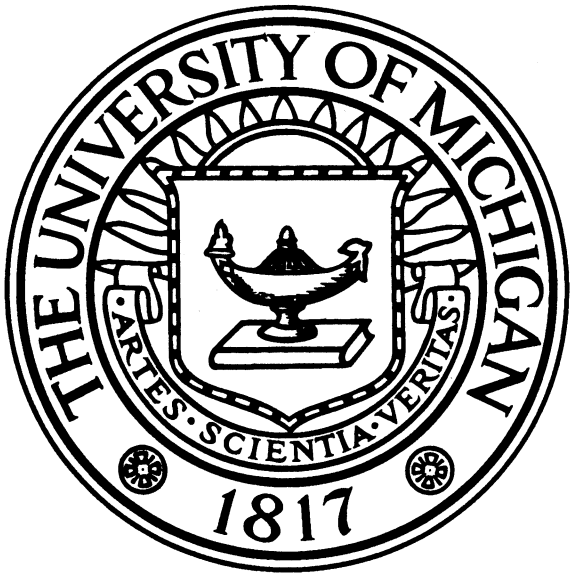
THE UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL

Department of Pathology

ANNUAL REPORT



1 JULY 2002 - 30 JUNE 2003

THE UNIVERSITY OF MICHIGAN

MEDICAL SCHOOL

Department of Pathology

ANNUAL REPORT

1 JULY 2002 - 30 JUNE 2003

LIST OF FACULTY

LIST OF FACULTY

Name	Rank	Institutional Affiliation
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	Clinical Associate Professor	The University of Michigan
Capps, Rodney D.	Assistant Professor	The University of Michigan
Chamberlain, Priscilla	Clinical Instructor II	Veterans Affairs Medical Center
Chensue, Stephen W.	Associate Professor	Veterans Affairs Medical Center
Chinnaiyan, Arul	Assistant Professor	The University of Michigan
Cho, Kathleen R.	Professor*	The University of Michigan
Cooling, Laura	Clinical Assistant Professor	The Universityof Michigan
D'Amato, Constance J.	Assistant Professor Emeritus	The University of Michigan
Dai, Yiran	Clinical 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
Elner, 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
Finn, William	Clinical Associate Professor	The University of Michigan
Flint, Andrew	Professor	The University of Michigan
Friedman, Bruce A.	Professor	The University of Michigan
Fullen, Douglas R.	Clinical Assistant Professor	The University of Michigan
Giacherio, Donald	Clinical Assistant 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
Headington, John T.	Professor Emeritus	The University of Michigan
Heidelberger, Kathleen P.	Professor Emeritus	The University of Michigan

Name	Rank	Institutional Affiliation
Hogaboam, Cory	Assistant Professor	The University of Michigan
Homeister, Jonathon	Lecturer	The University of Michigan
Inohara, Naohiro	Assistant Research Scientist	The University of Michigan
Johnson, Kent J.	Professor	The University of Michigan
Judd, W. John	Professor	The University of Michigan
Kaldjian, Eric	Adjunct Assistant Professor	Pfizer
Keller, Evan	Assistant Professor##	The University of Michigan
Keren, David F.	Clinical Professor	Warde Medical Laboratories
Killen, Paul D.	Associate Professor	The University of Michigan
Kleer, Celina	Assistant Professor	The University of Michigan
Krueger, Cynthia	Lecturer	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.	Clinical Assistant Professor+++	The University of Michigan
Lowe, John B.	Professor	The University of Michigan
Lowe, Lori	Clinical Associate Professor	The University of Michigan
Lucas, Peter	Lecturer	The University of Michigan
Lukacs, Nicholas	Associate Professor	The University of Michigan
McKeever, Paul E.	Professor	The University of Michigan
McKenna, Barbara J.	Clinical Associate Professor	The University of Michigan
Mellerick-Dressler, Dervla	Assistant Professor	The Universityof Michigan
Michael, Claire W.	Clinical 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	Clinical Assistant Professor	The University of Michigan
Nunez, Gabriel	Professor	The University of Michigan
Oberman, Harold A.	Professor Emeritus	The University of Michigan
Phan, Sem H.	Professor	The University of Michigan
Pierson, Carl L.	Assistant Professor	The University of Michigan
Ramsburgh, Stephen R.	Clinical Assistant Professor	The University of Michigan
Rasche, Rodolfo	Clinical Assistant Professor	The University of Michigan
Remick, Daniel G.	Professor	The University of Michigan
Ross, Charles W.	Associate Professor	The University of Michigan
Roulston, Diane	Clinical Associate Professor	The University of Michigan

Name	Rank	Institutional Affiliation
Ruiz, Robert	Clinical 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.	Clinical Assistant Professor	The University of Michigan
Silverman, Eugene M.	Clinical Associate Professor	The University of Michigan
Smith, Lisa	Clinical Assistant Professor	The University of Michigan
Stoolman, Lloyd M.	Professor	The University of Michigan
Su, Lyndon	Clinical Assistant Professor	The University of Michigan
Thorson, John	Clinical Assistant Professor	The University of Michigan
Till, Gerd O.	Professor	The University of Michigan
Valdez, Riccardo	Clinical Assistant Professor	The University of Michigan
Varani, James	Professor	The University of Michigan
Vincenz, Claudius	Research Investigator	The University of Michigan
Ward, Peter A.	Godfrey D. Stobbe Professor and Chairman	The University of Michigan
Warren, Jeffrey S.	Warthin/Weller Professor and Director, Clinical Pathology	The University of Michigan
Wilson, Thomas	Assistant Professor	The University of Michigan

* Joint Appointment, Department of Internal Medicine
** Joint Appointment, Dental School
*** 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 Urology
Joint Appointment, ULAM and Institute of Gerontology

DEPARTMENT OF PATHOLOGY
University of Michigan Medical School

2002

THE DEPARTMENT OF PATHOLOGY

Faculty, Residents and Fellows
Department of Pathology
October, 2002

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DEPARTMENTAL OVERVIEW

DEPARTMENTAL OVERVIEW
July 2002-June 2003

Introduction

The volume of activity involving both Surgical Pathology and the Clinical Laboratories continues to expand by approximately 4% per year with no evidence that this trend will be reversed. This has led to problems of compression and overloading in virtually the entire clinical laboratory system. In the late Spring of 2004, some clinical laboratory functions will be relocated to the Traverwood area (approximately 2 miles from UMMC) as a temporary adjustment. This is a stop-gap measure that does not address the long-term needs for the clinical laboratories. In addition, the Department desperately needs additional research space in which programmatic expansion can occur, especially as this relates to translational research which is moving ahead rapidly, employing both genomic and proteomic strategies. The Department of Pathology has played a key role in the use of genomic strategies as related to prostate cancer, lung and ovarian tumors. These tight-knit collaborations have greatly enhanced the institutional position, being at the "cutting edge" for the applications of genomics as a better way to understand behaviors of tumors. As indicated in the sections on teaching, research and service, the Department of Pathology continues to perform in an exemplary manner.

Teaching Activities

Faculty members continue to fill leadership roles as course directors, sequence coordinators, and serve 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 one fifth 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 the 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 five new students with two students receiving Ph.D. degrees. 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 our specialty by U.S. medical school graduates over the past three years. The program consists of 28 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, M.D. Anderson Hospitals, University of North Carolina and Memorial Sloan Kettering.

Clinical Service Activities

The Anatomic and Clinical Pathology Laboratories continue to provide excellent, full-spectrum service as the UMHS has continued to experience growth in ambulatory care activities and in many major clinical programs. 2002-2003 was marked by new faculty recruitments in Molecular Diagnostics, Microbiology, bone and soft tissue surgical pathology and cytopathology. The laboratories continued their trend of more laboratory procedures (approximately 5%) with a fixed number of staff. Efforts continue to be directed towards more aggressive control of laboratory utilization and the improvement of phlebotomy, central distribution and laboratory operations. In response to pressures to reduce our cost/unit of laboratory service and to improve operating efficiency, a more aggressive plan for laboratory and send-out test utilization was implemented. Augmentation of the capabilities of the Molecular Diagnostics, Blood Bank, Chemistry, Tissue Typing, Hematology, Microbiology, Cytogenetics, Cytopathology and Surgical Pathology Laboratories was contributory to this process. There was a marked improvement by clinical sites in compliance with the HCFA-mandated documentation rules. In 2002-2003, the Laboratories performed more than 3.2 million diagnosis laboratory analyses and more than 55,000 surgical pathology cases. The maintenance of high quality service, in the face of increasing complexity of

demands, is a testimony to the professionalism of the staff as well as the management capabilities of laboratory directors and senior laboratory personnel. Finally, as alluded to above, the Laboratories have responded to the institutional initiative to expand primary care capabilities within the region. This activity has been coupled with expansion of on-site point-of-care testing and data handling activities. The Laboratories continue to support the M-Labs outreach program. The Laboratories successfully completed the bi-annual College of American Pathologists (CAP) self-inspection. Maintenance of the delicate balance among quality service, cost-effective testing, utilization control and research and development, which characterizes an academic institution, will be a continuing challenge.

Research Activities

The Department of Pathology's research activities continue to be one of the many strengthens of our academic mission. The Department's faculty 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 expenditures of active grants and contracts credited to the Pathology Department's research efforts increased by approximately 3 million dollars when compared to the previous year's expenditures. The total research expenditures for 2003 were over $17 million; this included over $12 million in direct expenditures and $5 million in indirect expenditures. Faculty members in the Department of Pathology hold 73 active individual grants, which include 47 grants from the Federal government 41 NIH grants (2 Program Projects, 2 MERIT Awards, and 2 training grants) and 6 DOD grants. In one of these DOD Grants, the Department plays a leadership role in a research program with 5 different institutions. This program is a consortium dealing with therapeutic interventions to block the effects of bioterrorists' chemicals on the lung. In addition, another 26 grants originate from non-Federal sources, including, the American Heart Association, the Pew Charitable Trusts, American Lung Association, the MEDC Life Science Corridor Fund, and contract grants from a variety of 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 solid tumors and inflammatory diseases. The faculty actively publish in both the clinical and experimental arena and cover very diverse scientific interests, such as clinical pathology, anatomical pathology, and basic cellular and molecular mechanisms of disease. Our faculty participates in peer review of NIH grant applications 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.

Respectfully submitted,

Peter A. Ward, M.D.
Professor and Chairman

Steven L. Kunkel, Ph.D.
Co-director, Division of General Pathology

Joseph C. Fantone, M.D.
Director, Division of Anatomic Pathology

Jeffrey S. Warren, M.D.
Director, Division of Clinical Pathology

INDIVIDUAL FACULTY REPORTS

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

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

A. Surgical Pathology Services – 1 month.
B. Pathologist, Cardiac Transplant Team. Transplant biopsies – 2 weeks.

II. TEACHING ACTIVITIES:

A. Freshman Medical Class:
   1. Pathology 500, Course Director, Lecturer, "Basic Concepts of Disease" - 20 lecture hours.
   2. Multidisciplinary Conferences - 4 contact hours.
   3. Pathology 500, 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. Clinical Radiology-Pathology correlation Elective Course-2 lecture hours.

D. Dental School:
   1. Sophomore Dental Class (Path 580) - 2 lecture hours

E. Undergraduate LS&A/Graduate:
   1. Biology 224 - 1.5 lecture hours.
   2. Summer science academy – 4 lecture hours.

F. Hospital Conferences:
   1. Cardiovascular Pathology Case Conference - monthly.
   2. Cardiac Pathology teaching conference – monthly.

G. Community:
   1. Organizer, director, and lecturer of "Mini-Med. School", a six-week course for the public, Spring 2003.

H. Invited Lectures:
   1. Keynote Address-UM Medical School White Coat Ceremony, August 2002.
   2. Cardiology Grand Rounds, August 2002.

I. Production of Teaching Materials:
   1. Production of CD-Rom and syllabus for Histopathology Lab sequence of Pathology 500.

J. Honors:
   1. Lifetime achievement award in medical education, 2002.
   2. "TAMS" award, Class of 2003.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Pathologic-Radiologic correlation in aortic disease, with D. Williams.
B. Pathology of lesions produced by high intensity ultrasound, with Bioengineering staff and students.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL/UNIVERSITY:

A. Member, Curriculum Detail Design team; Patients and Populations sequence. Normal cell sequence.
B. Ombudsperson, Medical Faculty.
C. Member, ad hoc Search Committee for Chair, Department of Medical Education.
D. Member, Faculty Task Force to review Instructional Track.
E. Member, subcommittee for faculty, LCME review.

REGIONAL AND NATIONAL:

A. Editorial Board, Modern Pathology.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

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, Chelsea Internal Medicine Associates.
F. Laboratory Director, West Ann Arbor Health Care Facility.
G. Staff Practitioner, The Toledo Hospital, Toledo, Ohio
H. Consultant to Consultants in Laboratory Medicine, Toledo, Ohio

II. TEACHING ACTIVITIES:

A. House Officers:
   1. Lecturer, Clinical Pathology Grand Rounds.
   2. Lecturer, Clinical Pathology Didactic Lecture Series.
   3. Daily Sign-out and Interpretation of Laboratory Results.
   4. Clinical Pathology Curriculum Committee.
   5. Coordinator, Clinical Pathology Block B.

III. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Biochemistry Section, Clinical Pathology Laboratories.
B. Coordinator, Clinical Pathology Laboratory CME Program.
C. Clinical Pathology Discretionary Incentive Funds Committee.

REGIONAL AND NATIONAL:

A. Board of Directors, National Academy of Clinical Biochemistry (NACB).
B. Chair, NACB/AACC Professional Activities Committee.
C. Chair, NACB Awards Committee.
D. Annual Meeting Organizing Committee, American Association for Clinical Chemistry.
E. AACC Meeting Task Group, American Association for Clinical Chemistry.
F. Program Coordinating Commission, American Association for Clinical Chemistry.
G. House of Delegates, American Association for Clinical Chemistry.
H. Executive Committee/Journal Management Group, Clinical Chemistry Journal.
I. Member, Academy of Clinical Laboratory Physicians and Scientists.
J. Member, National Academy of Clinical Biochemistry.
K. Member, Association of Clinical Scientists.

L. Member, American Society for Mass Spectrometry.
M. Member, Society of Forensic Toxicology.

V. OTHER RELEVANT ACTIVITIES:

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.

EDITORIAL REVIEW ACTIVITIES:

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

AWARDS:

A. Clinical Chemist's Recognition Award, American Association for Clinical Chemistry.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. McMillin, G.A., Owen, W.E., Lambert, T.L., De, B.K., Frank, E.L., Bach P., Annesley, T.M., and Roberts, W.L.: Comparable effects of Digibind and DigiFab in thirteen digoxin immunoassays. Clin. Chem. 2002;48:1580-84.
2. Annesley, T.M.: Disposition of toxic drugs and chemicals in man. Clin. Chem. 2002;48:2085.
3. Annesley, T.M.: Poisoning and Laboratory Medicine. Clin. Biochem. 2003;36:321-322.
4. Tankanow, R., Tamer, H.R., Streetman, D.S., Smith, S.G., Welton, J.L., Annesley, T., Aaronson, K.D., and Bleske, B.E.: Interaction Study Between Digoxin and a Preparation of Hawthorn *(Crataegus oxyacantha).* J. Clin. Pharmacol., 2003;43:637-642.
5. Annesley, T.M.: Ion suppression in mass spectrometry. Clin. Chem. 2003, in press.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

A. General surgical pathology - four and one-half months.
B. Gastrointestinal and hepatic pathology services - six 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: mentor, 4 weeks with daily conferences

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 - (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. Adenomas of the duodenum: are there differences between sporadic and FAP-associated? With Paul Kowalski
D. Is hyperplasia of the interstitial cells of Cajal a common reaction to intramural masses in the gut? With Meryem Koker
E. The apoptotic form of microsopic colitis, with BJ McKenna
F. Are juvenile-like polyps in adults the same as in children? With Meryem Koker

G. What is the yield of significant microscopic disease in colorectal biopsies of adult patients with chronic diarrhea and normal endoscopic findings? With BJ McKenna
H. Is there such a thing as ectopic antral mucosa in the duodenal bulb? With Wei Xin
I. What is the cause of the autoimmune hepatitis-like recurrent hepatitis C in liver transplant recipients? With Wei Xin, Joel Greenson, and Robert Fontana
J. What is the rate of neoplastic progression in Barrett's mucosa during surveillance endoscopy and biopsy at the University of Michigan? With John Inadomi
K. What is the rate of neoplastic progression in ulcerative colitis during surveillance endoscopy and biopsy at the University of Michigan?
L. Marginal collagenous colitis: does it exist? With BJ McKenna, W Xin, M Anderson and L Evans
M. 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.

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, International Organization for Statistical Studies of Diseases of the Esophagus, Paris, France.
C. Member, Editorial Board, Human Pathology.
D. Member, Editorial Board, Modern Pathology.
E. Member, Editorial Board, American Journal of Surgical Pathology.
F. Ad hoc reviewer for American Journal of Pathology, Cancer, Gastroenterology, and American Journal of Gastroenterology.
G. Member of the Long Range Planning Committee, United States and Canadian Academy of Pathology, Inc
H. Member, Lung and Esophagus Task Force, American Joint Committee on Cancer, 2001-present

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "A whirlwind tour through esophagogastric inflammations and their complications" and "the role of the pathologist in the diagnosis and management of inflammatory bowel diseases, especially the colitides". Half day course, Pathology Update for Practicing Pathologists: Recent Advances and Selected Topics. American Society of Clinical Pathologists, Chicago, IL, July 13, 2002
2. "Whatever happened to the old ulcerative colitis we knew and loved?" and "Why is the gastroesophageal junction such a big deal when it is so small?" Update Course in Surgical Pathology, Ohio State University Medical Center, Columbus, Ohio, August 27, 2002
3. "Large cell minimally differentiated colon carcinoma" and "Small intestinal stromal tumors", presented at the Gastrointestinal Pathology Slide Seminar, 24th International Congress of the International Academy of Pathology, Amsterdam, the Netherlands, October 9, 2002
4. "GI Pathology", Diagnostic Problems in Anatomic and Clinical Pathology, Emory University School of Medicine, Atlanta, GA, October 19, 2002
5. "The gastrointestinal biopsy report: What's right, what's wrong and what doesn't matter?" With BJ McKenna, half day course, Annual meeting, American Society of Clinical Pathologists, Washington, DC, Oct 22, 2002
6. "What's up with gastrointestinal stromal tumors" and "Gastrointestinal biopsy reports: to err is human, but who will forgive you?" with Barbara J. McKenna, Second Annual Current Topics in Gastrointestinal Pathology, Johns Hopkins University School of Medicine, Baltimore MD, November 10-11, 2002
7. "Changing concepts in our understanding of ulcerative colitis", Twin Cities Pathology Society, Minneapolis, MN, November 21, 2002
8. "Dysplasia in the GI tract", Early Detection Research Network of the National Cancer Institute, Seventh Steering Committee Meeting, University of Alabama, Birmingham AL, January 31, 2003
9. "An iconoclastic view of dysplasia of the gut", Callendar-Binford Lecturer, Armed Forces Institute of Pathology, Washington, DC, February 27, 2003
10. "Why is the gastric cardia such a big deal when it is so small?" Visiting professor lecture, University of Washington, Seattle, WA, April 23, 2003
11. "Neoplastic diseases of the intestines", half day course, Pathology of the Gastrointestinal Tract, American Society of Clinical Pathologists, Chicago, IL, May 1, 2003
12. "Dysplasia can be a pain in the gut", Suffolk County Society of Pathologists, Port Jefferson, NY, May 22, 2003
13. "The changing face of ulcerative colitis", Department of Pathology, State University of New York at Stony Brook, Stony Brook, NY, May 23, 2003
14. "Dysplasia in the gut", Visiting Blue Grass Professor Lecture, University of Kentucky, Lexington, KY, June 6, 2003
15. The Gastrointestinal Biopsy Report, with BJ McKenna, 31st Annual Kentucky Society of Pathologists Spring Seminar, Versailles, KY, June 7, 2003

16. "New stuff in Barrett's mucosa and the gastric cardia"; "GI dysplasias, including Barrett's epithelium and ulcerative colitis"; "Idiopathic inflammatory bowel disease: changes with time and treatment"; "Gastrointestinal stromal tumors"; "Neoplasms of the appendix and anus"; Diagnosis of Gastrointestinal, Liver and Pancreatic Biopsies, California Pacific Medical Center Course, Alyeska, Alaska, June 23-26, 2003

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREEDJOURNALS:

1. McKenna BJ, Appelman HD: Dysplasia can be a pain in the gut. Pathology, 34:518-528, 2002
2. Chakrabarty S, Radjendirane V, Appelman H, Varani J: Extracellular calcium and calcium sensing receptor function in human colon carcinomas: promotion of E-cadherin expression and suppression of beta-catenin/TCF activation. Cancer Research. 63:67-71, 2003

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. Kaur P, Appelman HD, McKenna BJ: Computer-assisted image analysis separates benign from malignant gastric stromal tumors. Am J Clin Pathol. 118:638, 2002
2. Koker MM, Appelman HD: Do juvenile polyps age? Mod Pathol. 16:125A, 2003
3. McKenna BJ, Appelman HD: Biopsies of colonoscopically normal mucosa in adult patients with chronic diarrhea provide diagnostically relevant information in most cases. Mod Pathol. 16:128A, 2003
4. Xin W, McKenna BJ, Appelman HD: Gastric surface metaplasia in the duodenal bulb is not ectopic antral mucosa. Mod Pathol. 16:137A, 2003

MILA BLAIVAS, M.D., PH.D.
CLINICAL ASSOCIATE PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

A. 21 weeks of Surgical Neuropathology Service.
B. 54 days of Autopsy Service including weekend autopsy calls.
C. All muscle and nerve biopsies at the UMHS and referred by other hospitals in- and out-of-state throughout the year, including new anti-dystrophy workup (434 muscle biopsies and 110 nerve biopsies). 40% muscle biopsies with EM, 100% nerve biopsies with EM and 17 with teasing. Over 20 cases were tested with antidystrophy antibody (10-14) screen by IPOX.
D. Diagnostic EM on skin and other tissues for various rare disorders, 18 cases.
E. Cutting autopsied brains with Pathology House Officers, microscopic evaluation with the residents for the diagnosis.
F. Consulting on brain, muscle and nerve pathology, intradepartmental cases, VAH and other hospitals in MI and other states. 137 personal consults.

II. TEACHING ACTIVITIES:

A. Instructed residents, fellows and staff in Neurology, Rheumatology and Pediatrics and students on muscle, nerve and brain biopsies.
B. Lectures for medical and dental students; M-2 neuropathology labs.
C. Taught Pathology Residents how to perform and read-out autopsies.
D. Lectures on muscle, nerve and brain pathology to residents and fellows in Pathology, Neurology, Neurosurgery and Rheumatology.
E. Conferences on muscle and nerve cases with Neurology Department.
F. Neuropathology cases review with Pathology Residents.
G. Weekly and monthly conferences with Neuromuscular staff.
H. Conferences and lectures for Neurosurgery Residents and staff.
I. Pediatric Oncology conferences for brain tumor cases.
J. Personal tutoring of neurology and pathology residents on Neuropathology – 9 persons.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Collaboration with EMG group, neurosurgery, genetics, pediatrics, rheumatology, epilepsy and gynecology (Dr. J. Delancey group) on various projects.
B. National study group (ERSET), part of, for evaluation of temporal lobectomy/hippocampectomy cases.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Supervision of the muscle histochemistry and muscle and nerve biopsy handling.
B. Continuing improvement of interdepartmental and interinstitutional coordination of muscle and nerve biopsy service.
C. Improvements in immunoperoxidase stainings, expansion of anti-dystrophy workup.
D. Daily monitoring muscle histochemistry group performance.

MEDICAL SCHOOL:

A. Member of the Admissions Committee.

INVITED LECTURES:

1. Invited lecturer to St. Mary Hospital, Saginaw, September 2002.
2. Invited lecturer to the Nursing Homes Association, April 2003.

REGIONAL AND NATIONAL:

A. Consulting with outside pathologists, neurologists and family practitioners on muscle and nerve biopsies performance and interpretation, brain biopsies.
B. Member, American Association of Neuropathologists, IAP, CAP, PNS, and AAN.
C. Attended AANP meeting.
D. Ad-hoc reviewer for Archives of Pathology and Laboratory Medicine, Archives of Ophthalmology.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN PEER REVIEWED JOURNALS:

ARTICLES SUBMITTED FOR PUBLICATION:

1. Kocheril SV, Blaivas M: Dego's Disease Mimicking Vasculitis. Resubmitted to: Arthritis Care & Research.
2. Hedera P, Petty EM, Bui M, Blaivas M, Fink JK: The second kindred with distal myopathy linked to chromosome 14q (MPD1): Genetic and clinical analysis. Archives of Neurology 2003, in press.
3. *Fewel ME, Blaivas M, Thompson BG: Intradural metastatic pleural mesothelioma presenting with sudden deafness facial palsy, and Brown-Sequard syndrome. Submitted to Neurosurgery.
4. Herschner S, Blaivas M, Gells D: Biopsy of confirmed primary angiitis of the central nervous system with negative MRI and angiography. Submitted to Neurology.

5. Lagrange AH, Blaivas M, Gomez-Hassan D, Malow BA: Rasmussen's-like encephalitis presenting as new-onset narcolepsy, cataplexy, and epilepsy in an adult. Accepted to Epilepsy and Behavior.

CHAPTER IN BOOKS

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

1. Lagrange H, Blaivas M, Gomez-Hassan D, Malow B. A very Novel Case of New-Onset Narcolepsy, Cataplexy, and Epilepsy in a 40-Year-Old Business Professor. Presented at the American Epilepsy Society 56th Annual Meeting.
2. Nolan PC, Blaivas M, Techer JW: Inclusion body myositis with granuloma in muscle biopsy. To be presented at the AAEM meeting.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

B. Surgical Pathology sign out and consultations– 12 months
- 25% of SP cases

C. Cytology sign out and consultation – 12 months
- 50% of Pap Smears
- 50% of non-gynecological cases

II. TEACHING ACTIVITIES:

1. Pathology residents, SP – 506 hours
2. Pathology residents Cytology – 100 hours
3. M2 pathology lab – 50 hours
4. Lecture series for ENT residents – 25 hours
5. Cytology lectures to pathology and surgical residents as needed – 10 hours

II. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

None.

PENDING:

None.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

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:

EDITORIAL BOARDS:

None.

HONORS AND AWARDS

None.

PATENTS:

None.

INVITED LECTURES/SEMINARS:

None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

None.

BOOKS/CHAPTERS IN BOOKS:

None.

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

None.

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

ANNUAL DEPARTMENT REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES

A. Chief, Pathology and Laboratory Medicine Service (as of March 2001), 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 greivance 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. Technologists, technicians and hospital staff, ongoing continuing medical education instruction on clinical laboratory topics.

D. Research mentoring for post-doctoral, graduate, undergraduate, and high school trainees.

III. RESEARCH ACTIVITIES

SPONSORED SUPPORT:

A. Principal Investigator, Chemokine Deteminants 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. Cytokine manipulation of mycobacterial (Th1) and schistosomal (Th2) Ag mediated forms of hypersensitivity granuloma formation.

B. Regulation of chemokine receptor expression during Th1 and Th2 immune and inflammatory responses.

C. Role of chemotactic cytokines in granulomatous inflammation and Th1 and Th2 cell expression.

D. In vivo regulation of chemotactic cytokine production by leukocytes and stromal cells in the lung.

D. Analysis of eosinophil recruitment factors in type 2 granulomatous inflammation.

E. Dendritic cell chemokine receptor expression and in vivo migration.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Pathology Graduate Program Preliminary Exam Committee

B. Immunology Graduate Program's Preliminary Exam Committee

C. Member of graduate student thesis committees.

D. 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

B. Clinical Executive Board, VA Ann Arbor Healthcare System, voting member

C. Professional Standards Board, VA Ann Arbor Healthcare System, voting member

D. Invasive Proceedures Committee, VA Ann Arbor Healthcare System, voting member

E. Residency Review Board, VA Ann Arbor Healthcare System, voting member

F. Information Management Committee, VA Ann Arbor Healthcare System, voting member

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 evalulation for clinical and basic researchers.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Abrams, E. T., Brown, H., Chensue, S.W., Turner, G.D., Tadesse, E., Lema, V.M., Molyneux, M.E., Rochford, R., Meshnick, S.R. and Rogerson, S.J. Host Response to Malaria During Pregnancy: Placental Monocyte Recruitment Is Associated with Elevated beta Chemokine Expression. J. Immunol. 2003, 170:2759-2764.
2. Chiu, B., Freeman, C.M., Stolberg, V.R., Komuniecki, E., Lincoln, P.M., Kunkel, S. L. and Chensue, S. W. Cytokine-chemokine networks in experimental mycobacterial and schistosomal lung granuloma formation Am. J. Respir. Cell Mol. Biol. 2003, 29:106-16.
3. Kunkel, S.L., Chensue, S. W., Lukacs, N. and Hogaboam, C. Cytokine Phenotypes Serve as a Paradigm for Experimental Immune-Mediated Lung Diseases and Remodeling. Idiopathic pulmonary fibrosis. Am J Respir Cell Mol Biol. 2003, 29(3 Suppl 2): S63.(mycobacterial) and type-2 (schistosomal) immune responses. J. Leuk. Biol. 2002, 72:363-372.

BOOKS AND CHAPTERS IN BOOKS:

1. Chensue, S. W. and Kunkel, S. L. Cytokines and Chemokines in Granulomatous Inflammation. *In*, Granulomatous Infections and Inflammations:Cellular and Molecular Mechanisms. D.L. Boros ed., ASM Press Washington, D.C. pp 29-63. 2003.
2. Kunkel, S.L., Lukacs, N.W., Chensue, S.W, and Hogaboam, C. Cytokine Phenotypes and the Progression of Chronic Pulmonary Fibrosis. *In*, Idiopathic Pulmonary Fibrosis, J. Lynch ed., Marcel Dekker Inc., pp 303-321. 2003.

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

1. Freeman, C.M., Chiu, B-C., Stolberg, V.R. and Chensue, S. W. CCR8 is selectively expressed by an IL-10 producing antigen-specific memory CD4+ T cell population. FASEB J. 2003.
2. Chensue, S.W. Chemokine and Chemokine Receptor Dynamics during Type-1 and Type-2 Hypersensitivity-Type Pulmonary Inflammation" Keystone Symposia on Chemokines and Chemokine Receptors, Breckenridge, Colorado, January 7-12, 2003.

ARUL M. CHINNAIYAN, M.D., Ph.D.
ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Mentor, postdoctoral fellows: Chandan Kumar, Arun Sreekumar, Saravana Dhanasekaran, Rohit Mehra, Eric Albrecht (co-mentored with P.Ward)
B. Mentor, graduate students: Scott Tomlins (MSTP, Pathology), Qi Cao (Pathology), Jianjun Yu (Bioinformatics), Daniel Rhodes (MSTP, Pathology), Julie Kim (Bioinformatics), Viktoriya Resnick (Bioinformatics), Xiaoyu Jia (Pathology) Smita Lakhotia (Graduate Student, Indian Institute of Sciences),Ronglai Shen (Biostatistics Masters Student)
C. Mentor, Undergraduate Students: Shilpa Murthy, CMB Honors Research
D. Hosted international visiting scholars to train in microarray technology: Jian Huang, M.D. (Zhejiang University, China)
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.
F. Instructor, Biochemistry 491
G. Bioinformatics 511 Luncheon and Seminar
H. Biology of Cancer, ME.510.700, Seminar, Johns Hopkins Medical School
I. Co-Director, Bioinformatics 511
J. Cancer Biology Seminar Series, Lecturer, University of Michigan Medical School

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Molecular Classification of Prostate Cancer" American Cancer SocietyRSG-02-179-01-MGO, 07/01/02 – 06/30/06, 15% effort, $180,000/yr direct costs.
B. Principal Investigator, "The Role of Polycomb Group Proteins in Prostate Cancer" NIH R01 CA97063, 07/01/02 – 06/30/07, 20% effort, $178,000/yr direct costs.
C. Principal Investigator, "Transcriptome Analysis of Breast & Prostate Cancer Reveals Oncogenic Connections to Fatty Acid Metabolism", V Foundation N003689, 03/29/02 – 03/28/04, 0% effort, $50,000/yr direct costs.

D. Principal Investigator, "Development of Breast Cancer biomarkers Using DNA and Protein Microarray Technologies", Mary Kay Ash Charitable Foundation N003813, 07/01/02 – 06/30/04, 0% effort, $43,478/yr direct costs.

E. Principal Investigator, "A Functional Genomics Approach to Cancer", PEW Charitable Trust, 07/01/02 – 06/30/06, 0% effort, $55,556/yr direct costs.

F. Principal Investigator, "A Bioinformatics Approach to Cancer Profiling", Pilot Research Grant 2001N002824, University of Michigan, Bioinformatics Program, 07/01/01 – 12/31/02, 0% effort $75,000.

G. Principal Investigator, "The Role of Hepsin in Prostate Cancer", CapCURE Foundation, 2001 CapCURE Award N003299 01/01/02 – 12/31/02, 0% effort, $75,000.

H. Principal Investigator, "Molecular Classification of Prostate Cancer", Wendy Will Case Foundation, Bridging funds for re-submission of ACS grant, 12/01/01-11/31/02, 0%effort, $25,000.

I. Principal Investigator, "Functional Genomics Approach to Lethal Metastatic Prostate Cancer", Career Development Award, NCI P50 CA69568 (Pienta), 08/01/02 – 07/31/03, 25% effort, $70,000/yr direct costs.

J. Co-Principal Investigator, "Transcriptome Analysis of the EGFR Receptor in Breast Cancer, The Breast Cancer Foundation N003365 (Lippman), 10/01/01 – 09/30/02, 15% effort, $250,000/yr.

K. Co-Investigator, "Biological Differences between prostate cancer cells that metastasize to the bone versus soft tissue sites", Department of Defense DAMD17-02-1-0098 (Pienta), 11/01/01 – 10/31/04, 5% effort, $141,563/yr direct costs.

L. Co-Investigator, "Protective Effects of Anti-C5a in Sepsis", NIH (Ward), 12/01/01-11/30/06, 10% effort, $225,000/yr direct costs.

M. Principal Investigator, Pfizer, Inc. 12/15/02- 12/14/03, 0% effort $162,132/yr.

N. Principal Investigator, "Discovery of Cancer Biomarkers using High Throughout Multi-Blotting" (GMP Companies, Inc.) 12/01/02-11/30/05, 0%, $168, 827/yr.

O. Principal Investigator, "Functional Genomics Approach to Lethal Metastatic Prostate Cancer" S.P.O.R.E. in Prostate Cancer, Project 3, NCI P50 CA69568 (Pienta), 07/01/03 – 06/31/08, 15% effort, $144,578/yr.

P. Core Director, S.P.O.R.E. in Prostate Cancer, Tissue/Informatics Core of the UM Prostate SPORE, NCI P50 CA69568 (Pienta), 07/01/03– 06/30/08, 10% effort, $253,643/yr.

Q. Principal Investigator, "Dysregulation of the Corepressor CtBP in Prostate Cancer," Department of Defense, DOD PC020322, 1/2/03- 12/31/05, 15% effort, $125,000/yr direct costs.

PENDING:

None.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Pathology student recruitment activities (lunch, poster session)
B. Director of the Pathology DNA Microarray Research Lab
C. Director of the Prostate SPORE Tissue/Informatics Core

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

REGIONAL AND NATIONAL:

A. Ad hoc reviewer for the following Journals: *Nature, PNAS, Nature Genetics, American Journal of Pathology, Journal of Biomedical Informatics, Cancer Research, Neoplasia, Cell Death & Differentiation, Cytokine, Clinical Cancer Research, Molecular Diagnosis,* and the *Journal of Biological Chemistry.*
B. External grant reviewer for the National Science and Technology Board Biomedical Research Council (Singapore) and the Cancer Society of New Zealand, Inc.
C. Scientific Review Board, 2003 American Cancer Society, Grants Peer Review
D. Scientific Review Board, 2003 Department of Defense Prostate Cancer Research Peer Review Program
E. Scientific Review Board, 2003 Department of Defense Breast Cancer Concept Award Peer Review Program
F. Research Review Committee, 2003 Mary Kay Ash Charitable Foundation Research Review Committee.

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

EDITORIAL BOARDS:

A. Cancer Genomics and Proteomics

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

INVITED LECTURES/SEMINARS:

1. National Cancer Institute (NCI) SPORE meeting, Plenary presentation, "Functional Genomics of Prostate Cancer", July 16, 2002.
2. NCI Bioinformatics Meeting, Invited Speaker, "The Three B's of Prostate Cancer: Biology, Bioinformatics and Biomarkers", August 6, 2002.
3. UT Southwestern, Invited Speaker, "The Three B's of Prostate Cancer: Biology, Bioinformatics and Biomarkers", September 10, 2002.
4. "Celebrate Invention" Symposium, "Functional Genomics of Prostate Cancer", University of Michigan, October 11, 2002.
5. 81st Annual Meeting of GU Surgeons, Invited Speaker, "Functional Genomics of Prostate Cancer", October 19, 2002.
6. Clinical Pathology Grand Rounds (w/ Dr. Giacherio), October 25, 2002.
7. Prouts Neck Prostate Cancer Meeting, Invited Speaker, "The Three B's of Prostate Cancer: Biology, Bioinformatics and Biomarkers"November 8, 2002.
8. Pathology Bioinformatics Meeting, University of Michigan, Speaker, November 11, 2002.
9. MHCC / Prostate SPORE Meeting, Invited Speaker, "The Three B's of Prostate Cancer: Biology, Bioinformatics and Biomarkers", November 21, 2002.
10. UCSF Inter-Prostate SPORE Meeting, Invited Speaker, "The Three B's of Prostate Cancer: Biology, Bioinformatics and Biomarkers", December 3, 2002.
11. Society for Basic Urological Research, Tucson AZ, Invited Speaker, "The Three B's of Prostate Cancer: Biology, Bioinformatics and Biomarkers", December 7, 2002.
12. Astrazeneca, Invited Speaker, "The Three B's of Prostate Cancer: Biology, Bioinformatics and Biomarkers", January 13, 2003.
13. Cancer Center Grand Rounds, University of Wisconsin, Invited Speaker, "The Three B's of Prostate Cancer: Biology, Bioinformatics and Biomarkers", January 29, 2003.
14. Bioinformatics Program, University of Michigan, Invited Speaker, February 13, 2003.
15. Genentech, Invited Speaker, "The Three B's of Prostate Cancer: Biology, Bioinformatics and Biomarkers", February 18, 2003.
16. UC Davis Cancer Center, Invited Speaker, "The Three B's of Prostate Cancer: Biology, Bioinformatics and Biomarkers", February 20, 2003.
17. Pew 2002 Scholar Lecture, Grand Bahama Island, "The Three B's of Prostate Cancer: Biology, Bioinformatics and Biomarkers", March 10, 2003.

18. Johns Hopkins University, Sidney Kimmel Cancer Center, Invited Speaker, "The Three B's of Prostate Cancer: Biology, Bioinformatics and Biomarkers", April 21, 2003.
19. Medical College of Ohio, Invited Speaker, "The Three B's of Prostate Cancer: Biology, Bioinformatics and Biomarkers", Molecular Basis of Disease, April 29, 2003.
20. UCSF Cancer Center, Department of Pathology, Invited Speaker, "The Three B's of Prostate Cancer: Biology, Bioinformatics and Biomarkers", May 27, 2003.
21. Clinical Genomics Symposium, "The Three B's of Prostate Cancer: Biology, Bioinformatics and Biomarkers", Princeton, NJ, June 13, 2003.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Chay, C.H., Cooper, C.R., Gendernalik, J.D., Dhanasekaran, S.M., **Chinnaiyan, A.M.**, Rubin, M.A., Pienta, K.J. (2002) A functional thrombin receptor (PAR1) is expressed on bone-derived prostate cancer cell lines. *Urology*, 60:760-5.
2. Xin, W., Rhodes, D.R., Ingold, C., **Chinnaiyan, A.M.**, Rubin, M.A. (2002) Dysregulation of the Annexin Protein Family is Associated with Prostate Cancer Progression. *American Journal of Pathology*, 162(1):255-61.
3. Dash, A. Maine, I., Dhanasekaran, S.M., Barrette, T.R., **Chinnaiyan, A.M.**, Rubin, M.A. (2002) Changes in Differential Gene Expression Due to Warm Ischemia Time of Radical Prostatectomy Specimens. *American Journal of Pathology* 161:1743-8.
4. Varambally S., Dhanasekaran, S.M., Barrette, T.R., Sanda, M.G., Ghosh, D., Pienta, K.J., Sewalt, R.G.A.B., Otte, A.P., Rubin, M.A., **Chinnaiyan, A.M.** (2002). The Polycomb Group Protein EZH2 is Involved in Prostate Cancer Progression. *Nature*, 419:624-9.
5. Rios-Doria J, Day KC, Kuefer R, Rashid MG, **Chinnaiyan AM**, Rubin MA, Day ML. (2002). The role of calpain in the proteolytic cleavage of E-cadherin in prostate and mammary epithelial cells. *Journal of Biological Chemistry*, 278(2):1372-9.
6. Kumar-Sinha, C., Ignatoski, K.M., Lippman, M.E., Ethier, S.P., **Chinnaiyan, A.M.** (2003) Transcriptome Analysis of HER-2 Reveals A Molecular Connection to Fatty Acid Synthesis. *Cancer Research*, 63, 132-9.
7. Rhodes, D.R., Shen, R., Otte, A.P., **Chinnaiyan, A.M.**, Rubin, M.A. (2003) Molecular Biomarker Approach for Determining Risk of Prostate-Specific Antigen-Define Recurrence of Prostate Cancer. *Journal of the National Cancer Institute*, 95(9).
8. Yan, F., Sreekumar, A., Laxman, B., **Chinnaiyan, A.M.**, Lubman, D.M. (2003) Protein Microarrays Using Liquid Phase Fractionation of Cell Lysates. *Proteomics*, 3(7):1228-35.
9. Ghosh, D., **Chinnaiyan, A.M.** (2003) Tumor Classification from Combinations of Biomarkers in gene Expression Data Using LASSO and Support Vector Machines. *Bioinformatics*, Submitted.
10. Albrecht, E.A., **Chinnaiyan, A.M.**, Varambally, S., Kumar-Sinha, C., Barrette, T.R., Sarma, V.J., Ward, P.A. (2003) C5a-induced Gene Expression if Human Umbilical Vein Endothelial Cells. *American Journal of Pathology*, Submitted.
11. Mattfeldt, T., Kufer, R. **Chinnaiyan, A.M.**, Kestler, H.A., Rubin, M.A. (2003) Classification of prostatic lesions from gene expression data using supervised learning methods. *International Journal of Pattern Recognition and Artificial Intelligence*, Submitted.

12. Liu, T., Dhanasekaran, S.M., Jin, H., Tomlins, S.A., **Chinnaiyan, A.M.**, Phan, S.H. (2003) Induction of FIZZ1 Expression in Lung Injury and Fibrosis. *Journal of Clinical Investigation*, Submitted.
13. Sun YX, Wang J, Shelburne CE, Lopatin DE, **Chinnaiyan AM**, Rubin MA, Pienta KJ, Taichman RS. (2003) Expression of CXCR4 and CXCL12 (SDF-1) in human prostate cancers (PCa) in vivo. *Journal of Cell Biochemistry*, 89(3):462-73.
14. Ghosh D., Barrette T.R., Rhodes, D., **Chinnaiyan, A.M.** (2003) Statistical issues and methods for meta-analysis of microarrays in prostate cancer. *Functional Integrative Genomics*, July 22 [E pub ahead of print].
15. Kleer , C.G., Cao, Q., Varambally, S., Shen, R., Ota, I., Tomlins, S.A., Ghosh, D., Sewalt, R.G., Otte, A.P., Hayes, D.F., Sabel, M.S., Livant, D., Weiss, S.J., Rubin, M.A., **Chinnaiyan, A.M.** (2003) EZH2 is marker of aggressive breast cancer and promotes neoplastic transformation of breast epithelial cells. *Proceedings of the National Academy of Sciences*, 100(20):11606-11.

REVIEW ARTICLES:

1. Rhodes, D.R. and **Chinnaiyan, A.M.** DNA Microarrays: Implications for Clinical Medicine. (2002) Journal *of Investigative Surgery*, 15:275-9.2. Sreekumar A. and **Chinnaiyan, A.M.** (2002) The Use of Protein Microarrays in the Study of Cancer. A Supplement to *Biotechniques*, High-throughput Proteomics: Protein Microarrays, 46-53.
2. Sreekumar A, **Chinnaiyan AM.** (2002) Protein microarrays: a powerful tool to study cancer. *Curr Opin Mol Ther;* 4(6):587-3.
3. Kumar-Sinha, C. Rhodes, D.R., **Chinnaiyan, A.M.** (2003) Prostate Cancer Biomarkers: A Current Perspective, *Expert Review for Molecular Diagnostics*, 3(4): 459-70.

BOOKS/CHAPTERS IN BOOKS:

1. None.

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 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

A. Gynecological pathology consultation services and "Room G"/Gynecological Pathology sign out in surgical pathology – six months.

II. TEACHING ACTIVITIES:

A. Postdoctoral Fellows:
Responsible during the academic year for the following:
1. Donald Schwartz, Ph.D.
2. Yali Zhai, Ph.D.

B. Graduate students:
1. Neali Hendrix (Dept. of Pathology), faculty mentor, doctoral candidate, PIBS program
2. Kenute Myrie (Dept. of Human Genetics), thesis committee member, Ph.D. awarded 2002
Course Faculty, Pathology 581 – three lecture hours
Course Faculty, Pathology 580/630 – two lecture hours

C. Undergraduate students:
Lisa So

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, "FHIT Gene Alterations in Cervical Cancer Pathogenesis", NIH RO1 CA81587 (15% effort), September 1, 1998 - August 31, 2002. Final year is twelve month no cost extension.

B. Principal Investigator, Project 2 ("Molecular Profiling of Ovarian Cancer", 15% effort). NIH: U19 CA84953 (Hanash). "Toward a Molecular Classification of Tumors," September 30, 1999 – March 31, 2004.

C. Principal Investigator, "Oncogene Activation in Ovarian Cancer Pathogenesis", Department of Defense, OCRP OC000105 (15% effort), August 15, 2001 - August 14, 2004.

D. Principal Investigator, "Molecular Pathogenesis of Ovarian Endometrioid Adenocarcinomas", NIH RO1 CA94172 (30% effort), February 1, 2002 – January 31, 2007.

E. Co-Investigator (10% effort), "CDX2 Tumor Suppressor Pathway Defects in Colon Cancer", NIH R01 CA82223 (Fearon), August 15, 1999 – May 31, 2004.
F. Co-Investigator (10% effort), "The Role of β-Catenin/Tcf Pathway Defects in Cancer." NIH R01 CA85463 (Fearon), June 1 2000 – May 31, 2005.
G. Co-Investigator (5% effort), "Liquid Proteomics for Marker Screening of Ovarian Cancer", NIH RO1 CA100104 (Lubman), April 15 2003 – April 14, 2008

PENDING:

A. National Institutes of Health: 1P50CA98252-01 (09/03 – 09/08). SPORE in Cervical Cancer (Program PI: T.C. Wu); Role in Program: Principal Investigator, Project 2, Molecular Markers of Invasion in Cervical Cancer Progression (20% effort). Co-Investigator, Project 1, Markers of Progression to Cervical Cancer in Rural India (5% effort). Application reviewed by IRG in 06/02, priority score 153, funding anticipated pending final administrative approval.
B. Department of Defense, Ovarian Cancer Research Program: DAMD17-OC030117 (11/01/03 – 10/31/06). Development and Characterization of a Murine Model of Ovarian Endometrioid Adenocarcinoma Induced by Tissue Specific Expression of Oncogenic β-Catenin. Role in project: Mentor (5% effort) for New Investigator, Donald Schwartz, Ph.D.

PROJECTS UNDER STUDY:

A. Molecular profiling of ovarian epithelial tumors using 2-D gel approaches 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/ß-catenin/Tcf pathway defects in the pathogenesis of ovarian endometrioid adenocarcinomas.
E. 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, Curriculum Committee, 2002 – present
C. Department of Pathology Graduate Student Admissions Committee, 2002 – present
D. Department of Pathology, Committees for Long Range Planning in the Clinical Laboratories and Research (Chair), Spring 2003

INSTITUTIONAL:

A. Institutional Review Board, University of Michigan School of Medicine (IRB-MED), appointment from Feb 2001 – Jan 2005

REGIONAL AND NATIONAL:

A. Special Emphasis Panel, ZRG1 SSS-1(12)B Study Section, National Institutes of Health/National Cancer Institute, review of R41, R42, R43, and R44 applications, March 2003
B. Member, Special Conferences Committee, American Association for Cancer Research, 1999-2002
C. Member, Publications Committee, American Association for Cancer Research, 2002-present
D. Co-Organizer, 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. Chairperson, 2003 AACR – Women in Cancer Research – Charlotte Friend Memorial Lectureship Selection Committee, American Associate for Cancer Research
G. Member, 2003 AACR-Women in Cancer Research Brigid G. Leventhal Scholar Award Selection Committee
H. Secretary, International Society of Gynecological Pathologists, elected to two year term (2003-2004) renewable for two additional terms, not to exceed six years

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, *Molecular Diagnostic Pathology*
F. Member, Editorial Board, *The Women's Oncology Review*
G. Ad hoc reviewer for *American Journal of Pathology, British Journal of Cancer, Gynecologic Oncology, Laboratory Investigation, Journal of Pathology, American Journal of Obstetrics and Gynecology, Genes Chromosomes and Cancer, Journal of Clinical Investigation, Oncogene*

INVITED LECTURES/SEMINARS 2002-2003:

1. Cervical Cancer and Human Papillomaviruses. Annual Symposium of the Binford-Dammin Society of Infectious Disease Pathologists, United States and Canadian Academy of Pathology Annual Meeting, Chicago, Illinois, February 2002.
2. Ovarian Cancer: Molecular Clues to Pathogenesis and Tumor Classification: University of Michigan Department of Obstetrics and Gynecology. Ann Arbor, Michigan, May 2002.
3. Ovarian Cancer: Molecular Clues to Pathogenesis and Tumor Classification: Molecular Biology in Clinical Oncology Workshop, American Association for Cancer Research, The Given Institute, Aspen, Colorado, July 2002.

4. Ovarian Cancer: New Insights from Gene Expression Profiling. Fox Chase Cancer Center, Philadelphia, Pennsylvania, October, 2002.
5. Gene Expression Profiling of Ovarian Endometrioid Adenocarcinomas Identifies Novel Candidate Targets of β-catenin/Tcf Signaling. NCI Director's Challenge Principal Investigator Meeting, Bethesda, Maryland, November, 2002.
6. Ovarian Cancer: Insights from Gene Expression Profiling. National Cancer Institute, Bethesda, Maryland, January, 2003.
7. Molecular Pathology in Oncology: Overview and Selected Applications. Molecular Biology in Clinical Oncology Workshop, American Association for Cancer Research, The Given Institute, Aspen, Colorado, July 2003.
8. Borderline Ovarian Tumors – Molecular Biologist's Perspective. Borderline Ovarian Tumor Consensus Workshop, National Cancer Institute, Bethesda, Maryland, August 2003.

VI. PUBLICATIONS (2002-2003):

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Zhai, Y., Wu, R., Schwartz, D.R., Darrah, D., Kolligs, F.T., Nieman, M.T., Fearon E.R., and Cho, K.R. Role of ß-catenin/TCF Regulated Genes in Ovarian Endometrioid Adenocarcinomas. American Journal of Pathology 160:1229-38, 2002.
2. Kachman, M.T., Wang, H., Schwartz, D.R., Cho, K.R., and Lubman, D.M. A 2-D Liquid Separations/Mass Mapping Method for Interlysate Comparison of Ovarian Cancers. Analytical Chemistry 74:1779-1791, 2002.
3. Kolligs, F.T., Nieman, M.N., Winer, I., Hu, G., van Mater, D.S., Feng, Y., Smith, I.M., Wu, R., Zhai, Y., Cho, K.R., and Fearon, E.R. ITF-2, a downstream target of the Wnt/TCF pathway, is activated in human cancers with ß-catenin defects and promotes neoplastic transformation. Cancer Cell, 1:145-155, 2002.
4. Leung, J.Y., Kolligs, F.T., Wu, R., Zhai Y, Kuick R., Hanash, S., Cho, K.R., and Fearon, E.R. Activation of *AXIN2* Expression by ß-catenin/TCF: A Feedback Repressor Pathway Regulating Wnt Signaling. Journal of Biological Chemistry, 277:21657-65, 2002.
5. Wang, H., Kachman M.T., Schwartz, D.R., Cho, K.R., and Lubman, D.M. A protein molecular weight map of ES2 clear cell ovarian carcinoma cells using a 2-D liquid separations/mass mapping technique. Electrophoresis 21:3168-81, 2002.
6. Schwartz, D.R., Kardia, S.L.R., Shedden, K.A., Kuick, R., Michailidis, G., Taylor, J.M.G., Misek, D.E., Wu, R., Zhai,Y., Darrah, D.M., Reed, H., Ellenson, L.H., Giordano, T.J., Fearon, E.R., Hanash, S.M., and Cho, K.R. Gene expression in ovarian cancer reflects both morphology and biological behavior, distinguishing clear cell from other poor-prognosis ovarian carcinomas. Cancer Research 62:4722-4729, 2002.
7. Hinoi, T., Lucas, P.C., Kuick, R., Hanash, S., Cho, K.R., and Fearon, E.R. CDX2 regulates liver intestine-cadherin expression in normal and malignant colon epithelium and intestinal metaplasia. Gastroenterology 123:1565-1577, 2002.
8. Wu, R., Lin, L., Beer, D.G., Ellenson, L.H., Lamb, B.J., Rouillard, J.-M., Kuick, R., Hanash, S., Schwartz, D.R., Fearon E.R., and Cho, K.R. Amplification and Overexpression of the L-*MYC* Proto-Oncogene in Ovarian Carcinomas. American Journal of Pathology, 162:1603-1610, 2003.

9. Sherman-Baust, C.A., Weeraratna, A.T., Rangel, L.B.A., Pizer, E.S., Cho, K.R., Schwartz, D.R., Shock, T., and Morin, P. J. Remodeling of the extracellular matrix through overexpression of collage VI contributes to cisplatin resistance in ovarian cancer cells. Cancer Cell, 3:377-386, 2003.
10. Schwartz, D.R., Wu, R., Kardia, S.L.R., Levin, A.M., Huang, C.-C., Shedden, K., Kuick, R., Misek, D., Hanash, S., Taylor, J.M.G., Reed, H., Hendrix, N., Zhai, Y., Fearon, E.R., and Cho, K.R. Novel candidate targets of β-catenin/TCF signaling identified by gene expression profiling of ovarian endometrioid adenocarcinomas. Cancer Research, 63:2913-22, 2003.
11. Rangel, LB., Agarwal, R., D'Souza, T., Pizer, E.S., Alo, P.L., Lancaster, W.D., Gregoire, L., Schwartz, D.R., Cho, K.R., and Morin, P.J. Tight junction proteins claudin-3 and claudin-4 are frequently overexpressed in ovarian cancer but not in ovarian cystadenomas. Clinical Cancer Research 9:2567-75, 2003.
12. Shedden, K.A., Taylor, J.M.G., Giordano, T.J., Kuick, R., Misek D.E., Rennert, G., Schwartz, D.R., Gruber, S., Logsdon, C., Simeone, D., Greenson, J.K., Cho, K.R., Beer, D.G., Fearon, E.R., and Hanash, S. Accurate molecular classification of human cancers based on gene expression using a simple classifier with a pathologic tree-based framework. American Journal of Pathology (in press 2003).
13. Rangel, L.B.A., Sherman-Baust, C.A., Wernyj, R.P., Schwartz, D.R., Cho, K.R., and Morin, P.J. Characterization of novel human ovarian cancer-specific transcripts (HOST) identified by serial analysis of gene expression. Oncogene (in press, 2003).

BOOKS/CHAPTERS IN BOOKS:

1. Cho, K.R., and Ellenson L.H. Molecular Biology. In Blaustein's Pathology of the Female Genital Tract, 5th edition, ed. Robert J. Kurman, Springer-Verlag, New York, 2002.

LAURA COOLING, MD, MS
Clinical Assistant Professor II

Department of Pathology
Annual Department Report
1 July 2002-30 June 2003

I. CLINICAL ACTIVITES

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 Fellows
   b. Heme/Onc Nursing Staff (in-service lectures)
   c. Hematology case conference
      i. TTP in adolescent patient, role of plasma exchange
      ii. Management of severe HLA alloimmunization in aplastic anemia

B. Medical Students
1. Transfusion Medicine. Senior Therapeutics Course, Dept. of Pharmacology
2. Evaluation and management of platelet refractoriness. Hem/Onc residents, medical students and nursing staff.

