

**THE UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL**

Department of Pathology

ANNUAL REPORT



1 July 1999 - 30 June 2000

THE UNIVERSITY OF MICHIGAN

MEDICAL SCHOOL

Department of Pathology

ANNUAL REPORT



1 JULY 1999- 30 JUNE 2000

LIST OF FACULTY

LIST OF FACULTY

<u>Name</u>	<u>Rank</u>	<u>Institutional Affiliation</u>
Abell, Murray R	Professor Emeritus	The University of Michigan
Abrams, Gerald D.	Professor	The University of Michigan
Afify, Alaa M.	Clinical Assistant Professor	The University of Michigan
Al-Khafaji, Basim M.	Clinical Assistant Professor	The University of Michigan
Annesley, Thomas M.	Professor	The University of Michigan
Appelman, Henry, D.	Professor	The University of Michigan
Baker, James R.	Associate Professor	The University of Michigan
Barr Jr., Mason	Professor ⁺	The University of Michigan
Beals, Theodore F.	Assistant Professor	Veterans Affairs Medical Center
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
Cho, Kathleen R.	Associate Professor*	The University of Michigan
D'Amato, Constance J.	Assistant Professor	The University of Michigan
Davenport, Robertson	Associate Professor	The University of Michigan
de la Iglesia, Felix	Adjunct Professor**	Warner-Lambert; Parke Davis
Dressler, Gregory R.	Assistant Professor	The University of Michigan
Elnor, Victor M.	Associate Professor ⁺⁺	The University of Michigan
England, Barry G.	Associate Professor	The University of Michigan
Fantone, Joseph C.	Professor and Director, Anatomic Pathology	The University of Michigan
Fearon, Eric R.	Professor*	The University of Michigan
Finn, William	Clinical Assistant Professor	The University of Michigan
Flint, Andrew	Professor	The University of Michigan
Friedman, Bruce A.	Professor	The University of Michigan
Giacherio, Donald	Assistant Professor	The University of Michigan
Gikas, Paul W.	Professor Emeritus	The University of Michigan
Giordano, Thomas J.	Assistant Professor	The University of Michigan
Gordon, David	Adjunct Associate Professor	The University of Michigan
Greenson, Joel	Associate Professor and Director, Surgical Pathology	The University of Michigan
Headington, John T.	Professor Emeritus	The University of Michigan
Heidelberger, Kathleen P.	Professor	The University of Michigan
Hogaboam, Cory	Research Investigator	The University of Michigan
Johnson, Kent J.	Professor	The University of Michigan

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<u>Name</u>	<u>Rank</u>	<u>Institutional Affiliation</u>
Judd, W. John	Professor	The University of Michigan
Keller, Evan	Assistant Professor##	The University of Michigan
Keren, David F.	Clinical Professor	Warde Medical Laboratories
Killeen, Anthony A.	Assistant Professor	The University of Michigan
Killen, Paul D.	Associate Professor	The University of Michigan
Kunkel, Steven L.	Professor and Co-Director, Division of General Pathology	The University of Michigan
Lieberman, Richard W.	Clinical Assistant Professor+++	The University of Michigan
Lowe, Lori	Clinical Assistant Professor	The University of Michigan
Lowe, John B.	Professor	The University of Michigan
Lukacs, Nicholas	Assistant Research Scientist	The University of Michigan
McKeever, Paul E.	Associate Professor	The University of Michigan
Mellerick-Dressler, Dervla	Assistant Professor	The University of Michigan
Michael, Claire W.	Clinical Assistant Professor	The University of Michigan
Midgley, A. Rees	Professor	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
Nunez, Gabriel	Associate Professor	The University of Michigan
Oberman, Harold A.	Professor	The University of Michigan
Paulino, Augusto F.	Clinical Assistant Professor	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 Instructor II	The University of Michigan
Rasche, Rodolfo	Clinical Assistant Professor	The University of Michigan
Remick, Daniel G.	Associate Professor	The University of Michigan
Ross, Charles W.	Associate Professor	The University of Michigan
Rubin, Mark A.	Assistant Professor#	The University of Michigan
Schmidt, Robert W.	Professor Emeritus	The University of Michigan
Schnitzer, Bertram	Professor	The University of Michigan
Shanberge, Jacob N.	Clinical Professor	William Beaumont Hospital
Silverman, Eugene M.	Clinical Associate Professor	The University of Michigan
Stoolman, Lloyd M.	Associate Professor	The University of Michigan
Su, Lyndon	Clinical Assistant Professor	The University of Michigan

<u>Name</u>	<u>Rank</u>	<u>Institutional Affiliation</u>
Till, Gerd O.	Professor	The University of Michigan
Varani, James	Professor	The University of Michigan
Vincenz, Claudius	Research Investigator	The University of Michigan
Ward, Peter A.	Professor and Chairman	The University of Michigan
Warren, Jeffrey S.	Associate 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, Warner-Lambert, Parke Davis

+ 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



**Faculty, Residents and Fellows
Department of Pathology
October, 1999**

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DEPARTMENTAL OVERVIEW

DEPARTMENTAL OVERVIEW 1999-2000

Introduction

As described below, there has been an influx of new faculty into the Department, primarily involving replacements for open positions in Anatomic Pathology but also in response to greatly increased demands in diagnostic clinical areas (e.g. surgical pathology, cytopathology and dermatopathology). Several of the new diagnostic faculty have also brought research expertise that has direct applications to surgical pathology. The dental/medical student teaching programs of the Department have been enhanced by development of websites that students have found to be very accessible and convenient. The research enterprise of the Department continues to be very healthy, with a continued emphasis on basic and clinically relevant mechanisms of inflammation, apoptosis and neoplasia as well as new programs for bio-markers of solid tumors. Federal funding for these programs continues to exceed projections. The Department underwent an Internal Review, which was directed by Dr. Dan Remick. The External Review is scheduled for July 6-7, 2000. As has been the case for many years, the Department is short on space for faculty offices and for research laboratories. It should be noted that our research space has not increased for nearly 15 years in spite of very robust growth of the research enterprise of the Department. We continue to work actively with the Hospital to define options for relocation (out of the Pathology Building) of the Clinical laboratories.

Teaching Activities

Faculty members continue to fill leadership roles as course directors, sequence coordinators, and serve as Associate Dean for Medical Education in the Medical School curriculum. Several faculty members continue to be recognized as recipients of outstanding teaching awards and selection as graduation class marshals. Pathology laboratories continue to be a strength within the histology course and second year 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 exceptional evaluations. The Department continues to present a semester-long Dental Pathology course and a summer semester course to Medical Illustration students. Both courses continue to focus on the specific educational needs of these students and engage them in more inter-active learning activities, including the implementation of Web-based instruction. The Pathology graduate program was successful in recruiting two new students. 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 prosper despite declining national student interest in pathology residency training. The program consists of 28 house officers and fellows. Last year all graduates of the house officer program found desirable positions, in both academia and private practice, including fellowships at University of Michigan and Children's Hospital of Philadelphia.

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 several major clinical programs. 1999-2000 was marked by several new faculty recruitments and several new initiatives. 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. The Laboratories continued to reallocate resources needed to meet the continuing and marked increase in clinical activity experienced in 1999-2000. Augmentation of the capabilities of the Molecular Diagnostics, Blood Bank, Tissue Typing and Cytogenetics Laboratories was contributory to this process. There was a marked improvement by clinical sites in compliance with the HCFA-mandated documentation rules. In 1999-2000 the Laboratories performed more than 3 million diagnosis laboratory analyses and more than 50,000 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

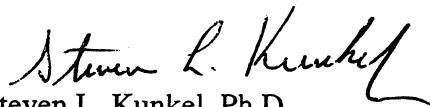
The Department of Pathology's research activities remain a strong and vibrant component of our academic mission. Faculty members continue to successfully compete for extramural research support, attract outstanding graduate and post-doctoral fellows from home and abroad, publish in highly visible, peer-reviewed scientific journals, and serve on numerous national and international scientific committees. During the past year, the expenditure of active grants and contracts credited to the Pathology Department's research efforts increased over one million dollars when compared to the previous year's expenditures. The total research expenditures for 1999-2000 were over \$11.5 million; this included approximately \$8.05 million in direct expenditures and \$3.5 million in indirect expenditures. Faculty in the Department of Pathology hold 67 individual grants from the National Institutes of Health, including a MERIT Award. Currently, the Department ranks 10th in terms of NIH support for academic Departments of Pathology. In addition, other support originates from the National Science Foundation, Department of Defense, American Heart Association, Environmental Protection Agency, American Lung Association, the American Cancer Society, and contract grants from industry.

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 SCOR. The faculty actively publish in both the clinical and experimental arena and cover very diverse scientific and molecular mechanisms of disease. This past year the faculty members in the Department of Pathology have collectively published hundreds of scholarly articles in numerous peer-reviewed scientific journals, with many of these articles appearing in journals with a high citation impact. Our faculty members participate 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 careers. Our faculty members 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 OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

- A. Surgical Pathology Services - 4 months.
- B. Necropsy Service - on call for consultation.
- C. Pathologist, Cardiac Transplant Team. Transplant biopsies - 9 months.
- D. Consultant for Gastrointestinal Pathology.
- E. Consultant for Cardiovascular Pathology.

II. TEACHING ACTIVITIES:

- A. Freshman Medical Class:
 - 1. Pathology 500, Course Director, Lecturer, "Basic Concepts of Disease" - 20 lecture hours.
 - 2. Multidisciplinary Conferences - 6 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. Cardiovascular Sequence - Pathology Lab Coordinator.
 - 2. 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. Macy Summer Science Academy - 1 lecture hour.
- F. Hospital Conferences:
 - 1. Cardiovascular Pathology Conference - monthly.
 - 2. Internal Medicine, Morbidity, Mortality Conference/CPC - quarterly
- G. House Officers:
 - 1. Training in Surgical and Necropsy Pathology.
- H. Invited Lectures:
 - 1. Keynote Address, Medical School White Coat Ceremony - August, 1999.
- I. Production of Teaching Materials:
 - 1. Production of CD-ROM for Histopathology Lab Portion of Pathology 500.
- J. Honors: Elected Class Marshall, Class of 2000

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Pathologic-Radiologic correlation in aortic disease, with D. Williams.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Member, Pathology House Officer Selection Committee.

MEDICAL SCHOOL/HOSPITAL/UNIVERSITY:

- A. Member, Historical Center for the Health Sciences Liaison Committee.
- B. Member, Component I Committee.
- C. Ombudsperson, Medical Faculty.
- D. Member, Medical School Executive Committee, through August, 1999.
- E. Member, Sesquicentennial Celebration Committee.

REGIONAL AND NATIONAL:

- A. Editorial Board, Modern Pathology.

V. PUBLICATIONS:

**ALAA M. AFIFY, M.D.
CLINICAL ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999-30 JUNE 2000**

I. CLINICAL ACTIVITIES:

- A. Cytopathology sign-out (in-house Gynecologic & Non-gynecologic cases) (10 months).
- B. Sign-out transfer cytology cases (TC) (5 months).
- C. Performance and interpretation of fine-needle aspirates at Cancer Center Clinic (5 months).
- D. Rapid interpretation of fine-needle aspirations performed by Clinicians and Radiologists (5months).
- E. Intradepartmental cytology consultations (12 months)
- F. Evaluation of immunohistochemistry control slides (12 months)
- G. Necropathy Service (5 weekends).

II. TEACHING ACTIVITIES:

- A. Residents and Cytopathology Fellow (12 months)
 - 1. Instruction in the evaluation, work-up and sign out of Gynecologic and Non-gynecologic cytopathology cases.
 - 2. Supervision and instruction in the performance, evaluation and interpretation of fine-needle aspirates from patients at the Cancer Center Clinic.
 - 3. Supervision and instruction in the evaluation and interpretation of the assisted invasive deep-seated fine-needle aspirates.
- B. Interdepartmental teaching lectures
 - 1. Didactic cytopathology lectures and microscopic oriented teaching lectures.
 - 2. Immunohistochemistry laboratory technologists teaching sessions.
- C. Laboratory instructor, M-2 pathology Labs.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- 1. Oncogenes expression in borderline serous ovarian carcinoma.
- 2. Expression of muscle markers in mesothelial cells and malignant cells obtained from body fluid cytologic specimen.
- 3. Expression of Thyroid Transcription Factor-1 in pulmonary and non- pulmonary adenocarcinoma obtained from body fluid cytologic specimen.
- 4. Fine-needle aspiration of spindle cell lesion of the head & neck: Diagnostic Accuracy, Cytologic Artifacts and Pitfalls.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

Director, Immunohistochemistry Laboratory

V. PUBLICATION:

ARTICLES PUBLISHED IN REFEREED JOURNALS:

1. Afify AM, Werness BA, Mark HF. HER-2/neu oncogene amplification in stage I and stage III ovarian papillary serous carcinoma. *Experimental & Molecular Pathology*. 66(2):163-9, 1999.
2. Werness B, Afify A.M, Eltabbakh GH, Huelsman K, Piver MS, Paterson JM. p53, c-erbB and K-67 expression in ovaries removed prophylactically from women with a family history of ovarian cancer. *International J of Gynecological Pathology*. 18(4):338-43, 1999.
3. Mark HF, Afify AM, Werness BA, Das S. Mark, Samy M. Trisomy 8 in stage I and stage III ovarian cancer detected by Fluorescent in-situ hybridization. *Experimental & Molecular Pathology*. 66(1):76-81, 1999.
4. Afify AM, Liu Jing, Al-Khafaji BM. Cytologic artifacts and pitfalls of thyroid fine-needle aspiration using ThinPrep ®: A comparative retrospective review. (Submitted).
5. Al-Khafaji BM and Afify AM. Salivary gland fine-needle aspiration using the ThinPrep ® Technique: Diagnostic accuracy, cytologic artifacts and pitfalls. (Submitted).

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

SCIENTIFIC POSTERS/ABSTRACT PRESENTATIONS:

1. Hyaluronic acid and CD44 aids in the differentiation between mesothelioma from adenocarcinoma in serous effusions. Poster presentation at USCAP meeting, 2000.
2. Cytologic artifacts and pitfalls of thyroid fine-needle aspiration using ThinPrep ®: A Comparative Retrospective Review. Poster presentation at USCAP meeting, 2000.
3. Salivary gland fine-needle aspiration using the ThinPrep ® Technique: Diagnostic Accuracy, Cytologic Artifacts and Pitfalls. Poster presentation at USCAP meeting, 2000.
4. Expression of p53, p21^{WAF1/CIP1} and Ki-67 in papillary serous carcinomas and serous tumors of low malignant potential. Poster presentation at USCAP meeting, 2000.
5. Endoscopic ultrasound-guided fine-needle aspiration of the pancreas: Diagnostic Utility & Accuracy. Poster presentation at annual scientific meeting of the American Society of Cytopathology, 2000.
6. Fine-needle aspiration of "Neck Masses" Using the ThinPrep® Technique: Diagnostic Accuracy, Cytologic Artifacts and Pitfalls. Poster presentation at annual scientific meeting of the American Society of Cytopathology, 2000.

**BASIM AL-KHAFAJI, M.D.
CLINICAL ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

- A. Cytopathology {10.5 months}
 - 1. Review & Signout of in-house cytology, Transfer cytology (TC), and intradepartmental cytology consultations. (Gynecologic & Non-Gyn).
 - 2. Performance of Fine Needle Aspiration (FNA), at Cancer Center Clinic, University Hospital, and Motts Children Hospital, to include rapid interpretation and assessment of FNAs performed by Clinicians and Radiologists (including CT, Ultrasound, Medical Procedures Unit, and outpatient clinics).
- B. Review & Signout of Genitourinary (TS) cases. {4 months}
- C. Performance, review, and signout of Autopsies. {5 weekend calls}

II. TEACHING ACTIVITIES:

- A. Cytopathology Fellow: {Full time}
 - 1. Microscopic sessions involving review of cytology preparations (Gyn & Non-Gyn).
 - 2. Supervision and instructing on performance of FNA.
 - 3. Supervision and instructing on rapid assessment of cytology preparations.
 - 4. Discussion and review of pertinent cytology literature with emphasis on diagnostic applications.
- B. Pathology Residents: {Full time}
 - 1. Introduction to the basic concepts of cytopathology through microscopic interaction.
 - 2. Instruction on FNA performance, and principles of cytopathology preparations.
- C. Medical Students:
 - 1. Pathology 600- Laboratory Instructor (24 contact hours)
 - 2. Interaction through their pathology rotation with emphasis on explaining the role of cytopathology and its interaction with the other specialties.
- D. Interdepartmental teaching lectures to include:
 - 1. Didactic Cytopathology lectures directed towards the pathology fellows and pathology residents. {three sessions}
 - 2. Microscopic oriented teaching lectures involving the residents and fellows. {three sessions}
- E. Mentor, Undergraduate Research Opportunity Program (UROP)
 - 1. Project title "DNA & Morphometric Image Analysis of Urinary Cytology", UROP project # 489, student (Sophia Saeed), winter and spring term.

2. Project title "Virtual Textbook of Cytopathology", UROP project # 603, students (Deepak K. Gupta, and Jenise Claiborne), winter and spring term.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

1. Assessment of Cytologic/Histologic correlation of nongynecological cytology with emphasis on the role of the Thin Prep technique
2. Diagnostic utility of Image morphometry in the follow-up of patients with TCC
3. Diagnostic utility of immunohistochemical markers in the follow-up of patients with TCC.
4. The diagnostic accuracy of US-guided FNA of the pancreatic masses.
5. AGUS (Atypical glandular cells of undetermined significance), identifying cytologic parameters based on cytologic/histologic and clinical follow-up.
6. Development of Web based, and Multimedia tools for cytopathology teaching, and cytopathology intra and interdepartmental consultations.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

1. Cytopathology Division Quality assurance & control.
2. Cytopathology Fellowship Training

REGIONAL & NATIONAL:

1. Elected, Member Educational Development Committee, American Society of Cytopathology.
2. Reviewer, Cancer/ Cancer Cytopathology Journal.

V. INVITED LECTURES/SEMINARS:

1. *The Virtual Textbooks: Web-based Education has the time come.* University of Texas, MD Anderson Cancer Center Faculty Development Seminar Feb 15th, 2000
2. *The Virtual Textbook of Cytopathology, Myth or Reality.* Michigan Society of Cytology, Livonia, MI, June 2000
3. *Glass Slides, Kodachromes, and Still Images: Time for Phase Retirement.* AIMCL June 2000 Meeting, University of Michigan, Ann Arbor, MI
4. *Fine Needle-Aspiration of Head & Neck Masses: The Best Kept Secrets.* Department of Otolaryngology, University of Michigan Medical School Otolaryngology for the Non Otolaryngologist: A Practical Update Seminar, October 99.

VI. AWARDS:

1. Best Web Site for advancing the field of Pathology through computer Technology. AP III 4th Annual Meeting, Pittsburgh, October 1999

VII. PUBLICATIONS:

ARTICLES PUBLISHED IN REFERRED JOURNALS:

1. Al-Khafaji, B. Neoplastic Lesions of the Oral cavity: The Common and Not so Common. *International Online Journal of Otorhinolaryngology* (Head & Neck Surgery). 3(2). 2000
2. Al-Khafaji, B. Cystic Lesions of the Neck: Differential Diagnoses with emphasis on FNA findings. *International Online Journal of Otorhinolaryngology* (Head & Neck Surgery). 3(2). 2000

ARTICLES SUBMITTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Al-Khafaji, B., Pasco-Miller, L., Zhang H. Z., Katz, RL. Chromosomal Aberrations in Renal cell Carcinoma: A Diagnostic & Prognostic Role for Cytopathology. (Cancer Cytopathology)
2. Afify A. Al-Khafaji, B., Cytologic Artifacts & Pitfalls of Thyroid FNA using ThinPrep: A Comparative Retrospective Review (Cancer Cytopathology)
3. Al-Khafaji, B., Afify A. Salivary Gland Fine-Needle Aspiration Using the ThinPrep[®] Technique: Diagnostic Accuracy, Cytologic Artifacts and Pitfalls. (Cancer Cytopathology)

ABSTRACTS PUBLISHED:

1. Al-Khafaji, B., Afify A. Salivary Gland FNA using the ThinPrep Technique: Diagnostic accuracy, Cytologic artifacts, & Pitfalls. *Modern Pathology* 13 (3), 41A, 2000. Presented in poster format at the Annual USCAP meeting, New Orleans March, 2000
2. Afify A., Al-Khafaji, B. Cytologic Artifacts & Pitfalls of Thyroid FNA using ThinPrep: A Comparative Retrospective Review. *Modern Pathology* 13 (3), 41A, 2000 Presented in poster format at the Annual USCAP meeting, New Orleans March, 2000
3. Al-Khafaji, B., Tranchida V., Afify A. Fine-needle aspiration of " Neck Masses" using the ThinPrep[®] Technique: Diagnostic accuracy, Cytologic artifacts, & Pitfalls. *Acta Cytologica* 44(5), 2000.
4. Afify A., Al-Khafaji, B. Cytologic Artifacts & Pitfalls of Thyroid FNA using ThinPrep: A Comparative Retrospective Review. *Acta Cytologica*, 44(5), 2000
5. Al-Khafaji, B., Lougee M. The Virtual Teaching Study Set: Myth or Reality. *Arch Pathol Lab Med* 124(6), 818, 2000

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL, TEACHING AND RESEARCH ACTIVITIES:

Sabbatical Year 1999-2000

Visiting Scientists, Parke-Davis Pharmaceutical, Ann Arbor Michigan

Projects:

1. SELDI Mass Spectrometry Assay Development – Insulin, VEGF
2. LC-MS-MS Characterization of Fosphenytoin Metabolites
3. Free and Total PSA by Solid Phase Immunoassay

SPONSORED SUPPORT:

Visiting Scientist Salary Support, Parke-Davis Pharmaceutical, \$25,000.

II. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Biochemistry Section, Clinical Pathology Laboratories
- B. M-Labs Technical Group
- C. Coordinator, Clinical Pathology Laboratory CME Program
- D. Clinical Pathology Discretionary Incentive Funds Committee

REGIONAL AND NATIONAL:

- A. Board of Directors, National Academy of Clinical Biochemistry
- B. House of Delegates, American Association for Clinical Chemistry
- C. Membership Committee, American Association for Clinical Chemistry
- D. Executive Committee/Journal Management Group, Clinical Chemistry Journal
- E. Member, Academy of Clinical Laboratory Physicians and Scientists
- F. Member, National Academy of Clinical Biochemistry
- G. Member, Association of Clinical Scientists
- H. Member, American Society for Mass Spectrometry

III. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

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

OTHER:

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

IV. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Judd, W.J., Storry, J.R., Annesley, T.M., Reid, M.E., Bensette M., Rohrkemper, D., and Valdez, R.: First example of a paraben-dependent antibody to an Rh antigen. *Transfusion*, 2000.
2. Roberts, W., Annesley, T., De, B., and Moyer, T.: Free phenytoin measurements by four immunoassays compared to HPLC. *Ther. Drug Monitor.*, 2000.

ABSTRACTS:

1. Shum, Y.Y, Bradbury., L., and Annesley, T.M.: Vascular endothelial analysis by SELDI-MS. *Proceedings of the 9th analytical research symposia*, 1999.
2. DE, B.K., Annesley, T.M., Moyer, T.P., and Roberts, W.L.: Evaluation of the Cobas Integra free phenytoin immunoassay. *Clin. Chem.* 2000;46:A192.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

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 - (1 1/2 hours/month).
 - 2. Liver Biopsy Conference - one hour per month.
 - 3. Gastrointestinal Biopsy Conference for Gastrointestinal fellows and staff, 3 hours

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Are there specific histologic types of colonic adenomas that are more likely to recur, with Klaus Lewin (UCLA) and members of the National Cancer Institute, Chemoprevention Branch
- B. 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 Harvard.
- C. What gastric stromal tumors are always benign"? with Carolyn Misick and members of the pathology department at the Cleveland Clinic
- D. Lymphocyte colitis, a comprehensive clinical/endoscopic/histologic study, with Rachel Vidal and members of the division of Gastroenterology.

- E. Anaplastic, lymphoma-like carcinoma arising in Barrett's mucosa, with BJ McKenna, T Nazeer, and A del Rosario, of Albany Medical Center
- F. Neoplasms of the small intestines, a survey, with BJ McKenna of Albany Medical Center
- G. Adenomas of the duodenum: are there differences between sporadic and FAP-associated? With Paul Kowalski
- H. Is hyperplasia of the interstitial cells of Cajal a common reaction to intramural masses in the gut? With Neil Bavakaty
- I. The apoptotic form of microscopic colitis, with a consortium of pathologists from around the country
- J. The status of the squamous mucosa next to segments of Barrett's esophagus, with WL Lo and Jeffrey Barnett

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Chairman, Advisory Committee on Appointments, Promotions and Tenure
- B. Internal Review Committee, 1999

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, International Organization for Statistical Studies of Diseases of the Esophagus, Paris, France.
- B. Visiting Pathologist for Regional Workshops on Pathologic Diagnosis in Inflammatory Bowel Disease, sponsored by the Crohn's and Colitis Foundation of America and the University of Chicago.
- C. Central Pathologist, Polyp Prevention Trial, National Cancer Institute, Washington, DC
- D. Member, Editorial Board, Human Pathology.
- E. Member, Editorial Board, Modern Pathology.
- F. Member, Editorial Board, American Journal of Surgical Pathology.
- G. Ad hoc reviewer for American Journal of Pathology, Gastroenterology, and American Journal of Gastroenterology.
- H. Member of the Council, member of the Ad hoc Nominating Committee, member of the Young Investigator's Committee, United States and Canadian Academy of Pathology, Inc

V. OTHER RELEVANT ACTIVITIES:

- 1. Distinguished Service Award Honoring George F. Stevenson, MD, the American Society of Clinical Pathologists, Oct 1999
- 2. Visiting Professor, Department of Pathology, University of Iowa, May, 2000

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 course, Chicago, IL, July, 23, 1999
2. "Cancers just above, within and just below the gastroesophageal junction: are they the same or different, and how do we know?" lecture at the Gastrointestinal Pathology Society course, Update on Esophageal Pathology, Annual meeting, American Society of Clinical Pathologists, New Orleans, LA, Sept 24, 1999
3. "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, New Orleans, LA, Sept 25, 1999
4. "Gastrointestinal biopsies that have either a differential diagnosis or no diagnosis", seminar for the Greater Detroit Pathology Society, Dearborn, MI, April 11, 2000
5. "Neoplastic diseases of the intestines", half day course, Pathology of the Gastrointestinal Tract, American Society of Clinical Pathologists, Aspen, CO, May 10, 2000
6. "Gastrointestinal stromal tumors are as annoying in the new millennium as they were in the old." Visiting Professor lecture, University of Iowa, Iowa City, IA, May 17, 2000
7. "Changing patterns and recognition of the pathology of inflammatory bowel diseases", lecture during the American Gastroenterological Association Clinical Symposium, San Diego, CA, May 24, 2000

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Tworek JA, Goldblum JR, Weiss SW, Greenson JK, Appelman HD. Stromal tumors of the abdominal colon: a clinicopathologic study of 20 cases. *Am J Surg Pathol.* 23:937-945, 1999
2. Tworek JA, Goldblum JR, Weiss SW, Greenson JK, Appelman HD. Stromal tumors of the anorectum: a clinicopathologic study of 22 cases. *Am J Surg Pathol.* 23:946-954, 1999
3. Appelman HD. Guest Editorial: The Carney triad: a lesson in observation, creativity, and perseverance. *Mayo Clin Proc.* 74:638-640, 1999
4. Kim B, Barnett JL, Kleer CS, Appelman HD. Endoscopic and histologic patchiness in treated ulcerative colitis. *Am J Gastroenterol.* 94:3258-3262, 1999
5. Fontana RJ, McCashland TM, Benner KG, Appelman HD, et al. Acute liver failure associated with prolonged use of bromfenac leading to liver transplantation. *Liver Transplantation and Surgery.* 5:480-484, 1999
6. Valdez R, Appelman HD, Bronner MP, Greenson JK. Diffuse duodenitis associated with ulcerative colitis, accepted for publication, *Am J Surg Pathol*

CHAPTERS AND BOOKS:

1. Kleer CG, Appelman HD: Pathology of Crohn's disease, accepted for publication, Surgical Clinics of North America, WB Saunders, Philadelphia, 2000
2. McKenna BJ, Appelman HD, Neoplasms of the small intestine, in Quigley EE and Marsh MN, eds.: The Small Intestine, Blackwell Scientific, Cambridge, MA, 2000
3. McKenna BJ, Appelman HD. Barrett's esophagus: morphologic considerations. in Orringer MB, ed.: Shackelford's Surgery Of The Alimentary Tract - Vol 1, The Esophagus. W B Saunders, Philadelphia, in press

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

1. Trupiano JK, Goldblum JR, Stewart RE, Appelman HD, Misick C: Gastric stromal tumors (GST): correlation of features with aggressive clinical behavior. Mod Pathol. 13:90A, 2000
2. Kresty LA, Stoner GD, Normolle D, Beer DG, Appelman H, et al. Analysis of Ki-67 and P53 in patients with non-dysplastic intestinal type Barrett's esophagus. Cancer Research, 2000

**THEODORE F. BEALS, M.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

- A. Diagnostic Electron Microscopy, Veterans Affairs Medical Center; Director of Electron Microscopy Center of Excellence.
- B. Cytopathology, Veterans Affairs Medical Center.
- C. Surgical Pathology, Veterans Affairs Medical Center.
- D. Fine Needle Aspiration, Veterans Affairs Medical Center.
- E. Autopsy Pathology, Veterans Affairs Medical Center.
- F. Tumor Board, Veterans Affairs Medical Center.
- G. Chief Pathology and Laboratory Medicine, Ann Arbor Veteran Affairs Health Systems.

II. TEACHING ACTIVITIES:

- A. Pathology House Officer elective: Diagnostic Electron Microscopy and Cytopathology.
- B. Diagnostic Electron Microscopy Case Conference.
- C. M2 Pathology Laboratory, Medical School

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Tumor suppressor gene loci on chromosome 18 and prognosis in squamous cell carcinoma. (Co-investigator, Thomas E. Carey PI)
- B. Head and Neck Oncology Program Project. (G.T.Wolf)

PROJECTS UNDER STUDY:

- A. Clinical relevance of ultrastructural characteristics of small cell carcinoma of lung.
- B. Utilization of plastic embedded cell blocks and electron microscopy in fine needle aspiration cytology.
- C. DNA content as a predictor of chemotherapeutic response and prognosis in squamous cell carcinoma of the larynx. (with C. Bradford).
- D. Differentiation of isolated renal tubular epithelial cells in culture (with D. Humes).
- E. Apoptosis in lung injury (with J.L. Curtis).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Electron Microscopy Committee.

MEDICAL SCHOOL/HOSPITAL:

- A. Clinical Executive Committee, Veterans Affairs Medical Center.
B. Professional Standards Board, Veterans Affairs Medical Center.
C. Invasive Procedures Review Committee, Veterans Affairs Medical Center.
D. Electron Microscopy Committee, Veterans Affairs Medical Center.
E. Information Management Committee, Veterans Affairs Medical Center.
F. Cancer Committee, Veterans Affairs Medical Center.
G. Coordinator of Data Processing for Pathology and Laboratory Medicine Service, Veterans Affairs Medical Center.
H. Dean's Committee, Veterans Affairs Medical Center.
I. Facility Management Committee, VISN#11, Department of Veteran Affairs.

REGIONAL AND NATIONAL:

- A. Department of Veteran Affairs, Veterans Health Administration, Patient Care Services, Chief Consultant Officer, Diagnostic Services Strategic Healthcare Group.
B. Department of Veterans Affairs, Veterans Health Administration, Director Pathology and Laboratory Medicine.
C. National Veterans Affairs Pathology Field Advisory Board.
D. Armed Forces Institute of Pathology, Scientific Advisory Board.
E. Association of Pathology Chairs, Veterans Affairs Committee, Consultant.
F. National Veterans Affairs Cytopathology Committee, Chair.
G. National Veterans Affairs Surgical Pathology Committee, Chair.
H. National Veterans Affairs Diagnostic Electron Microscopy Ad Hoc Advisory Group.
I. Pathology Intersociety Council, Member.
J. Department of Veterans Affairs, Veterans Health Administration, Office of Information Technology, Clinical Applications Requirement Group.
K. Department of Veterans Affairs, Veterans Health, Administration, Office of Information Technology, Laboratory Expert Panel on Government Computerized Patient Record.
L. National Committee for Clinical Laboratory Standards, Delegate.
M. Department of Veterans Affairs, Veterans Health Administration, Telemedicine Field Advisory Group.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Predictive markers for response to chemotherapy, organ preservation, and survival in patients with advanced laryngeal carcinoma. CR Bradford, GT Wolf, TE Carey, S Zhu, TF Beals, JM Truelson, KD McClatchey, SG Fisher Otolaryngol Head Neck Surg 121:534-8, 1999

BOOKS AND CHAPTERS IN BOOKS:

1. Successes in Autopsy Practice. Publication of Veterans Health Administration. 1999

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

1. Telemedicine in the Veterans Health Administration. The American Telemedicine Association Annual Meeting, 1999.
2. Early Onset Post-Irradiation Sarcoma of the Head and Neck. Am Acad Otol- Head and Neck Surg, 1999

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

- A. Six and a half months of Neuropathology Service.
- B. Three weeks of Autopsy Service and seven weekends autopsy calls.
- C. Muscle and nerve biopsies at the UMHS and referred by other hospitals in- and out-of-state throughout the year.
- D. Consultations on brain biopsies, autopsied brains and rheumatology cases.
- E. Coverage of muscle and nerve biopsies for MSU.
- F. Diagnoses on autopsied brains for ADRC program.

II. TEACHING ACTIVITIES:

- A. Taught residents, fellows and staff in Neurology, Rheumatology and Pediatrics and medical and dental students on muscle, nerve and brain biopsies.
- B. Taught Pathology Residents how to perform and read-out autopsies.
- C. Lectures on muscle, nerve and brain pathology to residents and fellows in Pathology, Neurology, and Neurosurgery.
- D. Conferences on muscle and nerve cases with Neurology Department.
- E. Neuropathology cases review with Pathology Residents.
- F. Weekly Conferences with Neuromuscular staff.
- G. Conferences and lectures for Neurosurgery Residents and staff.
- H. Monthly conferences for Rheumatology residents and staff.
- I. Personal tutoring of neurology and pathology residents on Neuropathology – 9 persons
- J. A month with a Japanese visiting pathologist from Nagoya.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Histology of animal models of rheumatoid arthritis with Arthritis and Rheumatology with Blake Roessler.
- B. Urethral musculature in aging and incontinence, with John DeLancey group, Obstetrics/Gynecology.
- C. Rat model in brain tumors growth and treatment, with Neurosurgery Department (Philip Kish, grant application submitted.)
- D. Co-investigator on P.E. McKeever, M.D. grant “Glioma Tissue Markers of Potential Diagnostic and Prognostic Value.”

- E. Evaluation of temporal lobectomy/hippocampectomy cases with Erasmo Passaro, M.D., and the epilepsy group (grant submitted).
- F. Several projects with the epilepsy Division of Neurology.
- G. Collaboration with EMG group, Radiology (S. Gebarski, M.D.), neurosurgery, pulmonary/internal medicine and ophthalmology on various projects.
- H. Supervision of histology/immunohistochemistry projects for residents, fellows and researchers in Neurosurgery, Neurology and Neuroscience labs.
- I. ADRC grant, co-investigator (diagnosis of dementia in autopsied brains).

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.
- D. Daily monitoring muscle histochemistry group performance.

MEDICAL SCHOOL:

- A. Member of the Admissions Committee.

REGIONAL AND NATIONAL:

- A. Neuropathology conferences for pathology residents, St. John Hospital in Detroit (until 8/00).
- B. Consulting with outside pathologists, neurologists and family practitioners on muscle and nerve biopsies performance and interpretation, brain biopsies.
- C. Invited lecture to Medical College of Ohio Neurology.
- D. Member, American Association of Neuropathologists, IAP, CAP, PNS, and AAN.
- E. Attended the meeting of American Association of Neuropathologists with posters presentation.
- F. AANP Awards Committee, member.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN PEER REVIEWED JOURNALS:

1. *Galasso JM, Stegman LD, Blaivas M, Harrison JK, Ross BD, Silverstein FS: Transplanted 9L gliosarcomas induce expression of the monocyte chemoattractant Protein-1 receptor, CCR2, in rat brain. *Experimental Neurology* 2000, 161:85-95.
2. *Alrawi A, Trobe JD, Blaivas M, Musch DC: Brain biopsy in primary angitis of the central nervous system.: *Neurology* 1999, 53:858-860.

3. *Pandit M, DeLancey OL, Iyengar J, Blaivas M, Ashton-Miller JA: Development of techniques to quantify urethral nerve size and distribution: histological methods. Accepted to Obstetrics and Gynecology.
4. *Pandit M, DeLancey JOL, Ashton-Miller JA, Iyengar J, Perocchini D, Blaivas M: Quantification of the intramuscular nerves within the female striated urogenital sphincter muscle. Accepted to Obstetrics and Gynecology.
5. *Smith AG, Blaivas M, Russel JR, Urbanits S, Grisold W, Feldman EL: The clinical and pathologic features of focal myositis. Muscle and Nerve, in press.
6. *Gorelick J, Ross DA, Merentette L, Switz K, Blaivas M: Sinonasal undifferentiated carcinoma: a case series and review of the literature. Neurosurgery, in press.
7. *Herrmann DN, Wald JJ, Blaivas M, Feldman EL: Granulomatous myositis, primary biliary cirrhosis, pancytopenia and thymoma: a case report and review of the literature. Muscle and Nerve, in press.
8. Scott RS, Blaivas M, et al: The pathology of REM sleep behaviour disorder with comorbid Lewy body dementia. Accepted to Neurology.

* Resident or Fellow

ARTICLES SUBMITTED FOR PUBLICATION:

1. *Rickman DS, Tyagi R, Zhu X-X, Bober MP, Song S, Blaivas M, Miser DE, Israel M, Ross DA, Kish PE, Hanash SM: The axonal cell adhesion molecule TAX-1 is aberrantly expressed in malignant gliomas: To: Nature.
2. *Fishman S, Blaivas M, Fink JK: Levodopa-carbidopa responsiveness in African-American subject with Machado-Joseph Disease type IV. To: Neurology.
3. Kish PE, Blaivas M, Strawderman M, Muraszko KM, Ross DA: Magnetic resonance imaging of ethyl-nitrosourea-induced rat gliomas: a model for experimental therapeutics of low-grade gliomas. To: Neuro-oncology.
4. *Flaherty KR, Wald J, Zeballos RJ, Blaivas M, Weisman IM, Schork MA, Zisman D, Rubenfire M, Martinez FJ: Unexplained exertional limitation: characterization in a large cohort discovered to have mitochondrial myopathy. To: Annals of Internal Medicine.

* Resident or Fellow

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

1. Gebarski SS, Blaivas M: Adult primary brain neoplasms: the role of the germinal matrices. Presented at RSNA 85th Scientific Assembly and Annual Meeting, 1999.
2. Pandit M, DeLancey JOL, Iyengar J, Blaivas M, Ashton-Miller J: Quantification of circular and longitudinal smooth muscle in the ventral wall of the female urethra. Presented at the American Urogynecology Society fall meeting, 1999.
3. Kish PE, Blaivas M, Strawderman M, Muraszko KM, Ross DA: Magnetic resonance imaging of ethyl-nitrosourea-induced rat gliomas; anti-progression effects of vitamin A. Presented at Neuro-Oncology Meeting, Fall 1999.

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4. Blaivas M, Greenberg HS, Gebarski SS: Sarcomatoid mesothelioma metastatic to spinal roots and probably to cranial nerves. *J Neuropathology* 59(5): 440, 2000. Presented at AANP Meeting, Atlanta, GA, June 8-11, 2000.
5. *Hedera P, Fink JK, Blaivas M: A family of three and one unrelated patient with CADASIL in Michigan. Diagnosis of brain and skin. *J Neuropathology* 59(5): 430, 2000. Presented at AANP Meeting, Atlanta, GA, June 8-11, 2000.
6. Blaivas M, Gebarski S: Complex "embryonal" glio-neuronal tumors in adults defy WHO classification. Admitted for presentation at the XIVth International Congress of Neuropathology, Birmingham, United Kingdom, September 2-9.
7. Gebarski S, Blaivas M: Oligoastrocytoma: a geminal matrix neoplasm. To be presented at the RSNA Annual Meeting, Chicago, IL, November/December 2000.

* Resident or Fellow

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

**ANNUAL DEPARTMENT REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

- A. Director, Clinical Laboratories, Veterans Affairs Medical Center, responsibilities include, equipment and methodology evaluation, review and consultation regarding quality management programs, personnel evaluation, counseling and grievance procedures.
- B. Hematology, daily evaluation of pathologist referred blood smears, bone marrow smears, Veterans Affairs Medical Center (approx 300 cases/1999).
- C. Surgical/Frozen Section Diagnosis (approx 250 cases/1999)
- D. Surgical Case Diagnosis (4 months in 1999, approx. 1800 cases) Veterans Affairs Medical Center.
- E. Autopsy Service, rotational basis, on call 13 weeks/year (staffing 11 cases in 1999).
- F. Special Chemistry/Immunology, daily interpretation of protein electrophoreses and problem ligand studies (approx 900 cases/1999), Veterans Affairs Medical Center.
- G. Blood Bank, consults and investigations, full time as needed, Veterans Affairs Medical Center.

II. TEACHING ACTIVITIES:

- A. Pathology house officers, Surgical Pathology/Autopsy supervision and instruction, (5 months/year)
- B. Medical Students, Pathology 600 laboratory (33 contact hours)
- C. Technologists, technicians and hospital staff, ongoing continuing medical education instruction on clinical laboratory topics.
- D. Graduate and undergraduate students, research project mentoring.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, Cytokine Cascades in Granuloma Formation, VAMC Merit Review Grant, (\$93,000 direct costs annually, 1997-2000).
- B. Principal Investigator, Chemokine Receptor Dynamics in Granuloma Formation, NIH AI43460 (\$115,000 direct costs annually, 1998-2001)
- C. Principal Investigator, Prostate Carcinoma Bone Metastasis in a SCID-hu Mouse Model, VERAM (\$5,000)
- D. Co-investigator, 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. Regulation of chemotactic cytokine production by leukocytes and stromal cells.
- E. Analysis of eosinophil recruitment factors in type 2 granulomatous inflammation.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

- A. Blood Utilization Review Committee, Veterans Affairs Medical Center, Chairman.
- B. Ambulatory Care Committee, Veterans Administration Medical Center.
- C. Personnel employment and annual evaluations.
- D. Anatomic Pathology Quality Assurance evaluation and reporting
- E. Editor, VALabs Newsletter.

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

V. OTHER RELEVANT ACTIVITIES:

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

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Bergerot, I., Arreaza, G.A., Cameron, M.J., Burdick, M.D., Strieter, R.M., Chensue, S.W., Chakrabarti, S., and Delovitch, T.L. Insulin B-chain reactive CD4 (+) regulatory T-cells induced by oral insulin treatment protect from type 1 diabetes by blocking the cytokine secretion and pancreatic infiltration of diabetogenic effector T-cells. *Diabetes*. 48:1720-1729, 1999
2. Hogaboam, G.M., Bone-Larson, C.L., Lipinski, S., Lukacs, N.W., Chensue, S.W., Strieter, R.M., and Kunkel, S.L. Differential monocyte chemoattractant protein-1 and chemokine receptor 2 expression by murine lung fibroblasts derived from Th1-and Th2-type pulmonary granuloma models. *J. Immunol*. 163:2193-2201, 1999
3. Moormann A.M., Sullivan A.D., Rochford R.A., Chensue S.W., Bock P.J., Nyirenda T., Meshnick S.R. Malaria and pregnancy: Placental cytokine expression and its relationship to intrauterine growth retardation. *J. Infect. Dis*. 180:1987-1993, 1999
4. Ruth, J.H, Warmington, K.S., Shang, X., Lincoln, P., Evanoff, H., Kunkel, S.L., and Chensue S.W. Interleukin-4 and -13 participation in mycobacterial (type-1) and schistosomal (type-2) antigen-elicited pulmonary granuloma formation: Multiparameter analysis of cellular recruitment, chemokine expression and cytokine networks. *Cytokine* 2000, in press.
5. Tong-Yuan Yang, Chen, S-C., Leach, M.W., Manfra, D., Homey, B., Wiekowski, M., Sullivan, L., Jenh, C-H., Narula, S.K., Chensue, S.W. and Lira, S.A. Transgenic expression of the chemokine receptor encoded by HHV8 induces an angioproliferative disease resembling Kaposi's sarcoma. *J. Exp. Med*. 2000, 191:445-453.
6. Matsukawa, A., Lukacs, N.W., Standiford, T. J., Chensue, S.W. and Kunkel, S.L. Overexpression of MCP-1 differentially alters development of Th1 and Th2 type responses in vivo. *J. Immunol*. 2000, in press.
7. Lukacs, N.W., Hogaboam, C., Chensue, S.W., Blease, K. and Kunkel, S.L. Type-1/Type-2 cytokine paradigm and the progression of pulmonary fibrosis. *Chest*, 2000, in press.
8. Kunkel, S.L. Chensue, S.W., Colletti, L., Standiford, T., Lukacs, N., Strieter, R.M. Cytokine networks and leukocyte recruitment. *Cytokines in Pulmonary Disease: Infection and Inflammation*. 2000, 141:19-35.

BOOKS AND CHAPTERS IN BOOKS:

1. Kunkel, S.L., Lukacs, N.W., Strieter, R.M., Standiford, T. and Chensue, S. W. The function of chemokines in health and disease. In, *Chemokines and Cancer*. pp. 3-19. 1999.

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

1. Qiu, B., Reich, F., Frait, K.A., and Chensue, S.W. Chemokine profiles during mycobacterial (type-1) and schistosomal (type-2) antigen-elicited lung granuloma formation. *FASEB J*. 2000, 14(4): A489.6.

2. Shang, X.Z., Frait, K.A. and Chensue, S.W. Chemokine receptor expression among CD4+ T cells participating in mycobacterial (Type-1) and schistosomal (Type-2) antigen-elicited granuloma formation. *FASEB J.* 2000, 14(6): A1096.
3. Hogabaom, C.M., Blease, K., Mehrad, B., Standiford, T.J., Lukacs, N.W., Chensue, S.W., Lu, B., Gerard, C., and Kunkel, S.L. Airway remodeling is absent in CCR1^{-/-} mice during chronic fungal allergic airway disease. *FASEB J.* 2000, 14(6): A1067.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

- A. Gynecological pathology consultation services – six months.

II. TEACHING ACTIVITIES:

- A. Postdoctoral Fellows:
Responsible during the current academic year for the following:
1. Denise C. Connolly, Ph.D.
 2. Rong Wu, M.D.
 3. Donald Schwartz, Ph.D.
 4. Ya-Li Zhai, Ph.D.
 5. Xiaodan Ren, Ph.D. (6 months)
 6. Amy Ferguson, M.D. (3 months)
- B. Graduate students:
Course Faculty, Pathology 581 – two lecture hours
- C. Undergraduate students:
Danielle Darrah
- D. House Officers:
Two staff consultation conferences
- E. Interdepartmental:
Multidisciplinary Gynecologic Oncology tumor board – one hour twice per month
Cancer Biology Journal Club: Faculty Supervisor
- F. National:
Course Faculty: Molecular Biology in Clinical Oncology Workshop, American Association for Cancer Research, The Given Institute, Aspen, Colorado.
- G. International:
Course Faculty: 10th Anniversary Annual Review Course on Gynecologic Oncology and Pathology, Kyoto, Japan

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Studies of the Molecular Pathogenesis of Cervical Cancer", NIH R29 CA64466 (50% effort), \$73,743 annual direct costs, April 1, 1995 – March 31, 2000.

- B. Principal Investigator, "FHIT Gene Alterations in Cervical Cancer Pathogenesis", NIH RO1 CA81587 (30% effort), \$171,441 annual direct costs, September 1, 1998 - August 31, 2001.
- C. Principal Investigator, Project 2 ("Molecular Profiling of Ovarian Cancer", 15% effort). NIH: U19 CA84953-01 (Hanash). "Toward a Molecular Classification of Tumors," Project #2 Annual Direct Costs: \$95,129, September 30, 1999 – March 31, 2004.
- D. Co-Investigator (10% effort), "CDX2 Tumor Suppressor Pathway Defects in Colon Cancer", NIH 1R01CA82223-01 (Fearon). Annual Direct Costs: \$147,301, August 15, 1999 – May 31, 2004.
- E. Co-Investigator (10% effort), "The Role of β -Catenin/Tcf Pathway Defects in Cancer." NIH 1R01CA85463-01 (Fearon)(6/1/00-5/31/05). Annual Direct Costs: \$200,000, June 1 2000 – May 31, 2005.
- F. Sponsor of postdoctoral fellow (Dr. Donald Schwartz) in the Cancer Biology Training Program, University of Michigan Comprehensive Cancer Center, NIH 5T32CA09676-08, salary support from July 1, 1999 – June 30, 2001.

PENDING: None

PROJECTS UNDER STUDY:

- A. Evaluation of loss of Fhit protein expression as a tumor progression and/or prognostic marker for cervical cancer.
- B. Development of an in vitro model of cervical cancer progression
- C. Molecular profiling of ovarian epithelial tumors using 2-D gel approaches and DNA microarray technologies.
- D. Identification and characterization of novel genes differentially expressed in ovarian carcinomas.
- E. Characterization of genetic alterations in poorly differentiated (anaplastic) colorectal carcinomas.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Departmental Self-Study Committee

REGIONAL AND NATIONAL:

- A. Member, Oral Biology and Medicine 1 Study Section, National Institutes of Health, 1998-2001.
- B. Member, Special Conferences Committee, American Association for Cancer Research, 1999-2002
- C. Co-Organizer, Molecular Biology in Clinical Oncology Workshop, American Association for Cancer Research, 2000.
- D. Member, National Comprehensive Cancer Center Panel for establishment of endometrial and cervical cancer treatment guidelines, 1997-present.

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. Ad hoc reviewer for *Journal of the National Cancer Institute*, *Journal of Clinical Investigation*, *Neoplasia*, *American Journal of Pathology*, *Laboratory Investigation*, *Modern Pathology*, *International Journal of Cancer*

INVITED LECTURES/SEMINARS:

- 1. Molecular Biology of Gynecological Tumors. Molecular Biology in Clinical Oncology Workshop, American Association for Cancer Research, The Given Institute, Aspen, Colorado, July 1999.
- 2. Molecular Biology of Cervical Cancer. Gynecologic Oncology Group Semi-Annual Meeting. Scottsdale, Arizona, July 1999.
- 3. 10th Annual Review Course on Gynecologic Oncology and Pathology. Lectures on "Molecular Biology of Ovarian Cancer", and "New Tools for Molecular Profiling of Human Cancer". Kyoto, Japan, November 1999.
- 4. Pathology Grand Rounds. "The Molecular Pathology of Cervical Cancer". Thomas Jefferson University Dept. of Pathology, Anatomy, and Cell Biology. Philadelphia, Pennsylvania, December 1999.
- 5. HPV and Beyond: The Molecular Biology of Cervical Cancer. Postgraduate Course at The Society of Gynecologic Oncologists (SGO) Annual Meeting. San Diego, California, February 2000.

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Szych, C., Staebler, A., Connolly, D.C., Wu, R., Cho, K.R., and Ronnett, B.M. Molecular Genetic Evidence Supporting the Appendiceal Origin of Pseudomyxoma Peritonei in Women. *American Journal of Pathology* 154:1849-55, 1999.
- 2. Wu, R., Connolly, D.C., Ren, X., Fearon, E.R., and Cho, K.R. Somatic Mutations of the *PPP2R1B* Candidate Tumor Suppressor Gene at Chromosome 11q23 are Infrequent in Ovarian Carcinomas. *Neoplasia* 1:311-314, 1999.
- 3. Connolly, D.C., Katabuchi, H., Cliby, W.A., and Cho K.R. Somatic Mutations in the *STK11/LKB1* Gene are Uncommon in Rare Gynecological Tumor Types Associated with Peutz-Jeghers Syndrome. *American Journal of Pathology* 156:339-345, 2000.

4. Wu, R., Connolly, D.C., Dunn, R.L., and Cho, K.R. Restored Expression of Fragile Histidine Triad (Fhit) Protein and Tumorigenicity of Cervical Carcinoma Cells. Journal of the National Cancer Institute 92:338-44, 2000.
5. Kolligs, F.T., Kolligs, B., Hajra, K.M., Hu, G., Tani, M., Cho, K.R., and Fearon, E.R. γ -Catenin is regulated by the APC tumor suppressor and its oncogenic activity is distinct from that of β -catenin. Genes and Development 14:1319-1331, 2000.
6. Connolly, D.C., Greenspan, D.L., Wu, R., Ren, X., Dunn, R.L., Shah, K.V. Jones, R.W., Bosch, F.X., Muñoz, N., and Cho, K.R. Loss of Fhit expression in invasive cervical carcinomas and intraepithelial lesions associated with invasive disease. Clinical Cancer Research (in press).

ARTICLES SUBMITTED OR IN PREPARATION:

1. Wu, R., Connolly, D.C., Bosch, F.X., Muñoz, N., and Cho, K.R. Somatic mutations of fibroblast growth factor receptor 3 (FGFR3) are uncommon in carcinomas of the uterine cervix (submitted).
2. Hough, C.D., Sherman-Baust, C.A., Pizer, E.S., Montz, F.J., Im, D.D., Rosenshein, N.B., Cho, K.R., Riggins, G.J., and Morin, P.J. Large-scale serial analysis of gene expression (SAGE) reveals genes differentially expressed in ovarian cancer (submitted).

BOOKS/CHAPTERS IN BOOKS:

1. Cho, K., and Hedrick, L. Molecular Biology. In Blaustein's Pathology of the Female Genital Tract, 5th edition, ed. Robert J. Kurman, Springer-Verlag, New York, Inc., in preparation.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

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

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. The Pathologic Examination of Human Autopsy Brains From Patients With Clinical Diagnosis of Alzheimer's, Huntington's, Pick's, and Other Dementing Diseases is being

done in collaboration with Drs. Roger Albin, Sid Gilman, and Norman Foster in the Michigan Alzheimer Disease Research Center, and 1999 - with R. Scott Turner, M.D., transgenic mouse model of plaques similar to Alzheimer's disease.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Anatomic Pathology Committee.
- B. Organize and teach the Neuropathology 858 Course.

