armstrong MB, Olobukola N, **Valdez R**, Park JM, Williams JA, Wechsler, DS. Testicular chloroma in a non-leukemic infant. Accepted for publication JPHO.
2. Bakshi NA, Ross CW, Finn WG, **Valdez R**, Ruiz R, Koujok K, Schnitzer B. Alk-positive anaplastic large cell lymphoma (ALCL) with primary bone involvement in children. Accepted for publication AJCP.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Bakshi NA, Finn WG, **Valdez R**, Ross CE, Schnitzer B. Fascin expression in diffuse large B-cell lymphoma (DLBCL), anaplastic large cell lymphoma (ALCL) and classical Hodgkin lymphoma (CHL). Submitted for publication.
2. Rawal A, Finn WG, Schnitzer B, **Valdez R**. Site-specific morphologic variations in extranodal marginal zone B-cell lymphoma (EMZL). Submitted for publication.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Grant MR, Schnitzer B, **Valdez R**, Finn WG. Malignant lymphomas of the retroperitoneum. Mod Pathol 2005;18(suppl 1): 232A.
2. Rawal A, Schnitzer B, Finn WG, **Valdez R**. Site-specific morphologic variations in extranodal marginal zone B-cell lymphoma (EMZL). Mod Pathol 2005;18(suppl 1): 248A.
3. Smith LB, **Valdez R**, Finn WG, Thorson JA. A rapid and comprehensive real time PCR assay for the detection of BCL2/IGH translocation in follicular lymphomas. Mod Pathol 2005;18(suppl 1): 251A.

BOOKS AND CHAPTERS IN BOOKS:

1. Yanik G, **Valdez R**, Ferrara J. Clinical Hematology Eds; Neil Young MD, Stan Gerson MD, Katherine High MD, Mosby Inc and Elsevier Publishing, NY. Chapter 97: Acute and Chronic Graft versus Host Disease (chapter submitted, publication expected in 2005).



**PETER A. WARD, M.D.
GODFREY D. STOBBE PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES

- A. These have been chiefly related to administrative responsibility for all clinical service functions of the Department.

II. TEACHING ACTIVITIES

- A. Post-doctoral fellows (2004-05):
1. Jayne Reuben, Ph.D.
 2. Hongwei Gao, Ph.D.
 3. Laszlo Marco Hoesel, M.D.
 4. Yong Han, M.D.
 5. Thomas Neff, M.D.
 6. Simona Neff, M.D.
 7. Cecilia Speyer, Ph.D.
- B. Graduate students
1. Kurt Bernacki, 2nd Semester Medical Student
- C. UROP Undergraduate Students:
1. Nick Rancilio
 2. Matthew Pianko
 3. Brandon Baugh
 4. Matthew Chung
- D. Undergraduate students:
1. Jeff Crawford, 2nd Year Undergrad (Calvin College)
 2. Eddie Martinez, 2nd Year Undergrad (U. of Mich.)

III. RESEARCH ACTIVITIES

HONORS

Distinguished Service Award, SHOCK Society, June 2005, Marco Island, Florida
Chugai Mentoring Award, American Society of Investigative Pathology, April 2005, San Diego, California

SPONSORED SUPPORT

- A. Principal Investigator, "Lung Immunopathology" (Training Grant) HL07517, \$227,536/yr., (5%) 06/01/96 - 05/31/06
- B. Principal Investigator, "Inflammatory Cells and Lung Injury" NIH/NHLBI PO1-HL31963, (Project 1), \$264,827 /yr. (25%) 02/01/05 - 01/31/10
- C. Principal Investigator; "Lung Injury by Oxygen Metabolites (MERIT) RO1- GM29507 NIH/NIGMS, (20%) \$312,396/yr, 07/01/05 - 06/30/09
- D. Principal Investigator, "Protective Effects of Anti-C5a in Sepsis," NIH/NIGMS RO1- GM61656, (20%) \$204,700/yr; 01/01/02 - 05/31/07
- E. Principal Investigator, "Mechanisms and Prevention of Lung Injury Caused by Exposure to Mustard Gas" DAMD 17-03-2-0054 USAMRMC, \$1,932,000 total, (5%), 08/15/03 - 08/14/05

IV. ADMINISTRATIVE ACTIVITIES

DEPARTMENTAL:

- A. Stobbe Professor and Chair, Department of Pathology.

MEDICAL SCHOOL/HOSPITAL:

- A. Medical School Executive Committee
- B. Senior Leadership Council
- C. Conflict of Interest Committee (Medical School)
- D. Technology Transfer Committee.
- E. Geriatric Center Executive Committee.
- F. Michigan Eye Bank Research Review Committee.
- G. Undergraduate Research Opportunity Program, University of Michigan.
- H. University of Michigan Cancer Center Executive Committee.

REGIONAL AND NATIONAL:

- A. American Association of Immunologists.
- B. American Society for Clinical Investigation.
- C. American Society for Investigative Pathology, representative to FASEB Board
- D. Association of American Physicians.
- E. American Thoracic Society.
- F. American Heart Association, Fellow
- G. Association of Pathology Chairmen
- H. American Association of University Pathologists
- I. A. James French Society of Pathologists, 1988-present.
- J. Institute of Medicine, National Academy of Sciences, July, 1990-present.
- K. Michigan Society of Pathologists.

- L. Michigan Thoracic Society, 1988-present.
- M. National Research Council.
 - 1. Chair and member, Council for Institute of Laboratory Animal Research, through June 30, 2005.
- N. Member, FASEB Board of Directors

V. OTHER RELEVANT ACTIVITIES

EDITORIAL BOARDS

- A. American Journal of Pathology, Editorial Board, 1982-present.
- B. American Review of Respiratory Diseases, Consulting Editor, 1977-present.
- C. Free Radical Biology & Medicine, Editorial Board, 1995-present.
- D. Journal of Clinical Investigation, Consulting Editor, 1995 - present.
- E. Journal of Experimental and Molecular Biology, 1999 – present
- F. Toxicologic Pathology, Editorial Board, 1988-present.

INVITED LECTURES/SEMINARS:

- 1. Invited Speaker, “Coagulation, Inflammation and Disease Relevance”, University of Michigan Medical School, Ann Arbor, Michigan, September 24, 2004.
- 2. Invited Speaker, West-Midwest APC/PDAS Regional Meeting; La Posada de Santa Fe Hotel, Santa Fe, NM; October 27, 2004.
- 3. Invited Participant, 3rd Innate Immunity Workshop, Crete, Greece; October 10, 2004.
- 4. Keynote Lecture, “Deflection of the Inflammatory Response in Sepsis”, Chugai Award for Meritorious Mentoring and Scholarship, American Society for Investigative Pathology Annual Meeting at Experimental Biology 2005, San Diego, California; April 4, 2005.
- 5. Invited Speaker, University of New Mexico, Albuquerque, NM; April 20, 2005
- 6. Invited Speaker, Burn & Shock Trauma Institute, Loyola University, Maywood, IL; May 5, 2005
- 7. Invited Speaker, American Thoracic Society 2005, San Diego, CA; May 19, 2005
- 8. Invited Speaker, EuroConference on Innate & Adaptive Immunity, Mecklenburg, Germany; June 1, 2005
- 9. Invited Speaker, 3rd Workshop on Complement Associated Diseases, Animal Models and Therapeutics, Rhodes, Greece; June 5, 2005

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS

1. Anaya-Prado, R., Toledo-Pereyra, L.H., Walsh, J., Guo, R.F., Reuben, J., and **Ward, P.A.**: Exogenous nitric oxide donor and related compounds protect against lung inflammatory response after hemorrhagic shock and resuscitation. *J Trauma*. 2004 Nov;57:980-988.
2. Speyer, C.L., Gao, H., Rancilio, N.J., Neff, T.A., Huffnagle, G.B., Sarma, J.V., and **Ward, P.A.**: Novel chemokine responsiveness and mobilization of neutrophils during sepsis. *Am J Pathol*. 2004 165:2187-2196.
3. Toledo-Pereyra, L.H., Lopez-Neblina, F., Reuben, J.S., Toledo, A.H., and **Ward, P.A.**: Selectin inhibition modulates Akt/MAPK signaling and chemokine expression after liver ischemia-reperfusion. *J Invest Surg*. 2004 17:303-313.
4. Huber-Lang, M.*, Sarma, J.V.*, Rittirsch, D.*, Schreiber, H., Weiss, M., Flierl, M., Younkin, E., Schneider, M., Suger-Wiedeck, H., Gebhard, F., McClintock, S.D., Neff, T., Zetoune, F., Brueckner, U., Guo, R.F., Monk, P.N., and **Ward, P.A.**: Changes in the novel orphan, C5a receptor (C5L2), during experimental sepsis and sepsis in humans. *J. Immunol*. 2005 174:1104-1110. *The three first authors contributed equally.
5. Neff, T.A., Guo, R.F., Neff, S.B., Sarma, J.V., Speyer, C.L., Gao, H., Bernacki, K.D., Huber-Lang, M., McGuire, S., Hoesel, L.M., Riedemann, N.C., Beck-Schimmer, B., Zetoune, F.S., **Ward, P.A.**: Relationship of acute lung inflammatory injury to Fas/FasL system. *Am J Pathol*. 2005 166(3):685-694.
6. Speyer, C.L., Rancilio, N.J., McClintock, S.D., Crawford, J.D., Gao, H., Sarma, J.V., and **Ward, P.A.**: Regulatory effects of estrogen on acute lung inflammation in mice. *Am J Physiol Cell Physiol*. 2005 288(4):C881-890.
7. Gao, H., Neff, T.A., Guo, R.F., Speyer, C.L., Sarma, J.V., Tomlins, S., Man, Y., Riedemann, N.C., Hoesel, L.M., Younkin, E.M., Zetoune, F.S., and **Ward, PA**: Evidence for a functional role of the second C5a receptor, C5L2. *FASEB J*. Epub March 22, 2005.
8. Farivar, A.S., Mackinnon-Patterson, B., McCourtie, A.S., Namkung, J., **Ward, P.A.**, and Mulligan, M.S.: Obliterative airway disease in rat tracheal allografts requires tumor necrosis factor alpha. *Exp Mol Pathol*. 2005 Jun;78(3):190-197.
9. Farivar, A.S., Mackinnon-Patterson, B., McCourtie, A.S., **Ward, P.A.**, and Mulligan, M.S.: The role of CC and CXC chemokines in cardiac allograft rejection in rats. *Exp Mol Pathol*. 2005 78(3):171-176.
10. Gerbitz, A., Ewing, P., Olkiewicz, K., Willmarth, N.E., Williams, D., Hildebrandt, G., Wilke, A., Liu, C., Eissner, G., Anereesen, R., Holler, E., Guo, R.F., **Ward, P.A.**, and Cooke, K.R.: A role for CD54 (intercellular adhesion molecule-1) in leukocyte recruitment to the lung during the development of experimental idiopathic pneumonia syndrome. *Transplantation*. 2005 79(5):536-542.
11. Hoesel, L.M.*, Neff, T.A.*, Neff, S.B., Younger, J.H., Olle, E.W., Gao, G., Pianko, M.J., Bernacki, K.D., Sarma, J.V., and **Ward, P.A.**: Harmful and protective roles of neutrophils in sepsis. *The two first authors contributed equally. *Shock* 2005 24(1):40-47.

**JEFFREY S. WARREN, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Director, Division of Clinical Pathology/Clinical Laboratories, May 1993-present.
- B. Director, Clinical Immunopathology Service; September 1989-present.
- C. Microbiology Laboratory; review of peripheral blood parasite smears; July 1996-present.
- D. Molecular Diagnostics Laboratory; signout of cases (3 weeks/year); July 1997-2005.
- E. Sendout Laboratory; Director, August 2002-July 2005.

II. TEACHING ACTIVITIES:

- A. "Current Topics in Immunopathology" journal club series: pathology residents, M4 students (37 contact hours).
- B. "Current Management Problems for Pathology Residents" series: pathology residents (6 contact hours).
- C. Clinical Pathology Grand Rounds:
 - 1. "Cases and images in immunopathology" (11/23/04).
 - 2. "Neonatal lupus syndromes" (12/14/04)
- D. Immunopathology signout: pathology residents, M-4 medical students, medical technology students (three times/week; 48 weeks/year).
- E. Immunopathology component of Block B (Clinical Pathology); ad hoc topical reviews: pathology residents (77 contact hours).
- F. Supervision of Research activities for:
 - 1. Anjali Desai, Ph.D. (Research Investigator); (6/15/96-present).
 - 2. Biofluid Repository Laboratory (Kun Li, M.D.)

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

None

PROJECTS UNDER STUDY:

- A. Modulation of proatherogenic endothelial and smooth muscle cell functions by erythropoietin, reactive oxygen intermediates, and reactive nitrogen intermediates.
- B. Role of erythropoietin in accelerated atherogenesis in ApoE (-/-) mice with drug-induced chronic renal disease.
- C. Measurement of NO production by endothelial cells using a chemical sensor. (Collaboration with Michael Meyerhoff, Ph.D., Department of Chemistry, University of Michigan).
- D. Pathophysiologic role of oxidants in uremia and its complications (collaboration with Rajiv Saran, M.D., Department of Internal Medicine, University of Michigan Medical School).

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL:

- A. Member, Steering Committee, et. al. Orders Management Program, University of Michigan Health System (25% effort).
- B. Professional Billing Compliance Committee, University of Michigan Medical School, 1999-present.

DEPARTMENTAL:

- A. Interviewer of Pathology Residency Candidates, 1989-present.
- B. Chairman, Laboratories Communications Committee, 1993-present.
- C. Chairman, Department of Pathology Quality Assurance Committee, 1993-present.
- D. Clinical Associate and Advisory Committee for Medical Technology Program, Eastern Michigan University, 1993-present.
- E. Chairman, Category Risk II Faculty Salary Planning Committee, Department of Pathology, 1996-present.

REGIONAL AND NATIONAL:

- A. Ad hoc referee for:
 - 1. American Journal of Pathology.
 - 2. Laboratory Investigation.
 - 3. Human Pathology.
 - 4. Journal of Applied Physiology.
 - 5. Lung.
 - 6. Blood.
 - 7. Journal of Laboratory and Clinical Medicine.
 - 8. Pediatric Research.
 - 9. Journal of Leukocyte Biology.
 - 10. American Review of Respiratory Disease.
 - 11. Chest.
 - 12. Journal of Pharmacology and Experimental Therapeutics.
 - 13. Circulation.
 - 14. Ophthalmology.
 - 15. American Journal of Respiratory Cell and Molecular Biology.
 - 16. Clinical Immunology and Immunopathology.
 - 17. Circulation Research.
 - 18. Journal of Immunology.
 - 19. Surgery.
 - 20. Reviews of Infectious Diseases.
 - 21. Infection and Immunity.
 - 22. Experimental Lung Research.
 - 23. Journal of Rheumatology.
 - 24. Clinical Infectious Diseases.
 - 25. Journal of Clinical Investigation.
 - 26. Cytometry.
 - 27. Biological Signals.
 - 28. Metabolism.

29. Molecular Medicine Today.
 30. American Journal of Respiratory and Critical Care Medicine.
 31. The Cancer Journal.
 32. British Journal of Pharmacology.
 33. Kidney International
- B. Member, Test Committee for Clinical Pathology, American Board of Pathology, 1999-2005.
 - C. Member, Council for Diagnostic Immunology and Molecular Pathology, American Society of Clinical Pathologists, 1998-present.
 - D. Member, Diagnostic Immunology Resource Committee, College of American Pathologist, 2000-present.
 - E. Past-President, Michigan Society of Pathologists, 2004.
 - F. Fellow Council, American Society of Clinical Pathologist
 - G. College of American Pathologists Inspection, Team Leader, University of Chicago Hospitals, Chicago, IL, October 5-6.

V. INVITED LECTURES/SEMINARS:

None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

None

ARTICLES SUBMITTED FOR PUBLICATION:

1. Desai A, Lankford H, Warren JS: Nitric oxide suppresses erythropoietin-induced monocyte chemoattractant protein-1 in endothelial cells: Implications for atherogenesis in chronic renal failure. (Submitted).
2. Desai A, Zhao Y, Warren JS: Development of atherosclerosis in Balb/c Apo E knockout mice. (Submitted).
3. Desai A, Zhao Y, Warren JS: Erythropoietin suppresses endothelial cell apoptosis: implications for atherogenesis in chronic kidney disease. (Submitted).

BOOKS/CHAPTERS IN BOOKS:

1. Warren JS: Immunopathology, in Rubin E (ed.) Pathology, 4th Edition, Lippincott-Williams and Wilkins, Philadelphia, PA, 2005.
2. Warren JS, Ward PA: The inflammatory response, in Lichtman MA, et. al. (eds.) Williams Hematology, 7th Edition, McGraw-Hill, New York, NY, (in press).
3. Warren JS: Immunoglobulin Quantification and Viscosity Measurement, in Keren DF (ed) Manual of Molecular and Clinical Laboratory Immunology, 7th Edition, American Society of Microbiology Press, Washington, DC, (in press).

**ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR,
MISCELLANEOUS PUBLICATIONS IN UNREFERRED JOURNALS:**

None

**THOMAS WILSON, M.D., Ph.D.
ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. CLINICAL ACTIVITIES:

- A. Assistant Director of the Molecular Diagnostics laboratory. Performed signout coverage in the director's absence and provided technical consultation and assistance in the implementation of new procedures.

II. TEACHING ACTIVITIES:

- A. Mentor, postdoctoral fellows: Rajashree Deshpande, Anandi Srinivasan, Leana Topper, Dongliang Wu
B. Mentor, graduate student fellows: Phil Palmbo (MSTP, CMB), James Daley (CMB)
C. Mentor, rotation student: Jennifer Keller (PIBS)
D. Mentor, undergraduate students: Renee Vander Laan, Brian Renard
E. Member, thesis committees: Tammy Morrish (Human Genetics), Marc Prindle (CMB), Anne Casper (Human Genetics), Sandra Durkin (Human Genetics), Rebecca Hausler (Biological Chemistry), Matthew Pratt-Hyatt (Biological Chemistry)
F. Member, preliminary examination committee: Scott Leiser (CMB), Karyolyn Oetjen (Pathology), Haitao Wen (Pathology), Sara Monroe (Pathology)
G. Member, Cellular and Molecular Biology Training Program
H. Path 581, 1 lecture, Neoplasia sectionmaster
I. Path 850, Coursemaster, research seminar series for graduate students
J. Two week full-time course in molecular biology and DNA repair, University of Michigan Postdoctoral Research Training Program

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Disposition of DNA Double-Strand Breaks Among Multiple Pathways of Repair", Pew Scholars Program in the Biomedical Sciences (8%), \$60,000/year (\$240,000/four years), 7/1/2000-6/30/2005 (final year is no cost extension).
B. Principal Investigator, "End Processing in DNA Double-Strand Break Repair", NIH/NCI 1 R01 CA090911-04 (27%), \$145,250/current year (\$601,750/four years), 4/1/2001-3/31/2005.

- C. Principal Investigator, "Systematic Genetic Analysis of Yeast NHEJ", NIH/NCI 1 R01 CA102563-01 (30%), \$157,500/current year (\$787,500/five years), 8/1/2004-7/31/2009.
- D. Mentor, University of Michigan Cancer Biology Training Grant Predoctoral Fellowship, Phillip L. Palmbo, 9/1/2004-8/31/2005
- E. Mentor, University of Michigan Rackham Predoctoral Fellowship, James M. Daley, 5/1/2005-4/30/2006
- F. Mentor, University of Michigan Summer Biomedical Research Fellowship, Renee M. Vander Laan, 5/1/2005-8/31/2005
- G. Mentor, University of Michigan Summer Biomedical Research Fellowship, Brian M. Renard, 5/1/2005-8/31/2005

PENDING:

- A. Principal Investigator, "End Processing in DNA Double-Strand Break Repair", NIH/NCI 2 R01 CA090911-05A1 (30%), \$175,000/first year (\$875,000/five years), 12/1/2005-11/30/2010.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Pathology student recruitment activities
- B. Chair and organizer, Pathology Research Seminar Series
- C. Member, Pathology Graduate Program Curriculum Committee

MEDICAL SCHOOL/HOSPITAL:

- A. Member, MSTP Career Advisory Panel
- B. MSTP student interviews
- C. Faculty candidate interviews/recruitment
- D. Member, committee for reorganization of residency training in Clinical Pathology

UNIVERSITY OF MICHIGAN:

- A. PIBS student interviews and recruitment dinners
- B. Member, Cellular and Molecular Biology Program Steering Committee

REGIONAL AND NATIONAL:

- A. None.

V. OTHER RELEVANT ACTIVITIES:

- A. Manuscript review, Genetics, MCB, Nature, DNA Repair, Cancer Research
- B. Biological Sciences Scholars Program, University of Michigan
- C. Pew Scholars Program in the Biomedical Sciences, Pew Charitable Trusts
- D. Member, Michigan Comprehensive Cancer Center
- E. Grant Review, Medical Research Council, UK

EDITORIAL BOARDS:

- A. None

HONORS AND AWARDS

- A. None.

PATENTS:

- A. None

INVITED LECTURES/SEMINARS:

1. "Reconstitution of bacterial nonhomologous end-joining (NHEJ) in yeast." American Society for Microbiology Conference on DNA Repair and Mutagenesis, Southampton, Bermuda, November 17, 2004.
2. "Separation of function mutants of Ku80 and Xrs2; evidence for a concerted NHEJ repairosome." Keystone Symposium on Genome Instability and Repair, Taos, New Mexico, March 19, 2005.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Deshpande R, Wilson TE. Identification of DNA 3' phosphatase active site residues and their differential role in DNA binding, Mg²⁺ coordination and catalysis. *Biochemistry*, 43:8579-89 (2004).
2. Della M, Palmboos PL, Tseng HM, Tonkin LM, Daley JM, Topper LM, Pitcher RS, Tomkinson AE, Wilson TE, Doherty AJ. Mycobacterial Ku and Ligase proteins constitute a two-component NHEJ repair machine. *Science* 306: 683-5 (2004). Phillip Palmboos, from the Wilson laboratory, acts as co-first author.
3. Daley JM, Wilson TE. Rejoining of DNA double-strand breaks as a function of overhang length. *Mol. Cell. Biol.* 25: 896-906 (2005).

4. Karumbati AS, Wilson TE. Abrogation of the Chk1-Pds1 checkpoint leads to tolerance of persistent single-strand breaks. *Genetics* 169: 1833-44 (2005).
5. Daley JM, Vander Laan RL, Suresh A, Wilson TE. DNA joint dependence of Pol X family polymerase action in nonhomologous end joining. *J. Biol. Chem.* In press.

ARTICLES SUBMITTED OR IN PREPARATION:

1. Palmbos PL, Wilson TE. Separation-of-function mutants of Ku80 and Xrs2 reveal a concerted NHEJ repairosome. *EMBO J.*
2. Pratt-Hyatt MJ, Kapadia1 KM, Wilson TE, Engelke DR. Increased recombination between active tRNA genes. *Nucl. Acids Res.*

BOOKS/CHAPTERS IN BOOKS:

1. Daley JM, Palmbos PL, Wu D, Wilson TE. Nonhomologous end joining in yeast. *Annual Review of Genetics.* In press.

**ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR,
MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:**

1. Pitcher RS, Wilson TE, Doherty AJ. New insights into NHEJ repair processes in prokaryotes. *Cell Cycle* 4: 675-78 (2005). Invited review.

SECTION REPORTS

ANATOMIC PATHOLOGY

DIVISION OF ANATOMIC PATHOLOGY

**ANNUAL REPORT
1 JULY 2004 - 30 JUNE 2005**

The Division of Anatomic Pathology continues to enjoy a strong national and international academic reputation while providing a breadth of expertise in support of the clinical, research and educational programs of the University of Michigan Health System, Medical School, and University. This past year two new faculty have joined the Division, Drs. Ma and Pang. These faculty bring additional expertise in dermatopathology and cytopathology, respectively.

During the past year surgical pathology implemented sub-specialty sign-out services in gastro-intestinal pathology and breast pathology in addition to the established services in genito-urinary pathology, gynecologic pathology, renal pathology, neuropathology and dermatopathology. Overall, the clinical activity in surgical pathology increased by approximately 4% with greatest increase associated with expansion of in-house programs and consultation cases. Additional space in support of the cytopathology service and histology laboratory was identified and renovations are proceeding. The dermatopathology service moved into new renovated space in medical science building 1.

Faculty research programs and extramural support continues to increase especially in programmatic areas associated with the Cancer Center, GI pathology, Breast pathology and SPORE in Urologic Disease. There continues to be expansion of core research facilities directed by faculty in the division including; tissue microarrays, laser capture microdissection, histology/immunoperoxidase/FISH, and tissue procurement.