III. RESEARCH ACTIVITIES

A. The Regulation and Biology of Globo-Series Glycosphingolipids
1. Chemical analysis of complex P and Luke related globo-gangliosides
2. Relationship of LKE phenotype on non-globo-glycoconjugates of human RBCs

3. Effect of inflammatory cytokines and retinoic acid on globo- and lacto-family in renal epithelial cells.
4. Molecular basis and regulation of Pk and Luke antigen expression in LKE.
5. Globo/lacto antigens in infectious disease

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

IV. 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.

V. ADMINISTRATIVE ACTIVITIES

DEPARTMENTAL

A. Associate Director, Transfusion Medicine

HOSPITAL

A. Transfusion Subcommittee

V. OTHER RELEVANT ACTIVITIES

INVITED LECTURES/SEMINARS:

1. Invited Lecturer, Internal Medicine Grand Rounds University of Michigan: Basics of Blood Transfusion Therapy. August 2002.
2. Invited Lecturer, Internal Medicine Grand Rounds, University of Michigan: Adverse Effects of Transfusion. September 2002.
3. Invited Speaker, Canadian Blood Services. Globo- Blood Group System. October 2002.
4. Invited Speaker, Canadian Blood Services and University of Toronto, Toronto, CA. Luke, Lewis and Luck. October 2002.
5. Invited Speaker, Carbohydrate Blood Group Workshop, American Association of Blood Banks 56th Annual Meeting, Orlando, FL. A "Globo"-al Perspective on ISBT Collection 209. October 2002.
6. Presenter, American Association of Blood Banks 56th Annual Meeting, Orlando, FL. Identification of two new single nucleotide polymorphisms in FUT3 (Lewis), associated with the Lewis null phenotype in African Americans. October 2002.
7. Presenter, American Association of Blood Banks 56th Annual Meeting, Orlando, FL. A missense mutation in □3GalT5, the glycosyltransferase responsible for galactosylgloboside and Lewis c synthesis, may be associated with the LKE-Weak phenotype in African Americans. October 2002.

8. Presenter, American Association of Blood Banks 56th Annual Meeting, Orlando, FL. The receptor for shiga toxin is commonly expressed by immature myeloid cells. October 2002.
9. Presenter, American Association of Blood Banks 56th Annual Meeting, Orlando, FL. Increased expression of a *para*-Forssman like glycosphingolipid on LKE-Weak Red Cells. October 2002.
10. Lecturer, Dept. of Surgery Resident Conference, University of Michigan. Basics of hemotherapy. April 2003.
11. Invited Speaker, Immunohematology Reference Laboratory Conference, American Association of Blood Banks, Las Vegas, NV. ABO antigens on human platelets. May 2003.
12. Invited Speaker, Annual Immunohematology Reference Laboratory Conference, American Association of Blood Banks, Las Vegas, NV. Blood and Bugs: the role of blood group antigens and infectious diseases. May 2003.
13. Lecturer, Clinical Pathology Grand Rounds, University of Michigan. Blood and bugs: an unhealthy synergism. May 2003.
14. Invited Speaker, Marion F. Beard Scientific Seminar, American Red Cross, Louisville, KY. Blood and Bugs: the role of blood group antigens and infectious diseases. June 2003.
15. Speaker, Current Topics in Blood Banking, University of Michigan. Working out the bugs; issues in platelet culturing and extended platelet storage. June 2003.
16. Presenter, Invitational Conference on Investigative Immunohematology. Increased autoantibody binding during platelet storage. June 2003.
17. Invited Speaker, Transfusion Medicine Seminar, Delta Blood Banks, Stockton, CA. ABO antigens and human blood platelets. July 2003.
18. Invited Speaker, Transfusion Medicine Seminar, Delta Blood Banks, Stockton, CA. Bugs and Blood: The role of blood group antigens in infectious diseases.

REVIEWER

Conn's Current Therapy
Journal of Lipid Research
Journal, Leukemia
Journal, Transfusion
Journal, Thrombosis and Hemostasis
Journal, Thrombosis Research
Scientific Abstracts, American Association Blood Bank 56th Annual Meeting

PROFESSIONAL MEMBERSHIPS

American Association of Blood Banks
Michigan Association of Blood Banks
    Education Committee
    Specialist in Blood Banking Subcommittee/Course Lecturer
Invitational Conference of Investigative Immunohematology
American Society of Clinical Apheresis
Alpha Omega Alpha

V. PUBLICATIONS

JOURNALS:

1. Cooling LLW, Zhang DS, Naides NS, Koerner TAW. Glycosphingolipid expression in acute nonlymphocytic leukemia: common expression of shiga toxin and parvovirus B19 receptors on early myeloblasts. Blood 2003; 101:711-721.
2. Cooling L, Gu Y. Indentification of two new single nucleotide polymorphisms in FUT3 associated with the Lewis null phenotype. Transfusion, in press.
3. Cooling L, Koerner TAW. Platelet-associated immunoglobulin increases during platelet storage. Transfusion, in press.

BOOKS/CHAPTERS IN BOOKS:

1. Rogers RL, Cooling LW. Therapeutic apheresis in pediatric patients. In Apheresis: Principles and Practice, 2nd edition (eds McLeod BC, Price TH, Weinstein R). AABB Press, 2003. In press.

PEER-REVIEWED ABSTRACTS:

1. Davenport R, Cooling L, Newman B. Acute pain transfusion reaction associated with transfusion of HLA class II antibodies. Submitted (in press?)
2. Cooling L, Hwang D. B2/B1, a monoclonal antibody against a bipotential neuroendocrine precursor in embryonic adrenal medulla, recognizes the Luke blood group antigen (GLOB3). Transfusion, in press.
3. Cooling L, Hwang D, Gu Y. The LKE-negative and LKE-weak RBC phenotypes do not reflect decreased RBC sialylation. Transfusion, in press.
4. Hwang D, Cooling L, Gu Y. Homozygosity for the galactosylgloboside synthase (□3GalT5)-T654 allele is associated with decreased LKE expression on LKE-weak RBC. Transfusion, in press.
5. Cooling L, Hwang D, Gu Y. Globoside synthase can regulate P^k and LKE expression on human RBC: evidence for the P^k-variant phenotype among some LKE-weak and LKE-negative donors. Transfusion, in press.
6. Woloskie S, Cooling L, Davenport R. Plasmapheresis complicated by protein S deficiency: maintaining a patent extracorporeal circuit. J Clin Apheresis 2003, in press.
7. Cooling L, Zhang DS, Koerner T. The receptor for shiga toxin is commonly expressed by immature myeloid cells. Transfusion 2002;42:S21.
8. Cooling L, Gu Y. Increased expression of a para-Forssman-like glycosphingolipid on LKE-weak red cells. Transfusion 2002;42:S34.
9. Cooling L, Gu Y, Copeland T. Identification of two new single nucleotide polymorphisms in FUT3 (Lewis), associated with the Lewis null phenotype in African Americans. Transfusion 2002;42:S36.
10. Cooling L, Gu Y, Judd WJ, Copeland T. A missense mutation in □3GalT5, the glycosyltranstransferase responsible for galactosylgloboside and Lewis c synthesis, may be associated with the LKE-weak phenotype in African Americans. Transfusion 2002;42:S32.

YIRAN DAI, M.D.
CLINICAL ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

A. Cytopathology (7 months)
   1. Review and Signout of in-house cytology, Transfer Cytology (TC) and intradepartmental and extradepartmental cytology consultations (Gyn & Non-Gyn).
   2. Performance of Fine Needle Aspirations (FNA) at the Cancer Center, University Hospital, and Mott Children's Hospital. Rapid interpretation of FNA performed at CT, Ultrasound, Medical Procedure Unit, and outpatient clinics.

B. Surgical Pathology (4 months)
   1. Review and Signout of Surgical Pathology (Room1, Room 2 and Room C)
   2. Review and Signout of Genitourinary biopsies and surgical resections (GU)

C. On call for intraoperative consultation (6 weeks)

II. TEACHING ACTIVITIES:

A. Fellows, residents and medical school students:
   1. Cytopathology:
      a. Introduction to the basic concepts of cytopathology through interaction at the microscope.
      b. Instruction on FNA performance and principles of cytopathology preparations.
      c. Supervision and instruction on rapid assessment of cytology preparations.
      d. Discussion and review of pertinent cytology literature with emphasis on diagnostic applications.
   2. Surgical Pathology:
      a. Instruction in surgical pathology diagnostic rooms
      b. Instruction in GU diagnostic room
      c. Instruction in intraoperative consultation
   3. Monthly cytopathology residents' conference
      Weekly cytopathology fellows' conference

B. Cytotechnologist:
   Cytopathology slide conferences.

C. Other education activities:
   National cytopathology teleconference.

III. RESEARCH ACTIVITIES:

PROJECTS UNDERSTUDY:

A. The overall effect of Thin Prep on the diagnosis of fibroadenoma.
B. The expression pattern of beta-catenin in mesothelial proliferative lesions and its diagnostic utilities.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Cytopathology division quality control and assurance

REGIONAL AND NATIONAL:

A. Elected member of Quality Control Committee, American Society of Cytopathology

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

Invited Lecturer, "Diagnostic cytology challenges in effusions". Teleconference. June, 2003.

VI. PUBLICATIONS:

ABSTRACT ACCEPTED FOR ASC

Yiran Dai, Celina G. Kleer, Claire W. Michael The overall effect of Thin Prep on the diagnosis of fibroadenoma. 2003 ASC meeting

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

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
I. Invited lecture: Risky business! Michigan Association of Blood Banks, Romulus, MI, September 12, 2002.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Pathophysiology of transfusion reactions.
B. Transfusion-transmitted West Nile Virus.
C. Cefotetan induced immune hemolysis.
D. Heparin-induced thrombocytopenia.
E. Cytodiagnosis of epitheliod hemangioendothelioma.

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. Scientific Section Coordinating Committee, American Association of Blood Banks.
C. Annual Meeting Program Planning Committee, American Association of Blood Banks.
D. Medical Advisory Committee, American Red Cross Southeastern Michigan Region.
E. Editorial Board, Transfusion.

VI. PUBLICATIONS:

ARTICLES ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Davenport RD. The red blood cell transfusion threshold: evidence and outcome. Cur Hematol Reports 1:142-148, 2002.

ARTICLES SUBMITTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Xin Wei, Davenport RD, Chang AE, Michael CW. The Exaggerated Pigmented Granulomatous Reaction to the Artificial Joint Implant Mimics Metastatic Melanoma. Diag Cytopathol (in press)
2. Reddy P, Reynolds C, Ratanatharathorn V, Davenport R, Silver S, Ayash L, Ferrara JLM, Uberti JP. West Nile virus encephalitis in a hematopoietic stem cell transplant recipient causing fatal CNS failure. Submitted to Bone Morrow Transplantation.
3. Pealer LN, Marfin AA, Petersen LR, Lanciotti RS, Page PL, Stramer SL, Stobierski MG, Signs K, Newman B, Goodman JL, Chamberland ME, and the West Nile Virus Transfusion Transmission Investigation Team. Transmission of West Nile Virus through blood transfusion—United States, 2002. Submitted to New England Journal of Medicine.

CHAPTERS IN BOOKS:

1. Davenport, RD: Hemolytic Transfusion Reaction. In: Simon TL, Dzik WH, Snyder EL, Stowell CP, Strauss RG (eds.): Rossi's Principles of Transfusion Medicine 3rd ed. Lippincott Williams and Wilkins, Philadelphia, PA, 2002.
2. Davenport RD: Blood Banking. In: Schmaier AH, Petruzzelli, LM (eds.): Hematology for the Medical Student. Lippincott Williams and Wilkins, Philadelphia, PA, 2003.
3. Davenport RD: Transfusion Therapy. In: Schmaier AH, Petruzzelli, LM (eds.): Hematology for the Medical Student. Lippincott Williams and Wilkins, Philadelphia, PA, 2003.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002-30 JUNE 2003

I. CLINICAL ACTIVITIES:

II. TEACHING ACTIVITIES:

None.

III. RESEARCH ACTIVITIES:

A. In vitro live cell organelle toxicity research using multiple, simultaneous fluorescent probes.

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

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

Editorial Board Member, Drug Metabolism Reviews.

INVITED LECTURES/SEMINARS:

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. J.R. Herman, L.A. Dethloff, E.J. McGuire, R.F. Parker, K.M. Walsh, A.W. Gough, H. Masuda and F.A. de la Iglesia. Rodent carcinogenicity with the thiazolidinedione antidiabetic agent troglitazone. Toxicol. Sci. 68:226-236, 2002.
2. H. Masuda, M.J. Adams, R.C. Secker, E. J. McGuire, J.R. Herman, D. Bailey and F.A. de la Iglesia. Reproductive Toxicology Studies with the Thiazolidinedione Antidiabetic Agent Troglitazone. J. Tox. Sci. In press, 2002.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Shi, M.M., Bleavins, M.R., Thompson, R.G., Chin, J.F., de la Iglesia, F.A, Candidate gene profiles for liver toxicity and metabolism in NIDDM patients receiving an antidiabetic thiazolidinedione (Submitted, 2002).
2. Bulera, S.J., Festerling, T.A., de la Iglesia, F.A. Gabapentin Activates MAP kinase In vivo and In vitro in pancreatic acinar cells from Wistar rats: a postulated mechanism for pancreatic acinar cell tumor formation (Submitted, 2002).
3. FA. de la Iglesia, J. Haskins, D. Farkas, D. Wilson, G. Bearman. Coherent Multiprobes and Quantitative Spectroscopic Multimode Microscopy for the study of simultaneous intracellular events. (Submitted, 2002)
4. 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 $_{1\text{-}48}$ in neonates with severe necrotizing enterocolitis. (Submitted, 2003)

BOOKS/CHAPTERS IN BOOKS:

1. F.A. de la Iglesia, J.R. Haskins and G. Feurer. Hepatotoxicity of Cardiovascular and Antidiabetic Drugs. In: Drug-Induced Liver Disease. N. Kaplovitz (Ed.) M. Dekker Publ. New York., 2002.

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

None.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

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.
C. Ph. D. Thesis Committee Member - Igor Nasonkin, Dept. of Genetics; Kris Coulter, Dept. of Genetics; Hoonkyo Soo, Dept. of Genetics; Yue Ge, Dept. of Genetics; Bryan MacDonald , Dept of Genetics; Brian Gummow, CMB; Collen Doyle, Dept. of Genetics, Ira Weiner, CMB; Rob Morrow, CMB.
D. Course Lectures - Path 581, 7.5 h; Path 582 course director; CDB 530, 3 h; CDB 680, 12h

MEDICAL SCHOOL/HOSPITALS:

A. First year Medical Students – Embryology, 2 h
B. Second Year Medical Students - Renal Section, 1 h

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Cell Migration, Chemoattraction and the RET/GDNF Pathway", NIH/NIDDK 1 R01 DK54723-04 (30% effort), 7/1/02 - 12/31/03, Annual Direct Costs $158,840.
C. 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.
C. Principal Investigator, Project #3 (20% effort), "Functional Analysis of RET Signaling in Renal Epithelial Cells", NIH/NIDDK, 2 P50 DK39255-11A1, O' Brien Renal Center Grant, "Mechanisms of Glomerular and Tubular Injury", Dr. Roger C. Wiggins, PI. 7/1/02 - 8/31/03, $76,066 Initial Budget Period.
D. Principal Investigator, Grant-in–Aid, Polycystic Kidney Disease Research Foundation, 2/1/03-6/30/03, $50,000.

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, Admissions Committee
B. Center for Organogenesis - Interim Co-Director, Steering Committee, Training Grant Review Committee, Advisory Committee, Seminar Committee (Chair)
C. Program in Biomedical Sciences (PIBS) - Admissions Committee

REGIONAL AND NATIONAL:

NIH Study Section, General Medicine B, Permanent Member
NCI Program Project, Reviewer, Columbia Univ. Site Visit
American Journal of Physiology, Editorial Reviews Board
Developmental Dynamics, Editorial Board
Human Frontiers in Sciences Program, reviewer
Irish National Research Council, reviewer
Australian Medical Research council, reviewer
Welcome Trust, reviewer

Reviewer for: Cell, Nature, Science, Mechanisms of Development, 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, Cell, Am. J. Pathology, Cancer Research

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. European Nephrogenesis Workshop IX, Royal College of Physicians, Dublin, Ireland
2. Developmental Gene Regulation, Max Planck Institute, Goettingen, Germany
3. Dept. of Anatomy, Indiana University School of Medicine, Indianapolis, IN
4. Dept. of Medicine, Vanderbilt University, Nashville, TN.
5. Dept. of Pathology, Boston University School of Medicine
6. NIDDK Workshop on Renal Development
7. St. Jude's Children's Research Hospital, Memphis, TN

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Cai, Y., Lechner, M.S., Nihalani, D., Prindle, M., Holzman, L.B. and Dressler, G.R. (2002) Phosphorylation of Pax2 by the c-Jun N-terminal kinase and enhanced Pax2 dependent transactivation. *J. Biol Chem.* 277, 1217-1222.
2. Tang, M.J., Cai, Y., Tsai, S.J., Wang, Y.K. and Dressler, G.R. (2002) Ureteric Bud Outgrowth in Response to RET Activation is Mediated by Phosphatidylinositol-3 Kinase. *Dev. Biol.* 243, 128-136.
3. Silberstein, G. B, Dressler, G.R. and Van Horn, K. (2002) Expression of the Pax2 oncogene in human breast cancer and its role in progesterone dependent mammary growth. *Oncogene* 21, 1009-1016.
4. Hoffmeister, A., Ropolo, A.,Vasseur, S., Mallo, G.V., Bodeker, H., Ritz-Laser, B., Dressler, G.R., Vaccaro, M.I., Dagorn, J.C., Moreno, S. and Iovanna, J.L. (2002) The HMG-I/Y-related protein p8 binds to p300 and Pax2 trans-activation-domain interacting protein to regulate the trans-activation activity of the Pax2A and Pax2B transcription factors on the glucagon gene promoter. *J. Biol. Chem.* 277, 22314-22319.
5. Dressler, G.R. (2002) Tubulogenesis in the developing mammalian kidney. *Trends Cell Biol.* 12, 390-395.
6. Cho, E.A., Prindle, M.J. and Dressler, G.R. (2003) The BRCT domain protein PTIP is required for progression through mitosis. *Mol. Cell. Biol.* 23, 1666-1673
7. Brophy, P.D., Lang, K.M. and Dressler, G.R. (2003) The Secreted Frizzled Related Protein SFRP2 Gene is Activated by the Pax2 Transcription Factor. *J. Biol. Chem.* in press.
8. Cai, Y., Brophy, P., Levitan, I. and Stefano, S. and Dressler, G.R. (2003) Groucho suppresses Pax2 transactivation by inhibition of JNK mediated phosphorylation. *EMBO J.*, in press.
9. Patel, S. and Dressler, G.R. (2003) Expression of Pax2 in the intermediate mesoderm is regulated by YY1. *Dev. Biol.*, in press/

ARTICLES SUBMITTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Lin, J., Cho, E.A., and Dressler, G.R. (2003) Kielin/Chordin-Like Protein 1, a Novel Secreted Inhibitor of TGF-□ and Activin Signaling. submitted

BOOK CHAPTERS:

1. Dressler, G.R. (2002) The Development of the Excretory System. In: *Mouse Development* (J. Rossant and P. Tam, eds.) Academic Press, NY, pp395-420.
2. Cho, E.A. and Dressler, G.R. (2003) The Formation and Development of Nephrons. In: *The kidney: Normal Development to Congenital Abnormalities* (P. D. Vize, A. S. Woolf, J. B. L. Bard, eds) Academic Press, pp195-210.
3. Gregory R. Dressler (2003) Cell Lineages and Stem Cells in the Embryonic Kidney. in *Handbook of Embryonic Stem Cells* (R. Lanza, ed.) Elsevier Science, in press.

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

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

ANNUAL DEPARTMENTAL REPORT
JULY 1 2001 – JUNE 30 2002

I. CLINICAL ACTIVITIES:

None

II. TEACHING ACTIVITIES:

A. Research Mentor:
1. Jennifer Lewis, Ph.D., postdoctoral fellow, 1999 - present.
2. Ezra Burstein, M.D., Lecturer, Department of Internal Medicine 2001 - present.
3. John Wilkinson, Ph.D., postdoctoral fellow, 2002 - present.

B. Thesis committee/examiner:
1. Molly Thomas, Pathology Graduate Program
2. Katie Johnson, Immunology Graduate Program
3. Lynn Kamen, Immunology Program
4. Brian Rudd, Pathology

C. Teaching:
1. Pathology 582
2. Immunology 850 (course director)

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Role of X-linked IAP (XIAP) in TGF-□ 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. Gerry Cohen, University of Leicester, England and Dr. Larry Boise, University of Miami.

C. Characterization of VIAF, 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. Gary Nabel, National Institute of Allergy and Infectious Diseases, Dr. Cisca Wijmenga, University Medical Center, Utrecht, and Dr. George Brewer, University of Michigan.

SPONSORED SUPPORT:

2002 - present	Startup funds from University of Michigan. Funding provided by Department of Pathology, UM Cancer Center and Biomedical Scholars Program (PI).
2003 - 2008	"Prevention of Mammary Cancer in Her-2neu Transgenic Mice," (5%). R01 (P.I. Merajver).
2004 – 2007	"Prostate cancer aggressiveness genes in hereditary prostate cancer," (15%). USARMC Prostate Cancer IDEA Award (Co-PI together with K. Cooney)

FELLOWSHIP AWARDS SERVING AS MENTOR:

2002 – 2004	T32 CA09676-10, NCI Postdoctoral Training Grant to John Wilkinson, Ph.D."The role of XIAP in the regulation of apoptosis"
2003 – 2006	American Gastroenterological Association Research Scholar Award to Ezra Burstein, M.D. "Characterization of a novel interacting partner of XIAP."

PENDING:

2004 - 2009	"Control of Apoptosis and Signaling by XIAP," R01 GM067827-01 (NIGMS). (Principal Investigator) (30%).
2004 – 2009	"SCF in eosinophilic airway inflammation, "R01 (Lukacs) (NIAID). PI. Lukacs (15%).

IV. ADMINISTRATIVE ACTIVITIES:

1. PIBS International Admissions Committee.
2. Immunology graduate program prelim committee
3. Organizing Committee, Gordon Research Conference on Cell Death, 2002.
4. Scientific Advisory Board, Aegera Therapeutics, 2002 - Present.
5. Temporary Reviewer, NIH Immunobiology Study Section, 2003.
6. Permanent Reviewer, NIH CDF-4 Study Section, 2003.
7. Permanent Reviewer, NIH CDF-6 Study Section, 2003.
8. Co-chair, AACR Symposium on Intracellular Apoptosis Signaling Molecules, 2003.
9. Reviewer, DOD prostate cancer study section, 2003

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL AND REVIEWING ACTIVITIES:

A. Editorial Board: *Journal of Biological Chemistry*, 2002 – 2007
Editorial Board: Biochemical Journal, 2003 - 2006

B. Reviewer (selected journals shown):
Cancer Cell,

Cell Death and Differentiation
Current Biology
EMBO Journal
Genes and Development
Immunity
Journal of Biological Chemistry
Molecular Cell
Nature Cell Biology
Nature Reviews Cancer
Oncogene
Proceedings of the National Academy of Sciences USA
Science

HONORS AND AWARDS:
Biomedical Scholar Award, University of Michigan, 2002.

INVITED LECTURES/SEMINARS:

1. Burnham Institute, La Jolla, CA (2003)
2. FASEB-American Sociey for Investigative Pathology Annual Meeting, San Diego, CA (2003)
3. AACR Annual Meeting, Minisymposium co-chair, Washington DC (2003)
4. Massachusetts General Hospital/Harvard Medical School, Cambridge MA (2003)
5. University of Massachusetts Cancer Center, Worcester MA (2002)
6. University of North Carolina at Chapel Hill, NC (2002)

VI. PUBLICATIONS:

1. Salvesen, G.A. and **Duckett, C.S.** IAP proteins: Blocking the road to death's door. *Nature Rev Cell Mol Biol* **3**: 401-410 (2002)
2. Bratton, S.B., Lewis, J., Butterworth, M., **Duckett, C.S.,** and Cohen, G.M. XIAP inhibition of caspase-3 preserves its association with the Apaf-1 apoptosome and prevents CD95- and Bax-induced apoptosis. *Cell Death and Diff.* **9**:881-892 (2002).
3. Hunter, A.M., Kottachchi, D., Lewis, J., **Duckett, C.S.**, Korneluk, R.G. and Liston, P. A novel ubiquitin fusion system bypasses the mitochondrial and generates biologically active Smac/DIABLO. J. Biol. Chem. **278**: 7494 – 7499 (2003).
4. Shin, H, Okada, K, Wilkinson, J.C., Solomon, K.M., **Duckett, C.S.**, Reed, J.C. and Salvesen, G.S. Identification of ubiquitination sites on the X-linked inhibitor of apoptosis protein. *Biochem. J.*, **373**:965-971 (2003).
5. Burstein, E. and **Duckett, C.S.** Dying for NF-□B? Control of cell death by transcriptional regulation of the apoptotic machinery. *Curr. Opinion Cell Biol.*, in press.
6. Beltrami, E., Plescia J., Wilkinson J.C., **Duckett, C.S.**, Altieri, D.C. Acute ablation of survivin uncovers p53-dependent mitotic checkpoint functions and control of mitochondrial apoptosis. *J. Biol. Chem.*, in press.
7. Ganesh, L., Burstein, E., Guha-Niyogi, A., Louder, M.K., Mascola, J.R., Klomp, L.W.J., Wijmenga, C., **Duckett, C.S**. and Nabel, G.J. Identification of a gene product, Murr1, which restricts HIV-1 replication in resting CD4+ lymphocytes. *Nature*, in press.

8. Burstein, E., Ganesh, L., Dick, R.D., van De Sluis, B., Wilkinson, J.C., 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.*, in press.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

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 AG12495-10S1 (McConnell) 2/01/03 - 11/30/03 10%
NIH $583,270
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 immunoassy techniques.

PENDING:

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

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 Womenís 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 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 ìdrugsî. 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 ìdrugî delivery.
3. 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.
4. 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.

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. Gauger PG, Mullan MH, Thompson NW, Matz KA, Doherty GM, England BG: An alternative analysis of intraoperative parathyroid hormone (IOPTH) data may improve ability to detect multigland disease. Archives of Surgery, in press 2003.
2. Flinn MV & BG England 2003. Childhood stress: endocrine and immune responses to psychosocial events. In: Social & Cultural Lives of Immune Systems, JM Wilce (Ed.), pp. 107-147. London: Routledge press.
3. Decker SD, MV Flinn, BG England, & C Worthman 2003. Cultural congruity and the cortisol stress response among Dominican men. In: Social & Cultural Lives of Immune Systems, JM Wilce (Ed.). London: Routledge press.
4. Wagner JD, MV Flinn, & BG England 2002. Hormonal response to competition among male coalitions. Evolution and Human Behavior23(6): 437-442.
5. Cason Z, Benghuzzi H, Tucci M, England B. TCPL delivery system as a model for E + P replacement therapy in post-ovariectomized adult rats mimicking a postmenopausal condition. **Biomed Sci Instrum**. 2003;39:529-34.

ABSTRACTS AND PAPERS AT SCIENTIFIC MEETINGS:

1. Quinlan RJ, Flinn MV, Leone DV, Quinlan MB, Gangestad SJ, Thornhill R, & England BG Tradeoffs between indirect parental investment and direct childcare: Long-term effects of household production and breastfeeding duration on children's cortisol levels, fluctuating asymmetry, and growth. (abstract) Proceedings of the Human Behavior and Evolution Society 2003.
2. Flinn MV, Noone, R & England, BG 2002. Longitudinal patterns of stress, family environment, and child health in a rural Caribbean village. (abstract) Abstracts of the American Anthropological Association Meetings 2002.
3. Flinn MV, Noone, R & England, BG 2002. Longitudinal patterns of cortisol reactivity, father absence, and maternal behavior in a rural Caribbean village. (abstract). Proceedings of the Human Behavior and Evolution Society 2002.
4. Nepomnaschy PA, McConnell D, Welch K, Strassmann BI and England BG (2003) Adrenal and Reproductive Hormone Changes in Parous Mayan Women in Rural Guatemala. Annual Meeting of the Human Biology Association, Tempe, Arizona.
5. Nepomnaschy PA, McConnell D, Welch K, Strassmann BI and England BG (2003) Stress and Reproduction in a Subsistence Population in Rural Guatemala. LIFE Spring Academy, Max Planck Institute & The University of Michigan, Ann Arbor, Michigan.
6. Nepomnaschy PA, McConnell D, Welch K, Strassmann BI and England BG (2003) Adrenal and Reproductive Hormone Changes in Parous Mayan Women in Rural Guatemala. Anita Payne Lectureship and Poster Day.Reproductive Sciences Program and Department of Obstetrics and Gynecology. The University of Michigan, Ann Arbor, Michigan.

7. Nepomnaschy PA, McConnell D, Welch K, Strassmann BI and England BG (2003) Adrenal and Reproductive Hormone Changes in Parous Mayan Women in Rural Guatemala. Reproductive Sciences Program Seminar Series.The University of Michigan, Ann Arbor, Michigan.
8. Gauger PG, Mullan MH, Thompson NW, Matz KA, Doherty GM, England BG. An alternative analysis of intraoperative parathyroid hormone monitoring data may improve detection of multiglandular disease. Frederick A. Coller Surgical Society, Sea Island, Georgia, October 18, 2002.
9. HA Benghuzzi and BG England, Long-term sustained delivery of Danazol, T and DHT alters HDL level in castrated rams, International Conference on Cardiovascular Medicine and Science, July 23-25, 2003, Bethesda, MD, USA, Abstract Published at the International Journal of Cardiovascular Medicine and Science, Vol. 6, No2, pp68, 2003.
10. H. Benghuzzi, M. Tucci, A. Tsao and B. England, The Use of TCPL Deliver System to Release Diosgenin as a Hormone Replacement Therapy in an Ovariectomized Rat Model. Abstract Accepted for Publication and Presentation at the 29th Annual Meeting of the Society for Biomaterials, Transactions. Reno, Nevada. April 30 – May 3, 2003, Abstract #216.
11. Felix Adah, Hamed Benghuzzi, Michelle Tucci, George Russell, Audrey Tsao, and Barry England, Sustained Delivery of Statin by Means of TCPL Delivery System and the Effect on Reproductive Hormones, The 19th Annual Meeting of the Academy of Surgical Research, October 3rd and 4th, 2003 at the St. Louis Radisson Hotel, St. Louis, MO.
12. Cason Z, Benghuzzi H, Tucci M, England B. TCPL delivery system as a model for E + P replacement therapy in post-ovariectomized adult rats mimicking a postmenopausal condition. Accepted for presentation and invited for manuscript submission at the 40th Annual Rocky Mountain Bioengineering Symposium, Biloxi, MS. April 11-13, 2003 [PubMed - indexed in MEDLINE]
13. Benghuzzi H, Tucci M, and England B*, Comparison Between Injectable and Sustained Delivery of DHEA or DHEA plus Estradiol, Society For Biomaterials, April 2002, Tampa, FL.
14. Benghuzzi Ham, Michelle Tucci, and Barry England, Pathophysiological Responses Associated with Sustained Delivery of Various DHEA Levels Using Adult Male Rodents, FASEB Journal, Abstract #144.7, P. A144, Vol. 16, Number 4, April 20-24, 2002
15. Benghuzzi_H, Tucci M, and England B*, Comparison Between Injectable and Sustained Delivery of DHEA or DHEA plus Estradiol,, Transactions, 28th Society For Biomaterials. April 24-27, 2002, Tampa, FL.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

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 Host Defense Course.
F. Medical Student Advisor (3rd and 4th year).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "An Integrated Curriculum for Multiculturalism, Spirituality, and End-of Life Care". Arthur Vining Davis Foundation. (2000-2002).
B. Co-Investigator, "University of Michigan Integrative Curriculum for Medicine and Allied Health." National Institutes of Health. R25-AT00812-01 (2001-2006).
C. 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. Coordinator - Educational Programs.
C. Director, Resident Training Program.
C. Chairman's Advisory Committee.
D. Department ACAPT Committee.
E. Research Space Advisory Committee.
F. 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. Medical School Curriculum Review Group (Chair)
H. LCME Review Committee (Chair).

REGIONAL AND NATIONAL:

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

V. AWARDS:

VI. OTHER RELEVANT ACTIVITIES:

VII. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Supiano, MA., Casey B. White, CW., and **Fantone,** JC., The Geriatrics Educational Consultant. Academic Medicine. 77(9):937-8, 2002.
2. Tang TS. **Fantone** JC. Bozynski ME. Adams BS. Implementation and Evaluation of an Undergraduate Sociocultural Medicine Program. Academic Medicine. 77(6):578-85, 2002

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002- 30 JUNE 2003

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.
   3. M-1 Histopathology Course (24 hours).
D. Dental and Graduate Students: Pathology 580/630: "Pathology of White Blood Cells" (Lecture) – 1 hour.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Optimization of Clinical Laboratory Hematology Practice.
B. Gene expression profiling of chronic lymphoproliferative disorders.
C. Utilization management and optimization for clinical laboratories.
D. Finn WG, Peterson LC (eds): *Hematopathology in Oncology*. Kluwer Academic Publishers, Boston (Book under contract; scheduled publication 2003 or 2004).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Associate Director of Clinical Pathology
B. Director, Hematopathology Section.
C. Chair, Long-Range Planning Committee for Clinical Laboratories.
D. Departmental Advisory Committee on appointment, promotion, and tenure
E. (ACAPT) (pathology) (Henry Appleman, M.D., Chair.)
F. Departmental Residency Selection Committee (Joseph Fantone, M.D., Chair).
G. Pathology Quality Assurance Committee (Jeffrey Warren, M.D., Chair).

REGIONAL/NATIONAL:

A. American Society of Clinical Pathologists, Check Path Planning Committee (Hematopathology).
B. College of American Pathologists, Hematology and Clinical Microscopy Resource Committee.
C. Society for Hematopathology, ASCP Companion Program Committee.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "The Pathologist's Role in the Evaluation of Peripheral Blood Abnormalities." Michigan Society of Pathologists, May 3, 2003.
2. "Update on Myelodysplastic Syndromes." Michigan Society of Pathologists, May 3, 2003.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Valdez R, McKeever P, Finn WG, Gebarski S, Schnitzer B: Composite germ cell tumor and B-cell non-Hodgkin's lymphoma arising in the sella turcica. Hum Pathol 33:1044-1047, 2002.

2. Uherova P, Schnitzer B, Valdez R, Ross CW, Finn WG: Nodular lymphocyte predominant Hodgkin lymphoma: an immunophenotypic reappraisal based on a single-institution experience. Am J Clin Pathol, 119:192-198, 2003.
3. Valdez R, Thorson J, Finn WG, Kleer CG, Schnitzer B: Lymphocytic mastitis: a molecular, immunophenotypic, and clinicopathologic evaluation of eleven cases. Mod Pathol 16(3):223-228, 2003.
4. Lantis KL, Harris RJ, Davis G, Renner N, Finn WG: Elimination of instrument-driven reflex manual differential leukocyte counts: optimization of manual blood smear review criteria in a high volume automated hematology laboratory. Am J Clin Pathol 119:656-662, 2003.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Brown W, Keeney M, Chin-Yee I, Johnson K, Lantis K, Finn W, Wolfe N, Kaplan S: Validation of body fluid analysis on the Coulter LH 750.

BOOKS AND CHAPTERS IN BOOKS:

1. Finn WG: Hematolymphoid system. In: *Yearbook of Pathology and Laboratory Medicine 2004.* Elsevier, Inc., in press.
2. Finn WG: Classification of lymphoma. In: *Hematology for the Medical Student.* Schmaier A, and Petruzzelli L, eds. Lippincott Williams & Wilkins 2003, pp185-195.

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

1. Selby D, Valdez R, Schnitzer B, Ross CW, Finn WG: Diagnostic criteria for acute erythroleukemia (letter). Blood 101:2895-2896, 2003.
2. Aller RD, Finn WG: New and improved: hematology analyzers. CAP Today 16(6):2078, 2003.
3. Finn WG: Inside Blood: Cytologic subtypes of grade 3 follicular lymphoma. Blood 101(6):2078, 2003.
4. Ramalingam P, Valdez R, Ross CW, Schnitzer B, Finn WG: Oct-2 andd BOB.1/OBF.1 expression in surface immunoglobulin-negative follicular lymphomas. Poster presentation, United States and Canadian Academy of Pathology Annual Meeting, Washington, DC, 2003. Mod Pathol 2003; 16(1)249A.
5. Ramalingam P, Finn W, Schnitzer B, Valdez R: Immunohistochemical expression of Oct2 in non-Hodgkin lymphomas evaluated by tissue microarray (TMA). Poster presentation, United States and Canadian Academy of Pathology Annual Meeting, Washington, DC, 2003. Mod Pathol 2003; 16(1)249A.
6. Kilgore S, Erba H, Valdez R, Finn W, Schnitzer B, Ross C: Mylotarg (Gemtuzumab Ozogamicin; CMA-676) in AML: predictive variables and response to treatment. Poster presentation, United States and Canadian Academy of Pathology Annual Meeting, Washington, DC, 2003. Mod Pathol 2003; 16(1)240A.
7. Selby D, Padmore R, Tuck M, Ross C, Schnitzer B, Finn W, Valdez R, Singleton T, Kaminski M: Characterization of bone marrow lymphoid aggregates in follicular lymphoma treated with [^{131}I] anti-B1 antibody. Poster presentation, United States and Canadian Academy of Pathology Annual Meeting, Washington, DC, 2003. Mod Pathol 2003; 16(1)251A.

8. Selby DM, Ross CW, Finn WG, Valdez R, Schnitzer B: CD10 and cyclin D1 expression in hairy cell leukemia. Poster presentation, United States and Canadian Academy of Pathology Annual Meeting, Washington, DC, 2003. Mod Pathol 2003; 16(1)251A.
9. Valdez R, Schnitzer B, Finn WG: Tissue microarray (TMA) analysis of surviving expression in benign lymphoid tissue and small B-cell non-Hodgkin lymphoma (NHL). Poster presentation, United States and Canadian Academy of Pathology Annual Meeting, Washington, DC, 2003. Mod Pathol 2003; 16(1)256A.
10. Finn WG: Classification of refractory anemia (letter). Leuk Res, in press.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2001 - 30 JUNE 2002

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
   2. Dermatopathology, Pathology Clerkship, MS IV
   3. 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. Immunohistochemical evaluation of sentinel lymph nodes for micrometastases: patterns of involvement and sensitivity of S100, HMB45 and melan-A immunostains (D. Karimipour, M.D., L. Lowe, M.D., L. Su, M.D., T. Johnson, M.D.)
B. CD5 expression by immunohistochemistry in cutaneous tumors of eccrine and apocrine differentiation (P. Bogner, M.D., L. Su, M.D.)
C. 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.)
D. 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.)
E. 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.)

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

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

None

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Su LD, Fullen DR, Lowe L, Uherova P, Schnitzer B, Valdez R. CD117 (KIT receptor) expression in Merkel cell carcinoma. Am J Dermatopathol. 2002 Aug;24(4):289-93.
2. Su LD, Fullen DR, Sondak VK, Johnson TM, Lowe L. Sentinel lymph node biopsy for patients with problematic spitzoid melanocytic lesions: a report on 18 patients. Cancer. 2003 Jan 15;97(2):499-507.
3. Fullen DR, Blobstein SH, McNutt NS. Asymptomatic pedunculated nodule on the leg of a 75-year-old man. Arch Dermatol. 2003 Jan;139(1):93-8.
4. Fullen DR, Jacobson SN, Valdez R, Novice FM, Lowe L. Granuloma annulare-like infiltrates with concomitant involvement by B-cell non-Hodgkin's lymphoma: report of a case. Am J Dermatopathol. 2003 Feb;25(1):57-61.
5. Fullen DR, Lowe L, Su LD. Antibody to S100a6 protein is a sensitive immunohistochemical marker for neurothekeoma. J Cutan Pathol. 2003 Feb;30(2):118-22.
6. Bogner PN, Fullen DR, Lowe L, Paulino A, Biermann JS, Sondak VK, Su LD. Lymphatic mapping and sentinel lymph node biopsy in the detection of early metastasis from sweat gland carcinoma. Cancer. 2003 May 1;97(9):2285-9.
7. Su LD, Fullen DR, Lowe L, Wang TS, Schwartz JL, Cimmino VM, Sondak VK, Johnson TM. Desmoplastic and neurotropic melanoma: analysis of 33 cases with lymphatic mapping and sentinel lymph node biopsy. (Submitted to Cancer).
8. Karimipour DJ, Lowe L, Su L, Hamilton T, Sondak V, Johnson TM, Fullen DR. Utility and sensitivity of standard immunostains and serial sectioning for melanoma sentinel lymph node biopsy. (Accepted for publication by J Am Acad Dermatol)

BOOKS/CHAPTERS IN BOOKS:

None

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

1. Bogner PN, Lowe L, Fullen DR, Biermann JS, Paulino AF, Sondak V, Su LD. "Lymphatic mapping and sentinel lymph node biopsy detects early metastasis of eccrine carcinoma." Poster presentation at the American Society of Dermatopathology 39th annual meeting, October 10-13, 2002.
2. Fullen DR, Lowe L, Su LD. "Antibody to S100A6 is a sensitive immunohistochemical marker for neurothekeoma." Poster presentation at the American Society of Dermatopathology 39th annual meeting, October 10-13, 2002.
3. Bogner PN, Su LD, Fullen DR. "Detection of CD5 by immunohistochemistry in cutaneous tumors of apocrine and eccrine origin." Accepted for poster presentation at the American Society of Dermatopathology 40th annual meeting, October 9-12, 2003.
4. Sturtz D, Smith DJ, Calderon MS, Fullen DR. "Giant folliculosebaceous cystic hamartoma of the upper extremity." Accepted for poster presentation at the American Society of Dermatopathology 40th annual meeting, October 9-12, 2003.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

A. Director, Chemistry Laboratory
B. Sign-out and interpretation of lipoprotein electrophoresis results.
C. 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.
D. Direct the workgroup overseeing the quality assurance programs for bedside blood glucose testing in the Medical Center.
E. Planning group for the approval and establishment of alternate site testing programs.
F. Technical Director for laboratories at U-M Health Centers off-site clinics.
G. Sign out of Triple Marker Screen results from maternal serum testing

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Pathology House Officers:
   1. Clinical Pathology Grand Rounds (2 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 – 1 hour continuing education lecture

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY

A. Evaluation of HPLC-MS methods for immunosuppressant drugs Tacrolimus and Sirolimus.
B. PSA and Percent free PSA levels in an African-American population (Flint Mens Health Study).
C. Evaluation of an enzymatic method for homocysteine determination.
D. Evaluation of EIA assays for extractable nuclear antigens.
E. Evaluation of Inhibin A assay in prenatal screening for Down Syndrome.

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

MEDICAL SCHOOL /HOSPITAL:

A. Clinical Information System Vendor Evaluation Decision Support Workgroup

REGIONAL AND NATIONAL:

A. Chair-Elect, Michigan Section AACC.
B. Treasurer, Michigan Section AACC.
C. Lipids and Lipoproteins Division Member
C. Ad hoc reviewer, Clinical Chemistry.

V. OTHER RELEVANT ACTIVITIES:

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

INVITED LECTURES/SEMINARS:

A. "Clinical Utility of Percent Free PSA in Screening for Prostate Cancer." Toledo Hospital,Toledo, OH, Oct 21, 2002.
B. "Impact of the New Cholesterol Testing Guidelines on the Clinical Laboratory." Dade Behring Laboratory Days Symposium, Cleveland, OH. November 13, 2002.
C. "Impact of the New Cholesterol Testing Guidelines on the Clinical Laboratory." Dade Behring Laboratory Days Symposium, Ann Arbor, MI November 15, 2002.
D. "Free PSA and Screening for Prostate Cancer." MSCLS Annual Meeting, Romulus, MI. April 9, 2003.

VI. PUBLICATIONS:

ARTICLES PUBLISHED IN REFEREED JOURNALS:

1. Clive, D., Rao, D., Giacherio, D., Gupta, M., Sackrison, J.L., and MacFarlane, G.D.: Analytical and clinical validation of a radioimmunoassay for the detection of 1,25 dihydroxyvitamin D. Clinical Biochemistry 2002; 35:517-521

ARTICLES SUBMITTED FOR PUBLICATION IN REFEREED JOURNALS

1. MacFarlane, G.D., Rao, D.S., Giacherio, D., Gupta, M., and Sackrison, J.L.: Hypervitaminosis D in midwestern urban centers. (submitted for publication, 2003).
2. McBryde, K.D., Kudelka, T.L., Kershaw, D.B., Brophy, P.D., Gardner, J.J., Bieniewicz, J.C., Mueller, B.A., Giacherio, D.A., and Smoyer, W.E.: Clearance of amino acids by hemodialysis in arginosuccinate synthetase deficiency. (submitted for publication 2003)
3. Sreekumar, A., Laxman, B., Rhodes, D.R., Bhagavathula, S., Giacherio, D., Sanda, M., Rubin, M., and Chinnaiyan, A.: Prostate cancer elicits a humoral response to □-methylacyl-CoA racemase. (submitted for publication 2003).

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

1. Patel, J., Annesley, T., and Giacherio, D.: A quick, simultaneous method of detection and quantitation of volatile alcohols and ethylene glycol by on column capillary gas chromatography of biological samples. Presented at Society of Forensic Toxicology Annual Meeting, Detroit, MI. Oct 16, 2002

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

A. General Surgical Pathology - four months.
B. Endocrine Surgical Pathology, Departmental and Outside Consultation - 12 months.
C. Immunoperoxidase Service - Outside Consultation - 12 months.
D. M-Labs Surgical Pathology Consultation - 12 months.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

A. Medical Students:
   1. 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 - 4 months.
C. Endocrine Surgical Pathology - 12 months as needed.
D. Consultation Conferences - four.
E. Molecular Pathology lectures.
F. Endocrine Pathology lectures.
C. Dental and Graduate Students:
   1. Endocrine Pathology lecture.
D. Interdepartmental:
   1. Endocrine Conference, Department of Surgery - monthly.
   2. Adrenal Cancer Conference - monthly.

EXTERNAL:

A. Michigan State Medical School.
   1. Endocrine Pathology - 2 lectures.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Co-Principal Investigator, "University of Michigan Endocrine Bank", Millie Schembechler Adrenal Cancer Research Fund, 1/1/01 to 12/31/02 ($100,000 direct costs), with Dr. Paul Gauger, Department of Surgery, 5% effort
B. 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
C. Co-Principal Investigator, "Towards a Molecular Classification of Tumors", NCI U19-CA84953, 9/99 to 3/04 ($951,282/yr direct costs for 4.5 yrs), with S. Hanash, Department of Pediatrics, Pathology Core Director, 20% effort
D. 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
E. Director, "Tissue Procurement Contract", Genentech, Inc., 5/99 to 5/2003 ($92,346 direct costs/year), 10% effort
F. Core Director, The University of Michigan Comprehensive Cancer Center, Tissue Procurement Service, 7-98 to present, 10% effort
G. Core Director, The University of Michigan Comprehensive Cancer Center, Laser Capture Microdissection Core, 1-99 to present
H. Core Director, The University of Michigan Comprehensive Cancer Center, Histology/Immunoperoxidase Service, 9-02 to present, 10% effort

PROJECTS UNDER STUDY:

A. Principal Investigator, "Gene Expression Profiles of Adrenal Cortical Neoplasms."
B. Principal Investigator, "Molecular Studies of Soft Tissue Sarcomas."
C. Principal Investigator, "Gene Expression Profiles of Thyroid Neoplasms."
D. Co-Investigator with Dr. Jim Baker, "Molecular Studies of Thyroiditis."
E. Co-Investigator, "Molecular Classification of Ovarian, Colonic and Thoracic Neoplasms."
F. Principal Investigator, "Gene Expression Profiles of Adrenomedullary Neoplasms."

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

NATIONAL:

A. Editorial Board, *Endocrine Pathology*

V. OTHER RELEVANT ACTIVITIES:

A. Consultant, Eli Lilly & Co.
B. Pathology Consultant, Asterand Corporation.

INVITED LECTURES/SEMINAR:

A. Invited Speaker, "DNA Microarray Analysis of Endocrine Tumors: What Can We Learn", Cleveland Clinic Foundation, Cleveland, Ohio
B. Pathology Ground Rounds, "DNA Microarray Analysis of Endocrine Tumors: What Can We Learn", Yale University School of Medicine, New Haven, Connecticut
C. Invited Speaker, "Gene Expression Studies of Lung Adenocarcinoma", Eli Lilly and Co., Indianapolis, Indiana
D. Invited Speaker, American Society of Investigative Pathology Companion Meeting at the United States and Canadian Academy of Pathology, "NCI Director's Challenge and Cancer Genome Anatomy Project: Interface with the Practicing Pathologist", Washington, D.C.
E. Invited Speaker, "Gene Expression Profiling of Endocrine Tumors", 6th Annual Affymetrix User Group Meeting, Chicago, Illinois

VI. PUBLICATIONS:

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

1. Beer DG, Kardia SLR, Huang C-C, Giordano TJ, Levin AL, Misek DE, Lin L, Chen G, Gharib TG, Thomas DG, Lizyness ML, Kuick R, Hayasaka S, Taylor JMG, Iannettoni MD, Orringer MB, Hanash S. Gene expression profiles predict survival of patients lung adenocarcinoma. Nat Med 2002:8;816-824.
2. Schwatrz DR, Kardia SLR, Shedden KA, Kuick R, Michailidis G, Taylor JMG, Misek DE, Wu R, Zhai Y, Darrah DM, Reed H, Ellenson LH, Giordano TJ, Hanash SM, Cho KR. Gene expression in ovarian cancer reflects both morphology and biological behavior, distinguishing clear cell from other poor-prognosis ovarian carcinomas. Cancer Res 2002:62;4722-4729.
3. Gharib TG, Chen G, Wang H, Huang C-C, Prescott MS, Misek DE, Thomas DG, Giordano TJ, Taylor JMG, Kardia S, Yee J, Orringer MB, Hanash S, Beer DG. Proteomic analysis of cytokeratin isoforms uncovers association with survival in lung adenocarcinoma. Neoplasia 2002:4;440-448.
4. Misek DE, Chang CL, Kuick R, Hinderer R, Giordano TJ, Beer DG, Hanash SM. Transforming properties of a Q18E mutation of the microtubule regulator Op18. Cancer Cell 2002:2;217-228.

5. Moran CJ, Arenberg DA, Huang CC, Giordano TJ, Thomas DG, Misek DE, Chen G, Iannettoni MD, Orringer MB, Hanash S, Beer DG. RANTES expression is a predictor of survival in stage I lung adenocarcinomas. Clin Cancer Res 2002:8;3803-3812.
6. Richards, ML, Gauger PG, Thompson W, Kloos RG, Giordano TJ. Pitfalls in the surgical treatment of insulinoma. Surgery 2002: 132;1040-1049.
7. Giordano TJ, Thomas DT, Kuick R, Lizyness M, Misek DE, Smith A, Sanders D, Aljundi RT, Gauger P, Thompson N, Taylor JMG, Hanash S. Distinct transcriptional profiles of adrenocortical tumors uncovered by DNA microarray analysis. Am J Pathol 2003:162;521-531.
8. Chen G, Wang H, Gharib TG, Huang CC, Thomas DG, Wang H, Shedden KA, Taylor JMG, Kardia SL, Misek DE, Giordano TJ, Iannettonni MD, Orringer MB, Hanash SM, Beer DG. Overexpression of oncoprotein 18 correlates with poor differentiation in lung adenocarcinomas. Mol Cell Proteomics 2003:2;107-116.
9. Chen G, Gharib TG, Thomas DG, Huang CC, Misek DE, Kuick RD, Giordano TJ, Iannettoni MD, Orringer MB, Hanash SM, Beer DG. Proteomic analysis of eIF-5A in lung adenocarcinomas. Proteomics 2003:3;496-504.
10. Logdson CD, Simeone DM, Binkely C, Arumugam T, Greenson JK, Giordano TJ, Misek DE, Kuick R, Hanash S. Molecular profiling of pancreatic adenocarcinoma and chronic pancreatitis identified multiple gene differentially regulated in pancreatic cancer. Cancer Res 2003:63;2649-2657.
11. Ferrara N, Frantz G, LeCouter J, Dillard-Telm L, Pham T, Draksharapu A, Giordano T, Peale F. Differential expression of the angiogenic factor genes VEGF and EG-VEGF in normal and polycystic human ovaries. Am J Pathol 2003:162;1881-1893.
12. Miller CT, Chen G, Gharib TG, Wang H, Thomas DG, Misek DE, Giordano TJ, Yee J, Orringer MB, Hanash SM, Beer DG. Increased c-crk proto-oncogene expression is associated with an aggressive phenotype in lung adenocarcinomas. Oncogene.
13. Beuschlein F, Looyenga BD, Reincke M, Giordano TJ, Hammer GD. Clinical impact of recent advances in the biology of adrenocortical cancer. Endocrinologist.
14. Richards ML, Thompson NW, Giordano TJ. Regression of type II carcinoids in MEN1 patients with ZES after surgical excision of all gastrinomas.
15. Schmalbach CE, Chepeha DB, Giordano TJ, Rubin MA, Teknos TN, Bradford CR, Wolf GT, Kuick R, Misek DE, Trask DK, Hanash S: Molecular Profiling Identifies Genes Associated with Metastatic Oral Cavity/Pharynx Squamous Cell Carcinoma. Arch Otolaryngol Head Neck Surg

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Chen G, Gharib T, Wang H, Huang C-C, Kuick R, Thomas D, Shedden KA, Misek DE, Taylor JMG, Giordano TJ, Kardia SLR, Iannettoni MD, Yee P, Hogg PJ, Orringer MB, Hanash SM, Beer DG. Proteins and pathways associated with poor survival in lung adenocarcinoma.
2. Lin J, Raoof DA, Thomas D, Greenson JK, Giordano TJ, Robinson GS, Barve RA, Orringer MB, Beer DG. L-type amino acid transporter-1 overexpression mediates uptake of melphalan in Barrett's adenocarcinoma.
3. Zahng L. Fu Z., Binkley C, Giordano TJ, Burant CF, Logsdon CD, Simeone DM. Raf kinase inhibitory protein (RKIP) inhibits beta cell proliferation.
4. 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.

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

1. Giordano T, Thomas D, Misek D, Lizyness M, Kuick R, Sanders D, Shioda T, Hanash S. Up-regulation of CITED1 in papillary carcinoma: Discovery via gene expression profiling and validation by tissue microarray-based immunohistochemistry. Presented as an Oral Abstract at the 2002 American Thyroid Association.
2. Giordano TJ, Thomas DT, Kuick R, Lizyness M, Misek DE, Smith A, Sanders D, Gauger P, Thompson N, Taylor JMG, Hanash S. Distinct molecular profiles of adrenocortical tumors uncovered by DNA microarray analysis. Presented at the November NCI Director's Challenge PI Meeting, Bethesda, Maryland.
3. Moran CJ, Arenberg DA, Huang C-C, Giordano TJ, Thomas DG, Misek DE, Chen G, Iannettoni MD, Hanash S, Beer DG. RANTES expression is a predictor of survival in stage I lung adenocarcinomas. Presented at the November NCI Director's Challenge PI Meeting, Bethesda, Maryland.
4. Shedden K, Giordano T, Taylor J, Kuick R, Cho K, Fearon E, Beer D, Hanash B. Accurate prediction of tissue of origin from gene expression data utilizing pathologists knowledge and simple classifiers. Presented at the November NCI Director's Challenge PI Meeting, Bethesda, Maryland.
5. Golembeski C, Thomas D, Lizyness M, Sanders D, Smith A, Misek D, Kuick R, Hanash S, Giordano T. Evaluation of galectin-3 as a marker of thyroid malignancy using DNA microarrays and tissue array immunohistochemistry. Presented at the 2003 United States and Canadian Academy of Pathology.
6. Smith L, Thomas D, Sanders D, Lizyness M, Smith A, Misek D, Kuick R, Hanash S, Shulkin B, Giordano T. Alpha-internexin, a novel marker of pheochromoctyoma: discovery by DNA microarray analysis and validation by tissue array immunohistochemistry. Presented at the 2003 United States and Canadian Academy of Pathology.
7. Giordano T, Lizyness M, Kuick R, Sanders D, Thomas D, Misek D, Smith A, Hanash S, Shulkin B. Distinct transcriptional profiles of metastasizing and non-metastasizing adrenal and extra-adrenal paragangliomas uncovered by DNA microarray analysis. Presented at the 2003 United States and Canadian Academy of Pathology.
8. Aljundi RT, Thomas D, Lizyness M, Sanders D, Kuick R, Misek D, Hanash S, Shioda T, Giordano T. CITED1, a potential new marker for papillary thyroid carcinoma: discovery by DNA microarray analysis and evaluation by tissue microarray immunohistochemistry. Presented at the 2003 United States and Canadian Academy of Pathology.
9. Hughes DPM, Thomas DG, Giordano TJ, Baker LH, McDonagh KT. Expression of EGFR family members in a panel of primary osteosarcoma cell lines. Proceedings of the AACR, Vol 44, March 2003.
10. Leu K, Thomas DG, Biermann S, Giordano T, Trent J, Pollock R, Baker L. A rationale for combination molecular targeted therapy in synovial sarcoma. Proceedings of the AACR, Vol 44, March 2003.
11. Lin J, Thomas DG, Giordano TJ, Robinson GS, Barve RA, Orringer MB, Beer DG. Melanoma-asscociated antigens 3 and 10: Potential targets for immunotherapy in Barrett's adenocarcinoma. Proceedings of the AACR, Vol 44, March 2003.