MEDICAL SCHOOL/HOSPITAL:

- A. Coordinator for the Neuroscience Sequence, 2nd year medical students.
- B. Neuroscience Curriculum Committee, Chairman.
- C. Coordinator for Neuropathology, Neuroscience Sequence.
- D. Neuroscience Examination Committee, Chairman.
- E. Admissions Committee, the University of Michigan Medical School.
- F. Curriculum Policy Committee (Elected).

REGIONAL AND NATIONAL:

- A. American Association of Neuropathologists.
- B. American Academy of Neurology.
- C. Society for Neuroscience.
- D. Michigan Chapter: Society for Neuroscience.

V. OTHER RELEVANT ACTIVITIES:

INVITED PRESENTATIONS:

- 1. "Alzheimer's Disease and Other Dementias," Alzheimer's Association, Eastern Michigan University and McCauley Health Center, March 2000.
- 2. "Brain Autopsy and its Importance in Diagnosis": 4th Alzheimer's Association Schreiber Conference, Kalamazoo, Michigan, May 2000.

VI. PUBLICATIONS:

ARTICLES ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS, BOOK CHAPTERS:

- 1. Kluin, K.J., Gilman, S., Foster, N.L., Sima, A.A.F., D'Amato, C.J., et al: Neuropathologic correlates of dysarthria in progressive supranuclear palsy. Revised for Archives of Neurology, June 2000.
- 2. Dickson, D.W., Liu, W.K., Hardy, J., Farrer, M., Mehta, N., Utti, R., Mark, M., Zimmerman, T., Golbe, L., Sage, J., D'Amato, C.J., et al: Widespread alterations in alpha-synuclein in multiple system atrophy. American J. Pathology, 1999, 155:1241-1251.

3. Sima, A.A.F., D'Amato, C, Foster, N.L.: Neuropathology of Chromosome -17- Linked Dementia. *Dement. Geriatr. Cogn. Disord.*, 1999, 10 (suppl):61-63.
4. Turner, R.S., D'Amato, C.J., Chervin, R.D., Blaivas, M.: The Pathology of REM sleep behavior disorder with comorbid Lewy body disease. In press, *Neurology*, 2000.

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

1. Alton, S.J., D'Amato, C.J., Gratsch, T.E., McDonough, K.L., Cerebellar implantation of embryo stem cell derived neuroepithelial progenitor cells. Society for Neuroscience, 2000.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

- A. Associate Medical Director, Blood Bank and Transfusion Service, University of Michigan Hospitals.

II. TEACHING ACTIVITIES:

- A. Introductory Course in Blood Banking/Transfusion Medicine for Pathology House Officers.
- B. Daily teaching rounds for Pathology House Officers assigned to the Blood Bank.
- C. Current Topics in Blood Banking Conference, Towsley Center for Continuing Medical Education.
- D. M4 Pharmacology course, Blood transfusion.
- E. Clinical Pathology Grand Rounds, Adverse effects of transfusion
- F. Michigan Association of Blood Banks, Non-hemolytic transfusion reactions
- G. Michigan Association of blood Banks, Immune responses
- H. American Association of Blood Banks, Regulation of immune responses

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "A Murine Model of Hemolytic Transfusion Reactions", National Blood Foundation.
- B. Principal Investigator, "Postmarketing Pharmacovigilance of SD-Plasma", V. I Technologies, Inc.
- C. Principal Investigator, "Evaluation of Solvent/Detergent-Treated Plasma, Isoagglutinin Depleted, in Normal Healthy Volunteers",

PROJECTS UNDER STUDY:

- A. Cytokine production in hemolytic transfusion reactions.
- B. Mechanisms of hypotensive transfusion reactions.
- C. Viral Safety of solvent/detergent treated plasma.
- D. Isoagglutinin-depleted plasma.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

- A. Transfusion Committee.

V. OTHER RELEVANT ACTIVITIES:

- A. Past-President, Michigan Association of Blood Banks.
B. Executive Committee, Michigan Association of Blood Banks.
C. Program Committee, Michigan Association of Blood Banks.
D. Scientific Section Coordinating Committee, American Association of Blood Banks.
E. Medical Advisory Committee, American Red Cross Southeastern Michigan Region.
F. Editorial Board, Transfusion.
G. Reviewer, Transfusion.
H. Reviewer, Chest.
I. Reviewer, American Journal of Clinical Pathology.
J. Reviewer, Journal of Clinical Investigation.

VI. PUBLICATIONS:

ARTICLES SUBMITTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Penezina OP, Davenport RD. The Expression of Platelet Activation-Specific Markers during short-term Storage of Citrated Whole Blood at Room Temperature. Submitted to Transfusion.

ABSTRACTS, AND PRESENTED PAPERS:

1. Fomovskaia GN, Haddock TF, Kubish GN, Penezina OP, Davenport RD. Nageotte chamber method for very low number of leukocytes counting validated for stored red blood cells. Transfusion 39:17S, 1999.
2. Penezina OP, Fomovskaya GN, Haddock TF, Davenport RD. Changes in the dextran purified human blood leukocyte cell subsets content after filtration via polyester filters coated with immobilized chondroitin sulfate A. Transfusion 39:41S, 1999.
3. Davenport RD, Fomovsky M. Serology and mortality in murine hemolytic transfusion reactions. Transfusion 39:81S, 1999.
4. Davenport RD, Butch SH. Fresh frozen plasma vs. reduced-risk plasma: Comparison of transfusion-transmitted disease risk in major surgery. Transfusion 39:99S, 1999.
5. Judd WJ, Davenport RD, Downs T. In-vitro analysis on isoagglutinin-depleted solvent detergent plasma: A "universal" plasma for transfusion. Transfusion 39:100S, 1999.

CHAPTERS IN BOOKS:

1. Davenport RD: The immune system: an overview. In: Vamvakas S, Blajchman MD (eds): Immunomodulatory Effects of Blood Transfusion. AABB Press, Bethesda, MD 1999.

2. Davenport, R. Transfusion-Associated fever. American Society of Clinical Pathologists Check Sample, Transfusion Medicine No. TM 99-5 (TM-233), 1999.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999-30 JUNE 2000**

I. CLINICAL ACTIVITIES:

- A. Co-Director, Genomic Pathology Laboratory

II. TEACHING ACTIVITIES:

- A. Graduate students:
1. Responsible during the current academic year for the following activities:
 - a. Graduate Student Training and Doctoral Committees
 - b. Joint Student Training in Pharmacology and Toxicology with Florida A&M School of Pharmacy, Toxicology Program
 - c. Direct Postdoctoral Fellowship Program in Experimental & Cellular Pathology

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Research activities with intramural support from Pfizer
- B. Collaborates with K. Johnson in the development of morphometric models for the evaluation of pathologic changes
- C. Consultant in quantitative microscopy, Morphology Core Lab
- D. Development of image analysis network system

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Co-Chair with Dr. Ward, Joint Research Fellowship Program

MEDICAL SCHOOL/HOSPITAL:

- A. None

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

- A. Editorial Board Member, Drug Metabolism Reviews

INVITED LECTURES/SEMINARS:

1. Retrospective on the Development of Analytical Microscopy Imaging. WIL Labs, Akron, Ohio, October 15, 1999.
2. Coherent Multiprobes and Quantitative Spectroscopic Multimode Microscopy for the Study of Simultaneous Intracellular (International Society of Analytical Cytology, Montpellier, France, May 2000).
3. Monitoring Simultaneous Subcellular Events in Vitro by Means of Coherent Multiprobe Fluorescence High Content Screening Workshop (Cellomics, Pittsburgh, Pennsylvania, June 2000).
4. Monitoring Simultaneous Subcellular Events in Vitro by Means of Coherent Multiprobe Fluorescence (Cambridge Health Tech Institute Fourth Annual Advances in Molecular Labels, Signaling & Detection). Washington DC, June 2000.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. M.A. Breider, A.W. Gough, J.R. Haskins, G. Sobocinski and F.A. de la Iglesia Effects of Troglitazone on Cell Proliferation in Murine Cardiac and Adipose Tissue. *Toxicol. Pathol* 27:545-552, 1999.
2. S.K. Duddy, S.M. Gorospe, J.M. Bleavins, F.A. de la Iglesia. Spontaneous and Thiazolidinedione-Associated B6C3F1 Mouse Hemangiosarcomas Exhibit Low *ras* Oncogene Mutation Frequencies *Tox. Appl. Pharm.* 160:133-140, 1999.
3. M.M. Shi, Myrand, S., Bleavins, M.R. and F.A. de la Iglesia. High Throughput Genotyping for the Detection of Single Nucleotide Polymorphism in NAD(P)H-Quinone Reductase (DT-Diaphorase) Using TaqMan Probes. *Mol. Pathol.* 52:295-299, 1999.
4. M.M. Shi, Myrand, S., Bleavins, M.R. and F.A. de la Iglesia. Genotyping for the Functionally Important Human CYP6*4 (B) Mutation Using TaqMan Probes. *Mol. Pathol. Protocols.* (Submitted 1999).
5. M.M. Shi, Bleavins, M.R. and F.A. de la Iglesia. Technologies for Detecting Genetic Polymorphisms in Pharmacogenomics. *Molecular Diagnostics* 4:343-351, 1999.
6. 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 Thiazolidindione Antidiabetic Agent Troglitazone. *J. Tox. Sci.* In press, 2000.
7. L. Dethloff, B. Barr, L. Bestervelt, S. Bulera, R. Sigler, M. LaGattuta and F.A. de la Iglesia. Gabapentin-Induced Mitogenic Activity in Rat Pancreatic Acinar Cells. *Pancreas Toxicological Sciences* 55:52-59, 2000.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Carlson, T., Jacobs, C., Gadam, P., de la Iglesia, F., Robertson, D. Aging results in an increase in the frequency of mutant ATPase submit 6 alleles isolated from *rattus norvegicus* hepatic mtDNA (submitted, April 2000).
2. Shi, M.M., Bleavins, M.R., Thompson, R.G., Chin, J.F., de la Iglesia, F., Candidate gene profiles for liver toxicity and metabolism in NIDDM patients receiving an antidiabetic thiazolidinedione (submitted, June 2000).
3. Bulera, S.J., Eddy, S.M., Ferguson, E., Jatko, T.A., Reindel, J.R., Bleavins, M.R., de la Iglesia, F.A. RNA expression in the early characterization of hepatotoxicants in high-density DNA microarrays (submitted, July 2000).

BOOKS/CHAPTERS IN BOOKS:

None.

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

1. de la Iglesia, F., Haskins, J., Farkas, D., Bearman, G. Coherent multiprobes and quantitative spectroscopic multimode microscopy for the study of simultaneous intracellular. *Cytometry* 39:suppl10):34-35, 2000.
2. Bulera, S., de la Iglesia, F. Letter to the Editor: Are selected short-term photogenotoxicity assays good predictors of photocarcinogenicity? *International Journal of Tox.* 19:63-64, 2000.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

- A. Rotation Students Supervised - Brian MacDonald, CMB; Jingmei Lin, Dept. of Pathology
- B. Post-doctoral Trainees Supervised - Eun Ah Cho, Ph.D.; Yi Cai, M.D., Ph.D.; Patrick Brophy, M.D.; Sanj Patel, M.D.
- C. Ph. D. Thesis Committee Member - Igor Nasonkin, Dept. of Genetics; Kris Coulter, Dept. of Genetics; Hoonkyo Soo, Dept. of Genetics; Pei-Jiun Chen, Dept. of Biology
- D. Course Lectures - Path 581, 4.5 hours; CDB 530, 3 hours; CDB 580, 3 hours

MEDICAL SCHOOL/HOSPITALS:

- A. Second Year Medical Students - Renal Section, one full lecture

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "PAX-2 in Normal and Cystic Epithelium Development", NIH/NIDDK R01 DK51043-02, (20%), September 30, 1995-August 31, 2000. Direct costs approximately \$90,000 requested annually.
- B. Principal Investigator, "Cell Migration, Chemoattraction and the RET/GDNF Pathway", NIH/NIDDK 1 R01 DK54723-01 (30% effort), 1/1/99 - 12/31/03, Annual Direct Costs \$158,840.
- C. Principal Investigator, "PAX2 Interacting Proteins in Development and Disease", NIH/NIDDK 1 R01 DK54740-01 (30% effort), 1/1/99 - 12/31/02, Annual Direct Costs \$158,840.
- D. 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. 9/1/98 - 8/31/03, \$76,066 Initial Budget Period.

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. Wnt and Frizzled signaling in the developing kidney

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Dept. of Pathology - Preliminary Exam Committee, Curriculum Committee
- B. Center for Organogenesis - Interim Co-Director, Steering Committee, Training Grant Review Committee, Advisory Committee, Seminar Committee (Chair)
- C. Program in Biomedical Sciences (PIBS) - Admissions Committee

REGIONAL AND NATIONAL:

- A. NIH Study Section, General Medicine B, Permanent Member
- B. NIDDK, Renal Program Project Grants, Ad-Hoc Reviewer
- C. American Journal of Physiology, Editorial Reviews Board
- D. Reviewer for: Mechanisms of Development, Development, Proceedings of the National Academy of Sciences, Developmental Dynamics, Journal of Biological Chemistry, Nature, 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:

- A. Membership in the American Society of Nephrology
- B. Membership in Society for Developmental Biology
- C. Membership in University of Michigan Comprehensive Cancer Center
- D. Membership in the Center for Organogenesis, University of Michigan

INVITED LECTURES/SEMINARS:

1. Dept. of Biochemistry, LSU Medical Center, New Orleans, LA.
2. Dept. of Anatomy, University of Kansas Medical School, Kansas City, KS.
3. Dept. of Biochemistry, Medical College of South Carolina, Charleston, SC.
4. Division of Developmental Biology, Children's Hospital, Univ. of Cincinnati, OH.

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Yang, Y., Jeanpierre, C., Dressler, G.R., Lacoste, M., Niaudet, P. and Gubler, M.-C. (1999) WT1 and Pax-2 podocyte expression in Denys-Drash syndrome and isolated diffuse mesangial sclerosis. *Am J. Pathol* 154, 181-192.
2. Dressler, G.R. (1999) Kidney development branches out. *Dev. Genetics* 24, 189-193.
3. Schwarz, M., Alvarez-Bolado, G., Dressler, G., Urbanek, P., Busslinger, M., and Gruss, P. (1999) Pax2/5 and Pax6 subdivide the early neural tube into three domains. *Mech. Dev.* 82, 29-39
4. Dressler, G. R. and Woolf, A. S. (1999) Pax2 in development and renal disease. *Int. J. Dev. Biol.* 43, 463-468.
5. Ostrom, L., Tang, M.-J., Gruss, P., and Dressler, G.R. (2000) Reduced *Pax2* gene dosage increases apoptosis and slows the progression of renal cystic disease. *Dev. Biol.* 219, 250-258
6. Mah, S.P., Saueressig, H., Goulding, M., Kintner, C., and Dressler, G.R. (2000) Kidney Development in Cadherin-6 Mutants: Delayed Mesenchyme-to-Epithelial Conversion and Loss of Nephrons. *Dev. Biol.* 223, 38-53.
7. Lechner, M.S. and Dressler, G.R. (2000) PTIP, a novel BRCT-domain protein interacts with the Pax2 and is associated with active chromatin. *Nuc. Acids Res.* 28, 2741-2751.

ARTICLES SUBMITTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Tang, M.J., Tsai, S.J., Wang, Y.K., Worby, C.A., Cai, Y. and Dressler, G.R. (2000) Chemotaxis of renal epithelial cells in response to RET activation is mediated by phosphatidylinositol 3-kinase. submitted

BOOK CHAPTERS:

1. Dressler, G.R. (2000) The development of the excretory system, in *Mouse Development* (J. Rossant and P. Tam, eds.) Academic Press

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

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

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. Instructor for Medical Student (M-4) rotation through Chemistry Laboratories.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. NIH: P60 DK 20572 (D. Greene) 12/01/97 - 11/30/02
Michigan Diabetes Research and Training Center
\$123,404 Direct Costs (Clinical Implementation Core)
Consultant with 5% Effort.
1. The major goals of this project provide laboratory support for diabetes related research conducted by the Michigan Diabetes Research and Training Center investigators.
- B. NIH/NIA U01 AG 12495 (AR Midgley) 06/01/99 - 05/31/03
Study of Women's Health Across the Nation: Menopause and Aging in Women
\$768,462 Direct Costs (Central Laboratory)
Associate Lab. Director with 10% Effort.
1. 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.

SCIENTIFIC COLLABORATIONS:

- A. University of Michigan; Reproductive Science Program: A. Rees Midgley Jr. M.D., and Daniel S. McConnell, Ph.D.: The major purpose of the Central Ligand Assay Satellite Services (CLASS) laboratory at the University of Michigan is to support the Multicenter National Study of Women's Health Across the Nation (SWAN) through state-of-the-science, automated assays for all major reproductive axis hormones, selected markers of

aging, other endocrine markers, and new ovarian markers which have the potential to define more accurately the menopausal transition and the characterize the postmenopause with greater precision.

- B. 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 "drugs". These delivery devices have proven capable of constant release of biological compounds into the circulation for as many as 12 months. These studies are continuing permitting increasingly tighter control in the rate and length of "drug" delivery.
- C. 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.
- D. University of Michigan: Jonathon A. Ship, D.M.D.: In the preceding study hormone concentrations in salivary secretions from children have provided invaluable information into the developmental physiology of children under natural conditions. Salivary flow rates are not different in healthy young and older adults although histomorphometric studies clearly show a decrease in acinar salivary producing cells across the human life span. It would be of interest to compare salivary hormone excretion patterns in subjects of advancing age. We are attempting to determine if a secretory reserve exists early in life, by determining if there is a difference in the ability of healthy human subjects' salivary glands to respond to an anticholinergic medication (glycopyrrolate).

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

- A. Director, Central Ligand Assay Laboratory.

MEDICAL SCHOOL/HOSPITAL:

- A. Consultant, Chemistry Core Facility, Diabetes Research and Training Center.
- B. Co-Director, Standards and Reagents Core Facility, Reproductive Sciences Program.
- 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 IN REFEREED JOURNALS:

1. Sisson JC. Thompson NW. Giordano TJ. England BG. Normolle DP. Serum Thyroglobulin Levels After Thyroxine Withdrawal In Patients With Low Risk Papillary Thyroid Carcinoma. *Thyroid*. 10(2):165-169, 2000 Feb.
2. Cason Z. Benghuzzi H. Tucci M. Scott A. England B. Assessment Of Endometrial Function During Sustained Delivery Of Estradiol And Estradiol Plus Progesterone In Ovariectomized Rats. *Biomedical Sciences Instrumentation*. 36:221-6, 2000.
3. Scott A. Higdon K. Benghuzzi H. Tucci M. Cason Z. England B. Tsao A. Hughes J. TCPL Drug Delivery System: The Effects Of Synthetic DHEA And Diosgenin Using An Ovariectomized Rat Model. *Biomedical Sciences Instrumentation*. 36:171-6, 2000.

ABSTRACTS AND PAPERS AT MEETINGS:

1. England BG, Gauger PA, Giacherio DA Thompson NW. Intra-Operative Parathyroid Hormone (PRH) Monitoring Using A Cart-Mounted Immulite Analyzer With Turbo Software. *Clinical Chemistry* 2000; 46 Suppl6: A476.
2. England BG, Walsh LA, Ghezzi DA, Giacherio DA, McConnell DS, Ship JA. Development Of A Blood Assay For Circulating Levels Of Glycopyrrolate: A Potent Antisialagogue. *Clinical Chemistry* 2000; 46 Suppl 6: A735.
3. McConnell DS, Midgley AR, Possley RM, England BG. A Sensitive Automated Chemiluminescent Immunoassay For Estradiol. *Clinical chemistry* 2000, 46 Suppl 6: A483.
4. Gauger PA, England BG, Thompson NW. "Experience with an Affordable System of Intra-operative Parathyroid Hormone Monitoring," invited presentation, Academy of Surgery of Detroit, Detroit, MI, April 13, 2000.
5. Gauger PA, England BG, Thompson NW. "Intraoperative Parathyroid Hormone Monitoring," invited presentation, University of Michigan Innovations 2000: Minimally Invasive Techniques in General and Cancer Surgery course, Grand Traverse, MI, July 14, 2000.
6. Gauger PA, England BG, Thompson NW. "Experience With an Affordable System of Intraoperative Parathyroid Hormone Monitoring," invited presentation, Frederick A. Collier Surgical Society, Ann Arbor, MI, October 21, 2000.
7. Flinn MV and England BG. Childhood Stress. Presented at "The Relationship System In Individual Variation And Functioning Conference. Presented at the Georgetown Family Center, Georgetown University Medical Center.
8. Mulkey C, England B and Flinn M Parenting Style And Cortisol Response. Presented at the Heartland Conference on Stress & the Family at the Center for Family Health, Kansas City MO.
9. Walsh LA, Ghezzi EM, Ship JA, England BG. Development of a Blood Assay for Circulating Levels of Glycopyrrolate: A Potent Antisialagogue. *International Association of Dental Research*. Washington DC. April 1-8, 2000.

SUBMITTED ARTICLES AND CHAPTERS:

1. England B.G. and J.B. Smart. Receptor Assays of the Clinical Laboratory, in, McClatchey, K.D. (ed.) *Clinical Laboratory Medicine*, 2nd Edition. Williams and Wilkins, Baltimore, MD, 2000

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

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. Pulmonary Pathology Conference (four per year to Pulmonary Division, Department of Internal Medicine).
- G. Medical Student Advisor (3rd and 4th year).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Co-Investigator, "Pulmonary Immune Responses to Inhaled Pathogens". NIH-R)1-HL5531601 (1998-2002)
- B. Principal Investigator, "An Integrated Curriculum for Multiculturalism, Spirituality, and End-of Life Care". Arthur Vining Davis Foundation. (2000-2002).

PROJECTS UNDER STUDY:

- A. Mechanisms of phagocytic cell-mediated tissue injury.
- B. Outcomes measures of undergraduate medical education.
- C. Assessment of professional values in medical student education

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director, Anatomic Pathology.
- B. Coordinator - Educational Programs.
- 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 Information Technology Advisory Committee.
- H. University of Michigan Distance Learning Committee.
- I. Medical School Strategic Planning Committee.

REGIONAL AND NATIONAL:

- A. ALA of Michigan, Grant Review Committee.
- B. USMLE, NBME Pathology Test Committee (Chair).
- C. Pathology Residency Review Committee. ACGME.

V. OTHER RELEVANT ACTIVITIES:

- 1. Invited speaker: Workshop on Medical Curriculum Reform, NYU Medical School, N.Y. 1999.
- 2. Invited speaker: Plenary Session on Professional Development in Medical Education, AAMC, Washington, D.C., 1999.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

- 1. Robins, L.S., White, C.B., Fantone, J.C., The Difficulty in Sustaining Curricular Reforms: A study of "Drift" at One School. *Academic Medicine*, 2000 (accepted for publication).
- 2. Alexander, G.L., Davis, W.K., Yan, Y.C. and Fantone, J.C., Following Medical School Graduates into Practice: Resident Directors' Assessments after the First year of Residency. *Academic Medicine* (accepted for publication).

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999- 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

- A. Medical Director, Clinical Hematology Laboratory.
- B. Diagnostic Hematopathology (Bone marrow biopsies, lymph nodes, blood smears, body fluids).
- C. Clinical Flow Cytometry Laboratory.
- D. Clinical Molecular Diagnostics Laboratory.
- E. 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.
 - 4. Hematopathology case conferences (2).
- B. Hematopathology teaching:
 - 1. Leukemia conference/biweekly.
 - 2. Lymphoma conference/weekly.
 - 3. Hematology conference/biweekly.
 - 4. Clinical Pathology Grand Rounds (two lectures).
 - 5. Clinical Pathology Case Conference/weekly.
 - 6. Department of Pathology Research Seminar (1 hour)
- C. Medical Students:
 - 1. M-2 Hematology Sequence: Section leader for laboratory sessions (12 hours).
 - 2. M-1 Histopathology Course (24 hours).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

None

PROJECTS UNDER STUDY:

- A. IgG expression in B-cell chronic lymphocytic leukemia.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Medical Director, Clinical Hematology Laboratory.
- B. Clinical Pathology Resident Training.
- C. Interviewer of residency candidates.

REGIONAL/NATIONAL:

- A. Editorial Board, Cytometry (Communications in Clinical Cytometry).
- B. Manuscript reviewer, Human Pathology.
- C. Contributing Editor, Yearbook of Pathology and Laboratory Medicine, Mosby, 2001.
- D. Reviewer of abstracts for American Society of Hematology 42nd Annual Meeting, December 2000.
- E. American Society of Clinical Pathologists, Check Path Planning Committee (Hematopathology).

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

None

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Kroft SH, Domiati-Saad R, Finn WG, Schnitzer B, Dawson DB, Singleton P, Ross CW: Precursor B-lymphoblastic transformation of grade I follicle center lymphoma. Am J Clin Pathol 113:411-418, 2000.
2. Yang B, Tubbs RR, Finn WG, Carlson A, Pettay J, His ED: Clinicopathologic reassessment of primary cutaneous B-cell lymphomas with immunophenotypic and molecular genetic characterization. Am J Surg Pathol 24:694-702, 2000.
3. Goolsby CL, Kuchnio M, Finn WG, Peterson L: Expansions of clonal and oligoclonal T cells in B cell chronic lymphocytic leukemia are primarily restricted to the T cytotoxic/suppressor cell population. Cytometry 42:188-195, 2000.
4. Bavikatty NR, Ross CW, Finn WG, Schnitzer B, Singleton TP: Anti-CD10 immunoperoxidase staining of paraffin-embedded acute leukemias: comparison with flow cytometric immunophenotyping. Hum Pathol (in press).

ARTICLES SUBMITTED FOR PUBLICATION:

1. Finn WG, Singleton TP, Schnitzer B, Ross CW, Stoolman LM: Adhesion molecule expression CD5 negative/CD10 negative chronic B-cell leukemias: comparison with non-Hodgkin's lymphomas and CD5 positive B-cell chronic lymphocytic leukemia.

BOOKS AND CHAPTERS IN BOOKS:

1. Finn WG: Hematolymphoid system. In: *Yearbook of Pathology and Laboratory Medicine 2001*. Raab SS, Dabbs DJ, Olson JD, Silverman JF, Stanley MW, eds. St. Louis, MO: Mosby, Inc., 2001 (in press).

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

1. Finn WG, Singleton TP, Schnitzer B, Ross CW, Stoolman LM: Adhesion molecule expression in CD5 negative, CD10 negative chronic B-cell leukemias. Poster presentation, United States and Canadian Academy of Pathology Annual Meeting, New Orleans, LA, 2000. *Mod Pathol* 2000; 13(1):148A, *Lab Invest* 2000; 82:148A.
2. Valdez R, Finn WG, Ross CW, Singleton TP, Tworek JA, Schnitzer B: Extranodal marginal zone B-cell lymphoma associated with Waldenstrom's macroglobulinemia. Poster presentation, United States and Canadian Academy of Pathology Annual Meeting, New Orleans, LA, 2000. *Mod Pathol* 2000; 13(1):165A, *Lab Invest* 2000; 82:165A.
3. Nangia R, Singleton TP, Ross CW, Finn WG, Padmore RF, Schnitzer B: Follicular Hodgkin's lymphoma: a clinicopathologic study. Poster presentation, United States and Canadian Academy of Pathology Annual Meeting, New Orleans, LA, 2000. *Mod Pathol* 2000; 13(1):158A, *Lab Invest* 2000;82:158A.
4. Uherova P, Singleton TP, Ross CW, Schnitzer B, Finn WG: The clinical significance of CD10 antigen expression in diffuse large B-cell lymphoma. Poster presentation, United States and Canadian Academy of Pathology Annual Meeting, New Orleans, LA, 2000. *Mod Pathol* 2000; 13(1):165A, *Lab Invest* 2000; 82:165A.
5. Nangia R, Kroft SH, Singleton TP, Ross CW, Finn WG, Schnitzer B: Splenic morphology in small B-cell lymphoproliferative disorders: a study of 48 well-characterized cases. Poster presentation, United States and Canadian Academy of Pathology Annual Meeting, New Orleans, LA, 2000. *Mod Pathol* 2000; 13(1):158A, *Lab Invest* 2000; 82:158A.
6. Petricek CM, Ross CW, Finn WG, Schnitzer B, Singleton TP: Utility of anti-CD117 in the flow cytometric analysis of acute leukemia. Poster presentation, United States and Canadian Academy of Pathology Annual Meeting, New Orleans, LA, 2000. *Mod Pathol* 2000; 13(1):160A, *Lab Invest* 2000; 82:160A.
7. Finn WG: Philadelphia chromosome-positive acute lymphoblastic leukemia (ALL) arising in the setting of existing B-CLL. Society of Hematopathology Case of the Quarter, February 2000.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

- A. Surgical Pathology Rotations, July (1/5), August (1/4), September (1/4), October (1/4), November (1/4), December (2/5), January (2/4), March (3/5), April (1/4), May (1/4), June (1/4)
- B. Ophthalmic Pathology Service – 52 weeks/year
- C. Autopsy Rotation – February (1/4)

II. TEACHING ACTIVITIES:

- A. Pathology 600
 - 1. Pathology of Valvular Disease, October, 1999
 - 2. The Vasculitides, October, 1999
 - 3. Obstructive Lung Disease - November, 1999
 - 4. Pulmonary Neoplasms - November, 1999
 - 5. Pathology of ARDS - November 1998
 - 6. Tissue Reactions to Infectious Agents - November, 1999
 - 7. Pulmonary Pathology Review for Medical Students November, 1998
 - 8. Gynecologic Pathology Review for Medical Students - April, 1999
 - 9. General Pathology Review for Medical Students - June, 2000
 - 10. Laboratory Instructor, September, 1999 - May, 2000
 - 11. Medical student question and answer sessions, October, 1999 - May, 2000
- B. Pathology 630:
 - 1. Respiratory Disease I - October, 1999
 - 2. Respiratory Disease II - November, 1999
- C. Residency Training:
 - 1. Diseases of the Chest I – March, 2000
 - 2. Diseases of the Chest II – March, 2000
 - 3. Surgical Pathology Consultant's Conference, December 1999
- D. Other educational activities:
 - 1. M4 student elective mentor, March, 2000,
 - 2. University of Michigan New Faculty Orientation, "Teaching Tips", September, 1999
 - 3. Center for Research on Learning and Teaching Workshops: "U.M. CourseTools, Multimedia, and Pedagogy: Putting the Pieces Together", March, 2000
 - 4. Member, M-2 Respiratory Sequence Committee, 1997-present
 - 5. Course Director, M-4 Student Pathology Clerkships

6. Radiology - Pathology Correlation Course Co-Director, April, 2000
7. M1 student mentor, February – May, 2000
8. M2 student mentor, September, 1999 - present
9. Nominated for American Association of Medical Colleges Humanism in Medical Education Award, 2000

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Interstitial Lung Diseases - Specialized Center of Research (1 P50 HL- 46487-01), Galen Toews, M.D. (Principal Investigator), Andrew Flint, M.D. (Co-Investigator).
- B. A Murine Model of Graft-Vs-Host Disease Lacrimal Gland Inflammation and Destruction: Histopathology, Immunopathology, and Intervention (Midwest Eye-Banks and Transplantation Center), Victor M. Elner, MD, PH.D(Principal Investigator), Andrew Flint MD (Co-Investigator)

PROJECTS UNDER STUDY:

- A. The separation of usual interstitial pneumonitis from nonspecific interstitial pneumonitis
- B. The cytopathologic features of vitreous fluids
- C. Immunochemical characterization of adenocystic carcinoma
- D. Interactive Teaching in Pathology

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

Interviewer of Pathology Surgical Pathology Fellowship Candidate, 2000

V. OTHER RELEVANT ACTIVITIES:

1. Member, Admissions Committee of the University of Michigan Medical School, 1995 - present
2. Member, Rules Committee, Senate Advisory Committee on University Affairs, 1999 – 2000
3. Resolution Officer, Office of Student Conflict Resolution, Division of Student Affairs, University of Michigan, 2000

EDITORIAL BOARDS:

Abstract Review Board, USCAP (Invited)

INVITED LECTURES/SEMINARS:

1. The Physician as Scientist, November, 1999 Inteflex 211, University of Michigan, Ann Arbor, MI,

VI. PUBLICATIONS:

1. Zisman DA, Lynch JP 3rd, Toews GB, Kazerooni EA, Flint A, Martinez: Cyclophosphamide Cyclophosphamide in the treatment of idiopathic pulmonary fibrosis. A prospective study in patients who failed corticosteroids. Chest, 2000 Jun; 117s(6):1619-1626
2. Flaherty KR, Toews GB, Lynch III JP, Kazerooni EA, Strawderman III RL, Hariharan K, Flint A, Martinez FJ: Steroids in idiopathic pulmonary fibrosis: Prospective comparative study of varying dosage regimens. Am J Respir Crit Care Med
3. Soong HK, Feil SH, Elnor VM, Elnor S, Flint A: Conjunctival mucoepidermoid carcinoma in a young HIV-infected man. Am j Ophth 128(5):640-3, 1999
4. Lynch III JP, Belperio J, Flint A, Martinez F: Bronchiolar complications of connective tissue disorders. Sem Resp Crit Care Med 20(2):149-155, 1999
5. Michael CW, Flint A: The cytologic features of Wegener's granulomatosis. Am J Clin Path 110(1):10-5, 1998
6. Brown RS, Leung JY, Kison PV, Zasadny DR, Flint A, Wahl RL: Glucose transporters and FDG uptake in untreated primary human non-small cell lung cancer. J Nuc Med 40(4):556-65, 1999
7. Michael CW, Flint A: The cytologic classification of Pulmonary Neuroendocrine tumors: how far can we go? Acta Cytol (abs) 2000
8. Flaherty K, Zisman D, Strawderman R, Lynch III JP, Kazerooni E, Toews G, Hariharan K, Gross B, Spizarny D, Cascade P, Flint A, Martinez F: Serial HRCT improves ability to follow patients with IPF during therapy. Am J Resp /Crit Care Med (abs) 1999; 159: A50
9. Flaherty K, Lynch III JP, Toews G, Hariharan K, Strawderman R, Streiter R, Kazerooni E, Flint A, Martinez F: High dose versus low dose corticosteroids in the treatment of idiopathic pulmonary fibrosis (IPF). Am J Resp Crit Care Med (abs)1999; 159: A50
10. Flaherty K, Martinez F, Peters-Golden M, Lynch III JP, Hariharan K, Kazerooni E, Flint A, Gross B, Toews G: Zileuton versus azathioprine: A randomized controlled trial of novel therapy for idiopathic pulmonary fibrosis (IPF). Eur Respir J (abs) 1999; 14:103S
11. Martinez F, Flaherty K, Flint A, Colby T, Lynch III JP, Hariharan K, Toews G: Survival and response to therapy in patients with NSIP versus UIP. Eur Respir J (abs)1999; 14:272S
12. Flaherty K, Flint A, Colby T, Toews G, Lynch III JP, Hariharan K, Martinez F: Inpatient variation of diagnosis obtained by open lung biopsy in patients with fibrotic lung disease. Eur Respir J (abs)1999; 14:273S
13. Kazerooni E, Flaherty K, Gross B, Toews G, Lynch III JP, Flint A, Colby T, Travis WD, Martinez F: Comparison of semiquantitative HRCT scoring in NSIP patients versus UIP at initial presentation. Society of Thoracic Radiology 2000
14. Flaherty K, Toews G, Peters-Golden M, Lynch III JP, Hariharan K, Kazerooni E, Flint A, Gross B, Martinez F: Randomized controlled trial of novel therapy for idiopathic pulmonary fibrosis: Zileuton versus azathioprine. Am J Respir Crit Care Med (abs)2000; 161:A374

15. Travis WD, Flaherty K, Colby TV, Flint A, Toews G, Lynch III JP, Kazerooni E, Gross B, Martinez F: Histologic patterns of interstitial pneumonia in patients with surgical lung biopsies of multiple lobes. *Am J Respir Crit Care Med* (abs) 2000; 161:A526.
16. Kazerooni E, Flaherty K, Gross B, Toews G, Lynch III JP, Flint A, Colby T, Travis WD, Martinez F.: Semiquantitative HRCT in NSIP vs UIP. *Am J Respir Crit Care Med* (abs)2000; 161; A527.
17. Flaherty K, Colby T, Travis W, Flint A, Toews G, Lynch III JP, Kazerooni E, Gross B, Martinez F: Survival in patients with histologic subsets of NSIP versus UIP. *Am J Respir Crit Care Med* (abs) 2000; 161:A708

SUBMITTED PUBLICATIONS:

1. Flaherty KR, Toews GB, Travis W, Colby T, Kazerooni EA, Gross BH, Jain A, Strawderman III RL, Flint A, Lynch III JP, Martinez FJ: Histopathological classification in patients with suspected IPF: Results of a large, well-characterized cohort. *Am J Respir Crit Care Med* (abs)

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

None

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999- 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

- A. Director, Pathology Data Systems.
- B. Director, Clinical Support Information Systems (encompasses information systems in Pathology, Radiology, Pharmacy, Radiation Oncology, Nuclear Medicine, Office of Clinical Affairs, Office of Graduate Medical Information, Medical Information Systems, Food and Nutrition Services, Social Work, and Respiratory Care), University of Michigan Health System.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

- A. Director of the Eighteenth Annual Symposium on Automated Information Management in the Clinical Laboratory (AIMC), Ann Arbor, Michigan, May 27-29, 1999. Meeting attracted 300 paid registrants and 28 vendors.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Use of the GroupWise Messaging System for support of clinical activities and clinic work processes; currently being prototyped in the Department of Physical Medicine and Rehabilitation.
- B. Policy development regarding confidentiality and security of email.
- C. The use Personal Digital Assistants (PDAs) for the transmission of laboratory test results to clinicians.
- D. Evolution of clinical laboratory web portals; e-commerce and the clinical laboratory.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Clinical Laboratory Directors Committee.

HOSPITAL:

- A. Chief Information Officer Executive Committee (CIOEC).
- B. Chairman, GroupWise Operations Committee.
- C. Chairman, Email Policy and Oversight Committee.
- D. Chairman, Clinical Support Information Systems Managers' Committee

UNIVERSITY:

- A. Executive Committee, Center for Statistical Consultation and Research (CSCAR).

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

- 1. A Primer on the Digital/Virtual Clinical Laboratory and Pathology Department. A lecture presented at the Anatomic Pathology, Informatics, and the Internet (APIII) Conference sponsored by the Division of Pathology Informatics, Department of Pathology, University of Pittsburgh Medical Center, Pittsburgh, PA, October 14, 1999.
- 2. The Digital/Virtual Pathology Department: Is This the Organizational Structure of the Future? A one-hour teleconference sponsored by the American Society of Clinical Pathologists (ASCP). March 22, 2000.
- 3. Web-LIS, E-Commerce, and the Clinical Laboratory Portal. A lecture presented at a symposium entitled "Lab 2002: Staying Ahead of the Curve" sponsored by the American Association of Clinical Chemistry (AACC), New York City, March 23, 2000.
- 4. Layman's Introduction to Emerging Internet and Computer Technology. A lecture presented at the 2000 Executive War College on Lab and Pathology Management, Seminar on Web-Based Laboratory Informatics Products, New Orleans, May 17, 2000.
- 5. The Future of the Clinical Laboratory Is Spelled IT: Implications and Prognostications. A lecture presented at the 18th annual symposium on Automated Information Management in the Clinical Laboratories (AIMCL), Ann Arbor, Michigan, May 31, 2000.
- 6. Challenges of Managing Patient Information in a Wired Culture. A breakout session presented at the annual meeting of the Clinical Laboratory Management Association (CLMA), Anaheim, California, June 28, 2000.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

None

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

- A. Director, Chemistry Laboratory
- B. Sign-out and interpretation of 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, Kellogg Hospitals.
- D. Direct the workgroup overseeing the quality assurance programs for bedside blood glucose testing in the Medical Center.
- E. Planning group for the 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 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.
- B. Postgraduate:
 - 1. Ph.D. Thesis Committees, Aaron Smith (5/96 to present), Department of Chemistry.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Development of an assay for gammahydroxybutyrate (GHB).
- B. Evaluation of methods for the rapid determination of PTH during parathyroidectomy cases.
- C. Evaluation of meters and data management systems for point of care testing.
- D. Implementation of Hemoglobin A1c testing by HPLC in the central lab, and by point of care immunoassay at satellite clinics.
- E. Evaluation of a new line probe technique for measuring extractable nuclear antigens (ENA).
- F. Development of methods to monitor serum caffeine levels.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Incentive Committee
- B. Quality Assurance Committee
- C. Chemistry Lab New Instrumentation Work Group
- D. M Labs / Central Distribution Work Group
- E. Director, Chemistry Laboratory
- F. Director, Point of Care Testing

MEDICAL SCHOOL /HOSPITAL:

- A. Ambulatory Care Operations and Planning Council
- B. Brighton Health Center Expansion Project Planning Group
- C. Emergency Department Expansion Project Work Group

REGIONAL AND NATIONAL:

- A. Executive Committee, Michigan Section AACC.
- B. Treasurer, Michigan Section AACC.
- C. Lipids and Lipoproteins Division Member, AACC
- D. Pediatric Clinical Chemistry Division Member, AACC
- E. Reviewer, Clinical Chemistry

V. PUBLICATIONS:

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

1. Intra-operative Parathyroid Hormone (PTH) monitoring using a cart-mounted Immulite analyzer with Turbo software. B.G. England, P. G Gauger, D.A. Giacherio, and N.W. Thompson. Clinical Chemistry 2000; 46 Suppl 6: A124.
2. Development of a blood assay for circulating levels of glycopyrrolate: a potent antisialogogue. B.G. England, L.A. Walsh, E.M. Ghezzi, D.A. Giacherio, D.S. Mcconnell, and J.A. Ship. Clinical Chemistry 2000; 46 Suppl 6: A188.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

- A. Renal Biopsy Service – 9 days.
- B. Autopsy Service – 9 days.

II. TEACHING ACTIVITIES:

- A. Histopathology Lab Section for M1 medical students – 16 hours.
- B. Urinary Sequence Lab for M2 medical studies – 8 hours.
- C. Lecture to House Officers – 1 hour.

III. RESEARCH ACTIVITIES:

None.

PROJECTS UNDER STUDY:

None.

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

MEDICAL SCHOOL/HOSPITAL:

- A. Member of Medical School Admission Committee.

REGIONAL AND NATIONAL:

- A. Chairman, Board of Directors, Public Citizen, Inc. (Ralph Nader, Initial Chairman and Founder).
- B. Reviewer for the “Journal of Urology” and “Urology”.

V. OTHER RELEVANT ACTIVITIES:

None.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

- A. General Surgical Pathology - four months.
- B. Endocrine Surgical Pathology, Departmental and Outside Consultation Services - 12 months.
- C. Her2/neu Immunoperoxidase service - Outside consultation.
- 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.
Component IV Pathology Elective mentor @ one month.
- B. House Officers:
 - 1. General Surgical Pathology - 4 months.
 - 2. Endocrine Surgical Pathology - 12 months as needed.
Consultation Conferences - four.
Molecular Pathology lecture.
Endocrine Pathology lecture.
- C. Dental and Graduate Students:
 - 1. Endocrine Pathology lecture.
- D. Interdepartmental:
 - 1. Endocrine Conference, Department of Surgery - monthly.
 - 2. Endocrinology and Metabolism Clinical Conference - occasional case presentations.
 - 3. Adrenal Cancer Conference - monthly.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. 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

- B. 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
- C. 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
- D. Director, "Tissue Procurement Contract", Genentech, Inc., 5/99 to 5/2000 (\$92,346 direct costs), 10% effort
- E. Principal Investigator, The University of Michigan Comprehensive Cancer Center, Millie Schembechler Adrenal Research Fund, "Gene Expression Profiles in Adrenal Cortical neoplasms using DNA Microarrays", 8/99 to 8/00 (\$15,000)

PROJECTS UNDER STUDY:

- A. Principal Investigator, "Molecular Studies of Adrenal Cortical Neoplasms."
- B. Principal Investigator, "Molecular Studies of Soft Tissue Sarcomas."
- C. Co-Investigator with Dr. Jim Baker, "Molecular Studies of Thyroiditis."
- D. Co-Investigator, "Molecular Classification of Ovarian, Colonic and Thoracic 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, Pathology Portion of Breast Cancer Core Facility
- E. Director, Frozen Tumor Bank
- F. Medical Institutional Review Board (IRB-Med), *ad hoc* member.
- G. Director, Laser Capture Microdissection Core
- H. Internal Review Committee
- I. MSTP M.D-Ph.D. Career Advisory Panel

NATIONAL:

- A. Editorial Board, *Endocrine Pathology*

V. OTHER RELEVANT ACTIVITIES:

- A. Consultant, Genentech Corporation.

INVITED LECTURES/SEMINAR:

1. Invited Speaker, "Running an Laser Capture Microdissection Core for a Large University-Based Cancer Center", National Institutes of Health Laser Capture Microdissection Conference, Bethesda, MD
2. Invited Speaker, "Adrenal Cortical Carcinoma", Genentech, Inc., Department of Pathology, San Francisco, CA
3. Invited Speaker, "Adrenal Cortical Carcinoma: Clinicopathologic Aspects and Pathogenesis", Millennium Pharmaceuticals, Inc., Boston, MA
4. Visiting Professor, "Thyroid Pathology and Associated Genetics", and "Pathogenesis of Adrenal Cortical Carcinoma", Emory University, Atlanta, GA

VI. PUBLICATIONS:

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

1. Wang SH, Koenig RJ, **Giordano TJ**, Myc A, Thompson NW, Baker JR. 1alpha,25-dihydroxyvitamin D3 up-regulates Bcl-2 expression and protects normal thyrocytes from programmed cell death. *Endocrinology* 1999;140:1649-1656.
2. Arscott PL, Stokes T, Myc A, **Giordano TJ**, Thompson NW, Baker JR. Fas (CD95) expression is up-regulated on papillary thyroid carcinoma. *J Clin Endocrinol Metab* 1999;84:4246-4252.
3. Sisson, JC, Thompson NW, **Giordano TJ**, England BG, Normolle DP. Serum thyroglobulin levels after thyroxine withdrawal in patients with low risk papillary thyroid carcinoma. *Thyroid*, 2000;10:165-169.
4. Kler CG, Bryant BR, **Giordano TJ**, Sobel M, and Merino MJ. Genetic changes in chromosome 1p and 17p in thyroid cancer progression. *Endocrine Pathology*, 2000;11:137-143.
5. Kintanar, EB, **Giordano TJ**, Thompson NW, and Michael CW. Granular cell tumor of trachea masquerading as Hurthle cell neoplasm on fine needle aspirate. *Diagn. Cytopathol.* 2000;22:379-382.
6. Kler CG, **Giordano TJ**, Merino MJ. Squamous cell carcinoma of the thyroid: An aggressive tumor associated with tall cell variant of papillary thyroid carcinoma. ??????
7. Pawlik TM, Richards ML, Burney R, **Giordano TJ**, Thompson NW. Intravagal Parathyroid Adenoma: Report of Two Cases.

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Bretz JD, Mesozzi E, **Giordano TJ**, Thompson NW and Baker, JR Jr. Inflammatory cytokine regulation of TRAIL-mediated apoptosis in thyroid epithelial cells.
2. Brichory FM, Misek DE, Yim A-M, Krause MC, **Giordano TJ**, Beer DG, and Hanash SM. Common occurrence of annexins I and II autoantibodies as a manifestation of an immune response in lung cancer.
3. Kler CG, **Giordano TJ**, Braun T, and Oberman HA. Pathologic features, proliferative activity and p53 expression in benign and malignant phyllodes tumors of the breast.

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

1. Mohl D, Schteingart D, Strieter R, and **Giordano TJ**. CXC chemokine (IL-8 and ENA-78) expression in adrenal cortical neoplasms. Presented at the 2000 Meeting of the United States and Canadian Academy of Pathology.
2. Valdez R, **Giordano TJ**, and Greenson JK. Endocrine cell (EC) hyperplasia of the stomach in graft-versus-host disease (GVHD). Presented at the 2000 Meeting of the United States and Canadian Academy of Pathology.
3. **Giordano TJ**. Co-chair, Proffered Papers Section in Endocrine Pathology, United States and Canadian Academy of Pathology, Spring Meeting, 2000.
4. Thomas D, Baker L, and **Giordano T**. Tissue microarray blocks: and efficient method for screening soft tissue and bony sarcomas. Presented at the 2000 Meeting of the Walther Cancer Institute

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

- A. General surgical pathology - four months
- B. Gastrointestinal and hepatic pathology consultation services - six months
- C. Liver transplant pathology - six months

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

- A. Medical Students:
 - 1. Pathology 600 - Laboratory Instructor (25 contact hours)
 - 2. GI Pathology Sequence, assisted Dr. Appelman (ten contact hours)
 - 3. GI Pathology Sequence, 2 hours full class lecture
 - 4. Preceptor for M-4 rotation (20 contact hours)
- 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 - May, 1999
 - 3. Gastrointestinal and hepatic pathology tutoring - six months
 - 4. Four consultation conferences
- D. Interdepartmental:
 - 1. Liver biopsy conference - one hour per month
 - 2. Multidisciplinary GI tumor board - 1-1/2 hours every other week
 - 3. GI pathology teaching sessions with GI fellows - one hour/week

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Co-investigator R01CA66560-01 (\$5,180,000) "Staging Breast Cancer with Positron Emission Tomography", 5% salary support, Richard L. Wahl, M.D. Principal investigator.
- B. Co-investigator R01ES07129- 01A2 (\$1,153,536) "DDT and Related Compounds and Pancreas Cancer", 5% salary support, David H. Garabrant, M.D. Principal investigator.

- C. 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.
- D. Co-Investigator N01-DK-9-2323 (\$1,433,559) "Hepatitis C Clinical Trial", 7% Salary Support, Anna Lok, M.D. Principal Investigator.

PROJECTS UNDER STUDY:

- A. Study of COX-2 expression in H. pylori gastritis with Division of Rheumatology.
- B. Study of molecular mechanisms in Barretts cancers, G-E junction cancers, and H. pylori cancers with Amy Ferguson and Tom Giordano.
- 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 PET scans in detecting metastases in breast cancer with Richard Wahl, Division of Nuclear Medicine.
- F. Study of etiology of pancreas cancer with David Garabrandt, School of Public Health.
Study of Granulomatous Appendicitis with Laura Lamps at the University of Arkansas.
Study of Barretts dysplasia grading with GI Study Group.
Study of Neuroendocrine Tumors of the Gut with Murray Resnick, M.D. Haifa, Israel
Study of Vascular proliferative lesions of the Gut with Neil Bavikatty, M.D.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director, Surgical Pathology
- B. Director, Surgical Pathology Fellowship Program.
- C. Quality Assurance Officer for Surgical Pathology
- D. Member, Residency Selection Committee
- E. Member, Departmental Incentive Committee
- F. Member, University Hospital Tissue Committee
- G. Member, University Hospital Operating Room 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. Webmaster, Hans Popper Hepatopathology Society
- I. Abstract reviewer, GI section of USCAP meeting
- J. Chairperson, Education Committee of the Gastrointestinal Pathology Society

- K. Judge for Resident Abstract competition, Hans Popper Hepatopathology Society
- L. Editorial Board member, The Online Journal of Digestive Diseases
- M. President-Elect, Gastrointestinal Pathology Society.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Moderator and Invited Speaker, GI Pathology Society Companion Meeting at ASCP Meeting, New Orleans, October, 1999.
2. Invited Speaker, Pathology Grand Rounds, Univ. of Michigan, Dept of Pathology, Jan. 2000.
3. Co-director of USCAP course entitled "Infectious Diseases of the GI tract," March, 2000.
4. Invited Panelist, Gastrointestinal Pathology Specialty Conference, USCAP Meeting, March 2000.
5. Moderator, GI Pathology Society Companion Meeting at USCAP meeting, March 2000.
6. Moderator, GI Pathology Society Companion Meeting at DDW meeting, May, 2000.
7. Faculty Member, ASCP Workshop - Surgical Pathology of the Gastrointestinal Tract, Aspen, Colorado, May 1999.
8. Invited Speaker, M-Labs Symposium, Ann Arbor, Michigan, May 2000.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Tworek JA, Goldblum JR, Weiss SW, Greenson JK, Appelman, HD. Stromal Tumors of the Abdominal Colon. *Am J Surg Pathol* 23:937-945, 1999.
2. Tworek JA, Goldblum JR, Weiss SW, Greenson JK, Appelman HD. Stromal Tumors of the Anorectum. *Am J Surg Pathol* 23:946-954, 1999.
3. Shureiqi I, Wojno K, Poore J, Reddy R, Moussalli MJ, Spindler S, Greenson JK, Normolle D, Hasan AA, Lawrence TS, Brenner DE: Decreased 13-S-hydroxyoxoctadecadienoic acid levels and 15-lipoxygenase,-1 expression in human colon cancers. *Carcinogenesis* 20:1985-95, 1999.
4. Valdez R, Bronner M, Appelman HD, Greenson JK: Diffuse Duodenitis Associated with Ulcerative Colitis. *American Journal of Surgical Pathology* (In Press).

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Montgomery E, Goldblum JR, Greenson JK, Haber MM, Lamps LW, Lauwers GY, et al: Dysplasia as a Predictive Marker for Invasive Carcinoma in Barrett's Esophagus, A Follow-up Study Based on 138 Cases from a Diagnostic Variability Study. *Human Pathology*
2. Montgomery E, Goldblum JR, Greenson JK, Haber MM, Lamps LW, Lauwers GY, et al: Diagnostic Reproducibility of the Diagnosis of Dysplasia in Barrett's Esophagus: A Reaffirmation. *Human Pathology*.

BOOKS/CHAPTERS IN BOOKS:

None.