Four senior residents completed surgical pathology fellowships. Five additional house officers completed fellowship training in cytopathology, urologic pathology, and hematopathology. All found excellent positions in sub-specialty fellowships (4), private practice (3), and academic faculty positions (2).

Currently we are actively recruiting for a new Director of Anatomic Pathology with planned expansion of translational research programs and future faculty recruitments. These are times of opportunity for the division, department and medical school and we are well positioned to continue as one of the pre-eminent academic divisions and departments in the country.

AUTOPSY SERVICE

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 2004 - 30 JUNE 2005

I. Timely Completion of Autopsy Reports:

The autopsy service continues to emphasize timely completion all our autopsy reports in order to communicate with our clinical colleagues and provide information to the families. The table below lists the autopsy completion time for different years. As of June, 2005 we closely track any autopsy that is older than 30 days until it is finished. This close tracking is accomplished by paging the house officer each day that their case is not complete. Since adopting this protocol on January 1, 2004, there has only been a single autopsy later than 60 days.

Time Interval	% completed in 60 days	% completed in 90 days	# of Autopsies
1995-96	40	58	541
1996- 97	64	89	565
1998-99	96	100	350
1999-2000	91	100	295
2000-2001	84	99	295
2001-2002	85	99	293
2003-2004	94	99	306
2004-2005	89	99	293

II. Autopsy Reporting on Careweb

Starting January 1, 2004, autopsy results have been available on Careweb. The front page from the autopsy report, the clinicopathological diagnosis, is placed on Careweb. Coupled with the improved turnaround time, this has significantly improved the utility of the autopsy service by providing timely feedback in an easily accessible manner. We are presently working to place all of the gross pathologic diagnoses on Careweb also.

III. Conferences:

We continue to present our cases at several different conferences. Pathology regularly participates in the weekly Death and Complications conference in the Department of Surgery. We also make presentations at the monthly Morbidity and Mortality conference in the Department of Internal Medicine. A continuing monthly conference in the Department of Internal Medicine has 4 autopsies presented each month. In contrast to the usual M&M conference where most of the presentation deals with the clinical story, the emphasis for this conference is on the autopsy findings and histopathology. These conferences run primarily by the first year pathology residents who have completed their autopsies. At

the request of the Department of Emergency Medicine, we are also making presentations twice a year to their house officers.

IV. Autopsy percentage:

We continue to determine the autopsy rate by clinical service in the hospital. The total number of deaths, number of cases and autopsy percentage for the 2004-05 year are listed below. This information as they shared with both the clinical chairs as well as the residency program directors of the University of Michigan. The figures below do not include the number of brain only autopsies performed.

	# of deaths	# of cases	% of deaths
Medicine	458	106	23%
Surgery	288	50	17%
Pediatrics	103	36	35%
Other services	27	8	30%
Total Hospital	876	200	23%

Hospital total 23%

V. Medical Examiner Cases:

The Department of Pathology continues to have a presence in Medical Examiner issues in the State of Michigan and Washtenaw County. Medical examiner autopsies continue to be done at the University of Michigan. Additionally, the Director of the Autopsy Service serves on the Executive Committee of the Michigan Association of Medical Examiners as well as being the Executive Editor of the Association's newsletter.

VI. Statistics:

This covers the time period July 1, 2004 to June 30, 2005.

Total number of autopsies performed	293
Hospital autopsies	200
Brain only	29
Medical examiner autopsies	60
Warm autopsies	4

Daniel G. Remick, M.D.
Director, Autopsy Service

CYTOPATHOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY

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Total gynecologic specimens for the year were 46,716; a 2.7% decrease from last year. (Expected decrease due to modified follow up recommendations for post-menopausal patients). Non-gynecologic specimens numbered 7,950, a 13.5% increase from last year. Fine needle aspirations totaled 1,806 for the current year, a 14.9% increase from last year. The laboratory continued to achieve the turnaround time for non-gynecologic specimens within 24-48 hours, and the turnaround time for the cervical smears have stabilized to an average of 4 working days.

At this time, we are approximately 96% converted to ThinPrep in gynecologic specimens. An amended report combining the original cytologic diagnosis and the HPV test by the Digene method has been effectively used.

The Laboratory Staff and faculty are enrolled in the newly established Proficiency Testing in compliance with the Centers for Medicare and Medicaid and are scheduled for the test in September 20.

The fine needle aspiration service established at the Taubman Center to assist with ultrasound guided thyroid aspirates performed by the Endocrinology Service has been successful and patients are routinely scheduled on Thursdays. The Fine Needle Aspiration Clinic in the CGC was successfully moved in May to another treatment room with minimal problems. We will continue to monitor its performance.

Our fellowship program continued to be highly successful. Drs. Michael Rhode and Ching Li completed their training with distinction. Dr. Yijun Pang was successfully recruited and joined our faculty in cytopathology effective in July of 2005.

The Cytopathology Section had excellent representation at national meetings with Seminars and posters presented by the cytology faculty. Dr. Michael was trained by TriPath Co. in North Carolina and received certification in interpreting SurePath gynecologic Preps.

Claire W. Michael, M.D.
Director, Cytopathology Laboratory

DERMATOPATHOLOGY SERVICE
DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
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The Dermatopathology Service receives diagnostic case material from four primary sources: (1) UMMC (ID) cases; (2) outside contractual (MD) cases; (3) personal consultation cases (DP); and (4) outside slides reviewed for referred patients (TD) cases.

Clinical Service

The clinical service volume is as follows:

	2002-2003	2003-2004	2004-2005
ID	6,811	6343	6888
MD	9,663	9514	8878
TD	1,698	1568	1758
DP	1,336	1577	1871
MISC	145	172	148
TOTAL	19,653	19,174	19,543

The Dermatopathology Service continues to be a high volume service, with greater than 19,000 cases signed out this year. We had an overall 2% growth in case load. The consult service experienced a 19% growth in volume. The clinical service load seen by each faculty member of the Dermatopathology Service, Dr. Su, Dr. Fullen, and Dr. Lowe, is substantial, with greater than 6,300 cases each.

We continue our active involvement in the University of Michigan Multidisciplinary Melanoma Clinic (MDMC) and Tumor Board (bi-weekly). This remains the largest melanoma program in the United States. Accordingly, the volume of difficult pigmented lesions seen by our service is substantial, as are the numbers of wide local excisions, biopsies, and sentinel lymph node biopsies generated by this busy clinic, all of which directly impact Dermatopathology. In addition, we have a very visible role in Cutaneous Lymphoma Conference and Tumor Board.

Education

The Dermatopathology Service continues its extensive and committed involvement with residency and medical student education in the both the Departments of Pathology and Dermatology. Teaching activities include daily instruction at the microscope during signout, weekly formal didactic sessions, weekly diagnostic conference, and active participation in the MSII Dermatology Core Sequence and Dermatopathology Laboratory. Dr. Lyndon Su and Dr. Douglas Fullen also actively participate in formal dermatopathology didactic sessions for our pathology residents.

Scholarly Activities

During this academic year, Dr. Doug Fullen was deservedly promoted to Associate Professor, effective September 1, 2005. We continue to be highly productive in scholarly activities and academic pursuits with numerous publications individually and/or collectively in well-respected peer reviewed journals. In addition, we have all actively participated at national meetings, either as invited speaker(s) and/or abstract/poster presentations.

Goals for 2005-2006

The Dermatopathology Service has successfully identified and recruited a fourth dermatopathologist. We welcome Dr. Linglei Ma, who will join us July 1, 2005. In addition, we are in the process of establishing a Dermatopathology Fellowship program.

Respectfully submitted,

Lori Lowe, M.D.
Director
Dermatopathology Service

NEUROPATHOLOGY SERVICE

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 2004– 30 JUNE 2005

Dr. Mila Blaivas, Ms. Constance J. D'Amato, Dr. Andrew P. Lieberman and Dr. Paul E. McKeever contributed to the Neuropathology Service. Ms. D'Amato is active emeritus.

I. CLINICAL ACTIVITIES:

1. There were over 1200 neurosurgical cases examined this year. There were many personal consult cases. (M.B. = 321)
2. The Diagnostic Unit of the Neuropathology Core Laboratory of the MADRC processed 24 dementia brain cases. Of these 24 brains, 20 were MADRC cases, 2 were neurology hospital patients, and 2 were from the Michigan Dementia Postmortem Network Program.
3. There were 439 muscle biopsies, 30% with electron microscopy. There were 93 peripheral nerve biopsies. There were 17-teased fiber preparations and 100 with electron microscopy. 6 skin or non-muscle/nerve tissue examined with electron microscopy. 29 muscle biopsies were examined with 10-16 anti-dystrophy antibodies in the IPOX laboratory.
4. There were over 300 University Hospital brains examined.
5. The Brain Tumor Board of the University of Michigan Cancer Center and Hospitals, supported weekly by a neuropathologist, reviewed neuropathology and clinical aspects of more than 150 difficult neuro-oncology cases.

II. TEACHING ACTIVITIES:

1. Medical Students: This year the neuropathology faculty taught in the Neurology two and one half week portion of the Neuroscience Sequence. Two one hour lectures were presented (APL), dementia and CNS tumors. There were two laboratories, two hours each (for half of the class and then repeated for the other half). Thus the faculty (CJD, APL, PEM) were involved in up to ten (10) hours of neuropathology teaching.
2. Dental Students: 3 lectures (PEM).
3. House Officers, Graduate Students, Postgraduate and other students and faculty: These included the following Continuing Medical Education accredited conferences: periodic conferences for Neurology; monthly Rheumatology Pathology Grand Rounds and occasional CPC conferences; monthly conferences where all biopsies are presented and interpreted; a weekly conference where abnormal brains are examined (including two or three weeks per month for dementia cases) with all clinicians invited; weekly nerve and muscle conferences; monthly nerve and muscle biopsy conferences. We provided

individual instruction on autopsies and biopsy material; bi-monthly conferences with Neuroradiology, Neurosurgery and Neuroradiology House Staff and every third month a microscopic conference for dementia brain cases. Weekly seminars were provided to neurological and neurosurgical house staff on clinical-pathological correlations.

4. Neuropathology 858, an evening course, given in the Fall, was taught by Dr. Lieberman and Ms. D'Amato.
5. Electives: Senior Medical Students, Pathology, Neurosurgery, and Neurology Residents were offered elective rotations in the Neuropathology Section.

III. RESEARCH ACTIVITIES:

1. Dr. Andrew Lieberman and Ms. D'Amato provided neuropathology support for MADRC. Dr. Lieberman was co-director of the Neuropathology core of MADRC.
2. Dr. Blaiwas collaborating with the EMG group (3 papers have been presented last Fall, 2 this summer, manuscripts in preparation), neurosurgery (manuscript in preparation), pediatrics, ophthalmology (Jonathan Trobe, M.D., Iris Ben-Bassat Mizrachi, M.D.), rheumatology (manuscript in preparation). Additionally, she is working with the Bioengineering Department and Neurosurgery Department, 2 projects under study, grant submitted for one of them. She is collaborating with Michael Wang, M.D., in the Department of Neurology and Neurophysiology, and group, on a grant to study CADASIL on mice model submitted to NIH (Co-investigator). Pilot project is under study. Finally she is involved with a national study group (ERSET, par of, for evaluation of temporal lobectomy/hippocampectomy cases.
3. Dr. McKeever and associates were determining differences in gene product expression in brain tumors. They assessed the predictive value of markers in brain tumor specimens. Stromal patterns as diagnostic tools in pituitary lesions were studied with Drs. Jason Jarzembowski and Ricardo Lloyd. He is characterizing neural cancer stem cells with Dr. Sean Morrison (5%); measuring tumor proliferation with Dr. Brian D. Ross (5%); measuring apoptosis in transgenic mice with Dr. Thomas Chenevert (5%); and characterizing gliomas in p53 altered mice with Dr. Yuan Zhu. He is finishing publications from a NIH funded project studying the prognostic potential of MIB-1 proliferation marker on brain tumors.
4. Dr. Lieberman's laboratory studies the mechanisms of neurodegeneration in Kennedy's disease and Niemann-Pick C. He is using cell culture and animal models to determine how the causative mutations lead to neuronal dysfunction and death. He is the principal investigator on grants from the NIH and Muscular Dystrophy Association that support his work.
5. University of Michigan Cancer Center faculty and staff with clinical research interests in brain tumors met and generated a number of project considerations with Pathology, Neurosurgery, Nuclear Medicine, Neuropathology, Neurology and Neuroradiology collaborations.
6. Collaboration with Neurology, Michigan State University, The Alzheimer's Association, Spectrum Health, and Wayne State University has established a registry for Alzheimer's disease and other dementias and degenerative diseases.

**SPECIAL STUDIES LABORATORY
(CLINICAL IMMUNOHISTOCHEMISTRY, DIAGNOSTIC MUSCLE STUDIES,
IMMUNOFLUORESCENCE AND IN SITU HYBRIDIZATION)**

**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

INTRODUCTION

The immunohistochemistry laboratory took an important step forward in efficiency and standardization in January 2005 with the addition of 5 new automated Ventana XT instruments. These new instruments have the ability to perform pretreatment for epitope retrieval, in addition to automated immunohistochemical staining. We have been updating and optimizing our antibody panel using Ventana prediluted antibodies to replace and supplement our other offerings. The diagnostic muscle studies laboratory remains a very busy service, and the laboratory has gained several new outside clients. Requests for direct immunofluorescence staining of renal, skin and heart specimens have increased slightly this year. Chromogenic in situ hybridization (CISH) plays an important role in the clinical diagnosis of HPV and EBV related diseases, and growth is anticipated in the number of tests offered.

CLINICAL IMMUNOHISTOCHEMISTRY

Year-end figures show that the average number of slides stained per day increased slightly, from 174 slides/day to 178 slides/day, representing a 2% increase over last year. Several new antibodies have been added to our menu, including MUC2, MUC5AC, MUC6, TFE3, OCT3/4, CD13, CD14, CD163 and CDX-2. Pretreatment for epitope retrieval from formalin-fixed tissue has been further standardized in two ways. First, online pretreatments available on the new Ventana XT instruments have decreased inter-operator variability for many of the different pretreatment methods we use. Second, we have added another pretreatment instrument, the Decloaker from Biocare, which performs pressure and temperature controlled epitope retrieval for procedures that cannot be performed by the Ventana XT. Continuing demand for new antibodies and special procedures like Chromavision and in situ hybridization (see below) have increased demands upon current staff, and will likely require changes in work organization in the coming year. As in the past, we have continued to score 100% on the biannual Immunohistochemistry CAP testing.

DIAGNOSTIC MUSCLE STUDIES

Under the direction of Dr. Blaiwas, this laboratory has continued to develop new diagnostic tools. The caseload for this service decreased slightly this year, although still remains high (398 biopsies compared to 424 muscle biopsies last year). In addition to the standard histochemistry panel, 17 frozen section antibodies are now available for the immunohistochemical diagnosis of muscular dystrophies. This capability has helped the lab to remain on the cutting edge of muscle disease pathologic diagnosis. However, this is a labor- and material-intensive process, as muscles require special processing and frozen sectioning, and a complete diagnostic workup (histochemistry and dystrophy panels) can entail up to 40 slides per case.

IMMUNOFLUORESCENCE

Under the direction of Drs. Killen, Johnson, Fullen and Gordon, this laboratory continues to stain skin, heart and renal biopsies using the automated Ventana ES immunostainer. The caseload increased slightly this year. There were 412 renal biopsies (361 last year), 312 skin biopsies (306 last year) and 56 heart biopsies (56 last year).

IN SITU HYBRIDIZATION

Chromogenic in situ hybridization (CISH) performed on paraffin embedded tissue sections has become a standard diagnostic test for both HPV and EBV related diseases. The number of cases remained steady over the past year and our Ventana Benchmark stainer is run most days of the week for these tests. In all likelihood we will continue to see more CISH tests added in the near future.

CONCLUSION

The clinical caseload continued to increase in the year 2005. Our future goals for the immunohistochemistry laboratory include further standardization of antigen retrieval and increased use of prediluted antibodies to enhance slide staining quality and increase efficiency. Expanded work hours (an afternoon shift) and/or overnight staining processes may be required in the coming year to better utilize laboratory resources and finish cases in a timely fashion.

CLINICAL PATHOLOGY

DIVISION OF CLINICAL PATHOLOGY

**DEPARTMENT OF PATHOLOGY
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The Clinical Laboratories continued to provide excellent, full-spectrum service (more than 850 different laboratory analyses) as the Health System continued to expand both its clinical volume and scope. The Molecular Diagnostics, Tissue Typing, and Immunopathology Laboratories were successfully relocated in December-January to incremental new laboratory space at Traverwood. Substantial effort has again been directed towards aggressive laboratory utilization control, the improvement of test ordering, laboratory logistics, and achievement of compliance with CMS-mandated rules on documentation of test-ordering indications. Department of Pathology personnel are critically involved at many levels of the \$74 million UMHS Orders Management Project” which promises to streamline patient care in the Hospitals and in so-called “Inpatient-like Venues”. Superimposed upon these efforts has been further development of computer links with M-Labs clients. In 2004-05 the Clinical Laboratories performed more than 3.5 million billable analyses (10 million individual measurements), supported a wide array of clinical and research programs, and added or replaced more than 50 testing methods. The maintenance of high quality services by the Clinical Laboratories, in the face of increasing complexity of demands, is testimony to the professionalism of the staff and the management capabilities of the laboratory directors and senior laboratory personnel. The Clinical Laboratories successfully completed the biannual College of American Pathologists on-site inspection in May, 2005. Maintenance of the delicate balance among quality service, cost effective testing, utilization control, and the research and development which characterizes an academic institution, will be a continuing challenge.

A major achievement was the continuing pursuit of an aggressive utilization management program. More than \$1.1M in direct laboratory cost avoidance and test utilization control was realized in 2004-05. This was made possible through educational meetings with selected clinical program directors and the support of the Clinical Decision Support Service.

Finally, the Clinical Laboratories have continued to respond to the change in scope and organization of UMHS patient care activities. In contrast to the early 1990s when 70% of laboratory testing volume came from inpatient services and 30% from ambulatory patients, the split is now 40:60 in the opposite direction. The laboratories currently support more than 30 UMHS-owned regional satellite facilities as well as many more patients who are M-Care subscribers. The Department was successful in the recruitment of a new M-Labs Program Director, Dr. Steven Mandell. In addition to excellence as a pathologist, Dr. Mandell brings great energy and expertise in outreach, informatics, management, and logistics.

Faculty and laboratory staff participated in a wide variety of intramural and extramural educational programs during 2004-05. For instance, the AIMCL (informatics) course in Las Vegas was again well attended, making it the most visible courses of its kind in the United States. The May AIMCL course brought together leaders from a variety of institutions and laboratory information technology fields to discuss the future of clinical pathology practice. These programs, along with the M-Labs educational

programs, are prominent examples of educational outreach activities. The recently revised clinical pathology residency training format, which organizes pathology residents into teams that rotated through four blocks of clinical laboratories that are grouped according to “relatedness of discipline”, was again updated in 2004-05. In keeping with a thematic approach, the 2005-06 version has established five rotation blocks and places greater emphasis on molecular diagnostics. The continued high quality of trainees in the Hematopathology Fellowship program has enhanced the service, educational, and academic missions of the Hematopathology group and the Department.

The academic achievements of faculty members within the Clinical Pathology Division have been outstanding. As a group, the CP faculty had approximately 80 articles published in peer-reviewed journals. Most faculty members played highly visible leadership roles in national organizations, courses, symposia, as well as on editorial boards, examining committees, and research review study sections; an illustration of their high levels of recognition throughout the United States (see individual reports). Numerous faculty members received extramural funding that supported a variety of scholarly activities (see individual reports).

The Clinical Pathology Division will continue to face new challenges. In addition to its ongoing academic enterprises, educational issues, leadership and development in quality assurance, and laboratory resource utilization in the context of the hospital cost efficiency program, the Division plans to continue its attention to informatics and the clinical molecular diagnostics program. It is anticipated that there will be increased emphasis on the recruitment of faculty who can successfully contribute to both the service and scholarly activities of the Department. Participation in the design of new clinical and research space under the leadership of our new Chairman, Dr. Jay Hess, is anticipated with great eagerness. Achievement of these objectives will require the continued commitment, professionalism, and hard work of the faculty, laboratory staff, administration, and house officers.

Jeffrey S. Warren, M.D.
Director, Clinical Pathology Division

**UNIVERSITY HOSPITALS BLOOD BANK
AND TRANSFUSION SERVICE**

**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

PATIENT CARE:

Blood component utilization increased relative to the previous year by 3.8% overall with 98,650 total components dispensed. There was an increase in all categories of blood components. Red Blood Cell utilization totaled 33,099 units. Platelet Concentrate utilization was totaled 48,909, reversing a downward trend seen in the previous three years. Increased overall utilization represents increased clinical activity. Notably, the volume of type and screen tests performed increased by 12% to 46,100. This is primarily due to increased activity in the Operating Rooms. Automation of type and screen processing permitted this growth to be accommodated without staffing increase.

Hematopoietic progenitor cell processing activity was comparable to the previous year with 458 total units processed. 224 HPC transplants were performed, with 386 units infused, for an average of 1.7 units per patient.

The Transfusion and Apheresis Service activity totaled 1678 patient encounters. This represents a 14% increase in activity compared to the previous year. Hematopoietic progenitor cell collections totaled 350, equivalent to the previous year, while 714 therapeutic apheresis procedures were performed, compared to 564. LDL apheresis experienced significant growth doubling the number of procedures to 104.

The Reference laboratory activity experienced 3% overall growth. However, there was an 18% increase in antibody identification studies and a 19% decrease in BMT testing. The latter most likely represents a transient drop due to turnover within the BMT program.

A total of 526 transfusion reaction investigations were performed. Of these, the largest categories were events not due to transfusion (275) and febrile non-hemolytic reactions (134).

EDUCATIONAL ACTIVITIES:

Members of the Blood Bank medical and technical staffs participated in Pathology house officer teaching, Hematology fellow teaching, M2 and M4 medical students teaching, the transfusion component of nursing orientation, and many interdepartmental conferences.

The 31st annual postgraduate course, "Current Topics in Blood Banking", was held on June 8-10, 2005. The course, under the direction of Mr. Judd, attracted over 100 technologists and physicians from throughout the United States. It continues to be one of the most popular postgraduate courses in the country devoted to blood bank topics. The Blood Bank and Transfusion Service medical and technical staffs were instrumental in planning, organizing and presenting this program.

PROFESSIONAL ACTIVITIES:

Members of the Blood Bank and Transfusion Service medical and technical staffs were active at the regional and national levels. Suzanne Butch served on committees of the American Association of Blood Banks, the Michigan Association of Blood Banks, ICCBBA, the American Society for Clinical Laboratory Science, the Michigan Society for Clinical Laboratory Science, and the National Certifying Agency of Clinical Laboratory Personnel. LouAnn Dake was a member of the AABB Immunohematology Reference Laboratories Accreditation Program Unit Committee, and presented at programs of the Michigan Association of Blood Banks and the Immunohematology Reference Laboratory Conference. Terry Downs was Co-chair of the Michigan Association of Blood Banks Spring Workshop. Ms. LouAnn Dake, Sandra Hoffmann, Suzanne Butch, and Margaret Stoe participated in assessment activities for the American Association of Blood Banks. Margaret Stoe served as President of the Michigan Association of Blood Banks.

RESEARCH ACTIVITIES:

Faculty research activities are documented in individual reports of Dr. Davenport, Dr. Cooling, and Mr. Judd. The Transfusion and Apheresis Service provided crucial support in leukocyte collection for General Clinical Research Center clinical research protocols.

Robertson D. Davenport, M.D.
Medical Director,
Blood Bank and Transfusion Service

CHEMICAL PATHOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY

ANNUAL REPORT

1 JULY 2004 - 30 JUNE 2005

The past year was once again marked by a steady increase in laboratory workload. The Chemistry Section experienced an approximate 5.5 % increase in overall test volume this year, performing nearly 5.4 million individual tests. The laboratory finished within its projected budget for the year and this workload was absorbed without the addition of incremental personnel.

The Chemistry Sections major focus this past year was on the selection of new chemistry and immunoassay instrumentation along with a lab automation track system. The laboratory committee for this selection process made 11 visits to other institutions to view equipment and configuration options. In conjunction with Pathology administration and medical center purchasing, the group selected the Bayer Diagnostics LabCell system as the best choice to meet the growth expectations of the Chemistry Section over the next five years. Two immunoassay instruments were installed in June with a projected go live date for clinical result reporting of mid September 2005. Installation of the new chemistry analyzers and track system is tentatively scheduled to begin in October 2005. Sophisticated computer "middleware" associated with the system should allow for significantly increased autoverification of test results and more individualized use of critical value reporting.