12. Chen G, Gharib TG, Thomas DG, Huang C-C, Misek DE, Giordano TJ, Iannettoni MD, Orringer MB, Hanash SM, Beer DG. Proteomic analysis of OP18 and eIF-5A in lung adenocarcinomas. Proceedings of the AACR, Vol 44, March 2003.
13. Thomas DG, Biermann S, Giordano TJ, Baker L. Telomerase reverse transcriptase (hTRT) expression in mesenchymal tumors. Proceedings of the AACR, Vol 44, March 2003.

DAVID GORDON, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

A. Supervision of Autopsies (~six weeks).
B. Cardiovascular Pathology Consultation (Autopsy Service and Surgical Pathology).
C. Cardiovascular Surgical Pathology (Heart biopsies +).

II. TEACHING ACTIVITIES:

A. Laboratory Instructor for Pathology Laboratories for M2 curriculum
B. Cardiovascular Pathology Lectures for M2 Cardiovascular Sequence
C. Cardiovascular Pathology Lectures for Dental and Graduate Student Pathology Course.
D. Conference organizer for monthly Pediatric Cardiology/Pathology Conference

III. RESEARCH ACTIVITIES:

A. Effects of ultrasound on heart muscle (Cardiology project)
B. Morphology Core Director: NIH PO1 HL57346 "Molecular Genetics Coagulation Disorders" 7/1/03 – 6-30-08. ; PI: D. Ginsburg
C. Member, Cardiovascular Center

SPONSORED SUPPORT:

A. Morphology Core Director: NIH PO1 HL57346 "Molecular Genetics Coagulation Disorders" 7/1/03 – 6-30-08. ; PI: D. Ginsburg

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

MEDICAL SCHOOL/HOSPITAL:

A. Assistant Dean for Diversity and Career Development (50% effort). This position coordinates the Medical School's diversity efforts, with programs targeting pre-medical students, medical students, house officers, faculty, and minority health/health disparities research.

V. PUBLICATIONS:

BOOKS AND CHAPTERS IN BOOKS:

1. **Gordon D**. "Transplant Arteriosclerosis". In: Topol, Fuster and Nabel (eds). Atherosclerosis and Coronary Artery Disease, 2004.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

A. General surgical pathology – Twenty-three weeks.
B. Gastrointestinal and hepatic pathology consultation services - four months.
C. Liver transplant pathology - 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
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, 2002.
   3. Gastrointestinal and hepatic pathology tutoring - four months.
   4. Four consultation conferences.
D. Interdepartmental:
   1. Liver biopsy conference - one hour per month.
   2. Multidisciplinary GI tumor board - 1hour every other week.
   3. GI pathology teaching sessions with GI fellows - one hour/month.
   4. GI and Liver path teaching to GI and transplant fellows – 2 hours/year

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Co-Investigator R01CA81488-01 ($4,547,772) "Molecular Epidemiology of Colorectal Cancer", 20% Salary Support, years 1-4, 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 Small cell carcinomas of the colon with GI Study Group
B. Study of fatty liver and steatohepatitis with Hari Conjeevaram in Division of Gastroenterogy..
C. NIH study of HCV with Anna Lok in Division of Gastroenterology.
D. NIH study of the Molecular Epidemiology of Colon Cancer in Israel.
E. Study of molecular classification of tumors with Stephen Gruber and Thomas Giordano
F. Study of molecular genetic changes in pancreas cancer with Diane Simione and Craig Logsdon
G. Study of Yersinia and Crohn's disease with Laura Lamps at the University of Arkansas.
H. Study of UC dysplasia grading with GI Study Group.
I. Study of Neuroendocrine Tumors of the Gut with Murray Resnick, M.D. Haifa, Israel
J. Study of Focal Active Colitis in children with Wei Xin, M.D.
K. Study of interval appendectomy specimens with Guangming Guo, M.D.
L. Study of Focally enhanced gastritis with Wei Xin, M.D.

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, 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. Past President, Gastrointestinal Pathology Society.
K. Editorial Board member, The Online Journal of Digestive Diseases
L. American Board of Pathology, Test Question Committee
M. Reviewer, American Journal of Gastroenterology
N. Reviewer, British Journal of Cancer
O. Reviewer, Journal of Clinical Oncology
P. Vogel Award Committee, USCAP

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Speaker, USCAP short course on GI pathology, Washington D.C., March 2003.
2. Faculty Member, ASCP Workshop – Surgical Pathology of the Gastrointestinal Tract, Chicago, Illinois, May 2003.
3. Invited Speaker, GI Pathology short course, International Academy of Pathology, Amsterdam, Netherlands, Oct. 2002.
4. Invited Speaker, GI Pathology slide seminar, International Academy of Pathology, Amsterdam, Netherlands, Oct. 2002.
5. Co-chair, GI Pathology slide seminar, International Academy of Pathology, Amsterdam, Netherlands, Oct. 2002

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Tzafra C, Herzog Y, Brodzky A, Greenson JK, Eldar S, Gluzman-Poltorak Z, Neufeld G, Resnick MB. Neuropilin-2 is a novel marker expressed in pancreatic islet cells and endocrine pancreatic tumors. Journal of Pathology 198:77-82, 2002.
2. Gruber SB, Ellis NA, Rennert G, Offit K, Scott KK, Almog R, Kolachana P, Bonner JD, Kirchoff T, Tomsho LP, Khedoudja N, Pierce H, Low M, Satagopan J, Rennert H, Huang H, Greenson JK, Groden J, Rappaport B, Shia J, Johnson S, Gregsen PK, Harris CC, Boyd J. *BLM* Heterozygosity and the Risk of Colorectal Cancer . Science 297: 2013, 2002.
3. Washington K, Greenson JK, Montgomery E, Shyr Y, Crissinger K, Polk DB, Barnard J, Lauwers GY. Histopathology of Ulcerative Colitis in Initial Rectal Biopsy in Children. Am J Surg Pathol 26:1441-1449, 2002.
4. Fontana RJ, Hamidullah H, Nghiem H, Greenson JK, Hussain H, Marrero J, Rudich S, McClure LA, Arenas J. Percutaneous Radiofrequency Thermal Ablation of
5. Hepatocellular Carcinoma: A Safe and Effective Bridge to Liver Transplantation. Liver Transpl 8:1165-1174, 2002.
6. Lamps LW, Madhusudhan KT, Havens JM, Greenson JK, Bronner MP, Chiles MC, Dean PJ, Scott MA. Pathogenic Yersinia DNA is Detected in Bowel and Mesenteric Lymph Nodes from Patients with Crohn's Disease. Am J Surg Pathol 27:220-227, 2003.
7. Greenson JK. Gastrointestinal stromal tumors and other mesenchymal lesions of the gut. Modern Pathol 16:366-375, 2003.
8. Greenson JK, Bonner JD, Ben-Yzhak O, Cohen HI, Miselevich I, Resnick MB, Trougouboff P, Tomsho LD, Kim E, Low M, Almog R, Rennert G, Gruber SB. Phenotype of Microsatellite Unstable Colorectal Carcinomas: Well-differentiated and focally mucinous tumors and the absence of dirty necrosis correlate with microsatellite instability. Am J Surg Pathol 27:563-570, 2003.
9. Logsdon CD, Simeone DM, Binkley C, Arumugam T, Greenson JK, Giordano TJ, Misek DE, Kuick R, Hanash S. Molecular Profiling of Pancreatic Adenocarcinoma and Chronic Pancreatitis Identifies Multiple Genes Differentially Regulated in Pancreatic Cancer. Cancer Research 63:2649-2657, 2003.

10. Xin W, Brown PI, Greenson JK. The clinical significance of focal active colitis in pediatric patients. Accepted to Am J Surg Pathol.
11. Guo G, Greenson JK. Histopathololgy of interval appendectomy specimens: Strong association with granulomatous and xanthogranulomatous appendicitis. Accepted to Am J Surg Pathol.
12. Ammori JB, Colletti LM, Zalupski MM, Eckhauser FE, Greenson JK, Dimick J,
13. Lawrence TS, McGinn CJ. Surgical resection following radiation therapy with concurrent gemcitabine in patients with previously unresectable adenocarcinoma of the pancreas. Accepted to Annals of Surgery.
11. Wai CT, Greenson JK, Fontana R, Kalbfleisch J, Marrero J, Conjeevaram H, Lok A. A simple novel non-invasive index is useful in predicting both significant fibrosis and cirrhosis in chronic hepatitis C (chc) patients. Accepted to Hepatology.
14. Akintola-Ogunremi O, Pfeifer JD, Tan BR, Zhu X, Hart J, Goldblum JR, Burgart L, Lauwers LY, Montgomery E, Lewin D, Washington K, Bronner M, Xiao S-Y, Greenson JK, et al. Protein expression and gene mutation of c-kit in colonic neuroendocrine carcinomas. Accepted to American Journal of Surgical Pathology.
15. Ogura Y, Lala S, Xin W, Smith E, Dowds TA1. Chen FF,
16. Zimmermann E, Tretiakova M, Cho JH, Hart J, Greenson JK, Keshav S
17. Nuñez G. Expression of NOD2 in Paneth Cells: A Possible Link to Crohn's Ileitis. Accepted to Gut.

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Lauwers GY, Goldblum JR, Burgart LJ, Bhan AK, Vauthey JN, **Greenson JK**. Expression Of Neurotrophin Receptors And Ret Protein In Duodenal Gangliocytic Paraganglioma: A Study Of 12 Cases. Submitted to Am J Surg Pathol.
2. Scheiman JM, **Greenson JK**, Lee, J , Cryer B. Impact of COX-2 Specific Inhibition on Human Helicobacter Pylori (HP) Gastritis: Implications for Ulcerogenesis and Carcinogenesis. Submitted to Gut
3. Askari FK, **Greenson JK**, Dick RD, Johnson VD, Brewer G. Treatment of Wilson's Disease with Zinc XVIII. Initial Treatment of the Hepatic Decompensation Presentation with Trientine and Zinc. Submitted to Journal of Laboratory and Clinical Medicine

BOOKS/CHAPTERS IN BOOKS:

1. Inflammatory Diseases of the Colon, in Surgical Pathology of the Gastrointestinal Tract, Liver, Biliary tract, and Pancreas. Edited by Robert D. Odze, John R. Goldblum, and James Crawford. Harcourt Health Sciences. In Press.
2. Sternberg's Diagnostic Surgical Pathology, Fourth Ed. Edited by Mills SM, Carter D, **Greenson JK**, Oberman HA, Reuter V, and Stoler MH. Lippincott, Williams & Wilkins, Philadelphia, PA. In Press.

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

1. Protein expression and gene mutation of c-kit in colonic neuroendocrine carcinomas. Akintola-Ogunremi O, Pfeifer JD, Tan BR, Zhu X, Hart J, Goldblum JR, Burgart L, Lauwers LY, Montgomery E, Lewin D, Washington K, Bronner M, Xiao S-Y, Greenson JK, et al. Platform presentation at USCAP meeting 2003, Mod Pathol 16:112A, 2003,

2. Sessile serrated colorectal polyp: A multi-institutional incidence study. Batts KP, Burgart LJ, Goldblum JR, Greenson JK, et al. Platform presentation at USCAP meeting 2003, Mod Pathol 16:113A, 2003.
3. Mixed hyperplastic/adenomatous colorectal polyps: A multi-institutional incidence study. Batts KP, Burgart LJ, Goldblum JR, Greenson JK, et al. Poster presentation at USCAP meeting 2003, Mod Pathol 16:114A, 2003.
4. Histopathololgy of interval appendectomy specimens: Strong association with granulomatous and xanthogranulomatous appendicitis. Guo G, Greenson JK. Poster presentation at USCAP meeting 2003, Mod Pathol 16:120A, 2003. Runner-up for resident award for best gastrointestinal pathology presentation.
5. The clinical significance of focal active colitis in pediatric patients. Xin W, Brown PI, Greenson JK. Platform presentation at USCAP meeting 2003, Mod Pathol 16:137A, 2003. Winner of resident award for best gastrointestinal pathology presentation.
6. Pathogenic *Yersinia enterocolitica* DNA is detected in gastrointestinal malakoplakia. Havens JM, Montgomery E, Greenson JK, Scott MA Lamps L. Poster presentation at USCAP meeting 2003, Mod Pathol 16:263A, 2003.

CORY M. HOGABOAM, Ph.D.
ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Graduate Students:
   1. Ph.D. Dissertation Committees, University of Michigan
      a. Claudia Jakubzick (Thesis successfully defended August 22, 2003)
      b. Allison Miller
      c. Betsy Pierce (Graduate Immunology Program)
      d. Tobias Rodriguez (Graduate Immunology Program)
      e. Matt Schaller (Graduate Immunology Program)
   2. Undergraduate Students, University of Michigan
      a. Esther Choi (spring/summer 2003)
   3. PIBS Graduate Student Laboratory Rotations, University of Michigan
      a. Megan Henderson
      b. Brian Moore
      b. Betsy Pierce
   4. Preliminary Examiner for Ph.D. Program, Graduate Immunology Program
      a. Malinda Schaefer
      b. Kelly Seidl
      c. Mike Khodadoust
   5. Formal Teaching, Dept. of Pathology
      a. Pathology 581: Inflammation and Sepsis
      b. Pathology 582: Systemic Inflammatory Responses

B. Postdoctoral Fellows:
   1. Jane Schuh, Ph.D.
   2. Claudia Benjamim, Ph.D.
   3. Traci Ness, Ph.D.
   4. Simona Neff, M.D.
   5. Nora Lin, M.D.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Co-investigator, Monokine gene expression/regulation in lung injury. R01 HL31237 (10%), $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 (15%), $162,578 per annum, 07/01/01 - 06/30/06.
D. Co-investigator, SCF in Liver Repair after Hepatectomy or Toxic Injury. R01 DK58106 (10%), $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 (10%). $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
I. characterized by persistent airway hyperreactivity, inflammation, and remodeling. Almirall Prodesfarma, S.A., $59,000 per annum. 12/01/03-11/31/04
J. 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.

PENDING:

A. Principal Investigator, *Role of CCR7, CCL19 and CCL21 in idiopathic interstitial pneumonia.* R01 HL076615-01 (20%), $225, 000 per annum, 04/01/04-03/31/09

PROJECTS UNDER STUDY:

Role of chemokines in airway remodeling due to allergic airway disease and asthma.
Role of chemokine receptors in airway remodeling due to allergic airway and asthma.
Role of chemokines and chemokine receptors in human interstitial fibrotic disease.
Novel approaches to targeting IL-4 and IL-13 in chronic allergic airway disease.
Role of IL-4 and IL-13 in chronic interstitial fibrotic disease.
Novel approaches to targeting IL-4 and IL-13 in human interstitial fibrotic disease.
Regulation of fibroblast activities during idiopathic interstitial pneumonias.
Role of chemokines and SCF in liver regeneration.
Role of CC chemokines in acute and chronic pulmonary inflammation.

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 (Associate Editor - July 1, 2002 – July 1, 2004)
   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

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:

Center for Scientific Review, ZRG1 IMB (01)
Fellowship (F32) and R15 Review.
NIAID, Division of Extramural Affairs, Scientific Review Program
Special Emphasis Review Panel, RFA AI-03-010 (Innovative Grants on Immune tolerance)

INVITED LECTURES/SEMINARS:

1. '*IL-13 receptor as a unique target in chronic pulmonary disease.*' 35th Brazilian Congress of Pharmacology, Aguas de Lindoia, Brazil. September 21-24, 2003.
2. '*Targeting IL-13 responsive cells in pulmonary disease.*' The 6th World Congress on Inflammation, Vancouver. B.C. August 1-7, 2003.
3. '*Balancing innate and acquired immune events: lessons learned from Aspergillus fumigatus.*' International society for human and animal mycology. San Antonio, TX. May 25-29, 2003.
4. '*Chemokines at the interface between innate and acquired immunity.*' Celgene, San Diego, CA. April 15, 2003.
5. '*Chemokines at the forefront of pulmonary anti-fungal and allergic responses to Aspergillus fumigatus.*' NCI, Fredrick, MD. March 21-22, 2003.

PATENTS

Method of treating allergen-induced airway disease.
University of Michigan and Micromet Inc.
Filed August 15, 2002.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICAITON IN REFERRED JOURNALS.

1. Jakubzick C., Kunkel S.L., Lukacs N.W., Joshi B.H., Puri R.K., Hogaboam C.M. Interleukin-13 fusion cytotoxin arrests Schistosoma mansoni egg-induced pulmonary granuloma formation in mice. Am. J. Pathol., 161(4): 1283-1297, 2002.
2. Oliveira S.H., Taub D.D., Nagel J., Smith R., Hogaboam C.M., Berlin A., Lukacs N.W. Stem cell factor induces eosinophil activation and degranulation: mediator release and gene array analysis. Blood, 100(13): 4291-4297, 2002.
3. Hogaboam C.M., Blease K., Schuh J.M. Cytokines and chemokines in allergic
4. bronchopulmonary aspergillosis (ABPA) and experimental Aspergillus-induced allergic airway or asthmatic disease. Front. Biosci. , 8(1): E147-E156, 2003.
5. Simpson K.J., Henderson N., Bone-Larson C.L., Lukacs N.W., Hogaboam C.M., Kunkel S.L. Chemokines in the pathogenesis of liver disease: so many players with poorly defined roles. Clin Sci (Lond). Jan; 104(1): 47-63, 2003.
6. Simpson K.J., Hogaboam C.M., Kunkel S.L. Harrison D.J., Bone-Larson C.L., Lukacs N.W. Stem cell factor attenuates liver damage in a murine model of acetaminophen-induced hepatic injury. Lab Invest. Feb; 83(2): 199-206, 2003.
7. Raman K., Kaplan M.H., Hogaboam C.M., Berlin A., Lukacs N.W. STAT4 Signal pathways regulate inflammation and airway physiology changes in allergic airway inflammation locally via alteration of chemokines. J. Immunol., Apr 1; 170(7): 3859-65, 2003.
8. Jakubzick C., Choi E.S., Kunkel S.L., Joshi B.H., Puri R.K., Hogaboam C.M. Impact of interleukin-13-responsiveness on the synthetic and proliferative properties of Th1- and Th2- type pulmonary granuloma fibroblasts. Am. J. Pathol., 162: 1475-1486, 2003.
9. Ajuebor M.N., Hogaboam C.M., Le T., Swain M.G. CCL2/MCP-1 directly inhibits NKT cell IL-4 production and is hepatoprotective during T cell-mediated hepatitis in the mouse. J. Immunol., 170: 5252-5259, 2003.
10. Lukacs N.W., Miller A.L., Hogaboam C.M. Chemokine receptors in asthma: searching for the correct immune targets. J. Immunol. 171: 11-15, 2003.
11. Ren X., Carpenter A., Hogaboam C.M., Colletti L.M. Mitogenic properties of endogenous and pharmacological doses of macrophage inflammatory protein-2 after 70% hepatectomy in the mouse. Am J Pathol. 163(2): 563-70, 2003.
12. Jakubzick C., Choi E.S., Joshi B.H., Keane M.P., Kunkel S.L., Puri R.K., Hogaboam C.M. Therapeutic attenuation of pulmonary fibrosis via targeting of IL-4 and IL-13 responsive cells. J. Immunol., 171: 2684-2693, 2003.
13. Kaminski N., Belperio J.A., Bitterman P.B., Chen L., Chensue S.W., Choi A.M., Dacic S., Dauber J.H., Du Bois R.M., Enghild J.J., Fattman C.L., Grutters J.C., Haegens A., Hanford L.E., Heintz N., Henson P.M., Hogaboam C., Kagan V.E., Keane M.P., Kunkel S.L., Land S., Loyd J.E., Lukacs N., MacPherson M., Manning B., Manning N., Martinelli M., Moller D.R., Morse D., Mossman B., Noble P.W., Nowak N., Oury T.D., Pardo A., Perez A., Petty T.L., Phan S.H., Ramos-Nino M.E., Ray P., Rogers R.M., Sato H.I., Scapoli L., Schaefer L.M., Selman M., Stern M., Strollo D.C., Tyurin V.A., Valnickova Z., Welsh K.I., Witzmann F.A., Yousem S.A., Strieter

R.M. Idiopathic pulmonary fibrosis. Am. J. Respir. Cell Mol. Biol. Sep; 29(3 Suppl 2): S1-S105, 2003.

14. Kunkel S.L., Chensue S.W., Lukacs N., Hogaboam C. The type 1/type 2-cytokine phenotype serves as a paradigm for the progression of chronic lung diseases and remodeling. Am. J. Respir. Cell Mol. Biol. S63-S66, 2003.
15. Stevens D.A. and participants in the Cystic Fibrosis Foundation Consensus Conference. Allergic Bronchopulmonary Aspergillosis in cystic fibrosis – State of the Art: Cystic Fibrosis Foundation Consensus Conference. Clin. Infect. Dis., Oct 1; 37 Suppl 3: S225-64, 2003.
16. Ness T.L., Hogaboam C.M., Strieter R.M., Kunkel S.L. Immunomodulatory role of CXR2 during experimental septic peritonitis. J. Immunol., in press.
17. Benjamim C. F., Hogaboam C.M., Lukacs N.W., Kunkel S.L. Septic mice are susceptible to Aspergillosis. Am. J. Pathol., in press.
18. Benjamim C. F., Hogaboam C.M., Kunkel S.L. Long-term pulmonary consequences of severe sepsis. J. Leuk. Biol., in press.
19. Hogaboam C.M., Ezekowitz R.A.B., Schuh J.M., Kunkel S.L. Diminished airway hyperresponsiveness but not airway remodeling in mannose-binding-lectin-A-deficient mice during chronic fungal asthma. J. Leuk. Biol., in press.
20. Neff S.B., Neff T.A., Kunkel S.L., Hogaboam C.M. Alterations in cytokine/chemokine expression during organ-to-organ communication established via acetaminophen-induced toxicity. Exp. Mol. Pathol., in press.
21. Ren X., Hogaboam C.M., Colletti L.M. Stem cell factor restores hepatocyte proliferation in IL-6 knockout mice following 70% hepatectomy. J. Clin. Invest., in press.
22. Schuh J.M., Jakubzick C., Blease K., Bruhl H., Xing Z., Mack M., Hogaboam C.M. Therapeutic intrapulmonary targeting of RANTES/CCL5-responsive cells prevents chronic fungal asthma. Eur. J. Immunol., in press.
23. Ajuebor M.N., Zagorski J., Kunkel S.L., Strieter R.M., Hogaboam C.M. Contrasting roles for CXCR2 during experimental colitis. Exp. Mol. Pathol., in press.
24. Kolodsick, J.E., Toews G.B., Jakubzick C., Hogaboam C.M., Moore T.A., McKenzie A., Wilke C.A., Chrisman C.J., Moore B.B. Protection from FITC-induced fibrosis in IL-13 deficient, but not IL-4 deficient mice: IL-13 mediates its profibrotic effects via direct activation of collagen synthesis in myofibroblasts. J. Immunol., in press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Ajuebor M.N., Hogaboam C.M., Le T., Proudfoot A.E.I., Swain M.G. CCL3/MIP-1α is pro-inflammatory in murine T cell-mediated hepatitis by recruiting CCR1-expressing IFN-γ producing CD4 (+) T cells to the liver. Gastroenterology, submitted.
2. Hildebrandt G.C., Duffner U.A., Olkiewicz K.M., Corrion L.A., Willmarth N.E., Williams D.L., Clouthier S., Hogaboam C.M., Reddy P.R., Moore B.B., Liu C., Yanik G., Cooke K.R. A critical role for CCR2: MCP-1 interactions in the development of idiopathic pneumonia syndrome after allogeneic bone marrow transplantation. Blood, submitted.
3. Ajuebor M.N., Proudfoot A.E.I., Kunkel S.L., Hogaboam C.M. The role of CCL3/MIP-1α in the pathogenesis of acute colitis. Gut, submitted.
4. Ramos C.D.L., Canetti C.A., Trindade de Souto J., Santana da Silva J., Hogaboam C.M. Cunha F.Q. MIP-1α/CCL3 acting on the CCR1 receptor mediates neutrophil migration in immune inflammation via sequential release of TNF-α and LTB_4. J. Immunol., submitted.

5. Jakubzick C., Choi E.S., 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. Augmented pulmonary IL-4 and IL-13 receptor subunit expression in Idiopathic Interstitial Pneumonia. J. Clin. Pathol., submitted.
6. Jakubzick C., Choi E.S., 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. Human pulmonary fibroblasts exhibit altered IL-4 and IL-13 receptor subunit expression in Idiopathic Interstitial Pneumonia. Am. J. Resp. Crit. Care Med., submitted.
7. *Jakubzick C., Choi E.S., 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 CCL7 expression in usual interstitial pneumonia. Am. J. Resp. Crit. Care Med., submitted.*

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

CHAPTERS:

1. Kunkel S.L., Lukacs N.W., Chensue S.W., Hogaboam C.M. Cytokine phenotypes and the progression of chronic pulmonary fibrosis. In: Lung Biology in Health and Disease Series. Idiopathic Pulmonary Fibrosis. Ed: Marcel Dekker, Inc., New York. April 2002.
2. Chensue S.W., Matsukawa A., Hogaboam C.M., Kunkel S.L. Chemokines in granulomatous lung inflammation. In: Chemokines in the Lung. Ed: R.M. Strieter, S.L. Kunkel, T.J. Standiford. Marcel Dekker, New York. 2002.
3. Hogaboam C.M., Schuh J.M., John A.E., Lukacs N.W. The role of chemokines in asthmatic airway responses. In: Chemokines in the Lung. Ed: R.M. Strieter, S.L. Kunkel, T.J. Standiford. Marcel Dekker, New York. 2002.
4. Hogaboam C.M., Kunkel S.L. The role of chemokines in linking innate and adaptive immunity. In: Innate Immunity. Ed: R.A.B. Ezekowitz, J. A. Hoffman. Humana Press, Totowa, NJ. 2002.
5. Schuh J.M., Kunkel S.L., Hogaboam, C.M. Mice knockouts for chemokines and chemokine receptors. In: Contemporary Immunology: Cytokine Knockouts. 2nd Edition Ed: G. Fantuzzi. Humana Press, Totowa, NJ. Chapter 19, pages 323-345, 2003.
6. Kunkel S.L., Lukacs N.W., Chensue S.W., Hogaboam C.M.
7. Cytokine phenotypes and the progression of chronic pulmonary fibrosis. In: Idiopathic pulmonary fibrosis. Ed: J. Lynch III Marcel Dekker, New York. In press, 2003.

BOOK REVIEWS:

1. M. Breitenbach, R. Crameri, and S.B. Lehrer. Fungal Allergy and Pathogenicity. Karger Publishers, Farmington, CT, USA, 2002. 310 pp.

ABSTRASTS:

1. Moore B.B., Wilke C.A., Thannickal V.J., Hogaboam C.M., Toews G.B., CCR2-mediated recruitment and activation of fibrocytes following acute lung injury. Am. J. Resp. Crit. Care Med. 167(7): A346, 2003.
2. Jakubzick C.J., Kunkel S.L., Martinez F.J., Flaherty K.R., Puri R.K., Toews G.B., Colby T.V., Travis W.D., Lynch III J.P., Hogaboam C.M., Augmented pulmonary IL-4 and IL-13 receptor

subunit expression in idiopathic interstitial pneumonia. Am. J. Resp. Crit. Care Med. 167(7): A840, 2003.

3. Benjamim C.F., Hogaboam C.M., Lukacs N.W., Kunkel S.L., Long-term immunosuppression to secondary fungal infection in septic mice. FASEB J., 17(5): A405.4, 2003.
4. Ness T., Matsukawa A., Hogaboam C.M., Kunkel S.L., The immunoregulatory role of TARC in the innate immune response to sepsis. FASEB J. 17(5): A762.10, 2003.
5. Jakubzick C., Choi E.S., Joshi B.H., Keane M.P., Kunkel S.L., Puri R.K., Hogaboam C.M., Reversal of experimental interstitial pulmonary fibrosis via targeting of IL-4 and IL-13 responsive cells. FASEB J. 17(5): A407.18, 2003.
6. Ajuebor M.N., Hogaboam C.M., Le T., Swain M.G., CCL3/MIP-1α, a crucial chemokine in the pathogenesis of T cell-mediated hepatitis in mice. FASEB J., 17(5): A162.10, 2003.
7. Schuh J.M., Thammavongsa V., Hogaboam C.M., The role of C10/CCL6 in a murine model of chronic fungal asthma. FASEB J., 17(5): A407.20, 2003.
8. Khan W.I., Varghese A.K., Blennerhassett P., Huang X., Gauldie J., Hogaboam C.M., Collins S.M., MCP-1 gene transfer enhances intestinal muscle contractility during nematode infection. Gastroenterology, 2003.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

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, "Nanomolecule-Based Agents for Pathogen Countermeasure", with James Baker, Allergy, 03/01/97 – 02/28/01, Dept of Defense.
D. Co-Investigator, "A New Approach to Treat Lupus Nephritis", with Gary Glick, Chemistry. National Institutes of Health, 02/22/00 – 02/21/04.
E. Principal Investigator, "Mechanisms of Vasculitis", Pfizer, Inc., 5/02 – 5/04
F. 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.
G. Co-Investigator with James Baker, "Nanoemulsions for Decontamination". DOD. Budget $3,100,000/year. 10/01/03.

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 aspiration pneumonitis.
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. Renal Pathology Conference - Biweekly.
C. Space Utilization Committee.
D. 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

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Sawada, S., Matsuda, Younger, J., Johnson, K.J., Bartlett, Hirschl, R.B.: Effects of partial liquid ventilation on unilateral lung injury in dogs. Chest 2002 Feb;121(2):566-72.
2. Reickert, C.A., Rich, P.B., Crotti, S., Mahler, S.A., Awad, S.S., Lynch, W.R., Johnson, K.J., Hirschl, R.B. Critical Care Medicine. 2002. 30:182-9.
3. Blatt, N.B., Bednarski, J.J., Warner, R.E., Johnson,K.J., Opipari, A.W. Jr. Glick, G,D: Benzodiazepine-induced superoxide signals B cell apoptosis: Mechanisitic insight and potential therapeutic utility. JCI, 2002. 110 (8):1123-32.
4. Bednarski, J.J., Warner, R.E., Rao,T., Leonetti, F., Yung, R., Richardson, B.C., Johnson, K.J., Ellman, J.A., Opipari, A.W., Jr. Glick, G.D. Attenuation of autoimmune disease in Fas-deficient mice by treatment with a cytotoxic benzodiazepine. Arthritis and Rheumatism. 2003. 148(3):757-66.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Warner, R.L., Lukacs, N., Shapiro, S.D., Varani, J., Johnson, K.J.: Role of metalloelastase in a model of allergic lung responses induced by cockroach allergen. Submitted for publication.
2. Warner, R.L., Younkin, E., Johnson, K.J., Varani, J.: Matrix metalloproteinase production by lung parenchymal cells. Submitted for publication.
3. Warner, R.L., Winter, H.C., Varani, J., Goldstein, I.J., Johnson, K.J.: Marasmius Oreades lectin induces kidney injury as a model of glomerular microangiopathic hemolytic anemia. Submitted for publication.
4. Kershaw, D.B., Bunchman, T.E., Johnson, K.J., Sedman, A.B., Kelsch, R.C.: Crescentic glomerulonephritis with subsequent hemolytic uremic syndrome in a child. Submitted for publication.
5. Varani, J., Hirschl, R., Dame, M. and Johnson, K.: Neutrophil infiltration is reduced during liquid ventilation: II. In Vitro analysis. Submitted for publication to Amer. J. Respiratory & Critical Care Medicine.
6. Sawyer, R.G., Chenault, R.H., Merion, R.M., Johnson, K.J., Kuta, E.G., and Hebert, C.A.: Antibody to interleukin-8 decreases systemic and pulmonary sequelae of sepsis: evidence for early chemokine regulation of cytokine activity in a porcine model of bacteremia. Submitted for publication.
7. J.D., Myc, A., Cao, Z., Johnson, K.J., Wright D.C., Brisker, J., and Baker, J.R.: Prevention of influenza A virus infection by non-ionic surfactant nanoemulsions in a murine model. Submitted for publication.
8. Heard, P.L., Bleavins, M.R., Johnson, K.J., Shi, M. and de la Iglesia, F.A.: Induction of Alanine Aminotransferase Gene Expression by Tacrine in Hep G2 Cells. Submitted for publication.

BOOKS AND CHAPTERS IN BOOKS:

1. Warren, J.S., Johnson, K.J. and Ward, P.A.: Phagocytes and reactive oxygen substances as mediators of acute lung injury, in, Hyers, T. (ed), Diffuse Alveolar Damage and Respiratory Failure, Futura Press, New York, In Press.
2. Till, G.O., Johnson, K.J. and Ward, P.A.: Oxygen free radicals in inflammation, in, Messmer, K. and Hammersen, F. (eds), Prog. Appl. Microcirc., Volume 9, Karger, Basel, In Press.
3. Ward, P.A., Warren, J.S. and Johnson, K.J.: Oxygen radicals, inflammation and tissue injury, in, Pryor, W. and Godber, S.L. (eds), Free Radical Biology and Medicine, In Press.
4. Varani, J. and Johnson, K.J.: Modulation of endothelial cell injury by all-trans retinoic acid: Role of the anti-inflammatory effects of RA, in, Jesaitis, A. (ed), Molecular basis of oxidative damage by leukocytes. CRC Press, In Press.

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

1. Roffi, C., Butler, A., Dednomdedieu, M., Johnson, K.J., Bleavins, M.: NMR of human biofluids: metabolites quantitation and correlation to metabolic pathways 43rd ENC (Experimental Nuclear Magnetic Resonance Conference), April 2002.
2. Johnson, K.J., Warner, R.L., Varani, J.: Role of stromelysin-1 in experimental acute lung injury. FASEB J. 16(4): A590.456.7, 2002.
3. Warner, R.L., Johnson, K.J., Varani, J.: Role of metalloelastase (MMP-12) in a model of experimental asthma. FASEB J. 16 (4) A590.456.8, 2002.
4. Warner, R.L., Younkin, E., Beltran, L., Johnson, K.J., Varani, J.: Lung parenchymal cells as a source of matrix metalloproteinases in lung inflammation. FASEB J. 16(4) A1207.909.6, 2002.
5. Cibrik, D.M., Johnson, K.J., Delnomdedieu, M.: Visual 3D NMR spectroscopy of urine from renal transplant patient. ATC Meeting, 2003.
6. Rem X,M., Johnson, K.J., Senior, R.M., Shipley, J.M., Carpenter, A., Colletti, L.: MMP-9 is important for hepatic regeneration. American College Surgery. 2003.
7. Warner, R.L., Nerusu, K., Bhavarathula, N., McClintock, S., Johnson, K.J., Varani, J.: Alveolar wall damage and neutrophil transmigration is defective in stromelysin-1-deficient mice. Experimental Biology. 15 (5)866.10. 2003
8. Warner, R.L., McClintock, S., Varani, J., Johnson, K.J.: Macrophage cytokine production is defective in stromelysin-1-deficient mice. Experimental Biology. 15(5). 866.11. 2003.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002- 30 JUNE 2003

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 immune hemolysis
   3. Present lecture on testing for weak D expression.

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 hemolsysis 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 8 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. Residency Training
   1. Provided instruction in immunohematology to six house-officers during their Blood Bank Rotation (over 150 contact hours)
   2. Provided instruction in immunohematology to seven hematology/oncology fellows (28 hours).

H. Current Topics in Blood Banking Conference, Towsley Center for Continuing Medical
I. Current Topics in Blood Banking Conference, Towsley Center for Continuing Medical Education:
J. Program Director – Planned and coordinated the June, 2003 Current Topics in Blood Banking Symposium and Preconference Workshops 11.5 hours
K. Presented Workshop entitled: Are we done yet? (1 5 contact hours)
L. Presented Workshop entitled: So you want to implement an electronic crossmatch? (1 contact hour)
M. Presented talk entitled: The test for weak D: why are you still doing it?
N. Moderated morning session on Transfusion Medicine topics

III. RESEARCH ACTIVITIES:

A. Judd WJ, Dake LR. Enzyme tests using anti-IgG gels. Vox Sang 2002;83(Suppl 2):154.
B. Cooling L, Gu Y, Judd WJ. A missense mutation in β3GalT5, the glycosyltransferase responsible for galactosylglobosie and Lewis c synthesase, may be associated with the LKE-weak phenotype in African Americans. Transfusion 2002;42(S):9.
C. Judd WJ, Butch S. Repeat antibody identification studies, how much is enough? Transfusion 2002;42(S):20.
D. Judd WJ, Moulds M, Schlanser G. Reactivity of FDA-approved monoclonal anti-D reagents with partial D RBCs. Transfusion 2002;42(S):20.
E. Afenyi-Annan AN, Judd WJ. Cefotetan induced immune-mediated hemolysis complicated by thrombocytopenia: alloimmune or thrombotic? Transfusion 2002;42(S):46.
F. Boonenberg C, Dake LR, Butch S, Judd WJ. Effective removal of isohemagglutinins from AS-3 Red Blood Cells for use in ABO incompatible heart transplants. Transfusion 2002;42(S):52.
G. Dake LR, Judd WJ. Weak D testing DAT-positive infants born to Rh-negative women in cases of fetal-maternal ABO incompatibility. Transfusion 2002;42(S):108.
H. Lectin studies, with Irwin Goldstein, PhD.
I. Studies on cefotetan-treated red cells with Robertson Davenport, MD.
J. Principal Investigator, field trial on automated blood typing system (Ortho Clinical Diagnostics).

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. Annual Meeting Program Committee.
   2. Specialist in Blood Banking Lecture Series Committee

B. American Association of Blood Banks:
   1. Scientific Abstract Review Committee.
   2. Editorial Board, Transfusion.
   3. Editorial Board, Immunohematology

C. Reviewer of articles submitted for publication in Transfusion, Immunohematology, Transfusion Medicine and Vox Sanguinus.

D. International Society of Blood Transfusion
   1. Member, WHO Committee on Blood Group Nomenclature

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES:

1. Where have all the lectins gone? Annual Meeting of the Michigan Association of Blood Banks, Detroit, MI, September 2002.
2. Management of the positive DAT. Annual Meeting of the Indiana Association of Blood Banks, Indianapolis, September 2002.
3. What is a clinically significant antibody? Blood Bank Day, Toronto General Hospital, Toronto, ONT, October 2002.
4. Controversies in immunohematology. Blood Bank Day, Toronto General Hospital, Toronto, ONT, October 2002.
5. What is weak D and should we test for it? Hurley Hospital, Flint, MI, May, 2003
6. The electronic crossmatch – a global perspective. 51st Annual Meeting of the Japanese Society for Transfusion Medicine, Fukuoaka, Japan, May 2003.
7. What is a clinically significant antibody? 51st Annual Meeting of the Japanese Society for Transfusion Medicine, Fukuoaka, Japan, May 2003.

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

1. Daniels GL, Cartron JP, Fletcher A, Garratty G, Henry S, Jorgensen J, Judd WJ, et al. International Society of Blood Transfusion Committee on terminology for red cell surface antigens: Vancouver Report. Vox Sang 2003;84:244-7.
2. Judd WJ. Current status of immunoprophylaxis with anti-D immunoglobulin (USA contributor). In: Engelfreit CP, Reesink HW. International forum. Vox Sang: *Accepted.*

EVAN KELLER
ASSOCIATE PROFESSOR
DEPARTMENT OF PATHOLOGY
ULAM AND INSTITUTE OF GERONTOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 – 30 JUNE 2003

I. RESEARCH ACTIVITIES:

1. National Institute of Aging (R01-AG-15904), "Ethanol-mediated osteoporosis and interleukin-6". (Keller, PI) 3/1/98-2/28/03 $748,000 direct cost; $260,200 indirect cost)
2. National Center for Research Resources. (T32 RR-07008-21) "Biomedical Research Training for Veterinary Scientists." (Keller, PI) 07/01/97-06/30/02 ($240,000 annual direct cost).
3. National Insitute of Aging. (R01) "Aging, gene expression and oxidative stress" (Keller; PI) 12/01/99-11/30/04 ($135,000 annual directs)
4. Dept. of Defense PC991111 "Interleukin-6 and prostate cancer progression" (Keller; Role: PI) 10/01/99-09/28/02 ($69,000 annual directs)
5. National Center for Research Resources (R01) "Development of mature zebrafish as an animal model." (Keller; Role: PI) ($225,000 annual directs FY1)
6. National Center for Research Resources. (T32) "Biomedical Research Training for Veterinary Scientists." Competitive Renewal ($280,000 annual direct costs FY1).
7. CaPCURE Awared. "Targeting skeletal metastasis" $75,000
8. National Institute on Aging. (P30-AG-13283) "Nathan Shock Center, Biology of Aging." (J. Faulkner, PI; Keller, Director Mutant and Transgenic Rodent Core) 07/01/00-06/30/05. ($84,889 Core Annual Directs).
9. National Cancer Institute (Project) in Prostate Cancer SPORE. "Targeting skeletal metastasis". (Keller:Project Leader; Spore PI, Pienta). $145,000 annual direct costs.
10. Department of Defense "Targeting Skeletal Metastasis" (Keller: PI) ($350,000 directs for three years).
11. Immunex (Gift) "For prostate cancer bone metastases research" (Keller: PI) 10/01 ($40,000).
12. Centocor (Contract) Biology of interleukin-6 in prostate cancer (Keller, PI) 7/03 ($40,000)

II. PENDING GRANTS

1. National Cancer Institute (P01) "The biology of prostate cancer skeletal metastases." (Keller: PI) ($1,189,000 annual directs FY1).
2. National Cancer Institute (R01) "Metastasis suppressor gene: Role of RKIP." (Keller: PI) $175,000 annual direct costs.
3. National Cancer Institute (R01) "VEGF and bone remodeling in skeletal metastases." (Keller, PI) $225,000 annual directs.

III. COLLABORATAIVE RESEARCH ACTIVITIES

EXTRAMURAL

1. Mark Day; Collaborator on R01 submission.
2. Kenneth van Golen; Consultant on R21 submission.
3. Eva Corey and Bob Vessella, U. Washington; Serum markers of prostate cancer skeletal metastasis.
4. Eva Feldman; Consultant, IGF , neuroblastoma and bone metastasis.

INTRAMURAL

1. National Cancer Institute (P30-CA-46592), "The University of Michigan Comprehensive Cancer Center Core Grant." (M. Wicha, P.I.; L Baker Director and Keller, Associate Director of Connective Tissue Oncology Program). ($1,865,046 annual directs).

IV. CLINICAL RESEARCH ACTIVITIES

1. SPORE Project Skeletal Metastasis Biomarkers.
2. Assay bone Remodeling markers. Dr. Larry Baker. Dept. of Medicine, UM.

V. PUBLICATIONS

1. Demiralp, B., H. Chen, A.J. Koh-Paige, E.T. Keller, and L.K. McCauley. Anabolic effects of parathyroid hormone during endochondral bone growth are dependent on c-fos. Endocrinology 143:4028-4047, 2002.
2. Stewart S, Shea DA, Tarnowski CP, Morris MD, D Wang Franceschi R, Lin DL and E Keller, Trends in early mineralization of murine calvarial osteoblastic cultures. A Raman microscopic study. Journal of Raman Spectroscopy. 33: 536-543, 2002.
3. Keller ET. Overview of metastasis and metastases. Journal of Musuloskeletal Neuronal Interactions. 2:567-569, 2002.
4. Keller ET, Yao Z. Applications of high-throughput methods to cancer metastases. Journal of Musuloskeletal Neuronal Interactions. 2:575-578, 2002.
5. Fujita H, Koshida K, Keller ET, Takahasi Y, Yoshimito T, Namiki M, Mizokami A. Cyclooxygenase-2 promotes prostate cancer progression. Prostate 53:232-240, 2002.
6. Khorram O, Colman RJ, Kemnitz JW, Magness RR, Zhang J, Yao Z, Keller ET. The influence of sex hormones on circulating nitric oxide (NOx) levels in Rhesus monkeys (Macaca mulatta). Med Sci Monit 8:BR489-95, 2002.
7. Cooper CR, Chay CH, Gendernalik JD, Lee HL, Bhatia J, Taichman RS, McCauley LK, Keller ET, Pienta KJ. Stromal factors involved in prostate carcinoma metastasis to the bone. Cancer (suppl) 97:739-747, 2003.
8. Keller ET and J. Brown JM. Osteoprotegerin (OPG), receptor activator of NF□B ligand (RANKL) and RANK in cancer metastasis. Research Advances in Cancer 3:81-93, 2003.
9. McCauley LK, Tozum TF, Kozloff KM, Koh-Paige AJ, Chen C, Demashkieh M, Cronovixh H, Richard V, Keller ET, Rosol TJ, Goldstein SA. Transgenic models of metabolic bone disease:

Impact of estrogen receptor deficiency on skeletal metabolism. Connect Tissue Res 44(Suppl. 1):250-263, 2003.

10. Murtha JM, Qi W, Keller ET.. Hematologic and serum biochemical values for zebrafish (Danio rerio). Comp Med 53:37-41, 2003.
11. Murtha JM, Qi W, Keller ET. Characterization of the Heat Shock Response in Mature Zebrafish (Danio rerio). Experimental Gerontol. 38:683-691, 2003.
12. Fu Z, Smith PC, Zhang L, Rubin M, Dunn RL, Yao Z, Keller ET. Effects of Raf Kinase Inhibitor Protein Expression on Suppression of Prostate Cancer Metastasis. J Natl Cancer Inst. 95:878-889, 2003. (Accompanying editorial JNCI 95:839-841, 2003).

ARTICLES ACCEPTED FOR PUBLICATION

1. Pfitzenmaier J, Quinn JE, Odman AM, Zhang J, Keller ET, Vessella RL, Corey E. Characterization of C4-2 prostate cancer bone metastases and their response to castration. J Bone Min Res. In Press.

PRESENTATIONS AT REGIONAL, NATIONAL OR INTERNATIONAL MEETINGS

ABSTRACTS

Over 10 abstracts presented at national meetings.

SEMINARS

1. "Introduction to Cancer Metastases" Invited Seminar. 32nd International Sun Valley Hard Tissue Workshop. Sun Valley, Idaho August, 2002.
2. "Applications of High Throughput Methods to Cancer Metastases" Invited Seminar. 32nd International Sun Valley Hard Tissue Workshop. Sun Valley, Idaho August, 2002.
3. "The biology of prostate cancer bone metastases" Invited seminar. Mt. Sinai Hospital, New York, April 2003.

VI. TEACHING AND MENTORING ACTIVITIES

COURSE SETTINGS

Director: ULAM Post-Doctoral Fellow Training Grant
Preceptor: Institute of Gerontology Training Grant
Preceptor: Clinical Cancer Immunology Training Grant
Preceptor: Cellular and Molecular Biology Program
Preceptor: Immunology Program Mentor
Preceptor: Urology training grant
Undergraduate research opportunity (UROP) mentor

MENTORED STUDENTS, POST-DOCTORAL FELLOWS AND FACULTY

Undergraduate/UROP Students

Jerdine Tan	UROP	2002-2003	UM Undergraduate
Rachel Roberts	Class	Spring 2003	UM Undergraduate
Lauren Wallner	Intern	2003	UM Undergraduate
Leigh Hagopian	Intern	2003	UM Undergraduate
Eva Marie Vandenbossche	Student help	2003	UM Undergraduate
Lindsay Dehne	UROP	Winter 2001	UM Undergraduate

Graduate Students

Jill Murtha, Pathology, Scientific Mentor, Pathology, Completed PhD
Zheng Fu, Immunology, Primary Advisor, Immunology, Completed PhD.
Paul Graf, CMB, Prelim committee, Pathology
Keni Rongguke, Thesis committee, Dental School, Bruce Rutherford Chair.
Meghan Brennan, Primary Advisor
Patrick Lester, Primary Advisor, Pathology

Postdoctoral Fellow

Yasuhide Kitagawa (Urologist from Kanazawa University, Japan)

Faculty

Jian Zhang, MD, PhD Research Scientist

VII. ADMINISTRATIVE SERVICE

ULAM

Director of Training Grant; Submit renewal.
Research Committee Representative

MEDICAL SCHOOL/HOSPITAL/UNIVERSITY

Rackham Student Appeals Committee
Associate Director, Connective Tissue Oncology Program (Cancer Center)
Colony for Aged Rodents Advisory Committee
Director, Transgenic and Mutant Rodent Core
Associate Director, Connective Tissue Oncology Program, Cancer Center

VIII. PROFESSIONAL ORGANIZATIONS

National Scientific Advisory Council: American Federation Aging Research
Scientific Advisory Committee: Institute for Advanced Studies on Aging.

IX. OTHER RELEVANT ACTIVITIES

Grant Reviews

1. External Scientific Grant Reviewer, VA Merit Review Board, Department of Veterans Affairs
2. American Federation for Aging Research
3. NIH: NIA, Program Project Review Committee
4. Department of Defense Pathobiology B: Prostate Cancer Grants
5. Department of Defense Bone Biology
6. NIA Comparative Aging SEP

Consulting

1. Centocor Pharmaceuticals, Philadelphia, PA
2. Vertex Pharmaceuticals, Boston, MA.

Manuscript Reviews

1. Ad hoc reviewer, *Journal of Clinical Investigation*
2. Ad hoc reviewer, *Cancer Research*
3. Ad hoc reviewer, *Neoplasia*
4. Ad hoc reviewer, *Prostate*

Meetings

1. Organized Connective Tissue Oncology Program Symposium 2003.

Publicity

1. Articles highlighting our work in BusinessWeek, BBC, NPR, Reuters, etc.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

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 (4 hours).
B. M2 Pathology Laboratory- Renal Sequence (16 hours).
C. Co-Coordinator - Renal Sequence (80 hours).
D. Renal Pathology for Pathology Residents (4 hours).
E. Renal Pathology for Nephrology Fellows Lectures (8 hours).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Co-Director, Molecular/Morphology Core, George M. O'Brien Renal Center, NIH-P50-DK39225, (5% Effort) $129,949/year, 8/1/98-7/30/03.
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, "ETB in regulation of renal sodium handling", NIH RO1-HL64720, (5% Effort) $225,00 direct costs/year, 5//01/01-4/30/04.
D. 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.

PENDING SUPPORT:

C. None.

PROJECTS UNDER STUDY:

A. Regulation of collagen IV gene expression.
B. Interstitial fibrosis as a predictor 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.
D. Reviewer:
    1. Kidney International.
    2. Journal of Clinical Investigation.
    3. Journal of American Society of Nephrology.

V. INVITED LECTURES AND SEMINARS:

None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Verma R, Wharram B, Kovari I, Kunkel R, Nihalani D, Wary KK, Wiggins RC, Killen PD, Holzman LB. Fyn binds to and phosphorylates the kidney slit diaphragm component Nephrin. J Biol Chem. 278:20716-20723, 2003.

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.

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

1. None.

CELINA G. KLEER, M.D.
ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
JULY 1, 2002 - JUNE 30, 2003

I. CLINICAL ACTIVITIES:

A. General surgical pathology, including frozen sections, and biopsies in diagnostic rooms I, II, and C with residents and fellows – 4 months
B. Breast pathology transfer and consultation service – 12 months
C. Review of breast cancer cases to be presented in the Breast Care Conference – 12 months

TEACHING ACTIVITIES:

A. Medical Students (M2 and M4)
Radiology-Pathology course for M4 students – 3 contact hours
Mentored four M4 students - 1 month

B. Pathology House Officers and Fellows
Surgical pathology diagnostic room instruction for house officers - 4 months
Two slide conferences on interesting cases in breast pathology – 2 contact hours
Two didactic lectures on breast pathology – 2 contact hours
Mentor for David Sturtz, HOIII, in the following project: Sturtz D, Schott AF and Kleer CG. Pathologic features of breast cancer associated with complete response to neoadjuvant chemotherapy. Platform presentation, USCAP meeting, Washington DC, March 2003.

C. Pathology Graduate Program
Natalie Whitfield, a first year pathology graduate student rotated in the lab from 4/29/03 to 6/16/03.

D. Interdepartamental
Breast Care Clinic tumor board – 12 months

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 (50%), $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 (30%), $451,531, 4/17/02 – 4/16/06.
C. **Principal Investigator,** *Role of EZH2 in the Development of Breast Cancer and its Clinical Utility as a Novel Biomarker,* John and Suzanne Munn Endowed Research Fund of the University of Michigan Comprehensive Cancer Center, G003191 (0%), $25,000, 7/1/03 – 6/30/04.
D. **Co-Investigator**, *Proteomics Alliance for Cancer*, PI Omenn, GR356 (5%), 8/01/02 - 7/31/05
E. **Co-Investigator**, PI S. Ethier. R01 CA100724-01 (0%),$603,250, 6/28/02-07

PENDING SUPPORT

A. **Principal Investigator,** *Role of LIBC (WISP3) in the Development of the Inflammatory Breast Cancer Phenotype*, National Institutes of Health, K08 CA 090876-01A1, (80%), $630,000
B. **Principal Investigator**, *Role of EZH2 in Breast Cancer Progression*, National Institutes of Health, RO1 CA107469-01, (30%) $1,250,000

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTAMENTAL:

A. Coordination of the breast pathology service.
B. Quality assurance of the breast pathology service.
C. Director, Breast Pathology Fellowship
D. Member of the Steering Committee for the Cancer and Aging initiative at the University of Michigan.
E. Medical School Admissions Committee, University of Michigan.

REGIONAL AND NATIONAL:

A. Reviewer, Breast Cancer Research
B. Reviewer, Breast Cancer Research and Treatment
C. Reviewer, Modern Pathology
D. Reviewer, Cancer Research

V. INVITED LECTURES:

1. "The polycomb group protein EZH2 is involved in breast cancer progression" Breast Oncology Meeting, University of Michigan, November 5, 2002.
2. "Difficult Diagnoses in Breast Pathology" VA Hospital, Ann Arbor, MI. November 21st, 2002.
3. "Characterization of RhoC, WISP3 and EZH2 as Markers of Aggressive Breast Cancer" Department of Pathology, Brigham and Women's Hospital, Harvard Medical School, February 25th, 2003.
4. "Characterizing Aggressive Breast Cancer Phenotypes: From Biology to Biomarkers" Cancer Center Grand Rounds, University of Michigan, March 14th, 2003.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Zhou M, Chinnaiyan AM, Kleer CG, Lucas PC and Rubin MA. Alpha-Methylacyl-CoA racemase: a novel tumor marker overexpressed in several human cancers and their precursor lesions. *Am J Surg Pathol.* 26(7): 926-931, 2002.
2. Kleer CG, Tseng MD, Gutsch DE, Rochford AR, Wu Z-F, Joynt LK, Helvie MA, Chang T, van Golen KL, Merajver SD. Epstein-Barr virus is implicated in the pathogenesis of breast fibroadenomas in immunocompromised hosts. *Modern Pathology* 15(7):759-764, 2002.

3. Pan Q, Kleer CG, van Golen KL, Irani J, Bottema KM, Bais C, De Carvalho M, Mesri EA, Robins DM, Dick R, Brewer GJ and Merajver SD. Copper deficiency induced by tetrathiomolybdate suppresses tumor growth and angiogenesis. Cancer Research 62(17):4854-9, 2002.
4. Valdez R, Thorson J, Finn WG, Schnitzer B, and Kleer CG. Lymphocytic Mastitis/ Diabetic Mastopathy: A Molecular, Immunophenotypic, and Clinicopathologic Evaluation of Eleven Cases. Modern Pathology 16: 223-228, 2003.
5. Rao DS, Bradley SV, Kumar PD, Hyun TS, Saint-Dic D, Oravecz-Wilson K, Kleer CG, and Ross TS. Altered receptor trafficking in Huntingtin Interacting Protein 1-transformed cells. Cancer Cell 3: 471-482, 2003.
6. Sabel MS, Schott AF, Kleer CG, Merajver SD, Cimmino V, Diehl KM, Hayes DF, Chang A, Pierce LJ. Sentinel Node Biopsy Prior to Neoadjuvant Chemotherapy. American Journal of Surgery 186:102-105, 2003.
7. Pan Q, Bao LW, Kleer CG, Brewer GJ, and Merajver SD. Antiangiogenic tetrathiomolybdate enhances doxorubicin therapy against breast carcinoma. Molecular Cancer Therapeutics 2:617-622, 2003.
8. 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, In Press.
9. Collisson EA, Kleer CG, Wu M, De A, Gambhir SV, Merajver SD, Kolodney MS. Atorvastatin Prevents RhoC Isoprenylation, Invasion and Metastasis in Human Melanoma Cells. Molecular Cancer Therapeutics, In Press.
10. 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. Proceedings of the National Academy of Sciences, In Press.
11. Kowalski PJ, Rubin MA and Kleer CG. E-Cadherin Expression in Primary Carcinomas of the Breast and its Distant Metastases. Breast Cancer Research, In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Kleer CG, Zhang Y, Pan Q, Merajver SD. WISP3 is a Secreted Tumor Suppressor Protein that Modulates IGF Signaling in Inflammatory Breast Cancer. Submitted.
2. Pan Q, Kleer CG, Bao LW, and Merajver SD Antiangiogenic tetrathiomolybdate protects against Her2/neu-induced breast carcinoma by hypoplastic remodeling of the mammary gland. Submitted.