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

1. Lamps LW, Madhusudhan KT, Greenson JK, Pierce RH, Massoll NA, Scott MA. *Yersinia enterocolitica*: A potentially important cause of granulomatous appendicitis. Poster presentation at USCAP Meeting, 2000. *Modern Pathol* 13:83A, 2000.
2. Lazenby AJ, Greenson JK, Wilcox CM, Winokur TS. Staining of Microsporidia Nuclei by Light Microscopy. Poster Presentation at USCAP Meeting, 2000. *Modern Pathol* 13:84A, 2000.
3. Montgomery E, Bronner M, Goldblum J, Greenson JK, Haber M, Lamps L, et al. Diagnostic Reproducibility of Dysplasia in Barrett's Esophagus (BE): A Reaffirmation. Poster Presentation at USCAP Meeting 2000. *Modern Pathol* 13:85A, 2000.
4. Montgomery E, Bronner M, Goldblum J, Greenson JK, Haber M, Lamps L, et al. Dysplasia as a Predictive Marker for Cancer in Barrett's Esophagus: A follow-up study based on consensus diagnoses in 151 cases from 10 institutions. Platform Presentation at USCAP Meeting 2000. *Modern Pathol* 13:85A, 2000.
5. Ormsby AH, Granlich TL, Montgomery E, Bronner M, Greenson JK, Haber M, et al. Cytokeratin Subsets (CK7/20) Immunostaining in Biopsies of Barrett's Esophagus (BE) and BE-related Dysplasia/Adenocarcinoma (ADC): A multi-institutional study. Platform Presentation at USCAP Meeting 2000. *Modern Pathol* 13:86A, 2000.
6. Valdez R, Giordano TJ, Greenson JK. Endocrine Cell (EC) Hyperplasia of the Stomach in Graft-versus-Host-Disease (GVHD). Poster Presentation at USCAP Meeting 2000. *Modern Pathol* 13:90A, 2000.

**KATHLEEN P. HEIDELBERGER, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 JUNE 2000**

60% Appointment
1 Month family care leave
6 months extended sick leave

I. CLINICAL ACTIVITIES:

- A. Pediatric Necropsies, daily, six months.
- B. Pediatric Surgical Consultation Cases, intra and extra mural, daily, six months.
- C. Placental Pathology, daily six months.
- D. Heart biopsy service, regular back-up for Dr. Gerald Abrams.
- E. Adult Necropsy Service, staff, thirteen weeks.
- F. Regular coverage for Dan Remick, M.D. as Director of Autopsy Service
- G. Continued to organize and maintain the Michigan Cardiac Registry, six months.
- H. Teratology Unit, histology, as necessary, approximately 40 cases per year.
- I. Children's Cancer Study Group, coordinate pathological material and data necessary for all children registered in national tumor protocols. (Collaborating investigator, NCI #2-U10-CA-02971-33, CCSG, R. Hutchinson, M.D., P.I.).

II. TEACHING ACTIVITIES:

- A. House Officers in Pathology, daily consultation on Pediatric cases in surgical reading rooms, six months.
- B. House Officers in Pathology, gross and microscopic supervision of most pediatric necropsies, six months, and adult cases, six weeks plus on-call weekends.
- C. Lecture on Pediatric Necropsy Pathology in Orientation for new House Officers in Pathology.
- D. Core curriculum lectures for House Officers in Pediatric Pathology, two.
- E. Individual gross and microscopic resident teaching in Placental Pathology.
- F. Gross Necropsy Conference, one hour/week, six months.
- G. Coordinate three core curriculum lectures in placenta: Pathology and OB/GYN residents.
- H. Consult conference (1), pediatric cases for pathology residents.
- I. Conferences: Faculty, house staff and students:
 - 1. Pediatric Cardiology Death Conference, monthly, six months.
 - 2. Pediatric Tumor Conference, twice monthly, six months.
 - 3. Pediatrics CPC/General Death Conference, quarterly (one approximately).
 - 4. Pediatric Liver-GI Conference, twice monthly, six months.
 - 5. Pediatric General Surgery Conference monthly, six months.

III. RESEARCH ACTIVITIES:

- A. Continued study of effects of various congenital heart defects on the pulmonary vasculature.
- B. Collaborative project with pediatric surgeons (Joseph Lelli, M.D., lead) on the correlation of the frozen section results in biliary atresia with post operative bilirubin levels and recovery.
- C. Project with Pediatric surgeons (C. Harmon, M.D.) VEGF (vascular endothelial growth factor) and thrombospondin expression in neuroblastoma.

PROJECTS UNDER STUDY:

- A. Collaborative project with pediatric surgeons (Dan Teitelbaum, M.D., lead) on the mechanisms of the effects of total parenteral nutrition on the gastrointestinal tract and liver in a mouse model. (See abstracts; manuscript submitted.)
- B. Continued follow-up (with Mason Barr, M.D. and Aileen Sedman, M.D.) of the abnormal kidney development and function in surviving twin(s) in twin transfusion syndrome.
- C. Correlation project with pediatric surgeons (Joseph Lelli, M.D. lead) on clinical diagnosis/management and outcome of appendicitis in children (see abstracts and publications).
- D. Study with Drs. Graziano and Ludomirsky (Pediatric Cardiology) on pulmonary venous wall properties in hypoplastic left ventricle syndrome with premature closure of foramen ovale. (See papers - published or accepted.) Presented 9/99 Midwest Pediatric Cardiology Society meeting.
- E. Study with James Geiger, M.D. (Pediatric surgery) on dendritic cell (and other) markers in ganglioneuroma and ganglioneuroblastoma.

ONGOING RESEARCH:

- A. Continuing correlation as co-investigator of histopathologic changes in neuroblastoma associated with cell/tumor maturity with different tissue gene expressions. (Valerie Castle, M.D., PI.)

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Departmental ACAPT.
- B. Administrative coverage for Dan Remick as Director of Autopsy Service in his absence.

MEDICAL SCHOOL/HOSPITAL:

- A. Executive Committee for Mott/Women's/Holden/Psychiatric Hospitals.

REGIONAL AND NATIONAL:

- A. Women's Liaison Officer, American Association of Medical Colleges.
- B. Member Distinction and Awards Committee, Society for Pediatric Pathology.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Influence of restrictive atrial septa on pulmonary vascular morphology in patients with hypoplastic left heart syndrome. Graziano JN, Heidelberger KP, Ensing G, Gomez CA and Ludomirsky A. Accepted for publication.
2. Lelli, J, Drongowski R, Raviz S, Wilke L, Heidelberger KP and Hirschl R: Historical changes in the postoperative treatment of appendicitis in children: Impact on medical outcome. Journal of Pediatric 2000 Surgery 35:239-245.

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

1. Lelli J, Drongowski R, Raviz S, Wilke L, Heidelberger KP and Hirschl R: Historical changes in the post-operative treatment of appendicitis in children: Impact on medical outcome. Paper presented at Am. Pediatric Surg. Assn. Annual meeting. May, 1999. Palm Springs, CA.
2. Forbush B, Kiristioglu I, Teitelbaum DH, Eisenbraun MD and Heidelberger KP: Multi Drug Resistance 2 Gene Expression in the Murine Liver: Relevance to the Development of Parenteral Nutrition - Associated Cholestasis. Surgical Forum, 1998, XLIX 569-570.

**CORY M. HOGABOAM, Ph.D.
RESEARCH INVESTIGATOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

- A. Graduate Students:
1. Ph.D. Dissertation Committees, University of Michigan
 - a. Cynthia Bone-Larson
 - b. Claudia Jakubzick
 2. Undergraduate Students, University of Michigan
 - a. Matthew Steinhauser
 - b. Joe Barber
- B. Postdoctoral Fellows:
1. Kate Blease, Ph.D.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

1. **Principal Investigator**, *Role of Monocyte Chemoattractant Protein-1 (MCP-1) and CC Chemokine Receptor-2 (CCR2) in Persistent Experimental Airway Hyperresponsiveness and Fibrosis Due to Aspergillus fumigatus*. American Lung Association Research Grant RG-039-N (8%), \$24 217 per annum, 1/7/99 - 6/30/01.
2. **Co-investigator**, *Stem Cell Factor and mast cells in allergic airway disease*. R01 HL58178 (15%), \$135 000 per annum, 9/1/99 - 8/30/03.
3. **Co-investigator**, *Monokine gene expression/regulation in lung injury*. R01 HL31237 (10%), \$200 000 per annum, 4/01/00 - 3/31/05.
4. **Principal Investigator**, *Role of IL-4, IL-13 and MCP-1 during Allergic Airway Fibrosis*. Research Contract from Novartis Pharmaceuticals (10%), \$102 178.50 per annum, 1/1/00 - 1/1/02.
5. **Co-investigator**, *Specialized Centers of Research - Pathobiology of Fibrotic Lung Disease*. P50 HL56402-04 (5%), \$1 300 000 per annum, 09/01/97 - 08/30/01.

PENDING SUPPORT:

1. **Principal Investigator**, *Nitric oxide regulation during allergic aspergillosis*. R01 HL66028-01 (35%), \$150 000 per annum, 10/1/00-9/30/05.

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 IL-13 in chronic allergic airway disease.
- Role of nitric oxide in chronic allergic airway disease.
- Regulation of fibroblast activities during chronic asthma.
- Role of chemokines in liver regeneration.
- Role of SCF in acute and chronic inflammation.
- 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)
- B. Journal peer-review
 - 1. Canadian Journal of Physiology and Pharmacology
 - 2. Journal of Gastrointestinal Motility
 - 3. American Journal of Physiology
 - 4. Gastroenterology
 - 5. American Journal of Pathology
 - 6. Journal of Clinical Investigation
 - 7. Journal of Leukocyte Biology
 - 8. Journal of Immunology
 - 9. Journal of Clinical Immunology
 - 10. American Journal of Respiratory Cell and Molecular Biology
 - 11. Infection and Immunity
 - 12. Blood
 - 13. Journal of Experimental Medicine
- C. Grant peer-review
 - 1. National Institutes of Health, National Heart, Lung and Blood Institute.
 - 2. Department of Veterans Affairs, Merit Review.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

- 1. Keystone Symposia, Santa Fe, NM. January 17-24, 1999. Title: '*IL-4 gene transfer in the treatment of experimental mucosal inflammation.*'
- 2. The Banff Inflammation Workshop, Banff, AB. March 4-11, 1999. Title: '*Chemokine and chemokine receptor contributions to allergic airway disease.*'

3. Michigan Gastrointestinal Peptide Research Center Retreat 1999, Ann Arbor, MI. Title: '*Viral based gene therapies in GI disease: combating the skeptics.*'
4. Schering-Plough Research Institute, Immunology Department, Kenilworth, NJ. May 25-26, 1999. Title: '*Role of fractalkine and V28 in acetaminophen-induced hepatic injury.*'
5. Novartis Pharmaceuticals, Respiratory Diseases Department, Horsham, UK. October 1-5, 1999. Title: '*Airway remodeling associated with allergic airway disease.*'
6. Trauma, Shock, Inflammation and Sepsis (5th World Congress), Munich, Germany. February 28-March 4, 2000. Title: '*Cell trafficking.*'
7. Wayne State University, Allergy and Immunology Program, Detroit, MI. April 11, 2000. Title: '*Mouse models of fungal allergic asthma.*'
8. Mucosal Inflammation Research Group, University of Calgary, Calgary, AB. June 19-25, 2000. Title: '*Hepatic regenerative properties of ELR-CXC chemokines during liver injury.*'
9. Pulmonary Research Group, University of Alberta, Edmonton, AB. June 19-25, 2000. Title: '*Novel roles for chemokines during allergic airway remodeling.*'

PODIUM PRESENTATIONS AT SCIENTIFIC MEETINGS:

1. FASEB 1999, Washington, DC. '*Novel CXCR2-dependent liver regenerative qualities of ELR-containing CXC chemokines.*'
2. FASEB 2000, San Diego, CA. '*Innate immune and airway remodeling roles for monocyte chemoattractant protein-1 during lung exposure to Aspergillus fumigatus conidia.*'
3. AAI 2000, Seattle, WA. '*Airway remodeling is absent in CCR1-/- mice during chronic fungal asthma.*'

OTHER:

1. FASEB 2000, San Diego, CA, Chair of Minisymposium: '*Chemokines in Inflammation and Disease*'

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICAITON IN REFERRED JOURNALS.

1. Steinhauer M.L, Hogaboam C.M., Kunkel S.L., Lukacs N.W., Strieter R.M., Standiford T.J. Interleukin-10 is a major mediator of sepsis-induced impairment in lung antibacterial host defense. *J. Immunol.*, 162: 392-399, 1999.
2. Campbell E., Hogaboam C.M., Lincoln P., Lukacs N.W. Stem cell factor-induced airway hyperreactivity in allergic and normal mice. *Am. J. Pathol.*, 154: 1259-1265, 1999.
3. Steinhauer M.L, Hogaboam C.M., Lukacs N.W., Strieter R.M., Kunkel S.L. Multiple roles for interleukin-12 in a model of acute septic peritonitis. *J. Immunol.*, 162: 5437-5443, 1999.
4. Warmington K.S., Boring L., Ruth J.H., Hogaboam C.M., Kunkel S.L., Charo I.R., Chensue S.W. Effect of CC chemokine receptor 2 (CCR2) knockout on type 2 (Schistosomal antigen-elicited) pulmonary granuloma formation: analysis of cellular recruitment and cytokine responses. *Am. J. Pathol.*, 154: 1407-1416, 1999.

5. Hogaboam C.M., Simpson K.J., Chensue S.W., Steinhauser M.L., Lukacs N.W., Gauldie J., Strieter R.M., Kunkel S.L. Macrophage inflammatory protein-2 gene therapy attenuates adenovirus- and acetaminophen-mediated hepatic injury. *Gene Therapy*, 6: 573-584, 1999.
6. Hogaboam C.M., C.S. Gallinat, Taub D.D, Strieter R.M., Kunkel S.L, Lukacs N.W. Immunomodulatory role of C10 chemokine in a murine model of allergic bronchopulmonary aspergillosis. *J. Immunol.*, 162: 6071-6079, 1999.
7. Hogaboam C.M., Bone-Larsen C.L., Lipinski S., Lukacs N.W., Strieter R.M., Chensue S.W., Kunkel S.L. Differential MCP-1 and CCR2 receptor expression by lung fibroblasts from murine Th1-type and Th2-type pulmonary granuloma models. *J. Immunol.*, 163: 2193-2201, 1999.
8. Hogaboam C.M., Bone-Larson C.L., Steinhauser M.L., Colletti L.M., Lukacs N.W., Strieter R.M., Simpson K.J., Kunkel S.L. Novel CXCR2-dependent liver regenerative qualities of ELR-containing CXC chemokines. *FASEB J.*, 13: 1565-1574, 1999.
9. Lukacs N.W., Oliveira SH, Hogaboam C.M. Chemokines and asthma: redundancy of function or a coordinated effort? *J. Clin. Invest.* Oct 15;104(8):995-999, 1999.
10. Jedrzkiewicz S., Kataeva G., Hogaboam C.M., Kunkel S.L., Strieter R.M, McKay D.M. Superantigen immune stimulation evokes epithelial monocyte chemoattractant protein-1 and RANTES production. *Infect. Immun.*, 67(11): 6198-6202, 1999.
11. Lukacs N.W., Hogaboam C.M., Campbell E., Kunkel S.L. Chemokines: function, regulation and alteration of inflammatory responses. *Chem. Immunol.* 72: 102-120, 1999.
12. Matsukawa A., Hogaboam C.M., Lukacs N.W., Lincoln P.M., Strieter R.M., Kunkel S.L. Endogenous monocyte chemoattractant protein-1 protects mice in a model of acute septic peritonitis. Cross talk between MCP-1 and LTB₄. *J. Immunol.* 163: 6148-6154, 1999.
13. Barbara, G., Xing Z., Hogaboam C.M., Gauldie J., Collins S.M. IL-10 gene transfer prevents experimental colitis in rats. *Gut*, 46: 344-349, 2000.
14. Hogaboam C.M., Mehrad B, Blease K., Steinhauser M.L., Standiford T.J., Kunkel S.L, Lukacs N.W. Chronic airway hyperreactivity, goblet cell hyperplasia and peribronchial fibrosis during allergic airway disease induced by *Aspergillus fumigatus*. *Am. J. Pathol.*, 156: 723-732, 2000.
15. Matsukawa A., Hogaboam C.M., Lukacs N.W., Lincoln P.M., Strieter R.M., Kunkel S.L. Expression and contribution of endogenous IL-13 in an experimental model of sepsis. *J. Immunol.*, 164: 2738-2744, 2000.
16. Padol I, Huang J.Q., Hogaboam C.M., Hunt R.H. Therapeutic effects of the endothelin receptor antagonist RO-48-5695 in the TNBS/DNBS rat model of colitis. *Eur. J. Gastro. Hepatol.*, 12(3): 257-266, 2000.
17. Matsukawa A., Hogaboam C.M., Lukacs N.W., Lincoln P.M., Strieter R.M., Kunkel S.L. Endogenous MCP-1 influences systemic cytokine balance in a murine model of acute septic peritonitis. *Exp. Mol. Pathol.*, 68(2): 77-84, 2000.
18. Hogaboam C.M., Bone-Larson C.L., Steinhauser M.L., Matsukawa A., Gosling J., Boring L, Charo I.F., Simpson K.J., Lukacs N.W., Kunkel S.L. Exaggerated hepatic injury due to acetaminophen challenge in mice lacking CC Chemokine Receptor 2. *Am. J. Pathol.*, 156: 1245-1252, 2000.
19. Matsukawa A., Hogaboam C.M., Lukacs N.W., Lincoln P.M., Evanoff H.L., Kunkel S.L. Pivotal role of macrophage-derived chemokine in the innate immune response. *J. Immunol.*, 164: 5362-5368, 2000.
20. Hogaboam C.M., Bone-Larson C.L., Matsukawa A., Steinhauser M.L., Blease K., Lukacs N.W., Kunkel S.L. Therapeutic use of chemokines. *Curr. Pharm. Des.*, 6(6): 651-663, 2000.

ARTICLES ACCEPTED FOR PUBLICATION:

1. Blease K., Kunkel S.L, Hogaboam C.M. Acute inhibition of nitric oxide exacerbates airway hyperresponsiveness, eosinophilia and C-C Chemokine generation in a murine model Allergic Bronchopulmonary Aspergillosis. *Inflammation Research*, in press, 2000.
2. Blease K., Mehrad B., Standiford T.J., Lukacs N.W., Gosling J., Boring L., Charo I.F., Kunkel S.L, Hogaboam C.M. Enhanced pulmonary allergic responses to *Aspergillus* in CCR2^{-/-} mice. *J. Immunol.*, in press, 2000.
3. Blease K., Mehrad B., Standiford T.J, Lukacs N.W., Kunkel S.L., Chensue S.W., Lu B., Gerard C.J., Hogaboam C.M. Airway remodeling is absent in CCR1^{-/-} mice during chronic fungal allergic airway disease. *J. Immunol.*, in press, 2000.
4. Bone-Larson C.L., Hogaboam C.M., Steinhauser M.L., Lukacs N.W., Strieter R.M., Chensue S.W., Kunkel S.L. Novel protective effects of stem cell factor in a murine model of acute septic peritonitis. *Am. J. Pathol.*, in press, 2000.
5. Steinhauser M.L., Hogaboam C.M., Lukacs N.W., Strieter R.M., Kunkel S.L. C10 chemokine therapy promotes disease resolution and survival in an experimental model of bacterial sepsis. *Infect. Immun.*, in press, 2000.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Simpson K.J., Kunkel S.L., Harrison D.J., Hogaboam C.M., Lukacs N.W. Stem cell factor (SCF) attenuates liver damage and promotes regeneration in a murine model of acetaminophen-induced hepatic injury. *Gastroenterology*.
2. Bone-Larson C.L., Hogaboam C.M., Steinhauser M.L., Lukacs N.W., Strieter R.M., Chensue S.W., Kunkel S.L. Macrophage inflammatory protein-2 regulates the nuclear expression of hepatic transcription factors CCAAT/enhancer binding protein- β and signal transducer activator of transcription-3 during liver regeneration. *FASEB J.*
3. Ajuebor M.N., Hogaboam C.M., Kunkel S.L., Proudfoot A.E.I., Wallace J.L. The chemokine RANTES is a crucial mediator of the chronic phase of colitis in the rat. *J. Immunol.*
4. Matsukawa A., Lukacs N.W., Hogaboam C.M., Chensue S.W., Kunkel S.L. Chemokines and their receptors in cell-mediated immune responses in the lung. *Microscopy Research and Technique*.
5. Carollo M., Hogaboam C.M., Delaney S., Christie M.I., Perretti M. Temporal expression of chemokines and chemokine receptors in a model of mouse granuloma formation. Association with the different phases of the inflammatory response. *J. Immunol.*

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

1. Hogaboam C.M., Chensue S.W., Kunkel S.L. Role of C-C chemokines in Th1- and Th2-type pulmonary inflammation models. *Chemokines in Disease. Biology and Clinical Research*. Ed: C. Hebert. Humana Press. Chapter 9, pages 139-149, 1999.
2. Steinhauser M.L., Kunkel S.L., Hogaboam C.M. The role of cytokines in experimental models of sepsis. *ILAR Journal* Ed: P.A. Ward. National Research Council. 40: 142-150, 1999.

3. Bone-Larson C.L., Simpson K.J., Colletti L.M., Lukacs N.W., Lira S., Kunkel S.L., Hogaboam C.M. The role of chemokines in the immunopathology of the liver. *Immunological Reviews*. Ed: P. Parham. Munksgaard International Publishers. 170, 2000.
4. Hogaboam C.M., Bone-Larson C.L., Steinhauser M.L., Colletti L.M., Lukacs N.W., Strieter R.M., Simpson K.J., Kunkel S.L. Novel CXCR2-dependent liver regenerative qualities of ELR-containing CXC chemokines. *FASEB J.*, 13: A252.19, 1999.
5. Bone-Larson C.L., Hogaboam C.M., Steinhauser M.L., Lukacs N.W., Strieter R.M., Chensue S.W., Kunkel S.L. The multiple protective roles of stem cell factor in a murine model of fecal peritonitis. *FASEB J.*, 13: A750.6, 1999.
6. Galeazzi F., Vallance B.A., Hogaboam C.M., Collins S.M. Macrophages play a protective role during experimental colitis in the mouse. *Gastroenterology*, 116; A560, 1999.
7. Hogaboam C.M., Blease K., Mehrad B., Steinhauser M.L., Standiford T.J., Kunkel S.L., Lukacs N.W. A novel model of chronic allergic airway disease induced by *Aspergillus fumigatus*. *Am. J. Resp. Crit. Care Med.* 161(3): A843, 2000.
8. Blease K., Mehrad B., Kunkel S.L., Lukacs N.W., Hogaboam C.M. IL-18 neutralization exacerbates airway hyperresponsiveness and lung fibrosis in a chronic model of *Aspergillus fumigatus*-induced allergic airway disease. *Am. J. Resp. Crit. Care Med.* 161(3): A843, 2000.
9. Hogaboam C.M., Blease K., Mehrad B., Lukacs N.W., Standiford T.J., Kunkel S.L. Innate immune and airway remodeling roles for monocyte chemoattractant protein-1 during lung exposure to *Aspergillus fumigatus* conidia. *FASEB J.*, 14(4): A219.11, 2000.
10. Steinhauser M.L., Hogaboam C.M., Lukacs N.W., Kaplan M.H., Kunkel S.L. Extracellular and intracellular regulation of the CC chemokine C10. *FASEB J.*, 14(4): A137.11, 2000.
11. Gharaee-Kermani, M., Smith R., Bravo R., Hogaboam C.M., Kunkel S.L., Phan S. A role for eotaxin in bleomycin-induced lung fibrosis. *FASEB J.*, 14(4): A399.7, 2000.
12. Blease K., Mehrad B., Kunkel S.L., Lukacs N.W., Hogaboam C.M. Exacerbation of airway hyperresponsiveness and lung fibrosis by IL-18 neutralization in a chronic model of *Aspergillus fumigatus*-induced allergic airway disease. *FASEB J.*, 14(4): A448.2, 2000.
13. Matsukawa A., Hogaboam C.M., Lukacs N.W., Strieter R.M., Kunkel S.L. Crucial role of CC chemokine macrophage derived chemokine (MDC) in lethal septic peritonitis in mice. *FASEB J.*, 14(4): A489.7, 2000.
14. Hogaboam C.M., Blease K., Mehrad B., Standiford T.J., Lukacs N.W., Chensue S.W., Lu B., Gerard C.J., Kunkel S.L. Airway remodeling is absent in CCR1^{-/-} mice during chronic fungal allergic airway disease. *FASEB J.*, 14(6): A101.1, 2000.
15. Matsukawa A., Hogaboam C.M., Lukacs N.W., Knibbs R.N., Bullard D.C., Stoolman L.M., Kunkel S.L. Mice lacking E- and P-selectin are resistant to the lethality in a murine model of acute septic peritonitis. *FASEB J.*, 14(6): A149.15, 2000.

PATENTS:

Treatment of liver disease and injury with ELR-CXC chemokines, Filed August 9, 1999, Docket Number: 4100.000980, Provisional Serial Number: 60,147,855

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

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.

PENDING SUPPORT:

- A. Co-Principal Investigator, "MMPs in Prostate Cancer" 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. Visiting Professor and Lecture, University of Florida, Gainesville, Florida.

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

1. Gipson, T.S., Bless, N.M., Shanley, T.P., Crouch, L.D., Bleavins, M.R., Younkin, E.M., Sarma, V., Gibbs, D.F., Wongelawit, T., McConnell, P.C., Mueller, W.T., Johnson, K.J., and Ward, P.A.: Regulatory effects of endogenous protease inhibitors in acute lung inflammatory injury. *J. Immunol.*, 1999, 162:3653-3662.
2. Gibbs, D.F., Apel, I.J., Weiss, S.J., Johnson, K.J., and Varani, J.: Characterization of matrix metalloproteinases produced by rat alveolar macrophages. *Am. J. Respir. Cell Mol. Biol.*, 1999, 20:1136-1144.
3. Gibbs, D.F., Shanley, T.P., Warner, R.L., Murphy, H.S., Varani, J. and Johnson, K.J.: Role of matrix metalloproteinases in models of macrophage-dependent acute lung injury. *Am. J Respir. Cell Mol. Biol.*, 1999, 20:1145-1154.
4. Varani, J., Dame, M.K., Wojno, K., Schuger, L., and Johnson, K.J.: Characteristics of non-malignant and malignant human prostate in organ culture. *Lab. Invest.* 1999,79(6):723-731
5. Davidson, B.A., Knight, P.R., Helinski, J.D., Nader, N.D., Shanley, T.P., and Johnson, K.J.: The role of tumor necrosis factor- α in the pathogenesis of aspiration pneumonitis in rats. *Anesthesiology*, 1999;91(2):486-499.
6. Hamouda, T., Hayes, M.M., Cao, Z., Tonda, R., Johnson, K., Wright, D.C., Brisker, J., and Baker, J.R.: A novel surfactant nanoemulsion with broad-spectrum sporicidal activity against *Bacillus* species. *Journal Infectious Diseases*, 1999;180(6)1939-1949.
7. Nader, N.D., Knight, P.R., Bobela, I., Davidson, B.A., Johnson, K.J., and Morin, F.: High-dose nitric oxide inhalation increases lung injury after gastric aspiration. *Anesthesiology*. 1999;91(3):741-749.
8. Varani, J., Dame, M.K., Wojno, K., Schuger, L., and Johnson, K.J.: Characteristics of nonmalignant and malignant human prostate in organ culture. *Laboratory Investigation*. 79:723-731, 1999.
9. Donovan, B.W., Reuter, J.D., Zhengyi, C., Andrezej, M., Johnson, K.J., and Baker Jr., J.R.: Prevention of murine influenza A viral pneumonitis by surfactant nanoemulsions. *AntiViral Chemistry and Chemotherapy, Antiviral Chemistry & Chemotherapy 2000*; 11:41-49
10. Shanley, T.P., Davidson, B.A., Nader, N.D., Bless, N., Vasi, N., Ward, P.A., Johnson, K.J., and Knight, P.R.: The role of macrophage inflammatory protein-2 (MIP-2) in aspiration-induced lung injury. Accepted in *Critical Care Medicine*, 1999.
11. Warner, R.L., Bless, N.M., Lewis, C.S., Younkin, E., Beltran, L., Guo, R.F., Johnson, K.J., and Varani, J.: Time-dependent inhibition of immune complex lung injury by catalase: Relationship to alterations in macrophage and neutrophil matrix metalloproteinase elaboration, Accepted in *Free Rad. Biol. Med.*, 2000.

ARTICLES SUBMITTED FOR PUBLICATION:

1. 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.

2. 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.
3. 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.
4. O'Shea, K.S., Johnson, K.J., Gordon, D., Sliwkamski, M.X., and Erickson, S.L.: Effects of heregulin treatment on adult wild-type and ErbB2, ErbBC and heregulin heterozygous null mice. Submitted for publication.
5. O'Shea, S., Johnson, K.J., Gordon, D., Pisacane, P., Clark, R., Sliwkowski, M.X. and Erickson, S.L.: Effects of heregulin on adult breast and other epithelial tissues: an in vivo study of wildtype, heregulin, ErbB2 and ErbB3 heterozygous null mice. Submitted for publication.
6. Reuter, 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.
7. 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. Varani, J., Gibbs, D. F., Apel, I. J., Warner, R. L., Weiss, S. J., Johnson, K. J.: Characterization of matrix metalloproteinases produced by rat alveolar macrophages. Keystone Symposium, Macrophage Biology, January 1999.
2. Johnson, K. J., Gibbs, D. F., Shanley, T. P., Warner, R. L., and Varani, J.: The role of matrix metalloproteinases in models of acute lung injury: evidence for the alveolar macrophage as the source of the proteinases. Keystone Symposium, Macrophage Biology, January 1999.
3. Lake, K.D., Leavey, S.F., Ojo, A.O., Johnson, K.J., Punch, J.D., Bromberg, J.S., Campbell, D.A., Magee, J.C., Merion, R.M., Turcotte, J.G. and Leichtman, A.B.: The successful use of sirolimus in transplant recipients with hemolytic uremic syndrome. American Society of Transplant Surgeons, 1999.

4. Younkin, E.M., Warner, R.L., Bless, N.M., Varani, J., and Johnson, K.J.: In vitro effects of catalase on the production of matrix metalloproteinases (MMPs) by alveolar macrophages and neutrophils. *FASEB J.* 13(5)748.6, 1999.
5. Warner, R.L., Bless, N.M., Younkin, E.M., Varani, J., and Johnson, K.J.: Time-dependent effects of catalase administration on the reduction of matrix metalloproteinase (MMP) activity in acute lung alveolitis. *FASEB J.* 13(5)639.15, 1999.
6. Gough, A., Walsh, K., Johnson, K., Kennedy, J., Pegg, D., and de la Iglesia, F.: Nephrotoxicity of HIV protease inhibitor, CI-1029, in humans and monkeys. Submitted to ACVP Meeting, 2000.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

- A. Clinical Pathology Grand Rounds:
 - 1. Program Director.
 - 2. Presented lectures entitled "The electronic crossmatch."
- B. Anatomical Pathology Conferences:
 - 1. Program Coordinator.
- C. Core-Lecture Series in Blood Banking for 1st-year Pathology House Officers:
 - 1. Program Coordinator.
 - 2. Presented lectures on:
 - a) Pretransfusion testing.
 - b) Prenatal/perinatal testing.
 - c) Immune hemolysis.
 - d) Antibody identification.
- D. Clinical Pathology Case Study Conference:
 - 1. Program Coordinator.
 - 2. Participant.
- E. Fellows:
 - 1. Christin Martin, MD, Blood Bank Fellow.
- F. Pathology Residents:
 - 1. Residency Training Review Committee.
 - 2. Provided instruction in immunohematology to house-officers during their Blood Bank Rotation (over 200 contact hours).
 - 3. Obtained accreditation of a Transfusion Medicine Fellowship Training Program to the Accreditation Council for Graduate Medical Education.
- G. Current Topics in Blood Banking Conference, Towsley Center for Continuing Medical Education:
 - 1. Program Director - Planned and coordinated the June, 2000 Current Topics in Blood Banking Symposium and Preconference Workshops.
 - 2. Presented Workshop entitled: "Cases we have known and loved."
 - 3. Presented talk entitled: "Repeat antibody identification."
 - 4. Presented talk entitled: "Automation in the transfusion service"

5. Moderated morning session on Transfusion Medicine.

III. RESEARCH ACTIVITIES:

1. Judd WJ, Storry JR, Annesley TD, Reid ME, Bensette M, Dake L, Waddington S, Rohrkemper D, Valdez R. The first example of a Paraben-dependent anti-Rh. *Transfusion* 1999;39(S):79.
2. Judd WJ, Davenport RD, Suchi M. An 'enzyme-only' alloanti-C causing acute intravascular hemolysis. *Abstract submitted to AABB.*
3. Judd WJ, Dake L. PEG-adsorption of autoantibodies results in loss of concomitant alloantibody. *Abstract submitted to AABB.*
4. Judd WJ, Downs T, Davenport RD, Hammond D, Sing C, Pehta JC. In vitro analysis of isohemagglutinin-depleted solvent detergent plasma. Accepted for presentation at the International Society for Blood Transfusion Meeting, Vienna, Austria, July 2000.

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. Co-Chairman, Special Lecture Series Committee - coordinated a series of 60 lectures medical technologists seeking Certification as a Specialist in Blood Banking.
 2. Presented lectures on Rh and MN systems, prenatal testing, lectins and polyagglutination (6 contact hours) as part of Special Lecture Series.
 3. Member, Annual Meeting Program Committee.
- B. American Association of Blood Banks:
 1. Member, Scientific Abstract Review Committee.
 2. Member, Editorial Board, *Transfusion*.
- C. Reviewer of articles submitted for publication in *Transfusion*, *Immunohematology*, *Transfusion Medicine* and *Vox Sanguinis*.
- D. International Society of Blood Transfusion
 1. Member, WHO Committee on Blood Group Nomenclature

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES:

1. Modern approaches to pretransfusion testing. Ortho Clinical Diagnostics, Washington, DC, September, 1999.

2. Modern approaches to pretransfusion testing. Chicagoland Blood Bank Society, October, 1999.
3. The electronic crossmatch. Ontario Area Medical Technology Continuing Education Program, Toronto, April, 2000.
4. Clinical insignificance of a positive direct antiglobulin test. AABB Annual Meeting, San Francisco, CA, November, 1999.
5. Modern approaches to pretransfusion testing. AABB Annual Meeting, San Francisco, CA, November, 1999.
6. Cases I have know and loved. Toronto General Hospital, April, 2000.
7. The electronic crossmatch. Marion F. Beard Memorial Seminar. American Red Cross, Louisville, KY, June 2000.

PUBLICATIONS:

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

1. Elution – dissociation of antibody from red blood cells: theoretical and practical considerations. *Transfusion Medicine Reviews*, 1999;13:297-310.
2. Judd WJ, Storry JR, Annesley TD, Reid M, Bensette M, Waddington S, Dake L, Rohrkemper D, Valdez R. The first example of a paraben-dependent anti-Rh. *Transfusion*: Accepted.

CHAPTERS IN BOOKS:

1. Judd WJ. Blood groups. *In: Encyclopedia of Science and Technology*. New-York: McGraw-Hill, Accepted.
2. Judd WJ. Pretransfusion testing. *In: McClatchey KD, ed. Clinical laboratory medicine, ed 2*. Baltimore: Lippincott, Williams and Wilkins. Accepted.
3. Judd WJ. Issues in implementing an electronic (computer) crossmatch. *Ortho Clinical Diagnostics White Paper*. Accepted.

**EVAN T. KELLER, D.V.M., Ph.D.
ASSISTANT PROFESSOR OF COMPARATIVE MEDICINE AND PATHOLOGY
UNIT FOR LABORATORY ANIMAL MEDICINE AND
DEPARTMENT OF PATHOLOGY
ASSISTANT RESEARCH SCIENTIST
INSTITUTE OF GERONTOLOGY**

**ANNUAL DEPARTMENT REPORT
1 JULY 1999 – 30 JUNE 2000**

I. TEACHING ACTIVITIES:

- A. Lecturer, Pathology 581 Course, 6 contact hours
- B. Post-doctoral Fellows: Din-Lii Lin, Ph.D, Jin-Lu Dai, M.D., Pete Smith, D.V.M.
- C. Graduate Students: Jian Zhang, M.D., Jill Murtha, D.V.M., Zheng Fu.
- D. Undergraduate Students: Avni Patel, Richard Prebish
- E. Director, ULAM Post-doctoral Fellow Training Grant
- F. Institute of Gerontology Training Grant
- G. Immunology Training Program
- H. Committees, Henli Chen and Maya Williams

II. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Estrogen-modulated cytokine expression in osteoporosis in non-human primates.
- B. Role of interleukin-6 in ethanol-mediated osteoporosis
- C. Role of oxidative stress on cytokine induction in the brain.
- D. Oxidative stress and gene expression in aging.
- E. Role of interleukin-6 in prostate cancer resistance to chemotherapy.
- F. The biology of prostate cancer skeletal metastases.
 - 1. Osteoblastic lesions.
 - 2. Osteolytic activity.
- G. Heat shock protein response in zebrafish.

SPONSORED SUPPORT:

- 1. National Institute of Aging (R01-AG-11970), "Interleukin-6 and Osteoporosis" (Keller; PI), 5/1/95-4/30/02 (\$228,827 annual direct cost).
- 2. National Institute of Aging (R01-AG-15904), "Ethanol-mediated osteoporosis and interleukin-6." (Keller,PI) 3/1/98-2/28/03 (\$148,000 annual direct cost).
- 3. National Institute of Aging (R01-AG-15904), Supplement for "Ethanol-mediated osteoporosis and interleukin-6." (Keller, PI) 12/15/98-12/14/00 (\$61,000 annual direct cost).
- 4. National Insitute of Aging. (R01-AG-15884) "Aging, gene expression and oxidative stress" (Keller; PI) 12/01/99-11/30/02 (\$170,000 annual direct cost).

5. 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).
6. Department of Defense. (PC991111) "Interleukin-6 and prostate cancer progression." (Keller, PI) 06/01/00-05/30/03 (\$69,000 annual direct cost).
7. Parke-Davis Pharmaceuticals, (Gift) "For Bone Biology Research Development" (Keller: PI), 10/01/99 (\$50,000).
8. National Cancer Institute. SPORE in Prostate Cancer. "Inhibition of interleukin-6 to enhance prostate cancer chemotherapy." (Keller, PI), 10/01/99-9/28/00. (\$45,000 annual direct cost).
9. U. Michigan BMRC (Basic Science Program Project Planning Grant) "The biology of prostate cancer skeletal metastases." (Keller; Role: PI), 10/01/99-09/30/00 (\$10,000 annual direct cost).
10. National Cancer Institute (P30-CA-46592), "The University of Michigan Comprehensive Cancer Center Core Grant." (M. Wicha, P.I.; Keller, Associate Director of Connective Tissue Oncology Program) 6/1/96 - 5/31/01. (\$1,865,046 total grant annual directs)
11. 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).
12. U. Michigan BMRC (Equipment Grant). Light Cycler PCR Machine (Keller; Role: PI). 04/01/00 (\$48,175 annual direct cost).

CONSULTANT ACTIVITY:

1. Parke-Davis Pharmaceuticals, Bone Biology, Contact, Vijaykumar Baragi, PhD.

III. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Chair, Jody C. Ungerleider Memorial Award Committee

MEDICAL SCHOOL/HOSPITAL:

- A. Comparative Integrative Genomics Development Committee
- B. Colony for Aged Rodents Advisory Committee
- C. Associate Director, Connective Tissue Oncology Program, Cancer Center
- D. Director, Mutant and Transgenic Rodent Core, Nathan Shock Center
- E. Grant reviewer for OVPR
- F. Rackham Graduate Student Appeals Committee

REGIONAL AND NATIONAL:

- A. Deputy Editor, *Journal of Gerontology: Medical Sciences*
- B. Reviewer:
 1. *Cytokine*
 2. *Journal of Gerontology: Biological Sciences*

3. *Cancer Research*
- C. National Scientific Advisory Council, American Federation Aging Research
- D. Scientific Advisory Board, Institute for Advanced Studies in Aging
- E. Chair, Osteoporosis section. Serono Conference on Menopause
- F. Ad hoc reviewer, VA Merit Awards

OTHER RELEVANT ACTIVITIES:

A. Memberships:

1. Multipurpose Arthritis and Musculoskeletal Disease Center Faculty
2. Cancer Center
3. Cellular and Molecular Biology
4. Immunology Program

IV. INVITED LECTURES/SEMINARS:

1. "The role of interleukin-6 in prostate cancer pathophysiology," invited seminar. Michigan Consortium on Prostate Cancer Research, UM, March 2000.
2. "Alcohol-mediated bone loss and interleukin-6," invited seminar. Oral Health Sciences Seminar, School of Dentistry, University of Michigan, April 2000.
3. "Cross-talk between interleukin-6 and the androgen receptor," invited seminar. East Medical University, Shanghai, China, June 2000.
4. "Cross-talk between interleukin-6 and the androgen receptor." Invited seminar. Zhongshan Medical University, Guangzhou, China, June 2000.

V. AWARDS/HONORS:

1. Visiting Professorship, Dept. of Immunology, Tianjin Medical University, Tianjin China, 2000.

VI. PUBLICATIONS:

PUBLISHED ARTICLES:

1. Chiu KM, Keller ET, Crenshaw TD, Gravenstein S. Carnitine and dehydroepiandrosterone sulfate induce protein synthesis in porcine primary osteoblast-like cells. *Calcif Tissue Int.* 64:527-533, 1999.
2. Keller ET, Binkley NC, Stebler BA, Hall DM, Johnston G, Zhang J, Ershler WB. Ovariectomy does not induce osteopenia through interleukin-6 in rhesus monkeys (*Maccaca mulatta*). *Bone.* 26:55-62, 2000.
3. Chiu KM, Arnaud CD, Ju J, Mayes D, Bacchetti P, Weitz S, Keller ET. Correlation of estradiol, parathyroid hormone, interleukin-6 and interleukin-6 receptor during the normal menstrual cycle. *Bone.* 26:79-85, 2000.
4. Knezevic-Cuca J, Stansberry KB, Johnston G, Zhang J, Keller ET, Vinik AI, Pittenger GL. Neurotrophic role of interleukin-6 and soluble interleukin-6 receptors in N1E-115 neuroblastoma cells. *J Neuroimmunol.* 102:8-16, 2000.

5. Ershler WB, Keller ET. Age-associated increased IL-6 gene expression, late life diseases and frailty. *Ann Rev Medicine*. 51:245-270, 2000.

ARTICLES ACCEPTED FOR PUBLICATION:

1. Morris MD, Tarnowski CP, Timlin JA, Carden A, Dreier JL, Ignelzi MA, Jr., Lin D, Keller ET. Raman Imaging as a Probe of Chemical and Biomechanical Properties of Bone Tissue. *Society of Photo-Instrumentation Engineers Annual Proceedings*. In Press.
2. Mizokami A, Gotoh A, Yamada H, Keller ET, Matsumoto T. Tumor necrosis factor- represses androgen sensitivity in the LNCaP prostate cancer cell line. *J Urol*. In Press.
3. Muenchen H, Lin DL, Walsh MA, Keller ET, Pienta KJ. TNF-induced apoptosis in prostate cancer cells through inhibition of NF- κ B by an I κ B α "Super-Repressor." *Clin Cancer Res*. In Press.

ABSTRACTS:

1. Keller ET, Zhang J, Stebler B. Influence of immune factors on bone remodeling in rhesus monkeys (*Macaca mulatta*). *American Society for Bone and Mineral Research Annual Meeting*, 1999.
2. Zhang J, Murtha J, Habib P, Smith P, Keller ET. Ethanol induces hepatic lipid peroxidation through interleukin-6 in mice. *Oxygen Society Annual Meeting*, New Orleans, 1999.
3. Keller ET, Zhang J, Johnston G, Stebler B. Oxidative stress-mediated activation of NF κ B and the interleukin-6 promoter requires NF κ B-inducing kinase activity. *Gordon Conference on Aging*. Ventura, CA, 2000.
4. Lin D, Gopalakrishnan R, Franceschi RT, Keller ET. The bone metastatic LNCaP-derivative C4-2B prostate cancer cell line produces bone in vitro. *American Association for Cancer Research Annual Meeting*, San Francisco, 2000.
5. Lin D, Mizokami A, Keller ET. Interleukin-6 Induces Androgen Receptor Function through MAPK/ERK Kinase (MEK) in Prostate Cancer Cells. *American Association for Cancer Research Annual Meeting*, San Francisco, 2000.
6. Dai J, Zhang J, Lin D, Keller ET. Conditioned medium from the bone metastatic LNCaP-derivative C4-2B prostate cancer cell line induces osteoblasts to produce bone in vitro. *American Association for Cancer Research Annual Meeting*, San Francisco, 2000.
7. Zhang J, Keller ET. Osteoprotegerin (OPG) inhibits osteoclastogenesis induced by prostate cancer cells in vitro. *American Association for Cancer Research Annual Meeting*, San Francisco, 2000.
8. Smith PC, Dai JL, Keller ET. Anti-interleukin-6 antibody enhances chemotherapeutic-mediated inhibition of prostate cancer cell growth in vitro. *American Association for Cancer Research Annual Meeting*, San Francisco, 2000.
9. Bautch JC, Ferguson KJ, Ring DL, Keller ET. The effects of exercise on interleukin-6 (IL-6) levels in the synovial fluid of osteoarthritic knees. *Association of Rheumatology Health Professional Annual Meeting*, Philadelphia, 2000.

**ANTHONY A. KILLEEN, M.D., Ph.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

- A. Director of Molecular Diagnostics.
- B. Director of Clinical Chemistry Section.
- C. Interpretation and sign-out of protein electrophoretic analyses.

II. TEACHING ACTIVITIES:

- A. Lectures to House Staff on Clinical Pathology.
- B. Protein Sign-Out in Immunology Laboratory with 1-2 residents for 4-6 hours biweekly.
- C. Molecular Diagnostics Sign-Out with Residents.
- D. Lectures to Pathology House Staff and Faculty at Clinical Pathology Rounds.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Co-Investigator, "Genetics of CYP2A in cigarette smokers". E.F. Domino (Principal Investigator) 10% effort (Pending)

PROJECTS UNDER STUDY:

- A. Molecular Genetics of CYP21 (Steroid 21-hydroxylase).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director, Molecular Diagnostics Laboratory.
- B. Director, Clinical Chemistry Section.
- C. Member, Pathology Resident Selection Committee.
- D. Director, Fellowship Program in Chemical Pathology.
- E. Member, Departmental Internal Review Committee

OTHER DEPARTMENT:

- A. Director, Clinical Molecular Genetics Fellowship Program

REGIONAL AND NATIONAL:

- A. Past-Chair, Molecular Pathology Subdivision of American Association for Clinical Chemistry.
- B. Chair, Training and Education Committee, Association for Molecular Pathology.
- C. Editorial Board Member, Molecular Diagnosis, Clinical Molecular Diagnostics.
- D. Manuscript Reviewer, Clinical Chemistry, Molecular Diagnosis, and Clinical Molecular Diagnostics.
- E. Member, 2001 EduTrak Committee, American Association for Clinical Chemistry annual meeting.
- F. Moderator, EduTrak "Advances in the Pathogenesis and Diagnosis of Neurodegenerative Diseases", American Association for Clinical Chemistry 2000 meeting, San Francisco
- G. Member, College of American Pathologists Chemistry Resource Committee.

V. INVITED LECTURES AND SEMINARS:

- 1. Killeen AA: The Congenital Adrenal Hyperplasias. XXIII World Congress of Pathology, Brazil, September, 1999.
- 2. Killeen AA: Nucleic Acid Quantification. ASCP/CAP Fall Meeting, New Orleans, September, 1999.
- 3. Killeen AA: Nucleic Acid Quantification. ASCP/CAP Spring Meeting, Boston, April 2000.
- 4. Killeen AA: Basic Genetics. Lecture to the Michigan Association of Blood Banks, March 2000.

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

- 1. Zhou M, Sheldon S, Akel N, Killeen AA: Chromosomal aneuploidy in leukemic blast crisis: a potential source of error for interpretation of bone marrow engraftment analysis by VNTR amplification. *Mole Diag* 4:153-157, 1999.
- 2. Ozturk IC, Killeen AA: Molecular genetic factors in cardiovascular disease. *Arch Pathol Lab Med* 123:1219-1222, 1999.
- 3. Jone C, Killeen AA: Monitoring of bone marrow engraftment by PCR of D1S80 with capillary electrophoretic separation of amplicons. *Mole Diag* (in press).
- 4. Wei W-L, Ozturk IC, Palaniappan L, Rubenfire M, Killeen AA: Analysis of CYP21 coding polymorphisms in 3 ethnic populations: further evidence of non-amplifying CYP21 alleles among whites. *Mole Diag* 5:47-52, 2000.
- 5. Bavikatty NR, Killeen AA, Akel N, Schmaier AH: Association of the prothrombin 20210 (G to A) mutation with factor V Leiden in a Midwestern American population. *Am J Clin Pathol* (in press).

VII. BOOKS/CHAPTERS IN BOOKS:

- 1. Killeen AA: "Protocols in Molecular Pathology" (in press). Compilation of laboratory protocols in Molecular Pathology to be published by Humana Press in the "Methods in Molecular Medicine" series. Expected publication date: September 2000.

2. Ozturk IC, Killeen AA: Genotyping of ApoE. In: Killeen AA (ed.): Protocols in Molecular Pathology. Humana Press, (in press).
3. Killeen AA: Technologies in the Clinical Laboratory. In: Gruber S (ed.): Cancer Genetics, (in press).

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

1. Wei WL, Killeen AA: Identification of a frequent RsaI polymorphism in intron 6 of CYP21. Clin Chem (in press).
2. Killeen AA, Jiddou R, Sane KS: Identification of polymorphisms in intron 2 of the CYP21 gene. Am J Pathol 151:1490, 1997.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

- A. Board Certification, Anatomic Pathology.
- B. Diagnostic Renal Biopsy Service (28 weeks).
- C. Chief Renal Consultant.

II. TEACHING ACTIVITIES:

- A. M2 Pathology Lecture - Renal Sequence (3 hours).
- B. M2 Pathology Laboratory- Renal Sequence (12 hours).
- C. Co-Coordinator - Renal Sequence (60 hours).
- D. Anatomy and Cell Biology 530 (PIBS) (3 hours)
- E. Renal Pathology for Pathology Residents (4 hours).
- F. Renal Pathology for Nephrology Fellows Lectures (8 hours).
- G. Diagnostic Renal Pathology Rotations with Fellows (100 hours)
- H. Dissertation Committees (one).

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, "IGF-I is an Osmoprotectant in Neuroglial Cells", NIH-R01-DK38304, (5% Effort) \$103,045 direct costs/year, 3/1/98 to 2/28/2003
- C. Core Consultant, Molecular Biology Core, "Michigan Diabetes Research and Training Center", NIH-P60-DK20572, (5% Effort) \$100,000 direct costs/year, 4/1/98-3/31/03.

PENDING SUPPORT:

- A. Co-Investigator, "Chronic Allograft Nephropathy in the Elderly", NIH PO1-, (10% Effort) \$125,547 direct costs/year.

PROJECTS UNDER STUDY:

- A. Regulation of collagen IV gene expression.
- B. Interstitial fibrosis as a predictor of renal progression.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Anatomic Pathology Accessioning Committee.
- B. Digital Imaging Committee.

MEDICAL SCHOOL/HOSPITAL:

- A. Faculty recruitment, Departments of Internal Medicine, Pediatrics.
- B. Component II Curriculum development, M2 Urinary System.
- C. Assistant Director, Diagnostic Renal Biopsy 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. Laboratory Investigation.
 - 2. American Journal of Pathology.
 - 3. American Journal of Physiology.
 - 4. Journal of Clinical Investigation.
 - 5. Journal of Biological Chemistry.
 - 6. Journal of American Society of Nephrology.

V. INVITED LECTURES AND SEMINARS:

None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Porcellati F, Hosaka Y, Hlaing T, Togawa M, Larkin DD, Karihaloo A, Stevens MJ, Killen PD, Greene DA: Alternate splicing in human Na⁺-MI cotransporter gene yields differentially regulated transport isoforms. *Am J Physiol.* 276:C1325-1337, 1999.
2. Van Vliet AI, Van Alderwegen IE, Baelde HJ, de Heer E, Killen PD, Kalluri RK, Bruijn JA, Bergijk EC: Differential Expression of Collagen Type IV Alpha-chains in the Tubulointerstitial Compartment in Experimental Chronic Serum Sickness Nephritis. *J Pathol.* 189:279-287, 1999.
3. Lu W, Phillips CL, Killen PD, Hlaing T, Harrison WR, Elder FFB, Miner JH, Overbeek PA, Meisler MH: Insertional mutation of the collagen genes Col4a3 and Col4a4 in a mouse model of Alport syndrome. *Genomics* 61:113-124, 1999.
4. Abe A, Gregory S, Lee L, Killen PD, Brady RO, Kulkarni A, Shayman JA: Reduction of globotriaosylceramide in Fabry mice by substrate deprivation. *J Clin Invest* 105:1563-1571, 2000.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Todd-Turla KM, Schnermann JB, Briggs JP, Killen PD: Regulation of Renal Mineralocorticoid and Glucocorticoid Receptor mRNA in Response to Adrenalectomy and Corticosteroid Hormone Replacement. Submitted 1999.
2. Schieren G, Gattone VH, Killen PD: Aberrant expression of extracellular matrix genes is prominent in slowly progressive polycystic kidney disease in *pcy/pcy* mouse. Submitted 2000.

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

1. Nakashima E, Pop-Busui R, Larkin D, Stevens M, Killen PD, Towns R, and Greene DA: Post-Translational Regulation of the Sodium-Dependent *myo*-Inositol Cotransporter (SMIT) in Response to Hypertonicity. *J Am Soc Nephrol* 10:55a, 1999.
2. Duhme C, McNagny KM, Killen PD and Kershaw DB: Homozygous Disruption of the Murine Podocalyxin/MEP21 Gene Leads to Disordered Glomerular Structure and Neonatal Death. *J Am Soc Nephrol* 10:544a, 1999.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

- A. Diagnosis of surgical specimens, including frozen sections, and biopsies in diagnostic rooms I, II, and C with residents and fellows.
- B. Daily diagnosis of consultation cases and transfer cases (TS) in breast pathology referred from pathologists elsewhere in the U.S.
- C. Presentation of breast cancer cases at the weekly multidisciplinary Breast Care Conference.
- D. Diagnosis of heart transplant biopsies.