The Immunology Section of Chemistry completed a stressful but very successful move offsite to the Traverwood building in January of 2005. A second Dade-Behring ProSpec nephelometer was purchased and brought on-line with the move. The Immunology section also acquired a Dynex DSX automated ELISA system which allowed several changes in testing menu. The lab implemented an ELISA screening assay for extractable nuclear antigens, automated the assay for total hemolytic complement (CAE), and brought in-house testing for antibodies to cyclic citrullinated peptide (anti-CCP). The lab is proceeding with plans to implement testing for anti-beta₂glycoprotein I and also for free kappa and lambda light chains in the first half of fiscal year 2006.

Several assays were moved to more automated instrumentation. Hepatitis B surface antibody testing and Hepatitis B core antibody testing was moved to an automated chemiluminescent immunoassay format on the Vitros Eci analyzer. HIV 1,2 antibody serology testing along with Hepatitis A antibody testing were moved to an automated ELISA assay platform, the Diasorin EtiMax. These combined moves eliminated one workstation area within the lab and allowed the lab to shift personnel to better accommodate the continued growth in testing.

In the toxicology area, a second HPLC-mass spectrometer system was acquired, installed, and an assay for the immunosuppressant drug mycophenolic acid was developed and implemented. Testing for Tacrolimus was switched from a commercial immunoassay to the HPLC-MSMS system with a projected annual savings of \$100,00 per year. Development work on quantitative assays for tricyclic antidepressants was initiated, with a projected implementation date for these tests of fall 2006.

The Chemistry Laboratory continued its leadership role in Point of Care (POC) testing both within the hospitals and at the off-site health care centers. Testing for Hemoglobin A1c and microalbuminuria in diabetics and prothrombin time in patients on coumadin has continued to expand. Laboratory personnel have been active participants in the planning process for the new Surgery Center being built at the East Ann Arbor Campus and the infusion center at the Canton Health Center. Laboratory functions at both of these new sites will be supervised through the Chemistry Section. Laboratory staff have also been key participants in the drafting and implementation of institution wide point of care testing guidelines for nursing in order to comply with JCAHO accreditation checklists.

The lab has continued its active role in the supervision of bedside blood glucose monitoring programs at University Hospitals. The lab maintains quality control, linearity, and proficiency testing records on more than 130 whole blood glucose meters stationed throughout the institution. Results from these meters are now downloaded directly to a server in Pathology, and patient glucose results passed directly to the laboratory information system. Full implementation of this connectivity solution over this past year has allowed for a more complete capture of POC blood glucose testing values within the institution.

Educational efforts included the training of medical technology students from Ferris State University and Eastern Michigan University, and the time spent by Pathology residents gaining an overview of the various testing modalities employed by the laboratory as part of their the CP Block B rotation. Drs Giacherio, Annesley, and England spend time each week with residents in didactic sessions, as well as participate in the Clinical Pathology Grand Rounds lecture series. Further information on teaching and professional activities of the Chemistry Section faculty can be found in the individual faculty reports.

Donald Giacherio, Ph.D.
Director, Chemistry Laboratory

CLINICAL CYTOGENETICS LABORATORY

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 2004 - 30 JUNE 2005

Overview

After years of steady increases in cytogenetics testing, the overall number of tests performed and samples processed this past fiscal year was very similar to the previous year's numbers, with 2648 cytogenetics and 474 FISH studies performed (-2.3% and +1.7% respectively).

Thomas Glover, Ph.D. (Professor, Department of Human Genetics) continued to provide invaluable expertise and sign-out coverage of constitutional genetics cases. Lisa R. Smith, Ph.D. served as Assistant Director. Two full-time technologists were hired following two departures due to personal reasons.

Clinical Services

The number of samples sent for cytogenetic analysis decreased for constitutional studies (1192, -7.5%) and slightly increased for oncology studies (1456, +2.4%). The number of peripheral blood samples for constitutional studies leveled off after the dramatic increase experienced last year (699, -1.7%). Prenatal diagnosis studies decreased for the first time in four years in both categories (309 amniocenteses, -18%; 82 chorionic villus samples, -9.9%). Skin biopsies and products of conception also decreased in number (102, -7.3%).

For neoplasias, the number of bone marrow samples decreased relative to last year (1276, -6.0%), however, the in-house solid tumors and lymphoma samples rose dramatically (180, +177%) following incorporation of cytogenetics into the lymphoma work-up, as requested by the Hematopathology faculty. This increase more than compensated for the loss of bone marrow samples from the discontinuation of MLabs client Botsford Hospital last August.

The overall number of FISH studies performed was about the same as for the previous year (474, +1.7%). A new FISH test for microduplications of 15q was developed and is now offered for patients with developmental delay or mental retardation and autism or other behavioral problems. This led to an increase in single-probe constitutional FISH tests (190, +11%). However, there was a noticeable decrease in the number of subtelomeric FISH tests performed (84, -16%), due to the increasing sending out of samples for array CGH testing using BAC microarrays. Oncology FISH remained at much the same level as the previous year (200, +2.6%).

Education

Five Pathology residents, two Hematopathology fellows and six Genetic Counseling students came to the laboratory for rotations. The Pathology residents and fellows gave brief talks for the technologists in areas relevant to the case work in the laboratory, making a much-appreciated contribution to continuing education.

Two staff members participated in national and/or regional meetings: our lab supervisor presented a poster at a national cytogenetics meeting and one senior technologist gave a presentation at a regional cytogenetics conference.

Future Plans

Array CGH, e.g., with BAC microarrays, is rapidly becoming the standard of care for molecular cytogenetics testing. Microarray analysis is more rapid and less labor intensive than cytogenetic analysis and detects genetic imbalances at a much finer level of resolution. It tests hundreds of loci in one experiment, yet does not cost much more than a subtelomeric FISH analysis, for which 41 loci are examined. It is clear that our laboratory needs to move in this direction and we are investigating the possibility of developing this capacity in-house.

Demand for additional FISH testing remains high; thus, we are beginning studies for *P53* gene deletions in hematopoietic malignancies, microduplications of 22q for constitutional studies. Also under consideration is the use of FISH for minimal residual disease in leukemia, and FISH with fixed, paraffin-embedded tissues for oncology studies. However, implementation of this technology for clinical testing will require additional manpower and other resources in the laboratory.

Diane Roulston, Ph.D.
Clinical Associate Professor
Director, Clinical Cytogenetics Laboratory

HEMATOLOGY LABORATORY
DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005

Overview

The 2004-2005 academic year was a period of considerable transition in the hematopathology laboratories. This year we bid farewell to R. Jayne Harris, MT(ASCP), our “founding” Chief Technologist, after over 40 years of faithful service. Nancy Renner, MT(ASCP), SH, was promoted to Chief Technologist following Jayne’s retirement. Nancy’s previous position of Day Supervisor was subsequently filled by Usha Kota, MT(ASCP), who previously had served as the Senior Clinical Technologist in the Flow Cytometry area. We enthusiastically welcome these new members of our leadership team. We begin the 2005-2006 academic year with 3 open positions in a very competitive environment for medical technologist talent.

We underwent a very successful accreditation inspection by the College of American Pathologists this spring, thanks to the tireless efforts of our dedicated staff, particularly Kay Lynne Lantis, MT(ASCP), SH, and Mary Jane Liu, MT(ASCP). Kay Lynne also began the process of transitioning to on-line procedure manuals—a process we hope to continue for all procedures in the laboratory.

Substantial physical renovations were completed to accommodate installation of a new Beckman Coulter LH1500 automation line. The coagulation laboratory continued to grow and to adapt advanced coagulation testing to the automated BCS platform. Deployment of new cytometers and a new reporting system were well underway in the clinical flow cytometry laboratory.

Individual section reports are as follows:

1. **Clinical Hematology Laboratory and Bone Marrow Laboratory**

The Beckman Coulter 1500 automation line was successfully installed, and is currently handling a large percentage of our daily workflow. We plan a formal “go live” date in September 2005, following an additional site visit and certification by the manufacturer. The newly installed system includes automated slidemakers and stainers, along with a 2000-sample “stockyard” capable of retrieving and rerunning samples based on user commands entered into the line control software or through the laboratory information system. Line installation required substantial physical renovation to the laboratory. Since over 80% of our results are currently released via autoverification algorithms designed in our laboratory, this upgrade will allow a substantial majority of complete blood count

and differential count orders to be completed without manual intervention, holding promise for substantial gains in efficiency and productivity. We are currently working the staff in Central Distribution to optimize specimen handling and line loading procedures.

We continue our ongoing efforts to optimize operations in the hematology laboratory, and to strike the most appropriate balance between automated and manual testing methods. An enhanced, interlaboratory flagging system was developed by Jerry Davis, MT(ASCP), MPH, in order to more effectively select for samples that require manual review of red blood cell morphology for possible hemolytic anemia. We hope this system will serve as a model for automated interlaboratory “cross talk” for the optimization of clinical laboratory utilization.

In the bone marrow laboratory, we continue to expand the number of staff trained to perform differential counts of bone marrow samples. We are also working toward optimizing staffing levels in the bone marrow laboratory (including hiring a technologist to work a 2pm to 10pm “swing” shift) to accommodate continued increases in demand from the clinical services.

As in previous years, test volumes continue to increase. Our volume of complete blood count (CBC) orders rose almost 6% to nearly 419,000. Differential count orders rose almost 7% to over 251,000. Of these, only 14,385 (fewer than 6%) were performed manually, due to a continuation of our policies optimizing manual slide review (detailed in previous annual reports and in *Am J Clin Pathol* 2003; 119:656). Volumes of urinalysis and body fluid cell count orders have remained fairly stable.

2. **Coagulation Laboratory (Dr. Alvin Schmaier)**

The Coagulation Laboratory continues to grow in activity. There was 7.9% and 6.3% increase in inpatient and outpatient requests for the prothrombin time, respectively, with a total 135,103 tests performed. 56% of the PT are on inpatients. There was 8.1% and 6.5% increase in inpatient and outpatient requests for the activated partial thromboplastin time, respectively, with a total of 104,435 tests performed in the last fiscal year. The fastest growing test is the anti-factor Xa assay (23% increase) in both the inpatient and outpatient setting for the assessment of the level of low molecular weight heparin. 838 assays were performed in combined inpatient and outpatient settings. Anti-IIa assays increased from 30 performed last year to 72 this year (140% increase).

There also was a 4.6% increase in the Dimer assay with 7,113 tests performed in the last fiscal year. With the help of Dr. Thomas Wakefield, the assessment of the D-Dimer’s ability to screen for DVT was completed. A value of D-Dimer > 3.0 has a 64% sensitivity, 76% specificity, and 70% accuracy to predict that a patient has a proximal DVT in the right patient setting. A negative D-Dimer assay has an

80% likelihood of excluding a diagnosis of DVT. This clinical assessment material is published on CareWeb.

In addition to evaluation of these most commonly used assays, additional studies were performed to develop more automated specialized coagulation testing. The antithrombin functional assay with a normal range of 93-129% was evaluated for its reliability. There was no increase in the diagnosis of antithrombin deficiency as result of having a tighter normal range. To improve automation of antithrombin antigen and provide a result in similar form of units, an antithrombin LIA test was developed for the BCS. This assay has a normal range between 71-121%. Similarly, the free protein S antigen assay using a LIA-based technology was fully implemented. We are presently evaluating a protein S coagulant assay to add as an additional assay. Alternatively, we have switched from a protein C amidolytic assay to a protein C coagulation-based assay. This assay is more global in diagnosis, but is also influenced by additional coagulation factor entities such as factor V leiden.

We also had our platelet function testing methodology published this year (Am J Clin Path 123:172-183, 2005). This effort was intended to initiate a national effort to develop standards of practice for platelet function testing. As result of this publication, Dr. Schmaier who is presently the President of NASCOLA has been asked to participate on a CSCI committee to develop good guidelines for practice of platelet function testing.

Our program to evaluate the Platelet Function Analyzer (PFA) as an assay to assess platelet dysfunction is still on-going. This year we have accrued an additional 22 patients prospectively giving us a total of 42 evaluable patients. Since there are so many sub-diagnoses of platelet function disorders, at the rate of evaluable patient accrual, it will take an additional year of data collection to complete this evaluation of this instrumentation.

3. **Flow Cytometry Laboratory**

Beckman Coulter FC500 flow cytometers are now being installed and validated to replace our previous Coulter XL models. The FC500 platform allows for routine 5-color analysis, and brings with it a substantially more functional software package (Coulter CXP) that will allow for enhancements of data acquisition, data analysis, data storage, and report archiving. This upgrade will allow us to end our current practice of scanning printed output for digital storage on the server, and will allow us to instead directly transfer formatted data output to the server for archival storage. In addition, a new interface to our existing Oracle database was developed and installed, allowing us to continue the automated transfer of numerical data from the instrument to final reports for quantitative assays (T cell subset analyses, stem cell analyses, etc.).

Another substantial upgrade in the lab was the deployment of XPlain report generating software. This software allows for the rapid composition and verification of clinical flow cytometry reports by pathologists, and eliminates lag time between dictation and transcription of reports. The result has been a substantial decrease in turnaround times for leukemia/lymphoma immunophenotyping reports. This software also provides better quality assurance/ quality control tools to the staff.

The flow cytometry lab processed almost over 5500 test orders in the 2004-2005 academic year, including over 2,200 leukemia / lymphoma immunphenotyping orders. We continue to have a robust triage system, that results in the cancellation of a substantial percentage of unnecessary orders.

4. **Academic and Educational Efforts**

Directorship of the hematopathology fellowship program will transition from Dr. Bertram Schnitzer to Dr. Riccardo Valdez over the first few months of the 2005-2006 academic year. We thank Dr. Schnitzer for his outstanding service in creating the fellowship, which has produced several outstanding leaders in the field of hematopathology. We also look forward to Dr. Valdez's leadership. We bid farewell to our outgoing fellow Dr. Ajay Rawal, and we welcome this year's fellows, Drs. Tarek Rahmeh, Lauren Smith, and Michael Hayes.

We continue to be very active participants in all aspects of resident and medical student education, with our faculty teaching numerous small group sessions and lectures. Drs. Schmaier and Stoolman continue to serve as director and co-director, respectively, of the second year medical school hematology sequence, and Dr. Valdez continues his distinguished service on the Medical School admissions committee.

Our group also continues to enjoy regional and national recognition, with several of our members holding office or committee assignments in numerous national organizations (American Society for Clinical Pathology, College of American Pathologists, Society for Hematopathology, North American Specialized Coagulation Laboratory Association, International Society for Laboratory Hematology), publishing numerous peer-reviewed articles, serving on editorial boards, and enjoying invited speakerships.

5. **Goals for upcoming year**

Numerous projects for improvement of operations are either planned or underway. Renovations to make way for the automation project mandated temporary off-site relocation of some laboratory functions, and we plan to "re-unite" these areas into the main laboratory space. We plan to complete the

leadership transition following the recent appointment of a new Chief Technologist and new Day Supervisor. We will be busy completing the nearly complete installation of the hematology automation line and flow cytometry upgrades. We will need to consider the future of our automated coagulation analyzers, which are now over 5 years old.

We will continue our record of optimizing clinical laboratory operations, with plans to assess the feasibility of bringing up several new tests, including a flow cytometry based fetal red cell assay to either replace or augment the current manual Kleihauer-Betke procedure, single platform testing for CD4 counts and stem cell counts, routine 5-color flow cytometry panels, etc. We also hope to increase the participation of residents and fellows in these projects.

Finally, we hope to begin a strategic planning process for hematopathology at the University of Michigan, to coincide with the recent arrival of our new Chair, Dr. Hess, and with the proposed recruitment of new hematopathology faculty.

William G. Finn, M.D.
Director, Hematopathology
Associate Director, Clinical Pathology



HISTOCOMPATIBILITY AND IMMUNOGENETICS LABORATORY

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 2004 - 30 JUNE 2005

CLINICAL ACTIVITIES:

The Histocompatibility Laboratory moved to the Traverwood Building this past year, and the relocation was welcomed and successful. The laboratory continued to experience a steady increase in the overall clinical test volume, particularly in the area of antibody screening. The test menu remained unchanged from previous years with the exception of the imminent addition of another antibody screening assay, which utilizes the Luminex microsphere-based technology. This test will be an adjunct to the complement-dependent cytotoxicity (CDC), ELISA, and flow cytometric methods currently used to evaluate potential graft recipients for the presence of anti-HLA antibodies. Flow cytometric antibody screening and crossmatch studies are currently being performed by Allogen Laboratories in Cleveland, Ohio. A high rate and degree of pre-sensitization in our patient population (due to prior failed grafts or multiple blood product transfusions) continues to add significant complexity to the performance and interpretation of the laboratory tests performed in the HLA laboratory. DNA-based typing remains the primary technique used for the determination of HLA class I and class II alleles. The Luminex instrument is currently being used to perform high-throughput mid-resolution typing at a substantial cost savings over previously used methods. Nucleotide sequencing is used for select bone marrow (stem cell) transplant recipient and donor evaluations.

Last year's goal of developing a Cerner Classic (PathNet) program to electronically report panel reactive antibody (PRA) and anti-HLA antibody specificity results into CareWeb was achieved in FY2004 thanks to the diligent efforts of the senior laboratory staff (including Ms. Cindy Schall, Ms. Debra Dudek, and Ms. Lisa Kreuser), Ms. Kathy Davis and her Pathology Data Systems staff, and Mr. Thomas Morrow. The clinical staff in the transplant programs are now able to view all histocompatibility test results in CareWeb (rather than relying on facsimile copies of reports sent by the laboratory staff during regular laboratory hours; tissue typing results went online in FY2003). These two programs have enabled the laboratory to realize greater efficiency as well as more effective communication with the clinicians.

The HLA laboratory was inspected by the American Society for Histocompatibility and Immunogenetics (ASHI) and the College of American Pathologists (CAP) in FY2004 and did extremely well during both of these external evaluations. Inspectors were impressed by the new laboratory space, but even more forthcoming in their comments regarding the high quality of the work and documentation performed in the laboratory. During the summation, the ASHI inspector commented that the University of Michigan HLA laboratory was "the best laboratory he had inspected in (his) 25 years performing inspections".

Dr. Riccardo Valdez continued to devote a substantial portion of his professional effort to managing and directing the HLA laboratory. He has progressively become more involved in the day-to-day operations of the laboratory, and continues to: interpret complex test results on difficult cases, meet with the

clinical transplant services to discuss laboratory and patient issues, handle personnel issues, and manage billing and laboratory utilization matters. This year, Dr. Valdez drafted a laboratory services agreement between the University of Michigan Transplant Program and the Gift of Life Michigan, the latter is the regional organ procurement organization (OPO) that performs the final donor-recipient crossmatch testing and provides organ allocation for all clinical transplant programs in the state of Michigan. The establishment of such an agreement is a new United Network for Organ Sharing (UNOS) requirement. He was instrumental in developing and designing the test result format in the aforementioned Cerner Classic PRA program, and he actively participated in the validation of the program. In addition, Dr. Valdez continues to hold weekly meetings with the laboratory supervisor, monthly meetings with Dr. James Baker, and he attends business and educational meetings sponsored by the Gift of Life Michigan. Dr. Valdez will complete his last year of the ASHI required training for new laboratory directors in July 2005, and he will formally apply for certification as the laboratory director in FY2005.

TEACHING ACTIVITIES AND RESEARCH:

Dr. Valdez, Ms. Cynthia Schall (the Laboratory Supervisor), and other members of the laboratory were involved in the numerous teaching activities of the laboratory. Ms. Cynthia Schall coordinated the teaching activities for house officers rotating in the laboratory, and the senior laboratory personnel provided instruction in the basic principles and techniques of histocompatibility testing for pathology house officers, allergy fellows, renal medicine fellows, hematology/oncology fellows, and post-doctoral candidates from the Department of Hematology. Dr. Valdez and Ms. Schall completed several in-service lectures for the faculty and support staff in the solid organ transplant program. Members of the laboratory staff (including Cindy Schall, Debra Dudeck, and Judy Knakiewicz) were involved in activities related to training medical technology students. The previously described clinical research collaborations with the renal and heart transplant programs are ongoing. Dr. Valdez and Ms. Schall submitted two abstracts based on clinical work for the upcoming annual ASHI scientific meeting. Plans are currently underway to recruit and hire a doctoral scientist to expand the scholarly activities of the HLA laboratory.

NEW GOALS:

In addition to continuing to address the demand for more complex services from the Medical Center's various transplant programs, the laboratory's goals for the next year include: 1) to complete and submit the ASHI required director training portfolio for the formal accreditation of Dr. Valdez as the laboratory's medical director, 2) to successfully recruit an additional faculty member for the laboratory, 3) to build and grow a research program for the laboratory with the assistance of the doctoral scientist recruit, 4) to complete the validation of the Luminex instrument for antibody screening and to obtain ASHI certification for its use in the laboratory, 5) to continue to evaluate and validate in-house flow cytometric testing procedures, and, 6) to continue expand the resident educational experience in tissue typing to include exposure of the residents to renal and heart transplant biopsies.

Jeffrey S. Warren, M.D.
Director, Division of Clinical Pathology

Riccardo Valdez, M.D.
Assistant Professor of Pathology

CLINICAL IMMUNOPATHOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY

ANNUAL REPORT

1 JULY 2004- 30 JUNE 2005

I. OVERVIEW:

The Immunopathology Laboratory performed more than 70,000 analyses in 2003-04. John Lowe, M.D. and John Thorson, M.D., Ph.D. provided invaluable service to the laboratory in the interpretation of protein electrophoresis studies. Kent Johnson, M.D., and Paul Killen, M.D., Ph.D., also provided invaluable coverage of anti-neutrophil cytoplasmic antibody (ANCA) and anti-GBM studies.

II. CLINICAL SERVICES:

Integration of clinical immunopathology testing into the Chemistry Section has been fully realized. New procedures were implemented in the protein electrophoresis area, in the analysis of antibodies to extractable nuclear antigens, and in the measurement of several individual analytes previously measured by nephelometry.

III. RESEARCH AND DEVELOPMENT:

The Laboratory supported clinical studies of the effects of cytotoxic/immunosuppressive drugs on IgG, IgA and IgM as well as IgG subclass concentrations in lupus patients and in serum banking in conjunction with Dr. Joseph McCune (Department of Medicine, University of Michigan). Several commercially-financed methods and instrument evaluations were also carried out. These studies involved a new method for detection of antibodies to extractable nuclear antigens and antineutrophil cytoplasmic antibodies.

IV. QUALITY ASSURANCE:

The laboratory actively participated in the Division-wide utilization management program.

V. TEACHING/PROFESSIONAL:

Residents, M4 medical students, and medical technology students rotated through the laboratory. Clinical Pathology Grand Rounds included immunopathology presentations by Dr. David Keren (Warde Medical Laboratory, Ann Arbor), and Dr. Warren (see individual faculty report). Drs. Warren and Keren continued a weekly series of didactic sessions entitled "Current Topics in Immunopathology". Other professional activities of faculty and staff in the laboratory are summarized under individual reports.

Jeffrey S. Warren, M.D.
Director, Clinical Immunopathology Laboratory

CLINICAL MICROBIOLOGY / VIROLOGY LABORATORIES

**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

June 30, 2005 marked the end of Dr. Carl Pierson's appointment in the department, and he assumed the position of full-time retiree.

I. CLINICAL ACTIVITIES:

The Laboratory continued to experience significant increases in test volume with an approximately 11.6% increase compared to that of FY 2004-05, with a total testing volume of over 330,000 tests. While this increase is being seen relatively equally across all areas of the laboratory, we are continuing to see higher increases in our most complex testing areas, specifically in molecular diagnostics.

Molecular diagnostics continues to be a major growth area of the laboratory. Having successfully incorporated new automated testing for CT/NG and HCV viral loads during FY2003, a great deal of time was spent in FY2004-05 training technologists to perform these tests. Work continues in the lab to automate the specimen extraction procedures for additional nucleic acid amplification tests. A project begun by one of the Pathology residents (Kajal Sitwala) established parameters for the automated extraction of specimens for CMV viral load testing. This verification study should be completed and clinical testing begun early in FY2005-06. In addition, a new assay for the determination of HCV genotype was evaluated and brought into clinical testing this year. The results of our evaluation were presented at an international meeting in 2005. Our evaluation of a new test for EBV viral load assessment by real-time PCR should also be completed and clinical testing begun early in FY2005. Preliminary results of this evaluation were presented at an international meeting in 2005.