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

1. Sturtz DE, Schott AF, and Kleer CG. Pathologic features of breast cancer associated with complete response to neoadjuvant chemotherapy: importance of histologic type and grade. Platform presentation, USCAP meeting, Washington DC, 2003
2. Kleer CG, Zhang Y, Pan Q, Merajver SD. Characterization of WISP3, a novel tumor suppressor gene for inflammatory breast cancer, in normal breast and breast disease. Platform presentation, USCAP meeting, Washington DC, 2003

3. Kleer CG, Shen R, Wolf J, Rubin MA. Characterization of platelet derived growth factor receptor expression in breast cancer identifies inflammatory breast cancer as a potential target for treatment with PDGFRb inhibitors. Poster presentation, USCAP meeting, Washington DC, 2003
4. Kleer CG, Shen R, Chinnaiyan AM, Rubin MA. EZH2 is overexpressed during breast cancer progression and is a predictor of poor outcome in patients with breast cancer. Poster presentation, USCAP meeting, Washington DC, 2003.
5. Kleer CG, Zhang Y, Pan Q, Merajver SD. WISP3 is a secreted protein and modulates IGF signaling in inflammatory breast cancer. Minisymposium AACR Meeting, Washington DC, July 11-14, 2003.

CYNTHIA KRUEGER, M.D.
LECTURER
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

A. Cytopathology Service:
   1. Fine Needle Aspiration Service – 11 weeks
   2. Hospital Cytology Service (Gynecologic and Non-gynecologic specimens) – 15 weeks

II. TEACHING ACTIVITIES:

A. House Officers:
   1. Fine Needle Aspiration Cytology – 11 weeks
   2. Hospital Cytology Service – 15 weeks
   3. Cytopathology Teaching Conference – 1 hour

B. Cytotechnologists:
   1. Cytopathology Teaching Conference – 1 hour

III. OTHER RELEVENT ACTIVITIES:

INVITED LECTURES:

1. "The Latest Bethesda Classification and Clarification" Lecture at the Nineteenth M-Labs Symposium – **Everyday Issues in Cytopathology,** University of Michigan Health System, October 5, 2002.

STEVEN L. KUNKEL, Ph. D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

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. Member, Lung Immunopathology Post-doctoral Training Program (Pathology)
H. Member, Experimental Immunopathology 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. Chair, Pathology Graduate Examination Committee
M. Member, Graduate Teaching Award Review Committee
N. Supervised/serve on thesis committee the following postdoctoral fellows, graduate students, medical Students and undergraduates:
O. Fellows: Jane Schuh, Claudia Benjamim, Steven Lundy, Traci Ness, Graduate Students; Hiatal Chen, Clauda Jakubzick.
P. Undergraduate Students: Ester Choi, Kristin Carpenter, Ted Martens, Jillian Ewing, Susan Lewis
Q. Doctoral Thesis Committee Member/Orals Committee for the following graduate students: Molly Thomas, (Pathology), Allison Miller (Pathology), Sara Cheng (MSTP, CMB), Anavelys Ortiz-Suarez (CMB) Tania Gourley (Micro/Immuno), Tina Yee (Micro/Immunology), Phil Schaner (MSTP, Cell and Developmental Biology), John Marrow (MSTP, Neuroscience)
R. Oral Preliminary Examination Committee
S. Facilitator SROP Conference Research Roundtable

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 for Section II
D. SCOR Occupational and Immunological Lung Disease, P50HL-46487 Principal Investigator for Project 3
E. SCCOR Acute Lung Injury, P50HL60289, Principal Investigator Project 3

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. Operating Committee Pathology Graduate Program
B. Space Utilization and Research Committee
C. Interview candidates for graduate program
D. Divisional Co-Director of General Pathology
E. Chair, Graduate Program's Examination Committee
F. Member, Department of Pathology ACAPT Committee
G. 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

REGIONAL AND NATIONAL

A. Associate Editor, American Journal of Pathology
B Associate Editor, American Journal of Respiratory Cell and Molecular Biology
C. Associate Editor, Experimental and Molecular Pathology
D. Associate Editor, Shock
E. Editorial Board, Mediators of Inflammation
F. Co-Chair 2003 Keystone Conference on Biology of Chemokines
G. 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
H. Grant Reviewer, The Arthritis Society
I. Grant Reviewer, Veterans Administration
J. National Institutes of Health Study Section, Lung Biology and Pathology (ad hoc)
K. Chair, Publications Committee American Society of Investigative Pathology

V. OTHER RELEVANT ACTIVITIES:

A. National Institute of Allergy and Infectious Diseases. Board of Scientific Counselors, Laboratory of Host Defense and Clinical Investigation. Ad hoc. Bethesda, MD.
B. National Institute of Aging Site Visit, ad hoc reviewer, Baltimore, MD
C. National Institute of Allergy and Infectious Diseases. Permanent member, Board of Scientific Counselors, Laboratory of Host Defense and Clinical Investigation. 2003-

INVITED LECTURES AND SEMINARS:

1. Invited speaker, Models of emphysema: Speeding the pace of progress, Alpha 1 Foundation, September 2002 Airlie, Virginia
2. Invited speaker, Inflammatory lung diseases, Inflammation Research Association, October, 2002Sagamore, New York
3. Invited Speaker, Pittsburgh Lung Conference, University of Pittsburgh, October 2002 Pittsburgh PA.
4. Invited lecture, XXVII Brazilian Society of Immunology Congress, Salvadore, Brazil, October 2002.
5. Invited lecture, XXXIV Brazilian Congress on Pharmacology and Experimental Therapy, Aguas de Lindoia, Brazil, Oct 2002.

6. Invited Lecture. Therapeutic Effects of Humanized IL-8 Antibody, Utretch, Netherlands, November 2002.
7. Invited Lecture. Louisiana State University, New Orleans, LA, Nov 2002
8. Invited Speaker, Chronic Obstructive Pulmonary Disease: The Important Questions. Malta, December 2002.
9. Invited Speaker, Indiana University School of Medicine, Indianapolis, In January 2003.
10. Invited Speaker, Keystone Symposia; Regulatory and Effector Functions of Macrophages, Taos, NM Feb 2003
11. Invited Speaker, Abbott Bioscience Center, Wochester, MA March 2003
12. Invited Speaker, Immunobiology Center, Yale University, New Haven CT, March 2003
13. Keystone Speaker, Inflammation Research Association, Seattle WA, April 2003.
14. Invited Speaker, Innate Immunity: From flies to human, Academy of Science, Paris, France, May 2003.
15. Invited Speaker, Novartis Seminar series. Horsham, England June 2003

VI. PUBLICATIONS:

ARTICLES PUBLISHED IN REFEREED JOURNALS:

1. Schuh JM, Blease K, Kunkel SL, Hogaboam CM. Eotaxin/CCL11 is involved in acute, but not chronic, allergic airway responses to Aspergillusfumigatus. Am J Physiol Lung Cell Mol Physiol. 2002; Jul;283(1):L198-204.
2. Schuh JM, Power CA, Proudfoot AE, Kunkel SL, Lukacs NW, Hogaboam CM. Airway hyperresponsiveness, but not airway remodeling, is attenuated during chronic pulmonary allergic responses to Aspergillus in CCR4-mice.FASEB J. 2002; Aug 1;16(10):1313-1315.
3. Jakubzick C, Kunkel SL, Joshi BH, Puri RK, Hogaboam CM. Interleukin-13 Fusion Cytotoxin Arrests Schistosoma mansoni Egg-Induced Pulmonary Granuloma Formation in Mice. Am J Pathol. 2002; Oct;161(4):1283-97.
4. Weinberg JB, Lutzke ML, Efstathiou S, Kunkel SL, Rochford R. Elevated chemokine responses are maintained in lungs after clearance of viral infection. J Virol. 2002; Oct;76(20):10518-23.
5. Cheng SS, Lukacs NW, Kunkel SL. Eotaxin/CCL11 is a negative regulator of neutrophil recruitment in a murine model of endotoxemia. Exp Mol Pathol. 2002 Aug;73(1):1-8.
6. Garcia-Ramallo E, Marques T, Prats N, Beleta J, Kunkel SL, Godessart N. Resident cell chemokine expression serves as the major mechanism for leukocyte recruitment during local inflammation. J. Immunol 2002; Dec 1;169(11):6467-73.
7. Thomas MS, Kunkel SL, Lukacs NW. Differential role of IFN-gamma-inducible protein 10 kDa in a cockroach antigen-induced model of allergic airway hyperreactivity: systemic versus local effects. J Immunol. 2002; Dec 15;169(12):7045-53.
8. Tekkanat KK, Maassab H, Miller A, Berlin AA, Kunkel SL, Lukacs NW. RANTES (CCL5) production during primary respiratory syncytial virus infection exacerbates airway disease. Eur J Immunol. 2002; Nov;32(11):3276-84
9. Cheng, SS, Kunkel, SL. The evolving role of the neutrophil in chemokine networks. Chem Immunol Allergy 2003; 83:1-14.
10. Simpson KJ, Henderson NC, Bone-Larson CL, Lukacs NW, Hogaboam CM, Kunkel SL. Chemokines in the pathogenesis of liver disease: so many players with poorly defined roles. Clin Sci (Lond). 2003; Jan;104(1):47-63.

11. Simpson, K, Hogaboam, CM, Kunkel, SL, Harrison, DJ, Bone-Larson, C., Lukacs, NW. Stem cell attenuates liver damage in a murine model of acetaminophen-induced hepatic injury. 2003; Lab Invest.83:1-8.
12. Chiu BC, Freeman CM, Stolberg VR, Komuniecki E, Lincoln PM, Kunkel SL, Chensue SW. Cytokine-Chemokine Networks in Experimental Mycobacterial and Schistosomal Lung Granuloma Formation. Am J Respir Cell Mol Biol. 2003 29:106-116.
13. Jakubzick C, Kunkel SL, Joshi BH, Puri RK, Hogaboam CM. Interleukin-13 fusion cytotoxin arrests Schistosoma mansoni egg-induced pulmonary granuloma formation in mice. Am J Pathol. 2003; 161: 1283-1297.
14. Jakubzick C, Choi ES, Kunkel SL, Joshi BH, Puri RK, Hogaboam CM. Impact of Interleukin-13 responsiveness on the synthetic and proliferative properties of Th1- and Th2-type pulmonary granuloma fibroblasts. Am J Pathol. 2003 162(5):1475-86.

ANDREW P. LIEBERMAN, M.D., PH.D.
ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

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. (Post-Doctoral Fellow)
      b. Zhigang Yu, M.D. (Post-Doctoral Fellow)
      c. Christopher Pacheco (Thesis student)
   2. Rotating Graduate Students
      a. Christopher Pacheco, Neuroscience Graduate Program
      b. Mary Heng, Neuroscience Graduate Program
   3. Thesis committee member
      a. Valerie Drews, Neuroscience Graduate Program
   4. Preliminary examination committee member
      a. Michael Corradetti, Cell and Molecular Biology Graduate Program
      b. Qi Cau, Pathology Graduate Program
      c. Brian Rudd, Pathology 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, Pathology 858
F. Course director and instructor, Neuroscience 700
G. Lecturer, Pathology 581
H. Lecturer, Neuroscience 731
I. Member, Neuroscience Graduate Program

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Altered androgen receptor function due to CAG expansion", K02 NS44047 (75%), $156,250/year ($681,250/five years), July 1, 2002 – June 30, 2007.

B. Principal Investigator, "Altered androgen receptor function in Kennedy's disease", Muscular Dystrophy Association (5%, no salary support), $73,409/year ($219,000/three years), July 1, 2002 – June 30, 2005.
C. Principal Investigator, "Oxidative injury in a model of motor neuron disease", Michigan Alzheimer's Disease Research Center (0%, no salary support), $30,000/year, January 1, 2002 – December 31, 2002.
D. Director, "Neuropathology Core, Michigan Alzheimer's Disease Research Center", P50 AG08671 (S. Gilman, P.I.) (15%), $47,043/year

PROJECTS UNDER STUDY:

A. Mechanism of neurodegeneration in Kennedy's disease
B. Mechanism of neurodegeneration in Niemann – Pick C

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Member, Pathology Graduate Program Admissions Committee
B. Member, Pathology Graduate Program Preliminary Examination Committee
C. Member, Pathology Graduate Program Research Symposium Awards Committee
D. Pathology residency training program candidate interviews
E. Department of Pathology faculty candidate interview

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

UNIVERSITY OF MICHIGAN:

A. None

REGIONAL AND NATIONAL:

A. Member, Awards Committee, American Association of Neuropathologists
B. Manuscript review for:
    1. Experimental Neurology
    2. Molecular and Cellular Biology

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. None

HONORS AND AWARDS

A. None

PATENTS:

A. None

INVITED LECTURES/SEMINARS:

1. Invited Participant, Howard Hughes Medical Institute/Burroughs Wellcome Fund Course on Laboratory Management, Chevy Chase, Maryland, July 2002.
2. "Kennedy's Disease", Neuroscience Graduate Program Retreat, Howell Center, October 2002.
3. Invited Participant and Panel Discussant, Kennedy's Disease Association Conference "Reaching for the Stars", Baltimore, Maryland, October 2002.
4. "Transcriptional Dysregulation in Kennedy's Disease", Pathology Graduate Program Research Symposium, Ann Arbor, Michigan, January 2003.
5. Invited Lecturer, "Autopsy Diagnosis of Dementia", Alzheimer's Disease Educational Program, Edna Gates Conference Seminar on Dementia Care, Eastern Michigan University, Ann Arbor, Michigan, March 2003.
6. Invited Speaker and Panel Discussant, "Autopsy Diagnosis of Alzheimer's Disease and Other Neurodegenerative Disorders", Alzheimer's Association of Northwest Ohio Chapter Annual Meeting, Toledo, Ohio, April 2003.
7. "Altered androgen receptor function in Kennedy's disease." Department of Pathology Research Seminar Series, April 2003.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Lieberman A P, Harmison G, Strand A D, Olson J M, Fischbeck, K H. Altered transcriptional regulation in cells expressing the expanded polyglutamine androgen receptor. Hum Mol Genet, 17:1953-1965, 2002. (Cover illustration and editorial. See: Orr H T. Microarrays and polyglutamine disorders: reports from the Hereditary Disease Array Group. Hum Mol Genet, 17:1909-1910, 2002)

RICHARD W. LIEBERMAN, M.D.
CLINICAL ASSISTAN PROFESSOR
DEPARTMENTS OF PATHOLOGY AND
OBSTETRICS & GYNECOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

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. Michigan State University Medical Students
   1. M2 School of Human Medicine, Obstetrics & Gynecology Sequence: Three hours Gynecologic Pathology lectures; preparation of examination questions.
   2. M2 School of Osteopathic Medicine, Obstetrics & Gynecology Sequence: Two hours Gynecologic Pathology lectures; preparation of examination questions.

D. 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.

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. Diagnostic Hierarchy – schema development in MS Access, with link to Oracle 8i

SPONSORED SUPPORT:

None

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Member, Pathology Bioinformatics, Department of Pathology.

MEDICAL SCHOOL/HOSPITAL:

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

UNIVERSITY OF MICHIGAN:

None.

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "Web-based Imaging for Interactive Microscopy: Potential Applications for the Anatomic Pathologist" ASCP/CAP 2002 Meeting in Washington, D.C. October 2002.
2. "Managing High Throughput Tissue Microarray Data: The Unviersity of Michigan SPORE Model" Pathology BioInformatics Conference, Taubman Center, Ann Arbor, MI. November 2002.
3. "Clinical Implications of TBS 2001 – Update on management of abnormal cervical cytology". Update in Obstetrics and Gynecology, Taubman Center, Ann Arbor, MI. April 2003.
4. Five hours, clinical pathologic correlation lectures. 39th Annual Northern Michigan Summer Conference. Shanty Creek, Michigan. June 16-20, 2003.

VI. PUBLICATIONS:

ARTICLES PUBLISHED IN REFEREED JOURNALS:

1. Heller DS. Haefner HK. Hammoud M. **Lieberman** RW. Vulvar hidradenitis suppurativa. Immunohistochemical evaluation of apocrine and eccrine involvement. [Journal Article] *Journal of Reproductive Medicine. 47(9):695-700, 2002 Sep.*

ARTICLES SUBMITTED TO REFEREED JOURNALS:

1. Fetters 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)

BOOKS/CHAPTERS IN BOOKS:

None.

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.

JOHN B. LOWE, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

A. Clinical Immunology Diagnostic Service - sign out of serum and urine protein electrophoresis, immunofixation, and immunoelectrophoresis.

II. TEACHING ACTIVITIES:

A. Supervision of three postdoctoral fellows (Jonathon Homeister, M.D., Ph.D., Lan Zhou, M.D., Ph.D., and Stephanie Chervin, Ph.D.)
B. Supervision of one MSTP student (David Kim)
C. Supervision of two PhD students (Yunfan Ma – Pathology; Jeongsup Shim – Biomedical Engineering)
D. Lecturer – Postdoctoral Research Training Program
E. Member of four Ph.D. thesis committees (Stacey Arnold, Anavelys Ortiz-Suarez, Qin Li, Gabriel Maine)
F. Member, Cell and Molecular Biology Program Committee
G. Member, Pathology Department Ph.D. Program Committee
H. Member, Graduate Program in Immunology

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. "Glycoconjugate function in mammals". Source of award: Howard Hughes Medical Institute
B. Program Project - Project #2 Principal Investigator, "Carbohydrate-dependent adhesion of normal and tumor cells", NIH - CA71932 (20% effort), $732,109/five years direct cost, 07/08/96 - 02/28/07
C. Large Scale Collaborative Project Award "Protein-carbohydrate interactions in cell communication". Bridging Project Title "Fucosylated Glycan Structure and Function" (Lowe). NIH GM62116 (Paulson) (5% effort) $300,000/five year direct cost, 09/01/01 – 08/31/06

PROJECTS UNDER STUDY:

A. Structure and regulation of mammalian oligosaccharide genes. Efforts are focused on the isolation and analysis of gene(s) for human and murine glycosyltransferases, using mammalian gene transfer techniques, and on characterization of immune defects in glycosyltransferase knock-out mice.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Chair, Biomedical Scholars Program Committee
B. Member, Department of Pathology's Graduate Program Committee
C. Member, University of Michigan Technology Transfer Committee
D. Member, Biomedical Research Core Facilities Advisory Committee
E. Member, Biomedical Science Research Building Committee
F. Member, Life Sciences Institute Advisory Committee
G. Chair, Task Force on Molecular Medicine Recruitment for the Life Sciences Institute
H. Member, Executive Committee for the Life Sciences Institute
I. Member, Microarray/Microchip Technology Advisory Committee

REGIONAL AND NATIONAL:

A. Member, Scientific Advisory Board, The Ara Parseghian Medical Research Foundation (Niemann-Pick disease type C)
B. Member, Editorial Board of the European Journal of Biochemistry
C. Member, Editorial Board of Molecular Medicine
D. Consulting Reviewer for Proceedings of the National Academy of Sciences USA, Journal of Cell Biology, Journal of Experimental Medicine, Biochemistry, Journal of Immunology, Glycobiology, Cell, Science, Nature, Immunity, Nature Immunology, Blood

V. OTHER RELEVANT ACTIVITIES:

A. Howard Hughes Medical Institute, Investigator

VI. INVITED LECTURES AND SEMINARS:

1. Glycan-mediated, selectin-dependent leukocyte recruitment in innate and adaptive immunity. Boehringer-Ingelheim, Ridgeway, CT. August 2002.
2. Glycosylation in the control of leukocyte recruitment. Max Planck Institute Conferences. Ringberg, Germany, September 2002
3. Keynote Address: Mechanisms that control leukocyte recruitment and lymphocyte homing. Ernst Schering Foundation Workshop on Leukocyte Migration. Berlin, Germany, October 2002.
4. Glycosylation loci that control selectin-dependent leukocyte biology. Society for Glycobiology, Boston, MA. November 2002.
5. The Biology and biochemistry of fucosylation. 2003 Gordon Research Conference on Glycobiology. Ventura, CA. March 2003.
6. Fucosylation and the control of hematopoietic cell trafficking and differentiation. ASBMB, San Diego, CA. April 2003.
7. Glycosylation loci that control selectin-dependent leukocyte biology. University of Verona. Verna, Italy. September 2002.
8. Control of selectin ligands that dictate leukocyte recruitment. University of Insubria, Varese, Italy, September 2002.

9. Glycosylation loci that control leukocyte biology. Washington University Medical School Department of Pathology. St. Louis, MO. March 2003.
10. Glycosylation loci that control leukocyte biology. Department of Biochemistry, University of Arkansas School of Medicine. Little Rock, AK. April 2003.
11. Glycosylation in the control of leukocyte biology. Brigham and Women's Hospital Vascular Biology Program, Harvard Medical School, Boston, MA. April 2003.
12. Glycosylation events that control selectin-dependent leukocyte biology. UCSD School of Medicine Department of Pathology. La Jolla, CA. June 2003.

VII. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Chervin SM, Lowe JB, and Koreeda M. Synthesis and biological evaluation of a new sialyl Lewis x mimetic derived from lactose. J Org Chem 67::5654-5662, 2002.
2. Smith PL, Myers JT, Rogers CE, Zhou L, Petryniak B, Becker DJ, Homeister JW. and Lowe JB. Conditional control of selectin ligand expression and global fucosylation events in mice with a targeted mutation at the FX locus. J Cell Biol 158:801-815, 2002.
3. Lowe JB. Glycosylation in the control of selectin counter-receptor structure and function. Immunol Rev 186:19-36, 2002.
4. Thomsson KA, Hinojosa-Kurtzberg M, Axelsson KA, Domino SE, Lowe JB, Gendler SJ, and Hansson GC. Intestinal mucins from cystic fibrosis mice shown increased fucosylation due to an induced Fuc□1-2 glycosyltransferase. Biochem J 367(Pt 3):609-616, 2002.
5. Becker DJ, Myers JT, Ruff MM, Smith PL, Gillespie BW, Ginsburg D, and Lowe JB. Strain-specific modification of lethality in fucose-deficient mice. Mammalian Genome 14:130-139, 2003.
6. Mitoma J, Petryniak B, Hiraoka N, Yeh J-C, Lowe JB, and Fukuda M. Extended core 1 and core 2 branched O-glycans differentially modulate sialyl Lewis x-type L-selectin ligand activity. J Biol Chem 278:9953-9961, 2003.
7. Becker DJ and Lowe JB. Fucose: Biosynthesis and biological function in mammals. Glycobiology 13:41R-53R, 2003.
8. Lowe JB and Marth JD. Genetic approaches to glycan function in mammals. Ann Rev Biochem 2003, in press.
9. Lowe JB. Glycan-dependent leukocyte adhesion and recruitment in inflammation Curr Opin Cell Biol., 2003, in press.

ARTICLES SUBMITTED OR IN PREPARATION:

1. Becker DJ, Smith PL, Petryniak B, Kelly RJ, Myers JT, Wu B, Wang PG, and Lowe JB. Glycan-dependent regulation of GDP-mannose 4,6-dehydratase activity. In revision.
2. M'Rini C, Chang G, Schweitzer C, Cavanagh LL, Palframan RT, Warnock RA, Lowe JB, Quackenbush EJ, and von Andrian UH. A novel endothelial L-selectin ligand in lymph node medulla that is regulated by α(1,3)-Fucosyltransferase-IV. In revision.
3. Hiraoka N, Kawashima H, Petryniak B, Nakayama J, Mitoma J, Marth JD, Lowe JB, and Fukuda M. Core 2 Branching β1,6-*N*-Acetylglucosaminyltransferase and HEV-Restricted Sulfotransferase Collaboratively Control Lymphocyte Homing. Submitted.
4. Smith PL, Rogers CE, Myers JM, Petryniak B, and Lowe JB. Dysregulated expression of selectin ligands on fetal thymocytes in mice with a targeted disruption of the Galgt2 GalNAc transferase locus. In preparation.
5. Hiraiwa N, Domino S, Saunders T, and Lowe JB. Dominant pre-implantation lethality in mice directed by aberrant expression of an □(1,2)fucosyltransferase cDNA. In preparation.

6. Legault DJ, Kelly RJ, Smith PL, and Lowe JB. Glycan epitope recovery defines amino acid sequence requirements for□(1,3/1,4)fucosyltransferase acceptor substrate specificity. In preparation.
7. Pipia GG, Kale S, Smith PL, Kelly RJ, Rogers CM, Lowe JB, and Long MW. Selectin ligand pairs: negative modulators of human hematopoiesis. In preparation.
   Masayoshi Oh-eda M, Tsuboi S, Petryniak B, Lowe JB, and Fukuda M. Expression of E-selectin ligand oligosaccharides on Chinese hamster ovary cells by mouse fucosyltransferase IV and VII. In preparation.
8. Kale S, Chervin SM, Pipia G, Kelly RJ, Datta NS, Smith PL, Lowe JB, and Long MW. Selectin ligand-dependent homeostatic control of hematopoiesis. In preparation.

BOOKS AND CHAPTERS IN BOOKS:

1. Lowe JB. Glycosyltransferases and glycan structures contributing to the adhesive activities of L-, E-, and P-selectin counter-receptors. Biochem Soc Symp 33-45, 2002.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

A. Dermatopathology Service – 12 months.
B. Dermatopathology Consultation Service (including MLabs and Veterans Administration Hospital) – 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).
B. House Officers:
   1. Dermatopathology sign-out (Pathology and Dermatology Residents).
   2. Review of dermatopathology consultation material.
   3. Dermatopathology teaching conference (weekly-twice monthly).
C. Diagnostic Conference, Department of Dermatology (weekly).
D. Director of Diagnostic Conference, Department of Dermatology – (2 hours/month)
E. Hospital Conferences:
   1. Multidisciplinary Melanoma Conference (twice monthly).
F. Honors:
   1. Listed in the *Guide to America's Top Physicians*, 2003 edition by the Consumers' Research Council of America
   2. Listed in *Hour* Magazine's Best Doctors, October, 2002 edition

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. 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. 4/1/01-9/30/01 (Study ongoing through 2003) $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.
D. Abbott Co., "A phase II multi-center study of the safety and efficacy of adalimumab (D2E7) in subjects with moderate to severe chronic plaque psoriasis." Local principal investigator: Sewon Kang, M.D., Co-Investigator: Lori Lowe, M.D. 5/2003-6/2003.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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. Coordinator, QA/QC program (Mohs surgery slides), Cutaneous Surgery and Oncology Program, Department of Dermatology, University of Michigan
E. Member, Multidisciplinary Melanoma Program, University of Michigan Comprehensive Cancer Center

REGIONAL AND NATIONAL:

A. Editorial Board: *Cancer,* Associate Editor, Skin section
B. Member, North American Melanoma Pathology Study Group
C. Member, American Medical Women's Association Mentorship Program
D. Member, American Academy of Dermatology's Minority Medical Student Mentor Program
E. Ad hoc manuscript reviewer, *Journal of Cutaneous Pathology*
F. Ad hoc manuscript reviewer, *The American Journal of Dermatopathology*
G. Ad hoc manuscript reviewer, *Journal of the American Academy of Dermatology*
H. Ad hoc manuscript reviewer, *Archives of Dermatology*
I. Ad hoc manuscript reviewer, *Dermatologic Surgery*
J. Ad hoc manuscript reviewer, *Cancer*

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Interactive Session of Challenging Clinicopathological Cases: What Is Your Diagnosis?, faculty, American Society of Dermatopathology Annual Meeting, Phoenix, AZ, October, 2002.
2. Self-Assessment in Dermatopathology, faculty, American Society of Dermatopathology Annual Meeting, Phoenix, AZ, October, 2002.
3. "The Conundrum of Melanocytic Terminology: Atypical Nevi and Atypical Junctional Melanocytic Hyperplasia. What you need to know to manage your patient," invited seminar, Michigan Dermatologic Society Meeting, University of Michigan, Ann Arbor, Michigan, March, 2003.
4. "Cutaneous Manifestations of Rheumatologic Disease," invited seminar, 31st Annual Spring Update in Internal Medicine, University of Michigan, Ann Arbor, Michigan, May, 2003

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Schwartz JL, Wang TS, Hamilton TA, **Lowe L,** Sondak VK, Johnson TM: Thin primary cutaneous melanomas: associated detection patterns, lesion and patient characteristics. Cancer 95: 1562-1568, 2002.
2. Sheng H, Goich S, Wang A, Grachtchouk M, **Lowe L**, Mo R, Lin K, de Sauvage FJ, Sasaki H, Hui C, Dlugosz AA: Dissecting the oncogenic potential of Gli2: Deletion of an amino-terminal fragment alters skin tumor phenotype. Cancer Res 62: 5308-5316, 2002
3. Su LD, Fullen DR, **Lowe L**, Uherova P, Schnitzer B, Valdez R: CD117 (kit receptor) expression in Merkel cell carcinoma. Am J Derm Pathol 24: 289-293, 2002.
4. Su LD, Fullen DR, Sondak VK, Johnson TM, **Lowe L:** Sentinel lymph node biopsy for problematic spitzoid melanocytic lesions: a report of 18 cases. Cancer 97: 499-507, 2003.
5. Barr KL, **Lowe L**, Su LD: Mycobacterium marinum infection simulating interstitial granuloma annulare: A report of 2 cases. Am J Dermatopathol 25: 148-151, 2003.
6. Fullen DR, Jacobson SN, Valdez R, Novice FM, **Lowe L**: Granuloma annulare-like infiltrates with concomitant cutaneous involvement by B-cell non-Hodgkin's lymphoma: Report of a case. Am J Dermatopathol 25: 57-61, 2003
7. Fullen DR, **Lowe L,** Su LD: Antibody to S100 A6 protein is a sensitive immunohistochemical marker for neurothekeoma. J Cutan Pathol 30: 118-122, 2003.
8. Bogner PN, Fullen DR, **Lowe L**, Paulino A, Biermann JS, Sondak VK, Su LD: Lymphatic mapping and sentinel lymph node biopsy detects early metastasis of sweat gland carcinoma. Cancer 97: 2285-2289; 2003.
9. Grachtchouk V, Grachtchouk M, **Lowe L**, Johnson T, Wei L, Wang A, deSauvage F, Dlugosz AA: The magnitude of hedgehog signaling activity defines skin tumor phenotype. EMBO J 22: 2741-2751, 2003.
10. Bezanis G, Wang TS, Johnson TM, **Lowe L**: Verrucous plaques on the leg. Arch Dermatol 139:933-938, 2003.

11. Altman JF, **Lowe L**, Redman B, Esper P, Schwartz JL, Johnson TM, Haefner HK: Placental metastasis of maternal melanoma. J Am Acad Dermatol (in press).
12. Pacella SJ, **Lowe L,** Bradford C, Johnson TM, Rees R: The utility of sentinel lymph node biopsy in head and neck melanoma in the pediatric population. Plast Reconstr Surg (in press).
13. Karimipour DJ, **Lowe L**, Su L, Hamilton T, Sondak V, Johnson TM, Fullen D: Melanoma sentinel lymph node biopsy: utility and sensitivity of standard immunostains. J Am Acad Dermatol (in press).
14. Sondak VK, Taylor JMG, Wang Y, Sabel MS, **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 (in press).
15. Wechter ME, Gruber SB, Haefner HK, **Lowe L**, Schwartz JL, Reynolds KR, Johnston CM, Johnson TM: Vulvar melanoma: a report of 20 cases and review of the literature. J Am Acad Dermatol (in press).
16. Wechter ME, Reynolds KR, Haefner HK, **Lowe L**, Gruber SB, Schwartz JL, Johnston, CM, Johnson TM: Vulvar melanoma: Review of diagnosis, staging and therapy. Journal of Lower Genital Tract Disease (in press).

ARTICLES SUBMITTED FOR PUBLICATION:

1. Su LD, Fullen DR, **Lowe L**, Wang TS, Schwartz JL, Cimmino VM, Sondak VK, Johnson TM: Desmoplastic and neurotropic melanoma. Analysis of 57 cases, including 33 cases with lymphatic mapping and sentinel lymph node biopsy. Submitted to Cancer, 2003.

ABSTRACTS, BOOK REVIEWS, PRELIMINARY COMMUNICATIONS, PANEL DISCUSSIONS:

1. Barr KL, **Lowe L**, Su LD: Mycobacterium marinum infection simulating interstitial granuloma annulare: A report of two cases. J Cutan Pathol 30: 42, 2003.
2. Fullen DR, **Lowe L**, Su LD: Antibody to S100 A6 is a sensitive immunohistochemical marker for neurothekeoma. J Cutan Pathol 30: 60, 2003.
3. Bogner P, **Lowe L**, Fullen D, Biermann J, Paulino AF, Sondak V, Su L: Lymphatic mapping and sentinel lymph node biopsy detects early metastasis of eccrine carcinoma. J Cutan Pathol 30: 89, 2003.
4. Guitart J, **Lowe L**, Piepkorn M, Prieto VG, Rabkin MS, Shea CR, White W, Barnhill RL: Metastasizing thin melanoma or multiple primary melanomas? Arch Dermatol 139: 388-389, 2003.
5. Sabel MS, Taylor JM, Grover AC, **Lowe L**, Chang AE, Johnson TM, Sondak VK: Mitotic rate and younger age are predictors of sentinel lymph node positivity. Abstracts of the Society of Surgical Oncology 56th Annual Cancer Symposium, Ann Surg Oncol 10(suppl): S17, 2003.

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

ANNUAL DEPARTMENT REPORT
1 JULY 2001-30 JUNE 2002

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Pathology 585, Lecturer, Inflammation section, Summer, 2002, 2003
B. Pathology 580, Dental School. Lectures on Inflammation, cytokines and Chemokines
C. Pathology 581, Graduate Students. Lectures on Inflammation and Immune responses.
D. Pathology 643, Course Director, Immune mechanisms of Disease, Fall, 2002.
E. Post-doctoral fellows-Alison John, Steve Lundy
F. Graduate Students- Allison Miller, Molly Thomas, Matt Schaller, Brian Rudd

III. RESEARCH ACTIVITIES:

NIH SPONSORED SUPPORT:

A. Principal Investigator, "Role of C-C chemokines in eosinophil airway inflammation", RO1, 5/1/01-4/30/06, National Institutes of Health.
B. Principal Investigator, "SCF and mast cells in allergic airway inflammation", NIH R01. 9/1/99-8/30/03.
C. Principal Investigator, "Cockroach allergen-induced airway inflammation" NIH Program Project, Project IV with P.A. Ward, M.D., Program Director 3/1/99-2/28/04.
D. Co-Investigator, "Acute Lung Injury", Project 2, NIH Special Centers of Research (SCOR) grant, with Steven L. Kunkel, Ph.D., Ted Standiford, M.D. SCOR Director. 12/01/98 to 11/30/04.
E. Co-Investigator, "Fibrotic cytokine phenotypes in interstitial lung disease" Project 3, NIH Special Centers of Research (SCOR) grant, with Steven L. Kunkel, Ph.D. Galen B. Towes, M.D. SCOR Director.
F. Co-Investigator, "RETINAL CELL/LEUKOCYTE BINDING INDUCES CXC/CC CHEMOKINES", with Victor Elner, M.D., Ph.D. NIH RO1. 9/01/98 to 8/30/03.

INDUSTRIAL SUPPORT:

A. Anormed Corp. "Role of CxCR4 antagonists in allergic airway disease" 5/2002 to 6/2003.
B Berlex Biosciences "Role of Lipoxin and its analogs in attenuating allergen-induced airway disease" 12/2002 to 11/2003.

PROJECTS UNDER STUDY:

A. Regulation of cytokine and chemokines during eosinophilic airway inflammation.
B. Role of mast cells in chronic inflammation.
C. Role of cytokines and chemokine in RSV-induced airway inflammation.
D. Role of chemokines in autoimmune responses.
E. Role of stem cell factor (SCF) in acute and chronic inflammation.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

1. Immunology representative- Curriculum Committee for Joint Medical School Graduate program, PIBS.
2. Admissions Committee- Immunology Graduate Program in PIBS.
3. Cirriculum Committee for Pathology Graduate Program.
4. Preliminary exam committee for Pathology Graduate Program.
5. Immunology graduate examination Committee
6. Immunology Graduate Steering Committee

REGIONAL AND NATIONAL:

SECTION EDITOR:

1. Journal of Immunology
2. Journal of Interferon and Cytokine Research

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. European Respiratory Journal
6. Journal of Experimental Medicine
7. Journal of Leukocyte Biology
8. Cellular Immunology
9. BLOOD
10. Journal of Clinical Investigation

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. The role of chemokines and their receptors in pulmonary inflammation. Cleveland Clinic. Cleveland, Ohio 11/6/02.

2. Chemokines and their receptors in Airway disease. Keystone Symposium on Chemotactic Cytokines. Beaver Run, CO. January 7-12, 2003.
3. The role of chemokines and their receptors in asthmatic inflammation. IBC conference on Inflammatory mediator. Vienna, VA. June 2-4, 2003.
4. Airway inflammation and Disease. Eli Lilly, Indianapolis, IN, August, 26, 2003.

SESSION CHAIRS:

1. Role of cytokines in vasculitis responses. Exp. Biol. annual meeting, San Diego, CA. April, 2003.
2. Chemokines in Immunological responses. AAI annual meeting, Denver, CO, May, 2003.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED IN PEER-REVIEWED JOURNALS:

1. Oliveira, S.H.P., S. Lira, M. Miekowski, L. Sullivan, and N.W. Lukacs. Increased responsiveness of murine eosinophils to MIP-1b (CCL4) and TCA3 (CCL1) is mediated by their specific receptors, CCR5 and CCR8. J. Leuk. Biol. 71:1019-1025, 2002.
2. Mancuso, P., A. Gottschalk, S. M. Phare, M. Peters-Golden, N. W. Lukacs, and G. B. Huffnagle. Leptin-deficient mice exhibit impaired host defense in Gram-negative pneumonia. *J Immunol 168:4018, 2002.*
3. Cheng, S. S., N. W. Lukacs, and S. L. Kunkel. Eotaxin/CCL11 suppresses IL-8/CXCL8 secretion from human dermal microvascular endothelial cells. *J Immunol 168:2887, 2002.*
4. Blease, K., J. M. Schuh, C. Jakubzick, N. W. Lukacs, S. L. Kunkel, B. H. Joshi, R. K. Puri, M. H. Kaplan, and C. M. Hogaboam. Stat6-deficient mice develop airway hyperresponsiveness and peribronchial fibrosis during chronic fungal asthma. *Am J Pathol 160:481, 2002.*
5. Shang, XZ, K.A. Frait, N.W. Lukacs, S.L. Kunkel, and S.W. Chensue. Eosinophil mobilization to type-2 (Schistosomal antigen-induced) hypersensitivity pulmonary granulomas: Role of eotaxin and Monocyte chemotactic protein-3 (MCP-3). Am J. Pathol. 161:257-266, 2002.
6. Lukacs, N.W., A. John, A. Berlin, D.C. Bullard, R. Knibbs, and LM Stoolman. E- and P-Selectins are essential for the development of cockroach allergen-induced airway responses. J. Immunol. 169:2120-2125, 2002.
7. Sandra H.P. Oliveira, D.D. Taub, J. Nagel, R. Smith, and N.W. Lukacs. Stem cell factor (SCF) induces eosinophil activation and degranulation: mediator and gene array analysis. Blood 100(13):4291-7, 2002.
8. Kim K. Tekkanat, Aaron A. Berlin, Hussein Maassab, Steven L. Kunkel, Pam Lincoln, Holly Evanoff, and Nicholas Lukacs. Role of RANTES in the primary RSV infection and Lung function. Eur. J. Immunol. 32:3276-3284, 2002.
9. Molly Thomas, Steven L. Kunkel, and Nicholas W. Lukacs. Differential role of IP-10 during allergen-induced airway responses: Local vs. systemic effects. J. Immunol. 169: 7045-7053, 2002.
10. K. Simpson, S.L. Kunkel, D.J. Harrison, C.M. Hogaboam, and N.W. Lukacs. Stem cell factor (SCF) attenuates liver damage and promotes regeneration in a murine model of acetominophen-induced hepatic injury. Lab Invest 83:199-206, 2003.

11. Allison L. Miller, Robert M. Strieter, Samual Ho, H. Gruber, and N.W. Lukacs. Role of CxCR2 in RSV-induced mucus production and airway hyperreactivity. J. Immunol. 170(6):3348-56, 2003.
12. Kavita Raman, Mark H. Kaplan, Cory M. Hogaboam, Aaron Berlin, Steven L. Kunkel and N.W. Lukacs. STAT4 signal pathways regulate inflammation and airway physiology changes in allergic airway inflammation locally via alteration of chemokines. J.Immunol. 170:3859-3865, 2003.
13. Alison John, Aaron Berlin, and Nicholas W. Lukacs. Effect of RSV-induced CCL5 on allergic airway inflammation. Eur. J. Immunol. Jun;33(6):1677-85, 2003.
14. Pinho V, Oliveira SH, Souza DG, Vasconcelos D, Alessandri AL, Lukacs NW, Teixeira MM. The role of CCL22 (MDC) for the recruitment of eosinophils during allergic pleurisy in mice. J Leuk Biol. 73(3):356-62, 2003.
15. Lukacs, N.W., A.L. Miller, and C.M. Hogaboam. Chemokine receptors in Asthma: Searching for the correct immune targets. J. Immunol. 171(1):11-15, 2003.
16. Steve Lundy, Aaron A. Berlin, and Nicholas W. Lukacs. Interleukin-12 Independent downmodulation of cockroach antigen-induced asthma in mice by intranasal exposure to bacterial lipopolysaccharide. Amer. J. Pathol. (In Press).
17. Allison John, Nicholas W. Lukacs, Lloyd Stoolman, Robert Bergatze, and Jon Nagy. P selectin-specific nanoparticle technology in allergic asthma. FASEB J. (In Press).

BOOKS/CHAPTERS IN BOOKS:

1. Cory M. Hogaboam, Jane M. Schuh, Alison E. John, and Nicholas W. Lukacs. The role of chemokines in asthmatic inflammation. Ed. R.M. Strieter, S.L. Kunkel, T.J. Standiford. Marcel Dekker. 2002.
2. Lukacs, N.W. Cytokines, Chemokines, and asthmatic inflammation. CLI Journal. Oct., 2002.
3. Lukacs, N.W. MAI Interview on chemokines in asthma. MAI Journal. January, 2003.
4. S.L. Kunkel, NW Lukacs, SW Chensue, CM Hogaboam. Cytokine phenotypes and the progression of chronic pulmonary fibrosis. Idiopathis pulmonary fibrosis . ED. J. Lynch. Marcel Dekker, 2003.
5. John, Alison and N.W. Lukacs. The role of chemokines and their receptors in Asthma. Sarcoidosis. (In Press).

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 – 30 JUNE 2003

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. Neuroscience Sequence, Neuropathology for Second Year Medical Students.
   1. Prepared two laboratories and two lectures on brain tumors; toxic, metabolic, demyelinating and infectious diseases.
   2. Taught four laboratories.
   3. Senior medical student, Neuropathology elective.
B. House Officers:
   1. Brain cutting, sampling, microscopic examination and special stain instruction of pathology House Officers.
   2. Individual instruction of Pathology House Officers on neurosurgical biopsy material, 28 weeks.
   3. Review all neurosurgically removed material in the hospital in CME-approved biweekly conference, 28 weeks.
   4. Invited presentations of neuropathologic observations at Rheumatology, Ophthalmology and other joint clinical conferences.
   5. Pathology Resident's Tuesday AP Conference rotated with other faculty.
   6. One month House Officer Electives.
   7. Pathology Resident's Monday Special Conferences rotated with other faculty.
   8. Combined Neurosurgery, Neuroradiology, Neuropathology CPC.
   9. Autopsy call.
   10. Pathology Gross Conference.
   11. Various other conferences.
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": 41st Annual AFIP Kenneth M. Earle Memorial Neuropathology Review, Armed Forces Institutes of Pathology, Rockville, Maryland, 2003.

III. RESEARCH ACTIVITIES:

A. Immunohistochemical study of germ cell tumor with Dr. Riccardo Valdez.
B. Immunohistochemical study of craniopharyngiomas with Dr. Wei Xin.
C. Study of pituitary adenoma hypophyseal stroma with Dr. Jason Jarzembowski.

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.

REGIONAL AND NATIONAL:

A. Editorial Board, Journal of Histochemistry and Cytochemistry.
B. Editor, Histochemical Society Newletter.
C. Primary Review Pathologist, Children's Cancer Study Group CCG 9897 nationwide study of childhood low grade gliomas.
D. Reviewer for the following journals:
    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.
E. Member, Brain Tumor/EMF Study Scientific Advisory Panel, National Cancer Institute, Jonathan Samet, Chairman.
F. Member, Review Panel, Program for Treatment of Malignant Brain Tumors, National Cancer Institute, William Jewell, Chairman.
G. Member, Review Panel, Molecular Markers of Glioma Initiation and Progression, National Cancer Institute, Susan Naylor, Chairwoman.
H. M-Labs Neuropathology Services.

V. OTHER RELEVANT ACTIVITIES:

PROFESSIONAL ORGANIZATIONS:

A. Faculty of Graduate Program of Department of Pathology.
B. Member of the University of Michigan Cancer Center.
C. Member, International Academy of Pathology, 1972 --.
D. Member, Alpha Omega Alpha, Eta Chapter, 1972 –.
E. Member, American Association of Neuropathologists, 1978 --.
F. Member, Society of Neuroscience, 1983 --.
G. Member, American Association of Pathologists, 1984 --.
H. Member, Children's Cancer Study Group, 1985 --.
    1. Pathology Committee, 1989 --.
    2. Primary Review Pathologist for astrocytoma study, 1991 --.
       Review and determine correct diagnoses on cases put on study protocol.
I. Member, Histochemical Society, 1989 --.
    1. Constitution Advisor 1996 --.
       Make certain that Council functions in accord with constitution.
J. Lieutenant Colonel, U.S. Army Reserve Medical Corps, 1997 --.

PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Xin W, Rubin MA, **McKeever PE.**: Differential expression of cytokeratin 8 and 20 differentiate between craniopharyngioma and Rathke cleft cyst. Arch Pathol Lab Med 126:1174-8, 2002.
2. Valdez R, **McKeever PE**, Finn WG, Ross CW, Schnitzer B.: Composite germ cell tumor and high-grade B-cell lymphoma arising in the sella turcica: a report of one case. Human Pathol 33:1044-7, 2002.
3. Youkilis AS, Park P, **McKeever PE**, Chandler WF.: Parasagittal ependymoma resembling falcine meningioma. Am. J. Neuroradiol: 22: 1105-8, 2001.
4. Song DK, Boulis NM, **McKeever PE**, Quint DJ.: Angiotropic large cell lymphoma with imaging characteristics of CNS vasculitis. Am. J. Neuroradiol.: 23: 239-42, 2002.
5. 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.
6. Lin PT, Bijwaard K, **McKeever PE.**: Adult peripheral primitive neuroectodermal tumor of the cauda equina diagnosed by a combined immunohistochemical and molecular genetic analysis. (in preparation)
7. 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.
8. Lin PT, Bijwaard K, **McKeever PE.**: Adult peripheral primitive neuroectodermal tumor of the cauda equina diagnosed by a combined immunohistochemical and molecular genetic analysis. (in preparation).
9. **McKeever PE**, Junck L, Li L, Mena H, Tkacyzk A, Yan M.: Block age affects MIB-1 proliferation indices. (in preparation).

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., 2003, 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, Blaivas M, Gebarski SS: In: *Pituitary Tumors, Chapter 23*. Thapar K, Kovacs K, Scheithauer BW, Lloyd RV (Eds). The Humana Press Inc., Totowa, New Jersey, 2000. (in press).
4. 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.
5. McKeever PE: Immunohistochemistry of the nervous system. In: *Diagnostic Immunohistochemistry*. Dabbs DJ (Ed). Churchill Livingstone, 2002, pp.559-624.
6. McKeever PE, Boyer P: The brain, spinal cord, and meninges. In: *Diagnostic Surgical Pathology, 4th edition*. Sternberg SS, Antonioli DA, Carter D, Mills SE, Oberman HA (Eds). Lippincott, Philadelphia (in press).

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

A. General surgical pathology – six weeks
B. Genitourinary surgical pathology—six weeks
C. Hospital gynecologic and nongynecologic cytology—seven weeks
D. Fine needle aspiration cytology—seven weeks
E. Gastrointestinal and hepatic pathology services – seventeen weeks

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

A. Medical Students:
   1. Pathology 600 - laboratory 2-4 hours per week
   2. Senior Elective in Pathology: mentor, 4 weeks with daily conferences

B. House Officers:
   1. Surgical pathology diagnosing room instruction for assigned house officer—6 weeks
   2. Cytopathology fellow and assigned resident diagnostic teaching—14 weeks
   3. Gastrointestinal and hepatic pathology tutoring - full time
   4. Lectures in gastrointestinal and liver pathology, 2 hours
   5. Consult conferences, 4-5 hours
   6. Lectures in cytopathology, 3 hours
   7. Cytopathology fellows weekly case conferences, 40 hours
   8. Resident Morgue Rounds, 50 hours

C. Interdepartmental:
   1. G-I Tumor Conference - (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 microsopic 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. Is there such a thing as ectopic antral mucosa in the duodenal bulb? With Wei Xin and HD Appelman
E. Marginal collagenous colitis: does it exist? With HD Appelman, W Xin, M Anderson and L Evans
F. A study to correlate high resolution CT findings with histologic findings in resected small bowel for Crohn's disease, with Ellen Zimmerman, Peter Higgins, and others
G. Studies of acute pancreatitis in CFTR-/- mice, with Matthew DiMagno and others
H. Correlation of standard cytologic interpretation and molecular characterization of EUS-guided FNA specimens, with Michelle Anderson and others

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Resident Selection Committee
B. Pathology Faculty Library Renovation Project
C. Clinical Laboratories Long Term Planning Committee

MEDICAL SCHOOL/HOSPITAL:

A. Member, Admissions Committee

REGIONAL AND NATIONAL:

A. Commissioner for Graduate Medical Education in Pathology, American Society for Clinical Pathology
B. Member, Board of Directors, American Society for Clinical Pathology
C. Member, Publication Committee, American Society for Clinical Pathology
D. Advisor, Resident Physician Group, American Society for Clinical Pathology
E. Member, Task Force on Maintenance of Certification, American Society for Clinical Pathology
F. Co-Director, Resident Review Course, American Society for Clinical Pathology
G. Ambassador, United States and Canadian Academy of Pathology
H. President, A James French Society of Pathologists

VI. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "The gastrointestinal biopsy report: What's right, what's wrong and what doesn't matter?" With BJ McKenna, half day course, Annual meeting, American Society of Clinical Pathologists, Washington, DC, Oct 22, 2002;
2. "Non-IBD colitis" and "Gastrointestinal biopsy reports: to err is human, but who will forgive you?" with Henry D. Appelman, Second Annual Current Topics in Gastrointestinal Pathology, Johns Hopkins University School of Medicine, Baltimore MD, November 10-11, 2002

3. "Liver Pathology" and "Selected Cases in GI and Liver Pathology" at ASCP Resident Review Course, Hoffman Estates, Illinois, April, 2003
4. "Non-IBD Colitis", Visiting Blue Grass Professor Lecture, University of Kentucky, Lexington, KY, June 6, 2003
5. The Gastrointestinal Biopsy Report, with HD Appelman, 31st Annual Kentucky Society of Pathologists Spring Seminar, Versailles, KY, June 7, 2003

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREEDJOURNALS:

1. McKenna BJ, Appelman HD: Dysplasia can be a pain in the gut. Pathology, 34:518-528, 2002

CHAPTERS and BOOKS:

2. 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. Kaur P, Appelman HD, McKenna BJ: Computer-assisted image analysis separates benign from malignant gastric stromal tumors. Am J Clin Pathol. 118:638, 2002
2. McKenna BJ, Appelman HD: Biopsies of colonoscopically normal mucosa in adult patients with chronic diarrhea provide diagnostically relevant information in most cases. Mod Pathol. 16:128A, 2003
3. Xin W, McKenna BJ, Appelman HD: Gastric surface metaplasia in the duodenal bulb is not ectopic antral mucosa. Mod Pathol. 16:137A, 2003

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Medical School Students:
   1. Mentor for medical students' senior clerkship – six weeks.
   2. Introduction to cytology, second year medical students (30 minute lecture)
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.
   4. Monthly Cytopathology Resident Conference.
   5. Weekly Cytopathology Fellowship Conference
   6. Consult Case Conference.
   7. Anatomic Pathology Conference: 2/year-Review of Cytopathology
C. Other Education Activities:
   1. Cytotechnologists - Cytopathology Slide Conferences.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

1. 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.

PROJECTS UNDER STUDY:

1. Co-Investigator. (Principle Investigator: Daniel F. Hayes) Ductal lavage pilot study. Sponsored by the Daniel F. Hayes Breast Cancer Gift Fund.
2. Co-Investigator. (Principle Investigator: Lisa A. Newman, M.D., MPH, FACS) Feasibility study of evaluating breast cancer patients with ductal lavage.

3. Co-Investigator. (Principle investigator: David N. Riesman) Evaluation of BRG1/BRM in primary lung carcinoma.
4. Co-Investigator. (Principle investigator: Samir Hanash, M.D.) Global profiling of the cell surface proteome of cancer cells.
5. Fine needle aspiration of squamous lesions; Diagnostic features and pitfalls.
6. Dai Y, Michael CW. Application of Beta Catenin and Cyclin D1 in mesothelial lesions.
7. Sturm C, Michael CW. Cytologic features of microglandular hyperplasia.

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. Secretary, Papanicolaou Society of Cytopathology.
E. Member, American society of Clinical Pathologists, Non-Gynecologic Star Program
F. Member, American society of Cytopathology, Scientific Committee
G. Member, Abstract review committee, United States and Canadian Academy of Pathology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "ThinPrep in non-gynecologic specimens: our experience at the University of Michigan". Invited presentation, European Congress of Cytopathology. Antwerp, Belgium, September 18, 2002.
2. "Comparison between ThinPrep and TriPath in non-gynecologic specimens". Invited presentation, European Congress of Cytopathology. Antwerp, Belgium, September 17, 2002.
3. "Unknown slide seminar" Invited speaker, European Congress of Cytopathology. Antwerp, Belgium, September 18, 2002.
4. "Respiratory and effusion cytology session" Co-moderator, European Congress of Cytopathology. Antwerp, Belgium, September 17, 2002.
5. "Diagnostic cytology challenges in effusions". Microscopic tutorial, American Society of Clinical Pathology, October, 2002.

6. "Cytopathology of the Lung. Differential Diagnosis and Diagnostic Pitfalls". **Workshop**, American Society of Clinical Pathology, October, 2002.
7. "The interpretation of fine needle aspirates prepared by the ThinPrep technique". American society of cytopathology, Utah, November 9, 2002.
8. "The interpretation of cytologic specimens prepared by the ThinPrep technique". **Short Course**, United States and Canadian Academy of Pathology. Chicago, IL. March , 2003.
9. "Pulmonary cytopathology, microscopic session". Invited speaker, Rush Presbyterian Hospital, Chicago, IL. April 7, 2003.
10. "Neuroendocrine tumors of the lung: differential diagnosis and diagnostic pitfalls". Invited speaker, Rush Presbyterian Hospital, Chicago, IL. April 7, 2003.
11. "Neuroendocrine tumors of the lung: differential diagnosis and diagnostic pitfalls". **Teleconference,** Teleconference Network of Texas, May 2003.
12. ""Neuroendocrine tumors of the lung: differential diagnosis and diagnostic pitfalls". Michigan Society of Cytology, May, 2003
13. "Diagnostic cytology challenges in effusions". **Teleconference**, Teleconference Network of Texas, June 2003. Jointly presented with Yiran Dai, M.D.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Gong Y, Sun X, Michael CW, Attal S, Williamson BA, Bedrossian CWM. Immunocytochemistry of serous effusion specimens: a comparison of ThinPrep vs. cell block. Diagn. Cytopathol. 2003;28:1-5.
2. Shin BK, Wang H, Yim AM, Le Naour F, Brichory F, Jang JH, Zhao R, Puravs E, Tra J, Michael CW, Misek DE, Hanash S. Global profiling of the cell surface proteome of cancer cells uncovers an abundance of proteins with chaperone function. The Journal of Biologic Chemist. 2003;278(9):7607-7616.
3. Bavikatty NR, Michael CW. The cytologic features of small cell carcinoma on ThinPrep. Diagn. Cytopathol. (Diagn. Cytopathol. 2003;29:8-12).
4. Xin W, Raab S, Michael CW. Low grade urothelial carcinoma: Reappraisal of cytological criteria on ThinPrep. (Diagn. Cytopathol. 2003;29:125-129).
5. Liu W, Michael CW. Malignant mesothelioma versus adenocarcinoma in serous fluids: The everlasting challenge. Check Sample, American Society of Clinical pathology.
6. Xin W, Davenport R, Chang D, Michael CW. The Exaggerated Pigmented Granulomatous Reaction to the Artificial Joint Implant Mimics Metastatic Melanoma. (In press, Diagn cytopathol)

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED 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).
2. Anca M. Avram, , Christine Sturm, Claire W. Michael, Craig A. Jaffe, and James C. Sisson. Cryptococcal Thyroiditis and Hyperthyroidism.