II. TEACHING ACTIVITIES:

- A. Medical Students (M4)
 - 1. Presentation of interesting breast pathology cases in the radiology-pathology course (4 contact hours)
- B. Pathology House Officers and Fellows
 - 1. Slide conferences (3) on difficult consultation cases in breast pathology.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

Principal Investigator, "LIBC (Lost in Inflammatory Breast Cancer) Gene Targeted Mice: A Novel Model to Develop and Test Gene Targeted Therapies for Inflammatory Breast Cancer" (2000 Concept Award), Department of Defense Breast Cancer Program, \$75,750. Starting approximately September 2000.

PENDING:

Principal Investigator, "Role of LIBC in the Development of the Inflammatory Breast Cancer Phenotype", K08 Mentored Clinical Scientist Development Award. NIH (75%), \$430,726/five years.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Kleer C.G. and Michael, C.W. Fine-Needle Aspiration of Breast Carcinomas with Prominent Lymphocytic Infiltrate. *Diagnostic Cytopathology* 23:39-42, 2000.
2. Kleer CG, Giordano TJ, Merino MJ. Squamous cell carcinoma of the thyroid: An aggressive tumor associated with the tall cell variant of papillary thyroid carcinoma. *Modern Pathol*, In press.
3. Kleer CG, Bryant B, Giordano TJ, Sobel ME, Merino MJ. Genetic changes in chromosome 1p and 17p in thyroid cancer progression. *Endocrine Pathol*, In press.
4. Kleer CG, van Golen KL, Merajver SD. Inflammatory breast cancer: Clinical syndrome and molecular determinants. *Breast Cancer Research*, In Press.

BOOKS/CHAPTERS IN BOOKS:

1. Kleer CG and Appelman HD. Surgical Pathology of Crohn's Disease. In press in *Surgical Clinics of North America*.

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

1. Tseng, M.D., Gutsch, D.E., Helvie, M.A., van Golen, K.L., Merajver, S.D. and Kleer, C.G. Epstein-Barr virus is implicated in the pathogenesis of breast fibroadenomas in immunocompromised hosts. *Proceedings of the American Association for Cancer Research*, 41:74,A472, 2000. Presented at the AACR meeting in San Francisco, April, 2000.
2. Tan, L and Kleer, CG. E-cadherin, Gross cystic disease fluid protein-15 (GCDFP-15) and high molecular weight cytokeratin expression in in-situ carcinomas of the breast. Accepted as poster presentation at next ASCP meeting in San Diego, October, 2000.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

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 Pediatrics
- D. Academic Advisor, Immunology graduate program
- E. Member, Molecular mechanisms of Microbial Pathogenesis training grant program committee
- F. Operating committee Graduate Program in Immunology
- G. Member, Pathology graduate program committee
- H. Member, Lung Immunopathology Post-doctoral Training Program (Pathology)
- I. Member, Experimental Immunopathology Training Program (Pathology)
- J. Member, Pulmonary Cellular and Molecular Biology Training Program
- K. Member, Pediatric Training Grant "Cellular and Molecular Biology in Pediatrics"
- L. Member, Systems and Integrative Biology Training Program (Physiology)
- M. Chair, Pathology Graduate Examination committee
- N. Member, Graduate Teaching Award Review Committee
- O. Supervised the following postdoctoral fellows, graduate students, medical Students and undergraduates:
 - P. Fellows; Drs., Emma Campbell, Kate Blease, Kim Tekkanat, Akihiro Matsukawa, Sandra Oliveira. Graduate Students (MSTP); Sara Cheng, Cindi Bone-Larsen, Clauda Jakubzick, Medical students: Matt Steinhauser
 - Q. Undergraduate Students: Joe Barber, Rob Schrader, Matthew Slenderbrok
 - R. Doctoral Thesis Committee Member/Orals Committee for the following graduate students: Brian Lane (CMB), Joyce J. Lai (Public Health), David Cho (School of Public Health), Wannee Asavaroengchai (Pathology), Sara Cheng (MSTP, CMB), Cindi Bone-Larson (MSTP, Pathology), Jeff Bednarski (MSTP, CMB), Anavelys Ortiz-Suarez (CMB) Tania Gourley (Micro/Immuno)
 - S. Oral preliminary examination committee J. Zhang, Jing-mei Lin (Pathology)

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 SCOR Acute Lung Injury, P50HL60289, Principal Investigator Project 3.

PATENTS:

“Treatment of liver disease and injury with ELR CXC” Serial number 60/147,855, filed 2000.

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
- D. Role of cytokines in angiogenesis/tumorigenesis

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

MEDICAL SCHOOL/HOSPITAL/UNIVERSITY:

- A. Member, Committee on medical student research
- B. Member, search committee for the Robinson and Huetwell Professor of Rheumatology
- C. Medical school admission interview committee
- D. Medical scientist training program interviewer
- 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. External Scientific Advisory Committee, Univ. of Michigan Multi-purpose Arthritis Center
- K. Member, Human Research Coordinating Council

REGIONAL AND NATIONAL:

- A. Associate Editor, Journal of Clinical Investigation
- B. Senior Associate Editor, American Journal of Pathology
- C. Associate editor, American Journal of Respiratory Cell and Molecular Biology
- D. Associate Editor, Experimental and Molecular Pathology,
- E. Associate Editor, Shock
- F. Editorial board, Mediators of Inflammation
- G. Chair, 2000 Gordon Conference on Chemotactic Cytokines
- H. Co-Chair 2001 Keystone Conference on Biology of Chemokines
- I. Member, Advisory Board Xith International vascular Biology Meeting
- J. 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
- K. Grant Reviewer, The Arthritis Society
- L. Grant Reviewer, Veterans Administration
- M. National Institutes of Health Study Section, Lung Biology and Pathology,
- N. National Institutes of Health Study Section, Biological and Physiological Sciences special emphasis panel.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

- Invited Speaker, Workshop on Pulmonary Immunobiology and Inflammation, NIH,NHLBI, Aug 1999.
- Invited Speaker, Workshop on Acute Lung Injury (SCOR), NIH, HNLBI, September 1999.
- Invited Speaker Corixa, Seattle, WA September, 1999.
- Invited Speaker, University of Illinois Medical School, Chicago, IL September, 1999.
- Invited Speaker, Merck, Rahway, NJ, September, 1999
- Invited Speaker, University of Chicago, November 1999
- Invited Speaker, Novartis, Horsham, United Kingdom, October, 1999
- Invited Speaker, Experimental Models of Cardiovascular Disease, Society of Toxicology, Philadelphia, PA March 2000
- Invited Speaker, Chemokine Biology. Almirall Prodesfarma, Barcelona, Spain, April 2000.
- State of the Art Speaker. Aspen Lung Conference on Pulmonary Fibrosis. Aspen Co June 2000
- Invited Speaker, Woodrow Wilson National Fellowship Foundation Summer Science Institute. Princeton, NJ. July 2000.

VI. PUBLICATIONS:

ARTICLES PUBLISHED IN REFEREED JOURNALS:

1. Hogaboam, C.M., Bone-Larson, C., Lipinski, S., Lukacs, N.W., Chensue, S.W., Strieter, R.M., Kunkel, S.L. Differential monocyte chemoattractant protein-1 and chemokine receptor 2 expression by murine lung fibroblasts from Th1 and Th2-type pulmonary granulomas models. *J. Immunol.* 1999;163:2193-2201.
2. Campbell, E.M., Charo, I.F., Kunkel, S.L., Strieter, R.M., Boring, L., Gosling, J, Lukacs, N.W. Monocyte chemoattractant protein-1 mediates cockroach allergen-induced bronchial hyperreactivity in normal but not CCR2^{-/-} mice: The role of mast cells. *J. Immunol.* 1999;163;2160-2167.
3. Kunkel, S.L. Promiscuous chemokine receptors and their redundant ligands play an enigmatic role during HIV-1 infection. *Am. J. Respir. Cell. Mol. Biol.* 1999; 20:859-860.
4. Jedrzejewicz, S., Kataeva, G., Hogaboam, C.M., Kunkel, S.L., Strieter, R.M., McKay, D.M. Superantigen immune stimulation evokes epithelial monocyte chemoattractant protein 1 and RANTES production. *Infect Immun* 1999; 67;6198-6202.
5. Kunkel, S.L. Through the looking glass: the diverse in vivo activities of chemokines. *J Clin Invest* 1999; 104:1333-1334.
6. Matsukawa, A., Hogaboam, C.M., Lukacs, N.W., Lincoln, P.M., Strieter, R.M., Kunkel, S.L. Endogenous monocyte chemoattractant protein-1 (MCP-1) protects mice in a model of acute septic peritonitis: cross-talk between MCP-1 and leukotriene B4. *J. Immunol.*1999; 163:6148-6154.
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8. Matsukawa, A., Lukacs, N.W., Standiford, T.J., Chensue, S.W., Kunkel, S.L. Adenoviral-mediated overexpression of monocyte chemoattractant protein-1 differentially alters the development of Th1 and Th2 type responses in vivo. *J. Immunol.* 2000; 164:1699-1704.
9. Lane, T.E., Liu, M.T., Asensio, V.C., Paoletti, A.D., Campbell, I.L., Kunkel, S.L., Fox, H.S., Buchmeir, M.J. A central role for CD4(+) T cells and RANTES in virus-induced central nervous system inflammation and demyelination. *J. Virol* 2000; 74:1415-1424.
10. Hogaboam, C.M., Blease, K., Hedrad, B., Steinhäuser, M.L., Standiford, T.J. Kunkel, S.L. Lukacs, N.W. Chronic airway hyperreactivity, goblet cell hyperplasia, and peribronchial fibrosis during allergic airway disease induced by *Aspergillus fumigatus*. *Am J. Pathol.* 2000; 156:723-732.
11. Matsukawa, A, Hogaboam, C.M., Lukacs, N.W., Lincoln, P.M., Strieter, R.M., Kunkel, S.L. Endogenous MCP-1 influences systemic cytokine balance in a murine model of acute septic peritonitis. *Exp. Mol. Pathol.* 2000, 68:77-84.
12. Matsukawa, A., Hogaboam, C.M., Lukacs, N.W., Lincoln, P.M., Evanoff, H.L., Strieter, R.M. Kunkel, S.L. Expression and contribution of endogenous IL-13 in an experimental model of sepsis. *J. Immunol.* 2000; 164: 2738-2744.
13. Hogaboam, C.M., Bone-Larson, C., Matsukawa, A., Steinhäuser, M.L., Blease, K., Lukacs, N.W., Kunkel, S.L. Therapeutic use of chemokines. *Current Pharmaceut Design* 2000; 6:651-663.

14. Bone-Larson, C., Simpson, K.J., Colletti, L.M., Chen, S.C., Lliar, S., Kunkel, S.L., Hogaboam, C.M. The role of chemokines in the immunopathology of the liver. *Immunol Reviews*. 2000; 177:1-13.
15. Ignatowski, T.A., Kunkel, S.L., Spengler, R.N. Interactions between the alpha-2 adrenergic and the prostaglandin response in the regulation of macrophage-derived tumor necrosis factor. *Clin Immunol* 2000; 96:123-130.
16. Szekanecz, Z., halloran, M.M., Volin, M.V., Woods, J.M., Strieter, R.M., Haines, G.K., Kunkel, S.L., Burdick, M.D., Koch, A.W. Temporal expression of inflammatory cytokines and chemokines in rat adjuvant-induced arthritis. *Arthritis and Rheumatism*. 2000; 43:1266-1277.
17. Zhang, S., Lukacs, N.W., Lawless, V.A., Kunkel, S.L., Kaplan, M.H. Differential expression of chemokines in Th1 and Th2 cells is dependent on Stat6 but not Stat4. *J. Immunol*. 2000; 165:10-14.
18. Blease K, Mehrad B, Standiford TJ, Lukacs NW, Kunkel SL, Chensue SW, Lu B, Gerard CJ, Hogaboam CM. Airway Remodeling Is Absent in CCR1-/- Mice During Chronic Fungal Allergic Airway Disease. *J Immunol*. 2000;165:1564-1572.
19. Belperio JA, Burdick MD, Keane MP, Xue YY, Lynch JP 3rd, Daugherty BL, Kunkel SL, Strieter RM The role of the CC chemokine, RANTES, in acute lung allograft rejection.. *J Immunol*. 2000 165(1):461-72.
20. Ruth JH, Warmington KS, Shang X, Lincoln P, Evanoff H, Kunkel SL, Chensue SW. Interleukin 4 and 13 participation in mycobacterial (type-1) and schistosomal (type-2) antigen-elicited pulmonary granuloma formation: multiparameter analysis of cellular recruitment, chemokine expression and cytokine networks. *Cytokine*. 2000 May;12(5):432-44.
21. Arenberg DA, Keane MP, DiGiovine B, Kunkel SL, Strom SR, Burdick MD, Iannettoni MD, Strieter RM. Macrophage infiltration in human non-small-cell lung cancer: the role of CC chemokines. *Cancer Immunol Immunother*. 2000 May;49(2):63-70.
22. Matsukawa A, Hogaboam CM, Lukacs NW, Lincoln PM, Evanoff HL, Kunkel SL Pivotal role of the CC chemokine, macrophage-derived chemokine, in the innate immune response. *J Immunol*. 2000 164:5362-8.
23. Hogaboam CM, Bone-Larson CL, Steinhilber ML, Matsukawa A, Gosling J, Boring L, Charo IF, Simpson KJ, Lukacs NW, Kunkel SL. Exaggerated hepatic injury due to acetaminophen challenge in mice lacking C-C chemokine receptor 2. *Am J Pathol*. 2000 156:1245-52.
24. Simpson KJ, Lukacs NW, McGregor AH, Harrison DJ, Strieter RM, Kunkel SL. Inhibition of tumour necrosis factor alpha does not prevent experimental paracetamol-induced hepatic necrosis. *J Pathol*. 2000 Mar;190:489-94.
25. Campbell E, Kunkel SL, Strieter RM, Lukacs NW. Differential roles of IL-18 in allergic airway disease: induction of eotaxin by resident cell populations exacerbates eosinophil accumulation. *J Immunol*. 2000 164:1096-102.

BOOKS AND CHAPTERS IN BOOKS:

1. Kunkel, S.L., Phan, S.H., Lukacs, N.W., Hogaboam, C., Chensue, S.W. Chemokine/cytokine biology during the evolution of fibrotic disease. In *Inflammatory Processes; Molecular mechanisms and therapeutic opportunities*. Birkhauser Verlag, Basel, Switzerland.
2. Lukacs, N.W., C. Hogaboam, E. Campbell, and S.L. Kunkel. Chemokines: Function, regulation, and alteration of inflammatory responses. *Chemokines*. Ed. Alberto Montavani. Chemical Immunology. Karger.
3. Kunkel, S.L., Chensue, S.W., Colletti, L., Standiford, T.J., Lukacs, N., Strieter, R.M. Cytokine networks dictate leukocyte recruitment. in: *Cytokines in pulmonary infectious disease: Pathogenesis and therapeutic strategies*. edited by S. Nelson and T. Martin, Marcel Dekker, New York, N.Y.
4. The role of chemokines in the immunopathology of pulmonary disease. Kunkel SL, Lukacs NW, Strieter RM, Chensue SW. *Forum (Genova)*. 1999 Oct-Dec;9(4):339-55. Review
5. Kunkel, S.L., N.W. Lukacs, R.M. Strieter, and S.W. Chensue. The role of chemokines in the immunopathology of pulmonary disease. In: *Forum Trends in Experimental and Clinical Medicine*

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

1. Lukacs, N.W., T. Yang, M. Wiekowski, D.N. Cook, S.L. Kunkel, S.K. Narula, A. Zlotnik, S.A. Lira. Deletion of CCR8 attenuates eosinophil accumulation, Th2 cytokine production and airway hyperactivity in a cockroach allergen model of asthma. *ATS 2000*.
2. Hogaboam, C.M., K. Blease, B. Mehrad, M.L. Steinhauser, T.J. Standiford, S.L. Kunkel, and N.W. Lukacs. A Novel model of chronic allergic airway disease induced by *aspergillus fumigatus*. *ATS 2000*.
3. K. Blease, B. Mehrad, S.L. Kunkel, N.W. Lukacs, and C.M. Hogaboam. IL-18 Neutralization exacerbates airway hyperresponsiveness and lung fibrosis in a chronic model of *aspergillus fumigatus*-induced allergic airway disease. *ATS 2000*.
4. K.K. Tekkanat, D. Cho, H.F. Massaab, J. Lai, M. Kaplan, and N.W. Lukacs. Role of IL-12 in the regulation of airway hyperactivity in RSV Infection. *Exp. Biology 2000*.
5. M.L. Steinhauser, C.M. Hogaboam, N.W. Lukacs, M.H. Kaplan, and S.L. Kunkel. Extracellular and intracellular regulation of the CC chemokine C10. *Exp. Biology 2000*.
6. S.H.P. Oliveira, S.L. Kunkel, R.M. Strieter, and N.W. Lukacs. TNF and IL-4 upregulate CC Chemokine receptor expression on murine eosinophils. *Exp. Biology 2000*.
7. A. Matsukawa, C.M. Hogaboam, N.W. Lukacs, R.M. Strieter, and S.L. Kunkel. Crucial role of CC chemokine MDC in lethal septic peritonitis in mice. *Exp. Biology 2000*.
8. C.M. Hogaboam, K. Blease, B. Mehrad, T.J. Standiford, N.W. Lukacs, S.W. Chensue, B.Lu, C.J. Gerard, and S.L. Kunkel. Airway remodeling is absent in CCR1^{-/-} mice during chronic fungal allergic airway disease. *AAI 2000*.
9. K.K. Tekkanat, H. Masaab, D. Cho, J. Lai, and N.W. Lukacs. IL-13-induced airway hyperactivity and Mucous production during respiratory syncytial virus (RSV) infection. *AAI 2000*.
10. S.M. Zhang, N.W. Lukacs, V.A. Lawless, S.L. Kunkel, and M.H. Kaplan. Differential expression of chemokines in Th1 and Th2 cells is dependent on Stat6 but not Stat4. *AAI 2000*.

11. S.H.P. Oliveir and N.W. Lukacs. Differential activation of MDC and RANTES from eosinophils by Th1 and Th2 type cytokines. AAI 2000.
12. A. Matsukawa, C.M. Hogaboam, N.W. Lukacs, R.N. Knibbs, D.C. Bullard, L.M. Stoolman, and S.L. Kunkel. Mice lacking E- and P- selectin are resistant to the lethality in a murine model of acute septic peritonitis. AAI 2000.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

- A. Gynecologic Pathology Consultation - twelve months.
- B. Gynecologic Oncology Semimonthly Tumor Planning Conference - twelve months.
- C. Autopsy service – twelve months (18 weeks, 6 weekends).
- D. Gynecologic Oncology – Colposcopy Clinic, one half day/week, twelve months.

II. TEACHING ACTIVITIES:

- A. Residents:
 - 1. Review cases and supervise presentation of semimonthly Gynecologic Oncology Tumor Planning Conference – twelve months.
 - 2. Sign-out - Gynecologic Pathology and Autopsy cases. Placental pathology sign-out – twelve months.
 - 3. Instruction in the Gross Examination, frozen section diagnosis, and processing of Gynecologic Surgical specimens, July 1999.
 - 4. Instruction and supervision in the performance, presentation and sign-out of autopsy cases.
 - 5. Teaching Conferences- lecture in Gyn Pathology, Jan 2000.
 - 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, and other resources
- B. Medical Students:
 - 1. M2, Obstetrics & Gynecology Sequence: Four hours Gynecologic Pathology lectures; preparation of examination questions.
 - 2. M2, Obstetrics & Gynecology Sequence: Laboratory instruction.
 - 3. M2 resource web page in Gyn Pathology (<http://gynonc.path.med.umich.edu> – Web access to Gyn Pathology laboratory, lecture slides, and other resources
 - 4. M1 – Basic Pathology, Lab Instructor Spring 1999.
- C. Ob/Gyn Residents and Gynecologic Oncology Fellow:
 - 1. Semimonthly Tumor Planning Conference – twelve months.
 - 2. Colposcopy clinic staff – one-half day per week (twelve months).
 - 3. Lectures in Gynecologic Pathology to Gyn Oncology Service – two/year
 - 4. Gyn Pathology Rotation for 3rd year Gyn Oncology Rotation – one month

- D. Dental Students
 - 1. Pathology 631, Fall 1999. Lab lectures and lab practical.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. "Cost effectiveness of vaginal smear screening after total hysterectomy for benign disease". Project Investigator, Dr. Michael D. Fetters, Department of Family Medicine. Sponsored by Blue Cross Blue Shield of Michigan. Salary support – 3%.

PROJECTS UNDER STUDY:

- A. "Web Based Teaching in Gynecologic Oncology". An unrestricted Educational Grant from the Association of Professors in Gynecology and Obstetrics (APGO). Dr. James Lilja (2nd year Gyn Oncology Fellow), Dr. Richard W. Lieberman (Gynecologic Pathology), and Dr. Kevin Reynolds (Chief, Gynecologic Oncology Division).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Member, Pathology Informatics Planning Committee, Department of Pathology.
- B. Member, Pathology Informatics Exchange Program (PIX) with University of Michigan & University of Pittsburgh.

MEDICAL SCHOOL/HOSPITAL:

None.

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, Gerontology Research

- I. Editorial Reviewer, ASCP Check Samples

V. **OTHER RELEVANT ACTIVITIES:**

INVITED LECTURES/SEMINARS:

1. MLabs Symposia, October 1999. "Dysplasia and Carcinoma In Situ of the Cervix, Vagina and Vulva".
2. The 8th Annual Primary Health Care of Women, December 1999 at Towsley Center. "Highlights in Gynecologic Pathology: Clinical Pathologic Correlation of Selected Cases at the University of Michigan".
3. The American College of Obstetrics and Gynecology 5th District Winter Meeting, "Point Counterpoint: Thin Prep is the Gold Standard for Cytologic Screening of Cervical Cancer", February 2000.
4. The 15th MLabs Symposium, May 2000. "Reporting in Gynecologic Pathology: Case Presentations".
5. Automated Information Management in the Clinical Laboratory (AIMCL) 2000. "Innovations in Digital Imaging Technology in the Pathology Laboratory". Lecture given over the Internet from Washington, D.C. (Armed Forces Institute of Pathology) to Towsley Center.

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED IN REFEREED JOURNALS:

1. Lieberman RW, Henry MR, Laskin W, Walenga JF, Buckner S, O'Connor DM. "Colposcopy in pregnancy: Directed brush cytology compared with cervical biopsy." *Obstetrics & Gynecology*, 1999. 94(2): 198-203.
2. Taylor RT, Zeller J, Lieberman RW, O'Connor DM. "An analysis of two versus three grades for endometrial carcinoma." *Gynecologic Oncology*, 1999. 74(1): 3-6.

BOOKS/CHAPTERS IN BOOKS:

None.

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

None.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

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 four postdoctoral fellows (Steven Domino, M.D., Ph.D., Jonathon Homeister, M.D., Ph.D., Glenda Smithson, Ph.D., Lan Zhou, M.D., Ph.D.)
- B. Supervision of two MSTP students (Daniel Becker and David Kim)
- C. Lecturer - Postdoctoral Research Training Program
- D. Member of five Ph.D. thesis committees (Stephanie M. Chervin (Alt), Stacey Arnold, Paul Bock, Anavelys Ortiz-Suarez, and Gallia Levy)
- E. Member, Cell and Molecular Biology Program

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. "Oligosaccharide function during murine embryogenesis". Source of award: Howard Hughes Medical Institute
- B. Program Project - Project #2 Principal Investigator, "Carbohydrate-dependent adhesion of normal and tumor cells", NIH - CA71932 (25% effort), \$732,109/five years direct cost, 07/08/96 - 04/30/2001
- C. Program Project - Project #1 Principal Investigator, "Oligosaccharides as Anti-Inflammatory Agents", NIH AI33189, (15% effort), \$647,684/five years direct cost), 09/01/92 - 08/31/2000

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, Ad-Hoc Research Faculty Search Committee
- B. Chair, Neuropathology Faculty Search Committee
- C. Member, University of Michigan Health Services Strategic Planning Research Subcommittee.
- D. Member, Microarray and Microchip Technology Advisory Committee
- E. Member, Department of Pathology's Internal Review Committee
- F. Member, Department of Pathology's Graduate Program Committee
- G. Member, University of Michigan Technology Transfer Committee
- H. Member, Biomedical Research Core Facilities Advisory Committee

REGIONAL AND NATIONAL:

- A. Deputy Editor, The Journal of Clinical Investigation
- B. Member, Scientific Advisory Board, The Ara Parseghian Medical Research Foundation (Niemann-Pick disease type C)
- C. Member, Editorial Board of Glycobiology
- D. Member, Editorial Board of the European Journal of Biochemistry
- E. Consulting Reviewer for Proceedings of the National Academy of Sciences USA, Journal of Cell Biology, Journal of Experimental Medicine, Biochemistry, Journal of the American Chemical Society, Journal of Histochemistry and Cytochemistry, Journal of Immunology, Glycoconjugate Journal, and Transfusion
- F. External Referee, Transfusion Medicine SCOR Special Study Section, NIH
- G. Member, Howard Hughes Medical Institute International Scholars Program Grant Review Committee

V. OTHER RELEVANT ACTIVITIES:

- A. Howard Hughes Medical Institute, Investigator

VI. INVITED LECTURES AND SEMINARS:

1. Selectin ligand defects in glycosylation mutant mice. Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, Connecticut, August 1999
2. Selectin ligand defects in glycosylation mutant mice. University of Toronto, Toronto, Ontario, Canada, September 1999
3. Leukocyte trafficking defects in mammals with mutant glycosylation loci. Genentech, Inc., South San Francisco, California, October 1999
4. Leukocyte trafficking defects in mammals with mutant glycosylation loci. Roche Bioscience, Palo Alto, California, November 1999
5. Selectin ligand deficiency in fucosylation-deficient mice. The San Diego Glycobiology Symposium, La Jolla, CA, January 2000

6. Control of leukocyte trafficking by glycosylation loci. Hematology Grand Rounds. Mt. Sinai Medical School. New York City, NY, April 2000
7. Immune compromise in mice with selectin ligand deficiencies. The Second International Glycosyltransferase Symposium, Toronto, Ontario, Canada, May 2000
8. Glycosylation loci that control selectin ligand activity. University of Helsinki. Helsinki, Finland, June 2000

VII. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Weninger W, Ulfman LH, Cheng G, Lowe JB, and von Andrian UH. Leukocyte rolling in non-inflamed skin venules: role of selectins and $\alpha(1,3)$ -fucosyltransferase-IV and -VII in cutaneous immune surveillance. *Immunity* 2000, in press.
2. Williams DA, Tao W, Yang F, Kim C, Gu Y, Mansfield P, Levine JE, Petryniak B, Derrow C, Harris C, Jia B, Zheng Y, Ambruso D, Lowe JB, Atkinson SJ, Dinauer MC, Boxer L. A dominant negative mutation of the hematopoietic-specific RhoGTPase, Rac 2, is associated with a human phagocyte immunodeficiency. *Blood* 2000, in press.

ARTICLES SUBMITTED OR IN PREPARATION:

1. Homeister JH, Thall A, Petryniak B, Maly P, Rogers CE, Smith PL, Kelly RJ, Misra A, Chang G, Askari S, Smithson G, Marks RM, Hindsgaul O, von Andrian UH, and Lowe JB. The $\alpha(1,3)$ fucosyltransferases Fuc-TIV and Fuc-TVII co-cominantly control E-, P-, and L-selectin ligand activities on leukocytes and high endothelial venules. Submitted.
2. Huang M-C, Zollner O, Moll T, Maly P, Thall AD, Lowe JB, and Vestweber D. P-selectin glycoprotein ligand-1 and E-selectin ligand-1 are modified by different fucosyltransferases in mouse neutrophils. Submitted.
3. Smithson G, Rogers CE, Smith PL, Scheidegger EP, Petryniak B, Myers JT, Homeister JW, and Lowe JB. Multiple cellular immune defects account for faulty contact hypersensitivity response in fucosyltransferase-deficient mice. In preparation.
4. Becker DJ, Smith PL, Phillips ML, Etzioni A, Ketchum K, Sullivan FX, Kumar R, Paulson JC, and Lowe JB. A biochemical lesion interacting with GDP-D-mannose 4,6-dehydratase accounts for defective selectin ligands in leukocyte adhesion deficiency II syndrome. In preparation.
5. Masayoshi Oh-eda M, Tsuboi S, Petryniak B, Lowe JB, and Fukuda M. Reconstitution of E-selectin ligand oligosaccharides on CHO cells by expression of two distinct fucosyltransferases. Oligosaccharide structures synthesized by mouse fucosyltransferase IV and VII. In preparation.
6. Hiraiwa N, Domino S, Saunders T, and Lowe JB. Dominant pre-implantation lethality in mice directed by aberrant expression of an $\alpha(1,2)$ fucosyltransferase cDNA. In preparation.
7. Legault DJ, Kelly RJ, Smith PL, and Lowe JB. Acceptor substrate specificities of the $\alpha(1,3/1,4)$ fucosyltransferases are determined by single amino acid differences. In preparation.
8. Smith PL, Myers JT, Rogers CE, Petryniak B, and Lowe JB. The FX null mouse phenocopies the human leukocyte adhesion deficiency II syndrome. In preparation.
9. Smith PL, Myers JT, Rogers CE, Petryniak B, and Lowe JB. Phenotypic consequences of deletion of the CTNAcI GalNAc transferase locus in the mouse. In preparation.

10. Domino S, Hiraiwa N, and Lowe JB. Molecular cloning, genomic mapping, and expression of two Secretor blood group $\alpha(1,2)$ fucosyltransferase genes expressed in murine uterine epithelium and gastrointestinal tract. In preparation.

BOOKS AND CHAPTERS IN BOOKS:

1. Lowe JB and Marth J. Structures common to different types of glycans. In *Essentials of glycobiology*. Varki A., Cummings R, Esko J, Freeze H, Hart G, and Marth J. (eds). Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, pp. 211-252, 1999.
2. Lowe JB and Varki A. The glycosyltransferases. In *Essentials of glycobiology*. Varki A, Cummings R, Esko J, Freeze H, Hart G, and Marth J. (eds). Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, pp. 253-266, 1999.
3. Lowe JB and Freeze H. Naturally occurring genetic disorders of glycosylation. In *Essentials of glycobiology*. Varki A., Cummings R, Esko J, Freeze H, Hart G, and Marth J (eds). Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, pp. 479-498, 1999.
4. Cummings RD and Lowe JB. The selectins. In *Essentials of glycobiology*. Varki A., Cummings R, Esko J, Freeze H, Hart G, and Marth J (eds). Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, pp. 391-415, 1999.
5. Lowe JB. Red Cell Membrane Antigens. *The Molecular Basis of Blood Diseases*. Stamatoyannopoulos G, Nienhuis AW, Majerus PW, and Varmus H (eds.). W. B. Saunders Company, Orlando, Florida, in press, 2000.
6. Homeister JW and Lowe JB. Carbohydrate recognition in leukocyte-endothelial cell interaction. *Molecular Glycobiology*. In: *Frontiers in Molecular Biology*. Fukuda M (ed). Oxford University Press, Oxford, UK, in press, 2000.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000

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. Dermatopathology laboratory director and instructor, MS II Dermatology Sequence
 - 3. Dermatopathology, Pathology Clerkship, MS I and MS IV students (5 students).
- B. House Officers:
 - 1. Dermatopathology sign-out.
 - 2. Review of dermatopathology consultation material.
 - 3. Dermatopathology teaching conference/weekly.
- D. Diagnostic Conference, Department of Dermatology (weekly).
- E. Director of Diagnostic Conference, Department of Dermatology – 3-4/year
- F. Hospital Conferences:
 - 1. Multidisciplinary Melanoma Conference (twice monthly).
- G. Honors:
 - 1. Recognition in *The Best Doctors in America*, published by Woodward/White, Inc., 1999 Edition.
 - 2. Recognition in *The National Registry of Who's Who*, 2000 Edition.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Genes, environment, and melanoma (GEM) study (Multicenter collaborative investigation); local principal investigator: Stephen B. Gruber, M.D., Ph.D., MPH.
- B. Sunbelt Melanoma Trial (SMT): A multicenter trial of adjuvant interferon alpha-2b for melanoma patients with early lymph node metastasis detected by lymphatic mapping and sentinel lymph node biopsy. Local principal investigator: Alan Yahanda, M.D.
- C. Histologic features of thick non-metastasizing melanomas (cohort study – North American Melanoma Pathology Study Group).

- D. Histologic parameters of dysplastic nevi (cohort study – North American Pathology Study Group).
- E. Utility of Melan-A (MART 1) antigen expression in evaluation of sentinel lymph nodes for metastatic melanoma (V. Sondak, M.D., A. Yahanda, M.D., A. Chang, M.D., T. Johnson, M.D., and L. Su, M.D.).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director, Dermatopathology Service.
- B. Quality Assurance/Quality Control Program. Cutaneous Surgery and Oncology Unit.

REGIONAL AND NATIONAL:

- A. Program for Dermatology for the 21st Century-Dermatopathology Study Group, American Academy of Dermatology.
- B. Member, Dermatopathology Test Committee, American Board of Pathology.
- C. Member, Dermatopathology Test Committee, American Board of Dermatology.
- D. Member, North American Melanoma Pathology Study Group.
- 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: Photodermatology, Photoimmunology and Photomedicine.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

- 1. Basic Self-Assessment in Dermatopathology, American Academy of Dermatology Annual Meeting, San Francisco, CA, March, 2000.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Karimipour, D., Lowe, L., Blaivas, M., Sachs, D., Johnson, T.M.: Lafora Disease: diagnosis by skin biopsy. J Am Acad Dermatol 41:790-792, 1999.
- 2. Sachs, D.L., Lowe, L., Chang, A.E., Carson, E., Johnson, T.M.: Do primary small intestine melanomas exist?: report of a case. J Am Acad Dermatol 41:1042-1044, 1999.
- 3. Johnson, T.M., Saluja, A., Fader, D., Blum, D., Cotton, J., Wang, T.S., Lowe, L.: Isolated extragenital bowenoid papulosis of the neck. J Am Acad Dermatol 41:867-870, 1999.

4. Johnson, T.M., Sondak, V.K., Su, L.D., Headington, J.T., Kang, S., Lowe, L.: Is it a benign Spitz nevus or a malignant melanoma? *Primary Care and Cancer* 20:41-44, 2000.
5. Ratner, D., Lowe, L., Johnson, T.M., Fader, D.J.: Perineural spread in basal cell carcinomas treated with Mohs micrographic surgery. *Cancer* 88:1605-1613, 2000.
6. Johnson, T.M., Chang, A., Redman, B., Rees, R., Bradford, C., Riba, M., Lowe, L.: Management of melanoma using a multidisciplinary melanoma clinic model. *J Am Acad Dermatol* 42:820-826, 2000.
7. Johnson, T.M., Yahanda, A.M., Sondak, V.K., Cimmino, V., Lowe, L.: Melanoma: Role of sentinel node mapping. *Current Problems in Dermatology* (in press).
8. Bowen, G.M., Chang, A., Lowe, L., Hamilton, T., Patel, R., Johnson, T.M.: Solitary melanoma confined to the dermal/subcutaneous tissue: evidence for revisiting the staging classification. *Arch Dermatol* (in press).

BOOKS/CHAPTERS IN BOOKS:

1. Fazel, N., Wilczynski, S, Lowe, L., Su, L.: Clinical, histopathologic and molecular aspects of cutaneous human papillomavirus infections. In: Smoller, B.R. (ed): *Dermatologic Clinics: Updated on Dermatopathology* (Philadelphia, PA: W. B. Saunders Co., 1999), pp 521-536.
2. Lowe, L.: Deposition Disorders: Fitzpatrick, J.E., Aeling, J. (eds): *Secrets of Dermatology* (Philadelphia, PA: Hanley and Belfus, Inc., 2nd edition) (in press).
3. Sondak, V.K., Cimmino, V.M., Lowe, L., Johnson, T.M.: Dermatofibrosarcoma protuberans: What is the best surgical approach? *Surgical Oncology* (in press).

ABSTRACTS, BOOK REVIEWS, PRELIMINARY COMMUNICATIONS, PANEL DISCUSSIONS:

1. Lowe, L.: Book Review: *Surgical Dermatopathology*, edited by Maloney, Torres, Hoffman, Helm. *J Dermatol Treat* 11:137, 2000.
2. Grover, A.C., Moon, J., Chang, A.F., Johnson, T.M., Sondak, V.K., Cimmino, V.M., Lowe, L., Taylor, J.M.G., Yahanda, A.M.: Histological and clinical factors associated with positive sentinel lymph nodes in melanoma. Frederick A. Collier Surgical Society Annual Meeting, Ann Arbor, MI, October, 2000.

**NICHOLAS W. LUKACS, Ph.D.
ASSISTANT RESEARCH SCIENTIST
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENT REPORT
1 JULY 1999-30 JUNE 2000**

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

- A. Pathology 585, Lecturer, Inflammation section, Summer, 1999, 2000
- B. Pathology 581, Dental School and Pathology Grad. Students. Lectures on Inflammation, cytokines and Immunology
- C. Post-doctoral fellows- Kim Tekkanat and Sandra Oliveira
- D. Visiting Scientists- Akihiro Matsukawa
- E. Graduate Students- Allison Miller

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

Active

- A. Principal Investigator, "Role of C-C chemokines in eosinophil airway inflammation", R-29 FIRST Award, 7/1/96-6/30/01, National Institutes of Health.
- B. Principal Investigator, "SCF and mast cells in allergic airway inflammation", NIH R01. 9/1/99-8/30/04
- 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. Principal Investigator; Section III, "Rational Design of Adhesion Blocking Anti-Inflammatories" NIH SBIR grant. (Ligocyte Pharmaceuticals, Inc.) 7/1/00 to 6/30/03.
- E. 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.
- F. 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. Towses, M.D. SCOR Director.

PROJECTS UNDER STUDY:

- A. Regulation of cytokine and chemokines during eosinophilic airway inflammation.
- B. Role of mast cells in chronic inflammation.
- C. Regulation of chemokine production during cell-to-cell interactions.

- D. Role of chemokines in autoimmune responses.
- E. Adhesion molecules in chronic inflammatory responses.
- F. Role of stem cell factor (SCF) in acute and chronic inflammation

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

REGIONAL AND NATIONAL:

-Associate Editor-

Journal of Immunology

-Section Editor (beginning July 1, 2000)

Journal of Immunology

-ASIP Program Committee for Experimental Biology 2000 and 2001 meeting

-Reviewer for the following Journals:

- 1. Journal of Immunology
- 2. American Journal of Pathology
- 3. American Journal of Respiratory Cell and Molecular Biology
- 4. Infection and Immunity
- 5. Immunology Today
- 6. European Respiratory Journal
- 7. Journal of Experimental Medicine
- 8. Hepatology
- 9. Shock
- 10. Journal of Leukocyte Biology
- 11. Cellular Immunology
- 12. BLOOD
- 13. Journal of Clinical Investigation
- 14. Journal of Clinical Allergy

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

- 1. Use of Chemokines and their receptors in Asthma and eosinophil accumulation in tissue. Schering-Plough. July 19th, 1999.
- 2. Differential roles of IL-12 and IL-13 in immune response and induction of airway hyperreactivity during RSV infection. Novartis, Horsham, U.K. Oct. 4, 1999.

3. Cytokines and chemokines in RSV-induced pulmonary hyperreactivity. Schering-Plough. Dec. 6, 1999.
4. Tissue specific migration of lymphocytes. Allergic Disorders and treatment. Orlando, Florida. January 25th, 2000.
5. RSV-induced exacerbation of allergic asthma. Picower Institute. March 10th, 2000.
6. IL-4/IL-13. Chairman of Block symposium at AAI annual meeting, Seattle, WA. May 12th, 2000.
7. Regulation of leukocyte recruitment in inflammation. Moderator. ATS annual meeting, Toronto, Ontario. May 10th, 2000.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERREED JOURNALS:

1. C. M. Hogaboam, C. S. Gallinat, D. D. Taub, R. M. Strieter, S. L. Kunkel, and N.W. Lukacs. 1999. Immunomodulatory Role of C10 Chemokine in a Murine Model of Allergic Bronchopulmonary Aspergillosis. *J. Immunol.* 162:6071-6079.
2. Campbell, E., I.F. Charo, S.L. Kunkel, R.M. Strieter, L. Boring, J. Gosling, and N.W. Lukacs. 1999. Monocyte chemoattractant protein-1 mediates cockroach allergen-induced bronchial hyperreactivity in normal but not CCR2-/- mice: The role of mast cells. *J. Immunol.* 163:2160-2167.
3. Hogaboam, C.M., C.L. Bone-Larson, S. Lipinski, N.W. Lukacs, S.W. Chensue, R.M. Strieter, and S.L. Kunkel. 1999. Differential monocyte chemoattractant protein-1 and chemokine receptor 2 expression by murine lung fibroblasts derived from Th1- and Th2-type pulmonary granuloma models. *J. Immunol.* 163:2193-2201.
4. Campbell, E.M. and N.W. Lukacs. 1999. Cytokine and chemokine interactions in allergic airway inflammation. *ILAR Journal* 40:157-162.
5. Lukacs, N.W., S.H.P. Oliveira, and C.M. Hogaboam. 1999. Chemokines and asthma: Redundancy of function or coordinated effort. *J. Clin. Investigation.* 104(8):995-999.
6. Saavedra, M., B. Taylor, N. Lukacs, and P.L. Fidel, Jr. 1999. Local production of chemokines during vaginal Candidiasis. *Infect. Immun.* 67:5820-5826.
7. Campbell, E.M., S.L. Kunkel, R.M. Strieter, and N.W. Lukacs. 2000. Differential roles of interleukin-18 in allergic airway disease: Induction of eotaxin by resident cell populations exacerbates eosinophil accumulation. *J. Immunol.* 164:1096-1102.
8. Hogaboam, C.M., K. Blease, B. Mehrad, M.L. Steinhauser, T.J. Standiford, S.L. Kunkel, and N.W. Lukacs. 2000. Chronic airway hyperreactivity, goblet cell hyperplasia and peribronchial fibrosis during allergic airway disease induced by *A. fumigatus*. *Am. J. Pathol.* 156:723.
9. Matsukawa, A., N.W. Lukacs, T.J. Standiford, S.W. Chensue, and S.L. Kunkel. 2000. Overexpression of MCP-1 differentially alters the development of Th1 and Th2 type responses in vivo. *J. Immunol.* 164(4):1699-704.
10. Simpson, K.J., N.W. Lukacs, A.H. McGregor, D.J. Harrison, R.M. Strieter, and S.L. Kunkel. 2000. Inhibition of tumor necrosis factor alpha does not prevent experimental pracetamol-induced hepatic necrosis. *J. Pathol.* 190:489-494.

11. Matsukawa, A., C.M. Hogaboam, N.W. Lukacs, P.M. Lincoln, H.L. Evanoff, R.M. Strieter, and S.L. Kunkel. 2000. Expression and contribution of endogenous IL-13 in an experimental model of sepsis. *J. Immunol.* 164:2738-2744.
12. Matsukawa, A., C.M. Hogaboam, N.W. Lukacs, P.M. Lincoln, R.M. Strieter, and S.L. Kunkel. 2000. Endogenous MCP-1 influences systemic cytokine balance in a murine model of acute septic peritonitis. *Exp and Mol. Pathol.* 68:77-84.
13. Klein, A., A. Talvani, D.C. Cara, K.L. Gomes, N.W. Lukacs, and MM Teixeira. 2000. Stem cell factor plays a major role in the recruitment of eosinophils in allergic pleurisy in mice via the production of LTB4. *J. Immunol.* 164:4271-4276.
14. Wang, J., D.P. Snider, B.R. Hewlett, N.W. Lukacs, J. Gsuldie, H. Liang, and Z. Xing. 2000. Transgenic expression of granulocyte-macrophage colony-stimulating factor induces the differentiation and activation of a novel dendritic cell population in the lung. *Blood* 95:2337-2345.
15. Hogaboam CM, Bone-Larson CL, Steinhauer ML, Matsukawa A, Gosling J, Boring L, Charo IF, Simpson, KJ, Lukacs NW, Kunkel SL. 2000. Exaggerated Hepatic Injury Due to Acetaminophen Challenge in Mice Lacking C-C Chemokine Receptor 2. *Am J Pathol* 156:1245-1252.
16. Campbell, E.M. and N.W. Lukacs. Murine models of Airway Inflammation. *Methods in Molecular Biology: Chemokine Protocols.* 138:295-302.
17. Zhang, S., N.W. Lukacs, V.A. Lawless, S.L. Kunkel, and M.H. Kaplan. Differential expression of chemokines in T helper type 1 (Th1) and Th2 cells is dependent on Stat6 but not Stat4. *J. Immunol* 165:10-14.
18. Lukacs, N.W. 2000. Migration of helper T lymphocyte subsets into inflamed tissues. *J. Allergy and Clin Immunol.* (In Press).

BOOKS/CHAPTERS IN BOOKS:

1. Campbell, E., S.L. Kunkel, and N.W. Lukacs. 1999. Differential regulation of T cell responses by chemokines. Ed. Mark Rothenberg.
2. Kunkel, S.L., N.W. Lukacs, R.M. Strieter, and S.W. Chensue. 1999. The role of chemokines in the immunopathology of pulmonary disease. In: *Forum Trends in Experimental and Clinical Medicine.*
3. Lukacs, N.W. 1999. The role of chemokines in allergic airway inflammation. IN: *Chemokines in Disease; Biological and Clinical Research.* ED. C. A. Hebert. Humana Press Int.
4. Lukacs, N.W. and K.K. Tekkanat. 2000. Role of chemokines in asthmatic airway inflammation. *Immunological Reviews.* (In Press).
5. Lukacs, N.W., S.H.P. Oliveira, and C.M. Hogaboam. 2000. SCF-induced chemokine production, allergic airway inflammation and airway hyperreactivity. Mast cells and basophils. Ed. G. Marone, L.M. Lichtenstein, and S.J. Galli. Academic Press. pp 609-617.

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

1. Lukacs, N.W., T. Yang, M. Wiekowski, D.N. Cook, S.L. Kunkel, S.K. Narula, A. Zlotnik, S. A. Lira. Deletion of CCR8 attenuates eosinophil accumulation, Th2 cytokine production and airway hyperreactivity in a cockroach allergen model of asthma. *ATS* 2000.

2. Hogaboam, C.M., K. Blease, B. Mehrad, M.L. Steinhauser, T.J. Standiford, S.L. Kunkel, and N.W. Lukacs. A Novel model of chronic allergic airway disease induced by *aspergillus fumigatus*. ATS 2000.
3. K. Blease, B. Mehrad, S.L. Kunkel, N.W. Lukacs, and C.M. Hogaboam. IL-18 Neutralization exacerbates airway hyperresponsiveness and lung fibrosis in a chronic model of *aspergillus fumigatus*-induced allergic airway disease. ATS 2000.
4. K.K. Tekkanat, D. Cho, H.F. Massaab, J. Lai, M. Kaplan, and N.W. Lukacs. Role of IL-12 in the regulation of airway hyperreactivity in RSV Infection. *Exp. Biology* 2000.
5. M.L. Steinhauser, C.M. Hogaboam, N.W. Lukacs, M.H. Kaplan, and S.L. Kunkel. Extracellular and intracellular regulation of the CC chemokine C10. *Exp. Biology* 2000.
6. S.H.P. Oliveira, S.L. Kunkel, R.M. Strieter, and N.W. Lukacs. TNF and IL-4 upregulate CC Chemokine receptor expression on murine eosinophils. *Exp. Biology* 2000.
7. A. Matsukawa, C.M. Hogaboam, N.W. Lukacs, R.M. Strieter, and S.L. Kunkel. Crucial role of CC chemokine MDC in lethal septic peritonitis in mice. *Exp. Biology* 2000.
8. C.M. Hogaboam, K. Blease, B. Mehrad, T.J. Standiford, N.W. Lukacs, S.W. Chensue, B.Lu, C.J. Gerard, and S.L. Kunkel. Airway remodeling is absent in CCR1^{-/-} mice during chronic fungal allergic airway disease. AAI 2000.
9. K.K. Tekkanat, H. Masaab, D. Cho, J. Lai, and N.W. Lukacs. IL-13-induced airway hyperreactivity and Mucous production during respiratory syncytial virus (RSV) infection. AAI 2000.
10. S.M. Zhang, N.W. Lukacs, V.A. Lawless, S.L. Kunkel, and M.H. Kaplan. Differential expression of chemokines in Th1 and Th2 cells is dependent on Stat6 but not Stat4. AAI 2000.
11. S.H.P. Oliveir and N.W. Lukacs. Differential activation of MDC and RANTES from eosinophils by Th1 and Th2 type cytokines. AAI 2000.
12. A. Matsukawa, C.M. Hogaboam, N.W. Lukacs, R.N. Knibbs, D.C. Bullard, L.M. Stoolman, and S.L. Kunkel. Mice lacking E- and P- selectin are resistant to the lethality in a murine model of acute septic peritonitis. AAI 2000.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 – 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

- A. Daily surgical neuropathology and electron microscopic neuropathology, weekly Brain Tumor Board, review of neurosurgical, neuroradiologic, neuropathologic and clinical-pathologic correlation shared with Dr. Blaivas.
- B. Consultations on surgical neuropathology from other hospitals.
- C. Diagnostic neuropathology consultant, Veterans Administration Hospital.
- D. Examination of all University Hospital autopsy neuropathologic material – all duties previously done by Dr. Sima except peripheral nerve and ADRC: brain cutting, sampling, microscopic examination, and special stains.
- E. General autopsies.

II. TEACHING ACTIVITIES:

DEPARTMENTAL:

- A. Neuroscience Sequence, Neuropathology for Second Year Medical Students. Prepared two laboratories and two lectures on brain tumors; toxic, metabolic, demyelinating and infectious diseases. Taught four laboratories.
- 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, shared with Dr. Blaivas.
 - 3. Review all neurosurgically removed material in the hospital in CME-approved biweekly conference, shared with Dr. Blaivas.
 - 4. Various other conferences.
 - 5. Invited presentations of neuropathologic observations at joint clinical conferences.
 - 6. Pathology Resident's Tuesday AP Conference rotated with other faculty.
 - 7. One month House Officer Electives for Neurosurgery, Neurology, and Pathology.
 - 8. Pathology Resident's Monday Special Conferences.
 - 9. Combined Neurosurgery, Neuroradiology, Neuropathology CPC.
 - 10. Autopsy call.
 - 11. Pathology Gross Conference.
- C. Teach laboratory techniques to Research Assistants and UMMC Histologists.
- D. Other faculty: Brain Tumor Board.

REGIONAL AND NATIONAL:

- A. Faculty, "New Methods of Brain Tumor Analysis": 38th Annual AFIP Kenneth M. Earle Memorial Neuropathology Review, Armed Forces Institutes of Pathology, Rockville, Maryland, 2000.
- B. Armed Forces Institutes of Pathology Neuropathology Department, daily 1 p.m. 12-headed scope review, Washington, D.C.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. National Institutes of Health, Principal Investigator, "Glioma Markers of Potential Diagnostic and Prognostic Value" (\$562,806 for entire cost of project).

PROJECTS UNDER STUDY:

- A. Growth, spread and antigenicity of ENU-induced gliomas in rats with Constance D'Amato and Dr. Terry Hood.
- B. Magnetic resonance diffusion and cross relaxation of brain tumors with Drs. Thomas Chenevert and Brian Ross.
- C. Characterization of Rosai-Dorfman disease in brain with Drs. Michael Boland and Karin Muraszko.
- D. Viral vectors in glioma therapy with Drs. Julian Hoff and Brian Ross.
- E. Effects of BCNU on histopathology and MRI signals in experimental rat brain tumors with Drs. Brian Ross and Thomas Chenevert.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Chief, Section of Neuropathology.
- B. Director, Neuropathology Residence. Full accreditation from the Accreditation Council for Graduate Medical Education obtained in 1996.
- 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 Neuro-Oncology.
- B. Editorial Board, Journal of Histochemistry and Cytochemistry.
- C. Editor, Histochemical Society Newsletter.
- D. Primary Review Pathologist, Children's Cancer Study Group CCG 9897 nationwide study of childhood low grade gliomas.
- E. Reviewer for the following journals:
 - 1. Journal of Neuropathology and Experimental Neurology.
 - 2. Journal of Neurosurgery.
 - 3. Journal of Histochemistry and Cytochemistry.
 - 4. Journal of Neuro-oncology.
 - 5. American Journal of Pathology.
 - 6. Archives of Pathology and Laboratory Medicine.
- F. Member, Brain Tumor/EMF Study Scientific Advisory Panel, National Cancer Institute, Jonathan Samet, Chairman.
- G. Member, Review Panel, Program for Treatment of Malignant Brain Tumors, National Cancer Institute, William Jewell, Chairman.
- H. Member, Review Panel, Molecular Markers of Glioma Initiation and Progression, National Cancer Institute, Susan Naylor, Chairwoman.
- I. 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 --.
Decide on policies regarding handling of tumor specimens at annual meetings.
 - 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. Publication Committee 1995-1998.

- Monitor the Journal of Histochemistry and Cytochemistry and other HCS publications.
 2. Future Directions Committee 1994-1998.
 3. Constitution Advisor 1996 --.
Make certain Council functions in accord with constitution.
 4. Councilor, 1994-1998.
Review and vote upon policies regarding the Society's journal, annual meetings, membership, new directions, etc., at annual meetings and all during the year.
- J. Lieutenant Colonel, U.S. Army Reserve Medical Corps, 1997 --.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Figueroa BE, Quint DJ, McKeever PE, Changler WF. Extracranial metastatic meningioma. *British Journal of Radiology*. 72L513-6, 1999.
2. McKeever PE, Junck LR, Strawderman MS, Blaivas M, Tkaczyk A, Cates MA. Patient's youth predicts less proliferation of their glioblastomas. *Neurology* (in preparation)

BOOKS/CHAPTERS IN BOOKS:

1. McKeever PE: The Brain, Spinal Cord, and Meninges. Chapter 10 in: Sternberg SS, Antonioli DA, Carter D, Mills SE, Oberman HA (Eds): *Diagnostic Surgical Pathology, Third Edition*. Lippincott Williams & Wilkins, Philadelphia, 1999.
2. McKeever PE: Glial cell pathology. In: Smith BH and Adelman A, eds.: *Encyclopedia of Neuroscience*, Elsevier Science, 1999, p. 812-818.
3. Greenberg HS, Chandler WF, Ensminger WD, Junck L, Page MA, Gebarski SS, Hood TW, Stetson PL, Diaz RF, Hegarty T, Thornton A, Lichter AS, McKeever PE, Tankanow R: Radiosensitization with constant intra-arterial infusion of bromodeoxyuridine (BUDR) and focal external beam radiation in the treatment of malignant astrocytoma. In: *Infusion Systems in Medicine*. (In preparation.)
4. McKeever PE, Blaivas M, Gebarski SS: Pituitary Tumors. In: Thapar K, Kovacs K, Scheithauer BW, Lloyd RV (Eds): *The Humana Press Inc., Totowa, New Jersey, 2000*. (in press).
5. McKeever PE: Laboratory methods. In: Nelson JS, Parisi J, Schochet S (Eds): *Principles and Practice of Neuropathology*, Oxford, New York (in press).
6. McKeever PE: The nervous system. In: Dabbs DJ (Ed): *Comprehensive Diagnostic Immunohistochemistry*, Harcourt Brace & Co., Orlando (in press).
7. McKeever PE: The nervous system. In: Kohen E (Ed): *Fluorescent Probes in Oncology*, Imperial College Press, London (in press).