The laboratory is currently in the process of evaluating several responses to RFPs from commercial vendors for systems for automated bacterial identification and susceptibility testing to determine which of these systems would fit best in our lab. Following review of these RFPs, we plan to bring in appropriate systems for hands-on evaluation and have a decision completed by the middle of FY2005-6. We have also begun our evaluation of responses to an RFP for additional real-time nucleic acid amplification platforms for the lab to be able to handle the increasing volume and breadth of testing.

The laboratory has contributed a part-time position to the department's effort in the Orders Management Project that is targeted for completion early in FY2005-06.

In collaboration with Pharmacy, Infectious Diseases and Infection Control, we have generated several unit- and hospital-specific antibiograms to more closely track trends in antimicrobial resistance throughout the hospital and health system. These are being used to assess the appropriateness of antibiotic usage and determine whether changes in therapeutic recommendations or antibiotic formulary are required.

Several members of the laboratory were certified in the packaging and shipping of biological hazardous materials through an on-site training session with MDCH. The supervisory staff was also successful in hiring several new medical technologists to fill open positions.

II. RESEARCH ACTIVITIES:

The additional faculty depth in the laboratory during the past year has allowed for increased participation in a variety of research projects with collaborators from within UM, other universities, and with industry.

Dr. Newton is a co-investigator on an recently awarded 1.2 million dollar NIH grant with Dr. Arnold Monto at UM SPH, and will be providing 20% effort to provide technical expertise in influenza virus molecular diagnostics. Newton has developed a real-time PCR assay for detection of influenza virus that is being utilized as part of this study.

In collaboration with Binax, Inc., our laboratory completed a clinical trial of rapid antigen detection tests for adenovirus and parainfluenza virus in samples from pediatric patients.

Dr. Newton has established collaborations with investigators in the UM School of Dentistry evaluating novel therapeutics for the treatment of cold sores.

Dr. Newton has established collaborations with investigators in the UM Medical School evaluating expression virulence genes in enteric pathogens causing sepsis.

Dr. Newton has established collaborations with investigators in the UM Medical School developing novel molecular tests for the detection of fungi in clinical specimens.

The Laboratory is cooperating with a local company to evaluate a real-time PCR method for the direct bedside detection of group B Streptococcus in urogenital specimens.

We are collaborating with MDCH on a project for surveillance of MRSA in Michigan.

We are a clinical study site for two projects evaluating the in vitro activity of newly developed antibiotics—both projects are sponsored by pharmaceutical companies.

We are collaborating with multiple hospitals around the country on an NIH project evaluating emerging antibiotic resistance in Group A streptococci.

We are evaluating the performance of a new test to detect *Aspergillus* antigens in serum of immunocompromised patients, which can potentially be used to predict risk for developing disseminated disease.

The Laboratory responded to numerous IRB-approved requests from clinical services for specific laboratory data to fulfill research goals.

III. TEACHING ACTIVITIES:

All laboratory personnel continued to provide instruction to Pathology House Officers and Infectious Disease Fellows and residents on diagnostic procedures used in the Microbiology/Virology Laboratories. Several laboratory preceptorships for medical students, pharmacy students, and Pharm.D. residents were also provided during the year. Infectious Disease Laboratory rounds were held each weekday during which staff members and assigned Pathology House Officers interacted with ID team members to answer questions, demonstrate laboratory diagnostic procedures and discuss interesting findings. Numerous in-service education programs were held during the course of the year with individual technologists and Pathology House Officers giving presentations to staff members.

IV. PROFESSIONAL DEVELOPMENT:

Both supervisors and most of our Sr. Technologists attended one or more regional or national scientific meetings during the year. Several other staff members attended regional scientific meetings of interest. In addition, the Laboratory subscribed to two audioconference programs which provided a total of 10 conferences during the year that were available to all staff members and Pathology House Officers as part of our ongoing CME program. Monthly inservice programs were provided by Pathology residents and faculty.

V. GOALS FOR FY 2005-06

1. Continue process and efficiency improvements to accommodate an expected increase in test volume.
2. Expand our menu of nucleic acid tests to support the diagnostic needs of our clinical services, especially transplant programs.
3. Continue our transition to automated specimen extraction for appropriate nucleic acid amplification tests.
4. Continue our assessment of automated bacterial identification and susceptibility systems.
5. Continue our evaluation of the rapid NA amplification method for the detection of group B Streptococcus in urogenital specimens.
6. Assess current and future laboratory space and architectural requirements.
7. Assist in the selection of a new Laboratory Information System.

Respectfully submitted,

Duane Newton, Ph.D. Director
Carl L. Pierson, Ph.D., Co-Director
Clinical Microbiology/Virology Laboratory

MOLECULAR DIAGNOSTICS LABORATORY**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005****OVERVIEW**

All Laboratory operations were moved to newly renovated space in the Traverwood II facility near the North Campus. The Laboratory had a 6.5% increase in volume relative to the same period in the previous year. Several newly developed tests were validated and added to the Laboratory services menu. Plans for an expanded role for the Laboratory in Pathology resident teaching were developed and implemented.

CLINICAL SERVICES

The Laboratory currently employs one full time supervisor, five full time technologists, one of whom functions as a research and development technologist, and two part time technologists. All staff members are cross-trained in all areas of the laboratory. Tom Wilson, M.D., Ph.D., Assistant Director of the Laboratory, and Jeffrey Warren, M.D., provided assistance with sign out responsibilities.

In December 2004, the Laboratory completed a move of all operations to newly renovated space located in the Traverwood II complex at 2910 Huron Parkway in Ann Arbor. Comprising approximately 2,500 square feet, the space was specifically designed to enhance the functionality of the Laboratory's operations. The incremental space has allowed a significant expansion of routine clinical testing activities as well as research and development activities.

As of January 2005, HCV genotype analysis was discontinued following the introduction of this assay into the University of Michigan Hospital Clinical Microbiology/Virology Laboratory. Despite the discontinuation of this test, which accounted for approximately 10% of the Laboratory's test volume, the overall test volume increased to approximately 8,360 tests, representing a 6.5% increase relative to the same period last year. This change was in part due to across the board increases in test activity as well as the introduction of several new assays. Turn around times for tests performed in the Laboratory were essentially unchanged from the previous year, with an average of 5 days overall.

A variety of new assays were developed and/or validated for clinical use by the Laboratory during the past year. Assays developed in house include 1) a PCR-based assay for the detection of clonal populations of T lymphocytes, 2) a real time PCR assay for the detection and quantification of *BCR/ABL* transcripts in chronic myeloid leukemia, and 3) RT-PCR based assays for the detection of translocation specific transcripts that characterize alveolar rhabdomyosarcomas (*PAX3/FKHR*, *PAX7/FKHR*), desmoplastic small round cell tumors (*EWS/WT1*), and Ewing's sarcomas (*EWS/FLI1*, *EWS/ERG*). The Laboratory also participated in a collaborative effort with Third Wave Technologies, Inc., to validate a multiplex amplification/invasive oligonucleotide assay developed for *CFTR* mutation screening.

In May of 2005, the College of American Pathologists conducted an accreditation inspection of the Laboratory. No deficiencies were cited and no recommendations for improvement noted.

EDUCATION

Two senior level Pathology residents completed research projects in the Laboratory that were subsequently presented in poster or platform format at the 2005 USCAP meeting. In addition, several Pathology residents spent time in the laboratory during their CP Block D rotations, gaining an overview of all testing performed and participating in the review, interpretation and sign out of cases.

Educational activities of the Laboratory also included the training of Medical Technology students from Wayne State University and Eastern Michigan University, each of whom completed their CLS/MT clinical training in the Laboratory during a one-week rotation. Training included DNA and RNA extractions, polymerase chain reaction, Southern analysis, and an overview of all testing performed in the Laboratory.

In addition, students from the Genetic Counseling Program enrolled in the Advanced Clinical Concepts in Medical Genetics course each completed a 3-day rotation in the Laboratory. Training included basic laboratory techniques and assay result interpretation.

During the spring of 2005, preparations were made for an expanded rotation in Molecular Diagnostics for Pathology residents. This will be included as part of a new CP rotation designated Block E, scheduled to begin July 2005. During this rotation, residents will participate in a defined curriculum of activities and have opportunities to initiate or become involved in ongoing projects within the Laboratory.

FUTURE PLANS/RESEARCH AND DEVELOPMENT

Priorities for the next academic year will be 1) the identification and implementation of additional educational opportunities within the Laboratory for Pathology residents and fellows, 2) the development and validation of additional tests to be included on the Laboratory's menu of assays, and 3) the continuing conversion of many currently performed assays to state-of-the-art instrumentation platforms.

Plans are currently underway for the introduction of an accredited fellowship position in Molecular Genetic Pathology. This position would be based largely upon activities within the Laboratory as well as the Department of Pathology as a whole. It is anticipated that this position will be available at the beginning of the 2006-2007 academic year.

Validation of an in-house developed PCR-based assay for B-cell receptor gene (IGH) rearrangements is in progress and this assay will be available on a clinical basis within the next 2-3 months. This assay will be applicable to either fresh or formalin fixed tissue. In addition, in collaboration with Dr. John Judd and Dr. Robert Davenport, a real time PCR-based assay to genotype multiply transfused patients for RBC antigens is currently in development.

Several quantitative real time PCR assays to assess gene expression levels are being developed in consultation with the hematology/oncology and bone marrow transplant services, targeting the current and expected future needs of these groups. These include assays for *PML/RARA*, *TEL/AML1*, and a novel assay for the accurate quantification of hematopoietic chimerism in patients who have received allogeneic bone marrow transplantation. Based upon the use of insertion/deletion polymorphisms to distinguish donor derived cells from recipient cells, this assay has the potential to lower the detection limit for residual recipient cells by 2 to 3 orders of magnitude beyond current state of the art assays.

John A. Thorson, M.D., Ph.D.
Director, Molecular Diagnostics Laboratory

**SPECIMENT PROCUREMENT
(PHLEBOTOMY SERVICES AND CENTRAL DISTRIBUTION)**

**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

Specimen procurement is the front-end specimen collection and processing area for the Department of Pathology. This area includes Inpatient Phlebotomy (University Hospital and Mott Children's Hospital), Outpatient Phlebotomy (Cancer/Geriatric Center and the Taubman Center), and Central Distribution/Referral Laboratory. A total of 100.6 FTE's staff the three areas, responsible for 24-hour/7 day a week operations. The departments are directed by 1FTE manager, 3 FTE supervisors and 11.5 FTE clinic coordinators. The complex and specialized areas in Central Distribution, including Referral Laboratory Services also employs a Senior Medical Technologist and a Medical Technologist Training Coordinator. Budgeted Specimen Procurement salary and wages for FY 2005 are \$3,303,737, budgeted controllable expenses are \$731,960 and budgeted referral testing expenses are \$2,708,000.

Budget performance for FY 2005 appears consistent with responsibilities involved and the volume of work performed.

Inpatient Phlebotomy:

Volumes:

Inpatient phlebotomy volumes increased in FY 2005. A 9.7% increase was seen, resulting in 14,140 more patient draws. Patient acuity, along with 50 new hospital beds opened as of 1/17/05, drive this volume increase. This increase in volume was covered with existing personnel budget.

INPATIENT PHLEBOTOMY VOLUMES			
	<i>FY 2004</i>	<i>FY 2005</i>	<i>% Change</i>
<i>Inpatient Phlebotomy</i>	145,480	159,620	9.7

Expenses:

Inpatient salary/wage expenses were \$72,458 over budget (+8%) due primarily to overtime expenses associated with coverage of medical leaves of absence and open budgeted positions. Inpatient controllable expenses were over budget \$32,000 (+16%) due to increased patient volumes and the utilization of safer, single use products (saline, heparin) for central catheter line collections.

YTD TOTALS FY 2005	Inpatient Phlebotomy			
	Budget	Actual	Variance	% Variance
Salary/Wages	\$908,204	\$980,662	+\$72,458	+8.0
Expenses	\$197,650	\$230,309	+\$32,659	+16.5
Total	\$1,105,854	\$1,210,971	+\$105,117	+9.5

On-Going Activities/Future Activities:

In FY 2005, Inpatient Phlebotomy has:
 Investigated national certification options for staff phlebotomists to enhance competency documentation and professionalism of staff.
 Enhanced training and competency assessment/documentation for phlebotomy, indwelling line phlebotomy, and pediatric phlebotomy.
 Prepared staff for successful accreditation inspections by JCAHO and CAP.
 Participated in LIS vendor evaluations.
 Management staff were trained in the Risk Monitor Pro software for reporting patient safety issues.
 Unlabeled specimens, mislabeled specimens and other patient safety issues are now documented in the system.
 Participated in review of JW Thompson staff survey to understand strategies to retain/appreciate staff.
 Staff participated in Nursing Educational Blitz.

FY 2006 Goals:

Develop process for national certification of phlebotomy staff.
 Participate in process development for Order Management Project in University Hospital and Mott Children's Hospital.
 Participate/evaluate LIS vendors for LIS replacement project.

Outpatient Phlebotomy:**Volumes:**

Outpatient phlebotomy volumes increased in FY 2005. A 3.7 % increase was seen, resulting in 5,259 more patient draws. Outpatient clinic activity and patient acuity contribute to this increased volume. This increase in volume was covered with existing personnel budget.

OUTPATIENT PHLEBOTOMY VOLUMES			
	<i>FY 2004</i>	<i>FY 2005</i>	<i>% Change</i>
Cancer/Geriatric Center	54,172	56,926	5.1
Taubman Drawing Station, Floor #2	24,554	24,628	0.3
Taubman Drawing Station, Floor #3	65,195	67,626	3.7
TOTAL	143,921	149,180	3.7

Expenses:

Outpatient salary/wage expenses were \$51,842 over budget (+5.9%) due primarily to overtime expenses associated with coverage of medical leaves of absence and open budgeted positions. Outpatient controllable expenses were over budget \$48,268 (+22%) due to increased patient volumes and as a result the utilization of safer, single use products (saline, heparin) for central catheter line collections. In addition, expenses of \$44,000.00 were incurred as a result of port accessing and sample collection, now being performed in the Cancer/Geriatrics blood draw station.

YTD TOTALS	Outpatient Phlebotomy			
	Budget	Actual	Variance	% Variance
FY 2005				
Salary/Wages	\$875,711	\$927,553	+\$51,842	+5.9
Expenses	\$218,500	\$266,768	+\$48,268	+22.1
Total	\$1,094,211	\$1,194,321	+\$100,110	+9.1

On-Going Activities/Future Activities:

In FY 2005, Outpatient Phlebotomy has:

1. Investigated national certification options for staff phlebotomists to enhance competency documentation and professionalism of staff.
2. Enhanced training and competency assessment/documentation for phlebotomy, indwelling line phlebotomy, and pediatric phlebotomy.
3. Prepared staff for successful accreditation inspections by JCAHO and CAP.
4. Participated in LIS vendor evaluations.
5. Management staff were trained in the Risk Monitor Pro software for reporting safety patient issues. Unlabeled specimens, mislabeled specimens and other patient safety issues are now documented in the system.
6. Participated in review of JW Thompson staff survey to understand strategies to retain/appreciate staff.
7. Staff participated in Nursing Educational Blitz.

FY 2006 Goals:

1. Develop process for national certification of phlebotomy staff.
2. Participate/evaluate LIS vendors for LIS replacement project.
3. Assume responsibility for LPN staff performing port access/sample collection.
4. Train phlebotomy staff in CGC blood draw station to access/collect samples from port devices.
5. Open and assume responsibility for new Cardiovascular Center blood draw station.
6. Participate in evaluation of Web Portal product and utilization in clinic setting.

CENTRAL DISTRIBUTION:

Central Distribution continues to be the hub of pathology specimen processing activities. Volumes continue to increase and specimen-handling duties have become more demanding. Technology advances and the ensuing need for sophisticated testing involves a constant changing of tests ordered and changing of specimen requirements. Central Distribution staff continue to respond to these changes effectively.

Expenses:

Central Distribution salary/wage expenses were \$76,941 over budget (+5.1%) due primarily to overtime expenses associated with coverage of medical leaves of absence and open budgeted positions. In addition, high turnover rates for many of the department's positions, summer vacation coverage and critical staffing bonuses paid in order to guarantee staffing for the expected level of service (primarily on the midnight shift) contributed to this budget condition. Central Distribution controllable expenses were under budget \$21,777, or 6.9%.

YTD TOTALS FY 2005	Central Distribution			
	Budget	Actual	Variance	% Variance
Salary/Wages	\$1,519,822	\$1,596,763	\$76,941	5.1
Expenses	\$315,800	\$294,023	-\$21,777	-6.9
Total	\$1,835,622	\$1,890,786	\$55,164	3.0

On-Going Activities/Future Activities:

In FY 2005, Outpatient Phlebotomy has:

1. Prepared staff for successful accreditation inspections by JCAHO and CAP.
2. Participated in LIS vendor evaluations.
3. Management staff were trained in the Risk Monitor Pro software for reporting safety patient issues. Unlabeled specimens, mislabeled specimens and other patient safety issues are now documented in the system.
4. Participated in review of JW Thompson staff survey to understand strategies to retain/appreciate staff.
5. Staff participated in Nursing Educational Blitz.
6. Initiated efforts with management staff to streamline and simplify work processes in the department.

FY 2006 Goals:

1. Participate/evaluate LIS vendors for LIS replacement project.
2. Participate in evaluation of Web Portal product and utilization in clinic setting.
3. Participate in process development for Order Management Project in University Hospital and Mott Children's Hospital.
4. Continue working with management staff to develop strategies to simplify work processes within the department.
5. Continue working with management staff to address high turnover rate within the department.

Referral Laboratory Testing:

Referral Laboratory Testing continues to be an expensive, yet needed service and is an indication of overall volume demands in Central Distribution. New and rapidly changing test technologies and sophisticated testing protocols not performed on-site, along with patient acuity and complexity of patient conditions evaluated at our facility, contributes to the demand for this service.

Volumes:

Referral Laboratory test volumes have increased 11.5% over fiscal year 2004. There was a 101% increase in volume referred to one of our contracted/prime vendors, Specialty Laboratories, Santa Monica, CA. The 101% increase in volume being sent to Specialty Laboratories was due to suspension of referrals to this laboratory, pending quality/personnel licensure issues at the laboratory during the previous year. The problems were rectified to our satisfaction and referrals resumed in December, 2004.

REFERRAL LABORATORY TEST VOLUMES			
	<i>FY 2004</i>	<i>FY 2005</i>	<i>% Change</i>
<i>Mayo Medical Laboratories</i>	43,527	45,356	4.2
<i>Specialty Laboratories</i>	3,376	6,797	101.3
<i>Miscellaneous Laboratories</i>	6,259	7,136	14.0
TOTAL	53,162	59,289	11.5

Expenses:

Current fiscal year Referral Laboratory expenses are 28.6% over budget (\$774,015).

REFERRAL LABORATORY EXPENSES					
FY 2004			FY 2005		
Budget	Actual	% Variance	Budget	Actual	% Variance
\$2,208,504	\$3,095,106	40.1	\$2,708,000	\$3,482,015	28.6

This is directly related to the increased volume, as well as a slight increase in volume referred to "other", non-contracted reference laboratories. This shift has occurred over the past several years:

"Other" Referrals		
FY	Volume	% of Total
2003	6399	11.4
2004	6259	11.7
2005	7636	12.8

Testing performed at these non-contracted laboratories are often state-of-the-art, expensive molecular, genetics, and other specialized testing, that are often patent protected procedures which preclude volume pricing benefits. This is also reflected in the cost per test in fiscal year 2005 increasing to \$61.53 from \$58.22 in fiscal year 2004.

Contracted pricing with our prime vendors (Mayo Medical Laboratories, Rochester, MN and Specialty Laboratories, Santa Monica, CA) has allowed us to minimize regular price increases and is a valuable strategy in controlling these costs. For FY 2005, 80% of the \$3,482,015 fiscal year expense was paid out on contracted pricing:

FY 2005		
Laboratory	Expense	% of Total
Mayo Medical Laboratories	\$2,419,537	69%
Specialty Laboratories	\$398,685	11%
Other Laboratories	\$663,793	19%
Total	\$3,482,015	

On-Going Activities/Future Activities:

In FY 2005, Referral Testing activities have included:

1. Development of a new “integrated” interface with Mayo Medical Laboratories to facilitate easier order entry and procedure billing processes.
2. Expansion of orderable test procedures on the Specialty Laboratory interface to facilitate order entry and result reporting.
3. Dr. Steven Mandell has been involved in assessing physician referral lab requests for medical appropriateness and supporting the department’s efforts to send testing that is appropriate through our prime vendors, when possible.
4. Referral Lab staff have been vigilant in directing test requests through the prime vendors whenever possible.
5. Referral test volumes are communicated regularly to appropriate departmental staff for assessment of make/buy decisions in order to reduce referral costs. Of the top 15 referred tests by cost, 7 are in the process of being evaluated for performance on site.

FY 2006 Goals:

1. Continue to provide information on frequently referred tests to appropriate staff, for make/buy decision making.
2. Continue to fine-tune interfaces with primary vendors, in order to streamline order entry, result reporting, and billing processes.
3. Participate in the development of processes for the Order Management Project.
4. Participate in the evaluation/selection of Laboratory Information System vendors for the LIS replacement project.
5. Participate in the evaluation/selection of Web Portal Vendors.

Submitted by:
Harry Neusius

GENERAL PATHOLOGY

**BIOINFORMATICS CORE
(COMPREHENSIVE CANCER CENTER)**

**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. OVERVIEW:

Bioinformatics, which is the convergence of biology, information science, and computation will play a critical role in the future of cancer biology and translational science. The University of Michigan Comprehensive Cancer Center (UMCCC) has multiple informatics and data resources that support clinical and basic research. Many of these resources were developed to meet the specific needs of individuals and were not designed to share data or integrate with other information systems. In the past, informatics efforts have been spread across the Cancer Center without a unifying organizational structure. The presence of such an organizational structure allows for easier access to available resources and domain expertise. A robust informatics infrastructure is vital so that investigators can continue to focus on their work without being mired in the technical details necessary to run a data-intensive research operation. Recognizing this, the Cancer Center leadership established the UMCCC Bioinformatics Core in July of 2004. The newly established Division of Pathology Informatics (circa July 2005) will serve to host the Cancer Center Core for mutual integration and leveraging of assets and expertise. In the next Annual report (2006) this Core will be assimilated into the Division of Pathology Informatics.

The mission of the Core is to support the informatics needs of both clinical and basic science investigators by providing the technological infrastructure and informatics/regulatory (e.g., security, HIPAA) expertise to ensure the reliable and secure acquisition, storage, analysis, and application of biomedical data from both patients and biospecimens in order to promote the quality of peer-reviewed publications as well as faster translational (i.e., bench to bedside) medicine that will ultimately lead to novel discoveries and improved patient care.

The foundation of the Core is built upon two UMCCC-developed bioinformatics assets, Oncomine, a cancer microarray compendium and data mining platform, and Profiler, a web-based tissue biomarker evaluation system. In addition, the Core integrates a Clinical Outcomes Database/Registry (COD/R) which is an institutionally supported clinical research database system that now involves collaborative efforts with industry. Oncomine, Profiler, and COD/R are applications already actively being used by UMCCC investigators. Tools and Services provided by this Core include 1) support, integration and further development of Oncomine (e.g., myOncomine), Profiler, and COD/R, 2) participation in and interface with the Cancer Biomedical Informatics Grid (caBIG) initiative, 3) education/consulting with regards to bioinformatics applications, 4) custom

programming, and 5) data integration and annotation. As data-intensive research increases at the Cancer Center, the Bioinformatics Core will continue to work towards expanding its capabilities and services in order to meet the growing demands of the investigators and also establish the UMCCC as a national leader in the field of cancer bioinformatics and its application to patient care.

II. RESEARCH AND DEVELOPMENT:

The Bioinformatics Core has worked to support all of the initiatives as outlined above. A summary follows:

Oncomine/myOncomine

Oncomine (www.oncomine.org) is an internationally recognized and utilized bioinformatics infrastructure for cancer genomics research developed at the UMCCC using developmental funds from the UMCCC, the Department of Pathology and the Dean's Office. A biologist can come to the Oncomine website and ask basic questions such as: 1) What cancer or cancer subtypes is my gene of interest dysregulated in?, 2) What are the top genes that distinguish metastatic cancer from clinically localized disease?, or 3) What genes may serve as biomarkers for a particular cancer or cancer sub-type? Results are generated with primary analytical methods such as hierarchical clustering and statistically-based differential expression analysis, usually with careful consideration for multiple-hypothesis testing. The lead developer of this project is Daniel Rhodes.