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

1. Michael CW. Color atlas of Cancer Cytopathology, Edited by Takahashi M. Lippincott williams &Wilkins, 2000. **Book review**. AJCP 2002;2:332
2. Bhattacharya B, Bengana C, Kluskens L, Reddy VB, Michael CW, Gattuso P. The role of E-Cadherin, Calretinin and Vimentin in differentiating reactive mesothelial cells and mesothelioma from malignant epithelial effusions.

A. REES MIDGLEY, M.D.
PROFESSOR EMERITUS
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. MEDICAL SCHOOL

None

II. DENTAL SCHOOL

Pathology 631 Laboratory, Instructor for semester, ≈50 students, 2-4 contact hours/week.

III. RESIDENT TRAINING/CONTACT HOURS

None

IV. PATHOLOGY GRADUATE PROGRAM/CONTACT HOURS

None

V. POSTDOCTORAL FELLOWS, GRADUATES & UNDERGRADUATES

1. Graduate students - None
2. Postdoctoral Fellows - None
3. Other students:
   Brett Lantz, undergraduate student

VI. CONTINUING MEDICAL EDUCATION/OTHER EDUCATIONAL ACTIVITIES

A. Advised students who worked on research projects

B. During final year of phased retirement, continued to work on our multimedia, Web-based learning initiative in our non-profit, 501(c)(3) start-up company, inDepthLearning. This project is focused on using novel approaches and state-of-the-art technologies to help anyone regardless of reading ability (ranging persons reading at grade school to professional levels) to learn what they need and want to know about reproduction, reproductive health and sexuality. This project was funded by the U.S. Department of Education's Fund for the Improvement of Postsecondary Education (FIPSE). Created a new, complementary, for-profit company, NotABook Publishing, Inc. focused on using web-based, motivational tools for publishing. NotABook was recently awarded a Small Business Innovative Research grant from the NIH, "Adherence to Antiretrovirals in People Living with HIV" and inDepthLearning will be receiving an NIH R25 educational grant on June 1, "Reaching Teenage Drinkers via the Internet."

RICHARD A. MILLER, M.D., Ph.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY
SENIOR RESEARCH SCIENTIST
INSTITUTE OF GERONTOLOGY
RESEARCH SCIENTIST
ANN ARBOR V.A. MEDICAL CENTER

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

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.
   2. Immunology Program Prelim Exam Committee
   3. Ph.D. Dissertation Committees, University of Michigan:
      a. Yadira Hernandez
      b. Omer Yilmaz
4. Ph.D. Dissertation Advisor:
      a. Anavelys Ortiz-Suarez
      b. Scott Berger
      c. Adam Salmon
      d. Yayi Chang
      e. Norma DeJesus

B. Postdoctoral Fellows:
      a. James Harper
      b. Amir Sadighi-Akha
      c. Shin Murakami
      d. Scott Maynard

C. In Lab:
   1. Gonzalo Garcia, Ph.D.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, R. A. Miller "Genetic Control of Longevity in Mice," NIH/NIA 1-R01-AG11687-10 (8%), $291,292 direct costs/year, 9/1/93–11/30/03.

B. Principal Investigator, R. A. Miller, "Genetics of Age-Sensitive Traits in Mice," NIH/NIA 1-P01-AG-16699-05 (20%), $637,739 direct costs/year, 5/99–4/04.

C. Principal Investigator, R. A. Miller, "Wild Derived Mouse Stocks: New Models for Aging Research," NIH/NIA R01-AG13711-07 (10%), $200,000 direct costs/year, 9/1/00 - 8/31/05.

D. Principal Investigator, R. A. Miller, "Activation Defects in T Cells of Aged Mice," NIH/NIA R01-AG19619-03 (15%), $250,000 direct costs/year, 9/30/00 – 8/31/05.

E. Principal Investigator, J. Faulkner, "Nathan Shock Center of Excellence in the Basic Biology of Aging," NIH P30-AG13283-08, $139,000 direct costs/year, 9/1/95 – 6/30/05. Dr. Miller directs the Gene Expression Profiling Core and the "Laboratory for Anti-Geric Testing, Evaluation and Research."

F. Principal Investigator, J. Halter, "Claude D. Pepper Older Americans Independence Center," NIH P30-AG08808-13 (20%), $919,621 direct costs/year, 9/1/99 - 8/31/04. Subproject: "Weight Gain Trajectory and Life Span in Mice" and "Research Development Core".

G. Principal Investigator, Andrzej Bartke, Southern Illinois University, NIH R01-AG19899-01 (2%), $175,000, 12/1/01 – 11/30/06. Interaction of caloric restriction with longevity genes (Bartke, PI). Subcontract: Gene expression and biomarkers in dwarf mice (Miller), $32,894/year.

H. Program Director, R. A. Miller, "Research Training in Experimental Immunology," NIH T32-AI-07413-10 (5%), $244,867 direct costs/year, 9/15/98 – 8/31/03.

I. Principal Investigator, R. A. Miller, "Laboratory for Anti-Geric Testing, Evaluation and Research," NIH/NIA U01-AG022303-01 (5%), $219,679 direct costs/year, 7/03 – 6/08.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Experimental Immunology Training 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. Program Executive Committee
E. Member, Rheumatology Training Program
F. 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

HONORS AND AWARDS:

A. None.

INVITED LECTURES/SEMINARS:

2002

1. UM Division of Geriatric Medicine, "Introduction to Aging Research," July 9.
2. Symposium on Frontiers in Aging Research, Seattle, WA. "From Barn to Benchtop: Not Your Father's Aging Rodent." September 17-18.
3. Central Society for Clinical Research, Annual Meeting, Chicago, IL. "Genetics of Aging and Gene Expression in Mice." September 26.
4. Swarthmore College Biology Program, Swarthmore, PA. "From Barn to Benchtop: Not Your Father's Aging Rodent." September 27.
5. Shock Center Symposium on Dietary Restriction, Bandera, TX. "Gene Expression Analysis in Calorically Restriced Mice." October 13.
6. Department of Physiology, University of Texas Health Science Center, San Antonio, TX. "Not Your Father's Aging Rodent: New Mouse Models for Biogerontology." October 14.
7. University of Michigan Institute of Gerontology, Ann Arbor, MI. "From Barn to Benchtop: Not Your Father's Aging Rodent." October 17.
8. University of Michigan Bioinformatics Series, Ann Arbor, MI. "Gene Expression and Gene Mapping in Aging Mice." October 31
9. Microarray Analysis Work Group, School of Public Health, Ann Arbor, MI. "Gene Expression Studies in Aging Mice." November 4.
10. Gerontology Society of America Annual Meeting, Chicago, IL. "Longevity and Maturation in Wild-Derived Mouse Stocks." November 22.
11. American Federation for Aging Research Board Meeting, New York, NY. "Aging: Progress and Political Obstacles." December 1

2003

1. Learning in Retirement lecture series, Kellogg Eye Center, Ann Arbor, MI. "Extending Human Life Span: Scientific Prospects and Political Obstacles." January 8.
2. Tennessee Mouse Genetics Consortium, Nashville, TN. "Gene Mapping Studies of Aging Mice." January 16.
3. Geriatrics Grand Rounds, Duke University, Durham, NC. "Gene Mapping and Gene Expression in Aging Mice." January 28.
4. Duke University Distinguished Lecture Series in Aging, Durham, NC. "Extending Human Life Span: Scientific Prospects and Political Obstacles." January 28.
5. University of Michigan Institute of Gerontology, Ann Arbor, MI. "Gene Expression Analysis of Aging: Triumph and Tragedy on the Front Lines." February 19.
6. University of Chicago, Department of Psychology, Chicago, IL. "Gene Mapping and Gene Expression Analyses of Aging in Mice." March 5.
7. Gordon Conference on Aging, Ventura, CA. "Evolution of Aging: Experimental Systems." March 11.
8. NIA Workshop on Array Analyses in Aging, Ventura, CA. "Cell Biology of Slow-Aging Mice: Gene Expression Systems." March 15.
9. Sex and Gene Expression Group, Annual Meeting, Winston-Salem, NC. "Gender Effects on Genetics of Aging in Mice." March 21.
10. Boston University Department of Biochemistry, Boston, MA. "Genetics of Aging in Mice." April 1
11. Boston University Immunology Program, Boston, MA. "Defective Activation Pathways in T Cells from Aged Mice" April 2
12. University of Chicago Department of Psychology, Chicago, IL. "Gene Expression and Gene Mapping in Aging Mice." April 16
13. University of Pennsylvania School of Medicine, Philadelphia, PA. "Not Your Father's Aging Rodent: Genetics and Immunology from Barn to Benchtop." April 17
14. University of Washington School of Medicine, Seattle, WA. "Gene Expression Analyses of Aging: Triumph and Tragedy on the Front Lines." April 28
15. University of Michigan Geriatrics Center Retreat, Ann Arbor, MI. "The NIH Peer Review System: The Steep and Thorny Path to Funding." May 6.
16. Annual Meeting of the American Association of Immunologists, Denver, CO. Plenary lecture: "The Aging/Cancer Nexus." May 10.
17. Duke University School of Medicine, "Not Your Father's Aging Rodent: Genetics and Immunology from Barn to Benchtop." May 12.
18. 4th International ImAginE Meeting on Aging and Immunity, Kolybari, Crete. Plenary lecture: "Genetic and Biochemical Studies of Aging in Mice." May 21.
19. SAGE Crossroads Webcast on "Exciting Developments in Aging Research". Washington, DC. May 28.
20. Summer Training Course in Aging Research, Novato, CA. "Vertebrate Animal Models for Aging Research." June 11
21. American Federation for Aging Research Annual Grantee Meeting. Santa Barbara, CA. " Vertebrate Animal Models for Aging Research" and "Extending Human Life Span." June 12, 13.
22. Longevity Assurance Gene Consortium Annual Meeting, San Francisco, CA. "Genetics of Aging and Age-Sensitive Traits in Mice." June 25.

23. Genecor, Inc., Department of Immunology, Palo Alto, CA. "The Aging/Cancer Nexus." June 27.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Miller, R. A. and C. Chrisp. 2002. T cell subset patterns that predict resistance to spontaneous lymphoma, mammary adenocarcinoma, and fibrosarcoma in mice. J. Immunol., 169:1619-1625
2. Miller, R. A., A. U. Jackson, A. T. Galecki, and D. T. Burke. 2003. Genetic polymorphisms in mouse genes regulating age-sensitive and age-stable T cell subsets in mice. Genes and Immunity, 4:30-39.
3. Miller, R. A., J. M. Harper, A. Galecki, and D. T. Burke. 2002. Big mice die young: early-life body weight predicts longevity in genetically heterogeneous mice. Aging Cell 1:22-29.
4. Miller, R. A., Y. Chang, A. T. Galecki, K. Al-Regaiey, J. J. Kopchick, and A. Bartke. 2002. Gene expression patterns in calorically restricted mice: partial overlap with long-lived mutant mice. Molecular Endocrinology 16:2657-2666.
5. Ortiz-Suarez, A., and R. A. Miller. 2002. In vivo expansion of aged T cells from an IFN-producing CD8 subset with atypically high CD28 levels. Clinical Immunology 104:282-292.
6. Volkman, S. K. A.T. Galecki, D. T. Burke, M. R. Paczas, M. R. Moalli, R. A. Miller, and S. A. Goldstein. 2003. Quantitative trait loci for femoral size and shape in a genetically heterogeneous mouse population. Journal of Bone and Mineral Research 18:1497-1505.
7. Murakami, S., A. Salmon, and R. A. Miller. 2003. Multiplex stress resistance in cells from long-lived dwarf mice. FASEB Journal express article 10.1096/fj.02-1092fje.
8. Garcia, G. G., and R. A. Miller. 2002. Age-dependent defects in TCR-triggered cytoskeletal rearrangement in $CD4^+$ T cells. Journal of Immunology 169:5021-5027.
9. Harper, J. M., N. Wolf, A. T. Galecki, S. L. Pinkosky, and R. A. Miller. Hormone levels and cataract scores as sex-specific, mid-life predictors of longevity in genetically heterogeneous mice. Mech. Ageing and Development 124:801-810.
10. Xu, S., N. Yi, D. Burke, A. Galecki, and R. A. Miller. An EM algorithm for mapping binary disease loci: application to fibrosarcoma in a four-way cross mouse family. Genetical Research, in press.
11. Ortiz-Suarez, A., and R. A. Miller. Antigen-independent expansion of $CD28^{hi}$ CD8 cells from aged mice: cytokine requirements and signal transduction pathways. J. Gerontol. Biol. Sci., in press
12. Harper, J. M., A. T. Galecki, D. T. Burke, S. L. Pinkosky, and R. A. Miller. Quantitative trait loci for insulin-like growth factor-I, leptin, thyroxine, and corticosterone in genetically heterogeneous mice. Physiological Genomics, in press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Garcia, G. G., and R. A. Miller. O-Sialoglycoprotein endopeptidase corrects age-associated defects in mouse T cell synapse formation without altering CD43 exclusion. Submitted.
2. Wolf, N., A. Galecki, R. D. Lipman, S. Chen, D. Burke, and R. A. Miller. Quantitative trait locus mapping for age-related cataract severity and synechia prevalence using four-way cross mice. Submitted.

BOOKS/CHAPTERS IN BOOKS:

None

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

A. Surgical Pathology and Frozen Section Diagnosis (17 weels/year)
B. Autopsy Service, rotational basis, on call 13 weeks/year (staffing 15-20 cases/year).
D. Case presentations at Morbidity and Mortality Conferences.
E. Case presentations at weekly Urologic Pathology Conferences
F. Coordinator, "Topics in Pathology", CME accredited lecture series

II. TEACHING ACTIVITITES:

A. Post-Doctoral Fellows
   1. Research co-advisor to post-doctoral fellow: Dr. Matthew Adams, Dept. of Rheumatology, University of Michigan. supported by Arthritis Foundation of Michigan

B. House Officers
   1. Pathology house officers, Autopsy supervision and instruction (13 weeks /year)
   2. Pathology house officers, Surgical Pathology supervision and instruction, (5 months/year)
   3. Lecture and Case presentations at weekly Urologic Pathology Conferences

C. Graduate students:
   1. Course Director, Pathology 585, Lecture and Laboratory course for Medical Illustration Graduate students (15 hrs)
   2. Laboratory Instructor, pathology 600 (M2 pathology course)

D. Undergraduate students:

III. RESEARCH ACTVITIES:

SPONSORED SUPPORT:

A. Co-Investigator "Gender-specific T cell homing and autoimmunity" (B. Richardson, Internal Medicine, PI) NIH RO1AI42753 12/98 - 11/03 ($1,609,959)
B. Co-Investigator, " Molecular Mechanisms of Lung Host Defense" (J Curtis, PI)Research EnhancementAward Program (REAP)Veteran's Administration 10/01/98-09/30/03 ($1,350,000)
C. Co-investigator, "Metabolic imaging of Renal and Prostate Cancer using C-11 Acetate" (S. Snyder, PI) RO1-CA089448-01 12/01/01-11/31/04 ($1,801,214)
D. Co-Investigator. " Lung Injury by Oxygen Metabolites" NIH/NIGMS R37 GM29507. National Institute of Health (Peter A. Ward, PI). 07/01/01 - 06/30/06 ($1,123,824).

PROJECTS UNDER STUDY:

A. Endothelial cell responses in inflammation
   1. The enzyme source of endothelial cell oxidants
   2. The role of endothelial cell derived oxidants in signaling and cell injury
   3. Repertoire of endothelial cell derived cytokines and their role in inflammation

B. Gender-specific effects of hormones on T cells and endothelial cells in autoimmunity
   1. Effect of estrogen on endothelial cell estrogen reception expression
   2. The role of estrogen in endothelial cell adhesion molecule expression and lymphocyte homing

C. Gender-specific effects of hormones on dendritic cells in autoimmunity
   1. Effect of estrogen on antigen presention by dendritic cells
   2. Role of estrogen in the autoimmune response to antigen

IV. ADMINISTRATIVE ACTIVITIES:

MEMBERSHIP IN PROFESSIONAL SOCIETIES:

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)

DEPARTMENTAL:

A. 2001-present Chief, Histopathology, Pathology and Laboratory Medicine, VAAHS
B. Chief, Clinical Electron Microscopy, Pathology and Laboratory Medicine, VAAHS

MEDICAL SCHOOL/HOSPITAL:

A. Member, Admissions committee of the University of Michigan Medical School, 1999-present

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)
2. New York Academy of Science (1991)
3. American Society for Investigative Pathology (Fellow,1995)
4. 1996 Institutional Liason to University of Michigan
5. American Society of Clinical Pathologists (Fellow, 1995)
6. American Association of University Women (1995)
7. The A. James French Society of Pathologists (1996)
8. Society for Experimental Biology and Medicine (2000)
9. The Oxygen Society (2001)
10. Society for Free Radical Research International (2001)
11. The Nitric Oxide Society (2001)

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:

BOOKS/CHAPTERS IN BOOKS:

1. Murphy, H. S., J. Varani and P. A. Ward. Biology of Endothelial Cells: Role of the Endothelium in Lung Inflammation. Middleton's Allergy: Principles and Practice. N. F. Adkinson. Mosby St Louis. 2003.
2. Murphy, H.S., Ward, P.A. Inflammation. In Pathology. E. Rubin (ed) Lippincott-Raven New York (in press).

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Shang, X-Z, Chiu, B-C, Stolberg, V, Lukacs, N.W., Kunkel, S. L., Murphy, H.S., Chensue, S. W. Eosinophil Recuritment in Type-2 (Schistosomal Antigen-Induced) Hypersensitivity Pulmonary Granulomas: Source and Contribution of Monocyte Chemotactic Protein-3 (CCL7).). Am. J. Path. 161: 257-66, 2002.
2. Laudes IJ. Chu JC. Huber-Lang M. Guo RF. Riedemann NC. Sarma JV. Mahdi F. Murphy HS. Speyer C. Lu KT. Lambris JD. Zetoune FS. Ward PA. Expression and function of C5a receptor in mouse microvascular endothelial cells. J Immunol. 169(10):5962-70, 2002
3. Robey, T.C., Valimaa, T., Murphy, H.S., Mooney, D.J., Weatherly, R.A The use of internal "Knitted-type" stents in a rabbit tracheal reconstruction model. Arch. Otolaryng (Accepted for publication)

4. Hattori Y. Nerusu KC. Bhagavathula N. Brennan M. Hattori N. Murphy HS. Su LD. Wang TS. Johnson TM. Varani J. Vascular expression of matrix metalloproteinase-13 (collagenase-3) in basal cell carcinoma. *Experimental & Molecular Pathology. 74(3):230-7, 2003.*
5. Speyer, C L., T.A. Neff, R.L.Warner, R-F Guo, J.V. Sarma, N C Riedemann, . M. E. Murphy, H. S. Murphy, P.A. Ward. Regulatory effects of iNOS on Acute Lung Inflammatory Responses in Mice. Am. J Pathol (Accepted for Publication).
6. Montgomery, J. S., B. K. Hollenbeck, P. C. Fisher, H. S. Murphy, W. Underwood. Benign Paratesticular Schwannoma. J. Urol (accepted for publication).

SUBMITTED PUBLICATIONS:

1. Murphy, H. S., Q. Sun, B. A. Murphy, S. W. Chensue, B. C. Richardson, R. Yung. Tisssue Specific Estradiol Enhancement of Endothelial Cell Dependent Lymphocyte Recruitment. (Submitted for publication – Microvascular Research)
2. Toung, J., H. S. Murphy, M.E. P. Prince. Parotid Lipoma: A case report. (Submitted for publication.)
3. 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. (Submitted for publication- Neurosurgery).
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 (Submitted, Arch Otolaryngol - Head and Neck Surg.)
5. 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. (Submitted, Genes & Development).
6. R. L. Warner, H. C. Winter, C. L. Speyer, 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. (Submitted to Am. J. Pathol.)

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

1. Speyer, C.S., Ward, P.A., Murphy, H.S. Analysis of Nitric Oxide Synthase Activity in Mouse Dermal and Lung Microvascular Endothelial Cells. FASEB J. 16: A594 2002
2. H.S. Murphy, Q. Sun, B.A. Murphy, B.C. Richardson. Estradiol Enhances Antigen Presentation by Spleen Dendritic Cells. Keystone Symposium, 2003.
3. J Grimmer, E Alsberg, H.S.Murphy, H Kong, D. J. Mooney R. Weatherly, Tracheal Reconstruction in Rabbits using Polyglycolic-Acid (PGA) Mesh Embedded with Alginate-Encapsulated Chondrocytes. American Academy of Otolaryngology 2003.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

A. Consultation Service: Cytopathology/pulmonary pathology - 12 months.
B. Autopsy Service, occasional coverage.

II. TEACHING ACTIVITIES:

A. Pathology residents – Diagnostic consultations and lectures.
B. Dental and graduate students - Lectures (Dermatopathology).

III. RESEARCH ACTIVITIES:

A. History of cytopathology.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Advisory Committee on Appointments and Promotions.

REGIONAL AND NATIONAL:

A. Cytopathology, Editorial Advisory Board.
B. Acta Cytologica
   Associate Editor
   Editorial Advisory Board
   North American Review Board
C. International Academy of Cytology:
   International Board of Cytopathology, Member
D. Awards Committee, American Society of Cytopathology

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. Naylor, B.: a). Cytopathology of serous fluids, b). Cytology of mesothelioma, c). Transthoracic fine needle aspiration cytology, c) History of cytopathology. Lectures, Cytotechnology Training Program, Wayne State University, Detroit, Michigan, 2003.
2. Mesothelioma and the cytopathology laboratory. Cytoteleconference, American Society of Cytopathology, Ann Arbor, MI, April 2003.

DUANE W. NEWTON, Ph.D.
CLINICAL ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

A. Associate 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.

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. Lecturer, Clinical Microbiology, Wm. Beaumont Hospital Medical Technology Program
I. Clinical Pathology Grand Rounds, UM Dept. of Pathology.
   1. "Specimen Processing in the Clinical Virology Laboratory." Grand Rounds presentation, Clinical Pathology Division, Department of Pathology, University of Michigan Medical Center. 9/6/02.
   2. "West Nile virus in the U.S. and Michigan." Grand Rounds presentation, Clinical Pathology Division, Department of Pathology, University of Michigan Medical Center. 10/4/02.

J. Continuing Education Lecturer, UM Dept. of Pathology.
   1. "West Nile virus in the U.S. and Michigan." Continuing Education Seminar, Department of Pathology, University of Michigan Medical Center. 10/2/02.
   2. "West Nile virus in the U.S. and Michigan." Continuing Education Seminar, Clinical Microbiology and Virology Laboratories, University of Michigan Medical Center. 11/7/02.
   3. "Quality assurance activities in clinical microbiology." Continuing Education Seminar, Clinical Microbiology and Virology Laboratories, University of Michigan Medical Center. 1/14/03.
   4. "West Nile virus in the U.S. and Michigan." Brown-bag lunch seminar for Medical Technology students, Department of Pathology, University of Michigan Medical Center. 2/12/03.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. "Role of EBV and malaria co-infection in the pathogenesis of endemic Burkitt's lymphoma," Principal Investigator: Rosemary Rochford, UM School of Public Health.
B. "Serologic response to EBV infection in the presence and absence of malaria endemnicity," Principal Investigator: Duane Newton, Dept. of Pathology, University of Michigan.

PROJECTS UNDER STUDY:

A. "Real-Time" PCR for the rapid diagnosis of infectious diseases.
B. Use of the Cobas Monitor for the quantitation of HBV in patients with hepatitis.
C. Retrospective comparison of antimicrobic susceptibility profiles of bacteria isolated from pediatric patients and adult patients.
D. Use of the HandyLab bedside PCR device for detecting *Streptococcus agalactiae* during pregnancy.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Clinical Pathology Laboratory Directors Committee.
B. Quality Assurance Committee
C. Clinical Microbiology/Virology Senior Staff committee.
D. Consultant for "Consultants in Laboratory Medicine", ProMedica Health System, Toledo, OH.
E. Clinical Pathology Training Program Review Committee

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

REGIONAL/NATIONAL:

A. Corporate Liason Co-chair, South Central Association for Clinical Microbiology.
B. Rabies Working Group, Michigan Department of Community Health
C. Ad hoc reviewer, Journal of Clincal 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. "West Nile virus in the U.S. and Michigan." American Society for Microbiology, Michigan Branch Meeting. University of Michigan, Flint. Flint, MI. 10/12/02.
2. "West Nile and Other Arboviruses in the U.S." Distinguished Lecture Series, Biology Program of the College of Arts and Sciences, Governors State Univeristy, University Park, IL. 11/11/02.
3. "West Nile virus in the U.S. and Michigan." American Society for Clinical Chemistry, Michigan Branch Meeting. Windsor, Ontario. 11/21/02.
4. "West Nile virus in the U.S. and Michigan." Department of Biology Seminar Series, Eastern Michigan University, Ypsilanti, MI. 2/05/03.
5. "West Nile virus in the U.S. and Michigan." Department of Microbiology and Immunology Seminar Series, Wayne State University, Detroit, MI. 2/05/03.
6. "West Nile and Other Arboviruses in the U.S." 6th Annual Infectious Diseases Update, Promedica Health System, Toledo, OH. 4/02/03.
7. "Update on HIV Testing." Michigan Society for Clinical Laboratory Science (MSCLS) Annual Meeting, DoubleTree Hotel, Romulus, MI. 4/11/03.
8. "Update on West Nile Virus and SARS." Association for Professionals in Infection Control and Epidemiology (APIC), Greater Detroit Chapter Meeting, 5/9/03.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. **D.W.** Newton, C.F. Mellen, B.D. Baxter, R.L. Atmar, and M.A. Menegus. 2002. Practical and sensitive screening strategy for detection of influenza virus. *Journal of Clinical Microbiology* 40:4343-4356.

BOOKS/ CHAPTERS IN BOOKS:

1. "West Nile virus." In APIC Text of Infection Control and Epidemiology, submitted.
2. "Rabies." In APIC Text of Infection Control and Epidemiology, submitted.

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

1. D.W. Newton. "Laboratory Methods for Detection of West Nile Virus," *Advance for Laboratory Professionals*, submitted.
2. D.W. Newton, N.J. Turner, and W.D. LeBar. 2003. Performance of Binax Flu A, Flu B, and RSV on specimens submitted in M4 transport – a multicenter evaluation. Poster presented at the 19th Annual Clinical Virology Symposium and Annual Meeting of the Pan American Society for Clinical Virology, Clearwater, FL.
3. C.L. Young, D.W. Newton, C.L. Pierson. 2003. Clinical use of swab extraction tube system (S.E.T.S.) for Gram stain and bacterial culture. Poster presented at the 103rd General Meeting of the American Society for Microbiology, Washington, DC.
4. C.L. Young, J.T. Rudrik, D.W. Newton, C.L. Pierson. 2003. Four year comparison of Premier EHEC and molecular testing for the detection of shiga toxin I- and II-producing *Escherichia coli*. Poster presented at the 103rd General Meeting of the American Society for Microbiology, Washington, DC.
5. D.W. Newton. "West Nile Update," M-Labs Spectrum, 17(3):3-5, 2003

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Supervised, Theresa Dowds, Peter Lucas, Linda McAllister-Lucas, Mathias Chamaillard, Nesrin Ozoren, Christine MacDonald, Ruth Alvarez, Lech Czerski, Yasumasa Nishito, and Yasunori Ogura, Cyrus Piraka, Postdoctoral Fellows.
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:

CURRENT:

A. Principal Investigator, "Genetic regulation of apoptotic cell death," National Institutes of Health, $813,000 (total direct costs), 6/1/99-5/31/04.
B. Principal Investigator, "Role of Apaf-1/Caspase-9 Pathway in tumor development in the breast" US Army Medical Grant; $50,000.
C. Principal Investigator, "Ciper: a novel NF-κB-activating gene involved in Cancer," National Institutes of Health, $1,000,000 (total direct costs), 1/7/00-6/30/05.
D. Principal Investigator, "Characteriation of chimeric c-IAP2/MALT-1 in Lymphoma", Michigan Life Science Corridor Fund, $620,507 (total direct costs), 2/15/01-2/14/04.
E. Principal Investigator, "Nod2: A Susceptibility Gene for Crohn's Disease" National Institutes of Health, $1,000,000 (total direct costs), 7/1/02-6/30/04

PROJECTS UNDER STUDY:

A. Role of Ciper/Bcl10 Pathway in Signal transduction and lymphoma development.
B. Molecular regulation of apoptosis by Bcl-2 family members.
C. Role of Nod Family in Innate Immunity and Crohn's disease

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:

UNIVERSITY OF MICHIGAN:

2002 Invited Speaker, "Nods: Apaf-1-like Molecules Regulating the Host Response to Pathogens:, School of Dentistry Oral Health Sciences Seminar Series, University of Michigan, January 10

2002 Invited Speaker, "Nods: Apaf-1-Related Molecules Involved in Pathogen Recognition", Hearing and Chemical Senses Seminar Series, University of Michigan, December 18, 2002

2003 Invited Speaker, "Role of Bcl10 in lymphoid Survival and MALT lymphoma", Cancer Center Research Seminar, University of Michigan, February 11, 2003

2003 Invited Speaker, "NODs: Intracellular Sensors of Bacteria linked to Inflammatory Disease", Department of Pathology Research Seminar Series, University of Michigan, March 3, 2003

NATIONAL/INTERNATIONAL:

1. Invited Keynote Speaker, "The Nod2 Gene and Crohn's Disease", Symposium "Genomics of Chronic Inflammatory Disorders", Kiel, Germany, July 5
2. Invited Speaker, "Mecanismos de apoptosis dependientes de la mitocondria: su regulacion y alteraciones en cancer", Escuela de Oncologia "Severo Ochoa", Santander, Spain, July 22, 2002
3. Invited Speaker, "Mecanismos moleculares asociados a patogenia del linfoma MALT", Escuela de Oncologia "Severo Ochoa", Santander, Spain, July 22, 2002
4. Invited Speaker "NODS: A family of Apaf-1-related proteins involved in Bacterial Recognition", 6th Joint Meeting of the Japan Society of Histochemistry and the US Histochemical Society", Seattle, WA, July 18, 2002
5. Guest Lecturer "Biology of Bcl10/MALT1", Recent Developments in Gastrick MALt lymphoma, University College, London, September 20, 2002
6. Invited Speaker "Sepis gets the NOD", 42nd ICAAC, San Diego, CA, Sept. 6, 2002
7. Invited Speaker "Intracellular Recognition of Pathways and Crohn's Disease", The University of Texas Southwestern Medical Center, Dallas, TX, October 22, 2002
8. Invited Speaker "Function of NOD2 in mice and humans", Center for the Study of Inflammatory Bowel Disease, Harvard University, Boston, MA, November 22, 2002
9. Invited Speaker "Intracellular Recognition of Pathways and Crohn's Disease", University of Illinois Medical School, Chicago, IL, November 25, 2002
10. Invited Speaker "Intracellular Recognition of Pathways and Crohn's Disease", Department of Immunology, University of Washington Medical School, Seattle, WA, December 10, 2002
11. Invited Speaker "Intracellular Recognition of Pathways and Crohn's Disease", Medical College of Ohio, Toledo, OH, December 19, 2002
12. Invited Speaker, "NOD2 and Crohn's Disease", Keystone Symposium "Linking Innate with Adaptive Immune Responses", New Mexico, USA, January 30, 2003
13. Invited Speaker, "NODs: Intracellular Sensors of Bacteria linked to Inflammatory Disease", Pfizer, Ann Arbor, MI, March 6, 2003
14. Invited Speaker, "Nods: A protein Family involved in Bacterial Recognition linked to Inflammatory Disease", Suny at Buffalo, Buffalo, NY, March 10, 2003
15. Invited Speaker, "Intracellular Recognition of Bacterial Pathogens and Human Disease", Vanderbilt University, Nashville, TN, March 24, 2003
16. Invited Speaker, Keynote Address, "NOD2 Function and its Role in Inflammatory Bowel Disease", Keystone Symposium "The Regulation of Mucosal Inflammation", Keystone, CO, April 1, 2003
17. Invited Speaker, "NOD2 function and Crohn's disease", 3rd Intntl. Meeting on Inflammatory Bowel Diseases, Capri, Italy, April 13, 2003
18. Invited Speaker, "Nods: Intracellular sensors of bacteria.", EMBO Worshop On Pattern Recognition Proteins And Receptors, Trest, Czech Republic, May 14, 2003
19. Invited Speaker, "The Bcl10 Signaling Pathway and MALT Lymphoma", Center for Scientific Review, CAMP, MEP, National Institute of Health "Paths to Perdition: Tumor Suppressors and Apoptosis", June 19, 2003
20. Invited Speaker, "The NOD family and its role in mucosal inflammation and apoptosis", Falk Symposium "Mechanisms of Intestinal Inflammation: Implications for Therapeutic Intervention in IBD", Berlin, Germany, June 10, 2003

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNAL:

1. Kobayashi K, Inohara N, Hernandez LD, Galan JE, Nuñez G, Janeway C, Medzhitov R, Flavell RA. RICK/Rip2/CARDIAK mediates signalling for receptors of the innate and adaptive immune systems. Nature 416:194-199 (2002).
2. Liu JR, Opipari AW, Tan L, Jiang Y, Zhang Y, Tang H, Nuñez G. Dysfunctional apoptosome activation in ovarian cancer: Implications for chemoresistance. Cancer Res; 62:924-931 (2002).
3. Nor JE, Hu Y, Song W, Spencer DM, Nuñez G. Ablation of microvessels in vivo upon dimerization of iCaspase-9. Gene Therapy 9:444-451 (2002).
4. Inohara N, Nuñez G. A conserved domain in MD-2 related protein family involved in innate immunity and lipid metabolism. Trends Biochem Sci 27:219-221 (2002)
5. Muto A, Ruland J, McAllister-Lucas LM, Lucas PC, Yamaoka S, Chen FF, Lin A, Mak TW, Nuñez G, Inohara, N PKK mediates Bcl10-independent NF-kappa B activation induced by phorbol ester. J Biol Chem.; 277:31871-31876 (2002).
6. Gutierrez O,. Pipaon C, Inohara N, Fontalba A, Ogura Y, Prosper F, Nuñez G, Fernandez-Luna JL. Induction of Nod2 in myelomonocytic and intestinal Ephithelial cellsvia nuclear factor-kB activiation. J Biol Chem 227:41701-41705 (2002).
7. Wang D, You Y, Case SM, McAllister Lucas LM, Wang L, DiStefano PS, Nuñez G, Bertin J, LinX. A requirement for CARMA1 in TCR-induced NF-kappaB activation. Nat Immunol. 3:830-835 (2002).
8. Inoue N, Tamura K, Kinouchi Y, Fukuda Y, Takahashi S, Ogura Y, Inohara N, Nuñez G, Kishi Y, Koike Y, Shimosegawa T, Shimoyama T, Hibi T. Lack of common NOD2 variants in Japanese patients with Crohn's disease. Gastroenterology. 123:86-91(2002).
9. Wang X, Kuivaniemi H, Bonavita G, Mutkus L, Mau U, Blau E, Inohara N, Nuñez G, Tromp G, Williams CJ. CARD15 mutations in familial granulomatosis syndromes: a study of the original Blau syndrome kindred and other families with large-vessel arteritis and cranial neuropathy. Arthritis Rheum 46:3041-3045(2002).
10. Masumoto J, Zhou W, Chen FF, Su F, Kuwada JY, Hidaka E, Katsuyama T, Sagara J, Taniguchi S, Ngo-Hazelett P, Postlethwait JH, Nuñez G, Inohara N. Caspy: A Zebrafish caspase activated by ASC oligomerization required for pharyngeal Arch development. J Biol Chem 278:4268-4276 (2003).
11. Bonen DK, Ogura Y, Nicolae DL, Inohara N, Saab L, Tanabe T, Chen FF, Foster SJ, Duerr RH, Brant SR, Cho JH, Nuñez G. Crohn's disease-associated NOD2 variants share a signaling defect in response to lipopolysaccharide and peptidoglycan. Gastroenterology 124:140-146 (2003).
12. Inohara N, Ogura Y, Fontalba A, Gutierrez O, Pons F, Crespo J, Fukase K, Inamura S, Kusumoto S, Hashimoto M, Foster SJ, Moran AP, Fernandez-Luna JL, Nuñez G. Host recognition of bacterial muramyl dipeptide mediated through NOD2: implications for Crohn's disease. J Biol Chem 278:5509-55012 (2003)
13. Dowds TA, Maumoto J, Chen F, Ogura Y, Inohara N, Nuñez G. Regulation of cryopyrin/Pypaf1 signaling by pyrin, the familial Mediterranean fever gene product. Biochemical and Biophysical Research Communications 302:575–580, 2003

14. Masumoto J, Dowds TA, Schaner P, Chen F, Ogura Y, Li M, Zhu L, Katsuyama T, Sagara J, Taniguchi S, Gumucio D, Nuñez G, Inohara N. ASC Is an Activating Adaptor for NF-□B and Caspase-8-Dependent Apoptosis. Biochem Biophys Res Commun 303:69-73, 2003
15. Ogura Y, Saab L, Chen F, Benito A, Inohara N, Nuñez G. Genetic Variation and Activity of Mouse Nod2, a Susceptibility Gene for Crohn's Disease. Genomics 81:369-377, 2003
16. Merino J, Diez MA, Muniz M, Buelta L, Nuñez G, Lopez-Hoyos M, Merino R. Inhibition of B-cell death does not restore T-cell-dependent immune responses in CD40-deficient mice. Immunology 109:504-509, 2003
17. Lala S, Ogura Y, Osborne C, Hor SY, Bromfield A, Davies S, Ogunbiyi O, Nuñez G, Keshav S. Crohn's disease and the NOD2 gene: a role for paneth cells. Gastroenterology, 125:47-57, 2003
18. Chamaillard M, Hashimoto M, Horie Y, Masumoto J, Qiu S, Saab L, Ogura Y, Kawasaki A, Fukase K, Kusumoto S, Valvano MA, Foster SJ, Mak TW, Nuñez G, Inohara N. An essential role for NOD1 in host recognition of bacterial peptidoglycan containing diaminopimelic acid. Nat Immunol, 4:702-707, 2003

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

A. Autopsy Service.

II. TEACHING ACTIVITIES:

A. Lecturer, Pathology 580/630 and 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

III. RESEARCH ACTIVITES:

A. Principal Investigator, "Mechanisms of pulmonary fibrosis," NIH, R37, HL28737 MERIT Award.
B. Principal Investigator, "Myofibroblasts in pulmonary fibrosis," NIH, RO-1, HL 52285.
C. Project Leader, Project III, "Macrophage function in lung injury and fibrosis," NIH, PO-1, HL 31963.
D. Co-investigator, SCOR in Human idiopathic pulmonary fibrosis, NIH, P-50 HL 56402.

PROJECTS UNDER STUDY:

A. Mechanisms of lung injury and fibrosis.
B. Cytokine regulation of fibroblast function
C. Smad regulation of the α-smooth muscle actin 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. Role of eosinophils 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.
B. Member, Departmental Research and Space Advisory Committee.
C. 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. Lung.
C. Reviewer/site visitor for NIH Program Project/Study Sections and VA grant proposals.

INVITED LECTURES/SEMINARS:

1. Invited Speaker, "Fibroblast phenotypes in pulmonary fibrosis", First Pittsburgh International Lung Conference, Nemacolin Woods, PA, 2002
2. Invited Speaker, "Fibroblasts and pulmonary fibrosis", Department of Internal Medicine, University of California at Davis, Davis, CA, 2002
3. Session Chair, "Molecular mechanism of pulmonary fibrosis", American Thoracic Society Annual Meeting, Seattle, WA, 2003
4. Invited Speaker, "Fibroblasts and animal models of lung remodeling", Schering-Plough Research Institute, Kenilworth, NJ, 2003

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Huaux, F., Liu, T., McGarry, B., Ullenbruch, M., and Phan, S.H.: Dual roles of interleukin-4 (IL-4) in lung injury and fibrosis. J. Immunol. 2003; 170:2083-2092.
2. Brewer, G.J., Ullenbruch, M.R., Dick, R., Olivarez, L. and Phan, S.H.: Tetrathiomolybdate copper reduction therapy protects against bleomycin-induced pulmonary fibrosis in mice. J. Lab. Clin. Med. 2003; 141:210-216.
3. Swartz, R.D., Crofford, L.J., Phan, S.H., and Su, L.D.: Nephropathic fibrosing dermopathy: A novel cutaneous fibrosing disorder in patients with renal failure. Am. J. Med. 2003; 114:563-572.
4. Cutroneo, K.R. and Phan, S.H.: TGFβ1-induced Smad3 binding to the Smad7 gene: knockout of Smad7 gene transcription by sense phosphorothioate oligos, autoregulation and effect on TGFβ1 secretion: bleomycin acts through TGFβ1. J. Cell. Biochem. 2003; 89:474-483.
5. Hu, B., Wu, Z., and Phan, S.H.: Smad3 mediates transforming growth factor β induced α-smooth muscle actin gene expression in myofibroblast differentiation. Am. J. Respir. Cell Molec. Biol. 2003; 29:397-404.
6. Yang, Y., Zhe, X., Phan, S.H., Ullenbruch, M., and Schuger, S.: Involvement of SRF Isoforms in Myofibroblast Differentiation During Bleomycin-Induced Lung Injury. Am. J. Respir. Cell Mol. Biol. 2003; in press

BOOKS/CHAPTERS IN BOOKS/REVIEWS:

1. Phan, S.H.: The myofibroblast in pulmonary fibrosis. Chest. 2002; 122: 286S-289S.
2. Phan, S.H.: Fibroblast phenotypes in pulmonary fibrosis. Am J Respir Cell Molec Biol. 2003; 29:S87-S92.

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

1. Hu B, Wu Z, **Phan SH**: Smad3 mediates transforming growth factor β induced α-smooth muscle actin gene expression in myofibroblast differentiation. FASEB J. 2003;17:A605
2. Liu T, Dhanasekaran S, Jin H, Hu B, McGarry B, Ullenbruch M, Chinnaiyan A, **Phan SH**: Lung expression and potential role of FIZZ1 in bleomycin-induced lung fibrosis. 2003;167:A25
3. Hashimoto N, Jin H, **Phan SH**,: BM derived fibroblast-like cells producing collagen type I might play a critical role in the pathogenesis of BLM-induced fibrosis model.. Am. J. Resp. Crit. Care Med. 2003;167:A345
4. Gharaee-Kermani M, McGarry B, Jin H, **Phan SH**: Role of C-C chemokine receptor 2 (CCR2) in lung fibrosis and fibroblast activation. Am. J. Resp. Crit. Care Med. 2003;167:A347
5. Huaux F, Liu T, McGarry B, Ullenbruch M, Wang J, Xing Z, **Phan SH**: Pulmonary eosinophils and T lymphocytes possess distinct roles in the extension of blm-induced lung injury and fibrosis. Am. J. Resp. Crit. Care Med. 2003;167:A761

STEPHEN RAMSBURGH, M.D.
CLINICAL INSTRUCTOR II
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 – 30 JUNE 2003

I. CLINICAL ACTIVITIES:

A. General Surgical Pathology - 32 weeks

II. TEACHING ACTIVITIES:

A. Medical Students:
   1. M2 Pathology Lab – 70 hours
   2. Applied Clinical Anatomy – 4 hours
      Musculoskeletal System

B. House Officers:
   1. General Surgical Pathology – 30 weeks
   2. Resident Teaching Conference – 60 hours
   3. Consultation Conferences – 4 hours
   4. Intraoperative consultation – 70 hours
   5. Surgical Pathology Elective – 80 hours for senior level residents

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

None.

PENDING:

None.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

None.

MEDICAL SCHOOL/HOSPITAL:

None.

UNIVERSITY OF MICHIGAN:

None.

REGIONAL AND NATIONAL:

None.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

None.

HONORS AND AWARDS

Resident Teaching Award - 2003

PATENTS:

None.

INVITED LECTURES/SEMINARS:

None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

None.

BOOKS/CHAPTERS IN BOOKS:

Surgical Pathology: A Reference (publication pending).

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

None.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

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. 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.

C. Autopsy coverage at the University Hospitals, for weekdays and weekends. Autopsy coverage is also provided to Trillium Hospital, in Albion and Forest Health Medical Center, Ypsilanti.

D. Review peripheral smears at Forest Health Hospital and University of Michigan Health Service.

E. Clinical Pathology consults for M-Labs client hospitals.

F. Cytopathology: provide coverage in gynecologic, non-gyn and FNA services (performance of aspirate/interpretation) at U of M Hospitals for 20 weeks.

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 (20th Symposium in May, 2003), 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.
   1. Contacts with pathologists from client hospitals and others, as part of our support to pathologists; this includes providing occasional coverage;
   2. Laboratory network activity:
   3. Joint Venture Hospital Laboratory – (JVHL) QA committee, which meets approximately once every three months.
   4. M-Labs Network for M-care members. Coordinating M-Labs QA activities with D. Moss; monthly review of occurrence reports.

B. Medical Director of the University of Michigan Health Service Laboratory, and Forest Health Medical Center in Ypsilanti.
C. Active medical staff member at Forest Health Medical Center and Community Health Center of Branch Co (Coldwater). Conduct Tissue Review and Transfusion Review meetings. Attend their medical staff meetings.
D. Intra-departmental meetings (e.g., Cytopathology)

V. OTHER:

A. Inspector, for the CAP Accreditation Program. Performed two inspections.
B. QA Review through Peer Review Organization of Michigan (PROM), for other hospitals in Michigan.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

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. Pathology 600, Provided written critiques of student autopsy write-ups (167).
D. Laboratory Instructor, Pathology 600 (M2 pathology course), year long
E. Thesis Committee - Andrew Merry, Kellie Breen, Department of Physiology, Erin Gatza, Department of Immunology, Jill Murtha Department of Pathology
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, Jiyoun Kim, Ph.D., Liyu Xin, M.D., Ph.D., Hong Yan Xiao, M.D., Ekram El Laban, M.D.
G. Graduate Students – Andrew Merry, Kellie Breen, Laura McKinley, Jill Murtha
H. Undergraduate Students - Andrew Riskin, Teri Thomas

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. Oxident 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. Pricipal Investigator, "Regulation of IL-8 gene expression: four years, GM50401 $870,822, 1995- 2004. 20% effort
C. Principal Investigator, "Chemokines in the Pathogenesis of Asthma", ES09589, project #3, $1,180,00, 1998 – 2003. 10% 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.
F. Co-Investigator, "Can Paraxonase be Used to Treat Endotoxemia and Sepsis", Life Sciences Initiative, Bert LaDu Principal Investigator, $150,000, 2000-2003. 2% effort
G. Co-Investigator, NIH HD040112, "Neuroimmunology/Cytokine Alterations In Vulvodynia" Principal Investigator, Barbara Reed, $375,000, 2000 – 2003

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
B. Member, Task Force on Promotions and Tenure – Instructional Track
C. Member, Biomedical Research Council Undergraduate Research Council
D. Reviewer, Biomedical Research Council grants
E. Pathology representative to Medical Device Explant Committee
F. Representative for Pathology to Program in Biomedical Sciences (PIBS) Admissions Committee

REGIONAL AND NATIONAL:

A. Executive Committee, Michigan Association of Medical Examiners.
B. Deputy Medical Examiner for Washtenaw County.
C. Regular member National Institutes of Health, Surgery, Anesthesiology and Trauma Study Section Oct 1999 to June 2003
D. Member, American Society of Investigative Pathology Education Committee

E. Member, Michigan Coalation on Donation
F. Publications Committee, International Cytokine Society
G. Awards Committee, Shock Society
H. Organizer, Shock Society Young Investigator's Research Forum
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.

V. OTHER RELEVANT ACTIVITIES:

A. Editorial Board: Shock
B. Reviewer:
1. Journal of Immunology
2. Journal Leukocyte Biology
3. American Journal of Pathology
4. Shock, reviewed
5. American Journal of Physiology
6. American Journal of Respiratory Cell and Molecular Biology
7. American Journal of Respiratory and Critical Care Medicine
8. Cellular Immunology
9. Journal of Endotoxin Research
10. Cytokine
11. Grant Reviewer, Veterans Administration

INVITED LECTURES/SEMINARS:

2002 Visiting Professor, Washington State University, Pullman, Washington, *Understanding the Inflammatory Response to Sepsis to Guide Therapy*
2002 Chair, Experimental Biology Poster Discussion Session Pulmonary Inflammation, New Orleans
2002 Chair Experimental Biology Poster Discussion Session, Vascular Biology, New Orleans
2002 Moderator, Therapies in Treatment of Shock, Shock Society Meeting, Big Sky Montana
2002 External Reviewer, SCCOR grant, SUNY – Buffalo, Buffalo, New York
2002 Invited Speaker, *State of Michigan Response to Bioterrorism*, Michigan Association of Medical Examiners, Mt. Clemens, Michigan
2003 Organizer and Moderator, Magic Bullets for the Treatment of Sepsis Shock Society meeting

VI. PUBLICATIONS:

ARTICLES PUBLISHED

1. Xing, L., and Remick, D.G. 2003. Relative cytokine and cytokine inhibitor production by mononuclear cells and neutrophils. *Shock* 20:10-16.
2. Remick, D.G., Bolgos, G.L., Siddiqui, J., Shin, J., and Nemzek, J.A. 2002. Six at six: interleukin 6 measured 6 hours after the initiation of sepsis predicts mortality over 3 days. *Shock* 17:463-467.

3. Remick, D.G., Bolgos, G.R., Siddiqui, J., Shin, J., and Nemzek, J.A. 2002. Six at six: interleukin-6 measured 6 h after the initiation of sepsis predicts mortality over 3 days. *Shock* 17:463-467.
4. Steinstraesser, L., Tack, B.F., Waring, A.J., Hong, T., Boo, L.M., Fan, M.H., Remick, D.I., Su, G.L., Lehrer, R.I., and Wang, S.C. 2002. Activity of novispirin G10 against Pseudomonas aeruginosa in vitro and in infected burns. *Antimicrob Agents Chemother* 46:1837-1844.
5. Remick, D.G. 2002. Mediators of Sepsis. In *Sepsis and Multiple Organ Dysfunction.* E.A. Deitch, J.L. Vincent, and A. Windsor, editors. New York, New York: W.B. Saunders. 63-72.
6. Remick, D.G. 2002. Protein Analysis and Bioassays of Cytokines and Cytokine Receptors. In *Manual of Clinical and Laboratory Immunology.* N.R. Rose, R.G. Hamilton, and B. Detrick, editors. Washington, D.C.: ASM Press. 320-337.
7. Xiao, H., Jepkorir, C.J., Harvey, K., and Remick, D.G. 2002. Thrombin-induced platelet microparticles improved the aggregability of cryopreserved platelets. *Cryobiology* 44:179-188.
8. Su, G.L., Goyert, S.M., Fan, M.H., Aminlari, A., Gong, K.Q., Klein, R.D., Myc, A., Alarcon, W.H., Steinstraesser, L., Remick, D.G., et al. 2002. Activation of human and mouse Kupffer cells by lipopolysaccharide is mediated by CD14. *American Journal of Physiology Gastrointestinal & Liver Physiology* 283.
9. Nemzek, J.A., Ebong, S.J., Kim, J., Bolgos, G.L., and Remick, D.G. 2002. Keratinocyte growth factor pretreatment is associated with decreased macrophage inflammatory protein-2alpha concentrations and reduced neutrophil recruitment in acid aspiration lung injury. *Shock* 18:501-506.
10. Fan, M.H., Klein, R.D., Steinstraesser, L., Merry, A.C., Nemzek, J.A., Remick, D.G., Wang, S.C., and Su, G.L. 2002. An essential role for lipopolysaccharide-binding protein in pulmonary innate immune responses. *Shock* 18:248-254.
11. Wang, X., Ebong, S.J., Call, D.R., Newcomb, D.E., Bolgos, G.R., and Remick, D.G. 2002. Calcitonin gene-related peptide partially reverses decreased production of chemokines KC and MIP-2 following murine sepsis. *Inflammation* 26:167-174.
12. Remick, D.G. 2003. Cytokine therapeutics for the treatment of sepsis: why has nothing worked? *Curr Pharm Des* 9:75-82.
13. Steinstraesser, L., Burghard, O., Nemzek, J., Fan, M.H., Merry, A., Remick, D.I., Su, G.L., Steinau, H.U., and Wang, S.C. 2003. Protegrin-1 increases bacterial clearance in sepsis but decreases survival. *Crit Care Med* 31:221-226.
14. Zeng, X., Dai, J., Remick, D.G., and Wang, X. 2003. Homocysteine mediated expression and secretion of monocyte chemoattractant protein-1 and interleukin-8 in human monocytes. *Circ Res* 93:311-320.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002- 30 JUNE 2003

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. Molecular Diagnostics sign-out.
   5. Hematopathology case conferences.
   6. Hematopathology lecturer.

C. Hematopathology teaching:
   1. Leukemia conference/biweekly.
   2. Lymphoma conference/weekly.
   3. Hematology conference/biweekly.
   4. Clinical Pathology Grand Rounds (one lecture).
   6. Clinical Pathology Case Conference/weekly.
   7. Cutaneous Lymphoma Conference/monthly.
   8. Lecturer in flow cytometry to hematology/oncology fellows, Department of Internal Medicine and Department of Pediatrics.
   9. Multiple myeloma conference/biweekly
   10. Lecturer, "Hematologic Coups: A practical approach to challenging cases in hematolymphoid diagnosis", American Society of Clinical Pathology National Meeting

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Immunophenotypic profiling of leukemias and lymphomas by flow cytometry and immunohistochemistry.
B. Radioimmunotherapy for B-cell lymphoma.
C. Immunotherapy for acute myelogenous leukemia
D. Gene expression profiling of chronic lymphoproliferative disorders.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Clinical Flow Cytometry Laboratory.
Coordinator, CP resident teaching program.

B. Clinical Pathology Incentive Distribution Committee.
C. Pathology Faculty Incentive Committee.
D. Interviewer of residency candidates.

REGIONAL/NATIONAL:

A. Central pathology reviewer, multicenter study of I^{131} anti-B1 radioimmunotherapy for B-cell lymphoma, Corixa Pharmaceutical.
B. American Society of Clinical Pathologists, CheckPath Expert Review Panel, Hematopathology.
C. Manuscript reviewer, Archives of Pathology and Laboratory Medicine.
D. Manuscript reviewer, Clinical Cytometry.
E. Manuscript reviewer, Human Pathology

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Valdez R, Kroft SH, Ross CW, Schnitzer B, Peterson LC, Singleton TP, Finn WG: Cerebrospinal fluid involvement by mantle cell lymphoma. Mod Pathol 15:1073-1079, 2002.
2. Uherova P, Schnitzer B, Valdez R, Ross CW, Finn WG. Nodular lymphocyte predominant Hodgkin lymphoma: An immunophenotypic reappraisal based on a single-institution experience. Am J Clin Pathol 119:192-198, 2003.
3. Kansal R, Ross CW, Singleton TP, Finn WG, Schnitzer B. The histopathology of splenic small B-cell lymphomas: A study of 42 cases with a definitive diagnosis by the World Health Organization Classification. Am J Clin Pathol (in press).

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

1. Ramalingam P, Valdez R, Ross CW, Schnitzer B, Finn WG: Oct-2 and BOB.1/OBF.1 expression in surface immunoglobulin-negative follicular lymphomas. Poster presentation, United States and Canadian Academy of Pathology Annual Meeting, Washington, DC, 2003. Mod Pathol 2003; 16(1)249A.
2. Kilgore S, Erba H, Valdez R, Finn W, Schnitzer B, Ross C: Mylotarg (Gemtuzumab Ozogamicin; CMA-676) in AML: predictive variable and response to treatment. Poster presentation, United States and Canadian Academy of Pathology Annual Meeting, Washington, DC, 2003. Mod Pathol 2003; 16(1)240A.
3. Selby D, Padmore R, Tuck M, Ross C, Schnitzer B, Finn W, Valdez R, Singleton T, Kaminski M: Characterization of bone marrow lymphoid aggregates in follicular lymphoma treatedwith [^{131}I] anti-B1 antibody. Poster presentation, United States and Canadian Academy of Pathology Annual Meeting, Washington, DC, 2003. Mod Pathol 2003; 16(1) 251A.
4. Selby DM, Ross CW, Finn WG, Valdez R, Schnitzer B: CD10 and cyclin D1 expression in hairy cell leukemia. Poster presentation, United States and Canadian Academy of Pathology Annual Meeting, Washington, DC, 2003. Mod Pathol 2003; 16(1) 251A.
5. Selby D, Valdez R, Schnitzer B, Ross CW, Finn WG. Diagnostic criteria for acute erythroleukemia (letter to editor). Blood 101:2895-2896, 2003.