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

1. McKeever PE: Neurofilament (NF) and synaptophysin stains reveal diagnostic and prognostic patterns of interaction between normal and neoplastic tissues. 51st Annual Meeting of the Histochemical Society, New Orleans, 2000.

DERVLA MELLERICK-DRESSLER, Ph.D
ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Graduate students:

1. Course Lectures - Path 581, 4.5 hours; CDB 530, 3 hours

B. Undergraduate students:

1. Mentored NSF Developmental Neurobiology Training Fellows Sophie Laoa, Jeffrey Fisher and Heather Liu

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, NIH RO3 "The *Drosophila* embryonic CNS; a novel model for PCBs neurotoxicity" PI. 35% effort (\$150,000 9.99-8.02)
- B. Principal Investigator, National Science Foundation " Studies on the role and regulation of the *ventral nervous system defective* homeobox gene during *Drosophila* neurogenesis." 50% effort (3.1.97-2.28.2000; \$283,509)
- C. Principal Investigator, NIH RO3 " Identification of targets of the *ventral nervous system defective/NK-2* gene using a novel yeast selection system" 35% effort (12.1 97-11.30.99; \$152,355).

PENDING:

- A. Principal Investigator, NIH R01 " How does the *Drosophila vnd* homeobox gene integrate positional information?" 50% effort (\$800,000 8/15/00-7/30/04).
- B. Co-Investigator, "Epithelial Cell Signaling and Differentiation " 40% effort, (\$980,000 1/1/01-12/3103)

PROJECTS UNDER STUDY:

- A. The identification of mechanisms underlying Regulated Vnd expression at the transcriptional and post-translational level
- B. The establishment of *Drosophila* as a novel assay for potential neurotoxins

- C. The elucidation of the role of the homeobox gene GTX in CNS development
- D. Understanding the role of the CV2 protein in wingless and BMP signaling

IV. **ADMINISTRATIVE ACTIVITIES:**

MEDICAL SCHOOL/HOSPITAL:

- A. Organogenesis Center Seminar Committee member

V. **OTHER RELEVANT ACTIVITIES:**

Member of the Genetics Society of America

INVITED LECTURES/SEMINARS:

1. Invited Lecturer, "Homeobox genes and Dorsal-Ventral Patterning of the Developing CNS" MUSC Biochemistry Department, Charleston, August 29, 1999.
2. Invited Lecturer, "*Drosophila* CNS dorsal-ventral patterning: Regulated *vnd* expression is required for neuronal localization and pathfinding". 41st Annual *Drosophila* Research Conference, Pittsburgh, March 25, 2000.

VI. **PUBLICATIONS:**

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

1. Mellerick, D., Modica, V. *Drosophila* CNS dorsal-ventral patterning: Regulated *vnd* expression is required for neuronal localization and pathfinding. *A. Dros. Res. Conf.* 41 2000 :103

ARTICLES SUBMITTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Mellerick, D.M. and Modica, V. *Drosophila* CNS dorsal-ventral patterning: Regulated *vnd* expression is required for neuronal localization, numbers and pathfinding. Submitted

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

- A. Cytopathology - six months.
- B. Breast Cancer Clinic, Cytopathology and back-up Histopathology – twelve months.
- C. Consultation Service, Department of Pathology:
 - 1. Cytopathology - twelve months.
 - 2. Breast pathology - back up, twelve months.
- D. Necropsy Service - four weekends.

II. TEACHING ACTIVITIES:

- A. Medical School Students:
 - 1. 1999-Present: Introduction to cytopathology, Histology course, Year I Medical students.
 - 2. 1999-Present: Mentor for medical students' senior clerkship.
- B. Residents and Cytopathology Fellow:
 - 1. Sign out; Gynecologic and Non-Gynecologic Cytology cases.
 - 2. Instruction in the performance and interpretation of fine needle aspirates.
 - 3. Monthly Cytopathology Conference.
 - 4. Consult Case Conference - four/year.
 - 5. Anatomic Pathology Conference: 2/year-Review of Cytopathology
- C. Other Education Activities:
 - 1. Cytotechnologists - Cytopathology Conferences – four/year.
 - 2. Endocrinology grand round: Fine needle aspiration of the thyroid gland, August 3, 1999.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Co-Investigator 1 UO1 CA68291-01 (\$8,798.00-direct cost) "Retinoids and Intermediate Biomarkers for CIN II and III", 9% effort, National Institute of Health.
- B. National Institute of Health, Co-Investigator (DRDA#98-1650), New Screening Method for Early Detection of Breast Cancer (5% effort) (pending approval of supplement)

PROJECTS UNDER STUDY:

1. Michael CW, Georgy B, Elhosseiny, Collin B. The cytologic spectrum and diagnostic pitfalls of apocrine lesions of the breast. (Manuscript near completion)
2. Merajver SD, Michael CW. Genomic deletions in tumors from families with breast and ovarian cancer
3. Michael CW, Tworek J, Wojno JK. The use of newly marketed antibodies in conjunction with the routine panel in the evaluation of serosal fluids.
4. Michael CW, Collin B, Flint A. Neuroendocrine tumors of the lung: Cytologic features and differential diagnosis.
5. Michael CW, Weiss S. Deciduoid mesothelioma in a young male: a cytohistologic correlation with electron microscopy and immunohistochemistry.
6. Michael CW, Bedrossian CW. Evaluation of mesothelioma in situ by routine immunohistochemical stains and proliferative markers.
7. Michael CW, Pass HI. Can the presence of SV40 and its receptor have diagnostic utility in separating mesothelia from adenocarcinoma in body fluids.
8. Michael CW, Lui J. Fine needle aspirates of the breast: The University of Michigan Experience before and after the implementation of the ThinPrep technique.
9. Bavikaty N, Michael CW. Ultrasound guided transbronchial fine needle aspirates : Diagnostic accuracy and pitfalls.
10. Tworek JA, Michael CW. Fine needle aspirates of lymphocyte rich lesions: Cytologic diagnosis based on the revised REAL classification with flow-cytometry and biopsy follow-up.
11. Tworek JA, Michael CW. Evaluation of fine needle aspirates of small blue cell tumors prepared by the ThinPrep technique.
12. Akdas G, Michael CW. Review of fine needle aspirates of melanoma prepared by the ThinPrep technique.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director, Cytopathology Laboratory.
- B. Director, Cytopathology Fellowship.

MEDICAL SCHOOL/HOSPITAL:

None.

REGIONAL AND NATIONAL:

- A. Reviewer, Diagnostic Cytopathology.
- B. Reviewer, Cancer Cytopathology.
- C. Reviewer, CAP Check Sample.
- D. Member, Quality Control Committee, Papanicolaou Society of Cytopathology.

- E. Member, Nomination Committee, Papanicolaou Society of Cytopathology.
- F. Chair, American Society of Cytopathology, Committee of Public Information.
- G. Chair, Research Task Force, Papanicolaou Society of Cytopathology.
- H. Member, Abstract review committee, United States and Canadian Academy of Pathology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "The interpretation of fine needle aspirates prepared by the ThinPrep technique" Teleconference, Teleconference Network of Texas, October 26, 1999
2. "Everything You Always Wanted to Know About the ASC But Never Asked" American Society of Cytopathology National Meeting, Sacramento, CA, November 3, 1999.
3. "Pap smears in the 90's and beyond". 8th Annual Primary Healthcare of Women's Course, Ann Arbor, MI, December 2, 1999. Sponsored by the Department of Gynecology and Family Practice.
4. "Pitfalls in pulmonary cytology" Teleconference, Teleconference Network of Texas, January 25, 2000.
5. "Neuroendocrine tumors of the lung: differential diagnosis and diagnostic pitfalls". Teleconference, American Society of Cytopathology, April 2000.
6. "The interpretation of cytologic specimens prepared by the ThinPrep technique". Michigan Society of Cytology, Livonia, MI, June 2000.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Michael CW, Naylor B. Amyloid in cytologic specimens: Differential diagnosis and diagnostic pitfalls. *Acta Cytologica* 1999;43:746-755.
2. Rochester AB, Roubidoux MA, Michael CW, Patterson SK. Mammographic localization of small lesions of ductal carcinoma in situ. *Journal of Women's Imaging* 1999;1:6-10.
3. Rock CL, Michael CW, Reynolds RK, Ruffin MT. Prevention of Cervix cancer. *Crit Rev Oncol Hematol* 2000;33(3):169-85.
4. Kintanar BK, Giordano TJ, Thompson NW, Michael CW. Granular cell tumor of trachea masquerading as Hurthle cell neoplasm on fine needle aspirate: a case report. *Diagn Cytopathol* 2000;22:379-382.
5. Michael CW, Hunter B. Interpretation of fine needle aspirates processed by the ThinPrep technique: Cytologic artifacts and diagnostic pitfalls. *Diagn. Cytopathol.* 2000;23:6-13.
6. Kleer CG, Michael CW. Fine-needle aspiration of breast carcinomas with prominent lymphocytic infiltrate. *Diagn Cytopathol* 2000;23:37-42.
7. Michael CW, McConnell J, Pecott J, Afify AM, Al-Khafaji. Comparison of the ThinPrep and AutoCyte liquid based to preparations in non-gynecologic specimens. *Diagn Cytopathol.* (accepted)

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Michael CW, Buschmann B. Can true papillary neoplasms and their mimickers be accurately classified by cytology. Submitted to cancer Cytopathol.
2. Tworek JA, Michael CW. Parotid gland mucosa associated lymphoma and their cytologic mimics. Submitted to Diagn Cytopathol.

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

1. Michael CW, McConnell J, Afify A, Al-Khafaji B, Pecott J. Comparison of the ThinPrep and AutoCyte liquid based preparations in nongynecologic specimens. *Mod Pathol* 1999;12:49A.
2. Theoharis C, Michael CW. The utility of Melan-A in conjunction with S-100 and HMB-45 in the work-up of melanoma in cytologic specimens. *Mod Pathol* 2000;13:56A.
3. Afify A, Michael C, Stern R. hyaluronic acid and CD44 aids in the differentiation between mesothelioma and adenocarcinoma in serous effusions. *Mod Pathol* 2000;13:40A.
4. Liu J, Michael CW. Fibroadenoma versus ductal carcinoma in breast aspirates: The gray zone. Scheduled for poster presentation, American Society of Cytopathology National Meeting, Philadelphia, Pennsylvania, November 7-11, 2000.
5. Michael CW, Collins B, Flint A. The cytologic classification of pulmonary neuroendocrine tumors: how far can we go? Scheduled for poster presentation, American Society of Cytopathology National Meeting, Philadelphia, Pennsylvania. November 7-11, 2000.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. LEADERSHIP & MANAGEMENT ACCOMPLISHMENTS:

OVERVIEW:

- Guided the Reproductive Sciences Program (RSP) through discussions and actions required to close the unit following an unexpected decision in late March by the Vice President for Research, Fawwaz Ulaby. This decision came after receipt of superb external and internal reviews, the decision to recruit a new world-class leader, an advertisement in Science claiming "outstanding resources" to be provided, recruitment of many outstanding applicants, and interviewing of three with the top two invited back for a second visit. Then, at a meeting on March 23 with the Provost and Deans of Medicine, LS&A and SPH, the Vice President learned that no units were willing to provide the needed and claimed resources. Thus, at a special meeting of the RSP Executive Committee and the Search Committee on March 28, it was announced without any prior discussion or involvement of faculty or myself that RSP would be closed effective the end of August. Subsequently, when it was recognized that closure would be easier from a budgetary standpoint if effected before the start of the next fiscal year, July 1, closure was moved up to June 30.
- Prior to the notice of closure, continued to develop groundwork for transition to new leadership. Met with newly constituted RSP Executive Committee that included administrative representation from the Medical School, LS&A, and SPH. Began moving in new directions marked by emphasis on the impact of environmental change on reproduction and underlying molecular mechanisms. Held a successful conference on the effects of rising carbon dioxide on life forms and potentially reproduction. Subsequent to this conference, developed applications for support of new initiatives in this area. Received continued funding for another five years of our NIH training grant. Continued to stimulate discussions and plans for developing a U01 center to replace our prior P30 center. The new environmental initiatives will be key to this development. Discussions are continue on ways to develop other multi-investigator programmatic grants in areas like reproductive neuroecology and reproductive toxicology.
- Continued to operate our Central Laboratory in an NIH-funded Study of Women's Health Across the Nation as the premier laboratory doing large-scale analyses of reproductive hormones. Services of the laboratory continue to expand. We are now delivering approximately 20,000 determinations of hormone concentrations in serum and urine each month.
- Continued working as founder and principal mover on a large scale, multimedia, CD and Web-based learning project, the Reproductive Learning Collaboratory. This project is focused on using novel approaches and state-of-the-art technologies to help anyone regardless of reading or cognitive ability (ranging from grade school level students and

reading disabled adults to health care professionals) to learn what they need and want to know about reproduction, reproductive health and sexuality. This project is funded by the U.S. Department of Education's Fund for the Improvement of Postsecondary Education (FIPSE). With assistance of three graphics illustrators, several textual content developers (including 17 undergraduate research opportunity students – UROP), and two technical programming assistants, nearly completed a multi-level, dynamically-interactive website on birth control and started another on sexually transmitted diseases. In addition to the funded application for post-secondary education (U.S. Dept of Education), we submitted proposals for use in middle level schools (NSF). Approaching schools is made possible by a new key idea: providing school systems and teachers with ways to customize content. With this addition, initiated, coordinated (14 investigators) and submitted a grant to NASA involving environmental science learning.

- In preparation for retirement, formed a new company, inDepthLearning.com, Inc.

A. REPRODUCTIVE SCIENCES PROGRAM RESEARCH RELATED

1. Director, Standards and Reagents Core Facility (NIH P30 Center)
2. Director, Central Laboratory, Study of Women Across the Nation (NIH SWAN)

B. UNIVERSITY

1. Director, Reproductive Sciences Program.
2. Member, Biomedical Engineering
3. Member, Michigan Cancer Center, 1993-
4. Member, RUTH International Advisory Panel, 1997- (Raloxifene Use for the Heart)
5. Member, Steering Committee for Environmental Issues and Research on Campus, 1998-

C. REGIONAL AND NATIONAL

1. Member, NIDDK Endocrinology Research Program Advisory Committee, 1986-
2. Member, NIDDK Hormone Distribution Program Subcommittee, 1986-
3. Member, NIH Reviewers Reserve, 1989-

II. PERSONAL ACCOMPLISHMENTS IN RESEARCH & SCHOLARSHIP

A. TEACHING ACTIVITIES

1. Lectures:

Served as a primary instructor for a full semester four hours/week laboratory course for dental and health professional students, Pathology 630/631, Fall 1999

2. Graduate students:

None.

3. Supervision/Mentorship of other students:

Undergraduate Students included: Brea Aldorfer and Aaron Varani

UROP Students included: Jessica Alter, Michael Ascher, Josiah Avery, Sarah Bowersox, Rebecca Casas, Abigail Clark, Hugh Ferguson, Adam Hamilton, Teri Hammock, Klint Kesto, Jenny Li, Nishita Patel, Rasheeda Prince, Amy Sanghvi, Alex Sopheia, Jynifer Warren, Christa Wimberly

4. Service on Other Dissertation Committees:

None.

B. RESEARCH ACTIVITIES:

1. Current Active Support (direct costs; full term of project)

NIH, U01-AG 12495, A.R. Midgley, P.I., Menopause and Aging in Women: Central Laboratory, 10/01/99 - 09/30/03, \$1,465,338, 20%. Competitive renewal application funded for an additional 4 years.

NIH, U01-AG 12495 SUPPLEMENT, A.R. Midgley, P.I., Hormonal Predictors of Perimenopausal Morbidity, 05/29/96 - 07/31/99, \$2,894,204.

NIH, T32-HD 07048, D. Foster, P.I., Training Program in Reproductive Endocrinology, 07/01/00 - 06/30/05, (no salary support).

2. Proposal Writing (Funded)

Wrote a proposal to UROP for evaluation of our website, Evaluation of a Dynamic, Multi-Reading Level, Birth Control Module, 6/1/00-12/15/00, \$4,777

3. Proposal Writing (Not-Funded)

Supplement to FIPSE grant, "Off-campus and community-based delivery of educational programs that improve rural access: An innovative approach to help all people learn what they need and want to know."

4. Proposal Writing (Submitted)

On behalf of inDepthLearning.com, submitted proposals involving University of Michigan investigators to:

- Michigan Life Sciences Corridor, "Life Sciences Learning: A New, Multilevel, Dynamic Paradigm," \$1,437,116.
- National Cancer Institute, "An Innovative Web-Based System for Cancer Education" (Lewis Kleinsmith, PI), \$1,618,037.

And, on behalf of inDepthLearning.com, developed proposals involving University of Michigan investigators (submitted for the August 1, 2000 deadline) to:

- National Cancer Institute, Phase I Small Business Research Grant, "An Innovative, Web-Based System for Skin Cancer Education" (Lewis Kleinsmith, PI), \$100,000.
- National Institute of Allergies and Infectious Diseases, Phase I Small Business Research Grant, "An Innovative, Web-Based System for AIDS Education" with Sandro Cinti as

Principal Consultant, \$100,000.

- National Science Foundation, Informal Science Education Initiative, "Beyond the Headlines of Science: Educating the Public about Scientific Advances," \$2,727,096 (five years).

5. Scientific Collaborations

Pediatrics: Vasantha Padmanabhan: involvement in computer-controlled perfusion system and study of ovarian development.

6. Projects Under Study

- Development of a novel, multi-reading level, hyperlinked, reproductive learning environment for persons of all ages from 7 to 70 and available in forms accessible in homes, libraries, schools and clinics.
- Development and utilization of a computer-controlled perfusion system for on-line analysis of cellular responses to pulsatile and other controlled signaling and use of this system to assist in modeling the LH surge (being phased out, but continued by colleague Vasantha Padmanabhan)

C. OTHER RELEVANT ACTIVITIES

1. Lectures/Seminars/Meetings:

July 26, 1999, Conference call NIH grant review
July 31-Aug 3, 1999, Society for Study of Reproduction meeting, Pullman WA
September 3, 1999, Global Change Workshop, U of M
September 27, 1999, RSP Seminar: Learning about Reproduction Dynamically
December 1, 1999, Meeting with FIPSE administrators, Washington, DC
December 2-3, 1999, SWAN Steering Cmt mtg, Washington, DC
March 10, 2000, Michigan Assn of Computer Users in Learning (MACUL) conference, Grand Rapids
June 27-29, 2000, SWAN Steering Cmt mtg, Los Angeles, CA

2. Other Activities

Implementing chemiluminescence-based, solid state, two site immunoassays to replace and improve upon radioimmunoassays (and thereby reduction in usage of radioactive isotopes).

D. PUBLICATIONS:

1. Articles Published/In Press

1. Midgley, A.R., McConnell, D.S., England, B.G., Gonzalez, K., Davis, M., Possley, R., Kitzsteiner, S., Skurnick, J., Crawford, S., Santoro, N., Lasley, B. Ensuring reliability of assay results in a large, longitudinal, multiethnic, multicenter, cooperative study of the menopausal transition. *Clinical Chemistry*, Under revision after favorable review.

2. Articles in Preparation

1. England, B.G., Midgley, A.R., Jr., McConnell, D.S. A sensitive fully automated chemiluminescent immunoassay for estradiol.
2. McConnell, D.S., England, B.G., Midgley, A.R. Automated immunoassay of human gonadotropins in urine.

3. Abstracts

1. Midgley A.R, Rossi B.V., Reproductive Learning Collaboratory: Learning what you need and want to know about reproductive biology, reproductive health and sexuality. Society for the Study of Reproduction, July 31-Aug 3, 1999.
2. Midgley AR, Rossi BV, and Buberniak, Risa. CD-Based, Web-Enhanced Health Education System: Learning What You Need and Want to Know about Reproductive Biology, Reproductive Health, and Sexuality. RSP Poster Day, 1999.
3. Eight other related abstracts presented by UROP students at UROP symposia on March 29, April 5, and April 9, 2000.

III. DEVELOPMENTAL OBJECTIVES FOR 1999-2000

- A. After 32 years, turn over directorship of RSP to my successor!
- B. Obtain expansion funding for the concept behind the Reproductive Learning Collaboratory.
- C. Publish on the Web our first two units: Birth Control and Sexually Transmitted Infections.
- D. Complete and submit several manuscripts describing novel methodological approaches developed by the Central Laboratory.
- E. Develop assays of urinary hormones needed by the U01 Collaborative Centers on the perimenopause.

IV. EVALUATION OF GOALS AND OBJECTIVES SET LAST YEAR

1. After 31 years, turn over directorship of RSP to my successor.
 - Completed in that RSP has been disbanded as an OVPR unit.
2. Obtain external funding for the Reproductive Learning Collaboratory.
 - Done. Received major grant from the U.S. Department of Education (FIPSE).
3. Bring the Reproductive Learning Collaboratory Web site to a usable (albeit content-limited) state.
 - This is nearly finished. A final version will be published this Fall.
4. Complete and submit several manuscripts describing novel methodological approaches developed by the Central Laboratory.
 - The review of a key article was held up pending verification of stability of assays over a period of time. This has now been completed with excellent results. The resulting manuscript will be re-submitted as soon as the analyses are completed. With this manuscript finished, progress on the others can proceed.
5. Develop assays of urinary hormones needed by the U01 Collaborative Centers on the perimenopause.
 - Done. Assays now running for luteinizing hormone, follicle stimulating hormone, estrone conjugates, pregnanediol glucuronide, and creatinine and work progressing on new methods for inhibin, activin, and follistatin.

**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 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Graduate students:

1. Responsible during the current academic year for teaching activities for the following:
 - a. Human Growth and Development Course "Biology of Aging", 1 hour.
 - b. PIBS 501: Genetics of Aging and Longevity, 1 hour and Activation Defects in T Cells, 2 hours.
 - c. PIBS 502, Research Responsibility Course, 12 hours.
2. Program Director, "Experimental Immunopathology Training Grant."
3. Ph.D. Dissertation Committees, University of Michigan:
 - a. Anne Jackson
 - b. Pamela Bennett-Baker
 - c. Wannee Asavaroengchai
 - d. Meera Nathan
 - e. Tyler Sisk
 - f. Tania Gourley
 - g. Yadira Hernandez
4. Ph.D. Dissertation Advisor:
 - a. Michael Eisenbraun.
 - b. Anavelys Ortiz-Suarez.
5. Undergraduate students:
 - a. Ashwin Pamidi
 - b. Mary Jo Dubois

B. Postdoctoral Fellows:

1. Ami Tamir, Ph.D.
2. Ph.D. Dissertation Advisor
 - a. Michael Eisenbraun

- C. In Lab:
 - 1. Igor Dozmorov, Ph.D.
 - 2. Gonzalo Garcia, Ph.D.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Activation Defects in Aging T Cells", NIH AG-09801 (8%), \$170,741 direct costs/year, 8/1/90 - 7/31/99. MERIT award.
- B. Principal Investigator, "Genetics of Age-Sensitive Traits in Mice", NIH AG-16699 (20%), \$647,937 direct costs/year, 5/1/99 - 4/30/04.
- C. Principal Investigator, "Genetic Control of Longevity in Mice", NIH AG-11687 (8%), \$119,174 direct costs/year, 9/1/93 - 8/31/03.
- D. Principal Investigator, "New T Cell Subsets Defined by P-glycoprotein in Aging Mice", NIH R01-AG03978 (0%), \$158,141 direct costs/year, 12/1/95 - 11/30/99.
- E. Director, "Research Development Core", NIH AG-13283 (10%), \$89,400 direct costs/year, 9/1/98 - 6/30/00. (Component of Nathan Shock Center of Excellence for Basic Biology of Aging, John Faulkner, Program Director).
- F. Director, "Core Facility for Aged Rodents", NIH AG-08808 (5%), \$64,627 direct costs/year, 9/1/94 - 8/31/99. (Component of Claude Pepper Older Americans Independence Center, J. Halter, Program Director).
- G. Director, "Research Development Core", NIH AG-08808 (15%), \$155,270 direct costs/year, 9/1/94 - 8/31/99. (Component of Claude Pepper Older Americans Independence Center, J. Halter, Program Director).
- H. Project Director, "Prevention of Disease by Immunotonic Agents in Mice", NIH AG-08808 (5%), \$51,757 direct costs/year, 9/1/94 - 8/31/99. (Component of Claude Pepper Older Americans Independence Center, J. Halter, Program Director).
- I. Program Director, "Research Training in Experimental Immunopathology", NIH T32-AI-07413 (0%), \$244,353 direct costs/year, 4/1/92 - 8/31/03.
- J. Principal Investigator, "Wild Derived Mouse Stocks: New Models for Aging Research," NIH R01-AG13711 (5%), \$155,728 direct costs/year, 9/1/96 - 8/31/99.
- K. Course Director, "Summer Training Courses in Experimental Aging Research", NIH/NIA R13-AG12917 (0%), \$33,566 direct costs/year, 4/1/95 - 3/31/03.

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, Rheumatology Training Program
- D. Director, Research Development Core, Geriatrics Center

- E. Associate Director for Research, Geriatrics Center
- F. Director, Immunology Training Program
- G. Member, Program in Biomedical Sciences
- H. Director, Research Development Core, Nathan Shock Center
- I. Operating Committee, Immunology PhD program
- J. Associate Director, Nathan Shock Center for Aging

REGIONAL AND NATIONAL:

- A. Board of Scientific Advisors, Buck Center for Research on Aging.
- B. Fellow, Gerontological Society of America.
- C. Research Committee, American Federation for Aging Research.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

- A. Journal of Gerontology: Biological Sciences.
- B. Journal of the American Geriatrics Society. (Section Editor).
- C. Aging: Clinical and Experimental Research
- D. Mechanisms of Ageing and Development
- E. Experimental Gerontology

HONORS AND AWARDS:

- A. None.

INVITED LECTURES/SEMINARS:

1999

1. International Training Course in Signal Transduction, Santiago, Chile. "Signal Transduction Defects in T Cells from Aged Mice." Speaker, July 22 – 26.
2. National Research Council meeting on "Collecting Bio-indicators and Genetic Information in Household Surveys," Bethesda, MD. Speaker, August 19.
3. NIA/NHLBI Workshop on "Sleep and Host Defense Mechanisms," Bethesda, MD. "Aging of the Immune System." Speaker, August 24 – 26.
4. Biochemical Society Meeting, Cork, Ireland. "Immunosenescence: Primer and Prospectus." Speaker, September 6 – 8.
5. NIA Meeting on A Facility For Intervention Studies, San Antonio, TX. "Selection of Rodent Models and Immune Endpoints." Speaker, September 14 – 16.
6. "New Biology of Aging" Symposium, Kansas City, MO. "T Cell Aging in Mice: Genetic and Biochemical Analyses." Speaker, September 26 – 29.
7. Buck Center for Research on Aging, Novato, CA. "Are There Genes for Aging?" October 1.
8. University of Alabama, Birmingham, AL. "Genetic Analysis of Lifespan and Aging in Mice". Speaker, December 14.

2000

1. Workshop on Collecting Biological Indicators and Genetic Information in Household Surveys, Washington, DC. "Biomarkers and Genetics of Aging in Mice." Speaker, February 10 – 11.
2. Sigma Xi Lecture, Southern Illinois University, Carbondale, IL. "Are There Genes for Aging?" Speaker, February 16.
3. Annual Pepper Centers Meeting, UCLA, Santa Monica, CA. "Development and Exploitation of New Mouse Models for Aging." Speaker, February 17.
4. Ohio State University, Columbus, OH. "Aging – Genetics and Biochemistry." Speaker, February 21.
5. "Winning NIH Grants" workshop, University of Michigan, "Revising Applications." Speaker, April 8.
6. Biological Breakthroughs Expert Panel, RAND, Santa Monica, CA. Panel discussion. Speaker, April 12.
7. Geriatrics Center Research Retreat on Bone Marrow Transplantation in the Elderly, University of Michigan. "The Steep and Thorny Path to Grant Funding". Session Chair, April 27-28.
8. Nathan Shock Center Symposium on Genetics of Aging and Longevity, University of Michigan. Session Chair, May 1 – 2.
9. ULAM Brown-Bag Seminar Series, University of Michigan. "Dwarf Mice." Speaker, May 4.
10. Molecular Mechanisms of Aging, Hakone, Japan. "Genetic Analysis of Aging in Mice." Speaker, May 7 – 9.
11. American Association of Immunologists Annual Meeting, Seattle. "Protein Kinase Defects in T Cells from Aging Mice." Speaker, May 13 – 14.
12. American Clinical Oncology Society, New Orleans, "Mouse Genes for Aging and Cancer." Speaker, May 20 – 21.
13. 23rd Annual Meeting of the American Aging Association, Boston, MA. "Statistical Analysis of Gene Expression Data." Speaker, June 2.
14. 8th Annual Summer Training Course in Aging Research, Berkeley, CA.. "Theories of Aging" and "Vertebrate Animal Models." Course Director, June 11 – 15.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Tamir, A., and R. A. Miller.: Aging impairs induction of cyclin-dependent kinases and down-regulation of p27 in mouse CD4+ cells. *Cellular Immunology* 198:11-20, 1999.
2. Miller, R. A., R. Dysko, C. Chrisp, R. Seguin, L. Linsalata, G. Buehner, J. M. Harper and S. Austad.: Mouse stocks derived from tropical islands: new models for genetic analysis of life history traits. *J. Zoology*, 250:95-104, 2000.
3. Miller, R. A., and C. Chrisp.: Lifelong treatment with oral DHEA sulfate does not preserve immune function, prevent disease, or improve survival in genetically heterogeneous mice. *J. American Geriatrics Society*, 47:960-966, 1999.
4. Yang, D. and R. A. Miller.: Cluster formation by protein kinase C during murine T cell activation: effect of age. *Cellular Immunology*, 195:28-36, 1999.
5. Miller, R. A.: Kleemeier Award Lecture: Are There Genes for Aging? *J. Gerontology: Biological Sciences*, 54A:B297-B307, 1999.

6. Kirk, C. J., A. M. Freilich, and R. A. Miller.: Age-related decline in activation of JNK by TCR and CD28-mediated signals in murine T lymphocytes. *Cellular Immunology* 197:75-82, 1999.
7. Kirk, C. J., and R. A. Miller.: Age-sensitive and insensitive pathways leading to JNK activation in mouse CD4 T cells. *Cellular Immunology* 197:83-90, 1999.
8. Eisenbraun, M. D. and R. A. Miller.: *mdr 1a*-encoded P-glycoprotein is not required for peripheral T cell proliferation, cytokine release, or cytotoxic effector function in mice. *J. Immunol.* 163:2621-2627, 1999.
9. Eisenbraun, M. D., D. H. Teitelbaum, R. L. Mosley, and R. A. Miller.: Altered development of intestinal intraepithelial lymphocytes in P-glycoprotein-deficient mice. *Dev. Comp. Immunol.*, in press.
10. Miller, R. A., C. Chrisp, and W. Atchley.: Differential longevity in mouse stocks selected for early life growth trajectory. *J. Gerontol. Biol. Sci.*, in press.
11. Miller, R. A., D. Burke, and N. Nadon.: Announcement: four-way cross mouse stocks: a new, genetically heterogeneous resource for aging research. *J. Gerontol. Biol. Sci.*, 54A; B358, 1999.
12. Miller, R. A. and N. Nadon.: Principles of animal use for gerontological research. *J. Gerontol. Biol. Sci.*, 55A:B117 – 124, 2000.
13. Warner, H. R., D. Ingram, R. A. Miller, N. L. Nadon, A. G. Richardson.: Workshop report: program for testing biological interventions to promote healthy aging. *Mechanisms of Ageing and Development*, in press.
14. Miller, R. A. and S. Austad.: Large animals in the fast lane (letter). *Science* 285:199, 1999.
15. Eisenbraun, M. D., A. Tamir, and R. A. Miller.: Altered composition of the immunological synapse in an anergic, age-dependent memory T cell subset. *J. Immunology*, in press.
16. Tamir, A., M. D. Eisenbraun, G. G. Garcia, and R. A. Miller.: Age-dependent alterations in the assembly of signal transduction complexes at the site of T cell/APC interaction. *J. Immunol.*, in press.
17. Miller, R. A., S. Austad, D. Burke, C. Chrisp, R. Dysko, A. Galecki, A. Jackson, and V. Monnier.: Exotic mice as models for aging research: polemic and prospectus. *Neurobiology of Aging*, 20:217-231, 1999.
18. Miller, R.A.: Telomere diminution as a cause of immune failure in old age: an unfashionable demurrer. *Biochemical Society Transactions* 28: 241-245, 2000.
19. Miller, R.A.: Effect of aging on T lymphocyte activation. *Vaccine* 18:1654-1660, 2000.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Dozmorov, I., A. Bartke, and R. A. Miller.: Array-based expression analysis of mouse liver genes: effect of age and of the longevity mutant. Submitted.
2. Jackson, A. U., A. T. Galecki, C. Chrisp, D. T. Burke, and R. A. Miller.: Mouse loci associated with life span exhibit coordinated control of neoplastic and non-neoplastic disease. Submitted.

BOOKS/CHAPTERS IN BOOKS:

1. Kirk, C. J., and R. A. Miller.: Raf-1 protein kinase activity in T cells from aged mice. In: Methods in Molecular Medicine: Aging Methods and Protocols, Y. Barnett and C. Barnett, eds., Humana Press. pp 85 – 96, 2000.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

- A. Surgical Pathology and Frozen Section Diagnosis (5 months/year)
- B. Autopsy Service, rotational basis, on call 13 weeks/year (staffing 15-20 cases/year).
- C. Case presentations at Tumor Board
- 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 ACTIVITIES:

- 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 and NRSA
- B. House Officers
 - 1. Pathology house officers, Autopsy supervision and instruction (13 weeks /year)
 - 2. Pathology house officers, Surgical Pathology supervision and instruction, (23 weeks/year)
 - 3. Lecture and Case presentations at Urologic Pathology Conferences (25 conferences/year)
- C. Graduate students:
 - 1. Course Director, Pathology 585, Lecture and Laboratory course for Graduate students (22 hrs)
 - 2. Laboratory Instructor, pathology 600 (M2 pathology course)

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator: "Endothelial Cell Matrix Metalloproteinases in Human Prostate Cancer" Veteran's Administration VERAM 10/1/99-9/30/00 (\$15,000)
- B. Co-Investigator "Gender-specific T cell homing and autoimmunity" (B. Richardson, Internal Medicine, PI) NIH 12/98 - 11/03 (\$1,760,000)
- C. Co-Investigator, "Host Defense of the Lung" Research Enhancement Award Program (REAP) Veteran's Administration 11/98-10/03 (\$1,350,000)
- D. Collaborator. Lung Injury by Oxygen Metabolites NIH/NIGMS R37 GM29507. National Institute of Health (Peter A. Ward, Principal Investigator). 7/97-6/01. (\$1,123,824)

- E. Co-mentor, Matthew Adams, M.D., Arthritis Foundation, Michigan Chapter. 1/98-12/99 (\$20,000/ year)
- F. Collaborator, Matthew Adams, M.D., " Gender-specific T cell homing and autoimmunity" NIH-NRSA Award, 09/01/99-08/31/01 (\$85,028)

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 receptor expression
 - 2. The role of estrogen in endothelial cell adhesion molecule expression and lymphocyte homing
 - 3. Effect of estrogen on endothelial cell cytokine expression
- C. Role of prostate endothelial cells in malignancy

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Autopsy Quality Assurance Review

MEDICAL SCHOOL/HOSPITAL:

- A. Member, Admissions Committee of the University of Michigan Medical School, 1999-
- B. Member, Research and Development Committee, Veterans Affairs Medical Center, 1999-

REGIONAL AND NATIONAL:

- A. Membership in National Organizations
 - American Society for Investigative Pathology
 - American Society of Clinical Pathologists
 - The A. James French Society of Pathologists
 - American Association for the Advancement of Science
 - New York Academy of Science
 - American Association of University Women

V. OTHER RELEVANT ACTIVITIES:

- A. Reviewer for
 - Clinical Immunology and Immunopathology
 - Biochemical pharmacology
 - Shock
 - Free Radical Biology and Medicine
 - American Journal of Pathology

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

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Murphy, H.S., R. Warner, N. Bakopolous, M. Dame, J Varani, P.A. Ward. Endothelial cell determinants of susceptibility to neutrophil-mediated killing. *Shock* 12 (2):11-117, 1999
2. Gibbs DF. Shanley TP. Warner RL. Murphy HS. Varani J. Johnson KJ. Role of matrix metalloproteinases in models of macrophage-dependent acute lung injury. Evidence for alveolar macrophage as source of proteinases. *Am. J. Res. Cell Mol. Biol.* 20(6):1145-54, 1999
3. Robey, T.C., Eiselt, P.M., Murphy, H.S., Mooney, D.J., Weatherly, R.A. Biodegradable external tracheal stents and their use in a rabbit tracheal reconstruction model. *Laryngoscope* (in Press).
4. Robey, T.C., Valimaa, T., Murphy, H.S., Mooney, D.J., Weatherly, R.A The use of internal bioabsorbable LGA "finger-type" stents in a rabbit tracheal reconstruction model. *Arch. Otolaryng.* (in Press).

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

1. Murphy, H. S., Yu, C. 2000 Functional Expression of p47 Component of NADPH Oxidase in Endothelial Cells. *J. Mol Cell Cardiol* 32: A32.
2. Murphy, H.S., Yu, C., Dame, M., Warner, R., Varani, R. 2000 NO-induced HSP-70 expression in endothelial cells. *J. Mol Cell Cardiol.* 32: A48.
3. Robey, T.C., Valimma, T., Murphy, H.S., Mooney, D.J., Weatherly, R.A 2000.. The Use of Internal Bioabsorbable PLLA stents in a rabbit tracheal reconstruction model. Lamberson Research Conference. Univ. of Mich.

SUBMITTED PUBLICATIONS:

1. Murphy, H.S. Yu, C. Quddus, J. Functional Expression of the p47 Component of Endothelial Cell NAD(P)H Oxidase. *Biochem. Biophys. Res. Comun.* (submitted for publication).
2. Robey, T.C., Valimma, T., Murphy, H.S., Mooney, D.J., Weatherly, R.A. The Use of Internal Bioabsorbable PLLA stents in a rabbit tracheal reconstruction model. *Arch. Otolaryng.* (submitted for Publication).
3. Varani J, Dame M, Schmidt T, Zeigler M, Murphy HS, Wojno K, and Johnson K. Elaboration of matrix metalloproteinases by human prostate in organ culture and by prostate-derived cells. (Submitted for publication).
4. Warner R., Kang S., Murphy H., Varani J. Skin inflammation due to ultraviolet radiation is associated with induction of nitric oxide. (Submitted for publication).

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

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. Cytopathology.
- B. Tumors of zooplankton.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Advisory Committee on Appointments and Promotions.

REGIONAL AND NATIONAL:

- A. Cytopathology, Editorial Advisory Board.
- B. Acta Cytologica, Editorial Advisory Board.
Associate Editor, North American Review Board.
- C. Diagnostic Cytopathology, Consulting Editor.
- D. International Academy of Cytology:
International Board of Cytopathology, Member.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

- 1. Naylor, B.: The century for cytopathology. Lecture, Annual Scientific Meeting of American Society of Cytopathology, Sacramento, California, November, 1999.

2. Naylor, B.: a). Cytopathology of serous fluids, b). Mesothelioma, c). Transthoracic fine needle aspiration cytology, c) History of cytopathology. Lectures, Cytotechnology Training Program, Henry Ford Hospital, Detroit, Michigan, 2000.
3. Naylor, B.: Tumors on zooplankton: a preliminary histologic analysis (Lecture). Workshop on tumor-like abnormalities in zooplankton. Great Lakes Environmental Research Laboratory, U.S. Department of Commerce, National Oceanic and Atmospheric Administration, Muskegon, Michigan, November, 1999.
4. Omair, M., Naylor, B., Beals, T.F., Jude, D.J., and Vanderploeg, H.A.: Histological analysis of Great Lakes zooplankton tumors. Platform presentation, Conference of the International Association for Great Lakes Research, Cornwall, Ontario, Canada, April, 2000.

HONORS AND AWARDS:

None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Michael, C.W. and Naylor, B.: Amyloid in cytologic specimens: Differential diagnosis and diagnostic pitfalls. *Acta Cytol.*, 1999; 43:746-755.

BOOKS/CHAPTERS IN BOOKS:

None.

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

None.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

- A. Supervised Luis Del Peso, Adalberto Benito, Victor Gonzalez-Muñoz, Yuanming Hu, Naohiro Inohara, Peter Lucas, Rebecca Liu, Jacques Nöre, and Yasunori Ogura, Postdoctoral Fellows.
- B. Supervised Mary Benedict, Scott Burger, Jingurei Lin, and Alice Young, graduate students.
- C. Laboratory Instructor, Pathology 630/631. Full semester, two hours/week.
- D. Department of Pathology, Graduate Program Course 581, University of Michigan, Ann Arbor, Michigan, (1 lecture).
- E. Instructor, Microbiology and Immunology 553, Cancer Biology Training Program, University of Michigan, (1 lecture).
- F. 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, "Bcl-x_s-mediated apoptosis of Kaposi's sarcoma cells," National Institutes of Health, \$1,282,648 (total direct costs), 9/1/95-8/31/00.
- C. Principal Investigator, "Molecular analysis of Bcl-x_s-induced apoptosis in breast cancer," US Army Medical Research and Material Command, Fort Detrick, Frederick, MD \$801,917 (total).
- D. Principal Investigator, "HRK, A novel apoptosis regulatory gene," National Institutes of Health, \$746,005 (total annual direct costs), 3/1/98-2/28/02.
- E. Principal Investigator, "Molecular interactions of Bcl-2 family members," US Army Medical Grant; fellowship for Mary Benedict, Graduate Student Research Assistant. \$51,000.

- F. Principal Investigator, "Ciper: a novel NF- κ B-activating gene involved in Cancer," National Institutes of Health, \$1,000,000 (total direct costs), 1/7/00-6/30/05.

PENDING

- A. Principal Investigator, "Characterization of chimeric c-IAP2/MALT-1 in Lymphoma," Michigan Life Science Corridor Fund, \$620,507 (total direct costs), 01/01/01-12/31-03.

PROJECTS UNDER STUDY:

- A. Molecular characterization of the programmed cell death pathway in mammals and *C. elegans*.
- B. Molecular regulation of Bcl-2 family members.
- C. Gene therapy using Bcl-2 proteins as targets for cancer cell killing.

IV. DEPARTMENTAL:

- A. Member, University of Michigan Cancer Center, Ann Arbor, MI.
- B. Member, Transgenic Core Committee, Multipurpose Arthritis Center, University of Michigan, Ann Arbor, MI.
- C. Member, Comprehensive Examination Committee, Pathology Graduate Program, University of Michigan, Ann Arbor, MI.
- D. Member, Admissions Committee, Molecular and Cellular Biology, Graduate Program, University of Michigan, Ann Arbor, MI.
- E. Member, Hybridoma Core Committee, Multipurpose Arthritis Center, University of Michigan, Ann Arbor, MI.

MEDICAL SCHOOL/HOSPITAL:

- A. Co-Director, Cell Biology Program, University of Michigan Cancer Center.
- B. Member, Transgenic Core Facility Committee, Multipurpose.
- C. Member, Faculty Search Committee, Rheumatology Division, and Department of Microbiology/Immunology.
- D. Reviewer, Departmental Grants and Summer Student Scholarship Program.
- E. Member, Search Committee to find Chairman of Department of Radiation Oncology, University of Michigan Medical School, Ann Arbor, MI.
- F. Member, Hybridoma Core Committee, Multipurpose Arthritis Center, University of Michigan, Ann Arbor, Michigan.
- G. Member, Admission Committee, Program in Biomedical Sciences (PIBS), Graduate Program, University of Michigan, Ann Arbor, Michigan.
- H. Member, Biomedical Research Core Facilities (BRCF), University of Michigan, Ann Arbor, Michigan.
- I. Member, Biomedical Research Council, University of Michigan, Ann Arbor, Michigan.
- J. Member, Presidential Life Sciences Commission, 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:

1. Invited Speaker, "Regulation of the Cell Death Machinery," Rackham Arthritis Research Unit Seminar Series, University of Michigan Medical School, October 20, 1999.
2. Invited Speaker, "Regulation of the Cell Death Machinery," Pediatric Hematology/Oncology Conference, University of Michigan Medical School, December 1, 1999.
3. Invited Speaker, "Regulation of Apoptosis by the Apaf-1-Caspase-9 Pathway," Michigan Diabetes Research and Training Center, Sheldon Auditorium, Towsley Center, University of Michigan Medical School, March 11, 2000.

National and International:

1. Invited Speaker, "Mecanismos Moleculares que Regulan la Muerte Celular Programada o Apoptosis," Societat Catalana de Biologia Seminari Especial, University of Barcelona, Barcelona, Spain, June 11.
2. Invited Speaker, "Regulation of Apoptosis by Bcl-2 Family," European Society of Hematology, Barcelona, Spain, June 9-12.
3. Invited Speaker, "Regulation of the Cell Death Machinery," Department of Pathology, New York University School of Medicine, New York, NY, July 13, 1999.
4. Invited Speaker, "Regulation of the Cell Death Machinery," Cancer Center Seminar Series, University of Pittsburg Medical School, December 1, 1999.
5. Invited Speaker, "Regulation of Programmed Cell Death," St. Judes Children Hospital, Memphis, TN, December 10, 1999.
6. Invited Speaker, "New Insights into the Role of Mitochondria and Cytoplasmic Proteins in the Initiation of Apoptosis," New York Academy of Science Symposium, Rockefeller University, New York City, December 16, 1999.
7. Invited Speaker, "Regulation of the Cell Death Machinery," New York Medical College, New York, December 17, 1999.
8. Invited Faculty, Graduate Course in Apoptosis and Cell Cycle, Institute Venezolano de Investigaciones Cientificas, Caracas, Venezuela, January 25-28, 2000.
9. Invited Speaker, "Programmed Cell Death Regulation: Basic Mechanisms and Therapeutic Opportunities", American Association for Cancer Research, Hyatt Regency Lake Tahoe, Incline Village, NV, February 28, 2000.
10. Invited Speaker, "Regulation of the Cell Death Machinery," Dana-Farber Cancer Institute, Seminars in Oncology, Cambridge, MA, March 7, 2000.

11. Invited Speaker, "Regulation of the Cell Death Machinery," University of Iowa Medical School, Iowa City, IA, April 5, 2000.
12. Invited Speaker, "Regulation of the Cell Death Machinery", Department of Biochemistry and Biophysics, The Univ of Pennsylvania, Philadelphia, May 2, 2000.
13. Invited Speaker, "Regulation of the Cell Death Machinery", Department of Microbiology and Immunology, Tufts University Med School, Boston, MA, May 3, 2000.
14. Invited Speaker, "Regulation of Apoptosis by CED-4, Apaf-1 and Nod1", FASEB summer courses, Meeting on Signal Transduction, Coppertown, CO, July 2-7, 2000.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNAL:

1. Wu D, Hu Y, Chen P-J, Chen S, Nuñez G*, Ellis RE*. *C. elegans* MAC-1, and essential member of the AAA family of ATPases, can bind CED-4 and prevent cell death. *Development*. 126(9):2021-2031 (1999). *joint senior authors
2. Koseki T, Inohara N, Chen S, Carrio R, Merino J, Hottinger MO, Nabel GJ, Nuñez G. CIPER: A novel NF-kappaB-activating protein containing a caspase-recruitment domain with homology to herpes virus-2 protein E10. *J Biol Chem*. 274(15):9955-9961 (1999).
3. Inohara N, Koseki N, del Peso L, Hu Y, Yee C, Chen S, Carrio R, Merino J, Liu D, Ni J, Nuñez G. Nod1, an Apaf-1-like activator of caspase-9 and nuclear factor kappaB. *J Biol Chem*. 274(21):14560-14567 (1999).
4. Tang ED, Nuñez G, Barr FG, Guan KL. Negative regulation of the forkhead transcription factor FKHR by Akt. *J Biol Chem*. 274(24):16741-16746 (1999).
5. Catlett-Falcone R, Landowski TH, Oshiro MM, Turkson J, Levitzki A, Savino R, Ciliberto G, Mocinski L, Nuñez G, Dalton WS, Jove R. Interleukin 6-dependent stat3 signaling induces *bcl-x* gene expression and confers resistance to apoptosis in human myeloma tumor cells. *Immunity*. 10:105-115 (1999).
6. Hu Y, Benedict MA, Ding L, Nuñez G. Role of cytochrome c and dATP/ATP hydrolysis in Apaf-1-mediated caspase-9 activation and apoptosis. *EMBO J*. 18(13):3586-3595 (1999).
7. Silva M, Benito A, Sanz C, Prosper F, Ekhterae D, Nuñez G, Fernandez-Luna JL. Erythropoietin can induce the expression of bcl-xL through Stat5 in erythropoietin-dependent progenitor cell lines. *J Biol Chem*. 274(32):22165-22173 (1999).
8. Inohara N, Nuñez G. Genes with homology to DFF/CIDEs found in *Drosophila melanogaster*. *Cell Death Diff*. 6:823-824 (1999).
9. Tsukahara T, Kannagi M, Ohashi T, Kato H, Arai M, Nuñez G, Iwanaga Y, Yamamoto N, Ohtani K, Nakamura M, Fujii M. Induction of Bcl-xL expression by human T-cell leukemia virus type 1 tax through NF-kB in apoptosis-resistant T-cell transfectants with tax. *J Virol*. 73(10):7981-7987 (1999).
10. del Peso L, Gonzalez VM, Hernandez R, Barr FG, Nuñez G. Regulation of the forkhead transcription factor FKHR, but not the PAX3-FKHR fusion protein, by the serine/threonine kinase Akt. *Oncogene*. 18:7328-7333 (1999).
11. Ekhterae D, Lin Z, Brosius FC, Nuñez G. ARC inhibits cytochrome c release from mitochondria and protects against hypoxia-induced apoptosis in heart-derived H9c2 cells. *Circ Res*. 85(12):e70-e77 (1999).

12. Igaki T, Kanuka H, Inohara N, Sawamoto K, Nuñez G, Okano H, Miura Masayuki. Drob-1, a Drosophila member of the Bcl-2/CED-9 family that promotes cell death. *Proc Natl Acad Sci USA*. 97(2):662-667 (2000).
13. NicAmhloaibh R, Heenan K, Cleary O, Touhey S, O'Loughlin C, Nuñez G, Clynes M. Altered expression of Bcl-2 family mRNAs affect chemoresistance in a low-level multi-drug resistant variant of a human lung carcinoma cell line overexpressing mdr-1mRNA. *Int J Cancer*. 82(3):368-376 (1999).
14. Wells AD, Li XC, Li Y, Walsh M, Zheng XX, Wu Z, Nuñez G, Tang A, Sayegh M, Hancock WW, Strom TB, Turka LA. Requirement for T cell apoptosis in the induction of peripheral transplantation tolerance. *Nature Med*. 5(11):1303-1307 (1999).
15. Page C, Lin HJ, Jin Y, Castle VP, Nunez G, Huang M, Lin J. Overexpression of Akt/AKT can modulate chemotherapy-induced apoptosis. *Anticancer Res*. 20:407-16, (2000).
16. Liu R, Page C, Beidler DR, Wicha MS, Núñez G. Overexpression of Bcl-x_L promotes chemotherapy resistance of mammary tumors in a syngeneic mouse model. *Am J Pathol*. 155(6):1861-1867. (1999).
17. Sanz C, Benito A, Inohara N, Ekhterae D, Nuñez G, Fernandez-Luna JL. Specific and rapid induction of pro-apoptotic Hrk after growth factor withdrawal in hematopoietic progenitor cells. *Blood*. . 95(9):2742-72751 (2000).
18. Benedict MA, Hu Y, Inohara N, Nuñez G. Expression and functional analysis of Apaf-1 isoforms. Extra WD-40 repeat is required for cytochrome c binding and regulated activation of procaspase-9. *J Biol Chem*. 275:8461-8468 (2000).

**HAROLD A. OBERMAN, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999- 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

- A. Director, Blood Bank and Transfusion Service, University Hospitals.
- B. Diagnosis of surgical specimens from University Hospital patients.
- C. Diagnosis of surgical specimens from M-Labs.
- D. Diagnosis of consultation breast cases from pathologists elsewhere in the U.S. Chair, Transfusion Committee, Medical Staff
- E. Member of Executive Committee, University of Michigan Breast Care Center.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

- A. Lectures on breast pathology and transfusion medicine to sophomore class in system sequences. (six contact hours)
- B. Laboratory course for sophomore medical students (Pathology 600)
- C. Daily case review with pathology house officer assigned to blood bank.
- D. Presentation of Grand Rounds to Department of Radiation Oncology, "Invasive Carcinomas of the Breast". August 12, 1999.
- E. Postgraduate course, "Current Topics in Blood Banking", Planning Committee.
- F. Lectures on Transfusion Medicine presented to Pathology and Hematology/Oncology House Officers.
- G. Seminars and lectures on Pathology of Breast to Pathology House Officers. Presentation of consultation slide conferences (4) on pathology of the breast to pathology house officers.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. New Ultrasound Methods for Cancer Diagnosis and Treatment (3-5 years at 5 % effort)
- B. Microvascular and Structural Imaging of Breast Cancer (3-5 years at 3 % effort)
- C. Microinvasive carcinoma of the breast (with L Pierce)
- D. Correlation of histopathology and molecular pathology with prognosis of cystosarcoma phyllodes (with C. Kleer)
- E. Phase II evaluation of primary chemotherapy with doxorubicin/doectaxel in operable stage I and II breast cancer (L. Baker and A. Schott, P.I.)