Oncomine has continued to add innovative and powerful features such as pathway analysis, interactome analysis and transcriptional motif and chromosomal region enrichment analysis. Oncomine has also continued to add new datasets to its compendium, now with over 130 datasets and 10,000 profiled tissue samples representing 30 distinct tissue types. The Oncomine programming team has also developed myOncomine, which contains all of the functionality of the regular version but adds additional value for UMCCC investigators. It contains facilities for users to output their data in formats suitable for further statistical analyses in other software. This version will allow for the private uploading, viewing, linking, and analysis of their own data and this highly automated process is being coordinated with the UMCCC Microarray Core Facility so that once it is up and running, gene expression data will be transferred seamlessly from the Microarray Core to myOncomine.

Profiler

Profiler is a web-based pathology, biomarker analysis, and tissue microarray evaluation/visualization system. The Profiler system works in conjunction with the UMCCC Tissue Core run by Dr. Thomas Giordano. The tissue core scans the images

and transfers them electronically to the Profiler system, where investigators can log in remotely via the web interface and view and score the scanned images. Advantages of the system include the ability to view extremely high-resolution images on a computer screen as well as the ability for more than one pathologist to score the same sample, allowing differences in scoring between pathologists to be taken into consideration.

Based on feedback from various UMCCC and Pathology faculty, the Bioinformatics Core has been working to enhance Profiler to better serve the needs of its users. Originally designed to work only with Prostate tissue, it has since been expanded, based on requests by UMCCC investigators, to include other tissue types as well. These include the capacity to evaluate various parameters related to head and neck tissues (larynx and lymph nodes) in addition to breast tissue (see Appendix). Also based on UMCCC investigator input, the Core is working with Dr. Celina Kleer (UMCCC Breast Cancer Program member) and Dr. Rajal Shah (Prostate SPORE Tissue Core) to incorporate automated semi-quantitative systems (e.g., Chromovision, AQUA) for the analysis of tissue biomarkers into the Profiler system.

In addition to supporting the current user base and adding more tissue types to support cancer center driven research, plans are currently underway to allow for the integration of Profiler data with that of other systems such as the COD/R so that investigators can merge patient-specific data from disparate databases. This plan is in line with the caBIG initiative and will serve as a foundation for our ability to later connect to the national grid once in place.

Clinical Outcomes Database / Registry (COD/R) Systems

COD/R (currently known as Velos and the Cancer Registry) is an institutionally supported database system which will serve as a common platform for clinical research. In March 2005, the University made a strategic decision to end development of its own clinical outcomes database system (BioDBx) and purchase one provided by the commercial vendor Velos. Velos *eResearch* is a commercially available web-based application for managing clinical trials and outcomes research

The Bioinformatics Core is aiding in migrating data from the previous database (BioDBx) to eResearch for UMCCC members and is providing domain expertise to ensure that standards are adopted for this new system to better allow for the transfer of data between disparate systems. Using this product should allow for data to be better shared between the COD/R and other Bioinformatics Core components, such as Profiler and myOncomine. Efforts are also underway to develop a standardized specimen inventory management system to better track the flow of samples. This effort also includes a barcoding initiative.

Although currently contained in a separate database, the University of Michigan's hospital-based cancer registry is being enhanced by the Bioinformatics Core to move it

from a simple database used for reporting to one that serves Cancer Center members for clinical outcomes research as well.

The registry is being brought up-to-date by replacing the paper-based abstracting method with a highly efficient informatics tool for case identification and data abstraction, known as the Registry Case Finding Engine (CaFE). This will have several benefits. First, it will speed up the process of case identification dramatically. Second, it will free up time for the abstracters to focus more on data collection instead of patient identification. Third, it will remove the need for a person to read through all pathology reports unrelated to cancer, lessening the privacy concerns raised by HIPAA. We have gained programmatic access to our clinical data repository for this purpose. The ultimate goal is transform the registry from one that has mainly served the UMCCC for the purposes of reporting to one that will provide reporting as well as data abstraction services for IRB-approved UMCCC investigator studies.

PubMed Query Search Tool (QUEST)

PubMed Quest is an application written on behalf of the Cancer Center leadership to provide a simple, efficient, and standard way in which to track publications generated by the various cores at the Cancer Center. This tool, available from our website, allows for bulk searching of publications based on a list of investigators provided to the system. Features include the ability to restrict the searched base on location (such as Ann Arbor), dates of publication, and journal titles, as well as topics. It can also automatically mark all publications that represent either intra- or inter-programmatic collaborations (or both) as well as highlighting the names of all Cancer Center members in each citation.

caBIG (Cancer Biomedical Informatics Grid)

The Cancer Biomedical Informatics Grid (caBIG) initiative seeks to provide the integration of data from Cancer Centers throughout the country. The Bioinformatics Core has been involved in the caBIG initiative in order to represent and promote the interest of investigators at the UMCCC. As the caBIG community develops new systems and tools, the Bioinformatics Core will become ever more needed to ensure the broad dissemination of this knowledge to the Cancer Center as well as planning UMCCC's strategic direction as future informatics initiatives should unfold in order to maintain caBIG compliance. In the near future caBIG compliance may not only be an asset to research but may also be required in order to receive funding from the NIH.

Dr. Hanauer and Mr. Kevin Smith have been representing the UMCCC in caBIG and have been participating in both the Integrated Cancer Research (ICR) General Workspace and the Clinical Trials Management System (CTMS) Workspace meetings. They also serve as the liaison from the CTMS to the ICR workspaces in order to facilitate greater knowledge transfer and collaboration across caBIG workspaces.

Publications

The following is a list of publications in 2004-2005 that have utilized at least one aspect of the tools provided by the Bioinformatics Core:

Hofer MD, Fecko A, Shen R, Setlur SR, Pienta KG, Tomlins SA, Chinnaiyan AM, Rubin MA. Expression of the platelet-derived growth factor receptor in prostate cancer and treatment implications with tyrosine kinase inhibitors. *Neoplasia* 6(5):503-12, 2004.

Santagata S, Demichelis F, Riva A, Varambally S, Hofer MD, Kutok JL, Kim R, Tang J, Montie JE, Chinnaiyan AM, Rubin MA, Aster JC. JAGGED1 expression is associated with prostate cancer metastasis and recurrence. *Cancer Res.* 1;64(19):6854-7, 2004.

Shah RB, Mehra R, Chinnaiyan AM, Shen R, Ghosh D, Zhou M, Macvicar GR, Varambally S, Harwood J, Bismar TA, Kim R, Rubin MA, Pienta KJ. (2004) Androgen-independent prostate cancer is a heterogeneous group of diseases: lessons from a rapid autopsy program. *Cancer Res* 64(24):9209-16, 2004.

Shen R, Ghosh D, Chinnaiyan AM. Prognostic meta-signature of breast cancer developed by two-stage mixture modeling of microarray data. *BMC Genomics* 14;5(1):94, 2004.

Rubin MA, Varambally S, Beroukim R, Tomlins SA, Rhodes DR, Paris PL, Hofer MD, Storz-Schweizer M, Kuefer R, Fletcher JA, Byrne JA, Pienta KJ, Collins C, Sellers WR, Chinnaiyan AM. Overexpression, Amplification and Androgen-regulation of TPD52 in Prostate Cancer. *Cancer Res* 1;64(11):3814-22, 2004.

Sreekumar A, Laxman B, Rhodes DR, Bhagavathula S, Harwood J, Giacherio ., Ghosh D, Sanda MG, Rubin MA, Chinnaiyan AM. Humoral Immune Response to alpha-Methyl-CoA Racemase and Prostate Cancer *Journal of the National Cancer Institute*, 96(11):834-43, 2004.

Rubin MA, Zerkowski MP, Camp RL, Kuefer R, Hofer MD, Chinnaiyan AM, Rimm DL. Quantitative determination of expression of the prostate cancer protein alpha-methylacyl-CoA racemase using automated quantitative analysis (AQUA): a novel paradigm for automated and continuous biomarker measurements. *Am J Pathol* 164(3):831-40, 2004.

Kumar-Sinha C, Shah RB, Laxman B, Tomlins SA, Harwood J, Schmitz W, Conzelmann E, Sanda MG, Wei JT, Rubin MA, Chinnaiyan AM. Elevated alpha-methylacyl-CoA racemase enzymatic activity in prostate cancer. *Am J Pathol* 164(3):787-93, 2004.

Hofer MD, Kuefer R, Varambally S, Li H, Ma J, Shapiro GI, Gschwend JE, Hautmann RE, Sanda MG, Giehl K, Menke A, Chinnaiyan AM, Rubin MA. The role of metastasis-associated protein 1 in prostate cancer progression. *Cancer Res* 1;64(3):825-9, 2004.

Rhodes DR, Yu J, Shanker K, Deshpande N, Varambally R, Ghosh D, Barrette T, Pandey A, Chinnaiyan AM. Large scale meta-analysis of cancer microarray data identifies commone transcriptional profiles of neoplastic transformation and progression. *Proceedings of the National Academy of Sciences* 101(25):9309-14, 2004.

Ghosh DR, Chinnaiyan AM. Classification and selection of biomarkers in genomic data using LASSO. The University of Michigan Department of Biostatistics Working Paper Series, 2004 <http://www.bepress.com/umichbiostat/paper42>

Rhodes DR, Chinnaiyan AM. Bioinformatics strategies for translating genome-wide expression analyses into clinically useful cancer markers. *Ann N Y Acad Sci* 1020:32-40, 2004.

Rhodes DR., Yu J, Shanker K, Deshpande N, Varambally R, Ghosh D, Barrette T, Pandey A, Chinnaiyan AM. ONCOMINE: a cancer microarray database and integrated data-mining platform. *Neoplasia* 6(1):1-6., 2004.

Dhanasekaran SM, Dash A, Yu J, Maine IP, Laxman B, Tomlins SA, Creighton CJ, Menon A, Rubin MA, Chinnaiyan AM. Molecular profiling of human prostate tissues: insights into gene expression patterns of prostate development during puberty. *FASEB J* 19(2):243-5, 2005.

Ghosh D, Chinnaiyan AM. Covariate adjustment in the analysis of microarray data from clinical studies. *Funct Integr Genomics* 5(1):18-27, 2005.

Chinnaiyan AM. ONCOMINE and caBIG Advance Cancer Bioinformatics. *The Scientist* April 13, 2005, 19:6.

Rhodes DR, Kalyana-Sundaram S, Mahavisno V, Ghosh D, Barrette TR, Chinnaiyan AM. (2005) Mining for Regulatory Programs in the Cancer Transcriptome. *Nature Genetics* (In Press).

Rhodes DR, Chinnaiyan AM. Integrative Analysis of the Cancer Transcriptome. *Nature Genetics* 2005. (In Press).

Loberg RD, Wojno K, Day LL, Pienta KJ. Analysis of Membrane-Bound Complement Regulatory Proteins in Prostate Cancer. *Urology* (Submitted Feb 2005).

Rhodes, D.R., Tomlins, S.A., Varambally, S. Mahavisno, V., Barrette, T., Kalyana-Sundaram, S., Ghosh, D., Pandey, A. and Chinnaiyan, A.M. (2005) Integrative Prediction of the Human Protein Interaction Network and Application to Cancer Biology. *Nature Biotechnology* (In Press).

Grant Applications

Cancer Center Support Grant (PI, M. Wicha), P30 CA46592, \$3,434,955 direct costs, UMCCC Bioinformatics Core, \$250K/direct costs/ yr (Director, A. Chinnaiyan). Pending

caBIG, Funded in the Integrated Cancer Research Workspace and the Clinical Trial Management Workspace.

III. FUTURE GOALS:

The goals of the Bioinformatics Core in the following year include:

- A. Continuing to support the current applications offered through the core.
- B. Continuing to enhance the existing applications such as:
 - 1. Oncomine/myOncomine:
 - a. Enhancing the functionality of the myOncomine application
 - i. Working with the DNA Microarray core to ensure rapid transfer of data files from the core directly into Oncomine
 - ii. The addition of more public datasets
 - iii. Further education sessions to increase awareness and use of Oncomine/myOnomine
- C. Profiler:
 - 1. Developing the ability to score new tissue types as the need arises from investigators
 - 2. Improving the application to ensure that it works well for pathologists using the system to score images.
- D. COD/R
 - 1. Developing “hooks” in the CDR database to directly import data into the Velos database system
 - 2. Develop an infrastructure and business model to assist the deployment of databases for Cancer Center investigators
 - 3. Enhance the timeliness and functionality of the cancer registry and transform it to a valuable data repository of clinical information that could be used by investigators
- E. Continue participation in caBIG to ensure that the University of Michigan is aware of the ongoing developments and to allow for the rapid adoption of tools and services provided by caBIG when they are ready for distribution/adoption.

- F. Become the central resource for Cancer Center and Pathology investigators who have informatics needs that they are unable to manage on their own.
- G. Integrate UMCCC Bioinformatics Core Activities into the Division of Pathology Informatics.
- H. Develop informatics expertise in the area of proteomics

IV. TEACHING/PROFESSIONAL:

Education

Providing education for the use of the tools and services provided is another goal of the Bioinformatics Core. In July 2005, the Core hosted an education seminar on the use of OncoPrint for Cancer Center Investigators. The class, held in the Learning Resource Center, had approximately 40 individuals show up the 30 computer terminals provided. Because of the success of the initial class, another class will be held at the end of August 2005 and will be strictly limited to 30 participants. We anticipate that other classes will follow.

Consulting

Drawing upon the expertise of Bioinformatics Core members, the core has been meeting with multiple individuals from the Cancer Center to discuss and analyze informatics needs including database design and support issues. Efforts have also been made to help investigators utilize the data already located in the cancer registry database to avoid duplication of effort. Discussions have taken place with Douglas Blayney, Kathy Cooney, Sami Malek, Sandra Wong, John Wei, and Mike Sabel.

Arul M. Chinnaiyan, M.D., Ph.D.
Director, Bioinformatics Core

David A. Hanauer, M.D., M.S.
Assistant Director, Bioinformatics Core

DEPARTMENT OF PATHOLOGY EDUCATIONAL PROGRAMS

**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

The Department of Pathology continues to offer a number of diverse programs within the Medical School, Dental School, School of Public Health, College of Literature, Science and the Arts, and the Rackham School of Graduate Studies. These include: courses requiring formal lecture and laboratory exercises, senior medical student Pathology clerkships, and research training for undergraduate, graduate, and medical students, as well as postdoctoral fellows. Within the Medical Center, Departmental teaching activities extend not only to medical students, but also house officers and the staff of many clinical departments in the form of regularly scheduled clinical conferences. Departmental teaching also extends to practitioners in the region and nation through continuing medical education programs, workshops and seminars offered through The University of Michigan, and professional organizations including the United States and Canada Association of Pathologists (USCAP), and American Society of Clinical Pathologists (ASCP).

Medical Student Education:

Pathology faculty continue to provide outstanding leadership (e.g. course directors, sequence coordinators, Associate Dean of Medical Education) and excellent teaching in the first two years of the medical student curriculum. Faculty continue to be recognized as recipients of student teaching awards. Efforts to increase student active learning experiences in a web-based teaching format continue with the development of the "Virtual Microscope" and interactive laboratory exercises. Elective fourth year clerkships in General Pathology and specialty experiences continue to be highly evaluated by students and meet important curriculum educational goals.

Residency Training:

The Department offers both individual and combined residency training in Anatomic and Clinical Pathology as well as fellowships in Cytopathology, Hematopathology, Surgical Pathology, Blood Bank/Transfusion Medicine, Breast Pathology and Urologic Pathology. Approximately 30 residents and fellows receive training annually. Residents continue to be very academically active, with multiple presentations at national meetings and first author publications. Several residents continue to provide strong support to the medical

student educational programs through their involvement as laboratory instructors, mentors and tutors to students. Six house officers and 9 fellows completed training this past year. Graduates found desirable fellowships (9), faculty positions (2) at academic health centers and employment in private practice (5).

Graduate Program:

The Department's doctoral graduate program continues to expand and thrive (approx. 12 students) with a focus on providing excellent training in preparation for student's careers as scientific investigators. The quality of the faculty and training offered is reflected by the continued interest of MSTP students and the completion of doctoral theses by four students and one master's degree this past year. Two training grants within the Department continue to serve as important sources of support for graduate students and post-doctoral fellows. The Department of Pathology is an active participant with other basic science departments in the Program in Biomedical Science (PIBS). This program involves a joint recruitment effort of biomedical graduate programs to recruit the very best students to the University of Michigan and allow them to delay selection of specific departments until they have completed their first year of study. Several faculty serve on both the curriculum and admissions committees for the program. An annual Pathology Research Symposium was implemented this past year and well received by students and faculty.

University / CME: Programs:

Department faculty continue to offer high quality laboratory research opportunities to both undergraduate and medical students, a Dental student pathology course with lab, CME programs, and individual teaching in the other schools of the University including Public Health. The Pathology Informatics and Blood Bank CME courses continue to be recognized as foremost programs in the country. Faculty continue to develop internet based educational modules that can be linked established and future CME programs. The fall A.J. French Society meeting continues to be a focal point for CME especially for graduates of our resident training programs.

M-LABS

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 2004 - 30 JUNE 2005

I. OVERVIEW:

MLabs, established in 1985, is the University of Michigan Health System's outreach laboratory program. Its role is to extend the pathology department's clinical laboratory services and faculty expertise to regional hospitals, clinics, physician offices and other healthcare settings; work that otherwise might be sent outside the region or state, to national reference laboratories. This model proved to be successful, capitalizing on the quality reputation of the University, the Health Care System and the department, and the dedication and drive of several key individuals to guide and support the growth of the program; MLabs has continued to grow since its inception.

With competition in the marketplace and advances in laboratory automation and informatics, quality in clinical laboratory testing is now *assumed* by our clients and laboratory services are increasingly being viewed as a negotiable "commodity" with work going to the lowest bidder. As such, MLabs is able to distinguish itself from its competitors by offering specialty expertise, a testing menu, and university programs not available at local or regional levels from national reference laboratories.

MLabs is expected to grow and further enhance its services, capacity and operations and will do so sharing in the progress of the clinical laboratories. The Mission Statement below describes this intent and reflects the client advocate role that MLabs must play in the advancement of departmental operations; it reflects MLabs continued commitment to respond and remain responsible to the competitive marketplace.

II. MLABS MISSION STATEMENT

1. To develop and enhance MLabs; to increase its scope and profitability.
2. To represent the "voice" of the outreach client and patient in seeking constant improvement in all University laboratory, clinical, administrative, informatics, compliance and business operations where they might impact MLabs services; to do the same when dealing with external vendors who provide support services to the department that might impact MLabs services.
3. To maintain price competitiveness in our target markets; to ever seek improvement in the revenue/cost ratio for the MLabs test menu.

4. To enrich the academic mission of the department by providing laboratory specimens of interest to the faculty, residents and students as well as opportunities to expand the faculty's reputation and reach into the regions we serve as educators, experts, supportive colleagues and researchers.
5. To support the mission of the University of Michigan Health System (UMHS) by providing outpatient laboratory services to M-Care through a network (or networks) of hospitals' laboratories.

III. MLABS WORKFORCE:

We welcome two key members to the MLabs team this year in the roles of MLabs Program Director and Information Technology Support Specialist. Dr. Steven Mandell was recruited from the Detroit Medical Center and Wayne State University, returning to his home and training grounds in Ann Arbor (U.M. B.S. '83, M.D. '87, Res Path AP/CP '91, Surg Path Fellow '92). Dr. Mandell has expertise in laboratory administration, informatics, process improvement initiatives and general pathology. Mr. Stephen Goyette was recruited from Oakwood Hospital. Mr. Goyette is a medical technologist with a specialist certificate in chemistry from the ASCP. He served as the chemistry supervisor at Oakwood's DRCL before venturing into laboratory informatics as an application specialist for a new LIS install. He served as an LIS systems analyst for the past 7 years before joining our ranks.

They join a truly pleasant, dedicated, effective, creative and experienced team who embody the spirit of the client in all of our operations.

Faculty

Program Director	Steven H. Mandell, M.D., Assistant Professor
Associate Director	Rodolfo F. H. Rasche, M.D., Assistant Professor
Past Director	Eugene Silverman, M.D., Associate Professor Emeritus

Administrative Staff

Program Manager	Susan Valliere, BS, MT (ASCP)
Operations Supervisor	Deborah Moss, BS, MBA, MT (ASCP)SM
Account Representative	Melissa Brown, MT (ASCP)
Managed Care/Financial Analyst	Deirdre Fidler, MHSA, BS, MT (ASCP)
Information Technology Support Specialist	Steve Goyette, BS, MT (ASCP)SC

This listing only represents those specifically dedicated to MLabs service. In reality, the success of our operation is dependent on many partners in administration, the faculty, Pathology Data Systems, the clinical labs, health care center sites and central distribution who are too numerous to list here but without whose contribution we would not succeed.

IV. MLABS OPERATIONS - ANNUAL ACTIVITY:

Markets Served and Market Changes

The MLabs Program plays a significant role in providing reference laboratory services to the Michigan and Northern Ohio regions.

<u>MARKET SEGMENTS SERVED</u>	
Dermatology Drug Testing / Psychiatry and Drug Counseling General Surgery and Surgical Subspecialty Practices Hospitals – Full Coverage Hospitals – Reference and Esoteric Testing Independent Laboratories Industry Health Services Laboratory Networks Managed Care Medical and Medical Subspecialty Practices Medical Oncology	Multi-Specialty Clinics Neurology Obstetrics and Gynecology Ophthalmology Pathology Consultations Pediatrics Podiatry Research Industry - Commercial Specialty Clinics Visiting Nurse Associations

MANAGED CARE

M-CARE

In 1996, M-CARE and the Regents of the University of Michigan, through the Department of Pathology MLabs Program, established a capitated contract for the provision of outpatient laboratory services to M-CARE members. MLabs provides these services through a network of subcontracted laboratories throughout the State as well as directly by MLabs for physician offices locally. The MLabs/M-CARE laboratory agreement has made a significant contribution to the MLabs Program, allowing MLabs personnel the opportunity to gain valuable experience running a statewide laboratory network, negotiating managed care capitated contracts, and maintaining visibility and standing in the managed care arena.

LABORATORY NETWORKS

Joint Venture Hospital Laboratories (JVHL)

JVHL is the largest laboratory network in Michigan and is organized as a limited liability company in Michigan, equally owned by its hospital laboratory members. The University of Michigan Health System (MLabs) became an equity member of JVHL in 1997.

MLabs personnel coordinate all of the Departmental issues pertaining to contractual obligations to JVHL (e.g., Quality Assurance and HEDIS reporting). The University is represented on JVHL's Executive, Quality Assurance, Operations, and Marketing Committees by the MLabs Program Director and Chief Department Administrator.

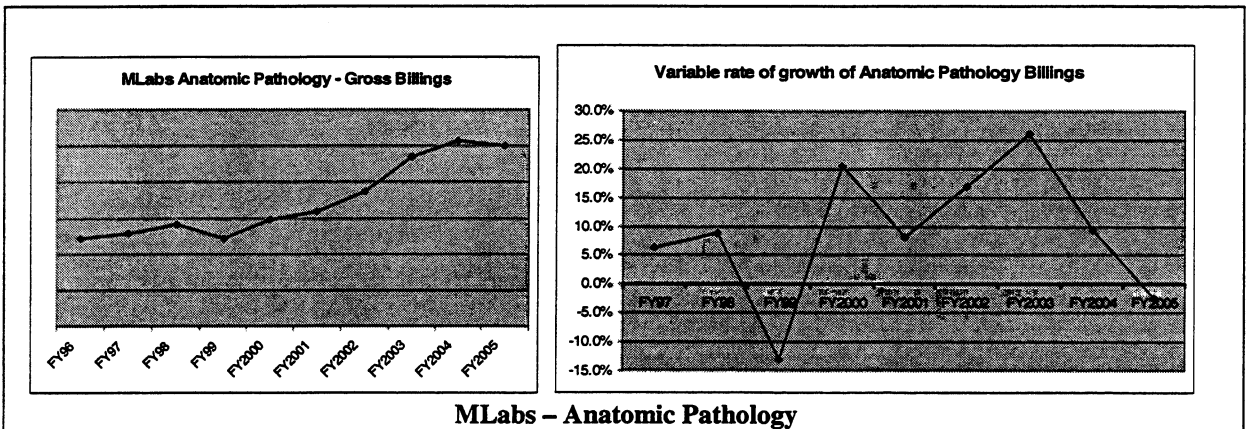
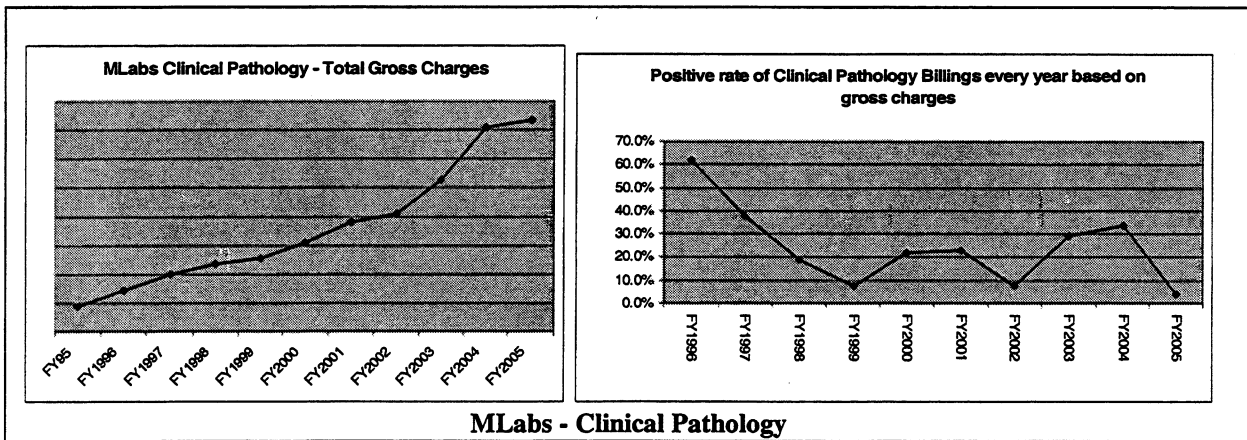
Great Lakes Laboratory Network (GLN)

MLabs became a member of GLN in 1996. MLabs does not participate in managed care contracts through GLN; our membership is primarily advisory through representatives on the Executive and Steering committees.