DIANE ROULSTON, Ph.D.
CLINICAL ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

A. Director, Clinical Cytogenetics Laboratory

II. TEACHING ACTIVITIES:

A. House Officers and Fellows
   1. Rotations in Cytogenetics
      a. Pathology residents (N=6)
      b. Hematopathology fellows (N=3)
      c. Genetics fellows (N=2)
      d. Hematology/Oncology fellows (N=2)

B. Clinical Cytogenetics teaching
   1. Abnormal Cytogenetics Case Conference (Biweekly) for technologists, residents, fellows, and faculty
   2. Leukemia Conference (Biweekly)
   3. Pediatric Genetics Post-clinic Conference (Weekly)
   4. Joint Genetics Conference (Monthly)
   5. Teratology Conference (Weekly)
   6. Pediatric Tumor Conference (4 cases)
   7. BMT Morbidity & Mortality Conference (1 case)
   8. Hematology Conference (2 cases)
   9. Clinical Pathology Grand Rounds
      a. "Cytogenetics of Hematologic Malignant Diseases" 2/21/03

III. RESEARCH ACTIVITIES:

A. N/A

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Clinical Cytogenetics Laboratory
B. Interviewer
   1. Pathology Residency Candidates
   2. Hematopathology Fellow Candidates

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: October 2002.
   2. Fellow, American College of Medical Genetics
   3. Peer Reviews: *Oncogene, Blood*

B. 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

C. Southwest Oncology Group (SWOG)

D. Director of an Approved Laboratory; submit cases for review

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Wechsler DW, Alexander BM, Engstrom LD, Motto DG, **Roulston D.** A novel inversion of 11q in an infant leukemia fuses *MLL* to *CALM*, a clathrin assembly protein gene. Genes Chromosomes & Cancer, 36:26-36. 2003.

ABSTRACTS:

1. Heerema NA, Shuster J, Biegel J, Camitta B, Cooley LD, Hirsch B, Magenis HE, Patil S, Pettenati MJ, Pullen J, Raimondi SC, Rao K, Schneider NR, **Roulston D**, Sanger W, Sather HN, Sutcliff MJ, vanTuinen P, Watson MS, Carroll AJ. Pattern of extra chromosomes in pediatric hyperdiploid (50 to 67 chromosomes) acute lymphoblastic lymphoma (ALL) is modal number (mn) dependent. American Society of Hematology 44th Annual Meeting, Philadelphia PA, December 6-10, 2002.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 – 30 JUNE 2003

I. CLINICAL ACTIVITIES:

A. Consultant, pediatric surgical pathology, full time
B. Consultant, pediatric autopsy pathology, full time
C. Consultant, Teratology histopathology, full time
D. Diagnostic Hematopathology, 1-2 weeks/month
E. Medical Director, Special Studies Laboratory (see separate report)
F. Pathology co-ordinator, Children's Oncology Group cases
G. Consultant, placental pathology, as needed

II. TEACHING ACTIVITIES:

A. Medical Students
   1. M2 Pathology Laboratory (~32 hours)
B. Dental Students
   1. Pathology Lecture and Laboratory (~3 hours)
C. Pathology House Officers:
   1. Pathology Consult Conferences, Rhabdomyosarcoma, Spindle cell neoplasms (2 hours)
   2. Pathology Teaching Conferences, Neuroblastoma (1 hour)
   3. Hematopathology In House Signout (~1 week per month, ~ 15 hours per month)
   4. Pediatric Autopsy Pathology cases and signout (up to 1 hour per week)
D. Interdepartmental:
   1. Lymphoma Conference (2 hours per month)
   2. Pediatric GI Pathology Case Conference (2 hours per month)
   3. Pediatric GI Pathology Teaching Conference (2 hours per month)
   4. Pediatric Hematology Oncology Fellow Pathology Tutorials (2 hours per month)
   5. Pediatric Hematology Oncology Wednesday Morning Teaching Conference (1 hour per month)
   6. Pediatric Hematology Oncology Tumor Board (2 hours per month)
   7. Pediatric Surgery, Radiology, Pathology Conference (1 hour per month)
   8. Pathology contributor for Pediatric Surgery, Radiology, Pathology Conference teaching case web presentations, Pediatric Surgery internal website (http://www.surgery.med.umich.edu/i/peds/Internal_site.htm)
   9. Pediatric Morbidity & Mortality Conference (1 hour per quarter)
   10. Pediatric Pulmonology Conference (up to 1 hour per month)
   11. Sarcoma Tumor Board (6 hours per month, 1/03 to 7/03)

III. RESEARCH ACTIVITIES:

A. Case study of intestinal infantile fibrosarcoma with Drs. Islam and Geiger of Pediatric Surgery (manuscript submitted)
B. Case study of nasopharyngeal neuroblastoma with Drs. Lau and Trobe of Neuro-Ophthalmology (manuscript submitted)
C. Case study of aggressive pediatric hepatic angiomyolipoma with Drs. McKinney and Geiger of Pediatric Surgery (manuscript in preparation)
D. Series report on radiology-pathology correlation in pediatric myofibroma with Dr. Hernandez of Pediatric Radiology.
E. Collaborator in ongoing studies of neuroblastoma with Dr. Castle of Pediatric Hematology Oncology

IV. ADMINISTRATIVE ACTIVITIES:

A. Executive Committee, Mott Hospital

V. PUBLICATIONS:

1. AF Nascimento, R Ruiz, JL Hornick, CD Fletcher. Calcifying fibrous 'pseudotumor': clinicopathologic study of 15 cases and analysis of its relationship to inflammatory myofibroblastic tumor. Int J Surg Pathol. 2002 Jul;10(3):189-96.

ALVIN H. SCHMAIER, M.D.
PROFESSOR
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 – 30 JUNE 2003

I. CLINICAL ACTIVITIES:

A. Professor of Internal Medicine.
B. Professor of Pathology.
C. Director, Coagulation Laboratory

II. TEACHING ACTIVITIES (Department of Pathology):

A. Pathology House Officers:
   1. Responsible during the current academic year for teaching activities for the following:
      a. Residents participated in twice weekly sign-out rounds by laboratory direct of specialized coagulation testing.
      b. Formal lecture for 4th year medical student elective clinical pathology course.

B. Medical School: M2 Hematology Course Director

III. RESEARCH DESCRIPTION

A. Dr. Schmaier's major investigative work is on the physiology and function of the plasma kallikrein/kinin system (KKS). The Schmaier laboratory made a fundamental discovery that the endothelial cell enzyme prolylcarboxypeptidase (PRCP) activates plasma prekallikrein when bound to high molecular weight kininogen (*JBC 277:17962-17969, 2002*). This year we have prepared a recombinant PRCP and examined its biochemistry. We have also prepared PRCP KO mice and are starting to examine their physiology. Other mouse models have been developed to determine if the plasma kallikrein/kinin system is a physiologic counterbalance of the renin angiotensin system (*Am J. Physiol 285:R1, 2003).*.

B. Second, the research efforts to develop a novel class of selective inhibitors of □-thrombin activation of platelet have made good progress. An agent termed "Thrombostatin™" has been developed as an inhibitor of □-thrombin cleaving the cloned thrombin receptors, PAR1. The mechanism of Thrombostatin™ as a binder to the thrombin cleavage site on protease activated receptor 1 (PAR1) and the active site of thrombin has been defined (*Am J Physiol 285:H183, 2003).* Studies examining the interaction of Thrombostatin™ with protease activated receptor 4 (PAR4) are also underway.

IV. HONORS & AWARDS:

None

V. IMPORTANT LECTURES:

1. 9/12/02: Michigan Association of Blood Banks, Romulus MI, "*New Therapeutic Products for the Management Coagulopathies*"
2. 11/15/02: Dade Symposium, Ann Arbor, MI., "*New Anti-Platelet and Anti-Coagulant Drugs And the Assays to Monitor Them*"
3. 12/7/02: American Society of Hematology: Grantsmanship Workshop, Philadelphia, PA, "*Mock Study Section and Management of an NIH Grant Rejection*"
4. 12/8/02: American Society of Hematology: Subcommittee of Clinical Laboratory Hematology, Chairman"*Translating Genomics and Proteomics into the Clinical Laboratory*"
5. 12/8/02: American Society of Hematology: Oral Abstract Presentation; "*Reduced Rate of Bradykinin Metabolism Protects the Mouse from Thrombosis*"
6. 1/07/03: Life Science Strategy Seminar, Business School, University of Michigan: "*Corporate Strategy, Organization and Culture (A), Merck*"1/14/03: Life Science Strategy Seminar, Business School, University of Michigan: "*Corporate Strategy, Organization and Culture (A),Eli Lille*"
7. 1/28/03: Life Science Strategy Seminar, Business School, University of Michigan: "*Corporate Strategy, Organization and Culture (A),Genzyme: Engineering the Market for Orphan Drugs*"
8. 2/11/03: Life Science Strategy Seminar, Business School, University of Michigan: "*Corporate Strategy, Organization and Culture (A), Millennium Pharmaceuticals-Growth by Mergers and Acquistions*"
9. 6/10/03: Division of Clinical Pharmacology, Department of Internal Medicine, Vanderbilt University, Nashville, TN *"The Plasma Kallikrein/Kinin System Interacts with the Renin Angiotensin System*"

VI. NATIONAL OR REGIONAL COMMITTEE ASSIGNMENTS:

1. Chairman: Scientific Subcommittee on Clinical Laboratory Hematology, American Society of Hematology, 2002
2. Central Society for Clinical Research: Hematology/Oncology Subspeciality Chairman
3. NASCOLA: North American Specialized Coagulation Laboratory Association – Vice President & Executive Committee

VII. INDIVIDUAL EDITORIAL BOARDS:

1. Editorial Board: Thrombosis and Haemostasis, Section Editor

VIII. NIH STUDY SECTIONS OR OTHER FEDERAL ADVISORY BOARDS:

1. NIH NHLBI: PPG Review Committee, 2002
2. NIH NHLBI: ZRG1 SSS-0 10B and SSS-0 12B Special Emphasis Panel Study Section, 2001-2004

IX. PEER-REVIEWED PUBLICATIONS:

1. Moreira, C.R., Schmaier, A.H., Mahdi, F., da Motta, G., Nader, H.B., Shariat-Madar, Z. Identification of prolylcarboxypeptidase as the cell matrix-associated prekallikrein activator. FEBS Letters. 523:167-170, 2002.
2. Chay, C.H., Cooper, C.R., Gendernalik, J.D., Dhanasekaran, S.M., Chinnaiyan, A.M., Rubin, M.A., Schmaier, A.H., Pienta, K.J. A functional thrombin receptor (PAR1) is expressed on bone-derived prostate cancer cell lines. Urology. 60:760-765, 2002.
3. Abela, G.S., Huang. R., Ma. H., Prieto. A.R., Lei, M., Schmaier AH, Schwartz, K.A., Davis, J.M. Laser-light scattering (LLS), a new method for continuous monitoring of platelet activation in circulating fluid. J. Lab. Clin. Med. 141:50-57, 2003.
4. Jahroudi, N., Schmaier, A., Srikanth, S., Mahdi, F., Lutka, F., Bowser, R. Von Willebrand factor promoter targets the expression of amyloid precursor protein to brain vascular endothelial cells of transgenic mice. J of Alzheimer's Disease. 5:149-158, 2003.
5. Krijanovski, Y., Proulle, V., Mahdi, F., Dreyfus, M., Muller-Esterl, W., Schmaier, A.H. Characterization of molecular defects of Fitzgerald trait and another novel high molecular weight kininogen deficient patient: Insights into structural requirements for kininogen expression. Blood. 101:4430-4436, 2003.
6. Hasan, A.A.K., Warnock, M., Nieman, M., Srikanth, S., Mahdi, F., Krishnan, R., Tulinsky, A., Schmaier, A.H. The mechanisms of Arg-Pro-Pro-Gly-Phe inhibition of thrombin. Amer J. Physiol Heart and Circ. Physiol. 285:H183-H193, 2003.
7. Jaffa, A.A., Durazo-Arvizu, R., Zheng, D., Lackland, D.T., Srikanth, S., Garvey, W.T., Schmaier, A.H., and the DCCT/EDIC Study Group. Plasma prekallikrein: a risk marker for hypertension and nephrology in type-1 diabetes. Diabetes. 52:1215-1221, 2003.
8. Wang, J., Even, M.A., Chen, X., Schmaier, A.H., Waite, J.H., Chen, Z. Detection of amide I signals of interfacial proteins in situ using SFG. J. American Chemical Society. In Press, 2003.

REVIEW PAPERS

1. Schmaier, A.H. Contributions of the plasma kallikrein/kinin system to disseminated intravascular coagulation. In: Disseminated Intravascular Coagulation, Eds. Ten Cate H, Levi M. Landes Bioscience. Georgetown, TX, 2003, pp.110-117.
2. Schmaier, A.H., Petruzzelli, L.M. Introduction to hematology. In:Hematology for the Medical Student. Schmaier, A.H., Petruzzelli, L.M. (eds). Lippincott, Williams & Wilkins, Baltimore, 2003, pp 1-4.
3. Schmaier, A.H. Principles of Hemostasis. In:Hematology for the Medical Student. Schmaier, A.H., Petruzzelli, L.M. (eds). Lippincott, Williams & Wilkins, Baltimore, 2003, pp. 71-77.
4. Schmaier, A.H. Approach to the bleeding patient . In:Hematology for the Medical Student. Schmaier, A.H., Petruzzelli, L.M. (eds). Lippincott, Williams & Wilkins, Baltimore, 2003, pp. 79-83.
5. Schmaier, A.H. Acquired bleeding disorders. In:Hematology for the Medical

Student. Schmaier, A.H., Petruzzelli, L.M. (eds). Lippincott, Williams & Wilkins, Baltimore, 2003, pp. 99-104.

6. Schmaier, A.H. Evaluation of thrombosis. In:Hematology for the Medical Student. Schmaier, A.H., Petruzzelli,L.M. (eds). Lippincott, Williams & Wilkins, Baltimore, 2003, pp. 121-126.
7. Bockenstedt, P., Schmaier, A.H. Platelet function and disorders. In:Hematology for the Medical Student.Schmaier, A.H., Petruzzelli, L.M. (eds). Lippincott, Williams & Wilkins, Baltimore, 2003, pp. 105-120.
8. Shariat-Madar, Z., Schmaier, A.H. Assembly and activation of the plasma kallikrein/kinin system: A new interpretation. International Immunopharmacology. 2:1841-1849, 2002.
9. Schmaier, A.H. The NIH grant review process and what to do if your grant is not funded. Hematology 2002. The American Society of Hematology Education Book, December 2002.
10. Schmaier, A.H., Finn,W.G., Petruzzelli, L.M. Atlas images. In: Hematology for the Medical Student.Schmaier, A.H., Petruzzelli, L.M. (eds). Lippincott, Williams & Wilkins. Baltimore, 2003, pp Appendix 1-12 .
11. Schmaier, A.H. The kallikrein/kinin and the renin angiotensin systems have a multi-layered interaction. Amer.J. Physiol: Regulatory, Integrative and Comparative Physiology. 285:R1-R13, 2003.

BOOKS:

1. Schmaier, A.H., Petruzzelli, L.M. (eds). Hematology for Medical Students. Lippincott, Williams & Wilkins, Baltimore, 2003.

PATENTS:

1. Schmaier, A.H. and Hasan, A.A.K. U.S. Patent No.: 6,544,750; Peptide Analogs as Selective Inhibitors of Thrombin Activation of Protease Activated Receptor 1. Date of Issue 4/8/03.
2. Schmaier, A.H. and Hasan, A.A.K. Synthetic Peptide Analogs of Arg-Pro-Pro-Gly-Phe As Selective Inhibitors of Thrombin and Thrombin Activation of Protease Activated Receptors 1 And 4. (pending), Submitted 5/1/03

X. CURRENT GRANT SUPPORT

1. **PO1-HL57346**, 2003-2008, "Molecular Genetics of Coagulation Disorders", D. Ginsburg, P.I. Core A. ($750,000 Direct Costs to Dr. Schmaier)
2. **R42-HL61981,** 2001-2003, "Thrombostatin in the Folts Model", AH Schmaier, PI, Subcontract to the
3. University of Michigan ($344,976 Total Costs to Dr. Schmaier at U of M subcontract)
4. RO1-HL65194, **2000-2004, "Plasma Protein Phenotyping of Prothrombotic Mice", A.H. Schmaier, P.I. ($604,128 Total Costs)**

5. **Michigan Life Science Corridor Grant**, 2001-2004, "Thrombostatin-A Novel Anti-Platelet Agent", AH Schmaier, P.I., ($745,793 subcontract to U of Michigan, HI Mosberg, and BR Lucchesi PI)
6. **RO1-HL52779**,2001-2005, "Regulation of Kinin Delivery on HUVEC", A.H. Schmaier, P.I. ($1,678,075 Total Costs)
7. **P01 CA69568,** 2002-2003, "The Role of Protease Activated Receptor-1 (PAR-1) in Prostate Cancer Metastasis", K. Pienta, P.I. ($16,670 Direct Costs to Dr. Schmaier)
8. **R43-GM** 2003-2004, "Oral Delivery of Thrombostatin" , J. Hilfinger, P.I. ($56,000 Total Costs)

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

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. Society for Hematopathology, Executive Committee
   1. Past President.
B. Children's Cancer Study Group: Review of in-house cases of lymphoma cases.
C. Member, Hematology Workshop Review Committee, American Society of Clinical Pathologists.
D. Hematology Planning Committee, American Society of Clinical Pathologists.
E. Bylaws Committee, Society for Hematopathology.
F. 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) Reactive Lymphadenopathies: Diagnosis and Differential Diagnosis; b) Non-Hodgkin's Lymphomas and their Differential Diagnosis; c) Hodgkin's Disease; d) Differential Diagnosis of Hodgkin's Disease; e) A Practical Approach to Diagnosis and Classification of Lymphomas and Leukemias by Immunohistochemistry, Flow Cytometry and Molecular Genetic Analysis; f) Extranodal Lymphomas and, g) Acute Lymphoblastic Leukemias, Orlando, FL, November 2002.
2. "Visiting Professor" Department of Pathology, University of Texas, Southwestern Medical Center, Dallas TX, February 2003.
3. "Visiting Professor" Department of Pathology, Yale University, New Haven, CT, April 2003.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Uherova P, Valdez R, Ross CW, Schnitzer B, Fin WG: Nodular lymphocyte predominant Hodgkin lymphoma. An immunophenotypic reappraisal based on a single-institution experience. Am J Clin Pathol 119:192-198, 2003.
2. Valdez R, Thorson J, Finn WG, Schnitzer B, Kleer C: Lymphocytic mastitis and diabetic mastopathy: a molecular, immunophenotypic, and clinicopathologic evaluation of 11 cases. Mod Pathol 16:223-228, 2003

3. Kansal R, Ross CW, Kroft SH, Singleton TP, Finn WG, Schnitzer B: Histopathology of splenic small B-cell lymphomas: A study of 54 cases classified by flow cytometric immunophenotypic analysis or lymph node biopsy. Am J Clin Pathol (in press).

ARTICLES SUBMITTED FOR PUBLICATION:

BOOKS AND CHAPTERS IN BOOKS:

1. Hsi ED, Schnitzer B. In Jaffe ES, Harris NL, Vardiman J (eds). Diagnostic Hematopathology. Harcourt Health Sciences, 2003.

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

1. Kilgore S, Erba H, Valdez R, Finn WG, Schnitzer B, Ross CW: Mylotarg (Gemtuzumab Oxogamicin; CMA-676) in AML: Predictive variables and response to treatment. Mod Pathol 16:240A, 2003
2. Ramalingam P, Valdez R, Ross CW, Schnitzer B, Finn WG: Oct-2 and BOB.1/OBF.1 expression in surface immunoglobulin negative follicular lymphomas. Mod Pathol 16:249A, 2003
3. Ramalingam P, Finn WG, Schnitzer B, Valdez R: Immunohistochemical expression of Oct-2 in non-Hodgkin lymphomas evaluated by tissue microarray (TMA). Mod Pathol 16: 249A, 2003
4. Selby D, Padmore R, Tuck M, Ross CW, Schnitzer B, Finn WG, Valdez R, Singleton T, Kaminski M: Characterization of bone marrow lymphoid aggregates in follicular lymphoma treated with [131I] anti-B1 antibody. Mod Pathol 16:251A, 2003
5. Selby DM, Ross CW, Finn WG, Valdez R, Schnitzer B: CD10 and cyclin D1 expression in hairy cell leukemia. Mod Pathol 16:251A, 2003
6. Valdez R, Schnitzer B, Finn WG: Tissue microarray (TMA) analysis of survivin expression in benign lymphoid tissue and small B-cell non-Hodgkin lymphoma (NHL). Mod Pathol 16:256A, 2003
7. Selby, DM, Valdez, R, Schnitzer, B, Ross, CW, and Finn, WG: Diagnostic criteria for acute erythroleukemia. Blood 2003; 101:2895.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

A. Room #1 and 2 Surgical Pathology sign-out, 9 weeks/year
B. GU surgical subspeciality sign-out, 22 weeks/year
C. Genitourinary transfer cases (TS), daily, 12 months
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

II. TEACHING ACTIVITIES:

A. Residents didactic Anatomic Pathology Lectures, 2/year
B. Residents Consultation Conferences, 2/year
C. GU fellow and pathology resident training, daily, 12 months
D. Urology resident pathology lectures, monthly, 12 months
E. M2-Renal Sequence and Reproductive Sequence Lectures, 3/year
F. Laboratory Instructor, M2 GU/Renal Sequence Lab

III. RESEARCH ACTIVITIES:

1. Co-director for Prostate Cancer SPORE Tissue Core
2. Validation of Tissue Microarrays for Research, 12 months.

SPONSORED SUPPORT:

University of Michigan Prostate SPORE (Specialized Program for Research Excellence) Tissue Core Grant (Co-director tissue core)
Analysis of 8p loss in Human Prostate Cancer- Co Investigator, Ro1, 5RO1 CA 60948-08, (JA Macoska, PI), 4/01/01-3/31/05
Erb Signaling in Prostate Cancer Progression- Co Investigator, DRDA 1234, UMCC 1234; CRC 1234 E

PROJECTS UNDER STUDY:

A. Prostate Carcinoma with Predominant Foamy Features: Does it demonstrate an Aggressive Molecular Phenotype?
B. Utility of Basal Cell Cocktail (p63+34betaE12) in the Diagnosis of Atypical Prostate Glandular Proliferations
C. Comparison of Monoclonal Antibody (P504S) and Polyclonal Antibody to α-Methylacyl-CoA Racemase in Benign, Atypical and Malignant Prostate Tissues.
D. Use of tissue microarrays to identify markers associated with response to interleukin-2 in renal cell carcinoma.
E. Elevated α-Methylacyl-CoA Racemase Enzymatic Activity in Prostate Cancer and its Potential Clinical Utility

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. House officer, GU fellow and faculty Candidate Interviews.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Qiang W, **Shah** R, Panos JC, Giraldo AA, David CS and Kong YC. HLA-DR and HLA-DQ Polymorphism in Human Thyroglobulin-Induced Autoimmune Thyroiditis: DR3 and DQ8 Transgenic Mice are Susceptible. Human Immunology, 63:301-310, 2002.
2. **Shah R**, Zhou M, LeBlanc M, Snyder M and Rubin MA. Comparison of the Basal Cell-Specific Markers, 34βE12 and p63, in the Diagnosis of Prostate Cancer. Am J Surg Pathol, 26(9): 1161-1168, 2002.
3. Joshi DP, **Shah RB**, Montie JE, and Lee CT. Isolated Recurrent Renal Cell Carcinoma Metastatic to the Bladder. JNMA, September 2002
4. Zhou M, **Shah** R, Shen Ronglai and Rubin MA. Basal Cell Cocktail (34βE12+p63) improves the detection of Prostate Basal Cells. Am J Sug Pathol, Vol. 27, No. 3, 2003
5. Kunju Lakshmi, Rubin Mark, Chinnaiyan Arul and **Shah Rajal**. Diagnostic Utility of the Monoclonal Antibody P504S in the Work Up of Atypical Glandular Proliferations. Am J Clinical Pathol, In Press.

PRESENTATIONS:

1. "Diagnostic Utility of Basal Cell Cocktail (p63+34betaE12) in the Diagnosis of Atypical Prostate Glandular Proliferations". United and Canadian Academy of Pathology, Washington D.C., March, 2003 and American Urological Association Meeting, Chicago, April, 2003
2. "Diagnostic Utility of the Monoclonal Antibody P504S in the Work Up of Atypical Glandular Proliferations". United and Canadian Academy of Pathology, Washington D.C., March, 2003

3. "Comparison of Monoclonal Antibody (P504S) and Polyclonal Antibody to α-Methylacyl-CoA Racemase in Benign, Atypical and Malignant Prostate Tissues". United and Canadian Academy of Pathology, Washington D.C., March, 2003
4. "Prostate SPORE Tissue Core Info structure- University of Michigan Experience" Israeli delegation, June 25-26, 2003

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

1. Kunju Lakshmi, Rubin Mark, Shen Ronglai, Ingold Collette, Chinnaiyan Arul and **Shah Rajal**. Diagnostic Utility of the Monoclonal Antibody P504S in the Work Up of Prostate Carcinoma. Modern Pathol 16(1): 719, Jan 2003
2. **Shah Rajal**, Kunju Lakshmi, Shen Ronglai, LeBlank Michele and Rubin Mark. Utility of Basal Cell Cocktail (p63+34betaE12) in the Diagnosis of Atypical Prostate Glandular Proliferations. Modern Pathol, 16(1): 726, Jan 2003
3. Kunju Lakshmi, Rubin Mark, Shen Ronglai, Ingold Collette, Chinnaiyan Arul and **Shah Rajal**. Comparison of Monoclonal Antibody (P504S) and Polyclonal Antibody to α-Methylacyl-CoA Racemase in Benign, Atypical and Malignant Prostate Tissues. Modern Pathol, 16(1): 718, Jan 2003
4. O'Toole John, Norman Silas, Kriesche Herwig-Ulf, **Shah Rajal,** Johnson Kent, Arenas Juan, Cibrik Diane. IVIG for the treatment of Transplant BK Nephropathy
5. Zhou M, **Shah R**, Shen R, Rubin MA. Basal Cell Cocktail (34betaE12+p63) improves the detection of Prostate Basal Cells. Modern Pathol, 16(1): 807, Jan 2003

EUGENE M. SILVERMAN, M.D.
CLINICAL ASSOCIATE PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

A. Surgical Pathology Coverage of M-Labs cases, including most cases from:
   1. University of Michigan Health Service, non-dermatology cases, Ann Arbor, Michigan.
   2. Forest Health Medical Center, Ypsilanti, Michigan.
   3. Other various clients including numerous satellite sites and University acquired practices.

B. Rotation with other staff pathologists:
   1. Coverage at the University Hospitals of weekend autopsy call.

C. Clinical Pathology consults for M-Labs clients.

D. Surgical Pathology "Quickie" Anatomic Pathology consults for pathologists at M-Labs client hospitals and others.

II. TEACHING ACTIVITIES:

A. Review of microscopic material with residents in interesting M Labs surgical pathology cases.

III. RESEARCH ACTIVITIES:

None.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Michigan Health Corporation representative to Joint Venture Hospital Labs (JVHL).

B. Director, M-Labs:
   1. Provide leadership for and participate in planning, marketing, and implementation of M-Labs programs.
   2. Growth. In FY 2003, M Labs added 16 new physician offices and specialty service practices to our client list. These now number in 143 offices. The majority of these are related to our contract to provide coverage to MCare patients. There were no new full reference laboratory accounts. No contracts for services were terminated.
      This fiscal year, gross billings for clinical pathology services increased by 29% and gross billing for anatomic pathology services increased by 21%. Total

combined expected revenue from CP and AP billing increased by 27% over our last fiscal year.

M Labs submitted no proposals to prospective new clients during FY2003.

The department of Pathology rejected business opportunities to provide dermatopathology services to 5 dermatology practices.

3. Managed Care Activities

We have successfully renegotiated our contract of 4/1/01 M Care to provide outpatient lab services for all groups and products for M Care's commercial and Medicare products. M Labs prepares quarterly QA reports on lab services for M Care's QA department and have conducted a Physician Satisfaction Survey for M Labs subcontracted providers and reported the results to M Care. We assist M Care with resolution of laboratory service issues. We are actively engaged in contracting for delivery of HEDIS data for M Care to assist them in meeting requirements of the NCQA.

4. Networks. MLabs is a member of 2 laboratory networks, Great Lakes Laboratory Network (GLN) which consists of 28 hospital laboratories, predominantly in the western and northern parts of Michigan, and Joint Venture Hospital Laboratories (JVHL) which has grown to include 9 equity members and 72 participating member laboratories located in Michigan. JVHL has contracts for laboratory services with 14 managed care organizations including BCN.

I serve on the JVHL Executive committee that is striving to improve the financial rewards to its provider members, including UMHS, by reducing "leakage" to non-contracted providers and increasing reimbursement for contracted services.

MLabs coordinates the Pathology Department's issues concerning contractual obligations to JVHL and GLN. These include such items as BCN critical value list and HEDIS reporting.

C. Member Department of Pathology Incentive Committee.

D. Member, University of Michigan Networking Leads Committee.

E. Alternate Member, Peer Review Committee and Executive Committee, Forest Health Medical Center.

V. OTHER RELEVANT ACTIVITIES:

None.

VI. PUBLICATIONS:

None.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

A. Assistant Director, Cytogenetics Laboratory

II. TEACHING ACTIVITIES:

A. House Officers and Fellows
   1. Rotations in Cytogenetics
      a. Pathology Fellows (N=3)
      b. Pathology Residents (N=6)
      c. Pediatric/Medical Genetics Residents (N=1)
      d. Hematology/Oncology Fellows (N=1)

B. Clinical Cytogenetics
   1. Abnormal Cytogenetics Case Conference (Biweekly)--- technologists, residents, and fellows
   2. Leukemia Conference (Biweekly)
   3. Pediatric Genetics Post-clinic Conference (Weekly)
   4. Joint Genetics Conference (Monthly)
   5. Clinical Pathology Grand Rounds
      a. "Cytogenetics of Solid Tumors" 02/28/03

III. RESEARCH ACTIVITIES:

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

PROJECTS UNDER STUDY:

1. "Study of origin and role of fibrotic tissue in the development of Obliterative Bronchiolitis"
2. PI: Vibha Lama, MD; Dept of Pulmonary and Critical Care + 8 Co-PI

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

V. PUBLICATIONS:

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

1. Soule S., Baldridge L., Kirkpatrick K., Cheng L., Gilbert J.L., **Smith L.R.**, Thurston V.C., Vance G.H., Einhorn L., and Miller K. 2002. *HER-2/neu* Expression in Germ Cell Tumors. *Journal of Clinical Pathology.* 55:656-658.
2. Knox K.S., Behni M., **Smith L.R.**, Vance G.H., Busk M., Cummings O.W., Kwo P.Y., and Wilkes D.S. 2002. Acute Graft-Versus-Host Disease of the Lung After Liver Transplantation. *Liver Transplantation,* 8(10):968-971

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

A. **Flow Cytometry Diagnostic Service** - interpretation of cell surface marker studies in the evaluation of hematologic disorders, primary and secondary immune deficiencies and autoimmune processes.

B. **Autopsy Service**

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):** Dr. Okuyama's work focused on T-cell trafficking during active cellular immunotherapy for metastatic cancer. In collaboration with Dr. Craig, he established a treatment model using cultured dendritic cells that permits study of T-cell trafficking from vaccine-primed lymph nodes to the tumor sites. He showed that ovalbumin-specific, endogenous T-lymphoblasts can be detected in tumor-draining and vaccine-primed lymph nodes using an ovalbumin-peptide-specific (OVA-peptide), Class I restricted tetramer and flow cytometry. In conjunction with B16 melanoma cells engineered to express ovalbumin, they will evaluate the trafficking of OVA-specific T-cells from vaccine-primed lymph nodes into tumors after blockade of pertinent adhesion receptors and chemokines. In this manner, they will evaluate trafficking efficiency and dissect the recruitment pathways used by circulating tumor-suppressive T-cells during immunotherapy.
2. **Randall Knibbs, Ph.D., Research Scientist (1/94-present)** - Dr. Knibbs assumed primary responsibility for the project exploring the trafficking and priming efficiency of cultured dendritic cells that overexpress lymph node homing receptors. Studies to date indicate that one can augment trafficking from subcutaneous inoculation sites to draining lymph nodes using this approach. These data, if confirmed, will provide insight into the mechanism of DC trafficking from tissues into regional lymph nodes. Trafficking studies with highly enriched populations of transduced cells are planned. In addition, the priming activities of homing receptor transduced, peptide and/or tumor-lysate pulsed DC will be compared to standard DC. Finally, the ability of homing receptor transduced DC to suppress established subcutaneous tumors will be compared to standard DC for both OVA-transduced and native murine melanomas.
3. **Joseph Skitzki, MD (8/01-7/03) post-doctoral fellow** – Dr. Skitzki completed his post-doctoral training this year under the Surgical Oncology Training Grant.

His work focused on the trafficking and clinical activity of infused, tumor-reactive T-lymphoblasts during adoptive cellular immunotherapy for metastatic cancer. He showed that trafficking into tumor-bearing tissues occurred immediately after infusion and subsequently from donor cells proliferating in secondary lymphoid organs. Importantly, the infused cells that entered tumors within 48 hours accounted for >90% of the tumor suppressive activity measured at two-weeks indicating that the initial influx into metastatic lesions is crucial to clinical activity. Finally, he showed that the selectin family of adhesion receptors is essential for optimal suppression of subcutaneous tumor-implants by adoptive immunotherapy. These studies were invited for oral presentation at three national meetings and two manuscripts covering the work are currently under development. In addition, Dr. Skitzki received the outstanding young investigator award (chosen from > 40 participants) after presentation of his work at the Med-West Regional Surgery Research Symposium.

4. **Undergraduate and graduate research assistants**: Mentored two undergraduate students in the laboratory participating in work/study programs and one rotating graduate student.

B. **Co-director, lecturer and seminar leader, M2 Hematology Sequence** (16 contact hours+120 hours administration/development).

1. Compiled "M2 HEMATOLOGY SEQUENCE SYLLABUS ONLINE" CD. This CD provided a comprehensive, computer-based tool for reviewing all printed and visual course content. It consisted of an outline of major topics linked to the relevant sections of the syllabus, PowerPoint Lectures and Web content.
2. Designed, authored and implemented the 6th generation of The Virtual Microscope-Hematopathology Interactive Syllabus (http://141.214.6.12/virtualheme99). The site incorporates high resolution (1900 X 1300 pixel) photomicrographs of blood smears, bone-marrow aspirates and lymph node sections in an interactive laboratory syllabus. Unique software allows user to pan across low-power images then magnify regions of interest. Questions (and answers) covering the pathophysiology, diagnosis and treatment of the hematologic malignancies are incorporated into the exercises. This "active" learning experience captures the essentials of the in-class laboratory exercises providing students with a flexible tool for preview and review. 1999 Computerworld-Smithsonian Award Finalist.

C. **Director, General Pathology Laboratory Course for Dental Students and co-director, General Pathology Lecture Course** (30 contact hours + 60 hours administration/development): Designed, authored and implemented 6th generation of The Virtual Microscope- Interactive web-based syllabus for General and Organ systems pathology for dental students (D2). URL= http://141.214.6.12/cyberscope631/ This site incorporates several hundred, high resolution (1900 X 1300 pixel) photographs of gross and microscopic specimens into an interactive laboratory syllabus. 1999 Computerworld-Smithsonian Award Finalist.

D. **M1 Host Defense Sequence** (4 contact + 20 development)**:** Lectured and developed CD-based courseware for lecture syllabus and case presentations.

E. **Advanced Topics in Immunology** (15 contact + 50 administration/development): Co-chaired (with Nicholas Lukacs, PhD) a graduate seminar series on Leukocyte Trafficking.

Graduate students prepared presentations in conjunction with the co-chairs using selected primary sources and reviews.

F. **Mini Medical School Lecture Series-- Gerald Abrams, Director** (1 contact hour + 20 hours development): Developed animated presentation on the Immune System for educated lay persons. Presented at the Mini Medical School Session Spring, 2003. Received commendation from the Dean based on evaluation by the Director and participants.

G. **Resident Teaching**: (30 contact hours)
   1. **Flow cytometry service, case sign-out** (3 months)
   2. **Autopsy service, weekend coverage**

III. RESEARCH ACTIVITIES:

A. **Principal Investigator (Kevin Mcdonagh, co-investigator)- Retroviral transgene induction of homing receptors on dendritic cells used for active immunotherapy: impact on trafficking, antigen priming and tumor suppression.** University of Michigan Comprehensive Cancer Center Innovation Award Program., $50,000 (direct); July 2003-June 2004.

B. **Principal Investigator (Kevin Mcdonagh, co-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- T Cell Trafficking in Adoptive Cellular Immunotherapy;** NIH, R01CA73059, 30% effort, $196,000 (annual, direct); April 2001 -Mar 2006

D. **Co-investigator on Project 2 and Co-director of the Immunology Core (with J. Mule, B. Redman and A.E. Chang, Surgical Oncology Division, University of Michigan)- Cellular Vaccines for Cancer Immunotherapy**, NIH P01CA59327, 15% 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 1999-June 2004.

G. **Co-investigator (with B. Richardson, Rheumatology Division, University of Michigan)- "Gender specific T-cell homing and autoimmunity";** NIH, R01AI42753, 0% effort, $187,000 (annual, direct); Apr 1998-Mar 2003.

H. **Trainer on three funded pre-/post-doctoral training grants: Translational Immunology (J. Mule, PI); Surgery Oncology Research (A.E. Chang, PI) and Immunopathology (R. Miller, PI).**

IV. ADMINISTRATIVE ACTIVITIES:

A. **Faculty Director, Medical Student Portal Project** (200+ hours administration, development, implementation):
   1. Initiated and co-directed (with Chris Chapman, Assistant Media Manager LRC) the development of a web-based Medical School Portal that provides tools for course design, management and delivery of the Medical School curriculum. This collaboration involved staff from the Medical School Learning Resource Center, Medical School Information Systems and the Media Union and culminated in the successful release of the application to the Medical School community on August 6th, 2003. The Portal facilitates faculty collaboration during course design, provides students with a flexible on-line academic calendar directly linked to essential educational resources and promotes on-line discussions within the Medical School community. When fully implemented, an "assignment" tool will help students and faculty track student-directed learning activities and a "search/retrieve" tool will help users find and retrieve educational resources when preparing for boards, assembling case presentations or developing courses.
   2. Provided training for faculty developing content for the Medical Student Portal.
   3. Coordinated long-range planning for Medical School Portal Project.

B. **Director, General Pathology Laboratory Course for Dental Students (Pathology 631) and co-director, General Pathology Lecture Course (Pathology 630)** - see educational activities.

C. **Co-Director, Hematology Sequence in Component II** - see educational activities.

D. **Director of Research Flow Cytometry Laboratory and Co-Director of Clinical Flow Cytometry Laboratory**- managed the development of new software to interface clinical flow cytometry instruments with the Laboratory Information System (Cerner Milleneum). Participated in the consolidation of Clinical Flow Cytometry and Hematology Laboratories. Managed the operation of the research flow cytometry instrument.

E. **Member, Medical School Curriculum Review Group**

F. **Member, Abnormal Organ Systems Task Force for Curriculum Redesign**

G. **Member, Medical School Admissions Committees**

H. **Member, Pathology/Immunology Graduate Program Admissions Committee**

V. OTHER RELEVANT ACTIVITIES:

A. EDITORIAL ACTIVITIES:

1. Journal of Experimental Medicine.
2. American Journal of Pathology.
3. Journal of Immunology (Associate Editor).

VI. PUBLICATIONS:

A. ARTICLES IN PEER REVIEWED PUBLICATIONS:

1. A. Matsukawa, N.W. Lukacs, C.M. Hogaboam, R.N. Knibbs, D.C. Bullard, S.L. Kunkel and **L.M. Stoolman**: Mice Genetically Lacking Endothelial Selectins are Resistant to the Lethality in a Murine Model of Septic Peritonitis. Exper. & Mol. Path. 2002. 72: 68.
2. B. Walcheck, A. Leppanen, R.N. Knibbs, **L.M. Stoolman**, S.R. Alexander, R.P. McEver. Sialyl-Lex formed on core 2-modified O-glycans is recognized by the mAb CHO-131: Distinction of cells expressing high affinity glycan ligands for P-selectin. 2002. Blood. 99:4063.
3. N. W. Lukacs, R.N. Knibbs, A. Johns, **L.M. Stoolman**: E- and P-selectin molecules are involved in the inflammatory responses during allergen-induced airway hyperractivity. J. Immunol. 169:2120.
4. M. Jutila, S. Kurk, L. Turk, R.N. Knibbs, **L.M. Stoolman:** L-selectin can serve as an E-selectin ligand on human T-cells. 2002. J. Immunol. 169:1768.
5. Jeffrey L. Curtis, Joanne Sonstein, Ronald A. Craig, Jill Todt, Randall N. Knibbs, Timothy Polak, Daniel C. Bullard, and **L.M. Stoolman**: Altered Lung Lymphocyte Recruitment in response to intratracheal particulate antigen challenge in mice lacking endothelial selectins is subset specific. 2002. J. Immunol. 169:2570
6. Wusi Maki, William G. Telford, Randall N. Knibbs, **L.M. Stoolman** and Sam T. Hwang: CC chemokine receptor-6 (CCR6) co-localizes with CD18 and enhances adhesion to activated endothelial cells in CCR6-transduced Jurkat T cells. J. Immunol. 169:2346.
7. Daniel, Myers DVM, Dianna Farris LVT, Angela Hawley MS, Shirley Wrobleski BS, Amy Chapman BS, **L.M. Stoolman MD**, Randy Knibbs PhD, Robert Strieter MD, Thomas Wakefield MD: Selectins and Interleukin-10 Influence Acute Thrombus Formation in a Mouse Model of Venous Thrombosis. 2002. J. Surgical Research. 108:212.
8. R.N. Knibbs, M.. Dame, M.R. Allen, Y. Ding, W.J. Hillegas, J. Varani, **L.M. Stoolman**. Sustained high yield production of recombinant proteins on transiently-transfected COS-7 cells grown on trimethylamine coated microcarrier beads. 2003. Biotechnology Progress. 19:9.

B. BOOK CHAPTERS:

1. **Stoolman. L.M.** 2003. Hematopoietic differentiation and the development of neoplastic diseases, in Hematology for Medical Students, A. Schmaier (ed.). Lippincott, Philadelphia, PA.

C. ABSTRACTS, BOOK REVIEWS, LETTERS TO THE EDITOR, MISCELLANEOUS UNREFEREED PUBLICATIONS:

1. **LM Stoolman**, Alvin Schmaier and Sequence Faculty, 2002. M2 HEMATOLOGY SEQUENCE SYLLABUS ONLINE CD.
2. **LM Stoolman,** Michael Lougee, Douglas Gibbs and Tom Peterson. 1998-2002 (updated annually). The Virtual Microscope- Interactive web-based syllabus for medical student (M2) Hematopathology laboratory. URL= http://141.214.6.12/virtualheme99/.

3. **LM Stoolman,** Michael Lougee, Douglas Gibbs, Tom Peterson and Gerald Abrams. 1998-2001 (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/.
4. **LM Stoolman**. 1999-2002 (updated annually). Hematopathology Unknown Exercises. Powerpoint-based excercise containing high resolution, annotated images and imbeded questions used by Medical Students (Hematology Sequence, year 2).
5. **LM Stoolman**. 1999-2002 (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 2) and Graduate Students (Pathology 581).
6. **L.M. Stoolman**, 1999-2002 (updated annually). Chronic Lymphocytic Leukemia: Interactive Case Study. Powerpoint based exercise including high-resolution images, animations, imbeded questions and hyperlinks from Case Study to source materials. Used by Medical Students (Host Defense Sequence, year 1).

LYNDON SU, M.D.
CLINICAL ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

A. Dermatopathology Service – (University Hospital and Transfer cases) – 12 months
B. Dermatopathology Consultation Service (including personal, M-Labs, and Veterans Administration Hospital 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. Role of apoptosis in melanoma progression and chemoresistance (Dr. Maria Soengas, Dr. Tim Johnson)
B. M-RNA expression microarray of Merkel cell carcinoma and other neuroendocrine tumors. (Dr. Tom Giordano, Dr. Lina Wasserman)

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:

VI. PUBLICATIONS:

ARTICLES PUBLISHED, ACCEPTED OR SUBMITTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Winer I, Normolle DP, Shureiqi I, Sondak VK, Johnson T, Su L, Brenner DE. Expression of 12-lipoxygenase as a biomarker for melanoma carcinogenesis. Melanoma Res. 2002 Oct;12(5):429-34.
2. Su LD, Fullen DR, Sondak VK, Johnson TM, Lowe L. Sentinel lymph node biopsy for patients with problematic spitzoid melanocytic lesions: a report on 18 patients. Cancer. 2003 Jan 15;97(2):499-507.
3. Petro A, Wegman PA, Su LD. Acral and ear papules and arthritis: fibroblastic rheumatism. A case report. Arch Dermatol. 2003 May;139(5):657-62.
4. Bogner PN, Fullen DR, Lowe L, Paulino A, Biermann JS, Sondak VK, Su LD. Lymphatic mapping and sentinel lymph node biopsy in the detection of early metastasis from sweat gland carcinoma. Cancer. 2003 May 1;97(9):2285-9.
5. Fullen DR, Lowe L, Su LD. Antibody to S100a6 protein is a sensitive immunohistochemical marker for neurothekeoma. J Cutan Pathol. 2003 Feb;30(2):118-22.
6. Hattori Y, Nerusu KC, Bhagavathula N, Brennan M, Hattori N, Murphy HS, Su LD, Wang TS, Johnson TM, Varani J. Vascular expression of matrix metalloproteinase-13 (collagenase-3) in basal cell carcinoma. Exp Mol Pathol. 2003 Jun;74(3):230-7.
7. Barr KL, Lowe L, Su LD. Mycobacterium marinum Infection Simulating Interstitial Granuloma Annulare: A Report of Two Cases. Am J Dermatopathol. 2003 Apr;25(2):148-51.
8. Swartz RD, Crofford LJ, Phan SH, Ike RW, Su LD. Nephrogenic fibrosing dermopathy: a novel cutaneous fibrosing disorder in patients with renal failure. Am J Med. 2003 May;114(7):563-72.
9. Su, L.D., Fullen, D.R., Lowe, L., Wang, T.S., Schwartz, J.L., Cimmino V.M., Sondak, V.K., Johnson, T.M. Desmoplastic and neurotropic melanoma: analysis of 33 cases with lymphatic mapping and sentinel lymph node biopsy. (Submitted to Cancer).
10. Karimipour, D.J., Lowe, L., Su, L., Hamilton, T., Sondak, V., Johnson, T.M., Fullen, D.F. Utility and sensitivity of standard immunostains and serial sectioning for melanoma sentinel lymph node biopsy. (Accepted for publication by J Am Acad Dermatol)

ABSTRACTS AND PRESENTED PAPERS:

1. Swartz RD, Crofford LJ, Phan SH, Ike RW, Su LD: "Nephrogenic fibrosing dermopathy: a novel cutaneous fibrosing disorder in patients with renal failure." Oral presentation at the American Society of Dermatopathology 39th annual meeting, October 10-13, 2002.
2. Bogner, P., Lowe, L., Fullen, D., Biermann, J., Paulino, A.F., Sondak, V., Su, L.D. "Lymphatic mapping and sentinel lymph node biopsy detects early metastasis of eccrine carcinoma." Poster presentation at the American Society of Dermatopathology 39th annual meeting, October 10-13, 2002.
3. Bogner, P., Lowe, L., Su, L., Fullen, D. "Detection of CD5 by immunohistochemistry in cutaneous tumors of apocrine and eccrine origin." Accepted for poster presentation at the American Society of Dermatopathology 40th annual meeting, October 9-12, 2003.

GERD O. TILL, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

A. 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:

A. 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:

INVITED LECTURES/SEMINARS:

Invited Speaker, "Protective effects of antioxidants on half-mustard gas-induced acute lung injury;" US Army Medical Research Institute of Chemical Defense, Aberdeen Proving Ground, Maryland, September 17-18, 2002

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. British Journal of Pharmacology
   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, Till GO, Smith MG, Ward PA. Protection from half-mustard-gas-induced acute lung injury in the rat. J. Appl. Toxicol. 22:257-262, 2002
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. McClintock SD, Till GO, Smith MG, Ward PA. Liposome-associated antioxidants protect from lung injury caused by 2-chloroethyl ethyl sulfide. (to be submitted)

4. Till GO, McClintock SD, Elford HL, Ward PA. Protective effects of polyhydroxyphenyl compounds on 2-chloroethyl-ethyl-sulfide-induced lung injury (to be submitted)

BOOKS AND CHAPTERS IN BOOKS:

None

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

1. Till GO. Book review in Arch. Pathol. Lab. Med. (in press) Methods in Molecular Biology, volume 196, "Oxidants and Antioxidants: Ultrastructure and and Molecular Biology Protocols" Edited by . D. Armstrong. Humana Press, 2002.

RICCARDO VALDEZ, M.D.
CLINICAL ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002- 30 JUNE 2003

I. CLINICAL ACTIVITIES:

A. Diagnostic Hematopathology (including peripheral blood and body fluid smears).
B. Clinical Hematology Laboratory.
C. Clinical Flow Cytometry Laboratory.
D. Hematopathology Consultation Cases (including M-Labs and Veteran's Hospital).
E. Tissue Typing/Histocompatibility Laboratory.
F. Diagnostic Heart Transplant Biopsies (ad hoc, 68 cases).
G. Blood Bank, attending coverage (ad hoc, 1 week).

II. TEACHING ACTIVITIES:

A. Medical Students:
   1. Laboratory Instructor, M2 General Pathology Course (32 hours).
   2. Rotation Mentor, M4 Pathology Elective (1 month).
   3. Laboratory Instructor, 2nd year Dental Student Pathology Course (9 hours).
   4. Co-Mentor, M4 Research elective [Michael Axelson] (5 hours)
   5. Faculty Mentor, Latin American-Native American Medical Student Association (5 hours)

B. House Officers:
   1. Sign-out of bone marrow biopsies, aspirate smears, peripheral 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 (2).

C. Hematopathology teaching:
   1. Leukemia conference/biweekly.
   2. Lymphoma conference/weekly.
   3. Hematology conference/biweekly.
   4. Multiple myeloma conference.
   5. Hematology/Oncology Morbidity and Mortality Conference.
   6. Internal Medicine Morbidity and Mortality Conference.
   7. Clinical Pathology Grand Rounds (one lecture).
   8. Clinical Pathology Case Conference/weekly.

D. Laboratory Staff:
   1. Hematology Laboratory monthly CME coordinator.
   2. Tissue Typing Laboratory Journal Club.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Gene expression profiling in small B-cell lymphoproliferative disorders and multiple myeloma.
B. Effects of novel hematopoietic malignancy therapies on bone marrow morphology.
C. Immunophenotyping of hematopoietic neoplasms.
D. Characterization of C57 black mouse hematopoiesis and hematolymphoid tumors following stem cell transplant (with Dr. Sean Morrison).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Tissue Typing/Histocompatibility Laboratory, Director in training.
B. Clinical Pathology Resident Training (coordinator, CPA Resident and Hematopathology Fellowship monthly rotations).
C. Interviewer for pathology residency program.

REGIONAL/NATIONAL:

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. **Valdez R**, Thorson J, Finn WG, Schnitzer B, Kleer CG. Lymphocytic mastitis: A Clinicopathologic, Immunophenotypic, and Molecular Evaluation of Eleven Cases. Mod Pathol 2003;16(3):223-228.
2. Fullen DR, Jacobson SN, **Valdez R**, Novice FM, Lowe L. Granuloma Annulare-like Infiltrates with Concomitant Cutaneous Involvement by B-cell Non-Hodgkin's Lymphoma: Report of a Case. Am J Dermatopathol 2003;25(1):57-61.
3. Uherova P, **Valdez R**, Ross CW, Schnitzer B, Finn WG. Nodular Lymphocyte Predominant Hodgkin Lymphoma: An Immunophenotypic Reappraisal Based on a Single-Institution Experience. Am J Clin Pathol 2003;119(2):192-198.
4. **Valdez R**, McKeever P, Finn WG, Gebarski S, Schnitzer B. Composite Germ Cell Tumor and B-cell Non-Hodgkin's Lymphoma Arising in the Sella Turcica. Human Pathology 2002;33(10):1044-1047.
5. Su LD, Fullen DR, Lowe L, Uherova P, Schnitzer B, **Valdez R**. CD117 (KIT receptor) Expression in Merkel Cell Carcinoma. Am J Dermatopathol 2002;24(4):289-293.
6. **Valdez R**, Ross CW, Singleton TP, Kroft SH, Peterson L, Schnitzer B, Finn WG. Cerebrospinal Fluid Involvement by Mantle Cell Lymphoma. Mod Pathol 2002;15(10):1073-1079.

ARTICLES SUBMITTED FOR PUBLICATION:

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

1. Kilgore S, Erba H, **Valdez R**, Finn WG, Schnitzer B, Ross CW: Mylotarg (Gemtuzumab Ozogamicin; CMA-676) in AML: Predictive Variables and Response to Treatment. Mod Pathol 16:240A, 2003
2. Ramalingam P, **Valdez R**, Ross CW, Schnitzer B, Finn WG: Oct-2 and BOB.1/OBF.1 Expression in Surface Immunoglobulin Negative Follicular Lymphomas. Mod Pathol 16:249A, 2003.
3. Ramalingam P, Finn WG, Schnitzer B, **Valdez R**: Immunohistochemical Expression of Oct-2 in Non-Hodgkin Lymphomas Evaluated by Tissue Microarray (TMA). Mod Pathol 16: 249A, 2003.
4. Selby D, Padmore R, Tuck M, Ross CW, Schnitzer B, Finn WG, **Valdez R**, Singleton T, Kaminski M: Characterization of Bone Marrow Lymphoid Aggregates in Follicular Lymphoma Treated with [131I] Anti-B1 Antibody. Mod Pathol 16:251A, 2003
5. Selby DM, Ross CW, Finn WG, **Valdez R**, Schnitzer B: CD10 and Cyclin D1 Expression in Hairy Cell Leukemia. Mod Pathol 16:251A, 2003.
6. **Valdez R**, Schnitzer B, Finn WG. Tissue Microarray (TMA) Analysis of Survivin Expression in Benign Lymphoid Tissue and Small B-cell Non-Hodgkin's Lymphoma (NHL). Mod Pathol 16:257A, 2003.
7. Selby DM, **Valdez R,** Schnitzer B, Ross CW, and Finn WG, et al. Diagnostic criteria for acute erythroleukemia. Blood 2003; 101:2895.

JAMES VARANI, PH.D.
PROFESSOR OF MICROBIOLOGY AND IMMUNOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

A. None.

II. TEACHING ACTIVITIES:

A. Mentor for students who worked in my laboratory over the past year, including five post-doctoral fellows, one pathology graduate student, one medical student, two SPH graduate students, three undergraduate students and two high school students.
B. Dissertation committee (committee chairman) for Jill Murtha.
C. Dissertation committee for Yayi Chang.
D. Thesis committee (committee chairman) for Ashish Lal (MPH degree)
E. Course director – Pathology 581. Tissue, cellular and molecular basis of disease.
F. Instructor – Pathology 581 – Tissue, cellular and molecular basis of disease.
G. Instructor – Pathology 600 – Pathology course for dental students.
H. Instructor – Pathology 582 – Tissue, cellular and molecular basis of disease
I. Instructor – Pathology 553 – Cancer Biology

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Retinoids for Diabetic Foot Ulcers." NIH DK59169.
B. Principal Investigator, "MMP-3 and acute lung injury." NIH NHLBI 70979
C. Principal Investigators, "Novel therapeuctic approach to psoriasis" NIH AR 44767
D. Principal Investigator, "Co-polymer – "Microcarrier culture system for human influenza vaccind production" HIH AI 50315
E. Principal Investigator on Project 10, "Retinoic Acid and Cells of the Skin," Johnson and Johnson Corporation.
F. Principal Investigator, "Cell culture, media, microcarrier system for Marek's Disease Vaccine" NIH AI 46876.

PROJECTS UNDER STUDY:

A. The biology of collagen destruction and repair in aging skin, photodamaged skin and diabetic skin.
B. Role of MMP-3 in acute and chronic lung injury.

C. The development of a microcarrier-based protocols for production of human influenza vaccine and for Marek's vaccine.
D. Role of EGF receptor function in benign hyperplastic skin disease.
E. Extracellular calcium sensing receptor as the mediator of epithelial cell proliferation and differentiation

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Member, Department of Pathology Advisory Committee on Appointments, Promotions and Tenure.
B. Member, Department of Pathology Graduate Program Committee
C. Member, Pathology Graduate Program Steering Committee
D. Member and chairman – Pathology Graduate Program Curriculum Revision Committee.
E. Member, Department of Pathology Graduate Program Comprehensive Exam Committee.