IV. ADMINISTRATIVE ACTIVITIES:

REGIONAL AND NATIONAL:

- A. American Association of Blood Banks
 - 1. Transfusion medicine research strategies committee
 - 2. Liaison to College of American Pathologists
 - 3. Associate editor, TRANSFUSION
- B. American Society of Clinical Pathologists
- C. College of American Pathologists
- D. Michigan Society of Pathologists
- E. Southeastern Michigan Region Red Cross Blood Program
 - 1. Board of Directors
 - 2. Medical Advisory Committee
- F. Consultant, Veteran's Administration Hospital, Ann Arbor
- G. Breast Cancer Advisory Committee, Michigan Department of Public Health

DEPARTMENTAL:

- A. Director, Transfusion Medicine program.
- B. Director, fellowship training program in Blood Banking/Transfusion Medicine.

MEDICAL SCHOOL/HOSPITAL/UNIVERSITY:

- A. Transfusion Committee, Chairman
- B. Breast Care Center
- C. Bone marrow homotransplantation task force
- D. Haematology sequence advisory committee, M-2 year

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

- A. Associate Editor, TRANSFUSION.
- B. Editorial Board, American Journal of Surgical Pathology.
- C. Editorial Board, American Journal of Clinical Pathology.
- D. Editorial Board, Modern Pathology
- E. Reviewer, Journal of the American Medical Association.
- F. Reviewer, Blood.
- G. Reviewer, Cancer.
- H. Reviewer, Human Pathology

HONORS:

- A. Founders Award, Michigan Association of Blood Banks. 1999.

INVITED LECTURES/PAPERS/SEMINARS:

1. Ductal Carcinoma in Situ of the Breast. Faculty seminars in Pathology. University of Michigan Department of Pathology. November 22, 1999.
2. Controversies in Ductal Carcinoma in Situ of the breast. Breast Care Center Forum. University of Michigan. December 8, 1999.
3. Problem solving in the blood bank. Workshop. Current Topics in Blood Banking. 26th annual symposium. University of Michigan. June 2, 1999.
4. Oberman HA, Goldman EB. Legal aspects of transfusion medicine. Current Topics in Blood Banking. 26th annual University of Michigan. June 3, 1999.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS

1. Wilson T.E., Helvie M.A., Oberman H.A., Joynt L.K. Pure and mixed mucinous carcinoma of the breast: Pathologic basis for differences in mammographic appearance. *Am. J. Radiol.* 1999;165: 285-289.
2. Oberman HA. Developments in pretransfusion testing and compatibility testing. *Transfusion.* 2000;40:134.
3. Oberman HA. Anticoagulation and preservation of stored blood. *Transfusion.* 2000;40:262,
4. Sazama S, DeChristopher PJ, Dodd R, Harrison CR, Oberman HA, et al. Practice parameter for the recognition, management and prevention of adverse consequences of blood transfusion. *Arch Pathol Lab Med.* 2000;124:61-70.

TEXTBOOKS, CHAPTERS IN TEXTBOOKS:

1. The Encyclopedia of Medical Imaging: Breast Imaging. (With Andersson, I. The NICER Institute. Oslo 1999.
2. Fibroadenomas, adenomas, cystosarcomas and hamartomas (Chapter 4). Atlas of Pathology of the Female Breast. Current Medicine. Philadelphia, PA. (in press)

LETTERS TO THE EDITOR:

1. Universal WBC reduction. Thurer RL, Luban NLC, AuBuchon JP, et al. *TRANSFUSION* 2000;40:751-752

**AUGUSTO FELIX G. PAULINO, M.D.
CLINICAL ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

- A. General Surgical Pathology – five months.
- B. Head and Neck Surgical Pathology, Departmental and Outside Consultation Services – 12 months.
- C. Bone and Soft Tissue Surgical Pathology, Departmental and Outside Consultation Services – 12 months.
- D. M-Labs Surgical Pathology Consultation – 12 months

II. TEACHING ACTIVITIES:

- A. Medical Students:
 - 1. M2: Musculoskeletal Sequence – 2 Lectures.
 - 2. M2: Pathology Laboratory
 - 3. M4: Radiology-Pathology Correlation
 - 4. M4: Preceptor for Pathology Elective
- B. House Officers:
 - 1. General Surgical Pathology – 5 months.
 - 2. Head and Neck Surgical Pathology – 12 months as needed.
 - 3. Bone and Soft Tissue Surgical Pathology – 12 months as needed.
 - 4. Consultation Conferences – four.
 - 5. Salivary Gland Pathology Lecture.
 - 6. Bone Pathology Lecture.
 - 7. Elective in Bone and Soft Tissue/Head and Neck Pathology.
- C. Interdepartmental:
 - 1. Pathology Conference for Oral/Maxillofacial Surgery Residents – monthly.
 - 2. Sarcoma Tumor Board – weekly.
 - 3. Pathology Conference for ENT Residents.
 - 4. Pathology Conference for Radiation Oncology Residents.
 - 5. M-Labs Symposium.
 - 6. Pathology Conference –VA Medical Center

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Co-Investigator "Predicting response to therapy and early detection of recurrent oral cancer", TE Carey (Principal Investigator).
- B. Co-Investigator "Phase I trial of gene therapy (using modified Fas ligand with a smooth muscle promoter in an adenoviral vector) in patients with locally-advanced or metastatic leiomyosarcoma or gastrointestinal stromal tumors", LH Baker (Principal Investigator).
- C. Co-Investigator "Phase II evaluation of 6 G/m² of ifosfamide plus doxorubicin and G-CSF in the treatment of poor prognosis soft tissue sarcomas", LH Baker (Principal Investigator).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. House Officer Candidate Interviews.

UNIVERSITY OF MICHIGAN:

- A. Co-chair, Homer H. Stryker Orthopaedic Pathology Conference.

REGIONAL AND NATIONAL:

- A. Member, Head and Neck Task Force, American Joint Committee on Cancer.
- B. Reviewer, Cancer.
- C. Reviewer, Journal of Surgical Oncology.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Paulino AFG, Singh B, Shah JP, Huvos AG. Basaloid squamous cell carcinoma of the head and neck. Laryngoscope (in press).
- 2. Propeck T, Quinn TJ, Jacobson JA, Paulino AFG, Habra G, Darian VB. Sonographic and MR imaging of bifid median nerve with anatomic and histologic correlation. AJR (in press).
- 3. Folpe AL, Goodman ZD, Ishak KG, Paulino AFG, Taboada EM, Meehan SA, Weiss SW. Clean cell myomelanocytic tumor of childhood and young adulthood: a novel member of the perivascular epithelioid clear cell family of tumors. Am J Surg Pathol (in press).
- 4. Snyder ML, Paulino AFG. Pathologic quiz case: an unusual salivary gland tumor. Arch Pathol Lab Med (in press).

5. Dawson LA, Anzai Y, Marsh L, Martel MK, Paulino A, Ship JA, Eisbruch A. Patterns of local-regional recurrence following parotid sparing conformal and segmental intensity modulated radiotherapy for head and neck cancer. *Int J Rad Oncol Biol Phys* 2000;46:1117-1126.
6. Paulino AFG, Singh B, Carew J, Shah JP, Huvos AG. Epstein-Barr virus in squamous carcinoma of the anterior nasal cavity. *Ann Diagn Pathol* 2000;4:1-6.
7. Snyder ML, Paulino AFG. Hybrid carcinoma of the salivary gland: salivary duct adenocarcinoma and adenoid cystic carcinoma. *Histopathol* 1999;35:380-383.

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

1. Propeck T, Quinn TJ, Jacobson JA, Paulino AFG, Habra G, Darian VB. Sonographic and MR imaging of bifid median nerve with anatomic and histologic correlation. Presented at the American Roentgen Ray Society meeting, May 2000.
2. D'Silva N, Polverini P, Paulino A, Hanks T. Malignant melanoma of the oral cavity. Presented at the oral pathology conference, Apr. 2000.
3. Bavikatty NR, Paulino AF. Histologic features fail to predict recurrence in conventional giant cell tumor of bone. Poster at the USCAP meeting, Mar. 2000.
4. Folpe AL, Goodman ZD, Ishak KG, Paulino A, Taboada E, Meehan SA, Weiss SW. Clear cell myomelanocytic tumor of falciform ligament/ligamentum teres in children and young adults. Poster at the USCAP meeting, Mar. 2000.
5. Dawson LA, Yoshimi A, Marsh L, Martel MK, Paulino A, Ship JA, Eisbruch A. Patterns of local-regional recurrence following parotid sparing conformal and segmental intensity modulated radiotherapy for head and neck cancer. Presented at the American Society for Therapeutic Radiology and Oncology meeting, Nov. 1999.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

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 ACTIVITIES:

- A. Principal Investigator, "Mechanisms of pulmonary fibrosis," NIH, RO-1, HL28737, (20% effort). 1996-2001 (years 14-19), (Total direct costs: \$811,365).
- B. Principal Investigator, "Myofibroblasts in pulmonary fibrosis," NIH, RO-1, HL 52285, (25% effort. 1998-2003 (years 06-10), (Total direct costs: \$906,614).
- C. Project Leader, Project III, "Macrophage function in lung injury and fibrosis," (P.A. Ward, Principal Investigator), NIH, PO-1, HL 31963, (25% effort), 1999-2004, (Total direct costs: \$512,859), Project III only.
- D. Co-investigator, Project 1, "Cytokine networks regulating inflammation of pulmonary fibrosis," (G.B. Toews, Principal Investigator), SCOR NIH, P-50 HL 56402, SCOR in Human idiopathic pulmonary fibrosis, Projects I & III (10% effort), 1996-2001, (Total direct costs \$828,155).

PROJECTS UNDER STUDY:

- A. Mechanisms of lung injury and fibrosis.
- B. Cytokine regulation of fibroblast function.
- C. Regulation of the α -smooth muscle actin promoter and gene expression.
- D. Myofibroblast differentiation and its regulation by cytokines.
- E. Cytokine regulation of myofibroblast apoptosis.
- F. Induction of telomerase expression in lung fibrosis.
- G. Role of eosinophils in pulmonary fibrosis.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

- A. Member, Medical Scientist Training Program Operating Committee.
- B. Member, Immunology Program Planning Committee
- C. 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.
- C. Reviewer/site visitor for NIH Program Project and VA grant proposals.

INVITED LECTURES/SEMINARS:

- 1. Invited Speaker "Eosinophils and pulmonary fibrosis", Eosinophils 1999, Lund Sweden, 1999
- 2. Invited Speaker "Cells, cytokines and lung fibrosis", University of California, Davis, CA, 1999
- 3. Invited Speaker/Consultant "Pathophysiology of pulmonary fibrosis", Schering-Plough, NJ, 2000
- 4. Session Chair "Molecular pathogenesis of fibrosis" at the 2000 Experimental Biology 2000 Annual Meeting, San Diego, CA, 2000

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

- 1. Zhang, H., and Phan, S.H.: Inhibition of myofibroblast apoptosis by transforming growth factor β_1 . Am. J. Resp. Cell Molec. Biol. 1999; 21:658-665.

2. Varani, J., Warner, R.L., Gharaee-Kermani, M., **Phan, S.H.**, Kang, S., Chung, J.H., Wang, Z.Q., Datta, S.C., Fisher, G.J., and Voorhees, J.J.: Vitamin A antagonizes decreased cell growth and elevated collagen-degrading matrix metalloproteinases and stimulates collagen accumulation in naturally aged human skin. *J. Invest. Dermatol.* 2000; 114:480-486.
3. Nozaki, Y., Liu, T., Hatano, K., Gharaee-Kermani, M., and Phan, S.H.: Induction of telomerase activity in fibroblasts from bleomycin-injured lungs. *Am. J. Resp. Cell Molec. Biol.* 2000; in press

BOOKS/CHAPTERS IN BOOKS:

1. Phan, S.H., Zhang, K., Zhang, H.Y., Gharaee-Kermani, M.: The myofibroblast as an inflammatory cell in pulmonary fibrosis. *Curr. Topics in Pathol.* 1999; 93:173-82.

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

1. Gharaee-Kermani M, Smith R, Bravo R, Hogaboam C, Kunkel S, **Phan SH**: A role for eotaxin in bleomycin-induced lung fibrosis. *FASEB J.* 2000; 14:A556
2. Gharaee-Kermani M, **Phan SH** and Baker J Jr.: Inhibition of transforming growth factor β 1 and β 2 expression in human and rat lung fibroblasts using antisense oligonucleotides complexed with starburst PAMAM dendrimers. *FASEB J.* 2000; 14:A555
3. Nozaki Y, Ullenbruch M, Roy, S, McGarry B, **Phan SH**: TGF β 1 regulation of α -smooth muscle actin gene expression in rat lung fibroblasts. *Am. J. Resp. Crit. Care Med.* 2000; 161:A750
4. Gharaee-Kermani M, Smith R, Ullenbruch M, McGarry B, Charo I, Lukacs N, Kunkel S, **Phan SH**: C-C chemokine receptor 2 is required for bleomycin-induced pulmonary fibrosis. *Am. J. Resp. Crit. Care Med.* 2000; 161:A750
5. Gharaee-Kermani M, **Phan SH** and Baker J: Specific transforming growth factor β 1 oligonucleotide antisense and starburst PAMAM dendrimers gene therapy in murine model of bleomycin induced pulmonary fibrosis. *Am. J. Resp. Crit. Care Med.* 2000; 161:A827

CARL L. PIERSON, Ph.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000

I. CLINICAL ACTIVITIES:

- A. Director, Clinical Microbiology/Virology Laboratories.
- B. Director, UMHC Saline Health Center Clinical Laboratory
- C. Director, UMHC Ypsilanti Family Practice Health Care Center Clinical Laboratory.
- D. Coordinator, Infectious Disease Microbiology Laboratory Rounds.
- E. Technical Consultant - M-Labs.
- F. New clinical test development, verification and implementation.

II. TEACHING ACTIVITIES:

- A. Instructor, Pathology House Officer Microbiology/Virology Program.
- B. Lecturer, Clinical Pathology Grand Rounds.
- C. Coordinator, Clinical Microbiology/Virology In-service Program.
- D. Instructor, Infectious Disease Laboratory Rounds.
- E. Lecturer, Epidemiology 680, "Hospital Epidemiology"

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. "Trends in Antimicrobial Resistance for Clinical Isolates of *Bacteroides sp.*", Principal Investigator: D. R. Snyderman, New England Medical Center, Boston, Massachusetts.
- B. "The incidence of sexually transmitted diseases among sex workers in Bali", Principal Investigator: Barbara Reed, School of Public Health, University of Michigan.
- C. "Evaluation of novasomes and dendrimers as barrier molecules for the prevention and treatment of infectious disease", Principal Investigator: James Baker, Jr., Dept. of Pathology, University of Michigan.
- D. "A Database Analysis and Retrospective Chart Review to Estimate the Impact of Extended Spectrum Beta Lactamases (ESBL) on Clinical and Economic Outcomes", Principal Investigator: Carl Pierson, Dept. of Pathology, University of Michigan.
- E. "Gatifloxacin Evaluation and Surveillance Study: Protocol 1273-BMS-099E", Principal Investigator: Carl Pierson, Dept. of Pathology, University of Michigan.
- F. "Comparative In Vitro Evaluation of Timentin vs Zosyn against Selected Bacteria", Principal Investigator: Carl Pierson, Dept. of Pathology, University of Michigan.
- G. "Zyvox Antimicrobial Potency Study (ZAPS)", Principal Investigator: Carl Pierson, Dept. of Pathology, University of Michigan.

- H. "In Vitro activity of Moxifloxacin against Clinically Significant Anaerobic Bacteria", Principal Investigator: Carl Pierson, Dept. of Pathology, University of Michigan.
- I. "Sterilization Efficiency of the Avenatech WD 240 Washer-Decontaminator Under In-Use Conditions", Principal Investigator: Carl Pierson, Dept. of Pathology, University of Michigan.
- J. "Susceptibility and Surveillance Study of Antimicrobial Resistance of Common Respiratory Pathogens", a multicenter study.

PROJECTS UNDER STUDY:

- A. Detection of the mecA resistance gene in staphylococci growing in blood culture bottles.
- B. Assessment of the clinical utility of IV Catheter cultures.
- C. Assessment of the efficiency of LE/Nitrate urine screening to reduce urine culture.
- D. Evaluation of microtiter and gradient strip methods for yeast antimicrobial susceptibility.
- E. Assessment of the accuracy of calculated MICs using the BioMIC system.
- F. Use of the Cobas Monitor for the quantitation of CMV in BMT patients.
- G. Identification of septic joint infections using broad-range PCR. Joint project with Dr. Krazan, Dept. of Pediatrics.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Clinical Pathology Laboratory Directors Committee.
- B. Chair, Clinical Microbiology/Virology Senior Staff committee.
- C. Chair, Clinical Microbiology/Virology Advisory Committee.
- D. UMHC Health Care Centers Laboratory Committee.

MEDICAL SCHOOL/HOSPITAL:

- A. Hospital Infection Control Committee.
- B. Antimicrobial Use subcommittee of the Pharmaceutical & Therapeutics Committee.
- C. Hospital Biodisaster Planning Committee

REGIONAL/NATIONAL:

- A. Executive Board, South Central Association for Clinical Microbiology.
- B. Executive Board, Michigan Branch-American Society for Microbiology
- C. Co-Chair, Michigan Microbiology Laboratory Directors Association.

V. OTHER RELEVANT ACTIVITIES:

PROFESSIONAL ORGANIZATIONS:

- A. American Society for Microbiology.
- B. European Congress for Clinical Microbiology and Infectious Diseases.

- C. Infectious Disease Society of America.
- D. South Central Association for Clinical Microbiology.

INVITED LECTURES/ SEMINARS:

1. "Drug Resistance in the Health Care Setting", Infection Control Symposium, Delta College, Saginaw, MI

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Snyderman DR, Jacobus, NV, McDermont, LA, Supran, S, Cuchural, GJ, Gorbach, SL, Hecht, DW, Harrell, H, Pierson, CL, Jenkins, S, Iannini, P, Rihs, J, and Finegold, S: A multicenter study of the in vitro susceptibility of the *Bacteroides fragilis* group, 1995-1996 with comparison of resistance trends from 1990-1996. 1999. Antimicrob. Agents Chemotherapy, 43:2417-2422.
2. Czermak, BJ, Sarma, V., Pierson, CL. Warner, RL Huber-Lang, M, Bess, NM, Schmal, H. Friedl, HP and Ward, PA: Protective effects of C5a blockade in sepsis. 1999; Nature Medicine 5(7):788-792.

BOOKS/ CHAPTERS IN BOOKS:

1. "Antimicrobial susceptibility testing". In Clinical Laboratory Medicine, K.D. McClatchey, ed., Lippincott Williams & Wilkins, 2nd Ed, *in press*

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

1. Cullen K, Young, C and Pierson, C: Evaluation of selective media for the recovery of *Haemophilus influenzae* from respiratory specimens of patients with cystic fibrosis. Abstract No. C112, 100th General Meeting, American Society for Microbiology, 2000, Los Angeles, CA, pg. 123.
2. Lobato, JA, Kolka, J, Hankerd, RE, and Pierson, CL. Relative detection of fecal parasites using a single vial collection system versus a standard 2-vial system. Abstract No. C235, 100th General Meeting, American Society for Microbiology, 2000, Los Angeles, CA, pg. 215.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

A. General Surgical Pathology – 24 weeks

II. TEACHING ACTIVITIES:

A. Graduate students:

1. M2 Pathology Lab – 70 hours

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

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:

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

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

- A. Surgical Pathology coverage of M-Labs cases, including most from the following hospitals/clinical practices:
 - 1. Trillium Community Hospital, Albion, MI;
 - 2. Addison Hospital, Addison, MI;
 - 3. University of Michigan Health Service;
 - 4. Livonia SurgiCenter and other University of Michigan Clinics and satellite sites;
 - 5. 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 Addison Hospital, Addison, MI.
- D. Perform bone marrow aspiration and biopsies at Trillium Hospital, Albion, MI.
- E. Review peripheral smears at Trillium Hospital, Addison Community Hospital and University of Michigan Health Service.
- F. Clinical Pathology consults for M-Labs client hospitals.
- G. Cytopathology: perform FNA services (performance of aspirate/interpretation) at U of M Hospitals and at Trillium Hospital.
Cover PAP smear interpretation and nongyn cytology read-out, one day a week.
Provide coverage for the Cytopathology Service when needed.
- H. Frozen sections at Trillium Hospital and the Livonia Surgical Center (U of M Facility).

II. TEACHING ACTIVITIES:

- A. Sign out M-Labs and University of Michigan autopsies with residents.
- B. Organize and lecture at the M-labs Symposium (15th Symposium in April 2000), 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 one day a week, with residents, fellow and, occasionally with medical students.
- D. In-service teaching to laboratory staff at Albion Community Hospital and the University of Michigan Health Service (UHS).
- E. Monthly colposcopy meetings with the Gyn medical staff at UHS.
- F. Gross Autopsy Conference, 6 hours.

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.
 - a. Marketing activities with potential new clients;
 - b. Contacts with pathologists from client hospitals and others, as part of our support to pathologists; this includes providing occasional coverage;
 - c. Laboratory network activity:
Joint Venture Hospital Laboratory – (JVHL) QA committee, which meets approximately once every three months.
Great Lakes Network – (GLN) Medical Affairs Committee, which meets as needed.
 - d. Coordinating M-Labs QA activities with D. Moss; monthly review of occurrence reports;
- B. Medical Director of the University of Michigan Health Service Laboratory.
- C. Active medical staff member at Trillium Hospital and Addison Community Hospital. Conduct Tissue Review and Transfusion Review meetings. Attend their medical staff meetings.
- D. Intra-departmental meetings (e.g., Cytopathology)

V. OTHER:

- A. Mentorship Program at the University of Michigan – Mentor
- B. Referee for the Hematology Survey, College of American Pathologists (CAP)
- C. Inspector, for the CAP Accreditation Program. Performed two inspections.
- D. 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 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

- A. Director, Autopsy Service.
- B. Director, Electron Microscopy Service
- C. Supervision of Autopsies-12 weeks, signed out 66 autopsies.
- D. Coordinator, Trauma/burn autopsy conference monthly
- E. Coordinator of Senior Staff Autopsy Call Schedule.
- F. Coordinator, Medical Examiner Investigators, University of Michigan
- G. 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. Lecturer, Pathology 600 Course, 1 contact hour
- D. Lecturer, Pathology 580 course (Dental School), 1 contact hour
- E. Pathology 600, Provided written critiques of student autopsy write-ups (167).
- F. Course Director, Pathology 800 Research Seminar Series in Pathology
- G. Lecturer, Pathology 581 Tissue, cellular and Molecular Basis of Disease, 3 contact hours
- H. Laboratory Instructor, Histopathology Laboratory for M1 students, 20 contact hours
- I. Laboratory Instructor Pathology 585, (Medical Illustrators course). 12 contact hours
- J. Laboratory Instructor, Pathology 600 (M2 pathology course), year long
- K. Thesis Committee - Andrew Merry
- L. Directed research of Michael O'Reilly, M.D. (Department of Anesthesiology), Stewart Wang, M.D., Ph.D., Richard Klein, M.D. (Department of Surgery), Susan Stern, M.D., (Department of Emergency Medicine), Grace Su, M.D., (Department of Medicine), Postdoctoral fellows, Samuel Ebong, Ph.D. Doug Call, Ph.D., Jean Nemzek, D.V.M. Jiyoun Kim, Ph.D., Liyu Xin, M.D., Ph.D.
- M. Visiting physician, Steven Kamiza, M.D.
- N. Medical Students – David Newcomb
- O. Graduate Students – Andrew Merry
- P. Undergraduate Students - Emily Beers, Antonia Eliason

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Regulation of gene expression of soluble mediators of inflammation using the following models:
 - 1. Endotoxin-stimulated human whole blood.
 - 2. Endotoxin injection in mice.
 - 3. Cecal ligation and puncture.
 - 4. 2 hit model of acid aspiration induced lung injury
- B. Toxic effects of immunomodulators.
- C. Pathophysiology of septic shock.
- D. Quantitation of mediators in septic shock.
- E. Cloning, sequencing, and expressing cytokines including mTNF, hTNF, mIL-6, hIL-8, mIL-18, mIL-1ra.
- F. Oxidant regulation of chemokine gene expression.
- G. Chemokines in the pathogenesis of murine asthma

SPONSORED SUPPORT:

- A. Principal Investigator, "The Role of Cytokines in Sepsis and Trauma", GM44918 \$906,182, 1990-2000.
- B. Principal Investigator, "Regulation of IL-8 gene expression: four years, GM50401 \$870,822, 1995- 2000.
- C. Principal Investigator, "Chemokines in the Pathogenesis of Asthma", ES09589, project #3, \$1,180,00, 1998 - 2002
- D. Principal Investigator, "Sulfazalazine modulation of cytokine production", Pharmacia-Upjohn, \$76,800, 1998 - 2000.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director - Autopsy Service.
- B. Director, Electron Microscopy Service.
- C. Interviewer - Candidates for faculty, house officer, postdoctoral, and graduate student positions.
- D. Co-ordinator of call schedule, both weekend and weekday, autopsy service.
- E. Coordinator, medical examiner investigator call schedule, University of Michigan

MEDICAL SCHOOL/HOSPITAL:

- A. Member, Medical School Admissions Committee
- B. Member, Biomedical Research Council Undergraduate Research Council

- C. Advisory Committee on, Appointments and Promotions and Tenure, Instructional Tract, 1997 – 2001
- D. Chair, Advisory Committee on, Appointments, Promotions and Tenure, Instruction Tract, 1999 – 2001.
- E. University Committee on Use and Care of Animals, 1997 – 2001
- F. Chair, University Committee on Use and Care of Animals, 1998 - 1999
- G. Reviewer, Biomedical Research Council grants
- H. Member, Strategic Planning Committee, including executive group, 1999 – 2000
- I. Pathology representative to Medical Device Explant Committee
- J. Representative for Pathology to Program in Biomedical Sciences (PIBS) Admissions Committee, 1999 - 2000
- K. Pathology Graduate Program Curriculum Revision Committee, 1999

REGIONAL AND NATIONAL:

- A. Chair, 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, Michigan Coalition on Donation
- E. Publications Committee, International Cytokine Society
- F. Awards Committee, Shock Society
- G. 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. Editorial Board: Journal of Immunology, Associate Editor
- C. Symposium Chair, Experimental Biology 2000, Mediators of Inflammation
- D. Reviewer:
 - 1. Journal of Immunology, reviewed 12 articles.
 - 2. Journal Leukocyte Biology, reviewed 1 article.
 - 3. American Journal of Pathology, reviewed 2 articles.
 - 4. Journal of Clinical Investigation, reviewed 2 articles.
 - 5. Infection and Immunity, reviewed 1 article.
 - 6. Shock, reviewed 20 articles.
 - 7. American Journal of Physiology, reviewed 1 article.
 - 8. Cytokine, reviewed 1 article
 - 9. American Journal of Respiratory Cell and Molecular Biology, reviewed 1 article
 - 10. Journal of American Geriatrics, reviewed 1 article
 - 11. Cellular Immunology, reviewed 1 article
 - 12. Annals of Internal Medicine, reviewed 1 article
 - 13. Grant Reviewer, Swiss Government, reviewed 1 grant
 - 14. Grant Reviewer, VA, reviewed 1 grant

INVITED LECTURES/SEMINARS:

- 1999 Visiting Professor, Beijing Medical University, Institute of Vascular Medicine, Beijing, China, *Reactive oxygen and the regulation of chemokines*
Invited Speaker, Shanghai Institute of Materia Medica, Shanghai, China *Regulation of Cytokine Gene Expression*
Visiting Professor, University of Natal, Durban South Africa, Department of Pathology, *Cytokine regulation by reactive oxygen and reactive nitrogen intermediates.*
Invited presentation, Pioneer High School Health Occupations Class, Ann Arbor, Michigan, *Value of Autopsies in Modern Society*
- 2000 Visiting Professor, Washington University School of Medicine, Department of Surgery, St. Louis, MO, *Sepsis, Nothing Works, But Have We Learned Anything?*
Visiting Professor, Cleveland Clinic Foundation, Department of Immunology Cleveland, Ohio, *Too Much Is Never Enough, The Inflammatory Response to Sepsis*
Invited Speaker, 5th International Congress on the Immune Consequences of Shock, Inflammation, and Sepsis, Munich, West Germany, *Combination Immunotherapy With Soluble Tnf Receptors (Tnf-Sr) Plus Interleukin 1 Receptor Antagonist (Il-1ra) Decreases Sepsis Mortality*

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Nemzek JA, Call DR, Ebong SJ, Newcomb DE, Bolgos GL, Remick DG. Immunopathology of a two-hit murine model of acid aspiration lung injury. *American Journal of Physiology; Lung Cellular and Molecular Physiology* 2000;278:L512-L520
2. Su GL, Klein RD, Aminlari A, Zhang HY, Steinstraesser L, Alarcon WH, Remick DG, Wang SC. Kupffer cell activation by lipopolysaccharide in rats: role for lipopolysaccharide binding protein and toll-like receptor 4. *Hepatology* 2000;31:932-6
3. Cooper PJ, Fekade D, Remick DG, Grint P, Wherry J, Griffin GE. Recombinant human interleukin-10 fails to alter proinflammatory cytokine production or physiologic changes associated with the Jarisch-Herxheimer reaction. *Journal of Infectious Diseases* 2000;181:203-9
4. Remick DG, Newcomb DE, Bolgos GL, Call DR. Comparison of the mortality and inflammatory response of two models of sepsis: lipopolysaccharide vs. cecal ligation and puncture. *Shock* 2000;13:110-6
5. Kronfol Z, Remick DG. Cytokines and the Brain: Implications for Clinical Psychiatry. *Am J Psychiatry* 2000;157:683-694
6. Cooper PJ, Awadzi K, Ottesen EA, Remick D, Nutman TB. Eosinophil sequestration and activation are associated with the onset and severity of systemic adverse reactions following the treatment of onchocerciasis with ivermectin. *Journal of Infectious Diseases* 1999;179:738-42
7. Hennein HA, Kiziltepe U, Barst S, Bocchieri KA, Hossain A, Call DR, Remick DG, Gold JP. Venovenous modified ultrafiltration after cardiopulmonary bypass in children: a prospective randomized study. *Journal of Thoracic & Cardiovascular Surgery* 1999;117:496-505

8. Granger J, Remick D, Call D, Ebong S, Taur A, Williams B, Nauss M, Millican J, O'Reilly M. A sandwich enzyme-linked immunoabsorbent assay for measurement of picogram quantities of murine granulocyte colony-stimulating factor. *Journal of Immunological Methods* 1999;225:145-56
9. Nemzek JA, Newcomb DE, Call DR, Remick DG. Plasma interference in an enzyme-linked immunosorbant assay using a commercial matched antibody pair. *Immunological Investigations* 1999;28:209-21
10. Mercer-Jones MA, Shrotri MS, Peyton JC, Remick DG, Cheadle WG. Neutrophil sequestration in liver and lung is differentially regulated by C-X-C chemokines during experimental peritonitis. *Inflammation* 1999;23:305-319
11. O'Reilly M, Newcomb DE, Remick D. Endotoxin, sepsis, and the primrose path. *Shock* 1999;12:411-420
12. Ebong S, Call D, Nemzek J, Bolgos G, Newcomb D, Remick D. Immunopathologic alterations in murine models of sepsis of increasing severity. *Infection & Immunity* 1999;67:6603-10
13. Mercer-Jones MA, Shrotri MS, Peyton JC, Remick DG, Cheadle WG. Neutrophil sequestration in liver and lung is differentially regulated by C-X-C chemokines during experimental peritonitis. *Inflammation* 1999;23:305-19

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

1. S.Ebong, S.Goyert, J.Nemzek, J.Kim, G.Bolgog, and D.Remick. Immunopathologic Alterations in CD14-Deficient Murine Sepsis *Exp Biol*, San Diego CA 2000
2. J. Nemzek, S.Ebong, G.Bolgog, and D.Remick. Effects of keratinocyte growth factor on acute lung injury in two-hit model *Exp Biol*, San Diego CA 2000
3. D. Remick, Genetic redundancy and the inflammatory response *Exp Biol*, San Diego CA 2000
4. J. Kim, J. Nemzek, S. Ebong, M. O'Reilly, The effect of different anesthetics on LPS induced cytokines in vivo *Exp Biol*, San Diego CA 2000
5. G. Bolgos, S., Ebong, D. Newcomb, J. Nemzek, D. Call, and D. Remick, TNF-SR + IL-1ra therapy improves sepsis survival *Exp Biol*, San Diego CA 2000
6. D. Remick, D. Call, S. Ebong, D. Newcomb, P. Nybom, J. Nemzek, and G. Bolgos, Prolonged Blockade Of Both Tnf And Il-1 Improves Survival Following Cecal Ligation And Puncture, *Shock Society, Snowbird Utah*, 2000
7. A Aminlari, RD Klein, HZ Zhang, D O'Donnell, S Wang, WA Alarcon, L Steinstraesser, SC Wang, DG Remick, GL Su, LPS Binding Protein Augmentation of Kupffer Cell Activation is Mediated by Toll Like Receptor 4. *Am. Assoc. Study of Liver Diseases*, 2000.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999- 30 JUNE 2000**

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).

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.
 - 5. Instructor, hematology portion of clinical pathology rotation, M4 clerkship in general pathology.
- 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. Cutaneous Lymphoma Conference.
 - 5. Clinical Pathology Grand Rounds (one lecture).
 - 6. Clinical Pathology Case Conference/weekly.
 - 7. Adult and Pediatric Hematology/Oncology Fellows Teaching Conference (two lectures).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

None.

PROJECTS UNDER STUDY:

- A. Immunophenotyping in acute and chronic leukemias.
- B. Histopathology, immunophenotyping, and genotyping of possible precursor lesions for lymphoma of mucosa-associated lymphoid tissue.
- C. Histopathology, immunophenotyping, and clinical features of anaplastic large cell lymphoma and mantle cell lymphoma.
- D. Radioimmunotherapy for B-cell lymphoma.

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.
- E. Pathology Department Internal Review Committee.

REGIONAL/NATIONAL:

- A. Pathology reviewer, multicenter study of I¹³¹ anti-B1 radioimmunotherapy for B-cell lymphoma, Coulter Pharmaceutical.
- B. Pathology reviewer, Zenarestat clinical trial, Parke-Davis/Warner Lambert Pharmaceutical.
- C. Hematology Council Member, Commission on Continuing Education, American Society of Clinical Pathologists.
- D. Manuscript Reviewer, American Journal of Pathology.
- E. Manuscript Reviewer, Archives of Pathology and Laboratory Medicine.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

- 1. Lecturer, "Hematologic Coups: A practical approach to challenging cases in hematology diagnosis", American Society of Clinical Pathologists Workshop, February, 2000.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Iravani S, Singleton TP, Ross CW, Schnitzer B. Precursor B lymphoblastic lymphoma presenting as lytic bone lesions. *Am J Clin Pathol* 112:836-843, 1999.
2. Kroft SH, Domiati-Saad R, Finn WG, Dawson B, Schnitzer B, Singleton TP, Ross CW. Precursor B-lymphoblastic transformation of Grade 1 follicle center lymphoma. *Am J Clin Pathol* 113:411-418, 2000.
3. Yang F, Tran T-A, Carlson JA, Hsi ED, Ross CW, Arber DA. Paraffin section immunophenotype of cutaneous and extracutaneous mast cell disease. *Am J Surg Pathol* 24:703-709, 2000.
4. Bavikatty NR, Ross CW, Finn WG, Schnitzer B and Singleton TP. Anti-CD10 immunoperoxidase staining of paraffin-embedded acute leukemias: comparison with flow cytometric immunophenotyping (in press, *Human Pathology*).
5. Skacel M, Ross CW, Hsi ED. Primary malignant lymphoma of the thyroid gland (in press, *Histopathology*).

ARTICLES SUBMITTED FOR PUBLICATION:

1. Finn WG, Singleton TP, Schnitzer B, Ross CW, Stoolman LM. Adhesion molecule expression in CD5-negative, CD10-negative chronic B-cell leukemias: comparison with non-Hodgkin's lymphomas and CD5-positive B-cell chronic lymphocytic leukemia.
2. Kaminski MS, Estes J, Zasadny KR, Francis IR, Ross CW, Tuck M, Regan D, et. al. Radioimmunotherapy with iodine I 131 tositumomab for relapsed or refractory B-cell non-Hodgkin's lymphoma: Updated results and long-term follow-up of the University of Michigan experience.
3. Misick CP, Ross CW, Strawderman MS, Kroft SH, Schnitzer B, Finn WG and Singleton TP. Apoptosis in myelodysplastic syndromes: p53, bcl-x, bcl-2, bax and TdT-Mediated dUTP-Nick End-Labeling.

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

1. Valdez R, Petricek CM, Finn WG, Singleton TP, Ross CW, Schnitzer B: Nodular lymphocyte predominance Hodgkin's disease and diffuse large cell lymphoma, B-cell phenotype. Proceedings of the 2nd Joint Meeting of the SH and EAHP, Tumor Progression in Lymphoma. Barcelona, September, 1999, p.I-16.
2. Kroft SH, Finn WG, Ross CW, Dawson DB, Singleton TP, Schnitzer B: Precursor B-lymphoblastic transformation of low grade follicle center lymphoma. Proceedings of the 2nd Joint Meeting of the SH and EAHP, Tumor Progression in Lymphoma. Barcelona, September, 1999, p. I-19.
3. Schnitzer B, Singleton TP, Ross CW, Sheldon S, Finn WG: Extramedullary myeloid cell tumor of differentiated monocytic cells followed by development of acute myelogenous leukemia, FAB

- M5b. Proceedings of the 2nd Joint Meeting, SH and EAHP, Barcelona, Spain, September 1999, p. I-30.
4. Finn WG, Sheldon S, Ross CW, Singleton TP, Schnitzer B: Philadelphia chromosome-positive acute lymphoblastic leukemia (ALL) arising in the setting of pre-existing B-cell chronic lymphocytic leukemia (CLL). Proceedings of the 2nd Joint Meeting, SH and EAHP, Barcelona, Spain, September 1999, p. II-3.
 5. Petricek C, Ross CW, Graham DM, Singleton TP, Finn WG, Schnitzer B: Grade II nodular sclerosis Hodgkin's disease with progression to lymphocyte depletion. Proceedings of the 2nd Joint Meeting, SH and EAHP, Tumor Progression in Lymphoma. Barcelona, Spain, September 1999, p. III-1.
 6. Petricek CM, Ross CW, Finn WG, Schnitzer B, Singleton TP: Utility of anti-CD117 in the flow cytometric analysis of acute leukemia. *Mod Pathol* 13:160A, 2000.
 7. Finn WG, Singleton TP, Schnitzer B, Ross CW, Stoolman LM: Adhesion molecule expression in CD5 negative (-), CD10 negative chronic B-cell leukemias. *Mod Pathol* 13:148A, 2000.
 8. Nangia R, Kroft SH, Singleton TP, Ross CW, Finn WG, Schnitzer B: Splenic morphology in small B-cell lymphoproliferative disorders (SBL): A study of 48 well-characterized cases.. *Mod Pathol* 13:158A, 2000.
 9. Nangia R, Singleton TP, Ross CW, Finn WG, Padmore RF, Schnitzer B: Follicular Hodgkin's lymphoma (FHL): A clinico-pathologic study. *Mod Pathol* 13:158A, 2000.
 10. Valdez R, Finn WG, Ross CW, Singleton TP, Tworek JA, Schnitzer B: Extranodal marginal zone B-cell lymphoma associated with Waldenstrom's macroglobulinemia. *Mod Pathol* 13:165A, 2000.
 11. Uherova P, Singleton TP, Ross CW, Schnitzer B, Finn WG: The clinical significance of CD10 antigen expression in diffuse large B-cell lymphoma. *Mod Pathol* 13:165A, 2000; 82:165A.
 12. Ross CW. Flow cytometric assay of neutrophil oxidative burst. *Mlabs Spectrum* 13(3):1-2, July 1999.

MARK A. RUBIN, M.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000

I. CLINICAL ACTIVITIES:

- A. Room #1 and 2 sign out, every 4-5 weeks, twelve months
- B. Bladder, prostate kidney, testicular and urinary bladder surgical consultation cases, intra and extra mural, daily, twelve months.
- C. Genitourinary Transfer Cases, daily, twelve months.
- D. GU fellow training, daily, twelve months
- E. Participation in Urology Tumor Board and Grand Rounds, biweekly, twelve months
- F. Ad hoc urologic pathology consultant for Urology, twelve months
- G. Rapid autopsies for men with advanced prostate tumors, 24/7 availability, twelve months

II. TEACHING ACTIVITIES:

- A. 1996-present Anatomic Pathology Journal Club
- B. 1995-present Second Year Medical School Pathology lectures (4 hours)
- C. 1998-present Urology resident pathology lectures (Monthly)
- D. 1998-present Forth Year Med. Student GU Radiology-Pathology Series (2 days)
- E. 1996-present Mentor medical and undergraduate students in research projects

III. RESEARCH ACTIVITIES:

- A. Development and Validation of Tissue Microarrays for Research, twelve months
- B. PI for Prostate Cancer SPORE Tissue Core and Blood/Serum Bank
- C. Translational projects in the field of prostate, bladder, and renal carcinoma
- D. Development of image oriented database for TMA
- E. Supervise translational research projects with Pathology and Urology residents

SPONSORED SUPPORT:

- A. Co-Investigator - P50 CA69568 - 08/01/00-07/31/01 - NIH - \$107,972 - 30% Effort
Tissue and Serum Core Resource for Prostate Cancer (Prostate SPORE grant)
- B. Co-Investigator - 5P30 CA46952 - -06/00-05/01 - NIH - \$64,850 - 10% Effort
Histopathology/Immunohistochemistry Core
- C. Project Director - MUNN Idea Award - 9/01/99-8/31/00 - \$10,000 - 0% Effort
Molecular Profiling to Distinguish Flat Urothelial Carcinoma in situ from Reactive
changes following BCG Therapy
- D. Principal Investigator - 99-3397 - 5/31/00-5/31/01 - NIH/NCI - \$236,859 - 20% Effort

- Development of Tissue Microarray Technology for the Prostate SPORE
- E. Principal Investigator- CA69568- 4/1/00-3/31/01-NIH/NCI-\$104,933- 10% Effort
Development of High-Density Tissue Microarray to Evaluate Prostate Cancer in African American Men: a collaboration with the departments of pathology and urology of Harlem Hospital (NY,NY)
 - F. Principal Investigator- 8/1/00-7/31/01-NIH/NCI -\$45,000- 10% Effort
Gene Expression Profile Analysis of Human Prostate Cancer Progression by Use of Laser Capture Microdissection and cDNA Expression Arrays.
 - G. Principal Investigator- 04/01/00 – 03/31/01-Genentech, Inc,- \$70,000-0% Effort
Biological Samples from Patients with Prostate Carcinoma and Development of TMA
 - H. Co-Investigator-R01CA79596-01A1- 07/01/99 – 06/30/04- NIH/NCI- \$186,666-5% Effort - Genetic Analysis of Hereditary Prostate Cancer Families.
 - I. Co-Investigator- R01CA82419- 04/01/00 – 03/31/04- NIH/NCI- \$157,000- 5% Effort
Modulating Tolerance for Prostate Cancer Antigen Vaccines.
 - J. Co-Investigator-CA69568-8/01/00 - 7/31/01-NCI/NIH \$70,000- 5% Effort
Prostate Elasticity Imaging - A New Technology for Early Detection and Monitoring of Prostate Pathology

PENDING SUPPORT:

- A. Co- Investigator- 99-070 - 7/01/00-6/30/02-NIH/NCI - 5% Effort - Quick Trials for Prostate Cancer Therapy.
- B. Co- Investigator- 7/01/01-6/30/04-DOD- 5% Effort - Role of the Human Polyomavirus, BKV, in Prostate Cancer

ONGOING RESEARCH:

- A. Molecular alterations associated with flat carcinoma in-situ and atypia of the bladder following BCG treatment. (Funded – Munn Award).
- B. Development and validation of tissue microarray for use in evaluating biomarkers: Inter-S.P.O.R.E. collaboration with Johns Hopkins and Baylor (Funded- S.P.O.R.E. supplement).
- C. Identification of HPV in men with penile carcinoma: collaborative study with Dr. W. Quint (Delft Holland), Dr. A. Cubillia (Paraguay), G. Ayalla (Baylor), and E Pirog (Cornell Medical School). (Funded through private sources.)
- D. Characterization of prostate carcinoma in African American men from the Harlem Hospital in New York city (Funded through the Office for Minority Research at the NCI/NIH).
- E. Characterization of E-Cadherin in prostate carcinoma
- F. Gene profiling of early neoplastic alterations in the prostate by cDNA expression arrays (Funded through SPORE Faculty Development Award)

IV. ADMINISTRATIVE ACTIVITIES:

- A. Director of Immunohistochemistry/Histology Cancer Center Core laboratory
- B. Director Prostate SPORE Tissue Core and Tissue Microarray Facility
- C. Prostate SPORE operating committee

MEMBERSHIPS AND OFFICES IN PROFESSIONAL SOCIETIES:

- A. 1996-present University of Michigan Comprehensive Cancer Center.
- B. 1996-present United States and Canadian Academy of Pathology.
- C. 1996-present New York Pathological Society.
- D. 1996-present International Urologic Pathology Society
- E. 1991-present Arztekammer Berlin (Germany).
- F. 2000-present SBUR (Society for Basic Urologic Research)

DEPARTMENTAL:

Director of Urologic Pathology Subdivision
GU Pathology Fellowship Supervisor
Faculty advisor for AP Journal club

MEDICAL SCHOOL/HOSPITAL:

- A. G.U. module for second year pathology course.
- B. Clinical Pathologic correlation course with Radiology (4th year).
- C. Co-Director for Tissue Core of the Comprehensive Cancer Center

REGIONAL AND NATIONAL:

- A. Editorial Board for Advances in Anatomic Pathology
- B. Ad Hoc Reviewer for American Journal of Pathology, Cancer Research, Urology, and Modern Pathology
- C. USCAP Abstract Review Board (2000-2003)-Genitourinary Section
- D. NCI working Group Participant (Advisor) on Tissue Microarrays – December 16 1999
- E. NCI/Special Emphasis Panel – RFACA99-012, Cooperative Prostate Cancer Tissue Resource – 12/3/99
- F. Department of Defense Prostate Cancer Molecular Biology Study Section, July 6-8, 2000

EXTRAMURAL INVITED PRESENTATIONS:

1. “WHO/ISUP Urothelial Lesions, 1999” Veterans Administration Hospital – Ann Arbor, MI on 4/12/99.
2. “Classification of Bladder Tumors” Thirteenth MLabs Symposium – Ann Arbor, MI on 5/15/99.
3. “Review of Gleason’s Grading for Prostate Cancer” Thirteenth MLabs Symposium – Ann Arbor, MI on 5/15/99.

4. "Potential use of tissue microarrays for large Network/Clinical trial studies: The Prostate S.P.O.R.E experience.," NCI/NIH working group meeting on tissue microarrays – Rockville, MD on December 16, 1999
5. "High-Density Tissue microarrays-The University of Michigan Prostate SPORE experience", 8th SPORE Investigators Workshop, Chantilly, Va., July 9-10, 2000
6. "Interpretation of Prostate Needle Biopsies with Carcinoma", ARTP (French Urologic Society) 9th Scientific Meeting, Paris, France, September 28, 2000.

V. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Mindel JS, Rubin MA, and Kharlamb AB: The Pupil Response to E-10 Hydroxynortriptyline in Rabbits with ocular sympathetic Paresis. *Journal of the Autonomic Nervous System* 1990, Vol. 30, 175-178.
2. Bonilla FA, Zaghouani H, Rubin MA, and Bona C: Vk Gene Usage, Idiotype Expression, and Antigen Binding among Clones Expressing the VHx24 Gene Family Derived from Naive And Anti-Idiotype Immune Balb/c Mice. *Journal of Immunology* 1990, Vol. 145, 616-622, No. 2.
3. Rubin MA, Snell JA, Tazelaar HD, Lack EE, Austenfeld JL, and Azumi N: Cardiac Papillary Fibroelastoma: An Immunohistochemical investigation and unusual clinical manifestations. *Modern Pathology* 1995, 8 (4): 402-407.
4. Staiman VR, O'Toole KM, Rubin MA, Lowe FC: Giant Malignant Fibrous Histiocytoma of the Testis/Spermatic Cord: Psychologic and Possible Etiologic Complications of Unethical Nazi Medical Experimentation. *Urology* 1996, 48 (6): 939-943.
5. Tsang P, Isreal H, Rubin MA: Oral Condyloma Acuminatum Associated with Human Papillomavirus and p53 Overexpression Mimicking Cyclosporin Effect in Transplant Patient. *Arch Pathol Lab Med*, 1996, 120:1129-1132.
6. Katz AE, de Vries GM, Benson MC, Buttyan RE, O'Toole K, Rubin MA, Stifelman M, Olsson CA. The Role of the Reverse-Transcriptase Polymerase Chain Reaction Assay for prostate-specific Antigen in the Selection of Patients for Radical Prostatectomies. *Urologic Clinics of North America* 1996, 23 (4): 541-550.
7. Zhang X, Chen MW, Ng A, Ng PY, Lee C., Rubin MA., Olsson CA, Buttyan R. Abnormal prostate development in C3 (1)-bcl-2 transgenic mice. *Prostate* 1997, 32(1): 16-26.
8. Ennis RD, Katz AE, de Vries GM, Heitjan DF, O'Toole KM, Rubin MA, Buttyan R, Benson MC, Schiff PB Detection of Circulating Prostate Cancer Cells via an Enhanced Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) Assay in Patients with Early Stage Prostate Cancer: Independence from other Pre-Treatment Characteristics. *Cancer* 1997, 79 (12): 2402-2408.
9. Rubin MA, Freter C, Cossman J, Azumi N. Case Report: Intravascular large cell lymphoma coexisting in hemangiomas of the skin. *Am. J Surg. Pathol* 1997, 21 (7): 860-864.
10. Rubin MA, Fang M, Stifelman MD, de Vries G, Buttyan R, Benson MC, Katz AE, Olsson CA, O'Toole K. Enhanced Reverse Transcriptase-PCR for Prostate Specific Antigen Combined with Needle Biopsy Results: A Superior Predictor of pT3 Disease. *Molecular Diagnosis* 1997, 2 (2): 135-145.

11. Han EK, Rubin MA, Lim, T., Arber N, Xing WQ, Weinstein IB. Cyclin D1 Expression in Human Prostate Carcinoma Cell Lines and Primary Tumors. *Prostate* 1998, 35(2): 95-101.
12. Rubin M.A., Parry JP, Singh B. Kaposi's Sarcoma-Associated Herpesvirus DNA Sequences: Lack of Expression in Prostatic Tissue of HIV-Negative Immunocompetent Men. *J Urology* 1998 (1): 146-148.
13. Ennis RD, Bozena KM, Rescigno J, Whitman AE, Heitjan DF, O'Toole KM, Rubin MA, Schiff PB Biologic Classification as an alternative to Anatomic Staging for Clinically Localized Prostate Cancer: A Proposal based on Patients Treated with External Beam Radiotherapy. *Urology* 1998, 51:265-270.
14. Ennis RD, Bozena KM, Heitjan DF, Rubin MA , O'Toole KM, Schiff PB Changes in Biochemical Disease-Free Survival Rates as a Result of Adoption of the Consensus Conference Definition in Patients with Clinically Localized Prostate Cancer Treated with External-Beam Radiotherapy. *Int J Radiation Oncology Biol Phys* 1998, 41: 511-517.
15. Rubin MA, de La Taille A, Bagiella E, Olsson CA, O'Toole KM. Cribriform Carcinoma of the Prostate and Cribriform Prostatic Intraepithelial Neoplasia: Incidence and Clinical Implications. *Am. J Surg. Pathol* 1998, 22 (7): 840-848.
16. Liu QY, Rubin MA, Omene C, Llederman S, Stein CA: Fas Ligand is Constitutively Secreted by Prostate Cancer Cells in Vitro. *Clin Cancer Res* 1998, 4 (7): 1803-1811
17. de la Taille A*, Rubin MA*, Bagiella E, Olsson CA, Buttyan RE, Burchardt T.O'Toole KM, Katz A: Can Perineural Invasion on Prostate Predict PSA Recurrence after Radical Prostatectomy? *J of Urology* 1999, 162(1): 103-6.
18. Rubin MA. Distinct Altered Patterns of p27KIP1 Gene Expression in Benign Prostatic hyperplasia and Prostatic Carcinoma. *NCI* 1999, 91(1): 91. [Letter].
19. Nastiuk KL, Mansukhani M, Kularatne,P, Rubin MA, Melamed J, Ittmann M, Krolewski JJ Common Mutations in BRCA1 and BRCA2 Do Not Increase The Relative Risk of Prostate Cancer in Young Jewish Men. *Prostate* 1999, 40(3): 172-7.
20. Shabisgh A, Tanji N, D'Agati V, Burchardt M, Rubin MA, Goluboff ET, Heitjan D, Kiss A: Early effects of castration on the vascular system of the rat ventral prostate gland. *Endocrinology* 1999, 140(4): 1920-6.
21. Rubin MA, Buyyouonouski M, Bagiella E, et al. Microvessel density in prostate cancer: lack of correlation with tumor grade, pathologic stage, and clinical outcome. *Urology* 1999; 53(3): 542-7.
22. Tickoo SK, Reuter VE, Amin MB, Srigley JR, Epstein JI, Min KW, Rubin MA, Ro JY: Renal Oncocytosis: A Morphologic Study of 14 cases. *AJSP* 1999 23(9): 1094-101.
23. Kambham N, Taylor JA, Troxel A, Rubin MA. Atypical Small Acinar Proliferation in Prostate Needle Biopsies. *J of Urologic Path* 1999 (10):177-187.
24. McKiernan JM, Buttyan R, Bander NH, de la Taille A, Stifelman MD, Emanuel ER, Bagiella E, Rubin MA, Katz AE, Olsson CA, Sawczuk IS: The Detection of Renal Carcinoma Cells in the Peripheral Blood with an Enhanced Reverse Transcriptase-polymerase Chain Reaction Assay for MN/CA9. *1999 Cancer* 1999 86(3)492-7.
25. de la Taille A, Katz A, Bagiella E, Olsson CA, O'Toole KM, Rubin MA: Perineural Invasion on Prostate Needle Biopsy: An Independent Predictor of Final Pathologic Stage. 1999. *Urology* 54(6): 1039-43
26. Vallorosi CJ, Day KC, Zhao X, Rashid MG Rubin MA Johnson KR, Wheelock MJ, Day ML. Truncation of the Beta-catenin Binding Domain of E-cadherin Precedes Epithelial Apoptosis During Prostate and Mammary Involution. *2000 J.B. Chem.* 275(5) 3328.