FINANCIAL

Gross billings for anatomic pathology decreased by 2.4% in 2005 and are likely accounted for by a discontinuation of muscle and nerve biopsy services for some accounts in addition to single client departures in each of our dermatology and hospital market segments.

Gross billings for clinical pathology increased by 3.9% for clinical pathology in 2005 and are likely accounted for by growth in a few of our clients' own outreach programs.



Client Enrichment and Education

MLabs coordinates continuing medical education activities for its clients, including a popular Saturday Anatomic Pathology Symposium (includes informal lectures, lunch and slide reviews at a multi-headed projection scope), attendance at the department's annual Blood Bank Conference, and other events. Client site training is also provided for a variety of in-service topics.

Service Volumes and Client Focused Service Enhancements

Client service assistants handled about 42,000 client calls this year.

Clients helped guide our service enhancements this year via their responses to our physician office customer satisfaction surveys and via constant interaction with our hospital clients.

Clients were overall very satisfied or satisfied with MLabs services but MLabs is seeking to exceed client's minimum expectations for satisfaction. To this end we have directed their comments into improving the following service aspects:

Billing Collections: established review process and communication protocol for key client's patients being sent for collections of overdue payments.

Blood Draw Station Availability and Convenience: department increased total number of stations by 4 in prominent locations around the Ann Arbor-Ypsilanti area in the past year.

Client Services Training: compiled educational material and client service standards for key client; employed web-based training/retraining and exam on client service techniques, standards and expectations for MLabs staff.

Communication / Problem Resolution Documentation: upgraded 4 hospital clients from 'Client Link' to 'Thin Client' GroupWise access, compliant exchange of protected health information, and improved tracking and resolution of problems.

Critical Result Notification: initiated evaluation of timely notification process for critical INR's identified by point of care testing on MLabs patients; implemented quality assurance processes for confirming all critical result notified.

EMR Reporting: implemented direct fax to client electronic medical record to improve reporting mechanisms; initiated and implemented redesigned reporting formats for several tests to improve interpretability and clinical utility.

Handbook Improvements: revised database and began process for transition to new combined in-house/MLabs online Handbook for single source of truth and improved utility and accuracy.

HIPAA Compliance: implemented Hypersend secure file transfer applications for exchange of protected health information (PHI) with clients without GroupWise availability.

Interface Conversions for Improved Workflow: assisted interfaced clients with conversion of Specialty Laboratory Sendouts to specific orderables, labels and manifests; likewise for on-site AP type clinical lab orders, converting XLABEL miscellaneous to specific laboratory locations on routing label.; conversion of Mayo Miscellaneous sendout orders to specific orderables, labels and manifests in process.

Phone Consultations: increased immediate or within minutes availability of medical director for phone consultation to near 100%.

Requisitions: redesigned and web-enabled client forms for specialty testing; initiated requisition redesign.

Web Based Patient Management, Ordering and Results: submitted requests for proposals and selected a vendor to implement MLabs Lab Web Portal; go live planned for 2nd quarter of next year.

MLabs Website: Initiated and implemented revisions of the website to be more user-friendly and better targeted towards client's needs; major revisions still ongoing.

Strategic Planning

In consideration of the client and patient advocacy role MLabs plays within the department, we have begun to advance the following process improvement initiatives over the past eight months:

1. Implement Lean and Six Sigma initiatives for Customer Service, Lab Operations and Office/Business Systems; 4 key personnel sent for Lean and/or Six Sigma training
2. Improved client services infrastructure
 - a. Staff: Phones: Rockwell phone operations reviewed and modified report requirements defined; service deficiencies for coverage areas identified and confirmed; requests for report modification for UMHS system placed with MCIT.
 - b. Fax: Explored and partially implemented desktop fax alternatives for sending and receiving
 - c. Quality assurance: Implemented automated QA recording, tracking and reporting for MLabs specimens/incidents using existing RM Pro module (no additional cost).
 - d. Hardware/Software upgrades: Converted division PC's to MCIT core image; updated to Acrobat 6.0, ACT! 2005 and Microsoft Visio 2003.
 - e. Printers: Discontinued redundant Market Watch service on remote printers.
 - f. Procedures: Rewritten in standard, common format with document control monitors; network drive enabled and linked to table of contents for easy look up and reference.
 - g. Client manual: Reorganized table of contents with links; network drive enabled for easy look up and reference
 - h. Surveys: Implemented Advisor 123-Survey tool for easy design, application, monitoring and interpretation of web-based surveys; available to the entire department or university for no additional cost.

3. Improve operations of key partners/vendors/clients
 - a. Change process control: Explored and defined stages for change process control with Mayo Medical Laboratories, PDS
 - b. Reviewed error correction process and report formats with Mayo Medical Laboratories Medical Director.
 - c. Developed strategy for reference lab insourcing and improved turnaround time.

In consideration of MLabs mission to grow, we have forwarded the following initiatives in marketing:

1. Expanding our brand identity and internal marketing opportunities
2. Evaluating market needs and areas of potential future growth
3. Strategies for establishing test menus for market segments or disease groups
4. Strategies for co-marketing opportunities with our clients or UMHS programs

V. BARRIERS TO SUCCESS:

The key to implementing these plans is strong, unified, unwavering, effective and committed leadership and the Chair, Medical Director of Clinical Laboratories, Associate Director of Clinical Laboratories, Chief Department Administrator, Clinical Laboratory Administrator, Medical Director of MLabs, MLabs Manager and Manager of Central Distribution and Phlebotomy all support MLabs initiatives; there are no barriers to keep us from committing to excellence.

VI. BENEFITS:

All strategies to improve laboratory operations and improve MLabs status in the marketplace will also function to improve operations for UMHS and yield positive benefits on the quality and efficiency of patient care. For instance, the lab web portal is intended to eliminate the rework and errors associated with transcribing manual requisitions into Pathnet; office bar coding of specimens in conjunction with interfaced orders from the web portal will decrease labeling errors and improve throughput of specimens resulting in decreased turnaround time and more efficient, effective patient care. Both of these initiatives will create significant efficiency in several divisions and permit capacity for additional work without requiring additional space.

Respectfully submitted by Steven H. Mandell, MD
Prepared by Dr. Mandell, Dr. Rasche and Ms. Valliere

PATHOLOGY RESEARCH MICROARRAY LABORATORY

**DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 2004- 30 JUNE 2005**

I. OVERVIEW:

The Pathology Research Microarray Laboratory was established in 1999-2000 as part of the larger Microarray Network at the University of Michigan Medical School. This array facility is in addition to the one in the Cancer Center, which is largely devoted to genetic analysis of solid tumors from humans. DNA microarray analysis is a powerful technology allowing for detailed gene expression studies of cell lines, animal models, and tissues (including pathologic specimens). With the sequencing of the human genome, it is now possible to monitor gene expression on a comprehensive, global scale as opposed to focusing on one gene at a time. Not only will this technology have an obvious application in the basic sciences, it has the potential of impacting the treatment and diagnosis of patients. As Pathology is a discipline comprised of both scientific investigation and clinical diagnosis, it is imperative that the Department play a role in the use and development of this technology. Clinical Pathology, in particular, has the opportunity of utilizing microarray technology to develop novel diagnostic and prognostic biomarkers.

The Pathology Research Microarray Laboratory functions to support the current and future research activities of the Department as well as Interdepartmental Programs. The primary focus of this facility is important in three areas in the study of human pathology including 1) inflammation, 2) apoptosis/cell death and 3) cancer. These studies are accomplished using characterized animal models as well as with human specimens and cell lines.

II. RESEARCH AND DEVELOPMENT:

While DNA microarray analysis is a potent technique to explore complex and interlocking systems, it is clear that this technology is in its infancy and that there are formidable problems in dealing with the multitude of data generated. Dr. Arul Chinnaiyan has carefully developed our Research Microarray Laboratory, beginning in 1999 when he visited the Brown and Botstein laboratories at Stanford in order to talk with experts and determine the best microarray system to meet our needs. Our microarray methodology is based primarily on techniques learned at the 1999 Cold Spring Harbor Workshop on DNA Microarrays.

Beginning October of 1999, the Lab has been assembling the equipment, clone sets, and supplies necessary to produce high-density cDNA microarrays including a robotic arrayer, microarray scanner, PCR machines, and liquid handling instrumentation. The Lab has successfully generated a 20K human cDNA chip, 10K rat cDNA chip and a 5K mouse cDNA chip. In 2005, we upgraded the robotic arrayer to 48 pins capacity and have been producing 32k human cDNA chips.

During this reporting period the following investigators have utilized the Microarray facilities:

1. Drs. Peter Ward and Vidya Sarma (Pathology), studies on sepsis and c5a.
2. Dr. Sem Phan (Pathology), studies using in vivo fibrosis models.
3. Dr. Dan Remick (Pathology, protein microarrays), sandwich antibody microarrays.
4. Dr. William Finn (Pathology), Profiling of hematologic malignancies (CLL and MCL).
5. Dr. Kenneth Pienta (Internal Medicine), gene expression mediated by PAR1.
6. Dr. Andrew Lieberman (Pathology), gene expression mediated by androgen receptor variants.
7. Dr. Sofia Merajver (Internal Medicine) Gene expression mediated by Rho family members.
8. Dr. Steven Ethier (Radiation Oncology) Gene expression mediated by FGFR family inhibitors.
9. Dr. Joseph Holoshitz (Internal Medicine) Gene expression of studies in identical twins with and without rheumatologic disease.
10. Dr. Kent Johnson (Pathology) and Pfizer Corporation- Development of antibody microarrays.
11. Dr. Paul Harari (Univ. of Wisconsin, Radiation Oncology) Gene expression mediated by Tarceva.
12. Dr. Celina Kleer (Pathology) Gene expression mediated by WISP.
13. Dr. Theodora Ross (Internal Medicine) Gene expression mediated by HIF1.
14. Dr. Naohiro Inohara (Pathology) (focuses on mechanistic studies to understand signaling pathways involved in apoptosis and innate immunity)
15. Drs. Chinnaiyan, Varambally, and Sreekumar (Pathology and Urology). Gene expression profiles of prostate cancer and benign prostatic hyperplasia. Gene expression mediated by EZH2 and AMACR. Development of protein microarray technologies for antibody microarrays and antigen microarrays for humoral immune response.

In addition to establishing DNA microarrays in the laboratory, a large effort has also been placed on devising a system to monitor protein levels and activity in a high-throughput fashion. Much of this activity has been assimilated into the newly established Proteomics Laboratory. While various genome scale methodologies to identify variations in DNA and RNA exist, an analogous "biochip" to explore protein function has been difficult to implement for various reasons. In this Lab we plan to establish a platform for the massively parallel analysis of protein levels, interactions, and function. One area for which we will implement both DNA and protein microarray technology is the development of novel cancer and inflammation biomarkers. Drs. Dan Remick and Kent Johnson are both working with the Microarray Lab in order to fabricate and test protein/antibody microarrays for their respective areas of interest. The protein array

platform has been successfully set up in Dr. Chinnaiyan's lab (Microarray Lab). We also purchased a new non-contact arrayer for protein chips. We are currently running both protein arrayers in their full capacity and produced protein arrays for different human cancers including: Prostate, Lung, Breast, Colon, and Bladder.

Publications

The following manuscripts include data made possible by the Microarray Lab:

Olle EW, Sreekumar A, Warner RL, McClintock SD, Chinnaiyan AM, Bleavins MR, Anderson TD, Johnson KJ. Development of an internally controlled antibody microarray. *Mol Cell Proteomics*. 2005, July 22.

Rubin MA, Bismar TA, Andren O, Mucci L, Kim R, Shen R, Ghosh D, Wei JT, Chinnaiyan AM, Adami HO, Kantoff PW, Johansson JE. Decreased alpha-methylacyl CoA racemase expression in localized prostate cancer is associated with an increased rate of biochemical recurrence and cancer-specific death. *Cancer Epidemiol Biomarkers Prev*. 2005 Jun;14(6):1424-32.

Witkiewicz AK, Varambally S, Shen R, Mehra R, Sabel MS, Ghosh D, Chinnaiyan AM, Rubin MA, Kleer CG. Alpha-methylacyl-CoA racemase protein expression is associated with the degree of differentiation in breast cancer using quantitative image analysis. *Cancer Epidemiol Biomarkers Prev*. 2005 Jun;14(6):1418-23.

Bradley SV, Oravec-Wilson KI, Bougeard G, Mizukami I, Li L, Munaco AJ, Sreekumar A, Corradetti MN, Chinnaiyan AM, Sanda MG, Ross TS. Serum antibodies to huntingtin interacting protein-1: a new blood test for prostate cancer. *Cancer Res*. 2005 May 15;65(10):4126-33.

Chinnaiyan P, Huang S, Vallabhaneni G, Armstrong E, Varambally S, Tomlins SA, Chinnaiyan AM, Harari PM. Mechanisms of enhanced radiation response following epidermal growth factor receptor signaling inhibition by erlotinib (Tarceva). *Cancer Res*. 2005 Apr 15;65(8):3328-35.

Thomas M, Yu Z, Dadgar N, Varambally S, Yu J, Chinnaiyan AM, Lieberman AP. The unfolded protein response modulates toxicity of the expanded glutamine androgen receptor. *J Biol Chem*. 2005 Jun 3;280(22):21264-71.

Narla G, Difeo A, Reeves HL, Schaid DJ, Hirshfeld J, Hod E, Katz A, Isaacs WB, Hebbing S, Komiya A, McDonnell SK, Wiley KE, Jacobsen SJ, Isaacs SD, Walsh PC, Zheng SL, Chang BL, Friedrichsen DM, Stanford JL, Ostrander EA, Chinnaiyan AM, Rubin MA, Xu J, Thibodeau SN, Friedman SL, Martignetti JA. A germline DNA polymorphism enhances alternative splicing of the KLF6 tumor suppressor gene and is associated with increased prostate cancer risk. *Cancer Res*. 2005 Feb 15;65(4):1213-22.

Shah RB, Mehra R, Chinnaiyan AM, Shen R, Ghosh D, Zhou M, Macvicar GR, Varambally S, Harwood J, Bismar TA, Kim R, Rubin MA, Pienta KJ. Androgen-independent prostate cancer is a heterogeneous group of diseases: lessons from a rapid autopsy program. *Cancer Res.* 2004 Dec 15;64(24):9209-16.

Dhanasekaran SM, Dash A, Yu J, Maine IP, Laxman B, Tomlins SA, Creighton CJ, Menon A, Rubin MA, Chinnaiyan AM. Molecular profiling of human prostate tissues: insights into gene expression patterns of prostate development during puberty. *FASEB J.* 2005 Feb;19(2):243-5. 2004 Nov 17.

Hofer MD, Fecko A, Shen R, Setlur SR, Pienta KG, Tomlins SA, Chinnaiyan AM, Rubin MA. Expression of the platelet-derived growth factor receptor in prostate cancer and treatment implications with tyrosine kinase inhibitors. *Neoplasia.* 2004 Sep-Oct;6(5):503-12.

Santagata S, Demichelis F, Riva A, Varambally S, Hofer MD, Kutok JL, Kim R, Tang J, Montie JE, Chinnaiyan AM, Rubin MA, Aster JC. JAGGED1 expression is associated with prostate cancer metastasis and recurrence. *Cancer Res.* 2004 Oct 1;64(19):6854-7.

Sreekumar A, Laxman B, Rhodes DR, Bhagavathula S, Harwood J, Giacherio D, Ghosh D, Sanda MG, Rubin MA, Chinnaiyan AM. Humoral immune response to alpha-methylacyl-CoA racemase and prostate cancer. *J Natl Cancer Inst.* 2004 Jun 2;96(11):834-43. Erratum in: *J Natl Cancer Inst.* 2004 Jul 21;96(14):1112.

Rubin MA, Varambally S, Beroukhim R, Tomlins SA, Rhodes DR, Paris PL, Hofer MD, Storz-Schweizer M, Kuefer R, Fletcher JA, Hsi BL, Byrne JA, Pienta KJ, Collins C, Sellers WR, Chinnaiyan AM. Overexpression, amplification, and androgen regulation of TPD52 in prostate cancer. *Cancer Res.* 2004 Jun 1;64(11):3814-22.

Paris PL, Andaya A, Fridlyand J, Jain AN, Weinberg V, Kowbel D, Brebner JH, Simko J, Watson JE, Volik S, Albertson DG, Pinkel D, Alers JC, van der Kwast TH, Vissers KJ, Schroder FH, Wildhagen MF, Febbo PG, Chinnaiyan AM, Pienta KJ, Carroll PR, Rubin MA, Collins C, van Dekken H. Whole genome scanning identifies genotypes associated with recurrence and metastasis in prostate tumors. *Hum Mol Genet.* 2004 Jul 1;13(13):1303-13. 2004 May 11.

Liu T, Dhanasekaran SM, Jin H, Hu B, Tomlins SA, Chinnaiyan AM, Phan SH. FIZZ1 stimulation of myofibroblast differentiation. *Am J Pathol.* 2004 Apr;164(4):1315-26.

Watson JE, Doggett NA, Albertson DG, Andaya A, Chinnaiyan A, van Dekken H, Ginzinger D, Haqq C, James K, Kamkar S, Kowbel D, Pinkel D, Schmitt L, Simko JP, Volik S, Weinberg VK, Paris PL, Collins C. Integration of high-resolution array comparative genomic hybridization analysis of chromosome 16q with expression array data refines common regions of loss at 16q23-qter and identifies underlying candidate tumor suppressor genes in prostate cancer. *Oncogene.* 2004 Apr 22;23(19):3487-94.

Wu M, Wu ZF, Kumar-Sinha C, Chinnaiyan A, Merajver SD. RhoC induces differential expression of genes involved in invasion and metastasis in MCF10A breast cells. *Breast Cancer Res Treat.* 2004 Mar;84(1):3-12.

Albrecht EA, Chinnaiyan AM, Varambally S, Kumar-Sinha C, Barrette TR, Sarma JV, Ward PA. C5a-induced gene expression in human umbilical vein endothelial cells. *Am J Pathol.* 2004 Mar;164(3):849-59.

Rubin MA, Zerkowski MP, Camp RL, Kuefer R, Hofer MD, Chinnaiyan AM, Rimm DL. Quantitative determination of expression of the prostate cancer protein alpha-methylacyl-CoA racemase using automated quantitative analysis (AQUA): a novel paradigm for automated and continuous biomarker measurements. *Am J Pathol.* 2004 Mar;164(3):831-40.

Kumar-Sinha C, Shah RB, Laxman B, Tomlins SA, Harwood J, Schmitz W, Conzelmann E, Sanda MG, Wei JT, Rubin MA, Chinnaiyan AM. Elevated alpha-methylacyl-CoA racemase enzymatic activity in prostate cancer. *Am J Pathol.* 2004 Mar;164(3):787-93.

Hofer MD, Kuefer R, Varambally S, Li H, Ma J, Shapiro GI, Gschwend JE, Hautmann RE, Sanda MG, Giehl K, Menke A, Chinnaiyan AM, Rubin MA. The role of metastasis-associated protein 1 in prostate cancer progression. *Cancer Res.* 2004 Feb 1;64(3):825-9.

Nyati MK, Maheshwari D, Hanasoge S, Sreekumar A, Rynkiewicz SD, Chinnaiyan AM, Leopold WR, Ethier SP, Lawrence TS. Radiosensitization by pan ErbB inhibitor CI-1033 in vitro and in vivo. *Clin Cancer Res.* 2004 Jan 15;10(2):691-700.

Knight PR, Sreekumar A, Siddiqui J, Laxman B, Copeland S, Chinnaiyan A, Remick DG. Development of a sensitive microarray immunoassay and comparison with standard enzyme-linked immunoassay for cytokine analysis. *Shock.* 2004 Jan;21(1):26-30.

Grant Applications

The Pathology Microarray Lab has supported the following grant applications by providing preliminary gene expression analyses:

“Molecular Classification of Prostate Cancer”, American Cancer Society, RSG-02-179-01-MGO, 07/01/02 – 06/30/06, 15%, \$180,000/yr; Principal Investigator (Chinnaiyan)

“Protective Effects of Anti-C5a in Sepsis”, National Institute of Health, GM61656 12/01/01-11/30/06, 5%, \$225,000/yr; (Principal Investigator: Ward)

R01, “Lung Injury by Oxygen Metabolites”; (Principal Investigator: P. Ward)

Microarray Supplement, “Sepsis Profiling”, (Principal Investigator: P. Ward)

U of M SPORE in Prostate Cancer, Principal Investigator: K. Pienta

DOD grant,” Biological Differences between prostate cancer cells that metastasize to the bone versus soft tissue sites”, (Principal Investigator: K. Pienta)

P01, Program Project on Prostate Cancer Bone Metastases; (Principal Investigator: E. Keller)

“The Role of Polycomb Group Proteins in Prostate Cancer”, National Institute of Health, R01 CA97063, 07/01/02 – 06/30/07, 20%, \$178,000/yr; Principal Investigator: Chinnaiyan

Glue Grant, U54 GM64351 “Inflammation and the Host Response to Injury”; Principal Investigator: Remick

Department of Defense, DOD PC020322; Principal Investigator: Chinnaiyan

“Epitomic Biomarkers of Prostate Space, U01 CA111275, 09/30/04-09/29/09, NIH, 10%, \$312,871/yr; Principal Investigator: Chinnaiyan

Pfizer Sponsored Research Agreement (Ward)

Principal Investigator, “Discovery of Cancer Biomarkers using High Throughput Multi-Blotting”, GMP Companies, Inc., 12/01/02-03/05, 0% effort, \$168, 827/yr direct costs.

III. FUTURE GOALS:

The future goals of the Pathology Microarray Lab in the next calendar year include:

1. Continue to support the research funding applications of Pathology faculty with preliminary data and bioinformatics expertise.
2. Continue to publish data using microarray technology in peer-reviewed journals to establish the Department in the fast moving field of genomics/proteomics.
3. Expand the rat, mouse, human DNA chips to include additional cDNA clones. Ultimately, we would like to develop a chip that can monitor the entire expressed genome.
4. Develop and utilize protein microarray technology to answer biologically important questions.
5. Train post-doctoral fellows and students in making and using microarrays.
6. Develop a unified bioinformatics platform for the analysis of DNA microarray, tissue microarray, protein microarray and clinical/pathology data.
7. Position our resources and expertise such that we can take advantage of opportunities in the emerging field of “clinical genomics”.