MEDICAL SCHOOL/HOSPITAL:

A. Member, Medical School Committee on Summer Research Opportunities.
C. Member, University of Michigan Cancer Center Basic Research Committee.
D. Member, Cancer Biology Research Training Grant Scientific Steering Committee.
E. Member, Department of Dermatology Research Training Grant Steering Committee.
F. Member, University Committee on Use and Care of Animals (UCUCA).
G. Member, Program in Biomedical Sciences (PIBS) Curriculum Committee
H. Member, Program in Biomedical Sciences (PIBS) Admissions Committee
I. Member, Program in Biomedical Sciences (PIBS) Steering Committee

UNIVERSITY:

A. Member, Graduate School Task Force on Non-Academic Misconduct

REGIONAL AND NATIONAL:

A. Editorial Board of Invasion and Metastasis.

B. Manuscript Review for:
1. American Journal of Pathology.
2. Cancer Research.
3. Experimental Cell Research.
4. International Journal of Cancer.
5. Journal of Investigative Dermatology.
6. Laboratory Investigation.
7. Invasion and Metastasis.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/PRESENTATIONS:

1. Invited speaker: Hamchung Lecture, National University of Korea, Seoul, Korea, September 14, 2002.
2. Invited speaker, Department of Biological Sciences, University of Indiana, October 15, 2002.
3. Invited speaker, Department of Pathology and Laboratory Medicine, MD Anderson Cancer Center, July 30, 2003.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Fligiel SEG, Datta SH, Fisher GJ, Voorhees JJ, Varani J. Ultrastructural and biochemical features of collagen damage in photoaged skin and by MMP-1 in vitro. *J. Invest. Dermatol.* 120:842-848, 2002.
2. Varani J, Petryniak J, Takagaki M, Dame MK, Petryniak B, Goldstein IJ. Differential expression of an a-galactosyl-cotnaining trisaccharide on high- and low-malignant murine sarcoma cells: Identification and regulation. *Clin. Exp. Metastasis* 19:1-8, 2002.
3. Moon SE, Bagavathula R, Varani J. Induction of matrix metalloproteinase-1 (MMP-1) during epidermal invasion of the stroma in human skin organ culture: Regulation through activation of MAPK pathways. Brit. J. Cancer 87:457-464, 2002.
4. Varani J, Perone P, Fligiel SEG, Fisher GJ, Voorhees JJ. Inhibition of type I procollagen production in photodamage: Correlation between presence of high molecular weight collagen fragments and reduced procollagen synthesis. *J. Invest. Dermatol.* 119:122-129, 2002.
5. Varani J, Perone P, Merfert MG, Moon SE, Larkin D, Stevens MJ. All-trans retinoic acid improves structure and function of diabetic rat skin in organ culture. *Diabetes* 51:3510-3516, 2002.
6. Knibbs RN, Dame M, Allen MR, Ding Y, Hillegas WJ, Varani J, Stoolman L. Sustained high yield production of recombinant proteins in transiently-transfected COS-7 cells grown on trimethylamine-coated microcrarrier beads. *Biotech. Progress* 19:9-15, 2002.
7. Hattori Y, Nerusu K, Bhagavathula N, Brennan M, Hattori N, Murphy HS, Su L, Wang TS, Johnson TM, Varani J. Vascular expression of matrix metalloproteinase-13 (collagenase-3) in basal cell carcinoma. *Exp. Molec. Pathol.* 74:230-237, 2003.
8. Fisher GJ, Kang S, Varani J, Bata-Csorgo Z, Wan Y, Datta S, Voorhees JJ. Mechanisms of photoaging and chronological skin aging. *Arch. Dermatol.* 138:1462-1470, 2002.
9. Chakrabarty S, Radjendirane V, Appelman H, Varani J. Extracellular calcium and calcium sensing receptor function in human colon carcinoma: Promotion of E-cadherin expression and suppression of b-catenin/TCF activation. *Cancer Res.* 63: 67-71 2003.
10. Fligiel SEG, Varani J, Datta SH, Kang S, Fisher GJ, Voorhees JJ. Collagen degradation in aged/photoaged skin in vivo and after exposure to MMP-1 *in vitro*. *J. Invest. Dermatol.* 120:842-848, 2003.

11. Brennan M, Bhatti H, Nerusu KC, Bhagavathula N, Kang S, Varani J, Voorhees JJ. Matrix metalloproteinase-1 is the major collagenolytic enzyme responsible for collagen damage in UV-irradiated human skin. *Photochem. Photobiol.* 73:43-48, 2003.
12. Varani J, Fligiel H, Zhang J, Aslam MN, Lu Y, Dehne L, Keller ET. Separation of retinoid-induced epidermal and dermal thickening from skin irritation. *Arch. Dermatol. Res.* (in press) 2003.
13. Bhagavathula N, Nerusu K, Ellis CN, Chittiboyina A, Avery MA, Christopher Ho CI, Benson SC, Pershadsingh HA, Kurtz TW, Varani J. Rosiglitzone inhibits biological responses in keratinocytes and signaling events that underlie responsiveness. *J. Invest. Dermatol.* (in press) 2003.
14. Lateef H, Sevens M, Varani J. All-trans retinoic acid suppresses matrix metalloproteinase production/activation and increases collagen synthesis in diabetic skin in organ culture. *Arch. Dermatol. Res.* (in press).
15. Varani J, Schuger L, Leonard C, Fligiel SEG, Kang S, Fisher GJ, Voorhees JJ. Reduced fibroblast interaction with intact collagen as a mechanism for depressed collagen synthesis in photoaged skin. *J. Invest. Dermatol.* (in press).

BOOKS AND CHAPTERS IN BOOKS:

1. Fisher GJ, Kang S, Varani J, Bata-Csorgo Z, Wan Y, Datta S, Voorhees. Mechanisms of Photoaging and Chronological Skin Aging. *Arch. Dermatol* 138:1462-1470, 2002.
2. Varani, J. Immunobiology of chemotaxis and metastases. *The Handbook of Cancer Immunology.* (in press).
3. Chakrabarty S, Varani J. Extracellular calcium and calcium sensing receptor function in human colon carcinoma: Role in promotion of E-cadherin expression and suppression of □-catenin/TCF activation. *Frontiers in Bioscience* (in press).
4. Varani J. Organ-cultured skin as a model for squamous epithelial cell invasion. *Frontiers in Bioscience* (in press).
5. Murphy H, Varani J, Ward PA: The Biology of Endothelial cells. *Allergy: Principals and practices.* Sixth Edition. E. Middleman, et al, eds. Mosbey, St. Louis, MO.
6. Murphy H, Varani J, Ward PA. Endothelial cell injury by neutrophils: Pathophysiology. *Perspectives in Lung Endothelial Barrier Function* (in press).

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

1. Fligiel SEG, Perone P, Varani J. Collagen destruction induced by metalloproteinase (MMP) treatment in vitro is similar to dermal collagen damage in photodamaged skin: An ultrastructural analysis. *J. Derm. Pathol.* 2002.
2. Varani J, Perone P, Fligiel SEG, Fisher GJ, Voorhees JJ. Inhibition of collagen production in photodamage. *J. Invest. Dermatol.* 2002.
3. Varani J. Factors influencing tumor cell motility in 3-dimensional collagen matrix cultures. *Keystone Symposium Proceedings.* 2003.
4. Varani J, Schuger L, Kang S, Fisher GJ, Voorhees JJ. Fragmented collagen, reduced mechanical tension and reduced interaction with intact collagen as a mechanism for depressed collagen synthesis in photoaged skin. *J. Invest. Dermatol* 2003.

5. Varani J. Assessment of Pregabalin for direct effects on endothelial cell proliferation in monolayer culture. Pfizer Technical Report. 2002.
6. Dame MK, Yu X, Garrido R, Bobrowski W, McDuffie JE, Albassam M, Varani J. A method for the isolation of endothelial cells and smooth muscle cells from individual canine coronary arteries. Pfizer Technical Report. 2003.

CLAUDIUS VINCENZ, PhD
RESEARCH INVESTIGATOR
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Graduate students:
Michael Zeidler, Student of the "Freie Universitaet in Berlin, Germany"

B. Courses: Pathology 581: Lectures on cellular pathology; Pathology 582: Module on poly-glutamine expansion disease (4 sessions).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

PENDING:

A. NIH RO1: Molecular analysis of the p75NTR homologue, NRADD

PROJECTS UNDER STUDY:

A. Studies on the biological activities and molecular mechanisms of NRADD, a novel transmembrane protein with a death domain.

B. Proteolytic processing of death receptors by γ-secretase.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

None

MEDICAL SCHOOL/HOSPITAL:

Member, University of Michigan Cancer Center
Member, University of Michigan Diabetes Research and Training Center

UNIVERSITY OF MICHIGAN:

None

REGIONAL AND NATIONAL:

A. Grant reviews: Italian Association for Cancer Research (Italy)
B. NOW MtC section (Netherlands)

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Reviewer for the following journals: The Journal of Cell Biology, Journal of Clinical Investigation, Cell Death and Differentiation, Trends in Immunology.

HONORS AND AWARDS:

None

PATENTS:

None

INVITED LECTURES/SEMINARS:

February 2003: Medical College of Ohio

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. NRADD, a novel membrane protein with a death domain involved in mediating apoptosis in response to ER stress. (2003) Cell Death and Differentiation 10, 580-591.

BOOKS/CHAPTERS IN BOOKS:

None

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

None

PETER A. WARD, M.D.
PROFESSOR AND CHAIRMAN
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

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 (2002-03):
   1. Ren-Feng Guo, M.D.
   2. Neils Reidemann, M.D.
   3. Ines Laudes, M.D.
   4. Cecelia Speyer, Ph.D.
   5. Eric Albrecht, Ph.D.
   6. Thomas Neff, M.D.
   7. Jayne Reuben, Ph.D.
   8. Hungwei Gao, Ph.D.

B. Graduate students
   1. Ms. Yun Jang Man, Winter Semester 2003
   2. Stephanie McGuire, First Semester Medical Student

C. UROP Undergraduate Students:
   1. Nick Rancilio

D. Undergraduate students:
   1. Lecture, College Honors Seminar 250 (LS&A), three hours.

III. RESEARCH ACTIVITIES

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, $246,249 /yr. (25%) $816,953/yr (all projects) 03/01/99 - 02/29/04

C Principal Investigator; "Lung Injury by Oxygen Metabolites (MERIT) RO1- GM29507 NIH/NIGMS, (20%) $204,700/yr, 07/01/01 - 06/30/05

D. Principal Investigator, "Protective Effects of Anti-C5a in Sepsis," NIH/NIGMS RO1-GM61656, (20%) $204,700/yr; 01/01/02 - 05/31/07

IV. ADMINISTRATIVE ACTIVITIES

DEPARTMENTAL:

A. Chair, Department of Pathology.

MEDICAL SCHOOL/HOSPITAL:

A. Advisory Committee for the Howard Hughes Medical Institute.
B. Cancer Center Executive Committee.
C. Clinical Chairs Council.
D. Conflict of Interest Committee.
E. Conflict of Interest and Commitment Committee
F. Faculty Group Practices Committee
G. Technology Transfer Committee.
H. Geriatric Center Executive Committee.
I. Michigan Eye Bank Research Review Committee.
J. Undergraduate Research Opportunity Program, University of Michigan.
K. University of Michigan Cancer Center Executive Committee.

UNIVERSITY OF MICHIGAN:

A. Michigan League Board of Governors, September, 1997 – June 2003

REGIONAL AND NATIONAL:

A. American Association of Immunologists.
B. American Society for Clinical Investigation.
C. Association of American Physicians.
D. American Thoracic Society.
E. Association of Pathology Chairmen
F. American Association of University Pathologists
F. A. James French Society of Pathologists, 1988-present.
G. Institute of Medicine, National Academy of Sciences, July, 1990-present.
H. Michigan Society of Pathologists.
I. Michigan Thoracic Society, 1988-present.
J. National Research Council.
    a. Chair and member, Council for Institute of Laboratory Animal Research.

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.
E. Journal of Experimental and Molecular Biology, 1999 – present
F. Toxicologic Pathology, Editorial Board, 1988-present.

INVITED LECTURES/SEMINARS:

1. Invited Lecturer, "Cytokines and Lung Injury"; University of Arizona College of Public Health, Tucson, AZ; January 16, 2003.
2. Invited Speaker, "Role of C5a and C5aR in Sepsis"; Keystone Symposia; Tahoe City, CA; March 10, 2003.
3. Invited Speaker, "Acute Lung Injury"; European Respiratory Society; Taormina, Italy; March 29, 2003.
4. Invited Participant, "Nobel Symposium No 124: Septicemia and Shock: Pathogenesis and Novel Therapeutic Strategies"; Karolinska Institutet; Stockholdm Sweden; May 15-17, 2003
5. Amberson Lecturer, ATS 2003, American Thoracic Society, Seattle, Washington; May 18, 2003
6. Invited Speaker, "Good Molecules Gone Bad", Twenty-sixth Annual Conference on Shock; Phoenix, AZ, June 7-10, 2003.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS

1. Riedemann, N.C., Guo, R.F., Neff, T.A., Laudes, I.J., Keller, K.A., Sarma, J.V., Markiewski, M.M., Mastellos, D., Strey, C.W., Pierson, C.L., Lambris, J.D., Zetoune, F.S., and **Ward, P.A.**: Increased C5a receptor expression in sepsis. J. Clin. Invest., 2002;110:101-108.
2. Anaya-Prado, R., and Ramos-Kelly, J.R., Toldeo-Pereyra, L.H., Walsh, J., and **Ward, P.A.**: Multiple selectin blockade with a small-molecule selectin inhibitor does not affect survival after a second inflammatory challenge with nonlethal LPS. J Invest. Surg., 2002;15:171-180.
3. Guo, R.F., Riedemann, N.C., Laudes, I.J., Sarma, V.J., Kunkel, R.G., Dilley, K.A., Paulauskis, J.D., and **Ward, P.A.:** Altered neutrophil trafficking during sepsis. J Immunol., 2002;169(1):307-314.
4. Riedemann, N.C., Guo, R.F., Laudes, I.J., Keller, K., Sarma, V.J., Padgaonkar, V., and **Ward, P.A.**: C5a receptor and thymocyte apoptosis in sepsis. FASEB J.; 2002:16(8):887-888
5. **Ward, P.A.** and Lentsch, A.B.: Endogenous regulation of the acute inflammatory response. Molecular and Cellular Biochemistry, 2002;234/235:225-228.
6. Beck-Schimmer, B., Madjdpour, C., Kneller, S., Ziergler, U., Pasch, T., Wuthrich, R.P., **Ward, P.A.,** and Schimmer, R.C.: Role of alveolar epithelial ICAM-1 in lipopolysaccharide-induced lung inflammation. Eur Respir J 2002 19(6):1142-1150.
7. Guo, R.F., and **Ward, P.A.**: Mediators and regulation of neutrophil accumulation in inflammatory responses in lung: Insights from the IgG immune complex model. Free Radical Biology and Medicine. 2002 33:303-310.

8. Guo, R.F., Lentsch, A.B., Sarma, J.V., Sun, L., Riedemann, N.C., McClintock, S.D., McGuire, S.R., Van Rooijen, N., and **Ward, P.A.:** Activator protein-1 activation in acute lung injury. Am J Pathol. 2002 161:275-282.
9. Anaya-Prado, R., Toledo-Pereyra, L.H., Lentsch, A.B., and **Ward, P.A.**: Ischemia/reperfusion injury. J Surg Res. 2002 105:248-258.
10. McClintock, S.D., Till, G.O., Smith, M.G., and **Ward, P.A.**: Protection from half-mustard gas-induced acute lung injury in the rat. J Appl Toxicol. 2002 22:257-262.
11. Riedemann NC, **Ward PA**: Oxidized lipid protects against sepsis. Nat Med 2002 8:1084-1085.
12. Shanley, T.P., Zhao, B., Macariola, D.R., Denenberg, A., Salzman, A.L., **Ward, P.A.**: Role of nitric oxide in acute lung inflammation: Lessons learned from the inducible nitric oxide synthase knockout mouse. Crit Care Med. 2002 9:1960-1968.
13. Huber-Lang, M.S., Younkin, E.M., Sarma, J.V., McGuire, S.R., Lu, K.T., Guo, R.F., Padgaonkar, V.A., Curnutte, J.T., Erickson, R., and **Ward, P.A.:** Complement-induced impairment of innate immunity during sepsis. J Immunol. 2002 169(6):3223-3231.
14. Huber-Lang, M.S., Riedemann, N.C., Sarma, J.V., Younkin, E.M., McGuire, S.R., Laudes, I.J., Lu, K.T., Guo, R., Neff, T.A., Padgaonkar, V.A., Lambris, J.D., Spruce, L, Mastellos, D., Zetoune, F.S., and **Ward, P.A.**: Protection of innate immunity by C5aR antagonist in septic mice. FASEB J. 2002 (12) 1567-1574.
15. Martinez-Mier, G., Toledo-Pereyra, L.H., McDuffie, J.E., Warner, R.L., Hsiao, C., Stapleton, S.R., and **Ward, P.A.:** Exogenous nitric oxide downregulates MIP-2 and MIP-1α chemokines and MAPK p44/42 after ischemia and reperfusion of the rat kidney. J Invest Surg. 2002 (15):287-296.
16. Laudes IJ, Chu JC, Huber-Lang M, Guo RF, Riedemann NC, Sarma JV, Mahdi F, Murphy HS, Speyer C, Lu KT, Lambris JD, Zetoune FS, and **Ward PA**: Expression and function of C5a receptor in mouse microvascular endothelial cells. J. Immunol. 2002 169(10):5962-5970.
17. Huber-Lang, M., Younkin, E.M., Sarma, J.V., Riedemann, N., McGuire, S.R., Lu, K.T., Kunkel, R., Younger, J.G., Zetoune F.S., and **Ward, P.A.**: Generation of C5a by phagocytic cells. Am. J. Pathol. 2002 161(5):1849-1859.
18. Naidu, B., Krishnadasan, B., Whyte, R.I., Warner, R.L., **Ward, P.A.**, and Mulligan, M.S. Regulatory role of IL-10 in experimental obliterative bronchiolitis in rats. Exp Mol Pathol 2002; 73(3): 164-170.
19. Riedemann, N.C., and **Ward, P.A.**: Complement in ischemia reperfusion injury. Invited Commentary Am J Pathol. 2003 162(2): 363-367.
20. Riedemann, N.C., Neff, T.A., Guo, R.F., Bernacki, K.D., Laudes, I.J., Sarma, J.V., Lambris, J.D., and **Ward, P.A.**: Protective effects of IL-6 blockade in sepsis are linked to reduced C5a receptor expression. J Immunol. 2003 170(1): 503-507.
21. Riedemann, N.C. and **Ward, P.A.**: Anti-inflammatory strategies for the treatment of sepsis. Expert Opin Biol Ther. 2003 3(2): 339-350.
22. Riedemann, N.C., Guo, R.F., and **Ward, P.A.**: Novel strategies for the treatment of sepsis. Nature Med. 2003 9(5): 517-524.
23. Huber-Lang, M.S., Sarma, J.V., McGuire, S.R., Lu, K.T., Padgaonkar, V.A., Younkin, E.M., Guo, R.F., Weber, C.H., Zuiderweg, R.R., Zetoune, F.S. and **Ward, P.A.**: Structure-function relationships of human C5a and C5aR. J Immunol., 2003 170(12):6115-6124.
24. Younger, J.G., Shankar-Sinha, S., Mickiewicz, M., Brinkman, A.S., Sarma, J.V., Younkin, E.M., Standiford, T.J., Zetoune, F.S., and **Ward, P.A.** Complement interactions with Pseudomonas aeruginosa and their proinflammatory consequences in vivo. Am. J. Resp. Cell Mol. Biol. 2003.
25. Riedemann, N.C., Guo, R.F., and **Ward, P.A.**: A key role of C5a/C5aR activation for the development of sepsis. Accepted J. Leukoc.Biol. 2003.

JEFFREY S. WARREN, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

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-present.
E. Molecular Diagnostics Laboratory; Interim Director, August 2002-June 2003.
F. Sendout Laboratory; Director, August 2002-present.

II. TEACHING ACTIVITIES:

A. "Current Topics in Immunopathology" journal club series: pathology residents, M4 students (44 contact hours).
B. "Current Management Problems for Pathology Residents" series: pathology residents (15 contact hours).
C. Clinical Pathology Grand Rounds:
   1. "Laboratory diagnosis of amyloidosis" (11/22/02).
   2. "Cases and images in immunopathology" (11/29/02).
D. Immunopathology signout: pathology residents, M-4 medical students, EMU medical technology students (three times/week; 48 weeks/year).
E. Immunopathology component of Block B (Clinical Pathology); ad hoc topical reviews: pathology residents (63 contact hours).
F. M-1 Host Defense sequence; "Autoimmunity and tumor immunology" (5/18/03); (1 contact hour); Case Studies (5/17/03; 5/18/03); (2 contact hours).
G. Supervision of Research activities for:
   1. Anjali Desai, Ph.D. (Research Investigator); (6/15/96-present).
   2. Kevin Coles (2003 UM graduate); (5/03-present).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

PROJECTS UNDER STUDY:

A. Role of cellular redox status and neutrophil-derived mediators in MCP-1-mediated pulmonary granulomatous vasculitis.
B. Modulation of proinflammatory endothelial and smooth muscle cell functions by erythropoietin, reactive oxygen intermediates, and reactive nitrogen intermediates.
C. Pathophysiologic role of oxidants in uremia and its complications (collaboration with Rajiv Saran, M.D., Department of Internal Medicine, University of Michigan Medical School).
D. Ischemia-reperfusion injury in perinatal rat brain (collaboration with Faye Silverstein, M.D., Departments of Pediatrics and Neurology, University of Michigan Medical School).

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL:

A. Member, Operations Improvement Committee, University of Michigan Health System 2000-present
B. Member, Professional Billing Compliance Committee, University of Michigan Medical School 1999-present.
C. Member, Executive Committee, University of Michigan Medical School, 1999-present.
D. Finance Subcommittee, advisory to Faculty Group Practice (FGP) Executive Committee, 1997-2003.
E. Member, Professional Billing Compliance Committee, 1999-present.
F. Dean's Advisory Committee (ad hoc substitute for Dr. Peter Ward), 1994-present.
G. Clinical Council (ad hoc substitute for Dr. Peter Ward), 1996-present.

DEPARTMENTAL:

A. Interviewer of Pathology Residency Candidates, 1989-present.
B. Interviewer of Pathology Graduate Program Candidates, 1990-present.
C. Chairman, Laboratories Communications Committee, 1993-present.
D. Chairman, Department of Pathology Quality Assurance Committee, 1993-present.
E. Clinical Associate and Advisory Committee for Medical Technology Program, Eastern Michigan University, 1993-present.
F. 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-present.

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. President, Michigan Society of Pathologists, 2003.

V. INVITED LECTURES/SEMINARS:

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Desai A, Miller MJ, Huang X, Warren JS: Nitric oxide modulates monocyte chemoattractant protein-1 expression in endothelial cells: implications for the pathogenesis of glucan-induced granulomatous vasculitis. Inflammation 27:221-231, 2003.
2. Rajiv S, Novak JE, Desai A, Abdulhayoglu E, Warren JS, et al. Impact of vitamin E on plasma asymmetric dimethylarginine (ADMA) in chronic kidney disease (CKD): a pilot study. Nephrol Dial Transplant 18:2415-2420, 2003.
3. Townson DH, Bowen JM, Remick DG, Warren JS, Keyes PL: Prolactin-induced regression of the rat corpus luteum: the effect of dexamethasone. J Endocrinology (in press).

ARTICLES SUBMITTED FOR PUBLICATION:

1. Szaflarski J, Liu XH, Warren JS, Silverstein FS: Treatment with antibody to monocyte chemoattractant protein-1 attenuates excitotoxic brain injury in perinatal rats. J Neuroscience (submitted).
2. Whetstone WD, Gomez HF, Ernsting KS, Miller MJ, Marks RM, Warren JS: Inhibition of dermonecrotic arachnidism with interleukin-8 monoclonal antibody. Acad Emerg Med (submitted).
3. Gomez HF, Greenfield DM, Miller MJ, Warren JS. Direct correlation of dermal inflammatory effects with intradermal migration of Loxosceles reclusa venom (submitted).
4. 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. Am J Pathol (submitted).

BOOKS/CHAPTERS IN BOOKS:

1. Hannon WH, Warren JS, Ivor L, et. al.: NCCLS. Clinical Evaluation of Immunoassays: Approved Guideline. MCCLS document I/LA21-A [ISBN 1-56238-455-4]. NCCLS, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2002.
2. Warren JS, Ward PA: The inflammatory response, in Beutler E, Lichtman MA, Coller BS, Kipps TJ and Seligsohn U (eds.) Williams' Hematology, 6th Edition, McGraw-Hill, New York, NY, (in press).
3. Warren JS: Leukocyte functional assays by flow cytometry, in Keren DF, McCoy JP, Carey JL, and Hanson CA (eds.) Flow Cytometry and Clinical Diagnostics, 3rd Edition, ASCP Press, Chicago, IL, (in press).
4. Warren JS: Immunodeficiency disease, in McClatchey KD (ed.) Clinical Laboratory Medicine, 2nd Edition, Lippincott Williams and Wilkins, Philadelphia, PA, (in press).
5. Warren JS: Immunopathology, in Rubin E (ed.) Pathology 4th Edition, Lippincott-Williams and Wilkins, Philadelphia, PA, ((in press).

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

THOMAS WILSON, M.D., Ph.D.
ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

I. CLINICAL ACTIVITIES:

A. Began active role as Assistant Director of the Molecular Diagnostics laboratory. Working under the guidance of Dr. John Thorson, I will assist with technology/test development, and provide backup with regards to sign-out, etc.

II. TEACHING ACTIVITIES:

A. Mentor, postdoctoral fellows: Rajashree Deshpande, Anandi Srinivasan, Leana Topper
B. Mentor, graduate student fellows: Phil Palmbos (MSTP, CMB), James Daley (CMB)
C. Mentor, rotation student: Fred Derheimer (PIBS)
D. Mentor, undergraduate students: Anthony Iacco, Monica Heger
E. Member, thesis committees: Tammy Morrish (Human Genetics), Jonathan Rios-Doria (CMB), Marc Prindle (CMB), Anne Casper (Human Genetics), Hui-Min Tseng (University of Texas Health Science Center at San Antonio, Molecular Medicine Program)
F. Member, preliminary examination committee: Matt Whorton (Pharmacology)
G. Member, Cellular and Molecular Biology Training Program
H. Path 581, 2 lectures
I. Path 582, 1 lecture, 1 discussion section
J. Path 850, Coursemaster, research seminar series for graduate students
K 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), 7/1/2000-6/30/2004.
B. Principal Investigator, "End Processing in DNA Double-Strand Break Repair", NIH/NCI 1 R01 CA90911-01 (27%), $145,250/current year ($601,750/four years), 4/1/2001-3/31/2005.
C. Principal Investigator, "Probing the mechanisms of gemcitabine action using a yeast genomic approach", University of Michigan Comprehensive Cancer Center Munn Research Grant (0%, no salary support), $15,000/year ($15,000/one year), 9/1/2001-8/31/2002.

D. Mentor, "Role of APC-Binding Protein BIM1 on Chromosome Dynamics", NIH NRSA 5 F32 GM064204-04, Leana Topper, Ph.D., postdoctoral fellow, 11/2002-8/2004

PENDING:

A. Principal Investigator, "Systematic Genetics Analysis of Yeast NHEJ", NIH/NCI R01, not funded (priority score 223). Revision in preparation.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Pathology student recruitment activities (lunch, poster session)
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: Eric Brown (BSSP), Hui Sun (BSSP, MCDB), Harmit Malik (BSSP, Human Genetics), JoAnn Sekiguchi (BSSP, Molecular Medicine), David Ferguson (BSSP, Pathology), Christine Canman (Pharmacology), Paul Andreassen (Pharmacology), Jim Ford (Pharmacology)

UNIVERSITY OF MICHIGAN:

A. PIBS student interviews and recruitment dinners
B. Member, Cellular and Molecular Biology Program Steering Committee

REGIONAL AND NATIONAL:

A. Pew Scholars Annual Meeting Planning Committee

V. OTHER RELEVANT ACTIVITIES:

A. Manuscript review, Genetics, MCB, TIBS
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

EDITORIAL BOARDS:

A. None

HONORS AND AWARDS

A. Invited participant (one of ~30 junior scientists invited from the United States) in the National Academy of Sciences 5th Annual Chinese-American Beckman Frontiers of Science Symposium, a multi-disciplinary event covering topics as diverse as galactic science to oceanography to biomedicine. Represented the fields of molecular biology/genetics.

PATENTS:

A. None

INVITED LECTURES/SEMINARS:

1. Systematic genetics analysis of nonhomologous end-joining. Department of Pathology, University of Michigan, Ann Arbor, MI, September 16, 2002
2. Strand breaks – not simple anymore! Department of Radiation Oncology, University of Michigan, Ann Arbor, MI, November 15, 2002.
3. Multiple mechanisms for removing 3' blocking lesions in DNA. Hôpital Maisonneuve-Rosemont, Centre de Recherche, Université de Montréal, Montreal, Canada, December 17, 2002.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Karathanasis E, **Wilson TE**. Enhancement of Saccharomyces cerevisiae end-joining efficiency by stationary phase transition but not by impairment of recombination. Genetics 161: 1015-27 (2002).
2. Vance JR, **Wilson TE**. Yeast Tdp1 and Rad1-Rad10 function as redundant pathways for repairing Top1 replicative damage. Proc Natl Acad Sci USA 99: 13669-74 (2002).
3. **Wilson TE**. A genomics-based screen for yeast mutants with an altered recombination/end-joining repair ratio. Genetics 162: 677-88 (2002).
4. **Wilson TE**, Palmbos PL, Topper, LM. Nonhomologous end-joining: bacteria join the chromosome break dance. TIBS 28: 62-66 (2003). *Invited review.*
5. Yu K, Chedin F, Hsieh CL, **Wilson TE**, Lieber MR. R-loops at immunoglobulin class switch regions in the chromosomes of stimulated B cells. Nat Immunol 4:442-51(2003).
6. Karumbati AS, Deshpande RA, Jilani A, Vance JR, Ramotar D, **Wilson TE**. The role of yeast DNA 3' phosphatase Tpp1 and Rad1/Rad10 endonuclease in processing spontaneous and induced base lesions. J Biol Chem; 278: 31434-43 (2003).

ARTICLES SUBMITTED OR IN PREPARATION:

1. Nonhomologous End Joining in Yeast. *Annual Review of Genetics*. Book chapter, due March, 2005.

BOOKS/CHAPTERS IN BOOKS:

1. None

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

1. Thimmarayappa J, Karathanasis E, **Wilson TE.** Roles of Pol4 and Mre11 in microhomology searching and end-processing during nonhomologous end-joining. Presented at the Genetics Society of America conference "Yeast Genetics and Molecular Biology", Madison, Wisconsin, July 2002.
2. Vance JR, **Wilson TE.** Yeast Tdp1 and Rad1-Rad10 function as redundant pathways for repairing Top1 replicative damage. Presented at the MD Anderson 55th Annual Symposium on Fundamental Cancer Research, Houston, Texas, October 2002.
3. **Wilson TE.** A genomics-based screen for yeast NHEJ mutants. Presented at the National Academy of Sciences 5th Annual Chinese-American Beckman Frontiers of Science Symposium, Irvine, California, October 2002.
4. Karumbati AS, Deshpande RA, Vance JR, **Wilson TE.** Mechanisms for repairing single-strand breaks during replication when base-excision repair fails. Environmental Mutagen Society Annual Meeting, Miami, FL, May 2003.

SECTION REPORTS

ANATOMIC PATHOLOGY

DIVISION OF ANATOMIC PATHOLOGY

ANNUAL REPORT
1 JULY 2002 - 30 JUNE 2003

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 three new faculty have joined the Division, Drs. Kunju, Pu, and Lucas. These faculty bring additional expertise in general surgical pathology as well as sub-specialty expertise in genitourinary pathology, cytology, and bone/soft tissue pathology, respectively.

Faculty research programs and extramural support continues to increase especially in programmatic areas associated with the Cancer Center, GI 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, ADRC and tissue procurement. Several faculty have expanded collaborations with biomedical research companies including Genetech (Calif.) and Parke-Davis (Mich.).

Three senior residents completed surgical pathology fellowships. Six additional house officers completed fellowship training in cytopathology, urologic pathology, and hematopathology. All found excellent positions in sub-specialty fellowships (3), private practice (2), and academic faculty positions (2).

Overall, the in-house clinical activity in surgical pathology and cytolopathology increased by approximately 5%. The dermatopathology service realized an 8% increase in cases. Additional space in support of the cytopathology service was identified and renovated. Plans for renovation of space in medical science building 1 are underway for expansion of the dermatopathology service. Currently we are actively recruiting to three open positions in cytopathology, head and neck surgical pathology and dermatopathology.

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 2002 - 30 JUNE 2003

I. Timely Completion of Autopsy Reports:

The autopsy service continues to emphasize timely completion all our autopsy reports. This has required active management of the autopsy late list and individually contacting both house officers and faculty when their cases are older than 30 days. Additionally, with the new incoming house officers we have made a strong statement that autopsies should be completed within 30 days. The table below lists the autopsy completion time for different years.

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
2002-2003	88	96	302

II. 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 2002-03 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.

	# of deaths	# of cases	% of deaths
Medicine	475	92	19%
Surgery	256	39	15%
Pediatrics	100	41	41%
Other services	36	4	4%
Total Hospital	***883***	***171***	***19%***

Hospital total 19%

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 new, monthly conference has been initiated in the Department of Internal Medicine where 4 autopsies are 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. This conferences run primarily by the first year pathology residents who have completed their autopsies. At the request of the Department of Emergency Medicine, we also making presentations twice a year to their house officers.

IV Medical Examiner Cases:

The Department of Pathology continues to have a presence in Medical Examiner issues in the State of Michigan and Washtenaw County. However, the Department of Pathology no longer provides medical examiner investigators to be on call for the Washtenaw County Medical Examiners office. The Medical Examiners office now provides staffing for investigators to be on call to investigate medical examiner deaths which arise at the University of Michigan. This has resulted in a cost-saving to the department since we are no longer providing on call pay.

VI Statistics:

This covers the time period July 1, 2002 to June 30, 2003.

Total number of autopsies performed	304
Hospital autopsies	255 (includes 74 brain only)
Medical examiner autopsies	49

Daniel G. Remick, M.D.
Director, Autopsy Service

CYTOPATHOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 2002 – 30 JUNE 2003

Total gynecologic specimens for the year were 50,828; a 5.4% increase from last year. Non-gynecologic specimens numbered 6,595; a 4.9% increase from last year. Fine needle aspirations totaled 1,528 for the current year. The laboratory continued to achieve the turnaround time for non-gynecologic specimens within 24-48 hours, and the turnaround time for the Papanicolaou smears have been stable at the current 5-7 working days.

Effective November 2002, the laboratory screening area was moved to the newly assigned space in the North Ingalls Building. Two of the cytotechs continue to rotate on a weekly basis through the hospital to provide non-gynecologic screening, overseeing the laboratory prep area, and back-up for the fine needle aspiration. A new cytotechnologist will join us in September of 2003. This position became available when Susan Clozza and Jenise Falan converted to part-time positions in June of 2003.

The T3000 processor (multislide processor) for the ThinPrep was installed in July 2002, and implementation of ThinPrep throughout the hospital system was initiated on a rolling system. At this time, we are approximately 90% converted to ThinPrep in gynecologic specimens. A third prep tech was recruited to support the ThinPrep conversion in the laboratory.

Our fellowship program continued to be highly successful. Dr. Wei Liu completed his training with distinction. Unfortunately, Dr. Theoharis, for personal reasons, had to interrupt his training for a leave of absence. Dr. Robert Pu was successfully recruited to join our faculty in cytopathology effective in September of 2003.

The Cytopathology Section had excellent representation at national and international meetings with several workshops and posters presented by the cytology faculty and residents.

Claire W. Michael, M.D.
Director, Cytopathology Laboratory

DERMATOPATHOLOGY SERVICE

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 – 30 JUNE 2003

The Dermatopathology Service receives diagnostic case material from six different sources: (1) UMMC (ID) cases; (2) outside contractual (MD) cases; (3) personal consultation cases (DP); (4) outside slides reviewed for referred patients (TD) cases; (5) miscellaneous intramural referrals (IE, IF, IS, MU) cases; (6) and informal consultations (intramural and VAH).

CLINICAL SERVICE

The clinical service volume has continued to increase and is as follows:

	2000-2001	2001-2002	2002-2003
ID	6,947	7,205	6,811
MD	6,381	7,248	9,663
TD	1,486	1,691	1,698
DP	876	1,244	1,336
MISC	87	126	145
TOTAL	15,777	17,514	19,653

Once again, the Dermatopathology Service has seen a significant increase in volume. The total number of cases for 2002-2003 was 19,653 which is a 12% increase when compared to the previous year. Our M-Labs (MD) case volume had the most gowth with a 33% increase compared to the previous year and, in fact, represents 64% of total M-Labs accessions. The clinical service load seen by each faculty member of the Dermatopathology Service, Dr. Su, Dr. Fullen, and Dr. Lowe, is substantial and exceeds any other surgical pathologist in the Department.

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 on Dermatopathology. Importantly, there is a 25% significant change in diagnosis for all patients referred to the MDMC after review by our service.

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

We continue to be highly productive in scholarly activities and academic pursuits. During this academic year (2002-2003), we have individually and/or collectively published 24 manuscripts (including in press) 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 2003-2004

Our primary goals for the next academic year are the recruitment of an additional faculty member and the establishment of a Dermatopathology Fellowship, while maintaining excellence in clinical service, education and academic pursuits.

Lori Lowe, M.D.
Director
Dermatopathology Service

NEUROPATHOLOGY SERVICE

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 2002– 30 JUNE 2003

Dr. Mila Blaivas, Ms. Constance J. D'Amato, Dr. Andrew 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. = 135)
2. The Diagnostic Unit of the Neuropathology Core Laboratory of the MADRC processed 74 dementia brain cases. Of these 74 brains, 63 were MADRC cases, 6 were neurology hospital patients, and 5 were from the Michigan Dementia Postmortem Network Program.
3. There were 434 muscle biopsies, 40% with electron microscopy. There were 110 peripheral nerve biopsies. There were 17-teased fiber preparations and 100 with electron microscopy. 18 skin or non-muscle/nerve tissue examined with electron microscopy. 23 muscle biopsies were examined with 10-14 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 eight weeks Neuroscience Sequence for our second year medical school curriculum. There were fourteen hours of neuropathology taught: six hours of lecture and eight hours in the laboratory.
2. Dental Students: 4 lectures.
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; Neuropathology 858, an 8-hour laboratory course; 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 clinico-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. Blaivas is working on the histology of animal models and human application in genetic treatment of rheumatoid arthritis with the Arthritis and Rheumatology Section with Blake Roessler; Neurology, Neuro-oncology, Genetics, Gynecology, and Pulmonary/Internal medicine on various projects.
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. He is finishing publications from a NIH funded project studying the prognostic potential of MIB-1 proliferation marker on brain tumors. He was the study pathologist for a multi-institutional study of treatments of low-grade astrocytoma for the Children's Cancer Group.
4. Dr. Lieberman's laboratory studies the mechanisms of neurodegeneration in Kennedy's disease, a disorder affecting motor neurons of the brain stem and spinal cord. He is using cell culture and animal models to determine how the causative mutation leads 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, NERVE AND MUSCLE DIAGNOSTIC STUDIES, IMMUNOFLUORESCENCE, AND IN SITU HYBRIDIZATION)

DEPARTMENT OF PATHOLOGY
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INTRODUCTION

Immunoperoxidase (IPOX) staining has continued to increase, and our antibody menu has been significantly expanded with the addition of 20 new antibodies in the past year. The muscle immunohistochemical panel continues to expand with new antibodies for the diagnosis of muscular dystrophies and now contains 15 antibodies. Demand for muscle histochemical staining continues steady, and the laboratory has continued to take on new muscle clients. Immunofluorescence remains busy with a large increase for the skin and heart specimens and a small increase in renal biopsies. In situ hybridization has become more important as a routine procedure in the clinical diagnosis of HPV and EBER.

CLINICAL IMMUNOHISTOCHEMISTRY

Year-end figures show that the average number of slides stained per day has increased from 131 slides/day to 151.5 slides/day representing a 15% increase over last year. Fifteen new antibodies have been added to the menu of antibody stains including Caldesmon, CD3 (new one), Melanoma cocktail, CD138, HHV8, NGFR, EGFR, CK 5/6, E Cadherin, Emerin, Laminin, Lamin A/C and a new breast panel for Chromavision. The Chromavision procedure requires special reagents, procedures and the Benchmark autostainer to accurately stain ER, PR and Her2-neu for quantitative analysis. Additionally, there are 5 new antibodies in development including WT1, Bob-1, Oct-2, P16-IK4a, and FLI-1.

To improve our services, we have been actively seeking written feedback from the clinical faculty on the quality and efficiency of the IPOX services. After a two-week introduction, during which all IPOX cases were accompanied by a new Quality Control worksheet, all of the main diagnostic areas have been stocked with worksheets for reporting problems. Direct meetings with the Hematopathology faculty, major users of the IPOX service, have identified new needs and areas for service improvement. As in the past, we have continued to score 100% on the biannual Immunohistochemistry CAP testing.

With the loss of one FTE in August 2000 and the ever-increasing workload, efficiency continues to be a top priority. The continuing demand for addition and workup of new antibodies, the increased utilization of laboratory services, and the institution of new special procedures like Chromavision will necessitate recruitment of additional laboratory staff in the coming year.

NERVE AND MUSCLE DIAGNOSTIC STUDIES

Under the direction of Dr. Blaivas this service has continued to develop new diagnostic tools this year. A panel of 15 frozen section antibodies is used routinely for the diagnosis of muscular dystrophies. The

caseload for this service has remained steady (364 muscles last year compared to 352 this year). The new dystrophy panel is often used on the same cases as the routine histochemistry panel, which can mean 35-40 stains will be performed on many cases. This has helped the lab to remain on the cutting edge of diagnosis of nerve and muscular disease.

IMMUNOFLUORESCENCE

Under the direction of Drs. Killen, Johnson and Gordon this laboratory continues to stain skin, heart and renal biopsies using the automated Ventana ES immunostainer. The caseload has increased steadily in all areas. There were 458 renal biopsies and 319 skin and heart biopsies. This represents an 8% increase in renal biopsies and a 66% increase in skin and heart biopsies. This dramatic increase has made it much harder for laboratory staff to perform immunofluorescence and simultaneously back up the IPOX technologist with their daily workload.

IN SITU HYBRIDIZATION

In situ hybridization is becoming a routine part of diagnosis for both HPV and EBER. The number of cases increased dramatically over the last year and the Ventana Benchmark stainer is run most days of the week for these tests. In all likelihood we will continue to see more tests using this technology in the near future.

CONCLUSION

The clinical load in all services continues to increase in the year 2003. Our future goals include continuing quality improvement and increased efficiency.

CLINICAL PATHOLOGY

DIVISION OF CLINICAL PATHOLOGY

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The Clinical Laboratories have continued to provide excellent, full-spectrum service (more than 820 different laboratory analyses) as the UMHS has expanded both its volume and scope in ambulatory care activities and experienced growth in several major clinical programs. Substantial effort has been directed towards aggressive laboratory utilization control, the improvement of test ordering, laboratory logistics, achievement of compliance with HCFA-mandated rules on documentation of test-ordering indications, and achievement of compliance with federal rules related to FDA approval of testing methods. Superimposed upon these efforts has been further development of computer links with M-Labs clients. In 2002-03 the Clinical Laboratories again performed more than 3 million billable analyses (10 million individual measurements), supported a wide array of clinical and research programs, and added or replaced more than 30 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 onsight in May, 2003. 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 initiative was achievement of a more aggressive utilization management program. More than $920,000 in direct laboratory cost avoidance and test utilization control was realized in 2002-03. This was made possible through educational meetings with each clinical department chairman, a series of extra-departmental educational presentations, publication of on-line (CareWeb) cost data, and, most effectively, direct utilization control policies and interventions.

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. These shifts have substantially increased our focus to informatics, logistics, and cost-containment.

Faculty and laboratory staff participated in a wide variety of intramural and extramural educational programs during 2002-03. For instance, the AIMCL (informatics) course was again well attended, making it among 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 revised clinical pathology residency training format (July, 1993), which organizes pathology residents into teams that rotate through three blocks of clinical laboratories that are grouped according to "relatedness of discipline", was again updated in 2002-03. In keeping with a thematic approach, the 2002-03 version

solidified the four rotation blocks and places greater emphasis on molecular diagnostics, coagulation, informatics, statistics, and management. 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 Department added a second slot in the Hematopathology Fellowship program and added a Blood Bank/Transfusion Medicine fellow.

The academic achievements of faculty members within the Clinical Pathology Division have been outstanding. As a group, the CP faculty had approximately 100 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. 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

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PATIENT CARE:

Blood component utilization decreased relative to the previous year by 3% overall with approximately 97,700 total components dispensed. Red Blood Cell utilization approximated 32,000 units with the majority being used in surgery. Platelet Concentrate utilization was approximately 47,600, continuing a decline in usage. Lower blood utilization occurred despite an increased clinical activity in high blood usage areas. This reflects the successful efforts of the medical staff to control costs.

Hematopoietic progenitor cell processing activity was comparable to the previous year with 419 total units processed. Most patients are continuing to reach the collection target in one procedure.

The transfusion and apheresis activity was also similar to the previous year with 1683 patient encounters. The proportion of progenitor cell collections and therapeutic apheresis procedures has remained steady. There continues to be significant activity in the areas of vascular heart transplant rejection, post-transplant recurrence of focal segmental glomerulosclerosis, and cryoglobulinemia. We successfully implemented low density lipoprotein apheresis for the treatment of refractory hypercholesterolemia.

Prestorage leukocyte-reduced Red Blood Cells and Platelet Concentrates were used almost exclusively.

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 30th annual postgraduate course, "Current Topics in Blood Banking", was held on June 5-7, 2002. 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, and was the first to be presented by a medical center rather than by a national blood program. 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. Ms. 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. Ms 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. Dr. Davenport served the American Association of Blood Banks on the Scientific Section Coordinating Committee, the Editorial Board of TRANSFUSION, and the Annual Meeting Program Planning Committee. Ms. Butch and Ms. Stoe served as Assessors for the American Association of Blood Banks. Ms. Stoe served on the Executive Board 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

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The past year was once again marked by an increase in laboratory workload. The Chemistry Section experienced an approximate 3 % increase in overall test volume this year. Included in this was a 5% increase in the more manual testing areas of Special Chemistry, Immunology, and Ligand Assay. This workload was absorbed without the addition of incremental personnel.

The Chemistry Section continued its efforts toward increasing levels of laboratory automation this past year. The section began the process of evaluating new high volume chemistry and immunoassay analyzers that would allow for further consolidation of workstations in the laboratory and achieve savings on reagent pricing. The goal is to acquire and implement new systems by late 2004. Considerable time and effort was spent on visits to view different analyzers in operation and gather performance data.

The laboratory evaluated and acquired a DPC Immulite 2000 chemiluminescent immunoassay analyzer for the special chemistry/RIA area. Multiple tests were moved to this automated, random access platform over the course of the year. These included Insulin, C-peptide, Growth hormone, DHEAS, Erythropoietin, Vitamin B12, Folic acid, and the components of the triple screen (AFP, hCG, unconjugated estriol).

Several assays were moved to other more automated platforms. Hepatitis C antibody testing was moved to a chemiluminescent immunoassay format on the Vitros ECi analyzer. This improved sensitivity assay allowed the lab to implement further reductions in the number of positive samples that required further confirmation by the RIBA assay, thus resulting in a considerable cost savings for the laboratory. Additional assays for Hepatitis B surface antigen and antibody were also moved to the Vitros ECi. An assay for BNP, a marker of congestive heart failure, was evaluated and implemented by the lab.

In the toxicology area, an HPLC-mass spectrometer system was acquired, installed, and development work begun on assays for the immunosuppressant drugs Sirolimus and Tacrolimus. A new atomic absorption analyzer for analysis of blood levels of lead, aluminum, copper, and zinc was acquired.

The Chemistry Laboratory continued its active 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 increased in scope and volume. The lab placed new Hemochron Signature Jr coagulation meters in the OR of University Hospital for PT and aPTT testing in its continued efforts to provide OR personnel with testing information that can result in reduced blood product utilization.

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 90 whole blood glucose meters stationed throughout the institution. Lab staff

worked with nursing personnel to complete the switch to AccuChek Inform glucose meters for all bedside testing. Results from these meters are now downloaded directly to a server in Pathology, and patient glucose results passed directly to the laboratory information system.

The laboratory staff contributed a significant amount of time and effort during the past year to the evaluation of new laboratory information system software for the department. Finally, credit should be given to all laboratory personnel who help with preparation for the CAP accreditation inspection. No major deficiencies were found in the Chemistry Section during the inspection.

Donald Giacherio, Ph.D.

CLINICAL CYTOGENETICS LABORATORY

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OVERVIEW

The laboratory had a 10.3% increase in the number of tests performed this year (N=2818) compared to last fiscal year, with a total of 2542 cytogenetics and 276 FISH studies performed (+9% and +19% 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. was hired to serve as Assistant Director and arrived in September 2002. Two full-time technologists were hired following two departures.

CLINICAL SERVICES

The number of samples sent for cytogenetics for constitutional studies increased, as did those sent due to malignancy. Constitutional blood samples were virtually unchanged (N= -5, -0.8%) while amniocentesis samples decreased (N= -18, -4.%); however, chorionic villus samples and tissues increased (N= +30, +38% and +34, +41%, respectively). The tissue culture service for fibroblasts to send out for biochemical studies increased substantially (N=+20, +87%).

For neoplasias, the number of bone marrows and solid tumors increased significantly (N=+119, +10.6%, and +30, +94%, respectively). In addition to covering these gains, we stopped sending bone marrow samples to Penrose St. Francis Hospital by the end of September 2002, so the technologists have had an especially busy year. Most of the gains in the bone marrow samples appears to be due to increased in-house activity, since the percentage of bone marrow samples sent through MLabs has remained between 12-15% of the volume since fall of 2001. The increasing value of cytogenetics studies for diagnosis of small round blue cell tumors and sarcomas is reflected in the gains seen for the labor-intensive solid tumor analysis.

Even greater growth was experienced for samples sent for FISH tests. Although the constitutional testing volume dropped (N= -21, -12.6%) the number sent for oncology tests more than offset that loss (N= +74, +132%). The increase in oncology FISH testing was due to the increasing use of BCR/ABL FISH to monitor the remission status of patients with CML treated with Gleevec (N= +46, +288%). These types of tests are more complex and thus more time-consuming than typical constitutional studies. A different constitutional test, Subtelomeric FISH, was implemented and a few clinical samples have been submitted recently for testing.

EDUCATION

A total of thirteen residents and fellows from several departments came to the laboratory for rotations. Six Pathology residents and three Hematopathology fellows, two fellows from Pediatric Genetics, and two fellows from Hematology/Oncology rotated through the laboratory. The Pathology and Genetics 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. In October Dr. Lisa Smith assumed responsibility for most of the teaching and direction of these rotations; without her considerable efforts we would not have been able to support this number.

FUTURE PLANS

As a consequence of the increased demand for both standard cytogenetics and FISH testing, we will need additional technological support, and efforts to hire an additional technologist are underway. However, additional laboratory or office space will be required if any further increase in volume is desired.

Diane Roulston, Ph.D.
Clinical Assistant Professor
Director, Clinical Cytogenetics

COMBINED HEMATOLOGY LABORATORY
(HEMATOLOGY, BONE MARROW, FLOW CYTOMETRY, COAGULATION)

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I. LABORATORY OPERATIONS

The combined hematopathology laboratories again continued to move forward with new initiatives despite facing increasing volumes and suboptimal staffing. The laboratories operated for most of the year with at least one open position, and with several long-term absences, without the benefit of incremental staff increases.

The laboratory passed its biennial on-site accreditation inspection by the College of American Pathologists with no deficiencies.

In response to employee concerns, the laboratories drafted a vision statement with a list of expectations that applies to all employees at all levels in the laboratories. Copies of the statement were distributed to all staff. In addition, an ongoing series of employee forum meetings was initiated. In these forums, employees' ideas are catalogued, with documentation made of specific actions taken in response to each idea, and a record of the acceptance or rejection of the idea. The forums were designed to increase employee participation and accountability in the decision-making process and operation of the laboratory.

Finally, regular focus meetings were established for each of the laboratory sections (hematology, bone marrow, flow cytometry, and coagulation). The focus meetings were designed to assure continued progress in addressing operations, programs, problems, and long range planning in each laboratory section.

Section specific reports are as follows:

A. COAGULATION LABORATORY

Three major accomplishments in the coagulation laboratory this year included the automation of an anti-IIa inhibitor assay, implementation of autoverification for prothrombin time (PT) and activated partial thromboplastin time (aPTT) orders, and updating of platelet aggregation and secretion assays.

The anti-IIa assay is used for the therapeutic monitoring of new classes of direct thrombin inhibitors currently in clinical use (argatroban and hirudin). This new assay has considerable advantages over the aPTT in monitoring these drugs, and replaces the manually-performed ecarin clotting time. This implementation has allowed the laboratory to expand this testing to 7-day-a-week availability, while markedly reducing the cost and labor-intensity of each test.

Autoverification of PT and aPTT tests began in the summer of 2003, with an immediate and positive impact on productivity in the laboratory. Analytical turnaround time for PTs and aPTTs were reduced by 66% with an approximate autoverification rate of 85%, and the new system allows for technologists to pay greater attention to manual tasks in the laboratory.

Last, the laboratory has updated its platelet function testing. In addition to validating it normal values for ADP-, epinephrine-, and collagen-induced platelet aggregation and secretion, the laboratory has added arachidonic acid- and gamma thrombin-induced platelet aggregation and secretion. These studies increase our array of examinations being performed on an individual platelet sample. Further, normal values have been obtained and we are prospectively getting values on patients with platelet function disorders to determine if the Dade-Berhing instrument PFA (Platelet Functional Analyzer) can be useful in the clinical arena.

Additional progress is also being made in the application of the advanced D-dimer assay, which was first offered last year. A validation trial is currently underway, with the cooperation of the department of surgery, for the establishment of discriminatory values for the prediction of deep venous thrombosis (DVT) and, presumably, pulmonary embolism.

B. HEMATOLOGY AND BONE MARROW LABORATORIES

Hematology and Bone Marrow Laboratories. As part of the continuing effort toward optimizing our approach to automated vs. manual hematology testing, a new set of criteria were established, based on quantitative thresholds, for technologists' interpretations of red blood cell abnormalities in peripheral blood smears. This approach is the first step in what we hope will be a more comprehensive, evidence-based overhaul of our policies regarding red cell morphology interpretation and reporting.

The "blood survey" test was streamlined to include a single panel that includes all tests commonly considered part of the "CBC" (including hemoglobin, hematocrit, RBC count, MCV, MCH, MCHC, platelet count, and MPV). In other words, all CBCs now include platelet counts as part of the order. This change was made in response to new panel definitions and charge codes as mandated by the federal Center for Medicare and Medicaid Services (CMS), and for the general optimization of our lab testing menu. We also made several other changes to our testing menu, mainly consisting of the deletion of tests that have become obsolete (such as urine hemosiderin), for which direct physician ordering was not appropriate (such as enzyme cytochemical staining of bone marrow smears) or for which reagents are no longer routinely available (such as the PK deficiency screen and GSSR assay).

The hematology laboratory successfully evaluated two new hematology analyzers (the Coulter LH755 and the Sysmex XE2100) with the goal of choosing one of those platforms to replace our current Coulter GenS analyzers some time in fiscal 2004.

C. FLOW CYTOMETRY LABORATORY

Attending staff continues to triage all requests for leukemia/lymphoma immunophenotyping, with cancellation of unwarranted requests. Of the 2554 specimens submitted for leukemia/lymphoma immunophenotyping, pathologist review lead to cancellation of 856 (34%) of these requests. Leukemia and lymphoma profiles are the most labor-intensive tests offered by the laboratory, and test volumes continue to grow.

Laboratory initiatives begun during the past year include: a program of regular CME sessions for technologists and faculty; a new communication/trouble-shooting log to help rotating technologists keep up with changes and procedures; addition of daily controls for stem cell and immunodeficiency assays per new CAP guidelines; validation study for CD34 stem cell assay in conformity with ISHAGE guidelines; participation in thorough on-site demonstration and "hands-on" evaluation of new instruments from two major vendors, in preparation for new instrument acquisition in the coming year.

II. LABORATORY GROWTH

A. COAGULATION LABORATORY

Coagulation laboratory. The laboratory performed 212,181 assays for PT, aPTT, fibrinogen, and advanced D-dimer, overall representing a 5% volume increase over FY 2002. Special coagulation testing increased by 9% to 12,903 tests performed.

B. HEMATOLOGY AND BONE MARROW LABORATORIES

Hematology and Bone Marrow Laboratories. Blood Survey (CBC) orders increased by 5% over FY 2002, to 365,068, and erythrocyte sedimentation rate orders increased by 13% to 20,309. Body fluid analysis increased by 4% to 6,531. As a result of our concerted effort last year to optimize the application of automated and manual differential leukocyte counts, the number of manual differential counts performed last year decreased by 48% to 11,805. Urinalysis orders also decreased by about 4%, to 50,664. The bone marrow lab continued to experience a relentless increase in volume with a 12% increase in bone marrow aspirates (to 1,619) and a 13% increase in bone marrow biopsies (to 1,691).