27. Rubin MA, Putzi M, Mucci N, Smith DC, Wojno K, Korenchuk S, Pienta K. Hormone Refractory Prostate Cancer: Rapid (“Warm”) Autopsy Study for Procurement of Metastatic Prostate Cancer. *Clin Cancer Res.* 2000 (6) 1038-1045
28. Mucci NR, Akdas G, Manely S, Rubin MA. Neuroendocrine Expression in Metastatic Prostate Cancer: Evaluation of High Throughput Tissue Microarrays to Detect Heterogeneous Protein Expression. *Human Path.* 2000 31(4) 406-414
29. Rubin MA, Gerstein A, Reid K, Bostwick DG, Cheng L, Parsons R, Papadopoulos N. 10q23.3 Loss of Heterozygosity is Higher in Lymph Node-Positive (pT2-3,N+) versus Lymph Node-Negative (pT2-3,N0) Prostate Cancer. *Human Path.* 2000 31(4) 504-508.
30. Rubin MA, Bassily N, Sanda M, Montie J, Strawderman MS, Wojno K: Relationship and Significance of Greatest Percentage of Tumor and Perineural Invasion on Needle Biopsy in Prostatic Adenocarcinoma. 2000 *AJSP* 24(2): 183-189.
31. Bassily N, Vallorosi CJ, Akdas G, Montie JE, Rubin MA: Coordinate Expression of Cytokeratins 7 and 20 in Prostate Adenocarcinoma and Bladder Urothelial Carcinoma. 2000 *AJCP* (113) 383-388.
32. Perrone EE, Theoharis C, Mucci NR, Cooney KA, and Rubin MA. Prostate Cancer Tumor Proliferation in African-American and White Men using High Density Tissue Microarray Technology. *JNCI* 2000 Vol. 92 (11) 3-5
33. Marcovish R, Wojno K, Wei JT, Rubin MA, Montie JE, Sanda MG: Bladder Neck Sparing Modification of Radical Prostatectomy Adversely Affects Surgical Margins in Pathologic T3a Prostate Cancer. In press *Urology*.
34. de la Taille A*, Rubin MA*, Olsson CA, Buttyan R., Bagiella E, Burchardt M, Katz AE. "Is Microvascular Invasion On Radical Prostatectomy Specimens A Useful Predictor Of PSA Recurrence For Prostate Cancer Patients?" In Press. *European Urology*
35. Zhang X, Lee C, Ng PY, Rubin MA, Shabsigh A, Buttyan R. Prostatic Neoplasia in Transgenic Mice with Prostate-directed Overexpression of the C-myc Oncoprotein. In press – *Prostate*.
36. Mucci NR, Rubin MA, Strawderman MS, Montie JE, Smith DC, Pienta KJ. Validation of Proliferation Index, p53, and bcl-2 Surrogate Endpoint Biomarkers for Prostate Cancer chemoprevention.. In Press. *JNCI*.
37. Hollenbeck BK, Bassily N, Wei JT, Montie JE, Hayasaka S, Taylor JMG, Rubin MA. Whole-Mounted Radical Prostatectomy Specimens Do Not Increase Detection of Adverse Pathologic Features: In press. *J Urology*.
38. Shah R, Bassily N, Wei J, Mucci N, Montie J, Sanda M, Rubin MA. Benign Prostatic Glands at Surgical Margins of Radical Prostatectomies: Frequency and Associated Risk Factors. In Press. *Urology*.
39. Rubin MA, Dunn R, Kambham N, Misick CP, O’Toole KM: Should a Gleason score be assigned to a minute focus of carcinoma on prostate biopsy? In press *AJSP*
40. Gerstein A, Zhao G, Almeida TA, Chess E, Shis IM, Isaacs, J, Buhler K, Pienta K, Rubin MA, Vessela R, Papadopoulos N. B-catenin, APC & hTRCP1 Alterations in Human Prostate Cancers. Accepted pending revisions. *Nature Medicine*.
41. Tewari A, El-Galley R, Issa M, Stricker H, Peabody J, PowSang J, Shukla A, Wajzman Z, Rubin M, Wei J, Montie J, Demers R, Johnson CC, Lameratto L, Shetty S, Farah R, Narayan P, Carlson G, Menon M. Genetic Adaptive Neural Network Model to Predict PSA Progression Following Radical Prostatectomy: A Multi Institutional Study. Submitted for publication

42. Nelson C*, Rubin MA*, Strawderman M, Montie JE, Sanda MG. Pre-Operative Parameters for Predicting Early Prostate Cancer Recurrence Following Radical Prostatectomy. Submitted for publication.
43. Chaib H, Rubin MA, Mucci NR, Li L, Taylor JMG, Rhim JS, Macoska JA. Activated in Prostate Cancer (AIPC): A PDZ Domain-Containing Protein Highly Expressed in Human Primary Prostate Tumors. Submitted for publication

*Equal Contribution

ABSTRACTS:

1. Azumi N, Rubin MA, Boyle L and Hartman D. Desmin, muscle specific actin, and alpha-smooth muscle actin expression In non-muscular sarcomas and sarcoma-like lesions. *Modern Pathol* 7:A3, 1994.
2. Rubin MA, Fang, M, Katz AE, Stifelman MD, de Vries GM, Benson MC: Enhanced reverse transcriptase-PCR for prostate specific antigen combined with needle biopsy results: a strong indicator of extraprostatic disease. *Modern Pathol* 9:A466, 1996.
3. Rubin MA, Ambinder R, Mann RB and Borowitz MJ. Histologic features fail to predict outcome in mantle cell lymphoma (MCL). *Modern Pathol* 9(1): A708, 1996.
4. Rubin MA, Katz AE, de Vries, GM, Benson MC, O'Toole K and Olsson CA. Enhanced RT-PCR for PSA: strong correlation with PSA-failure. *Pathol International* 46:A808, 1996.
5. Rubin MA. Intraductal prostate adenocarcinoma: strong correlation with aggressive clinical course. *Modern Pathol* 10:A503, 1997.
6. Rubin MA, Buyyounouski M, Katz AE, Olsson CA and Ennis RD. Microvessel density in prostate cancer: lack of correlation with tumor grade, pathologic stage, and clinical outcome. *Modern Pathol* 11:A540, 1998.
7. Rubin MA, Reid KA, Wang SI, Lequesne E, Olsson CA and Parsons R. *PTEN*, a putative prostate tumor suppressor gene: loss of heterozygosity in localized prostate cancer. *Modern Pathol* 11:A539, 1998.
8. Kambham N, Taylor JA and Rubin MA. Atypical small acinar proliferation: cop-out or clinically significant diagnostic category. *Modern Pathol* 11:A496, 1998
9. Tickoo SK, Reuter VE, Amin MB, Srigley JR, Epstein JE, Min KW, Rubin MA. Renal Oncocytosis: Morphology spectrum and morphogenetic considerations. *Modern Pathol* 11:A558, 1998.
10. Rubin MA, Reid K, Gerstein A, and Papadopoulos N. Laser Capture Microdissection of Achiral Prostatic: Adenocarcinoma for PCR Analysis. *US&C Academy of Path.* Mar.20-26,1999 Pg. 105A.
11. Vallorosi CJ, Bassily NH, Akdas G, Montie JE, & Rubin M, Ann Arbor, MI. Coordinate expression of cytokeratins 7 & 20 in Prostate adenocarcinoma and bladder urothelial carcinoma. 1999, AUA
12. Rubin MA, Reid KA, Gerstein A, Bostwick, L Cheng and Papadopoulos N. *PTEN*, A putative Prostate Tumor Suppressor Gene. *US&C Academy of Path.* Mar.20-26,1999:Pg. 106A.
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14. Rubin MA, Strawderman M, Bassily N, Williams JF, Sandra M, & Montie JE, Ann Arbor, MI. Prostate Cancer Staging: Evaluation of nomogram predicting unfavorable pathology. 1999, AUA.
15. Bassily NH, Montie JE, Pienta KJ, & Rubin MA, Ann Arbor, MI. Significance of Gleason pattern 4 as an independent prognostic indicator of postoperative PSA failure in prostatic adenocarcinoma. 1999, AUA.
16. Rubin M, De La Taille A, Olsson CA, Bagiella E, Sharir S, Burchardt T, Cao Y, & Katz AE, New York, NY. Microvessel Density as a predictor of PSA recurrence after radical prostatectomy: Comparison of CD-31 or CD-34 staining. 1999, AUA.
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18. Sandra MG, Wei JT, Nelson CP, Montie JE, Rubin MA. Favorable Clinical progression-free Survival after Radical Prostatectomy Based on Pre-Operative Parameters: A Framework for Counseling Patients. AUA, 1999
19. Bassily NH, Mucci NR, Proverbs-Singh T, Rubin MA. Use of High Throughput Tissue Microarray Technology to Evaluate Biomarkers for Prostate Cancer. USACAP, 2000.
20. Mucci NR, Proverbs-Singh T, Pienta KJ, Rubin MA. Prostrate Cancer Xenograft Profiling. USACAP 2000. Day ML, Vallorosi CJ, Rashid M, Day KC, Zhao X, Shah R, Amin A, Macoska J Rubin MA. E-cadherin Down Regulation in Prostate Carcinoma through Post Translational Protein Truncation. USACAP, 2000.
21. Shah R, Mucci NR, Pelok GD, Macoska J, Rubin MA. Proliferative Inflammatory Atrophy in Prostate Cancer: Implications as a Potential Neoplastic Precursor. USACAP, 2000.
22. Bassily NH, Mucci NR, Rubin MA. Preoperative Predictors of Gleason Pattern 4/5 Prostatic Adenocarcinoma in Radical Prostatectomies. USACAP, 2000.
23. Rubin MA, Theoharis C, Perrone EE, Mucci NR, Cooney KA. Prostrate Cancer Tumor Proliferation in African American and Caucasian Men using High Density Tissue Microarray Technology. USACAP, 2000.
24. Zhou M, Rubin MA. Prevalence and Location of Peripheral Nerve found on Prostate Needle Biopsy. USACAP, 2000.
25. Rubin MA, Kleter B, Zhou M, Ayala G, Cubilla AL, Quint WGV, Pirog EC. Detection of Human Papillomaviruses (HPV) in Penile Condyloma Dysplasia and Invasive Carcinomas using a Novel Line Probe Assay for Rapid Detection and Simultaneous Identification of 25 Different HPV types. USACAP, 2000.
26. Mucci NR, Strawderman M, Durka-Pelok G, Keyoumars F., Rubin MA, Pienta KJ. Validation of a Proliferation Index Surrogate Endpoint Biomarker for Prostate Cancer Chemoprevention. USACAP, 2000.
27. Chaib H, Rubin MA, Rhim JS, Macoska JA. Expression of the DIPC1 Gene is Downregulated in Human Prostate Tumors. AAC, 2000 (4751).
28. Chaib H, Rubin MA, Mucci NR, Rhim JS, Macoska JA. Isolation and Characterization of AIPC: A PDZ domain-containing Protein Highly Expressed in Human Primary Prostate Tumors. AAC, 2000 (2020).
29. Zhao X, Rubin MA, Hayward SW, Cunha GR, Day ML. Use of Tissue Recombination Technology to Study the Deletion of Retinoblastoma Gene in Prostate Tumorigenesis. AAC, 2000 (3585).

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31. Yoshida BA, Chekmareva MA, Dubauskas Z, Rubin MA, Yang X, Stadler W, Rinker-Schaeffer CW. MKK4/SEK1, A Putative Prostate Cancer Metastasis Suppressor Gene (MSG) Regulates Micrometastatic Growth. *AAC*, 2000 (4536).
32. Day KC, Vallorosi C, Zhao X, Rashid MG, Rubin MA, Day ML. Truncation of the Catenin Binding Domain of E-Cadherin Precedes Apoptosis of Mammary Epithelium. *AAC*, 2000 (1543).
33. Seifman BD, Williams AL, Rubin MA, Wolf, Jr. JS, The Functional Effects of Unilateral Endoscopic Laser Papillectomy. *AUA 2000* (1036).
34. Chaib H, Rubin MA, Mucci NR, Rhim JS, Macoska JA. Isolation and characterization of AIPC, a PDZ Domain – Containing Protein Highly Expressed in Human Primary Prostate Tumors. *AUA 2000* (140).
35. Rubin MA, Kleter B, Zhou M, Ayala G, Cubilla A, Quint WGV, Pirog EC. Detection of Human Papillomaviruses (HPV) in Penile Condyloma Dysplasia and Invasive Carcinomas using a Novel Line Probe Assay for Rapid Detection and Simultaneous Identification of 25 Different HPV Types. *AUA 2000* (630).
36. Issa M, El-Galley R, Narayan P, Wajsman Z, Shukla A, Po-Sang J, Rubin MA, Wei J, Montie J, Carson G, Stricker H, et al. Genetic Adaptive Neural Network Model to Predict PSA Progression Following Radical Prostatectomy: A Multi-Institutional Study. *AUA 2000* (847).
37. Williams AL, Marcovich R, Seifman BD, Rubin MA, Wolf, Jr. JS. Comparison of 2-Octyl Cyanoacrylate Adhesive, Fibrin Glue and Suturing for Wound Closure in the Porcine Urinary Tract. *AUA 2000* (31).
38. Rashid MG, Vallorosi CH, Sanda MG, Zhao X, Rubin MA, Montie JE, Day ML. Cleavage of E-Cadherin and its Association in Localized and Metastatic Prostate Cancer. *AUA 2000* (160).

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

- A. Director, Hematopathology
- 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 Southwest Oncology Group (SWOG) cases (circa 150/year).
- G. 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 and lymphomas.

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. Southwest Oncology Group
 - 1. Lymphoma Subcommittee.
 - 2. Leukemia Subcommittee.
- C. Children's Cancer Study Group: Review of in-house cases of lymphoma cases.
- D. Regional Center Review Pathologist, Southwest Oncology Group.
- E. Member, Review Panel for Lymphomas, Southwest Oncology Group.
- F. Member, Hematology Council, American Society of Clinical Pathologists.
- G. Member, Hematology Workshop Review Committee, American Society of Clinical Pathologists.
- H. Member, Quality Management Hematopathology Expert Review Panel, American Society of Clinical Pathologists.
- I. Bylaws Committee, Society for Hematopathology.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARD:

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

INVITED LECTURES/SEMINARS:

- 1. Schnitzer, B: Videomicroscopy Workshop, "Interesting Lymphoid Lesions," ASCP Workshop, New Orleans, LA, September, 1999.
- 2. Schnitzer, B: Hodgkin's Disease: A Practical Approach to Diagnosis and Differential Diagnosis, ASCP Workshop, New Orleans, LA, October, 1999.
- 3. "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, Vancouver, BC, October, 1999.
- 4. Schnitzer, B: "Lymphoma Classifications." Central Ohio Society of Pathologists, Columbus, OH, December, 1999.
- 5. "Reactive Lymphadenopathies," Tutorial on Neoplastic Hematopathology, Department of Laboratory Medicine and Pathology, Cornell University, Miami, Florida, February, 2000.

6. Schnitzer, B., Ross, CW and Singleton, T: "Hematologic Coups," ASCP Workshop, Las Vegas, NV, February, 2000.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Irvani S, Singleton TP, Ross CW, Schnitzer B: Precursor B-lymphoblastic lymphoma presenting as lytic bone lesions. *Am J Clin Pathol* 112:836-843, 1999.
2. Kroft SH, Finn WG, Schnitzer B, Dawson DB, Singleton TP, Ross CW: Precursor B-lymphoblastic transformation of grade I follicle center lymphoma. *Am J Clin Pathol* 113:411-418, 2000.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Grogan TM, Unger J, Miller TP, Kjeldsberg C, Tubbs R, LeBlanc M, Braziel R, Foucar K, Leith C, Spier C, Slovak ML, Nelson MA, Arber DA, Gulley M, Nathwani B, Schnitzer B, Fisher RI: The Hodgkin's-like and classic variants of anaplastic large cell lymphoma: A Southwest Oncology Group analysis: *Blood*. In Press.
2. Bavikatty NR, Ross CW, Finn WG, Schnitzer B, Singleton TP: CD10 detection in acute leukemia by immunohistochemistry in paraffin sections. *Human Pathol*. In Press.
3. Izbán KF, Ergin M, Huang Q, Qin J, Martinez RL, Schnitzer B, Ni H, Nickoloff BJ, Alkan S: Decreased NF- κ B expression by ubiquitin proteasome inhibition results in caspase-independent apoptosis in cultured Hodgkin and Reed-Sternberg cells.

BOOKS AND CHAPTERS IN BOOKS:

1. Reactive Lymphadenopathies. In: Knowles, D. (ed). *Neoplastic Hematopathology*, 2nd Ed. Williams & Wilkins, 2000.

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

1. Valdez R, Petricek CM, Finn WG, Singleton TP, Ross CW, Schnitzer B: Nodular lymphocyte predominance Hodgkin's disease and diffuse large cell lymphoma, B-cell phenotype. Proceedings of the 2nd Joint Meeting of the SH and EAP, Tumor Progression in Lymphoma. Barcelona, September, 1999. P. 1-16.
2. Kroft SH, Finn WG, Ross CW, Dawson DB, Singleton TP, Schnitzer B: Precursor B-lymphoblastic transformation of low grade follicle center lymphoma. Proceedings of the 2nd Joint Meeting of the SH and EAP, Tumor Progression in Lymphoma. Barcelona, September, 1999. P. 1-19.
3. Schnitzer B, Singleton TP, Ross CW, Sheldon S, Finn WG: Extramedullary myeloid cell tumor of differentiated monocytic cells followed by development of acute myelogenous leukemia, FABM5b. Proceedings of the 2nd Joint Meeting of the SH and EAP, Tumor Progression in Lymphoma. Barcelona, September, 1999. P. 1-30.

4. Finn WG, Sheldon S, Ross CW, Singleton TP, Schnitzer B: Philadelphia chromosome-positive acute lymphoblastic leukemia (ALL) arising in the setting of pre-existing B-CLL. Proceedings of the 2nd Joint Meeting of the SH and EAP, Tumor Progression in Lymphoma. Barcelona, September, 1999. P. II-3.
5. Petricek CM, Ross CW, Graham DM, Singleton TP, Schnitzer B: Grade II nodular sclerosis Hodgkin's disease with progression to lymphocyte depletion. Proceedings of the 2nd Joint Meeting of the SH and EAP, Tumor Progression in Lymphoma. Barcelona, September, 1999. p. III-1.
6. Petricek CM, Ross CW, Finn WG, Schnitzer B, Singleton TP: Utility of anti-CD117 in the flow cytometric analysis of acute leukemia. *Mod Pathol* 13:160A, 2000.
7. Finn WG, Singleton TP, Schnitzer B, Ross CW, Stoolman LS: Adhesion molecule expression in CD5 negative (-), CD18 negative chronic B-cell leukemias. *Mod Pathol* 13:148A, 2000.
8. Nangia R, Kroft SH, Singleton TP, Ross CW, Finn WG, Schnitzer B: Splenic morphology in small B-cell lymphoproliferative disorders (SBL): A study of 48 well-characterized cases. *Mod Pathol* 13:158A, 2000.
9. Nangia R, Singleton TP, Ross CW, Finn WG, Padmore RF, Schnitzer B: Follicular Hodgkin's lymphoma (FHL): A clinico-pathologic study. *Mod Pathol* 13:158A, 2000.
10. Valdez R, Finn WG, Ross CW, Singleton TP, Tworek JA, Schnitzer B: Extranodal marginal zone B-cell lymphoma associated with Waldenstrom's macroglobulinemia. *Mod Pathol* 13:165A, 2000.
11. Uherova P, Singleton TP, Ross CW, Schnitzer B, Finn WG: The clinical significance of CD10 antigen expression in diffuse large B-cell lymphoma. *Mod Pathol* 13:165A, 2000.

**JACOB N. SHANBERGE, M.D.
CLINICAL PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

- A. Weekly conferences on Coagulation, Thrombosis and Component Therapy for Blood Bank Residents, University of Michigan.
- B. Grand Rounds, Department of Pathology, University of Michigan, "Vascular Abnormalities as a Cause of Bleeding, April 7, 2000.

III. RESEARCH ACTIVITIES:

None.

IV. PUBLICATIONS:

None.

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

**ANNUAL DEPARTMENTAL REPORT
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I. CLINICAL ACTIVITIES:

- A. Surgical Pathology Coverage of M-Labs cases, including most cases from:
 - 1. Trillium Hospital, Albion, Michigan (including frozen sections).
 - 2. University of Michigan Health Service, non-dermatology cases, Ann Arbor, Michigan.
 - 3. Addison Community Hospital, Addison, Michigan.
 - 4. Other various clients including numerous satellite sites and University acquired practices.
- B. Autopsy Coverage for Trillium Hospital, Albion, Michigan, and Addison Hospital, Addison, Michigan.
- C. Rotation with other staff pathologists:
 - 1. Coverage at the University Hospitals of weekend and weekday autopsy call.
- D. Perform bone marrow aspiration and biopsies at Trillium Hospital, Albion, Michigan.
- E. Review peripheral blood smears at Trillium and Addison Community Hospitals.
- F. Clinical Pathology consults at Trillium and Addison Community Hospitals and other M-Labs clients.
- G. Surgical Pathology "Quickie" Anatomic Pathology consults for pathologists at M-Labs client hospitals.

II. TEACHING ACTIVITIES:

- A. Supervise residents in gross cutting of M-Labs cases and review microscopic material with residents in all interesting cases.
- B. Sign out some M-Labs and University of Michigan autopsies with residents.
- C. In-service teaching to laboratory staffs at Addison and Trillium Hospitals.

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 1999, MLabs added 12 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 (dermatopathology, flow cytometry, muscle and nerve biopsy), and a few were UMHS acquired practices. There was also one new full reference laboratory accounts, a hospital. One contract for services (EMU health system) was terminated.
This fiscal year, net billings for clinical pathology services increased by 21.8% and net billing for anatomic pathology services increased by 20.5%. Total combined billings increased by 21.4% over our last fiscal year.
MLabs submitted 2 proposals to prospective major clients during FY99. Of these, 1 was rejected, and one (to an existing client) was accepted.
3. Managed Care Activities
MLabs has expanded our agreement with MCare to supply outpatient laboratory services to include the majority of their provider groups (IDNs) for the HMO, POS, and Medicaid products. We are in active negotiation with MCare to develop a full-risk outpatient lab agreement for all groups and products to become effective 9/1/2000 (current target date).
MLabs continues to manage the MCare/MLabs agreement for Medicare HMO Program (Senior Plan). Five subcontracts are in place. We developed and implemented a system for reimbursement for testing done by other labs within network (Cross System Testing). We have finalized and facilitated most MCare HMO, POS, and Medicaid Contracts and Subcontracts. The other subcontracts are in progress.
We prepare quarterly QA reports on lab services for MCare's QA department and have conducted a Physician Satisfaction Survey for MLabs subcontracted providers and reported the results to MCare. We assist MCare with resolution of laboratory service issues.
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 10 managed care organizations, including Select Care, and a subcontract with MLabs for MCare work.
I serve on JVHL's Executive committee and its "elabs" committee.
We have succeeded in a cooperative effort of the 2 networks in a bid for the provision of laboratory services to Blue Care Network. Our bid was accepted and JVHL, in association with GLN has obtained and implemented a contract for provision of outpatient laboratory services for this large state-wide managed care product.
MLabs has actively worked for UMHS signing the Network Participation agreement with JVHL. UMHS signing of this agreement the last fiscal year has enabled us to participate in the BCN contract. Mlabs is preparing a proposal to

provide reference lab services to JVHL's new "elab" internal esoteric testing initiative.

- C. Member Department of Pathology Incentive Committee.
- D. Member, University of Michigan Networking Leads Committee.
- E. Department of Pathology representative to Managed Care Committee.
- F. Director, Laboratory at Trillium Hospital, Albion, Michigan.
- G. Director of Laboratories, Addison Community Hospital, Addison, Michigan.
- H. Chair, Tissue/Transfusion and Infection Control Committees, Trillium Hospital, and Addison Community Hospital.
- I. Member, Surgical and Medicine/Family Practice Committees, Trillium Hospital.
- J. Member, Executive Committee and Peer Review Committee, Addison Community Hospital.
- K. Plan and review Laboratory QA and CQI at Trillium and Addison Community Hospitals.
- L. Review Quality Control of Clinical Pathology tests at Trillium and Addison Community Hospitals.

V. OTHER RELEVANT ACTIVITIES:

None.

VI. PUBLICATIONS:

None.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

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 supervisor for undergraduate, post-doctoral and research-track investigators:**
 - 1. **Nobuhiro Takeshita, M.D., post-doctoral fellow (April 1998-present):** Dr. Takeshita is jointly supported by the L.M. Stoolman (Pathology) and A.E. Chang laboratories (Surgical Oncology) for work on T-cell trafficking during adoptive cellular immunotherapy for metastatic cancer. His research indicates that T-lymphoblasts grown from tumor-draining lymph node cells expressing binding site for the adhesion receptor P-selectin (so-called Plig^{high} cells) are 10-100 fold more potent than cells derived from unfractionated populations. Both the CD8, CD4 and NK-T cells contribute to the anti-tumor activities. As few as 1×10^6 cultured Plig^{high} cells completely suppress pulmonary metastases generated by infusion of 3×10^5 murine sarcoma cells. Their potency is further increased by pretreatment with proinflammatory cytokines that increase the recruitment of the adoptively transferred cells into tumor-bearing organs. The potency of the cultured Plig^{high} cells exceeds that reported for all previous forms of adoptive immunotherapy in the murine sarcoma model. Current efforts focus on defining the effector cell populations and activities that mediated the increased anti-tumor activities of the Plig^{high} population. In addition, pre-clinical studies in humans have begun (a focus of new P01 and R01 submissions).
 - 2. **Randall Knibbs, Ph.D., Research Scientist (January, 1994-present)** - Dr. Knibbs continued development of a microcarrier-based, high capacity transient transfection system. In addition, he developed a rapid purification system for the selectin-chimeras used in the adoptive immunotherapy project and purified several milligrams of these vital reagents for Dr. Takeshita's project. Dr. Knibbs assisted the PI in development of an SBIR project that will develop and test novel selectin inhibitors in several models of immunologically mediated disease in rodents. The project (coordinated by Jon Nagy, PhD at Ligocyte and Lloyd Stoolman, MD at the University of Michigan) was recently funded by the NIAID.

3. **Summer Research Opportunity Program Summer 1999, mentor:** Mentored Ms. Genese Reynolds (sophomore undergraduate), a pre-medical honors student interested in a career in pediatrics.
 4. **Undergraduate research assistants:** Hosted three undergraduate students in the laboratory during the academic year. These students actively participate in one of several ongoing research projects in the laboratory.
 5. **Graduate research assistants:** Hosted one Masters of Public Health student in the research laboratory.
- B. **Computerworld-Smithsonian Award Finalist for development of Internet-based courseware entitled: The Virtual Microscope-Interactive Laboratory Syllabii for Medical and Dental Pathology Courses.** This Award Program is jointly sponsored by the Smithsonian Institution and Computerworld Magazine. It solicits Case Studies from companies and individuals that illustrate the benefits of information technology to society as a whole. Thousands of Case Studies are submitted each year for consideration. In 1999, ~400 Case Studies were selected for inclusion in the American History Museum's Information Age Exhibit and added to the Smithsonian's Permanent Research Collection. **The Virtual Microscope** was selected as one of five finalists for the Computerworld-Smithsonian Award from the 75 Laureates in the Education and Academia Category. Judging criteria included the application's "benefit to society, difficulty, originality and the primacy of information technology in the definition or resolution of the task addressed". It was one of 15 Laureates in the category from the University of Michigan and the first from any unit of the institution to be selected as a Finalist in the Program.
- C. **Director, General Pathology Laboratory Course for Dental Students (Pathology 631) and co-director, General Pathology Lecture Course (Pathology 630):** The third generation Virtual Microscope Pathology Laboratory Interactive Syllabus was deployed for the course (<http://141.214.6.12/cyberscope631/>). The site incorporates high resolution (1900 X 1300 pixel) photographs of gross and microscopic specimens into an on-line version of the laboratory syllabus. An NT-Server in the Pathology Department houses the Livepicture Image Server dedicated to this project. The Livepicture Server software allows the user to pan across a low-power image and then magnify selected regions. Focus is maintained to the limits of photographic resolution. This "active" learning modality allows students to interact with specimens and slides much as they will in the laboratory. Consequently, it provides a unique approach to preview and review of laboratory material.
- D. **Co-director and lecturer, Hematology Sequence in Component II (Medical School 2nd year curriculum)-** Administered pathology component of sequence and co-directed course with Alvin Schmier, M.D. (Department of Internal Medicine and Pathology). The third generation of The Virtual Microscope-Hematopathology Interactive Syllabus was deployed for the course (<http://141.214.6.12/virtualheme99>). This site utilizes the image server and the general approach outlined above for the Dental Pathology Laboratory Website. New this year were two CD-based PowerPoint exercises. In addition, an image server capable of delivering completely digitized "Webslides" was developed so that alpha testing could begin in the Fall of 2000.
- E. **M1 Host Defense Sequence:** Lectured and developed CD-based courseware for lecture syllabus and case presentations.
- F. **Advanced Topics in Immunology:** Lecturer.

- G. **Pathology 581:** Co-director and lecturer.

III. RESEARCH ACTIVITIES:

ACTIVE SUPPORT (70% funded effort):

- A. **Principal Investigator- T Cell Trafficking in Adoptive Cellular Immunotherapy;** NIH, R01CA73059, 30% effort, \$180,000 (annual, direct); Apr 1998-Mar 2001.
- B. **Co-investigator and coordinator for Pathology Department section- “Rational Design of Adhesion Blocking Anti-Inflammatories”** (Jon O. Nagy, PI, Ligocyte Pharmaceuticals, Inc.); NIH, SBIR R43AI/GM43789, \$988,598 (annual, direct), 10% effort, Dec 99-Nov. NEW
- C. **Principal Investigator, project 3- "Structure of selectin-ligands synthesized by human T-lymphoblasts"**, NIH, P01AI33189 (Oligosaccharides as Anti-inflammatory Agents; PA Ward, Program Director), 15% effort, \$90,000 (annual, direct for the sub-project); Sept 1996-Aug 2000.
- D. **Co-investigator (with B. Richardson, Rheumatology Division, University of Michigan)- “Gender specific T-cell homing and autoimmunity”;** NIH, R01AI42753, 15% effort, \$187,000 (annual, direct); Apr 1998-Mar 2003 (NEW).
- E. **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 (NEW).
- F. **Co-investigator (with G. Kansas, Department of Microbiology/Immunology, Northwestern University)- “Leukocyte Recognition of P-selectin”;** American Cancer Society, \$120,000 (annual, direct), 5% effort, Jul 1999-June 2001.

IV. ADMINISTRATIVE ACTIVITIES:

- A. **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 Millenium). Participated in the consolidation of Clinical Flow Cytometry and Hematology Laboratories. Managed the operation of the research flow cytometry instruments (provided access for departmental investigators with grant support for flow cytometry).
- B. **Co-Director, Hematology Sequence in Component II and General Pathology 580/630/631-** see educational activities.
- C. **Member, Learning Resources Center Oversight Committee**
- D. **Member, Medical School InfoTech Committee**
- E. **Member, Medical School and MD/PhD Admissions Committees**
- F. **Member, Pathology/Immunology Graduate Program Admissions Committee**
- G. **Participant, Retreat on Medical School Sequence II Content**
- H. **Member, Pathology Website Committee**

V. **OTHER RELEVANT ACTIVITIES:**

EDITORIAL ACTIVITIES:

- A. Journal of Clinical Investigation.
- B. Journal of Biological Chemistry.
- C. Journal of Laboratory Investigation.
- D. Nature.
- E. Cell.
- F. Journal of Experimental Medicine.
- G. American Journal of Pathology.
- H. Journal of Immunology (Associate Editor).

VI. **PUBLICATIONS:**

ARTICLES IN PEER REVIEWED PUBLICATIONS:

1. Tanigawa, K., Craig, R.A., **Stoolman, L.M.**, Chang A.E. Effects of TNF- α on the in vitro maturation of tumor-reactive effector T-cells. 2000. J. Immunotherapy. Curtis JL, Wolber FM, Sonstein J, Craig
2. RA, Polak T, Knibbs RN, Todt J, Seitzman GD, **Stoolman LM**. Lymphocyte-endothelial cell adhesive interactions in lung immunity: lessons from the murine response to particulate antigen. 2000. Immunopharmacology (in press).
3. K. Tanigawa, K. Phillips, N. Takeshita, R.A. Craig , R.N. Knibbs, A.E. Chang and **L.M. Stoolman**. Tumor-specific responses in lymph nodes draining murine sarcomas are concentrated in cells expressing P-selectin binding sites (submitted).
4. **L.M. Stoolman**, R.A. Craig, M.J. Cameron, A.E. Chang. Ex-vivo expansion of human T-lymphocytes for adoptive immunotherapy: optimal growth conditions for expression of selectin ligands and attachment to vascular endothelium under shear (submitted).

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

1. K. Tanigawa, K. Phillips, R.A. Craig, R.N. Knibbs, A.E. Chang, **L.M. Stoolman**. Tumor-specific responses in lymph nodes draining murine sarcomas are concentrated in cells expressing P-selectin binding sites. 2000. Poster/Discussion session. AACR Annual Meeting, San Francisco, CA.
2. **LM Stoolman**, Michael Lougee, Douglas Gibbs and Tom Peterson. 1999. The Virtual Microscope- Interactive web-based syllabus for medical student (M2) Hematopathology laboratory. URL= <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.**
3. **LM Stoolman**, Michael Lougee, Douglas Gibbs, Tom Peterson and Gerald Abrams. 1999. 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 sites incorporates several hundred, high resolution (1900 X 1300 pixel) photographs of gross and microscopic specimens into an interactive laboratory syllabus. The features are as described above. **1999 Computerworld-Smithsonian Award Finalist.**
 4. **LM Stoolman**. 1999. Hematopathology Unknown Exercises. Interactive, CD-based excercises for medical student (M2) Hematopathology laboratory. CD-based publication used in M2-Heme sequence.
 5. **LM Stoolman**. 1999 & 2000. Leukocyte Pathophysiology and Leukocyte Trafficking. Interactive, CD-based syllabus and exercises including video clips and animations. CD-based publication used in Pathology 581 (Graduate Course) and Host Defense Sequence (M1 sequence).

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

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 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-monthly)
 - 5. Anatomic Pathology Core Conference – (2 per year)
 - 6. Anatomic Pathology Consultation Conference – (2 per year)
- C. Diagnostic Conference, Department of Dermatology – (weekly)
- D. Hospital Conferences:
 - 1. Multidisciplinary Cutaneous Lymphoma Conference (twice monthly)

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Sentinel lymph nodes in Merkel cell carcinoma. (Vernon Sondak, M.D., Alfred Chang, M.D., Timothy Johnson, M.D., Carol Bradford, M.D., Lori Lowe, M.D., Alan Yahanda, M.D., Vincent Cimmino, M.D.)
- B. Role of lipoxygenases in melanoma transformation. (Dean Brenner, M.D., Ira Winer, Vernon Sondak, M.D.)
- C. Dialysis dermopathy: a novel cutaneous fibrosing disorder in hemodialysis patients. (Shawn Cowper, M.D., Philip LeBoit, M.D., Howard S. Robin, M.D., Steven M. Steinberg, M.D., Samardeep Gupta, M.D.)
- D. Utility of melan-A immunostains in melanoma sentinel lymph nodes (Araba Afenyi-Annan, M.D.)

- E. Papular acantholytic dyskeratosis of the genitocrural region (Nasim Fasel, 4th year medical student and Hope Haefner, M.D.)

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Co-director, Dermatopathology Service

VI. PUBLICATIONS:

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

1. Su, L., Duncan, L.: Lymphoma- and leukemia-associated atypical CD30+ reactive cutaneous T-cell infiltrates. *J Cutan Pathol* 27:249-254, 2000.
2. Bowen, G.M., Peters, N.T., Fivenson, D.P., Su, L., Nousari, H.C., Anhalt, G.J., Cooper, K.D., Stevens, S.R.: Lichenoid dermatitis in paraneoplastic pemphigus. *Arch Dermatol* 136:652-656, 2000.
3. Natkunan, Y., Warnke, R.A., Haghighi, B., Kim, Y., Su, L., LeBoit, P.E., Kohler, S.K.: Co-expression of CD56 and CD30 in lymphomas with primary presentation in the skin: Clinicopathologic, immunohistochemical, and molecular analyses of seven cases. (Accepted in *Journal of Cutaneous Pathology*)
4. Romero, J.B., Rasmussen, J.E., Su, L.: Multiple light yellow papules: pseudoxanthoma elasticum-like papillary dermal elastolysis. A case report. (Accepted in *Archives of Dermatology*)
5. Sachs, D., Su, L., Dlugosz, A.: Annular ulcerated hip plaques: superficial granulomatous pyoderma. A case report. (Accepted in *Archives of Dermatology*)
6. Cowper, S.E., LeBoit, P.E., Robin, H.S., Steinberg, S.M., Su, L., Gupta, S.: Dialysis dermopathy: preliminary observations of a novel and evolving cutaneous fibrosing disorder in hemodialysis patients. (Accepted as a Research Letter to the Editor of *Lancet*)
7. Su, L., Kim, Y., Swetter, S., LeBoit, P., Kohler, S.K.: Interstitial mycosis fungoides: a variant of mycosis fungoides resembling inflammatory morphea and granuloma annulare (Submitted to *American Academy of Dermatology*)
8. Cherny, S., Mraz, S., Su, L., Harvell, J., Kohler, S.: Heteroduplex analysis of T-cell receptor gamma gene rearrangement as an adjuvant diagnostic tool in skin biopsies for erythroderma. (Submitted to *Journal of Cutaneous Pathology*)
9. Bowen, A.R., Sachs, D., Su, L., Bowen, G.M.: Enlarging necrotic mass of the scalp: Peripheral large T-cell lymphoma, CD30-negative. A case report. (Submitted to *Archives of Dermatology*)
10. Woo, J., Su, L., Kohler, S., Bowen, G.M.: Pseudolymphoma developing at the sites of subcutaneous vitamin K injections. A case report. (Submitted to *Archives of Dermatology*)

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

- A. None

II. TEACHING ACTIVITIES:

- A. Lecturer, 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. Principal Investigator , "Role of Cytokines and Adhesion Molecules in Thermal Injury", (NIH GM-48477).
B. Principal Investigator, "Effect of Polynitroxyl Albumin (PNA) on Protein Extravasation Following Thermal Burn Trauma" (SynZyme Technologies, LLC).
C. Co-Investigator, "Liquid Ventilation in ARDS" (NIH HL-54224)
D. Co-Investigator, "Lung Injury Produced by Oxygen Metabolites", (NIH GM-29507).
E. Co-Investigator, "Mechanisms and Prevention of Lung Injury Caused by Mustard Gas" (USAMRMC)

PENDING SUPPORT:

- A. None

PROJECTS UNDER STUDY:

- A. Role of leukocytes, inflammatory mediators, and adhesion molecules in thermal trauma-related cell and tissue injury.
B. Pathomechanisms of ischemia-reperfusion injury.
C. Pathophysiologic role of complement activation products in secondary lung injury.
D. Mechanisms and prevention of lung injury caused by 2-chloroethylethyl sulfide.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Interviewed candidates for faculty and postdoctoral positions
- B. Participation in undergraduate research program

MEDICAL SCHOOL/HOSPITAL:

- A. Course Director, Pathology 580/630
- B. Member Medical School Committee on Student Biomedical Research Programs
- C. Member Doctoral Thesis Committee
- D. Interviewed candidates for faculty positions
- E. Consultant for clinical research programs
- F. Reviewer of intra-departmental grant proposals

REGIONAL AND NATIONAL:

None

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

- A. Member Editorial Board, Immunopharmacology, 1998-present
- B. Member Editorial Advisory Board, Immunobiology, 1980- present
- C. Reviewer for the following scientific journals:
 - 1. American Journal of Pathology
 - 2. Immunopharmacology
 - 3. Journal of Applied Physiology
 - 4. Journal of Cataract and Refractive Surgery
 - 5. Journal of Clinical Investigation
 - 6. Journal of Leukocyte Biology
 - 7. Shock

INVITED LECTURES/SEMINARS:

- 1. Visiting Professor, Experimental Dermatology, University of Freiburg, Germany, June 20-21, 2000
- 2. Session Chair, General Aspects of Trauma and Critical Care Medicine, 7th Vienna Shock Forum, November 13-16, 1999, Vienna, Austria
- 3. Invited Speaker, Mechanisms of Dermal Burn Wound Edema Formation and Secondary Lung Injury, Seventh Vienna Shock Forum, November 13-16, 1999, Vienna, Austria

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Mulligan, M.S., Warner, R.L., Rittershaus, C.W., Thomas, L.J., Ryan, U.S., Foreman, K.E., Crouch, L.D., Till, G.O., Ward, P.A. Endothelial targeting and enhanced antiinflammatory effects of complement inhibitors possessing sialyl Lewis^x moieties. *J. Immunol.* 162: 4952-4959, 1999
2. Piccolo, M.T.S., Wang, Y., Verbrugge, S., Warner, R.L., Sannomiya, P., Piccolo, N.S., Piccolo, M.S., Hugli, T.E., Ward, P.A., Till, G.O. Role of chemotactic factors in neutrophil activation after thermal injury in rats. *Inflammation* 23:371-385, 1999
3. Seekamp, A., Hultquist, D.E., Till, G.O. Protection by vitamin B₂ against oxidant-mediated acute lung injury. *Inflammation* 23: 449-460, 1999
4. Piccolo, M.T.S., Wang, Y., Sannomiya, P., Piccolo, N.S., Piccolo, M.S., Hugli, T.E., Ward, P.A., Till, G.O. Chemotactic mediator requirements in lung injury following skin burns in rats. *Exp. Molec. Pathol.* 66: 220-226, 1999
5. Schlag, G., Redl, H., Till, G.O., Davies, J. Anti-L-selectin antibodies treatment of traumatic shock in baboons. *Crit. Care Med.* 27:1900-1907, 1999
6. Younger, J.G., Sasaki, N., Saleh, E.F., Hirschl, R.B., Ravage, Z.A., Ward, P.A., and Till, G.O. Detrimental effects of complement activation in hemorrhagic shock. *J. Appl. Physiol.* (in press)

BOOKS AND CHAPTERS IN BOOKS:

None

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

1. Till, G.O., Ravage, Z.B., and Piccolo, M.T.S. Mechanisms of dermal burn wound edema formation and secondary lung injury. *Shock* 12: 51-51, Suppl. 1, 1999
2. Younger, J.G., Sasaki, N., Nghiem, T., Hirschl, R.B., Till, G.O., and Ward, P.A. Physiological manifestations of systemic activation of complement. Proceedings, Society for Academic Emergency Medicine Scientific Meeting, San Francisco, May, 2000
3. Younger, J.G., Sasaki, N., Nghiem, T., Hirschl, R.B., Till, G.O., and Ward, P.A. Lung inflammation and function in a model of complement-mediated acute injury. Proceedings, Society for Academic Emergency Medicine Scientific Meeting, San Francisco, May, 2000
4. Younger, J.G., Sasaki, N., Nghiem, T., Till, G.O., and Ward, P.A. Systemic hemodynamic and metabolic effects of intravascular complement activation with CVF. *Shock* 13: 57-57, Suppl. 1, 2000

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

A. None.

II. TEACHING ACTIVITIES:

- A. Mentor for students who worked in my laboratory over the past year; includes three post-doctoral fellows, one pathology graduate student, and three undergraduate students.
- B. Course director – Pathology 581. Tissue, cellular and molecular basis of disease.
- C. Instructor – Pathology 600 – Pathology course for dental students.
- D. Instructor – Pathology 581 – Tissue, cellular and molecular basis of disease.
- E. Member, Pathology Graduate Program Steering Committee
- F. Member and chairman – Pathology Graduate Program Curriculum Revision Committee.
- G. Member, Department of Pathology Graduate Program Comprehensive Exam Committee.
- H. Director, Pathology Research Seminar Series.
- I. Member, PIBS Steering Committee
- J. Member, PIBS Curriculum Committee
- K. Member, PIBS Admission Committee
- L. Member, University of Michigan Minority Student Research Opportunities Program.
- M. Member, University of Michigan Student Research Opportunities Program.
- N. Member, Cancer Biology Training Grant Steering Committee.
- O. Member, Dermatological Sciences Training Grant Steering Committee

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Squamous Epithelial Invasion in Organ Culture," NIH CA60958.
- B. Principal Investigator, "Co-polymer - Trimethylamine microcarriers for high-density cell growth under serum-free conditions," HIH CA 74595.
- C. Principal Investigator on Project 10, "Retinoic Acid and Cells of the Skin," Johnson and Johnson Corporation..
- D. Principal Investigator, "Cell culture, media, microcarrier system for Marek's Disease Vaccine" NIH AI46876.

PROJECTS UNDER STUDY:

- A. The biology of human squamous carcinoma cell invasion
- B. The development of substrates for optimum growth of cells in large scale culture.
- C. Biological basis of photoaging and natural aging in skin.
- D. Development of a bioreactor culture system for Marek's disease vaccine.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Member, Department of Pathology Advisory Committee on Appointments, Promotions and Tenure.
- B. Member, Department of Pathology Graduate Program Committee

MEDICAL SCHOOL/HOSPITAL:

- A. Member, Medical School Committee on Summer Research Opportunities.
- B. Program Director, University of Michigan Cancer Center Program on Tumor Cell Metastasis and the Extracellular Matrix.
- 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, OSI Pharmaceuticals, Garden City, NY, July 13,14, 1999.
2. Invited speaker, Oxidative Stress, Skin Biology and Medicine, Kapandriti, Attiki, Greece, Sept. 13-16, 1999.
3. Johnson & Johnson Retinoid Symposium, Short Hills, New Jersey, May 15,16, 2000.
4. Invited Speaker, Williamsburg Foundation Conference on Vaccine Production Technology, Williamsburg, VA, Oct 10-14, 1999.
5. Invited Speaker, Keystone Symposium on Prostate Cancer and Growth Factor Signaling. Keystone, CO. Jan 22-29, 2000.

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Murphy HS, Bakopoulos N, Dame MK, Varani J, Ward PA. Heterogeneity of vascular endothelial cells: differences in susceptibility to neutrophil-mediated injury. *Microvascular Res.* 56:203-211, 1999.
2. Murphy HS, Warner RO, Dame MK, Varani J, Ward PA. Nitric oxide protects endothelial cells from oxidant injury. *Shock* 12:111-117, 1999.
3. Ginsburg I, Sadovnic M, Varani J, Tirosh O, Kohen R. Hemolysis of red blood cells induced by combinations of diethyldithiocarbamate (DDC) and divalent metal ions: Modulations by inhibitors of oxidants. *Free Rad. Res.* 195:1-13, 1999.
4. Gibbs DF, Shanley TP, Warner RO, Murphy HS, Varani J, Johnson KJ. The role of matrix metalloproteinases in models of acute lung injury: Evidence for the alveolar macrophage as the source of the proteinase. *Amer. J. Respir. Cell. Molecular Biol.* 20:1145-1154, 1999.
5. Gibbs DF, Apel IJ, Warner RO, Weiss SJ, Johnson KJ, Varani J. Characterization of matrix metalloproteinases produced by rat alveolar macrophages. *Amer. J. Respir. Cell. Molecular Biol.* 20:1136-1144, 1999.
6. Ginsburg I, Varani J, Singh N. PADMA-28, a traditional Tibetan herbal preparation inhibits the respiratory burst in human neutrophils, the killing of epithelial cells by oxidants and lipid peroxidation. *Inflammopharmacology* 7:47-62, 1999.
7. Varani J, Perone P, Chi Y, Schmidt T, Johnson T, Zeigler ME. Elaboration of matrix metalloproteinases and matrix metalloproteinase inhibitors by basal cell and squamous cell carcinomas of skin. *Brit. J. Cancer* 82:657-665, 2000.
8. Zouboulis CC, Tavakkol A, Elder JT, Varani J. Maintenance of human skin in organ culture: Role for insulin-like growth factor-1 receptor and epidermal growth factor receptor. *Arch. Dermatol. Res.* 291: 643-651, 1999.
9. Zeigler ME, Chi Y, Schmidt T, Varani J. Role of ERK and JNK pathways in regulating cell motility and matrix metalloproteinase 9 production in growth factor-stimulated human epidermal keratinocytes. *J. Cell. Physiol* 180:271-284, 1999.

10. Varani J, Dame MK, Wojno K, Schuger L, Johnson KJ. Characteristics of nonmalignant and malignant human prostate in organ culture. *Lab. Invest.* 79:723-731, 1999.
11. Ellis CN, Zeigler ME, Chi Y, Varani J, Fisher GJ, Pershadsingh HA, Stephen C. Benson, Theodore W. Kurtz: Troglitazone improves psoriasis and normalizes models of proliferative skin disease. *Arch. Dermatol.* 136:609-616, 2000.
12. Varani J., Warner R.O., Gharaee-Kermani M., Phan S.H., Kang S., Chung J., Wang Z-Q., Datta S.H., Fisher G.J., Voorhees J.J.: Vitamin A antagonizes elevated collagen-degrading matrix metalloproteinase and stimulates collagen accumulation in naturally-aged human skin. *J. Invest. Dermatol.* 114:480-489, 2000.
13. Chung JH, Kang S, Varani J, Lin J, Fisher GJ, Voorhees JJ. Decreased extracellular-signal-regulated kinase and increased stress-activated MAP kinase activities in aged human skin in vivo. *J. Invest. Dermatol.* (in press).

BOOKS AND CHAPTERS IN BOOKS:

1. Varani J, Ginsburg I. Protease-oxidant interactions in acute inflammation. In: Mohan, RH (ed.) *Research Advances in Pathology*, Global Research Network, Kerala, India (in press).

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

1. Varani J, Wang ZQ, Fisher GJ, Voorhees JJ. Reduced collagen production by fibroblasts in photoaged skin is normalized in fibroblasts cultured from photodamaged skin. *J. Invest. Dermatol.* 112:634, 1999.
2. Zeigler ME, Chi Y, Varani J. Differential activation of protein phosphatase activity by invasion and non-invasion promoting growth factors. *AACR Proceed.* 40, 694, 1999.
3. Chi Y, Zeigler ME, Varani J. Different roles of ERK and JNK signaling pathways in mediating invasive properties of HGF-stimulated human keratinocytes 40: 1313, 1999.
4. Varani J, Gibbs DF, Johnson KJ. Characterization of matrix metalloproteinases produced by rat alveolar macrophages. *Keystone Symposium on Macrophage Biology*, 1999.
5. Johnson KJ, Gibbs DF, Varani J. The role of matrix metalloproteinases in models of acute lung injury: Evidence for the alveolar macrophage as the source of the proteinase. *Keystone Symposium on Macrophage Biology*, 1999.
6. Varani J, Zeigler ME. Regulation of matrix metalloproteinase expression in organ-cultured human skin. *Keystone symposium on Signaling-2000*, 81:2000.
7. Varani J., Warner R.O., Gharaee-Kermani M., Phan S.H., Kang S., Chung J., Wang Z-Q., Datta S.H., Fisher G.J., Voorhees J.J.: Vitamin A antagonizes elevated collagen-degrading matrix metalloproteinase and stimulates collagen accumulation in naturally-aged human skin. *J. Invest. Dermatol.* 114:641, 2000.

**CLAUDIUS VINCENZ, PhD
RESEARCH INVESTIGATOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

- A. Graduate students:
Tom Hlaing, co-advisor with Dr. Peter A. Ward.
Johannes Bauer, Student of the "Freie Universitaet in Berlin, Germany"
Michael Zeidler, Student of the "Freie Universitaet in Berlin, Germany"
- B. Undergraduate students: All were part of UROP: Kary Dilley, Patrick Welch, Kashif Ali, Roshan Pai, Elizabeth Cook.
- C. Courses: Pathology 581 Lectures on cellular pathology (2 sessions), Lecture on polyglutamine expansion disease.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator: "Identification of Components of the Cell Death Pathway", NIH ES08111, \$1,315,155 / 5years, August 1, 1996 -July 31, 2001.
- B. Principal Investigator: "Identification of Components of the Cell Death Pathway", DOD 17-96-1-6085, \$811,316 / 4 years June 1, 1996 – May 31, 2000.
- C. Principal Investigator: "CD40 Signal transduction", NIH HD33881, \$677,079 / 4 years August 1, 1996 – July 31 , 2000.
- D. Principal Investigator: "Characterization of FAS associated death domain FADD", NIH AG13671, \$797,921 / 3 years April 11, 1996 – February 28 , 2000.
- E. Principal Investigator: "Signal Transduction by the Eck Receptor Tyrosin Kinase", NIH DK52201, \$1,110,609 / 4 years June 1, 1996 – May 31, 2000.

PENDING:

- A. Principal Investigator: "Study of Death receptors in Neuronal Systems", \$1,839,087 / 5 years December 1, 2000 – November 30, 2005
- B. Principal Investigator: "Mechanistic studies of A20, an inhibitor of NF- κ B", \$1,184,966 / 4 years April 1, 2001 – March 31, 2005

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:

None

PATENTS:

None

INVITED LECTURES/SEMINARS:

None

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Rigamonti, D., J. H. Bauer, C. De-Fraja, L. Conti, S. Sipione, C. Sciorati, E. Clementi, A. Hackam, M. R. Hayden, Y. Li, J. K. Cooper, C. A. Ross, S. Govoni, C. Vincenz, and E. Cattaneo. 2000. Wild-type Huntingtin protects from apoptosis upstream of Caspase-3. *Journal of Neuroscience* **20**:3705-13.