IV. TEACHING/PROFESSIONAL:

Terry Barrette, the Laboratory manager, has played an important role in setting up our microarray database and data analysis programs. Xuhong Cao, the Laboratory manager, has also played an important role in the overall lab managing and coordinating the basic lab research with the informatics projects, recently has successfully upgraded the arrayer to produce 32k Human chips that includes all the human cDNA in one chip. Dr. Chandan Kumar, a post-doctoral fellow in the lab, was instrumental in developing our cDNA microarray system as part of his training. In September of 2003, Dr. Kumar accepted a position as Senior Scientist at the Institute of Bioinformatics, Bangalore India where he setting up their Microarray capabilities. Sooryanaryana Varambally, Research Investigator, involves in many aspects of the microarray projects. Arun Sreekumar and George Wang, previously post-doctoral fellows in the lab were promoted to Research Investigators and involved in developing the protein microarray platform. Other postdoctoral fellows in the Department of Pathology that have received training in DNA or protein microarrays include: Saravana Dhanasekaran, Bharathi Laxman, Ira Maine (mentored by M. Rubin), Guoan Chen (mentored by D. Beer), Atreya Dash (mentored by M. Rubin), Monzy Thomas (mentored by A. Lieberman), Eric Albright (mentored by P.Ward), Tianju Wu (mentored by S.Phan), Li Zhu (mentored by G. Nuñez), and Thomas Neff (mentored by P. Ward). Similarly the following medical and graduate students received training in microarrays, microarray analysis and or QRT-PCR: Dan Rhodes (MSTP), Scott Tomlins (MSTP), Qi Cao (Pathology), Jianjun Yu (Bioinformatics), Chad Creighton (Bioinformatics), Patrick Lester (Pathology), Julie Kim (Bioinformatics), Viktoriya Resnick (Bioinformatics), Xiaoyu Jia (Pathology) Smita Lakhotia (Graduate Student, Indian Institute of Sciences), and Ronglai Shen (Biostatistics Masters Student).

Arul M. Chinnaiyan, M.D., Ph.D.
Director, Pathology Research Microarray Laboratory

Xuhong Cao, M.S.
Manager

PATHOLOGY DATA SYSTEMS ANNUAL REPORT

DEPARTMENT OF PATHOLOGY ANNUAL REPORT 1 JULY 2004- 30 JUNE 2005

Individual Laboratory Projects

- Development of software for the Molecular Diagnostic Laboratory to receive data feeds from the various instruments and communicate the data to PathNet.
- Assistance in the deployment of a new analyzer in Flow Cytometry called iCyte so that textual reports can be imported into PathNet.
- Continuing development of software for routing complex HLA results from our current “homebrew” Oracle-based system to CareWeb.
- Installation and customized enhancement of the Trestle telepathology and digital imaging system in Anatomic Pathology.
- Support for the installation of the ProView automated typing and screening instrument in the Blood Bank, requiring a new interface to PathNet.

MLabs Enhancements

- Improve the interfaces to pass orders and receive test results from the two reference labs to which the departments submits specimens, Specialty and Mayo Labs.
- Creation of an electronic allergen form for test ordering for Mayo Labs.

Adapting to New Standards and Billing Requirements

- Support for the conversion from our old barcode standard, Code 39, to a new standard, Code 128; this required a number of software modifications in PathNet on both the CP and the AP sides.
- Enhancement of ADT functions on the Oracle system in preparation for the deployment of advance billing

Standardization of PC/Laptop Software Images

- Deployment of the MCIT “core image” (standard PC software configuration) on approximately 250 departmental PCs and also resident and faculty laptop computers.

Network Architecture Modifications

- Pathology network “tree” migration from the UMHS to the UMMED configuration.

New Computer Acquisitions; New Lab and Space Acquisition; Decommissioning Old Systems

- Participation in the RFP development process and vendor selection for lab portal software in collaboration with MLabs.
- Participation in the laboratory move to Traverwood such that a full suite of IT services were available to all personnel.
- Refresh of the certification (test) environment of PathNet in order to prepare for the Eclipsys order management project.
- Participation in enhancements of the Medquist digital dictation system.
- Early planning for the relocation of PathNet hardware to the MCIT machine room in Arbor Lakes and other hardware to Med Sci I.
- Reactivation of the LIS RFP process for the acquisition of a new LIS, following capital funds allocation for the new system
- Decommissioning of the pathology wireless network after several years of operation and cutover to the MCIT wireless network.

Departmental Software and Hardware Improvements Not Specifically Related to a Specific Laboratory

- Improvements to the departmental web site including calendaring and an enhanced staff directory.
- Creation of a PDF forms server for the department whereby forms such as faculty absence can be completed and submitted electronically
- Enhancement of the SANS which is the storage area network serving the department

Inspection and Accreditation; Regulatory Changes

- Preparation for the CAP inspection (no PDS citations) including revision of the PDS manuals and review of the QC validation documents.
- HIPAA gap analysis in collaboration with MCIT to determine whether our currently security and confidentiality procedures are adequate.
- Organizing a system for the retrieval of old hardcopy lab test requisitions by medical record number, which will be invaluable at the time of audit by insurance companies seeking to match test requests with performed tests.

PROSTATE S.P.O.R.E. TISSUE/INFORMATICS CORE

**DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 2004- 30 JUNE 2005**

I. OVERVIEW:

This Core is administered by the Department of Pathology. The Core is primarily supported from funds provided by the University of Michigan Prostate SPORE grant (PI Kenneth Pienta), the Department of Urology, and the Department of Pathology. The aim of the University of Michigan Prostate SPORE Tissue Core is the collection of biological material with associated clinical information to facilitate translational research. Quality assurance is maintained by a staff of two pathologists (Drs. Shah and Chinnaiyan) and pathology fellow (Dr. Mehra). Clinical consent and patient participation is directed by a urologist with specialty interest in outcomes and quality of life research (Dr. Wei, Department of Urology). As a coordinated effort between Pathology, Urology, and SPORE researchers, the Tissue/Informatics Core has a comprehensive relational database that provides researchers a wide range of data on each sample under study. The Tissue/Informatics Core places patient confidentiality and clinical care as a top priority.

Since 1994 the Prostate Tissue Core has served an important role in the University of Michigan prostate SPORE. One of the main accomplishments of the Tissue Core is the establishment of a model Tissue Microarray (TMA) facility with associated infrastructure. This model has been tested at the University of Michigan site and has been used for managing clinical, pathology, and molecular data on over 1500 prostate cancer (PCa) patients dating back to 1995. This work done alone or in collaboration with other SPORE groups has led to many published studies. In May of 2004, Dr. Shah assumed leadership of the SPORE Tissue Core and is the lead surgical pathologist for the Michigan Prostate SPORE. Along with Dr. Shah, Dr. Chinnaiyan Co-directs the prostate SPORE lab and give research guidance to the core.

II. RESEARCH AND DEVELOPMENT:

Drs. Shah and Chinnaiyan are dedicated to maintain and improve the existing resources and capabilities of the SPORE Tissue Core. During this reporting period, a new perspective to the Tissue Core led to the development of new resources and technologies. These are delineated here:

1. Continued banking of genomic DNA, RNA/cDNA, and protein extracted from grossly dissected and laser-microdissected prostatic tissues.

2. Addition of an EDRN (Early Detection Research Network) needle biopsy cohort comprised of frozen needle biopsy tissues, serum, urine, and DNA from patients undergoing needle biopsy.
3. Established monthly meetings of a "Tissue Usage Committee" to ensure proper usage of tissues from the core, as well as, introduction of a "Specimen Request Form" for any and all requested specimens that come from the tissue core.
4. Continued banking of Urine from Radical Prostatectomy patients for protein analysis.
5. Use of real-time PCR technology for the validation of candidate differentially expressed prostate cancer genes.
6. Development of mRNA in situ hybridization and fluorescence in situ hybridization (FISH) of tissues and TMAs.
7. Continued development of a unified bioinformatics platform (designated "Profiler") to maintain and analyze inter-related clinical/pathology data, tissue microarray images/data, and gene expression/proteomics data.
8. On going inter-SPORE collaborations between Michigan and the Dana Farber HMS Cancer Center as well as between the intra-institution Prostate and Head& Neck SPOREs at Michigan.
9. Amendment of an IRB approval to keep all research biopsies collected and not just the biopsies from patients where cancer is found in the original 12 biopsy cores (Pending approval).
10. Validation of new biomarkers by immunohistochemistry.
11. Introduction of a barcoding system to label all future incoming samples.

The Tissue Core has been innovative in identifying and collecting prostate tissue samples. In addition to collecting samples from the prostatectomy cohort at the University of Michigan, metastatic hormone refractory prostate cancer is harvested from our Rapid Autopsy Program. Our Tissue Core performs a central histologic review by expert Genitourinary pathologists on all tissue entering the Core. The samples are carefully annotated by the support staff and entered into a relational database. New technology is employed when needed to help make the best use of these samples for research. Examples of this are the development of TMAs and tumor isolation protocols using laser capture microdissection. These annotated samples are made available to the SPORE projects, SPORE researchers, and other researchers under the direction of the Core PI. The Tissue Core works closely with the Biosatistics Core (PI Taylor) and Clinical Applications Core (PI Montie) in the development of TMAs, identification of representative study cohorts, and validation work. In summary, the Prostate Tissue Core has and continues to play a central role in the success of the University of Michigan Prostate SPORE Program.

III. PROGRESS/TASK REPORT:

The following projects have been completed or in progress in the Tissue/Informatics Core:

1. **14 Tissue Microarrays have been constructed:** A) TMA 91 LOA (3 arrays) Array (Drs. Shah/Chinniayan), TMA 92 Bladder Outcomes Array (Drs. Kunju/Shah/Lee), TMA 93 Mouse Prostate Array (Dr. Robbins), TMA 94 Salvage Prostatectomy Array (Drs. Shah/Ray), TMA 95 (2 arrays) Breast Carcinoma IN SITU (Dr. Kleer), TMA 96 Squamous Cell of the Oral Cavity (Dr. Carey), TMA 97 Mouse Screening Array (Robbins), TMA 98 (2 arrays) Warm Autopsy Array (Dr. Shah), TMA 99 Larynx Array (Dr. Carey), TMA 100 Progression Array (Dr. Shah).

2. **Profiler**
A bioinformatics infrastructure to analyze TMAs. The following were active users of the system: Rajal Shah (Pathology), Rohit Mehra (Pathology), Priya Kunju (Pathology), Celina Kleer (Pathology), Thomas Carey (Head and Neck), Carol Bradford (Head and Neck), Mark Rubin (Pathology), Kirk Wojno (Pathology), Matthias Hoffer (Dr. Rubin's lab, Brigham), Russel Taichman (School of Dentistry), Dan Rhodes (Pathology), Evan Keller (Pathology), Dr. Prince (Head and Neck), Tarek (Dr. Rubin's lab), and Katrina Cordell (Head and Neck).

3. **Laser Capture Microdissection Projects**
 - A. cDNA
 1. Prostate Cancer Progression (26 Caps of 10,000 Cells)
 - B. Comparative Genomic Hybridization
 - C. cDNA profiling of metastatic prostate cancer at different sites including prostate cancer epithelium and stroma (22 Caps of 12,000 cells)
 - D. CHIP on CHIP analysis (20 Caps of 10,000 cells)

4. **Serum collection**
 - A. Prostate cancer serum collection 945
 - B. Continued collecting only radical prostatectomy serums to make better use of freezer space and serum collection

5. **DNA collection**
 - A. Collection of DNA from Prostate Cancer Patients Peripheral Blood (499 specimens)

6. **Urine Collection**
 - A. 487 urine specimens have been procured.

7. **Tissue Bank collection**
 - A. Prostate cancer collection = 173 patients, 1353 blocks
 - B. Cystoprostatectomies = 11 specimens

8. **Rapid Autopsy Collection (Rapid Autopsies 32 and 36)**
 - A. Frozen blocks (657 total)
 - B. Paraffin blocks (944 total)

In summary, over the past 10 years, the University of Michigan Prostate SPORE Tissue Core has developed a mature tissue resource that maintains a large amount of clinical and pathology data. This resource has been used in over 83 peer-reviewed publications. The core has also developed an important TMA resource that allows for high-throughput evaluation of prostate tissues. Finally, the Tissue Core has developed important collaborations with other SPORE groups that will allow for important biomarker validation studies in the next few years.

Grant Applications Utilizing Tissue Core Resources

Principal Investigator (Chinnaiyan), "Epitomic Biomarkers of Prostate Space, U01 CA111275, 09/30/04-09/29/09, NIH, 10%, \$312,871/yr

Principal Investigator (Chinnaiyan), "Molecular Classification of Prostate Cancer", American Cancer Society, RSG-02-179-01-MGO, 07/01/02 - 06/30/06, 15%, \$180,000/yr

Principal Investigator (Chinnaiyan), "The Role of Polycomb Group Proteins in Prostate Cancer", National Institute of Health, R01 CA97063, 07/01/02 - 06/30/07, 20%, \$178,000/yr

Principal Investigator (Pienta), Co-Investigator (Chinnaiyan) Tissue/Informatics Core of the UM Prostate SPORE, NCI, SPORE in Prostate Cancer, A69568, 05/01/03- 05/30/08, 2.5%, \$253,643/yr

Principal Investigator (Pienta), Co-Investigator (Chinnaiyan), "Molecular Changes Associated with Prostate Carcinoma (PCa) Bone Metastases", R01 CA102872-01, NIH, (PI: Pienta), 09/24/03-08/31/07, 10%, \$173,280/yr

Publications during this reporting period using services provided by the Tissue/Informatics Core:

1. Rubin MA, Bismar TA, Andren O, Mucci L, Kim R, Shen R, Ghosh D, Wei JT, Chinnaiyan AM, Adami HO, Kantoff PW, Johansson JE. Decreased alpha-methylacyl CoA racemase expression in localized prostate cancer is associated with an increased rate of biochemical recurrence and cancer-specific death. *Cancer Epidemiol Biomarkers Prev.* 2005 Jun;14(6):1424-32.
2. Shah RB, Mehra R, Chinnaiyan AM, Shen R, Ghosh D, Zhou M, Macvicar GR, Varambally S, Harwood J, Bismar TA, Kim R, Rubin MA, Pienta KJ. Androgen-independent prostate cancer is a heterogeneous group of diseases: lessons from a rapid autopsy program. *Cancer Res.* 2004 Dec 15;64(24):9209-16.
3. Dhanasekaran SM, Dash A, Yu J, Maine IP, Laxman B, Tomlins SA, Creighton CJ, Menon A, Rubin MA, Chinnaiyan AM. Molecular profiling of human prostate tissues: insights into gene expression patterns of prostate development during puberty. *FASEB J.* 2005 Feb;19(2):243-5. Epub 2004 Nov 17.
4. Siu W, Dunn RL, Shah RB, Wei JT. Use of extended pattern technique for initial prostate biopsy. *J Urol.* 2005 Aug;174(2):505-9.
5. Shah RB, Kunju LP, Shen R, LeBlanc M, Zhou M, Rubin MA. Usefulness of basal cell cocktail (34betaE12 + p63) in the diagnosis of atypical prostate glandular proliferations. *Am J Clin Pathol.* 2004 Oct;122(4):517-23.
6. Das D, Shah RB, Imperiale MJ. Detection and expression of human BK virus sequences in neoplastic prostate tissues. *Oncogene.* 2004 Sep 16;23(42):7031-46.
7. Xiaoju Wang, Arun Sreekumar, Jianjun Yu, Sooryanarayana Varambally, Debashis Ghosh, Ronglai Shen, Donald Giacherio, Martin G. Sanda, Rohit Mehra, John Wei, James E. Montie, Kenneth J. Pienta, Mark A. Rubin, Arul M. Chinnaiyan. Epitomic Profiling of the Humoral Immune Response to Cancer. *New England Journal of Medicine.* In Press
8. Zheng Fu, Yasuhide Kitagawa, Ronglai Shen, Rajal Shah, Rohit Mehra, Daniel Rhodes, Atsushi Mizokami, Rodney Dunn, Arul M. Chinnaiyan, Zhi Yao, Evan T. Keller. The metastasis suppressor gene Raf kinase inhibitor protein (RKIP) is a novel independent prognostic marker in prostate cancer. *The Prostate.* In Press
9. Paris P.L., Andaya A., Fridlyand J., Jain A.N., Weinberg V., Kowbel D., Brebner J.H., Simko J., Watson J.E., Volik S., Albertson D.G., Pinkel D., Alers J.C., van der Kwast T.H., Vissers K.J., Schroder F.H., Wildhagen M.F., Febbo P.G., Chinnaiyan A.M., Pienta K.J., Carroll P.R., Rubin M.A., Collins C., van Dekken H. Whole genome scanning identifies genotypes associated with recurrence and metastasis in prostate tumors. *Hum Mol Genet.* 2004 Jul 1; 13(13):1303-1313.
10. Hofer M.D., Fecko A., Shen R., Setlur S.R., Pienta K.J., Tomlins S.A., Chinnaiyan A.M., Rubin M.A. Expression of the platelet-derived growth factor receptor in prostate cancer and treatment implications with tyrosine kinase inhibitors. *Neoplasia.* 2004 Sep-Oct; 6(5):503-512.
11. Loberg R.D., Neeley C.K., Adam-Day L.L., Fridman Y., St John L.N., Nixdorf S., Jackson P., Kalikin L.M., Pienta K.J. Differential expression analysis of MIM (MTSS1) splice variants and a functional role of MIM in prostate cancer cell biology. *Int J Oncol.* 2005 Jun; 26(6):1699-1705.

12. Sun Y.X., Schneider A., Jung Y., Wang J., Dai J., Wang J., Cook K., Osman N.I., Koh-Paige A.J., Shim H., Pienta K.J., Keller E.T., McCauley L.K., Taichman R.S. Skeletal localization and neutralization of the SDF-1(CXCL12)/CXCR4 axis blocks prostate cancer metastasis and growth in osseous sites in vivo. *J Bone Miner Res.* 2005 Feb; 20(2):318-329.
13. Kunju L, Chinnaiyan A, **Shah RB**. Comparison of Utility of Polyclonal and Monoclonal Antibody to alpha Methyl Acyl Co A Racemase (AMACR) in Work-up of Prostate Cancer. In press, *Histopathology*

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**PATHOLOGY PROTEOMICS LABORATORY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

I. OVERVIEW:

The Pathology Proteomics Laboratory was established in January 2005 as part of the proteomics initiative in the Department of Pathology. With the advent of DNA microarray analysis, detailed gene expression studies of cell lines, animal models, and tissues (including pathologic specimens) have been performed. Furthermore, the sequencing of human genome has allowed for monitoring gene expression on a comprehensive, global scale as opposed to focusing on one gene at a time. However, proteins are the final denominators of a cell's phenotype. Since there is little direct correlation between protein expression and transcript levels, it is essential to transition into analyzing the proteome in the context of disease progression. To this end, the Proteomics Laboratory has been employing state-of-art technologies that include protein microarrays, 2D-liquid phase protein fractionation, and mass spectrometry. Not only will these technologies have an obvious application in the basic sciences, they have the potential of impacting the treatment and diagnosis of patients. As Pathology is a discipline comprised of both scientific investigation and clinical diagnosis, it is imperative that the Department plays a role in the use and development of this technology. Clinical Pathology, in particular, has the opportunity of utilizing these technologies to develop novel diagnostic and prognostic biomarkers.

The Pathology Proteomics Laboratory functions to support the current and future research activities of the Department as well as Interdepartmental Programs. The primary focus of this facility is in two areas important in the study of human pathology including 1) inflammation and 2) cancer. These studies are accomplished using characterized animal models as well as with human specimens and cell lines.

The Proteomics Lab began with the installation of a Thermo-Finnigan LTQ ion trap mass spectrometer. In addition to the mass spectrometry, the Proteomics Lab is outfitted with a state-of-the art non-contact ink jet microarray for the fabrication of protein and phage-peptide microarrays. Other support equipment includes HPLC and the Beckman Proteome PF2D liquid fractionation system.

II. RESEARCH AND DEVELOPMENT:

While proteomics is an emerging field, it is clear that it is still in its infancy. Dr. Arun Sreekumar, a Research Investigator in the Department, has carefully developed our Proteomics Laboratory, beginning in January 2005 under the supervision of Dr. Arul Chinnaiyan. Dr. Sreekumar visited the demonstration sites for the Agilent and Thermo Finnigan mass spectrometers to identify the one that best suits the Departmental needs.

He also consulted local experts in the area, including Dr. David Lubman in the Department of Chemistry. Based on these deliberations, the Facility has thus acquired a Thermo-Finnigan 2D linear ion trap (LTQ) that is extensively being used for various ongoing collaborative projects. Many of the protocols being used have been developed keeping abreast of the latest publications in this field by various experts that include Drs. John Yates and Steven Gygi, among others.

While mass spectrometry-based proteomics is relatively new to the Department, we have developed a significant established expertise in the area of protein microarrays. Using phage protein microarrays, the laboratory has identified autoantibody signatures that are useful in the diagnosis of prostate cancer that has been accepted in the *New England Journal of Medicine*. Similarly, in collaboration with Dr. David Beer, these autoantibody profiling has been extended to lung cancer. A similar array approach using antibodies against inflammation was set up to study inflammation in the laboratories of Drs. Daniel Remick and Kent Johnson. The results of the study with Dr. Remick were published in the journal *SHOCK*. The manuscript containing results of the study with Dr. Johnson's laboratory has been accepted for publication in *Molecular and Cellular Proteomics*. The laboratory has also generated interactome data for a number of prostate cancer markers that include CTBP, EZH2 and GP73 allowing for delineating their functional roles during cancer development. This powerful technology is used by various investigators at the university including Drs. Gabriel Nunez (Pathology), Kent Johnson (Pathology) and Evan Keller (Urology). The collaborative effort with Dr. Nunez involves identification of signaling elements in the Nod pathway using a combination of co-immunoprecipitation and mass spectrometry. Furthermore, the laboratory has been using shot-gun proteomics to address the mechanism underlying development of hormone refractory prostate cancer. Both the protein microarray and mass spectrometry expertise of this laboratory was used in the collaborative study on identification of phosphorylation profiles in a breast cancer cell line treated with ERBB2 inhibitors. This study was carried out by our group in collaboration with the laboratories of Dr. David Lubman (Chemistry) and Dr Ethier (Radiation Oncology). A manuscript pertaining to the results of the study is under peer review.

In addition to establishing Proteomic technologies in the laboratory, a large effort has also been placed on devising a protein informatics framework to analyze the vast amount of data generated by all of the varied analyses listed above. This has involved implementation of various search algorithms for mass spectral data which include MASCOT and SEQUEST as well downstream programs for establishing accuracy of mass spectral identification. The latter includes PeptideProphet and ProteinProphet that were obtained as open source programs from Institute of Systems Biology. In addition, we are currently in the process of developing our own protein identification algorithm that would eliminate some of the inherent drawbacks that are found in most of the currently available open source programs.

During the first year of operation, the personnel of the Pathology Microarray Laboratory have:

1. Obtained the expertise required to generate protein microarrays, fractionate proteome in 2D-liquid phase and identify proteins by mass spectrometry.
2. Identified and assembled the infrastructure necessary to produce high-density protein and phage-peptide microarrays.
3. Established search algorithms and databases to analyze mass spectrometry data.
4. The laboratory generated proteomic data for various ongoing projects in collaboration with various laboratories at the University.

The laboratory has also published the following research articles in various pre-eminent journals:

1. Sreekumar A., Chinnaiyan A.M. (2002). The Use of Protein Microarrays to Study Cancer. *Biotechniques*. Suppl: 46-53.
2. Arun Sreekumar and Arul M. Chinnaiyan. (2002) Protein Microarrays: Powerful Tool to Study Cancer. *Cur. Op. Mol. Ther.* 4:587-593.
3. Yan F., Sreekumar A., Laxman B., Chinnaiyan A.M, Lubman D.M. (2003) Protein Microarrays Using Liquid Phase Fractionation of Cell Lysates. *Proteomics* (7): 1228-1235 (This article was ranked first in the Chemical Biology section by faculty of 1000 website).
4. Sreekumar A., Laxman B., Rhodes D.R., Bhagavathula S., Giacherio G., Ghosh D., Sanda M.G., Rubin M.A., Chinnaiyan A.M. (2004) Protein Microarray Analysis Reveals that Prostate Cancer Patients Elicit a Humoral Immune Response to α -Methylacyl-CoA Racemase. *JNCI* 96(10) 834-843.
5. Bradley S.V., Oravec-Wilson K.I., Bougeard G., Mizukami I., Munaco A.J., Sreekumar A., Chinnaiyan A.M., Li L., Corradetti M.N., Normolle D., Sanda M.G., Ross T.S. (2005) Autoantibodies to Huntington Interacting Protein-1: A new blood test for prostate cancer. *Cancer Res.* 15; 65(10):4126-33.
6. Xiao Wang, Jindan Yu, Sreekumar A., Sooryanarayana Varambally, Ronglai Shen, Donald Giacherio, Rohit Mehra, James E. Montie, Kenneth J.Pienta, Martin G. Sanda, Philip W. Kantoff, Mark A. Rubin, John T.Wei, Debashis Ghosh, Arul M. Chinnaiyan. Autoantibody signatures in Prostate Cancer (*New England Journal of Medicine: In Press*).
7. Olle E.W, Sreekumar A., Warner R.L., McClintock S.D., Chinnaiyan A.M., Paulauskis J.D., Bleavins M.R., Anderson T., Johnson K.J. Development of pseudo-two color antibody array: an internally controlled microarray (Accepted in *Molecular and Cellular Proteomics*).
8. Manoj Pal, Allison Moffa, Arun Sreekumar, Stephen P. Ethier, Arul M. Chinnaiyan and David M. Lubman. Differential Phosphoprotein Mapping in Cancer Cells Using Protein Microarrays Produced From 2-D Liquid Fractionation (Under peer review).