C. FLOW CYTOMETRY LABORATORY

Flow Cytometry Laboratory. Immunodeficiency monitoring studies and CD34 stem cell counts each experienced volume decreases in FY 2003 (3% and 11% decreases, respectively). However, leukemia/lymphoma immunophenotyping (the most labor intensive testing performed in the laboratory) continued to increase. Chronic leukemia/lymphoma phenotyping panels increased by 3%, and acute leukemia/lymphoma phenotyping panels increased by 2%.

M-Labs referrals continue to compromise a substantial part of the work volume, including 29% of all acute leukemia immunophenotyping panels, 49% of all chronic leukemia/lymphoma panels, and 28% of all immunodeficiency monitoring.

III. RESEARCH AND TEACHING ACTIVITIES

The hematopathology group continues to be academically productive. Despite increasing clinical service loads, members of our group published numerous papers in peer-reviewed scientific journals, and we continue to be active regionally, nationally, and internationally in hematopathology through invited lectures, participation in educational courses and workshops, and editorial activities with several hematology, hemostasis, flow cytometry, and pathology journals. Members of our group are also involved nationally in setting and maintaining standards for hematopathology practice through involvement in oversight bodies such as the American Society of Clinical Pathology CheckPath planning committee and expert panel in hematopathology, the College of American Pathologists hematology and clinical microscopy resource committee, and the executive committees of the Society for Hematopathology and the North American Specialized Coagulation Laboratory Association (NASCOLA).

We currently maintain two ACGME-accredited hematopathology fellowship positions. Our group is quite active in the teaching of pathology residents, including participation in formal rotations and several lectures in the Clinical Pathology Grand Rounds series. We are also quite active in teaching first and second-year medical students through involvement in first year histopathology and host-defense sequences, the second year hematology sequences (directed by Dr. Schmaier and co-directed by Dr. Stoolman) and the general pathology sequence for second year dental students (directed by Dr. Stoolman). Dr. Stoolman has also been involved in the Dean's initiative to redesign the preclinical medical school curriculum, and the newly designed system will begin this year for first year students and next year for second year students.

We continue our affiliation with the medical technology program at Ferris State University and Eastern Michigan University. To date this new affiliation has been quite successful. We have received excellent feedback from the students rotating through the laboratories, and this program continues to enhance our recruiting efforts during a time of continued critical shortage of medical technologists.

The hematology laboratory took part in a multi-institutional validation of the Coulter LH755 hematology analyzer for the automated performance of body fluid cell counts, and the results of this trial have been submitted for publication.

IV. FUTURE GOALS FOR THE COMBINED HEMATOPATHOLOGY LABORATORIES

We are hoping that FY 2004 will bring significant progress in our ability to perform high throughput analysis of our ever-increasing sample volume. We will initiate efforts to replace our flow cytometers with new instruments, including an automated sample preparation system. We also plan to purchase new automated hematology analyzers for the main hospital and Cancer Center laboratories, with the hope of integrating up-front automation as part of this acquisition. We will continue to refine our testing menus to optimally meet clinical demands and the needs of our patients.

William G. Finn, M.D.
Director, Hematopathology

Bertram Schnitzer, M.D.
Director, Hematopathology Fellowship Program

Charles W. Ross, M.D.
Director, Flow Cytometry

Lloyd M. Stoolman, M.D.
Co-Director, Flow Cytometry

Alvin Schmaier, M.D.
Director, Coagulation Laboratory

HISTOCOMPATIBILITY AND IMMUNOGENETICS LABORATORY
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CLINICAL ACTIVITIES:

The clinical activity as well as the overall case complexity in the Histocompatibility Laboratory continued to increase in FY 2002 due to robust and expanding clinical solid organ and bone marrow transplant programs (making the Laboratory one of the ten busiest in the United States).

DNA-based typing remains the primary technique used for the determination of HLA class I and class II alleles. This year the laboratory evaluated, validated, and received ASHI accreditation for the use of the microsphere technology based Luminex instrument to perform high-throughput mid-resolution typing at a substantial cost savings over previously used methods. The extent of HLA Class I and Class II antibody screening continues to increase as does the number of recipient/donor crossmatches performed annually. The degree of pre-sensitization in our patient population (due to prior failed grafts or blood product transfusions) adds significant complexity to the performance and interpretation of the laboratory test results. The Laboratory remains in the process of validating flow cytometry technology for HLA Class I and Class II antibody screening. Dr. Riccardo Valdez increasingly devoted a portion of his professional effort in the area of histocompatibility and immunogenetics in FY 2002 holding bi-weekly meetings with the laboratory supervisor, monthly meetings with Dr. James Baker, and attending educational and business meetings sponsored by the local organ procurement organization (Gift of Life Michigan). Dr. Valdez is working toward ASHI certification as a laboratory director.

TEACHING ACTIVITIES AND RESEARCH:

Ms. Cynthia Schall, the Laboratory Supervisor, and other members of the Laboratory were engaged in the teaching activities of the Laboratory, and they were effective in their work. Laboratory personnel provided instruction in the principles and techniques of histocompatibility testing for pathology house officers, allergy fellows, renal fellows, hematology/oncology fellows, and postdoctoral candidates from the Department of Hematology. Cynthia Schall oversaw the teaching activities for residents in the Laboratory and performed several in-service lectures for the support staff in the transplant programs. Dr. Valdez initiated a monthly journal club/literature review for the Laboratory staff and residents. Dr. Baker has continued to play an active role in ASHI. The Laboratory, in conjunction with the Renal Transplant Program, is preparing for involvement in a multicenter clinical trial assessing the effect of pre-transplant intravenous immunoglobulin administration on panel reactive antibodies (PRA) in pre-sensitized patients.

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) implementation of electronic records for tissue typing results and antibody screening test interpretations so that they can be displayed in CareWeb for viewing by the appropriate clinical staff, 2) continue to streamline laboratory procedures and testing algorithms to maximize laboratory efficiency, 3) expand the resident educational experience in tissue typing to include exposure of the residents to renal and heart transplant biopsies. Dr. Valdez will continue to develop expertise in tissue typing with special emphasis on studying the role of flow cytometry in pre-transplant evaluations and pursuing research projects in the Laboratory.

Jeffrey S. Warren, M.D.
Director, Division of Clinical Pathology

Riccardo Valdez, M.D.
Clinical Assistant Professor

CLINICAL IMMUNOPATHOLOGY LABORATORY

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I. OVERVIEW:

The Immunopathology Laboratory performed more than 65,000 analyses in 2001-02. John Lowe, M.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 coverage of anti-neutrophil cytoplasmic antibody (ANCA) and anti-GBM studies.

II. CLINICAL SERVICES:

Integration of clinical immunopathology testing into the Chemistry Section continued to progress. New procedures were implemented in the protein electrophoresis area, in the analysis of antibodies to extractable unclear 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 from Eastern Michigan University 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

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Duane Newton, Ph.D., joined the Pathology faculty on July 1, 2002, as a Clinical Assistant Professor of Pathology and Associate Director of the Clinical Microbiology/Virology Laboratory. Dr. Newton previous held the position of Director of the Virology and Immunology Laboratories at the Michigan Dept. of Community Health.

I. CLINICAL ACTIVITIES:

The Laboratory continued to experience significant increases in test volume with an 8% increase compared to that of FY 2002. Increased requests for blood culture, shiga-like toxin, antibiotic susceptibility, HPV genotyping, viral respiratory antigen screens and CMV serologies topped the list. Nucleic acid amplifications test for HBV and proviral HIV DNA were added to the test menu along with EIA procedures for two markers for celiac disease, gliadin and transglutaminase antibodies. Much effort was expended on responding to requests for West Nile Virus and Severe Acute Respiratory Syndrome (SARS) testing. Several technologists received certification for shipping biological hazardous materials. Much effort also went toward the Millennium computer upgrade project before it was discontinued. The supervisory staff was successful in hiring several new medical technologists to fill open positions. The Laboratory successfully passed its annual CAP Accreditation Inspection with flying colors!

II. RESEARCH ACTIVITIES:

- Much effort is going toward the use of nucleic acid amplification methods to either substitute for or augment traditional testing methods. New instrumentation has been received or is currently on order to increase efficiency in specimen preparation and test turn-around time, e.g., "real-time" PCR.
- 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. Clinical evaluation of the system is expected to begin late 2003.
- Procedures for determining yeast susceptibility to antifungal agents is underway.
- An evaluation of the Swab Extraction Tube System was completed and the data presented at a national meeting.
- The Laboratory cooperated with the Michigan Dept. of Community Health to compare EIA and molecular testing methods for the detection of Shiga toxin-producing isolates of E. coli. The data was presented at national meeting.
- The Laboratory responded to numerous IRB-approved requests from clinical services for specific laboratory data to fulfill research goals.

I. 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.

II. 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 14 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.

III. GOALS FOR FY 2004

1. Develop methods and procedures 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, e.g., EBV and enteroviruses.
3. Evaluate nucleic acid extraction and real-time amplification instruments to support the activities in item 2.
4. Initiate in-house yeast susceptibility testing.
5. Compete the first phase of the clinical 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.

Carl L. Pierson, Ph.D., Director
Duane Newton, Ph.D. Associate Director

Clinical Microbiology/Virology Laboratory

MOLECULAR DIAGNOSTICS LABORATORY

DEPARTMENT OF PATHOLOGY
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1 JULY 2002 - 30 JUNE 2003

OVERVIEW

The Laboratory had a 36% increase in volume during the year. Anthony Killeen, M.D., Ph.D., was succeeded by John Thorson, M.D., Ph.D., as Director of the Laboratory. The Laboratory acquired additional analytical equipment and has several new assays undergoing validation.

CLINICAL SERVICES

The Laboratory currently employs one full time supervisor, four full time technologists, and two part time technologists. All staff members are cross-trained in all areas of the laboratory.

In August 2002, Dr. Anthony Killeen departed as Director of the Laboratory. Jeffrey Warren, M.D., served as Interim Director until June 2003, at which time Dr. John Thorson assumed the role of Director. Charles Ross, M.D., and William Finn, M.D. both participated actively in the work-up and result interpretation of cases in molecular hematology.

The Laboratory saw an increase in annual volume to approximately 7,000 tests during the 2002-3 academic year. The growth in test volume was mostly accounted for by the addition of the Cystic Fibrosis assay. In addition there were significant increases in the number of requests for genetic tests of inherited thrombophilia risks.

During the past year, turn around times increased to an overall average of 5 - 6 business days. This was in part due to a decreased frequency in the number of times final reports were signed out each week and in part due to workload increases. Although extended relative to the previous reporting period, this is still within the published range and overall levels of service were not adversely affected.

In May 2003, the Laboratory underwent a successful accreditation inspection by the College of American Pathologists. No deficiencies were cited.

An increasing number of requests for cystic fibrosis mutation screening combined with recurrent reagent supply problems have prompted the decision to migrate this assay from the current Roche reverse hybridization platform to the Invader platform. This will result in a significant decrease in the turnaround time for approximately 90% of all patient samples submitted for this assay.

During the past academic year, the Laboratory acquired an ABI 310 Genetic Analyzer. This single capillary electrophoresis instrument will be used primarily for low volume applications such as B-and T-cell receptor gene rearrangement assays and occasional sequencing assays.

The Laboratory also acquired a MagnaPure LC automated nucleic acid extraction instrument. This instrument will greatly facilitate sample preparation, particularly for high volume assays such as cystic fibrosis screening, Factor V Leiden, and Prothrombin 20210 mutation analyses. Validation of this instrument is nearly complete and it is anticipated that it will be put into routine use early in the next academic year.

In order to service the anticipated future demand for assays performed on fixed, embedded tissue specimens, the Laboratory has recently acquired a microtome from the Histology Laboratory. This will allow the Laboratory to obtain appropriate specimen samples from tissue blocks for molecular diagnostics assays while ensuring the proper precautions to prevent carry-over of even minute amounts of tissue between specimens. Training in the use of this instrument and the validation of its use in clinical assays is currently underway.

EDUCATION

With the departure of the former Director in August 2002, the educational activities of the Laboratory were somewhat diminished for the 2002-2003 academic year. It is anticipated that the involvement of the laboratory in the education of Pathology residents, Medical Technology students, and others will return to a more normal level with the arrival of the new Director.

FUTURE PLANS

Planning for expansion of the Molecular Diagnostics Laboratory's clinical and research activities are currently underway. A top priority for the next academic year is the acquisition of instrumentation to perform real time PCR analyses. This will allow the Laboratory to perform quantitative assays for a number of diagnostically significant gene transcripts, including BCR/ABL, PML/RAR□, and BCL-1. In addition, this equipment will reduce the turn-around time associated with a number of currently performed assays, such as HFE and MTHFR mutation analyses.

Validation of PCR-based assays for B- and T-cell receptor gene rearrangements are nearly complete and these assays will be available on a clinical basis within the year. These assays will utilize the ABI 310 capillary electrophoresis instrument for analysis of results and their availability will eliminate a significant number of send out tests. Related to this, a procedure for the extraction of DNA from formalin fixed tissue is currently being validated and will allow these assays to be performed on fixed tissue blocks as well as fresh tissue specimens.

The acquisition of a high throughput capillary electrophoresis sequencing instrument is anticipated within the next year. This instrument will allow an expanded number of markers to be used for bone marrow engraftment analyses, thus eliminating the need to send a significant number of these assays to a reference laboratory. The use of this technology will also reduce the turn-around time for these assays and provide a true quantitative assessment of residual recipient cellularity. This instrument will also find use in a number of genotyping assays proposed as future additions to the Laboratory's menu.

Discussions with members of the Surgical Pathology faculty have identified a number of molecular-based assays which would be of value in the diagnosis of a variety of soft tumors, such as synovial sarcomas, Ewing's sarcoma, and rhabdomyosarcoma. For this purpose, reverse transcription real time PCR assays for the detection of chimeric transcripts will be developed. These assays will also require the isolation of RNA from fixed tissue. Planning and validation of these procedures is currently underway.

Finally, an expected future direction for the Laboratory is in the area of pharmacogenomics. A number of potential collaborative interactions have been identified with members of the University of Michigan Comprehensive Cancer Center for the development of both clinical and research based assays in this area. This would require the Laboratory to perform a number of high throughput genotyping assays, utilizing a mini-sequencing technology employing fluorescence polarization detection. Acquisition of instrumentation for this purpose is anticipated within the next year. With the availability of these types of assays in house, a significant and increasing demand for this information is anticipated.

John A. Thorson, M.D., Ph.D.
Director, Molecular Diagnostics Laboratory

Annual Report
Specimen Procurement
Phlebotomy Services and Central Distribution

Department of Pathology
July 1, 2002-June 30, 2003

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 96.75 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 2003 were $2,975,323.00.

Budget performance for FY 2003 appears consistent with responsibilities involved and the volume of work performed:

VOLUMES:

Combined inpatient and outpatient volumes were essentially unchanged from FY2002. Inpatient phlebotomy volumes increased 3.7 % (5,036 patient draws) and outpatient phlebotomy volumes decreased -3.6 % (-4,918 patient draws).

INPATIENT PHLEBOTOMY VOLUMES			
	FY2002	*FY2003*	*% Change*
Inpatient Phlebotomy	137,401	142,437	**3.7**

OUTPATIENT PHLEBOTOMY VOLUMES			
	FY2002	*FY2003*	*% Change*
Cancer/Geriatric Center	46,682	52,020	**11.4**
Taubman Drawing Station, Floor #2	25,924	21,570	**-16.8**
Taubman Drawing Station, Floor #3	65,795	59,893	**-9.0**
TOTAL	138,401	133,483	**-3.6**

Total Phlebotomy Volumes	275,802	275,920	**0.0**

New testing technology and sophisticated testing not performed on-site, along with patient acuity and complexity of patient conditions evaluated at our facility, resulted in an increase of 18.0% for referral testing volumes.

SEND OUT LABORATORY TEST VOLUMES			
	FY2002	**FY2003**	***% Change***
Mayo Medical Laboratories	29,330	41,741	**42.3**
Specialty Laboratories	4,781	0	**-100.0**
Miscellaneous Laboratories	5,834	5,399	**-7.5**
TOTAL	39,945	47,140	**18.0**

EXPENSES:

FY 2003 YTD variances for controllable expenses were +12% ($38,823) for Central Distribution, +2.7% ($4933) for Inpatient Phlebotomy, and -11.3 % ($24,206) for Outpatient Phlebotomy. Combined controllable expenses for Central Distribution, Inpatient Phlebotomy, and Outpatient Phlebotomy were +2.7 % ($19,550) overbudget.

Salary and wage expenses for FY 2003 were overbudget for all three areas. High turnover rates for many of the department's positions, summer vacations, several personnel medical leaves of absence, and critical staffing bonuses paid in order to guarantee staffing for the expected level of service- primarily for the midnight shift- resulted in salary and wage expenses being overbudget 5.0 % (+$165,049).

YTD TOTALS	CD		IP		OP		TOTAL	
FY 2003	**Budget**	**Actual**	**Budget**	**Actual**	**Budget**	**Actual**	**Budget**	**Actual**
Salary/Wages	$1,351,920	$1,448,156	$786,545	$861,900	$836,858	$830,316	$2,975,323	$3,140,372
Expenses	$321,468	$360,291	$181,361	$186,294	$213,564	$189,358	$716,393	$735,943
Total	$1,673,388	$1,808,447	$967,906	$1,048,194	$1,050,422	$1,019,674	$3,691,716	$3,876,315
VARIANCE		**$135,059**		**$80,288**		**-$30,748**		**$184,599**
% VARIANCE		**8.1**		**8.3**		**-2.9**		**5.0**

Fiscal year 2003 provided opportunity for continuation of several on-going projects by the three Specimen Procurement areas (Central Distribution, Inpatient Phlebotomy, and Outpatient Phlebotomy). These projects included:

a. Cerner Millennium Testing/Validation:

Phlebotomy and Central Distribution continued testing the Cerner Millenium product until January, 2003 when the project was put on hold. This project involved regular testing and validation of the general laboratory module, critical to Department of Pathology operations.

b. Staff Orientation/Training:

Phlebotomy and Central Distribution continued to fine-tune and expand on-line orientation and training materials. This included enhancements to the already on-line material used to orient new employees to Specimen Procurement. We also developed additional training materials, including video material that will be used to train staff on unit specific tasks. These materials included:

Strep Testing
Pregnancy Testing
Release of Blood Products in the ED Laboratory
Problems Solving of Blood Product Issues in the ED Laboratory
Blood Culture Collection
Patient Identification

Plans are to continue expanding the use of this technology in order to improve efficiency and efficacy of employee training and employee competency efforts.

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.

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. Referral Laboratory test volumes have increased 23.9% over fiscal year 2002. The increase in volume was primarily sent to Mayo Medical Laboratories and the decrease in volume going to "miscellaneous laboratories" is directly related to our efforts to direct testing to our prime vendor (Mayo Medical Laboratories) and away from non-prime vendors (Miscellaneous Laboratories).

SEND OUT LABORATORY TEST VOLUMES			
	FY 2002	FY 2003	*% Change*
Mayo Medical Laboratories	27,423	41,741	**52.2**
Specialty Laboratories	4,781	0	**-100.0**
Miscellaneous Laboratories	5,834	5,399	**-7.5**
TOTAL	38,038	47,140	**23.9**

*See #2, below.

Annual Send Out expenditures were 96% over budget. The discrepancy between budget and actual expenses continues to be related to several factors:

1. Increased physician requests for sophisticated and expensive state-of-the –art testing such as genetic, molecular, and other specialized testing.

2. Additional costs were incurred, beginning in April, 2002, as a result of Specialty Laboratories, one of our prime vendor referral laboratories, being deemed non-compliant with regulations primarily related to personnel licensing requirements. As a result, testing that was originally targeted to be sent by us to Specialty Laboratories was referred back to Mayo Medical Laboratories. A portion of the original cost savings expected from the Specialty Laboratories relationship was not realized. The relationship between the University of Michigan and Specialty Laboratories is currently in limbo and an assessment as to the benefits of resurrecting this relationship is expected in the near future.

SEND OUT LABORATORY EXPENSES					
FY2002			*FY2003*		
Budget	**Actual**	**% Variance**	***Budget***	**Actual**	**% *Variance***
$1,500,000	**$2,253,444**	**50.2**	**$1,534,500**	**$3,011,664**	**96.3**

QUALITY ASSURANCE MONITORS:

The department continues to monitor several quality assurance indicators to assess departmental performance. These included:

MONITOR	Description	Threshold	FY 2002 Performance
MLab Order Entry Accuracy	Review all ML ab (client) requisitions for order accuracy	<5%	2.3% Error Rate
Health Center Order Entry Accuracy	Review 10% of CD ordered Health Center requisitions for order accuracy	<5%	1.8 % Error Rate
Call Back Review	Review Call Back records for:		
	Correct Documentation	100%	95%
	Completed within 30 Minutes	85%	66%

The department is within threshold for Order Entry Accuracy (M Lab and Health Center specimens), but is not meeting the Call Back thresholds for documentation and completion time.
An action plan to address non-compliance with Call Back thresholds is being addressed.

INPATIENT PHLEBOTOMY:

Inpatient Phlebotomy Services continue to be responsible for both specimen collection (phlebotomy) and specimen transport in the University Hospital and Mott Children's Hospital. Patient draws for fiscal year 2003 have increased 3.7 % (+5036 patient draws) over fiscal year 2002.

INPATIENT PHLEBOTOMY VOLUMES			
	FY2002	*FY2003*	*% Change*
Inpatient Phlebotomy	137,401	142,437	**3.7**

Workflow redesign is being planned in order to better meet customer needs of having morning sweep collections into the laboratory by 8:30 AM. This will facilitate the earlier reporting of tests results and assist in getting patients discharged from the hospital as soon as possible.

OUTPATIENT PHLEBOTOMY:

Outpatient Phlebotomy Services continue to provide phlebotomy services to two blood drawing stations in the Taubman Center and one blood drawing station in the Cancer/Geriatric Center.

OUTPATIENT PHLEBOTOMY VOLUMES			
	FY2002	***FY2003***	***% Change***
Cancer/Geriatric Center	46,682	52,020	**11.4**
Taubman Drawing Station, Floor #2	25,924	21,570	**-16.8**
Taubman Drawing Station, Floor #3	65,795	59,893	**-9.0**
TOTAL	138,401	133,483	**-3.6**

Total outpatient phlebotomy volumes decreased a net of -3.6 % (-4918 patient draws). Decreased volumes were seen in the Taubman Blood Drawing Stations, with an increase of 11% (5338 patient draws) seen in the Cancer/Geriatric Center Blood Draw Station.

QUALITY ASSURANCE MONITORS:

The Outpatient Phlebotomy area does a monthly monitor of patient wait times. Modeled after a Mayo Clinic program that monitors the flow of patients one day a month through their blood drawing station, we collect data one day a month to assess performance. During fiscal year 2003, 80 to 98% of our patients were drawn within 30 minutes of arrival in the blood draw station. Most recent data shows 95% of Cancer/Geriatric patients are processed within the blood drawing station in under 20 minutes.

Submitted by:
Harry Neusius

GENERAL PATHOLOGY

M-LABS

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 2001 - 30 JUNE 2002

I. MISSION:

MLabs is the University of Michigan Health System's reference laboratory program, established in 1985. MLabs offers the high quality reference laboratory services and other resources of the Department of Pathology laboratories to hospitals, clinics, other institutions, and physician offices. MLabs mission is to ensure that the Department of Pathology laboratories: (1) remain financially strong, (2) receive sufficient laboratory specimens for teaching, training and research programs, and (3) to encourage increased productivity of the laboratory staff.

II. CURRENT STATUS:

Since its origin, the MLabs program has experienced continuous growth, most notably since 1994 at which time the University Hospital chose to increase resources devoted to it. Gross billings have increased fourfold in the last four years.

MLabs currently provides full anatomic pathology coverage and esoteric clinical laboratory services to one hospital and to the University of Michigan Health Service. MLabs is the primary reference laboratory and provides full esoteric laboratory testing to another 15 hospitals in Michigan and northern Ohio. MLabs does esoteric testing for a local pharmaceutical firm. MLabs also now provides daily courier service and receives laboratory testing from 143 physician offices/clinics .

III. GOALS:

1. To generate increased revenue and decreased unit operating cost of the University of Michigan Hospitals Clinical Laboratory System by outreach testing for:

- Reference laboratory services to hospitals.
- Group Practices.
- Physicians offices.
- Managed care organizations.
- Specific esoteric services such as renal biopsies, molecular diagnostics, cytogenetics, and flow cytometry, and other "centers of excellence".

2. Develop and participate in hospital laboratory networks to:

- Compete effectively for managed care laboratory testing.
- Reduce costs through test sharing and consolidation.

3. Through our outreach efforts, to build bridges to other institutions that will facilitate working arrangements between these institutions and other branches of the University of Michigan Health System.

4. To support the mission of the University of Michigan Hospital System by providing for outpatient laboratory services to M-Care through a network or networks of hospital laboratories which will be potential M-Labs clients.

IV. GROWTH:

- In FY2003, MLabs added 16 new physician offices and specialty service practices to our client list. The majority of these were related to our contract to provide coverage to MCare patients. Some were for specialty services, and a few were UMHS acquired practices.
- No new hospital full reference laboratory accounts.
- No contracts for services were terminated.
- MLabs submitted no proposals to prospective new clients during FY2003.
- Business opportunities were rejected by MLabs because the Department of Pathology could not provide the services which were requested. Five dermatology practices requested dermatopathology. These requests were denied. Estimated revenue for these services is $1,000,000.

IV. BILLING ACTIVITY:

- Gross billings for anatomic pathology increased by 21% and those for clinical pathology increased by 29%. Total combined expected revenue from billing increased by 27% from last year.

V. MANAGED CARE ACTIVITIES:

In the last six years, MLabs has contracted with MCare for provision of outpatient lab services, first to its Medicare members, and later for members enrolled in M Care's commercial and Medicaid products. MLabs subcontracted much of the work to M Care's provider hospital labs with benefits to hospitals and patients. These contracts are capitated, which will result in considerable savings to MCare over its previous fee for service contracts for these lab services.

In FY2003, we have successfully implemented our second renegotiated contract with M Care to provide outpatient laboratory services for all groups and products for M Care's commercial and Medicare products. M Labs prepares quarterly QA reports on lab services for M Care's QA department and have conducted a Physician Satisfaction Survey for M Labs subcontracted providers and reported the results to M Care. We assist M Care with resolution of laboratory service issues. We are actively engaged in contracting for delivery of HEDIS data for M Care to assist them in meeting requirements of NCQA and other certifying entities.

VI. NETWORK ACTIVITY:

In the past several years, hospitals throughout the country have been forming networks in order to cope with the evolving demands of a changing health care system including intense cost cutting by third party payors, reduction in inpatient laboratory testing, competition from commercial laboratories, and carve out of outpatient laboratory services (to large independent labs) from managed care contracts. The formation of laboratory networks gives hospital labs the geographic coverage which allows them to successfully compete in a managed care environment as well as to decrease unit costs and increase revenue streams through outreach activities.

MLabs has been positioning itself to deal with an increase in managed care testing by playing a key role in two laboratory networks. Great Lakes Laboratory Network (GLN) consists of 28 hospital laboratories, predominantly in the western and northern parts of Michigan; Joint Venture Hospital Laboratories (JVHL) has grown to include 9 equity members including UMHS, and 72 participating member laboratories located in Michigan. JVHL has contracts with 14 managed care organizations including Blue Care Network. M Labs is represented on the Executive Committee.

VII. PROSPECTS:

Looking ahead, we foresee an increasingly competitive market for outreach and esoteric laboratory testing. We are already experiencing fierce competition in the hospital reference laboratory market from increasingly consolidated large independent laboratories with a national presence who offer a broad range of esoteric testing at extremely competitive prices. Purchasing agreements among groups of hospitals and affiliations/consolidations among groups of hospitals may also dictate their use of reference laboratories other than MLabs.

In the next few years, MLabs will focus its efforts on maintaining and increasing its existing hospital client base. This will require some reduction in our pricing, some broadening of our test menu, and continued efforts to interface the Department of Pathology's information system with client hospital information systems. We may also enter into arrangements with client hospitals where we would provide some management of their outreach programs.

Our recently much increased physician office client base will require efforts to continue to make our services run smoothly. In addition to the managed care work contracted to MLabs, we will focus our efforts on obtaining the discretionary (pull-through) laboratory work from these physician clients.

MLabs plans to increase our efforts significantly in marketing specialty (niche) areas such as dermatopathology, renal pathology, cytogenetics, molecular diagnostics, neuropathology, hematopathology, and flow cytometry. We currently provide laboratory listing to 2 University Health Systems. We are working with a third health system to set up their laboratory and do their esoteric testing.

IX. IMPEDIMENTS:

As other hospital labs develop increasingly complex testing capabilities, the University of Michigan Clinical Laboratories must be increasingly innovative to bring more complex testing in-house in order to have a sufficient menu of complex testing to successfully compete in the hospital reference laboratory market. Investment in additional resources, personnel and space will be necessary if M Labs is to be able to accommodate the increased demand for esoteric testing where we have special expertise. So far, recently, additional resources have not been made available stifling growth in these areas. In addition, cost constraints have worked to reduce the scope and frequency of esoteric testing. If this trend continues, it would produce a downward spiral of reduction in volume leading to increased unit costs, leading and reduction in volume, etc.

Prepared by Eugene M. Silverman, M.D.

PATHOLOGY RESEARCH MICROARRAY LABORATORY

DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 2002- 30 JUNE 2003

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 entire human genome, it may soon be 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 in three areas important 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 2 years ago 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 attended by Dr. Chinnaiyan and taught by Drs. Joseph DeRisi (UCSF), Michael Eisen (Stanford), and Patrick Brown (Stanford), all of whom are renowned experts in the field.

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.

During this reporting period the following investigators have utilized the Microarray facilities:

1. Dr. Peter Ward (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. Marc Lippman (Internal Medicine), Gene expression mediated by ErbB family members.
7. Dr. Andrew Lieberman (Pathology), gene expression mediated by androgen receptor variants.
8. Dr. Mark Rubin (Brigham Woman's Hospital Pathology), prostate cancer profiling
9. Dr. Sofia Merajver (Internal Medicine) Gene expression mediated by Rho family members.
10. Dr. Steven Ethier (Radiation Oncology) Gene expression mediated by FGFR family inhibitors.
11. Dr. Joseph Holoshitz (Internal Medicine) Gene expression of studies in identical twins with and without rheumatogic disease.
12. Dr. Kent Johnson (Pathology) and Pfizer Corporation- Development of antibody microarrays.
13. Dr. Donna Livant (Radiation Oncology) Gene expression mediated by PHSCN.
14. Dr. Paul Harari (Univ. of Wisconsin, Radiation Oncology) Gene expression mediated by Tarceva.
15. Dr. Celina Kleer (Pathology) Gene expression mediated by WISP.
16. Dr. Theodora Ross (Internal Medicine) Gene expression mediated by HIF1.
17. Dr. Chinnaiyan (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. 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. Dr. Dan Remick and Dr. 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 following manuscripts include data made possible by the Microarray Lab:

1. Chay, C.H., Cooper, C.R., Gendernalik, J.D., Dhanasekaran, S.M., Chinnaiyan, A.M., Rubin, M.A., Pienta, K.J. (2002) A functional thrombin receptor (PAR1) is expressed on bone-derived prostate cancer cell lines. *Urology*, 60:760-5.
2. Xin, W., Rhodes, D.R., Ingold, C., Chinnaiyan, A.M., Rubin, M.A. (2002) Dysregulation of the Annexin Protein Family is Associated with Prostate Cancer Progression. *American Journal of Pathology*, 162(1):255-61.
3. Dash, A. Maine, I., Dhanasekaran, S.M., Barrette, T.R., Chinnaiyan, A.M., Rubin, M.A. (2002)

Changes in Differential Gene Expression Due to Warm Ischemia Time of Radical Prostatectomy Specimens. *American Journal of Pathology* 161:1743-8.

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6. Kumar-Sinha, C., Ignatoski, K.M., Lippman, M.E., Ethier, S.P., Chinnaiyan, A.M. (2003) Transcriptome Analysis of HER-2 Reveals A Molecular Connection to Fatty Acid Synthesis. *Cancer Research*, 63, 132-9.
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9. Albrecht, E.A., Chinnaiyan, A.M., Varambally, S., Kumar-Sinha, C., Barrette, T.R., Sarma, V.J., Ward, P.A. (2003) C5a-induced Gene Expression if Human Umbilical Vein Endothelial Cells. *American Journal of Pathology*, Submitted.
10. Mattfeldt, T., Kufer, R. Chinnaiyan, A.M., Kestler, H.A., Rubin, M.A. (2003) Classification of prostatic lesions from gene expression data using supervised learning methods. *International Journal of Pattern Recognition and Artificial Intelligence*, Submitted.
11. Liu, T., Dhanasekaran, S.M., Jin, H., Tomlins, S.A., Chinnaiyan, A.M., Phan, S.H. (2003) Induction of FIZZ1 Expression in Lung Injury and Fibrosis. *Journal of Clinical Investigation*, Submitted.
12. Sun YX, Wang J, Shelburne CE, Lopatin DE, Chinnaiyan AM, Rubin MA, Pienta KJ, Taichman RS. (2003) Expression of CXCR4 and CXCL12 (SDF-1) in human prostate cancers (PCa) in vivo. *Journal of Cell Biochemistry*, 89(3):462-73.
13. Ghosh D., Barrette T.R., Rhodes, D., Chinnaiyan, A.M. (2003) Statistical issues and methods for meta-analysis of microarrays in prostate cancer. *Functional Integrative Genomics*, July 22 [E pub ahead of print].
14. Kleer , C.G., Cao, Q., Varambally, S., Shen, R., Ota, I., Tomlins, S.A., Ghosh, D., Sewalt, R.G., Otte, A.P., Hayes, D.F., Sabel, M.S., Livant, D., Weiss, S.J., Rubin, M.A., Chinnaiyan, A.M. (2003) EZH2 is marker of aggressive breast cancer and promotes neoplastic transformation of breast epithelial cells. *Proceedings of the National Academy of Sciences*, 100(20):11606-11.

The Pathology Microarray Lab has supported the following grant applications by providing preliminary gene expression analyses:

ACS Beginning Investigator Grant, Molecular Classification of Prostate Cancer, P.I. A. Chinnaiyan

R01, Protective Effects of anti-c5a in Sepsis, P.I. P. Ward

R01, Lung Injury by Oxygen Metabolites, P.I. P. Ward

Microarray Supplement, Sepsis Profiling, P.I. P. Ward

U of M SPORE in Prostate Cancer, P.I. K. Pienta

DOD grant, Biological Differences between prostate cancer cells that metastasize to the bone versus soft tissue sites, P.I. K. Pienta

Breast Cancer Research Foundation, "Transcriptome Analysis of the EGFR Receptor in Breast Cancer, The Breast Cancer Foundation", PI M. Lippman

P01, Program Project on Prostate Cancer Bone Metastases, P.I. E. Keller

RO1, The Role of Polycomb Group Proteins in Prostate Cancer, P.I. Chinnaiyan

Glue Grant, U54 GM64351 Inflammation and the Host Response to Injury; P.I. D. Remick

Department of Defense, DOD PC020322 (Chinnaiyan)
Pfizer Sponsored Research Agreement (Ward)

GMP Sponsored Research Agreement (Chinnaiyan)

1. The Pathology Microrarray Lab can now produce 20K human cDNA arrays, 10K rat cDNA arrays, and 5K mouse cDNA arrays
2. A protein microarray platform is being optimized for use with clinical specimens and cell lines.

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 micorarrays.
6. Develop a unified bioinformatics platform for the analysis of DNA microarray, tissue micorarray, 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. 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, previously a post-doctoral fellow in the lab was promoted to Research Investigator. Arun Sreekumar, a Research Fellow, was 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, Ira Maine (mentored by M. Rubin), Atreya Dash (mentored by M. Rubin), Monzy Thomas (mentored by A. Lieberman), Eric Albright (mentored by P.Ward), 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). The Microarray Lab hosted international visiting scholars to train in microarray technology: Jian Huang, M.D. (Zhejiang University, China)

Arul M. Chinnaiyan, M.D., Ph.D.
Director, Pathology Research Microarray Laboratory

DEPARTMENT OF PATHOLOGY EDUCATIONAL PROGRAMS

ANNUAL REPORT
1 JULY 2002 - 30 JUNE 2003

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 combined residency training in Anatomic and Clinical Pathology as well as fellowships in Cytopathology, Hematopathology, Surgical Pathology, Blood Bank/Transfusion Medicine 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. Five house officers and nine fellows completed training this past year. Graduates found desirable fellowships and employment as well as faculty positons at the University of Michigan Hospitals.

Graduate Program:
The Department's doctoral graduate program continues to expand and thrive (approx. 15 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 two students 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 Michgan 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.

PROSTATE S.P.O.R.E. TISSUE/INFORMATICS CORE

DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 2002- 30 JUNE 2003

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. Chinnaiyan and Shah) and two pathology fellows (Drs. Mehra and Snyder). A urologist directs clinical consent and patient participation 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 September of 2002, Dr. Chinnaiyan assumed leadership of the SPORE Tissue Core. As Co-Director, Dr. Rajal Shah is the lead surgical pathologist for the Michigan Prostate SPORE.

II. RESEARCH AND DEVELOPMENT:

Drs. Chinnaiyan and Shah 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. Development of a bank of genomic DNA, RNA/cDNA, and protein extracted from grossly dissected and laser-microdissected prostatic tissues.
2. Introduction of quantitative real-time PCR technology for the validation of candidate differentially expressed prostate cancer genes.
3. Continued construction of TMAs from cases derived from the University of Ulm collaboration, which provides the SPORE with a rich source of hormone naïve prostatic tissues.
4. Development of Mayo Clinic TMAs for the validation of EZH2 and other biomarkers on independent patient cohorts.

5. Development of mRNA in situ hybridization and fluorescence in situ hybridization (FISH) of TMAs.
6. 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.
7. Establishment of a strong inter-SPORE collaboration between Michigan and the Dana Farber HMS Cancer Center as well as between the intra-institution Prostate and Head& Neck SPOREs at Michigan.

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 PCa is harvested from our Rapid Autopsy Program. We have also developed a program to collect hormone naive metastatic PCa from the University Clinic in Ulm, Germany. A recently developed protocol in conjunction with the Michigan Transplantation Society allows us to harvest benign prostate tissue from organ donors. 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. Twelve Tissue Microarrays have been constructed: 1) Prostate Transition Zone array TMA 67, 2) Bladder test array TMA 68, 3) Bladder Cancer TMA 69, 4) Larynx array (T.Carey) TMA 70, 5) Effect of Radiation on Xenograft Models (M. Nyati) TMA 71, 6) Larynx Ca. array (Carey) TMA 72, 7) Prostate Screening array TMA 73, 8) ENT test array (Carey) TMA 74, 9) Chromosome 8 array (Macoska) TMA 75, 10) Renal array (Shah, Kunju)TMA 76, 11) Screening hereditary array (Cooney) TMA 77, and 12) LOA array TMA 78.

2. Profiler - A bioinformatics infrastructure to analyze TMAs was updated to a second version. 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), Matthias Hoffer (Dr. Rubin's lab, Brigham), Russel Taichman (School of Dentistry), Dr. Cheville (Pathology), Dan Rhodes (Pathology), Evan Keller (Pathology), Dr. Lippman (Internal Medicine), Max Loda (Pathology, Brigham), Dr. Prince (Head and Neck), Tarek (Dr. Rubin's lab), and Zheng Fu from (Pathology).

3. LCM Projects- laser capture microdissection
   A) Arul Chinnaiyan (15 LCM caps) Reverse phase gel protein microarrays and RNA analysis
   B) Celina Kleer (31 LCM caps) – Breast cancer Amplicon project

4. Serum collection
   A) Re-started prostate cancer serum collection and restructured database (427 total)
   B) Started organizing and making aliquots to make better use of serum bank

5. DNA collection
   A) Bladder DNA for Dr. Lee 53
   B) Collection of DNA from Prostate Cancer Patients Peripheral Blood 202

6. Tissue Bank collections
   A) Prostate cancer collection (RRP) = 212
   B) Benign prostate from Cystoprostatectomy cases: 4
   C) Bladder cancer collection = 25
   D) Renal cancer = 4

7. Rapid Autopsy Collection (WA25-WA29)
   A) Frozen blocks (204 total)
   B) Paraffin blocks (165 total)

In summary, over the past 6 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 *70* 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.

Publications (Also includes published abstracts) during this reporting period using services provided by the Tissue/Informatics Core:

1. Fu Z, Smith PC, Zhang L, Rubin MA, Dunn RL, Yao Z, Keller ET. Effects of raf kinase inhibitor protein expression on suppression of prostate cancer metastasis. J Natl Cancer Inst. 2003 Jun 18; 95(12): 878-89.
2. De la Taille A, Viellefond A, Berger N, Boucher E, De Fromont M, Fondimare A, Molinie V, Piron D, Sibony M, Staroz F, Triller M, Peltier E, Thiounn N, Rubin MA. Evaluation of the interobserver reproducibility of Gleason grading of prostatic adenocarcinoma using tissue microarrays. Hum Pathol. 2003 May;34(5):444-9.
3. Sun YX, Wang J, Shelburne CE, Lopatin DE, Chinnaiyan AM, Rubin MA, Pienta KJ, Taichman RS. Expression of CXCR4 and CXCL12 (SDF-1) in human prostate cancers (PCa) in vivo. J Cell Biochem. 2003 Jun 1;89(3):462-73.
4. Chaib H, MacDonald JW, Vessella RL, Washburn JG, Quinn JE, Odman A, Rubin MA, Macoska JA. Haplo insufficiency and reduced expression of genes localized to the 8p

chromosomal region in human prostate tumors. Genes Chromosomes Cancer. 2003 Jul;37(3):306-13.

5. Rhodes DR, Sanda MG, Otte AP, Chinnaiyan AM, Rubin MA. Multiplex biomarker approach for determining risk of prostate-specific antigen-defined recurrence of prostate cancer. J Natl Cancer Inst. 2003 May 7;95(9):661-8.
6. Zhou M, Shah R, Shen R, Rubin MA. Basal cell cocktail (34betaE12 + p63) improves the detection of prostate basal cells. Am J Surg Pathol. 2003 Mar;27(3):365-71.
7. Xin W, Rhodes DR, Ingold C, Chinnaiyan AM, Rubin MA. Dysregulation of the annexin family protein family is associated with prostate cancer progression. Am J Pathol. 2003 Jan;162(1):255-61.
8. Dash A, Maine IP, Varambally S, Shen R, Chinnaiyan AM, Rubin MA. Changes in differential gene expression because of warm ischemia time of radical prostatectomy specimens. Am J Pathol. 2002 Nov;161(5):1743-8.
9. Rios-Doria J, Day KC, Kuefer R, Rashid MG, Chinnaiyan AM, Rubin MA, Day ML. The role of calpain in the proteolytic cleavage of E-cadherin in prostate and mammary epithelial cells. J Biol Chem. 2003 Jan 10;278(2):1372-9.
10. Varambally S, Dhanasekaran SM, Zhou M, Barrette TR, Kumar-Sinha C, Sanda MG, Ghosh D, Pienta KJ, Sewalt RG, Otte AP, Rubin MA, Chinnaiyan AM. The polycomb group protein EZH2 is involved in progression of prostate cancer. Nature. 2002 Oct 10;419(6907):624-9.
11. Kim WH, Rubin MA, Dunn RL. High-density tissue microarray. Am J Surg Pathol. 2002 Sep;26(9):1236-8; discussion 1237-8.
12. Shah RB, Zhou M, LeBlanc M, Snyder M, Rubin MA. Comparison of the basal cell-specific markers, 34betaE12 and p63, in the diagnosis of prostate cancer. Am J Surg Pathol. 2002 Sep;26(9):1161-8.
13. Kuefer R, Varambally S, Zhou M, Lucas PC, Loeffler M, Wolter H, Mattfeldt T, Hautmann RE, Gschwend JE, Barrette TR, Dunn RL, Chinnaiyan AM, Rubin MA. alpha-Methylacyl-CoA racemase: expression levels of this novel cancer biomarker depend on tumor differentiation. Am J Pathol. 2002 Sep;161(3):841-8.
14. Kumar-Sinha C, Rhodes DR, Yu J, Chinnaiyan AM. Prostate cancer biomarkers: a current perspective. Expert Rev Mol Diagn. 2003 Jul;3(4):459-70.
15. Yan F, Sreekumar A, Laxman B, Chinnaiyan AM, Lubman DM, Barder TJ. Protein microarrays using liquid phase fractionation of cell lysates. Proteomics. 2003 Jul;3(7):1228-35.
16. Fu Z, Smith PC, Zhang L, Rubin MA, Dunn RL, Yao Z, Keller ET. Effects of raf kinase inhibitor protein expression on suppression of prostate cancer metastasis. J Natl Cancer Inst. 2003 Jun 18;95(12):878-89.
17. Cooper CR, Chay CH, Gendernalik JD, Lee HL, Bhatia J, Taichman RS, McCauley LK, Keller ET, Pienta KJ. Stromal factors involved in prostate carcinoma metastasis to bone. Cancer. 2003 Feb 1;97(3 Suppl):739-47. Review.
18. Corey E, Quinn JE, Buhler KR, Nelson PS, Macoska JA, True LD, Vessella RL. LuCaP 35: a new model of prostate cancer progression to androgen independence. Prostate. 2003 Jun 1;55(4):239-46.
19. Zhou M, Shah R, Shen Ronglai and Rubin MA. Basal Cell Cocktail (34βE12+p63) improves the detection of Prostate Basal Cells. Am J Sug Pathol, Vol. 27, No. 3, 2003.
20. Kunju Lakshmi, Rubin Mark, Chinnaiyan Arul and Shah Rajal. Diagnostic Utility of the Monoclonal Antibody P504S in the Work Up of Atypical Glandular Proliferations. Am J Clinical Pathol, In Press.

21. Kunju Lakshmi, Rubin Mark, Shen Ronglai, Ingold Collette, Chinnaiyan Arul and Shah Rajal. Diagnostic Utility of the Monoclonal Antibody P504S in the Work Up of Prostate Carcinoma. Modern Pathol 16(1): 719, Jan 2003.
22. Shah Rajal, Kunju Lakshmi, Shen Ronglai, LeBlank Michele and Rubin Mark. Utility of Basal Cell Cocktail (p63+34betaE12) in the Diagnosis of Atypical Prostate Glandular Proliferations. Modern Pathol, 16(1): 726, Jan 2003.
23. Kunju Lakshmi, Rubin Mark, Shen Ronglai, Ingold Collette, Chinnaiyan Arul and Shah Rajal. Comparison of Monoclonal Antibody (P504S) and Polyclonal Antibody to α-Methylacyl-CoA Racemase in Benign, Atypical and Malignant Prostate Tissues. Modern Pathol, 16(1): 718, Jan 2003.
24. Zhou M, Shah R, Shen R, Rubin MA. Basal Cell Cocktail (34betaE12+p63) improves the detection of Prostate Basal Cells. Modern Pathol, 16(1): 807, Jan 2003.

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ANN ARBOR VA HEALTH SYSTEM
PATHOLOGY AND LABORATORY MEDICINE SERVICE

DEPARTMENT OF PATHOLOGY - UNIVERSITY OF MICHIGAN
ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

INTRODUCTION:

The VA Ann Arbor VA Healthcare System (VAAAHS) is a University of Michigan affilated 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 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, and a number of arranged electives including Diagnostic Electron Microscopy and special study programs in Surgical Pathology, Cytopathology and Digital Imaging. The VAAAHS laboratory was inspected in 2002 and retains full accreditation by the College of American Pathologists. The VAAAHS was 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 1 ½ decades. Digital images of selective 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.

Two ongoing reorganizational thrusts are underway at the VAAAHS. 1) The facility is refocusing its mode of healthcare delivery, downsizing inpatient care and greatly expanding its ambulatory care. In keeping with this change, a substantial capital improvement program is ongoing. Completed to date are Research Building, two additional parking structures and a 340,000 sq. ft. clinical addition. This building is attached to the existing hospital and provides space for ambulatory care, new surgical suites, post surgical recovered unit, vascular cath facilities, four intensive care units and a floor for diagnostic services (Pathology, Clinical Labs, Radiology and Nuclear Medicine). Pathology and Laboratory Medicine occupies 23,000 sq. ft on the third floor of the clinical addition. The previous structure is currently under complete remodeling to allow for current standards of inpatient privacy. Also included will be administrative offices, and additional research space. Current discussions concern a complete functional restructuring of the clinical labs. 2) 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. Ann Arbor is currently performing all surgical pathology for the Battle Creek/Grand Rapid facilities. The VISN has added an additional outpatient facility in Flint which is serviced by the Ann Arbor laboratory. A recent CARES review was implemented by the VA Secretary in order to project veteran medical care needs for the next two decades and based upon that review the VAAAHS will likely be facing increasing demand and expansion of services.

ANATOMICAL PATHOLOGY:

A. **Surgical Pathology**: 5,648 surgical cases were accessioned and reported during year 2002 continuing a steady increase over the prior reporting periods. The resident assigned to surgical pathology, usually a first year resident, acts as coordinator of the section and in that capacity 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:** 33 autopsies were performed during this year that is a rate of approximately 24% 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 VAAAHS 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.

C. **Cytology:** 2,363 cases were examined and diagnosed during this period. This is a slight increase over the last reporting year. Most of the cytology specimens are of diagnostic type, however the VAAAHS performs all PAP screening cytologies for the northern tier of VISN 11. Although there is not a formal rotation in cytology within the VAAAHS 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**: 60 electron microscopy cases were processed. 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 VAAAHS 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 VAAAHS 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 1,088,933 clinical pathology procedures were performed in the Ann Arbor and its affiliated Toledo oupatient laboratory. In Chemistry there were 776,838; in Hematology 99,026; in Urinalysis 13,672, in Microbiology 25,786 and in Blood Bank 19,754. The Toledo unit performed 94,603 tests. These figures represent productivity (billable) rather than weighted test numbers. A formal clinical pathology rotation has not been available for pathology residents although the 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 VAAAHS 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 participate 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. She and Dr. Chensue have research laboratories in Research Building 31 of the VAAAHS. All staff participate in various clinical studies and collaborate 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 was appointed as Chief of Service in 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 considers the practice of high quality medicine and the appropriate care of the veteran patients as its first and highest responsibility. 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 Pathology and Laboratory Medicine Service has maintained accreditation by the College of American Pathologists since the early 1960's. The Blood Bank maintains approval by the federal Food and Drug Administration. The partnership 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 newly constructed Clinical Addition now houses: Ambulatory Care, Surgical Suites, the Intensive Care Units, Nuclear Medicine, Radiology and the full Clinical and Anatomic Pathology laboratories.

Stephen W. Chensue, M.D., Ph.D.
Chief, Pathology and Laboratory Medicine Service
VA Ann Arbor Healthcare System

FINANCE AND ADMINISTRATION

DIVISION OF FINANCE AND ADMINISTRATION

DEPARTMENT OF PATHOLOGY - UNIVERSITY OF MICHIGAN
ANNUAL DEPARTMENTAL REPORT
1 JULY 2002 - 30 JUNE 2003

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 five units as follows:

A. ADMINISTRATIVE SUPPORT CENTER - PATHOLOGY LABORATORIES

Nancy A. Coray, Financial Analyst and Billing Coordinator
Deborah Day Jansen, Administrative Coordinator for Pathology Laboratories
Thomas D. Morrow, Assistant Administrator for Operations
Beverly J. Smith, Administrative Associate, Human Resources

Clinical Faculty Offices & Surgical Pathology Transcription, University Hospitals:

Deborah Day Jansen, Administrative Coordinator
Paulette Dozier, Office Manager, Surgical Pathology Transcription
Patricia Connolly, Office Manager, Clinical Faculty Offices

B. OFFICE OF ACADEMIC AND BUSINESS AFFAIRS - MEDICAL SCHOOL:

David R. Golden, Administrative Manager
Laura Hessler, Student Services Assistant
John E. Harris, Administrative Associate
Catherine A. Niemiec, Administrative Assistant

C. OFFICE OF THE CHAIRMAN:

Laura D. Blythe, Clinical Department Associate
Lynn A. McCain, Executive Medical Secretary
Jennifer Neff, Receptionist

D. PATHOLOGY PHOTOGRAPHY AND IMAGING CENTER:

Mark V. Deming, Senior Photographer
Elizabeth Horn, Photographer

E. CENTRAL DISTRIBUTION & PHLEBOTOMY SERVICES ADMINISTRATION:

Harry J. Neusius, Chief Technologist
Jill Bell, Laboratory Supervisor
Shellie Campbell, Laboratory Supervisor
Judith Nyhius, Laboratory Supervisor

All of the above sections reside in the Division of Finance and Administration. This Division is 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. 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.

I am pleased to recognize that very little turnover of staff occurred in FY 2003.

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. For Fiscal Year 2003, the Pathology Laboratories were over budget by less than 0.03% or $12,000. This accomplishment reflects our attentitiveness to cost containment and expense reduction. We have trained non-medical technology personnel with education in one of the sciences, to complete some of the tasks previously performed by medical technology staff. Additionally, we have implemented a program for medical technology students from area universities, i.e., Ferris State University, Eastern Michigan University, to be provided "on-site" internships. This program also serves as a "pre-recruitment" period for this group of students. Mr. Morrow was appointed as Chairman of a committee to re-design the website for the Department of Pathology. The new site was launched in June 2003.

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) the SPECTRUM Newsletter, and is responsible for all requisition modifications. Mrs. Jansen lead the Hospital and Health Services Blood Drive Program which was assigned to Pathology by Hospital Administration, and she has been able to increase the number of blood units collected through her innovative marketing techniques. Mrs. Jansen also manages the Surgical Transcription Unit and has assumed responsibility for the Faculty Office Suite in the Hospitals as well as the accessioning function in the Medical Science I Building. Staffing within the surgical transcription unit has stabilized and has resulted in timely processing of surgical pathology

reports. A major reorganization of the Clinical Faculty Offices was accomplished this past year including the addition of new faculty and staff and renovation to existing space. A new Office Manager was hired and in the interim, Mrs. Jansen assumed the day to day management of this unit.

Billing Coordinator: This individual, Ms. Nancy Coray, is responsible for processing and auditing all laboratory charges (gross charges of approximately $211,980,951, 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 438 FTEs). The Administrative Associate is responsible for the compilation of the Pathology Telephone Directory (on-line and hard copy) and serves as lead for the Department's Orientation Program.

OFFICE OF ACADEMIC AND BUSINESS AFFAIRS - MEDICAL SCHOOL:

This unit, which is managed by Mr. David Golden, is responsible for the Medical School all funds budget preparation and 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.

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 is coordinated in this office.

Mr. John Harris has assumed responsibility for oversight of the staff supporting our Research Programs. Ms. Catherine Niemiec is responsible for Human Resource issues for staff in the Medical School (approximately 134 FTEs) including our House Officer Program (24 FTEs), Post Doctoral Fellows (39 FTEs), and graduate students (34) as well as supervising the staff in the Pathology Education Office.

OFFICE OF THE CHAIRMAN:

In addition to providing support to the Chairman, Mrs. Lynn McCain is responsible for processing faculty appointments and promotions through our departmental ACAPT, the Medical School and University. She also assists the Division Directors with coordinating schedules for faculty recruits.

Mrs. Laura Blythe provides staff support to the Administrator, Mr. Eugene J. Napolitan. In addition, she is responsible for the supervision of faculty support staff, the Chairman's Office

Receptionist and temporary office staff. Additional responsibilities include Human Resources for faculty (70+) and other faculty related issues, such as travel and dues reimbursements and p-card reconciliation.

This past year has been an active recruiting period with the addition of five new faculty members. Recruitment efforts continue for several additional slots required for the continued expansion of services required by the Health System.

PATHOLOGY PHOTOGRAPHY AND IMAGING UNIT:

Mr. Mark Deming and Ms. Elizabeth Horn 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:

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. Neuisus 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. Neuisus, 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:

1. Grants and Contracts and Other Accounts:

241 active grants, contracts and other accounts

Total Extramural Direct Expenditures:	$12,151,608
Indirect Extramural Research Expenditures:	$ 5,003,032
Total Sponsored Projects:	$17,154,640

2. Faculty Group Practice Plan - Pathology:

Number of charge entries:	190,866
Gross Billings - Anatomic and Clinical Pathology:	$ 25,022,801
Collections	$ 9,169,121
Part A Payment:	$ 2,768,295
M-Labs Net Transfer:	$ 950,000

3. All Fund Expenditures – Medical School

Compensation & Benefits	$ 20,112,368
Commodities & Other Costs	$ 12,946,088
Total	$ 33,355,701

# of Funded Faculty	74.98
# of Funded Residents (includes 4 clinical fellows)	31.00
# of Funded FTE Research Projects (includes 15 graduate students, 44 pre & post-doctoral fellows)	159.00

4. Pathology Laboratories:

Number of billed tests reported by CDM :	3,168,236
Total Gross Revenue - Pathology Laboratories:	$211,980,951
Total Direct Expenses Pathology Laboratories:	$ 45,714,302

*Includes General Fund, Extramural Funds, FGP Professional Fee Income, Gift, etc.

Respectfully submitted,

Eugene J. Napolitan
Administrator