Grant Applications

The Pathology Proteomics Lab has supported the following grant applications by providing preliminary proteomic analyses:

R01 CA106402, NIH/NCI, "Protein Microarrays for the Humoral Response of Cancer", 06/15/04-05/31/09, (Principal Investigator: David Lubman)

Proteomics Alliance for Cancer Research, Michigan Technology Tri-Corridor Fund, (Principal Investigator: Gil Omenn)

"Profiling Prostate Cancer Using Protein Microarrays", DAMD17-03-1-0105, DOD, 02/01/03 – 01/31/05, (Principal Investigator: Arun Sreekumar)

"Epitomic Biomarkers of Prostate Cancer, U01 CA111275, 09/30/04-09/29/09, NIH, 10%, \$312,871/yr (Principal Investigator: Chinnaiyan)

Spore grant from University of Michigan Comprehensive Cancer Centre for project entitled Profiling Prostate Cancer Interactome using Protein Microarrays and Mass Spectrometry, (Principal Investigator: Arun Sreekumar)

III FUTURE GOALS:

The future goals of the Pathology Proteomics Lab in the next calendar year include:

1. Continue to support the research funding applications of Pathology faculty.
2. Continue to publish data using proteomics technology in peer-reviewed journals to establish the Department in the fast moving field of proteomics.
3. Develop and utilize protein microarray technology and mass spectrometry to answer biologically important questions.
4. Train post-doctoral fellows and students in proteomics.
5. Develop a unified bioinformatics platform for the analysis of mass spectrometry, protein microarray and clinical/pathology data.
6. Position our resources and expertise such that we can take advantage of opportunities in the emerging field of "clinical proteomics".
7. Transition and integrate activities into the Division of Translational Pathology.

IV. TEACHING/PROFESSIONAL:

Arun Sreekumar, Research Investigator who is in charge of the proteomics laboratory, has played an important role in setting the facility. He is currently training Drs. Adaikkalam Vellaichamy and TM Rajendiran on the various aspects of applying the technology to answer biologically relevant questions. Dr. Sreekumar is helping Barry Taylor, a bioinformatics graduate student to setup the protein-informatics capability. Javed Siddiqui (Research Associate, Remick lab), Eric Olle (Post Doctoral Fellow, Kent Johnson's lab), Kajal Sitwala (Pathology resident), Abhik Shah (Bioinformatics Graduate Student) and Manoj Pal (Chemistry Graduate Student) have all trained in various aspects of protein analysis/identification over the last year.

Arul M. Chinnaiyan, M.D., Ph.D.
Director

Arun Sreekumar, Ph.D.
Co-Director

**ANN ARBOR VA HEALTH SYSTEM
PATHOLOGY AND LABORATORY MEDICINE SERVICE**

**DEPARTMENT OF PATHOLOGY - UNIVERSITY OF MICHIGAN
ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

INTRODUCTION:

The VA Ann Arbor VA Healthcare System (VAAAHS) is a University of Michigan affiliated tertiary health care provider for veterans. It is one of three tertiary medical centers in the Veterans Integrated Service Network (VISN) #11 serving the veteran population of Michigan, and portions of Ohio, Indiana and Illinois. The VAAAHS Pathology and Laboratory Medicine Service maintains a close relationship with the University Department of Pathology at every level. All pathologists in the VAAAHS have medical school appointments and participate in university activities in a manner similar to other departmental sections. Recruitment for VAAAHS pathologists is a joint activity and candidates are selected on the basis of academic performance and potential as well as professional competence similar to any departmental candidate. There are currently four full-time pathology staff positions. Two and 1/2 resident training positions in the Department's program are supported with funds from the Department of Veterans Affairs. All residents serve monthly rotations in Surgical Pathology, Autopsy Pathology, with access to Diagnostic Electron Microscopy and special study programs in Surgical Pathology, Cytopathology and Digital Imaging. The VAAAHS laboratory retains full accreditation by the College of American Pathologists. The VAAAHS satellite laboratory at the Toledo Outpatient Clinic has been inspected by the JCAHO and is currently fully accredited. The medical center's Decentralized Hospital Computer System (*Vista*) is recognized as the most fully integrated medical information system. It combines all of the clinical management of the patient and has shifted to a computerized patient record system (CPRS) in year 2000. Data storage for all components of pathology and the clinical laboratories contains full patient information for 2 decades. Digital images of selected patient surgical, cytopathology, autopsy and ultrastructural specimen are stored as part of the patient medical record and are accessible to clinicians within minutes of case review.

In addition to the Toledo Outpatient clinic there are additional community based outpatient clinics (CBOCs) in Flint, Lansing and Jackson, Michigan. The VAAAHS Pathology and Laboratory Medicine Service (PALMS) provides specimen testing for these sites. The VAAAHS PALMS has successfully adapted to the shift to outpatient care and provides highest quality laboratory services in an environment of increasing demand. The VISN continues efforts toward an integrated health delivery system. Diagnostic Services will be a target for networking/consolidation among the current 8 independent facilities. This will result in additional sharing of service responsibilities, equipment standardization, VISN-wide reagent contracting, decreased cost of referred (send-out) testing to nonVA clinical labs and an increase in the workload in VAAAHS's anatomic pathology and the clinical labs. Due to overall testing volume, laboratory equipment standardization with blanket contracting promises to allow for substantial savings in laboratory costs. Vendor solicitation to provide standardized chemistry analyzers is to be issued for the fall of 2005.

Ann Arbor PALMS is currently performing all surgical pathology for the Battle Creek/Grand Rapid facilities. In addition, gynecologic cytopathology is performed for Detroit, Toledo and our affiliated CBOCs. A CARES review implemented by the VA Secretary in order to project veteran medical care needs for the next two decades indicated that the VA Ann Arbor Healthcare System will likely be facing increasing demand and the need to expand services.

ANATOMICAL PATHOLOGY:

- A. **Surgical Pathology:** 6,921 surgical cases were accessioned and reported during this period representing a 13% increase over the prior reporting period and continuing the trend of increasing workload. Greater than 95% of case diagnoses were reported in under 48 hr. The resident assigned to surgical pathology, usually a first year resident in training, has the opportunity to examine all of the specimens grossly and microscopically under close one-to-one mentoring by the staff pathologists. The resident interacts with the clinical teams. Weekly Urology Case Review Conference is held by Dr. Murphy. The residents assigned to autopsy and surgical pathology are primary presenters in clinical conferences. The residents obtain a broad educational experience and aid in providing high quality medical care. There is an extensive quality improvement program within Anatomical Pathology including regular consultations with the Armed Forces Institute of Pathology, University of Michigan, and other outside consultants. There is extensive quality assurance review and analysis of frozen sections, amended diagnoses, surgical appropriateness, turnaround times and follow-up of positive cancer diagnoses. The surgical and cytology readout stations are fully integrated into a hospital digital imaging system. Images are captured on cases of interest and when needed for documentation purposes. These are particularly useful in presentations to clinical teams reviewing specimens from their patients with the pathology staff and residents.
- B. **Autopsy Pathology:** 17 autopsies were performed during this year that is a rate of approximately 17 % of in-patient deaths. Assigned residents perform the autopsies, prepare the pathologic diagnosis, and present the case in conference to the staff pathologists and other residents. The resident cuts and otherwise prepares the tissue for the preparation of slides and then reviews them and makes a microscopic diagnosis. These steps are supervised by staff pathologists who permit a gradual increase in independence for the resident with increased experience. Several autopsies performed at the VAAHS are also presented at the extended Gross Conference at the University. The Department of Veterans Affairs maintains a policy to recognize the value of the autopsy and to encourage increased utilization. There is an expectation that all facilities will obtain permission to perform autopsies on at least 30% of their in-house deaths. However, to achieve this goal will require continued efforts to educate housestaff on the value of this procedure.
- C. **Cytology:** 3,287 cases were examined and diagnosed during this period. This is a 12% increase over the last reporting year. Most of the cytology specimens are of diagnostic type, however the VAAHS performs all PAP screening cytologies for the northern tier of VISN 11. Although there is not a formal rotation in cytology within the VAAHS the cytological material is readily available and is used as correlative information for surgical and autopsy pathology. This laboratory is a VA "Center of Excellence" in cytology.

- D. **Electron Microscopy:** 23 electron microscopy cases were processed, representing a continuing decline, likely due to the increased use of immunohistochemistry. Ultrastructural diagnosis is provided through sharing agreements with several Michigan hospitals. Some of the University of Michigan pathology specimens are processed and reported. The unit also serves several VAAHS research investigators. An elective rotation is available for pathology residents in electron microscopy. In other rotations the electron microscope findings are used to complement surgical or cytopathology diagnoses. This VAAHS is a "Center of Excellence" in electron microscopy and serves as consultant to other VA Medical Centers, to the University of Michigan Medical Center and to other hospitals by contract.

CLINICAL PATHOLOGY:

During the period of this report 1,447,233 clinical pathology procedures were performed in the Ann Arbor and its affiliated Toledo outpatient laboratory. In Chemistry there were 976,309; in Hematology 97,971; in Urinalysis 19,274, in Microbiology 30,745 and in Blood Bank 22,509; the Toledo unit performed 190,686 tests. A total of 75,695 phlebotomies were performed. These figures represent productivity (billable) rather than weighted test numbers. Residents may participate or observe clinical pathology procedures when this activity is appropriate in relation to their other rotations. Drs. Chensue, Utiger and Chamberlain oversee the clinical laboratory and make available interesting and pertinent clinical laboratory information available to residents as desired. Clinical Pathology and medical historical data is available to pathology residents via CPRS for their information in surgical pathology, autopsy pathology, and elective rotations.

EDUCATION AND TEACHING:

In surgical pathology the staff pathologists provide one-to-one mentoring during the surgical sign out time. In addition, there is a surgical pathology conference approximately every other week and an autopsy conference with the entire staff following each autopsy. Residents join in continuing educational activities in histopathology and cytopathology from the AFIP, CAP, and ASCP. Because of the closeness of various sections of the laboratory there is frequent consultation among the pathologists and the residents are involved throughout. Since the VAAHS is physically close to the University, the residents are expected to attend the appropriate teaching conferences at the University as well. The staff contribute to the laboratory and lecture portions of the second year medical students at the University of Michigan. The VA staff also participates in other ad hoc lectures and in a moderate number of seminars for the resident staff, most often given at the University of Michigan. Both Drs. Chensue and Murphy have made presentations at international pathology conferences. Through his research program Dr. Chensue also mentors post-doctoral fellows and graduate students.

RESEARCH:

The specific efforts of the pathology staff are included on individual reports. Dr. Stephen Chensue has strong funded research programs. He also participates in cooperative studies with other investigators at the University of Michigan. Dr. Murphy carries a full investigative program. Drs. Murphy and Chensue have research laboratories in Research Building 31 of the VAAAHS. All staff participates in various clinical studies and collaborates with a variety of investigators. The laboratory in general serves the VAAAHS research program by providing considerable technical support for clinical research and in some cases for more basic research in both anatomic and clinical pathology.

ADMINISTRATION:

Dr. Chensue has served as Chief of Service since March 2001. The staff pathologists at the VAMC serve in various capacities involving administrative tasks for the University of Michigan, such as the Resident Selection Committee, the Medical Student Admissions Committee, Graduate student preliminary exam and thesis committees, teaching faculty of the second year medical students as well as other graduate course in the medical, dental schools and the school of public health. At the VAAAHS, the pathology staff members serve on all major committees involved with institutional policies and procedures.

The VA's National Cytopathology Proficiency Program's administrative offices are located in the VAAAHS. All VA pathologists privileged in cytopathology are required to participate in a 16 glass slide comprehensive proficiency review annually. This is the largest comprehensive cytopathology proficiency program in the nation.

SUMMARY:

The VAAAHS Pathology and Laboratory Medicine Service hold the practice of high quality medicine and the appropriate care of the veteran patients as its first and highest responsibility. This is evidenced by continuing accreditation by external review agencies such as the College of American Pathologists (CAP), Joint Commission for the Accreditation of Hospitals Organization (JCAHO) and the Food and Drug Administration (FDA). There is close supervision of resident activities as they are involved with patient care. All staff members are privileged and evaluated in accordance with their training, experience, continuing education and participation in quality improvement activities. Within the service there is an extensive quality improvement program that integrates with that of the hospital as a whole. The affiliation with the University of Michigan serves to strengthen and improve the quality of patient care to our veterans. The teaching effort involving both residents and medical students is of benefit to the two institutions. The VAAAHS PALMS is positioned to continue delivery of high quality service to Veteran patients as demand for medical care continues to mount in the next decades.

In the Jan-Feb 2005 issue of the *Washington Monthly* the VA was recognized as providing “the highest quality care in the country.” It has been possible to achieve this status since the VA has not subject to the market demand to restrict health monitoring of patients. However, due to recent congressional budget limitations despite increasing veteran care demands VISN 11 has experienced significant budget shortfalls and will be faced with the serious challenge to maintain its high quality of care.

Stephen W. Chensue, M.D., Ph.D.
Chief, Pathology and Laboratory Medicine Service
VA Ann Arbor Healthcare System

ADMINISTRATION

DIVISION OF FINANCE AND ADMINISTRATION

**DEPARTMENT OF PATHOLOGY - UNIVERSITY OF MICHIGAN
ANNUAL DEPARTMENTAL REPORT
1 JULY 2004 - 30 JUNE 2005**

INTRODUCTION:

The Division of Finance and Administration, which is under the auspices of the Office of the Chairman and directed by Mr. Eugene J. Napolitan, Department Administrator is comprised of six units as follows:

- **ADMINISTRATIVE SUPPORT CENTER - PATHOLOGY LABORATORIES**
- **OFFICE OF ACADEMIC AND BUSINESS AFFAIRS - MEDICAL SCHOOL**
- **OFFICE OF THE CHAIRMAN**
- **PATHOLOGY PROFESSIONAL FEE BILLING OFFICE - KMS**
- **PATHOLOGY PHOTOGRAPHY AND IMAGING CENTER**
- **CENTRAL DISTRIBUTION & PHLEBOTOMY SERVICES ADMINISTRATION:**

This Division and its sections are responsible for the business, operational and fiscal affairs of the Department of Pathology as mandated by the policies of the Chairman, University of Michigan Health System (Medical School and Hospitals) and the University. The attached organization chart provides the detail of each section.

In addition to directing this division, Mr. Napolitan serves on various departmental, Health Systems and University Committees, several professional society committees and as a board director for several non-profit organizations.

Leadership provided by the Administrator for several new initiatives included collection of data and information thereby enhancing a successful succession plan for the new Chair, Jay L. Hess, M.D., Ph.D., including the transfer of Dr. Hess' research programs. Planning for a new Pathology Building has been initiated and Mr. Napolitan is a member of the lead team for this project. In addition, the activation of the Traverwood Clinical Laboratories and implementation of an automated accounting system to complement the reporting systems for the Medical School and University have been accomplished. Other initiatives for FY 2005 include the implementation of an automated Hematology diagnostic testing line to enhance turnaround time for laboratory testing, the development of a fund raising campaign with a goal to establish a collegiate professorship in the name of Harold A. Oberman, M.D.

In addition to the management of daily activities, each of the units has completed major projects which are summarized as follows:

ADMINISTRATIVE SUPPORT CENTER/PATHOLOGY LABORATORIES:

This unit is directed by Mr. Thomas Morrow, Assistant Administrator and is responsible for the business, operational and fiscal affairs of the Anatomic and Clinical Pathology Laboratories. This includes preparation and monitoring of all Hospitals laboratories revenue, expense and capital budgets, and personnel and payroll systems. Gross revenue for FY 2005 increased by 2.7% when compared to budget forecast for a total of \$286,573,138. For Fiscal Year 2005, the Pathology Laboratories expenditures amounted to \$52,839,998. Attentiveness to cost containment in the face of incremental activity allowed the laboratories to make increased margin contributions for the Hospital. Additionally, we have implemented a program for medical technology students from area universities, i.e., Ferris State University, Eastern Michigan University, Wayne State University, to be provided "on-site" internships. This program also serves as a "pre-recruitment" period for this group of students. Mr. Morrow served as the lead administrative representative in the implementation of a digital dictation system for the Department of Pathology. The new system is in place and is used by approximately 90% of our pathologists and surgical transcriptionists. Final implementation will be completed in this next Fiscal Year. He participated with the Section Chiefs for the implementation of automated analytical equipment in Hematology in July 2005, the selection of the Chemistry automated line, Bayer Plan scheduled to be completed in December 2005 and the laboratory portal which is vital to the growth of our MLabs Program which provides service to our Health Centers.

Administrative Coordinator: This individual, Mrs. Deborah Day Jansen, assists with the coordination of intra and inter laboratory activities for the anatomic and clinical pathology laboratories which include coordination of required proficiency tests; coordination of inspections required for continuing certification or licensure by the JCAH, CAP and MDPH; serving as departmental representative on the Safety Committee, Disaster Committee and as United Way Chairperson. In addition, the Administrative Coordinator acts as the liaison with the Hospital for renovation projects and coordinates the publication of the Pathology Laboratories Handbook (including on-line version), and is responsible for all requisition modifications. Mrs. Jansen also manages the Surgical Transcription Unit, the Faculty Office Suite in the Hospitals as well as the accessioning function in the Medical Science I Building. She was instrumental in the implementation of the Digital Dictation System and continues to work with faculty and staff in monitoring and improving use. Mrs. Jansen also served on the lead team for the activation of Traverwood Clinics and continues to oversee the operation requirements of this facility.

Billing Coordinator: This individual, Ms. Nancy Coray, is responsible for processing and auditing all laboratory charges (gross charges of approximately \$286,573,188, ensuring the accuracy of the daily billing files, correction of all errors with the appropriate Hospital department and responding to all questions regarding interdepartmental, MLabs or Hospital patient billings (technical portion). This position is also responsible for our billing system related to the MLabs Program. With the implementation of APC, timeliness of charges has improved dramatically.

Administrative Associate: This individual, Mrs. Beverly Smith, oversees the clerical support staff assigned to the Administrative Support Center and coordinates the Human Resources functions for Pathology Laboratories non-instructional staff (approximately 458 FTEs). She serves as lead for the Department's Orientation Program, coordinates the Medical Technology Internship Program and is a departmental representative for the Health System's Diversity Task Force.

OFFICE OF ACADEMIC AND BUSINESS AFFAIRS - MEDICAL SCHOOL:

Administrative Manager: Mr. David Golden, is responsible for the Medical School all funds budget preparation, new funds allocation model (FAM), variance reporting; tracking of all Medical School expenditures, professional fee billing operations (front end); general funds and teaching and administration funds; departmental renovation and remodeling; and management of the Word Processing Center. The major accomplishment of this unit was the implementation of a financial budgeting and monitoring system (UMS software) which resides on departmental servers. This system became fully operational in March 2005 and is interfaced with the University's Peoplesoft system.

All business and administrative functions associated with our sponsored research and education programs including coordination of the application process, receipt of grant awards, establishment of budgets, monitoring of expenditures and acting as liaison between the Principal Investigators, research sponsors and other University departments are now performed by staff in this unit. In addition, Human Resources functions associated with non-instructional staff (Medical School paid), house officers and post-doctoral fellows are coordinated in this office.

Administrative Associate: Mr. John Harris is responsible for oversight of the staff supporting our Research Programs and the daily management of the UMS system. Extramural sponsored expenditures for FY 2005 amounted to approximately \$16,051,320.

Administrative Assistant: Mrs. Catherine Bearman is responsible for Human Resource issues for staff in the Medical School (approximately 154 FTEs) including our House Officer Program (31 FTEs), Postdoctoral Fellows (39 FTEs), and graduate students (12). She also provides administrative oversight for staff in the Pathology Education Office and the faculty support staff in the Pathology Building. Mrs. Bearman also serves as the lead administrative staff member for facilities, including building maintenance and renovations.

OFFICE OF THE CHAIRMAN:

Executive Secretary: Mrs. Lynn McCain provides support to the Chair of the Department including management of his calendar, completing travel arrangements and preparation of manuscripts, abstracts, clinical consultations and all materials related to the search committees chaired by Dr. Hess. In FY2005, searches were initiated for the Director of Anatomic Pathology and the Director for Clinical Informatics.

Staff Associate: Mrs. Laura Blythe provides staff support to the Administrator, Mr. Eugene J. Napolitan. She serves as the human resource specialist for faculty including processing of faculty appointments, posting positions, payroll, effort reporting and all other human resource functions. In addition, she is an editor for the Department's website, supervises staff in the Office of the Chairman and in FY2005 served as the project lead for the digitization of former faculty and house officer files. This information is now accessible on the Department's web servers.

PATHOLOGY PROFESSIONAL FEE BILLING OFFICE:

The combined Pathology/Radiology Billing Office is managed by Mrs. Janice Taylor. She oversees 26 FTE staff and is responsible for the coding, accounts receivable management, and collections of professional fees for services provided in the Department of Pathology faculty.

PATHOLOGY PHOTOGRAPHY AND IMAGING UNIT:

Photographers: Mr. Mark Deming and Mrs. Elizabeth Walker are the photographers assigned to this service. They are responsible for a variety of photography and imaging services including those requested by our clinical and research faculty and house officer staff.

CENTRAL DISTRIBUTION AND PHLEBOTOMY SERVICES:

Chief Technologist: Mr. Harry J. Neusius is the Chief Technologist for these two laboratory services. All specimens directed to the Pathology Laboratories by the Taubman Clinics, patient floors and off-site health centers are received and accessioned by staff in this unit. The laboratory operates 24 hours per day, 7 days per week to provide the service required by UMHS. Phlebotomy Services are provided to the UMHS patient floors with designated "sweeps" and to UMHS outpatient services with three blood drawing stations located in the Hospitals and Cancer Center, and services available at most of the satellite sites. This unit has, historically, experienced a high rate of turnover in staff, especially on the afternoon and midnight shifts. Over the past year, Mr. Neusius and his supervisory staff have increased efforts to retain current staff. Cross-training with Phlebotomy Services has assisted in covering this critical service, specifically during the off-shifts. Laboratory procedures that are sent to reference laboratories represent a significant expense. A committee comprised of the Laboratory Director for Chemical Pathology, myself, Mr. Neusius, Thomas Morrow and Susan Valliere initiated a review of these procedures and by identifying two primary reference laboratories and performance of selected procedures "in house", have reduced this expense by \$200,000 annually.

SUMMARY OF FINANCIAL DATA FOR FY 2005:

1.	Grants and Contracts and Other Accounts:	
	244 active grants, contracts and other accounts	
	Total Extramural Direct Expenditures:	\$16,051,320
	Indirect Extramural Research Expenditures:	\$ 5,668,840
	Total Sponsored Projects:	\$21,720,160
2.	Faculty Group Practice Plan – Pathology Associates:	
	Number of charge entries:	205,366
	Gross Billings - Anatomic and Clinical Pathology:	\$ 27,860,898
	Net (FGP):	\$ 11,215,927
	Part A Payment – Laboratory & Administrative Supervision:	\$ 3,849,068
3.	All Fund Expenditures – Medical School	
	Compensation & Benefits	\$ 24,032,446
	Commodities & Other Costs	<u>\$ 13,889,104</u>
	Total	\$ 37,921,550
	# of Funded Faculty	74.98
	# of Funded Residents & Clinical Fellows	31.00
	# of Funded FTE Research Staff	154.00
	(includes 12 graduate students, 39 post-doctoral fellows)	
4.	Pathology Laboratories:	
	Number of billed tests reported by CDM :	3,980,000
	Total Gross Revenue - Pathology Laboratories:	\$286,573,138
	Total Direct Expenses Pathology Laboratories:	\$ 51,181,000
	# of FTE Staff	458

*Includes General Fund, Extramural Funds, FGP Professional Fee Income, Gift, etc.

Respectfully submitted,

Eugene J. Napolitan
Administrator