BOOKS/CHAPTERS IN BOOKS:

None

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

Meeting Abstracts:

1. DOD Area of Hope Meeting 2000. Atlanta, GA June 8-11, 2000 Inhibition of caspase-9 by Huntingtin
2. Mechanisms of Cell Death 2000. International Cell Death Society, El Escorial, Spain, May 6-10, 2000, Wt-Huntingtin protects from apoptosis upstream of Caspase 3
3. NF- κ B Regulation and Function: Keystone Meeting, Tahoe City, CA February 22 – 27, The Inhibitory profile of A20 suggests the generation of two NF- κ B activ activating signals by IKK β .

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

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 (1999-00):
1. Ren-Fang Guo, M.D.
 2. Markus Huber-Lang, M.D.
 3. Jacqueline Jordan, Ph.D.
 4. J. Eric McDuffie, Ph.D.

- B. UROP Undergraduate Students:
1. Kari Dilley, Sophomore
 2. Jennifer Loussia, Freshman
 3. Kristina Lu, Senior
 4. Stephanie McGuire, Junior
 5. Vishalee Padgaonkar, Senior

Research mentoring of two Research Scientists (Drs. Younger and Vincenz)
Gross Autopsy Conference

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

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Lung Immunopathology" (Training Grant), NHLBI-NIH-HL-07517 (5%), \$218,805/year, 6/1/86-5/31/01.
- B. Principal Investigator, "Lung Injury by Oxygen Metabolites", NIGMS-NIH-GM-29507 (20%), \$272,284/year (\$1,123,824/four years), 7/1/97-6/30/01.
- C. Principal Investigator, "Inflammatory Cells and Lung Injury", NHLBI-PO1-HL-31963 (25%), \$189,794/year (Proj. I) \$630,840 (all projects), 07/01/98 -03/01/04.
- D. Principal, Investigator, "Oligosaccharides as Inflammatory Agents", PO1-AI-33189 (10%), \$93,443/year (Proj. II) \$26,853/year (Core A), 09/01/98-08/31/00.
- E. Principal Investigator, "Rational Design of Adhesion Blocking Anti-Inflammatories" (LigoCyte) (10%), \$174,391/year; 06/15/00-06/14/01.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director, Division of General Pathology.

MEDICAL SCHOOL/HOSPITAL:

- A. Advisory Committee for the Howard Hughes Medical Institute.
B. Clinical Council.
Conflict of Interest Committee.
Technology Transfer Committee
C. Dean's Advisory Council.
E. Geriatric Center Executive Committee.
F. Howard Hughes Medical Institute Dean's Advisory Committee.
G. Internal Medicine Advisory Committee for the University of Michigan George M. O'Brien Renal and Urologic Center.
H. Michigan Eye Bank Research Review Committee.
I. Undergraduate Research Opportunity Program, University of Michigan.
J. University of Michigan Cancer Center Executive Committee.

UNIVERSITY OF MICHIGAN:

- A. Senate Assembly, September, 1995-present.
1. Chair, Medical Affairs Advisory Committee, Chair, September, 1996-present.
B. Senate Advisory Committee on University Affairs, 1998 – present.
C. Michigan League Board of Governors, September, 1997 – present.

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. A. James French Society of Pathologists, 1988-present.
G. Health Policy Agenda for the American People, Advisory Committee.
H. Institute of Medicine, National Academy of Sciences, July, 1990-present.
I. Michigan Society of Pathologists.
J. Michigan Thoracic Society, 1988-present.
K. National Research Council.
1. Chair, Institute of Laboratory Animal Research.
L. Universities Associated for Research and Education in Pathology, Inc., Board of Directors.

V. **OTHER RELEVANT ACTIVITIES:**

EDITORIAL BOARDS:

- A. American Journal of Pathology, Editorial Board, 1982-present.
- B. American Review of Respiratory Diseases, Consulting Editor, 1977-present.
- C. Biological Signals, Consulting Editor.
- D. Free Radical Biology & Medicine, Editorial Board, 1995-present.
- E. Journal of Clinical Investigation, Consulting Editor.
- F. Journal of Experimental and Molecular Biology, 1999 – present
- G. Toxicologic Pathology, Editorial Board, 1988-present.

HONORS AND AWARDS

None.

INVITED LECTURES/SEMINARS:

1. Invited Speaker, “Inflammatory lung disease”; 5th Altschul Symposium on Neuroinflammation, Saskatoon, Saskatchewan; August 19, 1999.
2. Invited Speaker, “Neutrophils: Innate Resistance and Adaptive Responses”; Society for Leukocyte Biology, 15th International Congress, Cambridge University, United Kingdom, September 24, 1999.
3. Invited Speaker, “Regulation of the Inflammatory Response”; Wayne State University Medical School, Michigan; November 30, 1999.
4. Keynote Address, “The Inflammatory Response”; NIH Workshop on Oral Diseases and Diabetes; Chevy Chase, Washington, DC; December 6, 1999.
5. Invited Speaker, “Harmful Effects of complement in Sepsis”, University of Louisville, Louisville, KY; March 14, 2000.

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Paine III, R.P., and Ward, P.A.: Cell adhesion molecules and pulmonary fibrosis. Am J Med, 1999;268-279.
2. Ginsburg, I., Ward, P.A., and Varani, J.: Can we learn from the pathogenetic strategies of group A hemolytic streptococci how tissues are injured and organs fail in post-infectious and inflammatory sequelae? FEMS Immunology and Medical Microbiology, 1999, 25:325-338.
3. Guo, R.F., Ward, P.A., Jordan, J.A., Huber-Lang, M., Warner, R.L. and Shi, M.M.: Eotaxin expression in sephadex-induced lung injury in rats. AJP 1999, 155;2001-2008.
4. Ramos-Kelly, J.R., Toledo-Pereyra, L.H., Jordan, J.A., Rivera-Chavez, F.A., Dixon, R.A.F., and Ward, P.A.: Upregulation of lung chemokines associated with hemorrhage is reversed with a small molecule multiple selectin inhibitor. J Am Coll Surg, 1999, 189:546-553.
5. Lentsch, A.B., Yoshidome, H., Warner, R.L., Cheadle, W.G., Ward, P.A., and Edwards, M.J.: Requirement for interleukin-12 in the pathogenesis of hepatic ischemia/reperfusion injury. Hepatology, 1999;30:1448-1453.

6. Bless, N.M., Huber-Lang, M., Guo, R.F., Warner, R.L., Schmal, H., Czermak, B.J., Shanley, T.P., Crouch, L.D., Lentsch, A.B., Sarma, V., Mulligan, M.S., Friedl, H.P. and Ward, P.A.: Role of CC chemokines (MIP-1 β , MCP-1, RANTES) in acute lung injury in rats. *J Immunol* 2000;164:2650-2659.
7. Kubes, P., and Ward, P.A.: Leukocyte recruitment and the acute inflammatory response. *Brain Pathol.* 2000;10:127-135.
8. Ward, P.A.: Adhesion protein protocols. *Arch Pathol Lab Med* 2000;124:332.
9. Lentsch, A.B., and Ward, P.A.: Regulation of inflammatory vascular damage. *J. Pathol.* 2000;190:343-348.
10. Mulligan, M.S., Lentsch, A.B., Huber-Lang, M., Guo, R.F., Sarma, V., Wright, C.D., Ulich, T.R., and Ward, P.A.: Anti-inflammatory effects of mutant forms of secretory leukocyte protease inhibitor. *Amer J Pathol.* 2000;156:1033-1039.
11. Mulligan, M.S., Warner, R.L., McDuffie, J.E., Bolling, S.F., Sarma, J.V., and Ward, P.A.: Regulatory role of Th-2 cytokines, IL-10 and IL-4, in cardiac allograft rejection. *Exp. Molecular Pathol.* 2000;69:1-9.
12. Ramos-Kelly, J.R., Toledo-Pereyra, L.H., Jordan, J., Rivera-Chavez, F., Rohs, T., Holevar, M., Dixon, R.A.F., Yun, E., and Ward, P.A.: Multiple selectin blockade with a small molecule inhibitor downregulates liver chemokine expression and neutrophil infiltration after hemorrhagic shock. *J. Trauma.* 2000;49:92-100.
13. Martinez-Mier, G., Toledo-Pereyra, L.H., McDuffie, E., Warner, R.L., and Ward, P.A.: L-selectin and chemokine response after liver ischemia and reperfusion. *J of Surgical Research*; 2000; 93:156-162.

BOOKS/CHAPTERS IN BOOKS

1. Ward, P.A. and Murphy, H.S.: Role of complement in endothelial cell activation. *Molecular and Cellular Basis of Inflammation.* Serhan, C.N. and Ward, P.A. (eds) Humana Press Inc., Totowa, New Jersey, pp. 1-27, 1999.
2. Fantone, J.C and Ward, P.A.: Inflammation, in, Rubin, E. and Farber, J.L. (eds.) *Pathology, Third Edition,* Lippincott-Raven Publishers, Philadelphia, Pennsylvania, pp. 36-75, 1999.
3. Johnson, K.J., Chensue, S.W. and Ward, P.A.: Immunopathology, in, Rubin, E. and Farber, J.L. (eds) *Pathology, Third Edition,* Lippincott-Raven Publishers, Philadelphia, Pennsylvania, pp. 104-142, 1999.
4. Ward, P.A. and Lentsch, A.B.: in *Sepsis and Organ Dysfunction from Basics to Clinical Approach.* Baue, A.E., Berlot, G., Gullo, A., Vincent, J.-L. (eds), Springer-Verlag Italia, Milano, pp. 55-62, 1999.
5. Maderazo, E.G. and Ward, P.A.: Leukocyte chemotaxis, in, *Manual of Clinical Laboratory Immunology, 3rd Ed.,* American Society for Microbiology, Washington, D.C., In Press.
6. Maderazo, E.G., Woronick, C.L. and Ward, P.A.: Inhibitors of chemotaxis, in, *Methods in Enzymology,* Academic Press, Orlando, Florida, In Press.
7. Morganroth, M.L., Till, G.O. and Ward, P.A.: Pathophysiology of ischemia-reperfusion lung injury, in Das, D.K. (ed), *Pathophysiology of Reperfusion Injury,* CRC Press, Inc., In Press.
8. Till, G.O., Friedl, H.P. and Ward, P.A.: Histamine-dependent modulation of oxygen radical production, in, Farr, C.H. (ed), *Proceedings of the Second International Conference of Bio-Oxidative Medicine,* In Press.
9. Till, G.O., Johnson, K.J. and Ward, P.A.: Oxygen free radicals in inflammation, in, Messmer, K. and Hammerson, R. (eds), *Progress in Applied Microcirculation, Volume 9,* Karger, Basel, In Press.
10. Till, G.O. and Ward, P.A.: Role of complement and neutrophils in experimental acute lung injury, in, Nuki, G. and Zvaifler, N. (eds) *The Lungs and Rheumatic Disease,* Butterworth's International Medical Reviews, Rheumatology 3, Butterworth and Co., England, In Press.
11. Till, G.O. and Ward, P.A.: The lung and rheumatic disease: Role of complement. *Butterworth's International Medical Reviews, Rheumatology 3,* In Press.

12. Till, G.O. and Ward, P.A.: Thermal injury and lung tissue damage, in, *Critical Topics in Pulmonary Pharmacology and Toxicology*, In Press.
13. Vaporciyan, A.A. and Ward, P.A.: The inflammatory response, in, Beutler, E., Lichtman, M.A., Collier, B.S. and Kipps, T.J. (eds), *Williams Hematology*, McGraw-Hill, Inc., New York, In Press.
14. Varani, J. and Ward, P.A.: The immunobiology of tumor cell chemotaxis, Waters, H. (ed), *Handbook of Cancer Immunology*, Garland STPM Press, In Press.
15. Ward, P.A.: Inflammation, Chapter 12, in, Bellanti, J.A. (ed), *Immunology in Medicine*, W.B. Saunders Company, Philadelphia, Pennsylvania, In Press.
16. Ward, P.A., Johnson, K.J. and Till, G.O.: Tissue injury as a consequence of oxygen radicals produced by phagocytic cells, in *Proceedings of Symposium by Comparative Respiratory Society*, Anaheim, California, In Press.
17. Ward, P.A., Johnson, K.J. and Till, G.O.: Animal models of oxidant lung injury, in, *Proceedings of Stressa Symposium in Zambon*, Italy, In Press.
18. Ward, P.A. and Murphy, H.S.: Complement activation products in endothelial cell activation, Koch, K. (ed), *American Chemical Society Symposium series book on Cell Adhesion and Migration*, In Press.
19. Ward, P.A.: Regulation of lung inflammatory injury in, Said, S. (ed), *Pro-inflammatory and anti-inflammatory peptides in Lung Biology in Health and Disease Series*, Marcel Dekker, Inc., New York, New York, In Press.
20. Ward, P.A. and Till, G.O.: The autodestructive consequences of thermal injury, Ninnemann, J. (ed), *the Immune Consequences of Thermal and Traumatic Injuries*, In Press.
21. Warren, J.S., Johnson, K.J. and Ward, P.A.: Phagocytes and reactive oxygen substances ad mediators of acute lung injury, in, Hyers, T. (ed), *Diffuse Alveolar Damage and Respiratory Failure*, Futura Press, New York, In Press.
22. Lentsch, A.B. and Ward, P.A.: Regulatory functions of secretory leukocyte protease inhibitor. Pandalai, S.G. (ed). In *Recent Research Developments in Immunology*. Research Signpost, Trivandrum, India. 1999;vol 1, part 1:pps. 31-35.

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

1. Guo, R.F., Hu, S.M., McDuffie, J.E., Sarma, V., Ward, P.A., and Shi, M.M.: Molecular cloning and functional characterization of a novel human CC chemokine. *Experimental Biology* 643.27:A844, 1999.
2. Guo, R.F., Jordan, J.A., Czermak, B.J., Huber-Lang, M., Ward, P.A., and Shi, M.M.: Eotaxin expression in Sephadex-induced pulmonary inflammation. *Experimental Biology* 643.30:A845, 1999.
3. Diehl, J.M., Warner, R.L., and Ward, P.A.: Adhesion molecule blockade decreases inflammatory mediator production from macrophages. *Experimental Biology* 750.1:A1017, 1999.
4. Jordan, J.A., Yun, E.C., Sarma, V.J., Czermak, B.J., Warner, R.L. and Ward, P.A.: The role of interleukin-17 in LPS-induced inflammatory lung injury. *Experimental Biology* 750.4:A1017, 1999.
5. Lentsch, A.B. and Ward, P.A.: Regulatory functions of secretory leukocyte protease inhibitor. *Recent Research Developments in Immunology*, Research Signpost, 1999. In Press.
6. Czermak, B.J., Friedl, H.P., and Ward, P.A.: Role and regulation of chemokines in rodent models of lung inflammation. Accepted in *ILAR Journal*, 1999.
7. Diehl, J.M., Warner, R.L., and Ward, P.A.: Adhesion molecule blockade decreases inflammatory mediator production from macrophages. *Experimental Biology* 750.1:A1017, 1999.
8. Jordan, J.A., Yun, E.C., Sarma, V.J., Czermak, B.J., Warner, R.L. and Ward, P.A.: The role of interleukin-17 in LPS-induced inflammatory lung injury. *Experimental Biology* 750.4:A1017, 1999.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

- A. Director, Division of Clinical Pathology/Clinical Laboratories, May 1993-present.
- B. Director, Clinical Immunopathology Service; September 1989-present.
- C. Interim Director, Clinical Cytogenetics Laboratory; September 1999-present.
- D. Interim Director, Tissue Typing Laboratory; March 2000-present.
- E. Microbiology Laboratory; review of peripheral blood parasite smears; July 1996-present.
- F. Molecular Diagnostics Laboratory; signout of cases (3 weeks/year); July 1997-present.

II. TEACHING ACTIVITIES:

- A. "Current Topics in Immunopathology" series: pathology residents, M4 students; (36 contact hours).
- B. Clinical Pathology Grand Rounds:
 - 1. "Professional reimbursement in pathology" (8/16/99).
 - 2. "Cases and images in immunopathology" (12/3/99).
 - 3. "Diagnosis and classification of systemic vasculitis: role of the clinical laboratory" (12/10/99)
 - 4. "ANA and ENA testing – beyond screening" (12/17/99)..
- C. Immunopathology signout: pathology residents, M-4 medical students, EMU medical technology students (three times/week; 26 weeks/year).
- D. Immunopathology component of Block B (Clinical Pathology); ad hoc topical reviews: pathology residents (47 contact hours).
- E. M-1 Host Defense sequence; "Autoimmunity and tumor immunology" (5/2/00); (1 contact hour).
- F. Supervision of Research activities for:
 - 1. Anjali Desai, Ph.D. (Research Investigator); (6/15/96-present).
 - 2. Hernan Gomez, M.D. (Assistant Professor; Emergency Medicine, University of Michigan); (6/1/96-present).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Oxidant-Induced Beta Chemokines in Granuloma Formation", NIH (RO1-HL48287), (40% effort), \$877,511; direct costs, 7/1/96-6/30/01.

- B. Co-Investigator, "Monocyte Chemoattractant Protein 1 in Corpus Luteum", NIH (RO1-HD33478), (10% effort), \$651,215; direct costs, 5/1/96-4/30/00 (Landis Keyes, Ph.D., Department of Physiology, University of Michigan, Principal Investigator).

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 the membrane attack complex (MAC) of complement, reactive oxygen intermediates, and reactive nitrogen intermediates.
- C. Pathophysiologic role of oxidants in uremia and its complications.
- D. Role of MCP-1 in luteolysis (collaboration with Landis Keyes, Ph.D., Department of Physiology, University of Michigan Medical School).
- E. Ischemia-reperfusion injury in perinatal rat brain (collaboration with Faye Silverstein, M.D., Departments of Pediatrics and Neurology, University of Michigan Medical School).
- F. Pathogenesis of Loxosceles reclusa venom-induced cell activation (collaboration with Hernan Gomez, M.D., Department of Surgery, Section of Emergency Medicine, University of Michigan, Ann Arbor, Michigan).

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL:

- A. Member, Executive Committee, University of Michigan Medical School, 1999-present.
- B. Finance Subcommittee, advisory to Faculty Group Practice (FGP) Executive Committee, 1997-present.
- C. Member, Task Force on Faculty Administrative Services, advisory to FGP Executive Committee and Chief Executive Officer, University of Michigan Health System, 1998-present.
- D. Member, Professional Billing Compliance Committee, 1999-present.
- E. Dean's Advisory Committee (ad hoc substitute for Dr. Peter Ward), 1994-present.
- F. 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.
- B. Member, Test Committee for Clinical Pathology, American Board of Pathology, 1999-present.
- C. Vice-Chair, Area Committee on Clinical Immunology and Ligand Assays, National Committee for Clinical Laboratory Standards, 1999-2000.
- D. Member, Council for Diagnostic Immunology and Molecular Pathology, American Society of Clinical Pathologists, 1998-present.
- E. Ad hoc Reviewer: Clinical Trials Review Committee; National Institutes of Health (NHBLI); Bethesda, MD; October 24-25, 1999.
- F. Ad hoc Reviewer; Clinical Trials Review Committee; National Institutes of Health (NHBLI); Bethesda, MD; June 26, 2000.

V. INVITED LECTURES/SEMINARS:

1. Warren JS: Diagnosis and classification of systemic vasculitis: role of the clinical laboratory. ASCP National Meeting, Orlando, FL, September 27, 1999.
2. Warren JS: Diagnostic immunology and molecular pathology update. ANA and ENA testing – beyond screening. ASCP National Meeting, Washington, D.C., October 29, 1999.
3. Warren JS: Induction of chemokine expression by the distal complement components C8 and C9 requires GPI-linked surface molecules. Indiana University, Indianapolis, IN, May 22, 2000.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Gomez HF, Miller MJ, Desai A, Warren JS: Loxosceles spider venom induces the production of α and β chemokines; Implications for the pathogenesis of dermonecrotic arachnidism. *Inflammation* 23:207-215, 1999.
2. Bowen JM, Towns R, Warren JS, Keyes PL: Luteal regression in the normally cycling rat: apoptosis, monocyte chemoattractant protein-1, and inflammatory cell involvement. *Biol Reproduction* 60:740-746, 1999.
3. Desai A, Miller MJ, Gomez HF, Warren JS: Loxosceles deserta spider venom induces NF- κ B-dependent chemokine production by endothelial cells. *J Toxicol Clin Toxicol* 37:447-456, 1999.
4. Desai A, Huang X, Warren JS: Intracellular glutathione redox status modulates MCP-1 expression in pulmonary granulomatous vasculitis. *Lab Invest* 79:837-847, 1999.
5. Gomez HF, Miller MJ, Trachy JW, Marks RM, Warren JS: Intradermal anti-Loxosceles Fab fragments attenuate dermonecrotic arachnidism. *Acad Emerg Med* 6:1195-1202, 1999.
6. Desai A, Lankford HA, Warren JS: Loxosceles deserta spider venom induces the expression of vascular endothelial growth factor (VEGF) in keratinocytes. *Inflammation* (in press).
7. Galasso JM, Miller MJ, Cowell RM, Harrison JK, Warren JS, Silverstein FS: Acute excitotoxic injury induces expression of monocyte chemoattractant protein-1 and its receptor CCR2 in neonatal rat brain. *Exp Neurol* (in press).
8. Miller MJ, Gomez HF, Snyder R, Warren JS: Detection of Loxosceles venom in lesional hair shafts and skin: application of a specific immunoassay to identify dermonecrotic arachnidism. *J Emerg Med* (in press).
9. Gomez HF, Miller MJ, Waggener MW, Warren JS: Antigenic cross-reactivity of venoms from medically important North American spider species. *Toxicon* (in press).
10. Galasso JM, Liu YQ, Szaflarski J, Warren JS, Silverstein FS: Monocyte chemoattractant protein-1 is a mediator of acute excitotoxic injury in neonatal rat brain. *Neuroscience* (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. Townson DH, Bowen JM, Remick DG, Warren JS, Keyes PL: The effect of dexamethasone on prolactin-induced luteolysis and macrophage infiltration in corpora lutea of the rat. *Biol Reproduction* (submitted).
3. Miller MJ, Desai A, Huang X, Warren JS: Nitric oxide modulates monocyte chemoattractant protein-1 expression in endothelial cells: implications for the pathogenesis of glucan-induced granulomatous vasculitis. *Am J Pathol* (submitted).
4. 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).
5. Desai A, Lankford HA, Warren JS: Homocysteine augments cytokine-induced chemokine expression in human vascular smooth muscle cells: implications for atherogenesis. *Circulation* (submitted).

BOOKS/CHAPTERS IN BOOKS:

1. Warren JS, Ward PA: The inflammatory response, in Beutler E, Lichtman MA, Collier BS, Kipps TJ and Seligsohn U (eds.) *Williams' Hematology*, 6th Edition, McGraw-Hill, New York, NY, (in press).
2. 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).
3. Warren JS: Immunodeficiency disease, in McClatchey KD (ed.) *Clinical Laboratory Medicine*, 2nd Edition, Lippincott Williams and Wilkins, Philadelphia, PA, (in press).

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

None

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

I. CLINICAL ACTIVITIES:

- A. Obtained Board Certification in Clinical Pathology, American Board of Pathology.

II. TEACHING ACTIVITIES:

- A. Graduate students:
Responsible during the current academic year for teaching activities for the following:
Path 581, 2 lectures
- B. Undergraduate students:
None.
- C. Postdoctoral fellows:
Research mentor to John R. Vance, Ph.D.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Disposition of DNA Double-Strand Breaks Among Multiple Pathways of Repair: Implications for Chromosomal Rearrangements in Cancer", American Cancer Society Institutional Research Grant 990733 (0%, no salary support), \$12,500/year (\$12,500/one year), 2/1/2000-1/31/2001.
- B. 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.
- C. Mentor, "Lung Immunopathology Training" (Training Grant), NIH 5T32HL07517, John R. Vance, Ph.D., postdoctoral fellow, 3/1/2000-2/28/2002.

PENDING:

- A. Principal Investigator, "End Processing in DNA Double-Strand Break Repair", NIH/NCI 1 R01 CA90911-01 (35%), \$225,000/year (\$1,025,000/five years), 4/1/2001-3/31/2006.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Faculty candidate interviews; Robert Hevner.

MEDICAL SCHOOL/HOSPITAL:

- A. Member, MSTP Career Advisory Panel.

UNIVERSITY OF MICHIGAN:

- A. None.

REGIONAL AND NATIONAL:

- A. None.

V. OTHER RELEVANT ACTIVITIES:

Member, College of American Pathologists.
Member, American Association for Cancer Research.
Member, Association for Molecular Pathology.
Member, American Society for Investigative Pathology.
Member, Genetics Society of America.

EDITORIAL BOARDS:

- A. None.

HONORS AND AWARDS

Biological Sciences Scholars Program, University of Michigan.
Pew Scholars Program in the Biomedical Sciences, Pew Charitable Trusts.

PATENTS:

- A. None.

INVITED LECTURES/SEMINARS:

1. Invited Speaker, "Interacting Pathways of DNA Double-Strand Break Repair in Genome Maintenance", Nephrology Basic Science Seminar, University of Michigan, April 4, 2000.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Wilson TE, Lieber MR. Efficient processing of DNA ends during yeast nonhomologous end-joining: evidence for a DNA polymerase β (*POLA*)-dependent pathway. *J. Biol Chem*; 274 (33):23599-609 (1999).

BOOKS/CHAPTERS IN BOOKS:

None.

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

1. Karathanasis E, Fathepure S, Wilson TE: Factors affecting the outcome of competition between homologous and nonhomologous DNA double-strand break repair. Accepted for presentation at Yeast Genetics and Molecular Biology, Genetics Society of America, Seattle, WA, July 2000.

SECTION REPORTS

ANATOMIC PATHOLOGY

DIVISION OF ANATOMIC PATHOLOGY

ANNUAL REPORT 1 JULY 1999 - 30 JUNE 2000

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 and educational programs of the University of Michigan Health System, Medical School, and University. This past year two new faculty have joined the Division, Drs. Douglas Fullen and Jing Liu. These faculty bring additional expertise in general surgical pathology as well as sub-specialty expertise in dermatopathology and cytology, 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, 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. Five additional house officers completed fellowship training in blood bank/transfusion medicine, cytopathology, urologic pathology, and hematopathology. All found excellent positions in sub-specialty (4) and research (1) fellowships, private practice (1), and academic faculty positions (2).

Overall, the in-house clinical activity in surgical pathology and cytopathology increased by approximately 8%. The dermatopathology service realized a 12% increase in cases. While the Medical Center Cost Efficiency Program (CEP) resulted in consolidation of laboratory functions and enhanced productivity in several areas over the past several years, any significant additional reductions in laboratory support in the context of increasing service volumes will negatively impact our ability to provide high quality service. Limitations in laboratory and faculty office space also hinder our ability to maximize productivity and accommodate the increased volumes and requests for expanded diagnostic services. However, re-design with expansion of the frozen section area is underway and will allow the department to support increased activity of the surgery service. New renovations to the autopsy suite were completed and have enhanced productivity, service to families, and increased safety. The efforts of Kathy Smiezney (Anatomic Pathology Laboratory Supervisor), Jim Pecott (Cytology Laboratory Supervisor) and all laboratory staff continue to be instrumental in successfully implementing the CEP and maintaining the high quality of our Anatomic Pathology laboratory services.

With continued expansion of clinical services and academic programs as well as future faculty retirements, it will be necessary in the next three years to recruit additional faculty especially in areas of pediatrics pathology, general surgical pathology, urologic pathology, cardiovascular pathology and cytopathology. 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 1999 - 30 JUNE 2000

I. Timely Completion of Autopsy Reports:

We continue to emphasize the timely completion of our autopsies. In order to meet the needs of the families, and our clinical colleagues, we are making a concerted effort to complete our cases within 60 days. All cases were completed in 90 days and virtually all were finished within 60 days for the 1999-2000 year. While this is a significant improvement, there has been some reduction in the number of cases completed within the allotted time frame. This will be addressed by having the dieners contact each faculty member each week when their name appears on the late list.

Time Interval	% completed in 60 days	% completed in 90 days	# of Autopsies
1995-96	40	58	541
1996- 97	64	89	565
1997- 98	64	85	424
1998-99	96	100	350
1999-2000	91	100	295

II. Autopsy percentage

We have begun to determine the autopsy rate by clinical service in the hospital. This is prepared every month by Paulette Dozier's staff. This information is provided to the departmental chairs on a regular basis. The autopsy percentage is for the 1999-2000 year is listed below.

Medicine 24%
Surgery 19%
Pediatrics 35%
Other services 42%

Hospital total 25%

III Conferences

At the request of the Bone Marrow Transplantation (BMT) team we have initiated a quarterly conference to review the deaths from this unit. This conference has been very well attended by the BMT physicians and has helped the autopsy service better define procedures for diagnosing graft versus host disease after death.

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. Locally, the hospital continues to provide medical

Department of Pathology Annual Report

examiner investigators for the University Hospital who are available on a 24 hour basis. Several house officers participate in this activity.

V. Statistics:

This covers the time period July 1, 1999 to June 30, 2000.

Total number of autopsies performed	295
Hospital autopsies	258
Medical examiner autopsies	37

Daniel G. Remick, M.D.

CYTOPATHOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY ANNUAL REPORT

1 JULY 1999 – 30 JUNE 2000

Total gynecologic specimens for the year were 42,756, representing a 12.4% increase over the previous year. Non-gynecologic specimens numbered 5,872; a 5.2% increase from last year. Fine needle aspirations performed by cytopathologists (an indicator of fine needle aspiration clinic usage in the cancer center) totaled 304 for the current year, a 13.4% increase over the previous fiscal year. In addition, the number of deep-seated fine needle aspirates performed in the Radiology Department or the endoscopy directed aspirates totaled 394 this year, representing a 20% increase over last year. The laboratory achieved the turnaround time for non-gynecologic specimens within 24-48 hours, and the Papanicolaou smears within 5 to 7 working days throughout most of the year despite the increased number of specimens accessioned. However, the last few months were very difficult in the Cytopathology laboratory due to the departure of one of the laboratory assistants and delayed replacement of the laboratory assistant for two months. To remedy the situation, the cytotechnologists were removed from screening on a rotating basis to assist with specimen preparation, resulting in prolonged GYN turnaround time from 5 to 22 working days. Non-gynecologic specimen turnaround time remained at 24 to 48 hours through this difficult period. Fortunately, with the appointment of Doug Mullen and additional measures putting the screening as top priority, our turnaround time is catching up to the normal range.

Mr. James Pecott was re-appointed President, as was Mrs. Jenise Gyurnek, Vice President, and Mr. Brian Smola, Web Chairman for the Michigan Society of Cytology. Drs. Afify and Al-Khafaji received their added qualification in Cytopathology in August of 1999.

Our fellowship program continued to be highly successful. Dr. Jing Liu completed her training with distinction, and joined our faculty as an instructor. Dr. Jim McConnell received his added qualification in Cytopathology in August of 1999. The changes in the fellowship structure and residency training in Cytopathology proved to be very successful with positive feedback from both the fellow and residents. Our Cytopathology fellowship had its first re-accreditation inspection in August and we are awaiting the board response. The department continues its active role in assessing the new technology and the ThinPrep technology for preparation of gynecologic smears was introduced this year. All cytopathologists and three cytotechnologists received formal training and were certified by Cytoc Corporation.

The Cytopathology Section had excellent representation at national and international meetings with several posters presented. Dr. Michael also presented a national teleconference sponsored by the American Society of Cytology and two teleconferences sponsored by the Teleconference Network of Texas. Dr. Naylor presented the "History of the Papanicolaou Smear" at the American Society of Cytopathology Annual Meeting. Dr. Al-Khafaji received first prize for "Best Website for Advancing the Field of Pathology through Computer Technology" at the AP III, 4th Annual Meeting.

Mr. James Pecott continued his involvement with the V500 Program. At this stage, the build is complete and we are currently editing some of the dictionaries, and troubleshooting cases (running from front to back), and SnoMed has been checked for cytology diagnostic entries. We are awaiting the suggested OCD on installation before the billing can be completed.

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

DERMATOPATHOLOGY SERVICE
DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 – 30 JUNE 2000

The Dermatopathology Service receives diagnostic case material from six different sources: (1) UMMC (ID) cases; (2) outside contractual (MD) cases; (3) personal consultation cases (LO, SU, HE); (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).

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

	1997-1998	1998-1999	1999-2000
ID	5,225	5,865	6,246
MD	4,138	4,401	6,153
TD	919	1,228	1,275
Consultation service	473	595	796

Once again, the Dermatopathology Service has seen tremendous growth with a significant increase in volume. Dermatopathology cases represented 32% of total surgical pathology accessions, excluding consultation cases. Overall, there has been a 40% increase in MD cases, a 34% increase in consultation cases, a 6% increase in ID cases and a 4% increase in TD cases. The total number of cases for 1999-2000 was 14,470, a 20% increase when compared to the previous year. During the past two years, the increase in volume has been a staggering 32% and has been seen by 1.6 FTE.

The Dermatopathology Service continues its extensive involvement with residency and medical student education in the Department of Dermatology. Teaching activities include weekly formal didactic sessions, weekly diagnostic conference, instruction at the microscope during signout, and active participation in the MSII Dermatology Sequence and Dermatopathology Laboratory. Dr. Lyndon Su has also significantly expanded formal dermatopathology didactic sessions for our pathology residents.

We continue our active involvement in the University of Michigan Multidisciplinary Melanoma Clinic (MDMC) and Tumor Board (bi-weekly). This is currently 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.

We are pleased that Dr Douglas Fullen will be joining the Pathology Department as our third dermatopathologist in July, 2000. Dr. Fullen received his residency training in anatomic and clinical

Department of Pathology Annual Report

pathology at the University of Michigan and completed subspecialty training in dermatopathology at Cornell University.

Lori Lowe, M.D.
Director, Dermatopathology Service

NEUROPATHOLOGY SERVICE
DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
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Dr. Mila Blaivas, Ms. Constance J. D'Amato, and Dr. Paul E. McKeever contributed to the Neuropathology Service.

I. CLINICAL ACTIVITIES:

1. There were over 1700 neurosurgical cases examined this year. There were over 250 personal consult cases.
2. The Diagnostic Unit of the Neuropathology Core Laboratory of the MADRC processed 61 dementia brain cases. Of these 61 brains, 41 were MADRC hospital cases, 12 were neurology hospital patients, and 3 were from the Michigan Dementia Postmortem Network Program.
3. There were 312 muscle biopsies, 50 with electron microscopy. There were 75 peripheral nerve biopsies. There were 10-teased fiber preparations and 75 with electron microscopy. (Some muscle and nerve biopsies were done as personal consult cases.) 17 skin or non-muscle nerve tissue examined with electron microscopy.
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 130 difficult neuro-oncology cases.
6. There are two neuropathology quality assurance meetings scheduled each month, and attended as necessary.

II. TEACHING ACTIVITIES:

1. Medical Students: This year the neuropathology faculty taught in the eight week 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 include periodic CME accredited conferences where Neurology, monthly CME accredited Rheumatology Pathology Grand Rounds and occasional CPC conferences, twice monthly Continuing Medical Education (CME) accredited conferences where all biopsies are presented and interpreted; a weekly conference where abnormal brains are examined (including one week for dementia cases) with all clinicians invited; weekly nerve and muscle conferences accredited for CME, monthly nerve and muscle biopsy conference accredited for CME; 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 are provided to neurological and neurosurgical house staff on clinico-pathological correlations.

4. Electives: Pathology, Neurosurgery, Neurology Residents and a UROP student chose elective rotations in the Neuropathology Section.
5. A pathologist from Nagoya, Japan spent a month in Neuropathology Service.

III. RESEARCH ACTIVITIES:

1. D. Blaivas and Ms. D'Amato provided neuropathology support for MADRC. Ms. D'Amato is Core Coordinator of the Diagnostic Neuropathology Core of MADRC. She has also been working with two investigators who are supported by the 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 and Timothy Laing; Urethral musculature in aging and incontinence, with John DeLancey group, Obstetrics/Gynecology; Rat model in brain tumors growth and treatment, with Brian Ross, Philip Kish; Neurosurgery, (Grant application submitted); Quantitative evaluation of temporal lobectomy/hippocampectomy cases with Dr Erasmo Passarois group; Collaboration with EMG group, Radiology (S. Gebarski, M.D.) Neurology, Neuro-oncology, Pediatric Genetics, Pulmonary/Internal medicine and Ophthalmology on various projects.
3. Dr. McKeever and associates are determining the extent and cause of differences in gene product expression in brain tumors. They are assessing the predictive value of markers in brain tumor specimens. He is principal investigator on a NIH funded project studying the prognostic potential of MIB-1 proliferation marker on brain tumors. He is the study pathologist for a multi-institutional transferrin receptor targeted glioma treatment protocol, and for a multi-institutional study of treatments of low-grade astrocytoma, the latter as study pathologist for the Children's Cancer Group.
4. 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.
5. Collaboration with Neurology, Michigan State University, The Alzheimer's Association, Henry Ford Hospital, Butterworth and Blodgett Hospitals, and Wayne State University has established a registry for Alzheimer's disease and other dementias and degenerative diseases.

**SPECIAL STUDIES LABORATORY
(CLINICAL IMMUNOHISTOCHEMISTRY, IMMUNOFLUORESCENCE AND NEURAL AND
MUSCULAR STUDIES)**

**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 July 1999—30 June 2000**

INTRODUCTION

The Clinical Immunohistochemistry Laboratory continues to grow and provide excellent high quality service. During the last year there has been a 10.4% increase in case load which has translated into a 4.8% increase in total slide volume for the clinical laboratory compared to last year.

CLINICAL IMMUNOHISTOCHEMISTRY

Year end figures show that the average number of slides per day has increased from 108 slides/day to 113.5 slides/day which represents a 4.8% increase. In January we added a third automated immunostainer to the laboratory. This newest immunostainer is from Dako Corporation. It has enabled us to perform the FDA approved stain for Her-2/ neu. To fully utilize the instrument we have also worked up several antibodies that were still on the bench and these are now done on the Dako stainer. These antibodies include Progesterone receptor, CMV, Hepatitis Surface and Core, Kappa , Lambda , C-kit, Uroplakin and E-Cadherin. This has enabled us to decrease turnaround time for these antibodies.

We have been able to implement two cost cutting measures this year in the Clinical Immunohistochemistry Laboratory. The first measure involved the removal of hematoxylin counterstain from the automated Ventana. By performing the counterstain procedure on the bench we have saved time as well as money. A Ventana dispenser of hematoxylin will stain 250 slides and will cost \$55.00. This works out to a yearly cost of \$6,417. By using stain from Surgipath and staining manually the annual cost is now \$100 thus saving \$6,300 per year. The second cost cutting measure involved changing our Progesterone staining procedure. We have switched from Abbott Laboratories to Dako Corporation. for our antibody. This has decreased the cost per slide from \$19.44/slide to \$0.44/slide. Estimating the volume of Progesterone slides per year to be 625 this would account for an annual savings of \$11,875.

We have added several new antibodies to our ordering menu this year including C-kit, Uroplakin, E-Cadherin, and Myogenin. Several more are in the developmental stage.

As always, the current number of 4 FTEs is working at full capacity to keep up with the ever increasing workload for Clinical Immunohistochemistry as well as the other two areas of the lab. The year 2000 has shown a substantial increase in all three work areas. Additionally, we continue to help the Cancer Center Immunohistochemical Laboratory with the completion of USCAP projects which must be completed in July and August . This usually involves hundreds of slides to stain.

We continue to do well on our biannual CAP Proficiency testing. We have scored 100% for this fiscal year. We did not have a CAP inspection this year but we have continued to prepare for 2001, including making inventory of all of our chemicals and their expiration dates as mandated by CAP.

Looking to the future, we are anxiously waiting for Ventana to release their new automated In Situ instrument. This is projected to be released in the fall of 2000 and we will get one into the lab as soon as possible.

Other goals for the lab include keeping up with the newest antibodies that make the University of Michigan a cutting edge institution and working to further streamline current procedures.

IMMUNOFLUORESCENCE

Under the direction of Dr. Killen and Dr. Johnson, the Immunofluorescence laboratory continues to stain skin, heart and renal biopsies using the automated Ventana immunostainer. Our case load has continued to increase in all areas of this service. Renal biopsies raised from 405 to 447 a 10% increase, and skins and hearts from 162 to 210 a 30% increase.

NEURAL AND MUSCULAR STUDIES

This service under the direction of Dr. Blaiwas has maintained its current patient load with 255 muscles and 64 nerves. After an educational visit to the Mayo Clinic, we have added three additional stains to the current muscle panel. These have aided in the diagnostic process and thus aided in patient care. Finally, we have taken over the nerve teasing service that was previously done in another area. There are usually 12 nerve teasings done each year and each one takes approx. four hours to do.

CONCLUSION

The clinical load in all services continues to increase in the year 2000. Our future goals include establishing In Situ hybridization in the lab and continuing with quality improvement and increased efficiency.

Alaa Afify, M.D.

Director of Clinical Immunohistochemistry for Anatomic Pathology

Kristina Fields B.S.

Senior Clinical Special Studies Laboratory

SURGICAL PATHOLOGY SERVICE

**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

The Surgical Pathology Division continues to grow at an unprecedented rate having experienced a 10% increase in volume compared to last year. This year, the Division saw 36,527 in-house surgical specimens, 3,689 personal consults, and 10,773 M-Lab cases. Any further increase in volume will require increases in personnel and space, including the addition of a pathology assistant.

Our ever-increasing volume has provided many new challenges to the histology laboratory and despite superb guidance and leadership from Ms. Kathy Smieszny, the lab has suffered from employee turnover. Not only is our volume higher than most nearby histology laboratories, but our pay scale is not competitive enough to retain valued employees. We have planned a new and enlarged gross room/frozen section area that we hope will be completed in the upcoming year. The scheduled increase in the number of operating rooms coupled with the increase in operating room hours and the increased demand for tissue procurement make the enlargement of this area of critical importance.

Our surgical pathology fellowship program continues to be highly successful. All of this year's graduates are staying on at the medical center for additional fellowship training.

Despite our dramatically increasing service commitments, the Surgical Pathology Division has maintained its productivity at national meetings. At this year's USCAP meeting, our faculty presented 20 abstracts, directed a short course, and moderated or spoke at numerous companion meetings/subspecialty conferences. Our faculty also taught several courses at the annual ASCP meeting. In addition to these accomplishments, the level of NIH funding among the surgical pathology faculty has never been higher.

As always, it is an honor to work with such outstanding colleagues.

Joel K. Greenson, M.D.
Director, Surgical Pathology

CLINICAL PATHOLOGY

DIVISION OF CLINICAL PATHOLOGY

**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

The Clinical Laboratories have continued to provide excellent, full-spectrum service (more than 800 different laboratory analyses) as the UMHS has expanded both its volume and scope in ambulatory care activities, experienced growth in several major clinical programs, and promoted the expansion of M-Care activities. Substantial effort has been directed towards 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, software conversion to a Y2K-compliant clinical laboratory information system, and most recently, initiation of implementation of the Cerner Millennium software upgrade. In 1999-00 the Clinical Laboratories again performed more than 3 million billable analyses, supported a wide array of clinical and research programs, and added or replaced numerous 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 self-inspection in May, 2000. 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 UMHS-wide compliance with new HCFA-mandated rules related to documentation of justification for laboratory test ordering. In conjunction with the UMHS Compliance Committee, a system-wide requirement for the entry of ICD-9 diagnosis codes on all ambulatory test requests was realized. (Ambulatory patients account for approximately 50% of all clinical laboratory test volume). In conjunction with institutional enforcement of this mandate, the Division has endeavored to improve test ordering through redesign and control of requisition content, direct cooperation with ambulatory care management, improvement of collection of demographic information at the point of test ordering, and the provision of periodic audit data for use by the Division, the Compliance Committee, and the Clinical Departments.

An additional initiative was an intensified effort to more tightly regulate esoteric test utilization and sendouts. We expect this effort to result in substantial additional direct cost savings.

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 approximately 50% each. 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 on informatics, logistics, and cost-containment.

Faculty and laboratory staff participated in a wide variety of intramural and extramural educational programs during 1999-00. For instance, the 27th annual Blood Bank/Transfusion Medicine course and the 18th Laboratory Information Systems (LIS) course were again well attended, making them among the most visible courses of their kinds in the United States. The May LIS course was again linked to a highly successful Executive Briefing which 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 updated in 1998-99. In keeping with a thematic approach, the 1999-00 version solidified the four rotation blocks and place 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 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**

**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

PATIENT CARE:

Blood component utilization manifested a modest increase during this year, likely related to increased surgical activity. Moreover, the transfusion service was engaged in study of new program additions and modifications related to posttransfusion infectious disease and variations in component provision.

There was increased reliance on peripheral blood progenitor cells, rather than bone marrow, for transplantation purposes. This had a pronounced impact on both the transfusion and apheresis area and on the main laboratory of the blood bank.

The transfusion and apheresis area continues to require more space for additional cell separators as well as for patient accommodation. Not only is space needed for support of the BMT program through peripheral blood progenitor cell procurement, but also for therapeutic apheresis procedures. Indications for the latter were primarily TTP, hyperviscosity syndromes, leukapheresis for leukemic patients, heart transplant acute rejection and neurologic diseases, especially myasthenia gravis and CIDP. Without additional space the laboratory is unable to implement liposorber apheresis for lowering of LDL cholesterol in patients with homozygous familial hypercholesterolemia. The current space compromises patient privacy and patient safety. The main laboratory space also is inadequate for bone marrow or stem cell processing, as the technical staff of the latter area has tripled and the number of liquid nitrogen storage tanks has increased in relation to the number of harvesting procedures.

Prestorage leukocyte reduction of all cellular blood components is in the process of national assessment. This will have several benefits for our patients, including reduction of febrile nonhemolytic transfusion reactions, reduction of alloimmunization to platelet transfusions with reduced incidence of refractoriness to platelet transfusions, and reduced transfusion-related cytomegalovirus infection.

The laboratory staff participated in editing the newest biannual edition of Blood Transfusion Policies and Standard Practices. This is distributed to all physicians and students, as well as patient care units, involved in blood transfusion.

Members of the staff actively supported interdepartmental functions. Mrs. Hoffman worked closely with the Bone Marrow Transplantation Program and also coordinated orders for HLA-matched Single Donor Platelets from our blood suppliers. The reference laboratory section supported the Department of Obstetrics and Gynecology. Ms. Butch led the Quality Management program of the clinical laboratories of the Department of Pathology and Mrs. Stoe chaired the Department's Laboratory Safety Committee

EDUCATIONAL ACTIVITIES:

The medical, technical and nursing staffs of the Blood Bank/Transfusion Service were actively involved in educational programs within the institution and at regional and national meetings. A two-week Blood Bank orientation program for Pathology House Officers was presented on two occasions during the year so that this information would be provided in proximity to the individual's lab rotation. Three hours of lecture were provided for the sophomore medical class in the context of the hematology segment, and a presentation on Transfusion Medicine was provided for the medical student senior elective course in Pharmacology and Therapeutics. Hematology fellows in internal medicine and Pediatrics rotated through the laboratory. In addition, the laboratory supported the medical technology training programs of Eastern Michigan University and Ferris State College.

Members of the Blood Bank medical and technical staffs were active participants in the biweekly hematology teaching conference. The 27th annual postgraduate course, "Current Topics in Blood Banking", was held on June 7-98, 2000. The course, under the direction of Mr. Judd, attracted over 150 technologists and physicians from throughout the United States and Canada. 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. Members of the Blood Bank and Transfusion Service staff presented Workshops on a variety of topics, and Ms. Butch, Mr. Judd, Mr. Meade and Drs. Oberman and Davenport participated in the plenary sessions of the symposium.

Blood Bank and Transfusion Service medical and technical staff participated in the annual meeting of the American Association of Blood Banks, providing poster presentations, courses and lectures covering a variety of topics. In addition, members of the laboratory presented invited lectures to a variety of regional and national blood banking organizations and state societies.

Aside from the lectures and presentations noted in the individual faculty reports of Mr. Judd and Drs. Davenport and Oberman, Mrs. Stoe, Mrs. Dake, Mrs. Hoffman, Mr. Meade and Ms. Butch were active in educational programs of the University of Michigan Health Center and the Michigan Association of Blood Banks. Ms. Butch was particularly active on the national scene, lecturing and authoring papers on computer utilization in the blood bank, preadmission testing of patients' blood and comparison of the infectious disease risk of plasma components.

PROFESSIONAL ACTIVITIES:

Members of the Blood Bank and Transfusion Service medical and technical staffs were active at the regional and national levels. Dr. Oberman served as Associate Editor of TRANSFUSION and was a member of the Research Initiatives Committee of the American Association of Blood Banks. Ms. Butch also served on the Information Systems Committee and on the Chief Technologist's Forum of the American Association of Blood Banks. In addition, she chaired the ad hoc coding and reimbursement committee of the NCCLS Committee on clinical Laboratory Standards. She served on the Michigan Association of Blood banks program committee and on the International Council on Commonality in Blood Banking Automation. Dr. Davenport serves on the Scientific Section of the American Association of Blood Banks and is a member of the editorial board of TRANSFUSION. In addition, members of the technical staff participated in the Inspection and Accreditation program of the American

Association of Blood Banks. Dr. Oberman's, Dr. Davenport's, and Mr. Judd's activities are further noted in their individual faculty reports.

RESEARCH ACTIVITIES:

The individual reports of Drs. Oberman, Davenport and a Mr. Judd record their publications and investigative efforts related to Blood Banking and Transfusion Medicine.

Harold A. Oberman, M.D.
Director, Blood Bank and Transfusion Service

CLINICAL CYTOGENETICS LABORATORY

**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

The Clinical Cytogenetics Laboratory experienced stable case volume (approximately 2100 cases overall; 1100 bone marrow, 600 prenatal, and 400 constitutional genetics) in 1999-2000. The laboratory underwent profound change as the long-time director, Dr. Susan Sheldon departed in late 1999. Dr. Thomas Glover (University of Michigan, Departments of Human Genetics and Pediatrics) rejoined the laboratory as a consultant and ably provided clinical expertise, signout coverage, and important linkage to the clinical departments in the areas of prenatal and constitutional genetics. Bone marrow cases were prepared within the laboratory and sent out to another consultant, Dr. Daniel VanDyke at the Henry Ford Hospital. The laboratory staff and supervisor, Ms. Beth Cox, are to be commended for their adaptability and professionalism during a difficult transition period. Plans to upgrade the armamentarium and infrastructure of the laboratory were launched in preparation for the arrival of a permanent director.

Following a national search, Dr. Diane Roulston (University of Chicago) was successfully recruited to direct the laboratory beginning in August, 2000. Dr. Roulston is a very highly recommended, broadly-trained, and experienced cytogeneticist with particular expertise in the area of hematologic oncology. The Department of Pathology is very enthusiastic about the arrival of Dr. Roulston and the prospect of future progress in this important area.

Jeffrey S. Warren, M.D.
Interim Director, Clinical Cytogenetics

**COMBINED HEMATOLOGY LABORATORY
(HEMATOLOGY, BONE MARROW, FLOW CYTOMETRY, COAGULATION)**

**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1999-30 JUNE 2000**

I. HEMATOLOGY AND BONE MARROW:

- A. Completed implementation of automated slidemaker module for Beckman-Coulter GenS instruments in main hematology laboratory, including automated rules/decision system establishing criteria for making of slides from blood samples.
- B. The automated rules system instituted in January 2000 resulted in an ability to verify more automated differential counts. As a result, manual differential counts (a test order generated within the laboratory only after failure of automated differential counts) decreased by over 9% to 46,862 for FY 2000.
- C. Began beta-testing of automated slide staining system in collaboration with Beckman-Coulter, Inc.
- D. Refined criteria for review of blood and body fluid smears by pathologist.
- E. Successfully implemented cross-training program between bone marrow and flow cytometry laboratories, allowing for flexible service coverage while maintaining specialized expertise.
- F. Extended bone marrow laboratory service coverage to 6 p.m. daily.
- G. Test volumes continue to increase in the hematology laboratory:

Test	Volume Fiscal 2000	Change from Previous year
Complete blood counts	317,353	+6.4%
Body fluid samples	6,578	+11.2%
Urine samples	48,415	+0.4%
Erythrocyte Sedimentation Rates	11,554	+8.8%
Reticulocyte counts	4,849	-0.5%
Bone marrow aspirates	1,620	+3.3%
Bone core biopsies	1,651	-1.5%
Other specialized heme testing (sickle prep, Kleihauer-Betke, osmotic frag., inulin screen, etc.)	1,433	+6.4%

II. FLOW CYTOMETRY

The Clinical Flow Cytometry section processed about 5600 specimens, a volume increase of 5% from the previous year. The percentage change in volume (relative to 1998-99) is listed below for each of the major test categories:

<u>Test Category</u>	<u>Change from 1998-99</u>
Immunodeficiency monitoring	+10%
CD34 stem cell counts	-7%
Chronic leukemia/lymphoma phenotyping	+6%
Acute leukemia phenotyping	+53%
T-cell subset monitoring in organ transplant recipients	+27%
Antiplatelet antibody testing	-45%

M-Labs referrals continue to comprise a substantial part of the work volume, including 31% of all acute leukemia immunophenotyping panels, 46% of all chronic leukemia/lymphoma panels, and 37% of all immunodeficiency monitoring.

Attending staff continue to triage all requests for leukemia/lymphoma immunophenotyping, with cancellation of unwarranted requests. Of the 2049 specimens submitted for leukemia/lymphoma immunophenotyping, pathologist review lead to cancellation of 702 of these requests.

Leukemia and lymphoma profiles are the most labor-intensive tests offered by the laboratory, and test volumes continue to show substantial growth. Because of this increased workload and the reduction of 0.5 FTE in technical staffing during the past year, the research, development and teaching functions of the lab have been largely curtailed.

III. COAGULATION

A. Laboratory Staffing:

1. The laboratory has been fully integrated with the staff of the main hematology laboratory.
2. 4.0 FTEs perform coagulation laboratory studies. One individual is full-time; 4.5 individuals are part-time.
3. Having an extra 0.5 individual has improved coverage of the laboratory. At present, there are two individuals performing specialized coagulation testing daily in the laboratory.

B. New Programs in the Laboratory:

1. The training and implementation of anti-factor Xa assays for heparin and any low molecular weight heparin (enoxaparin, dalteparin, danaparoid sodium) is on a routine basis, 24 h/day for patients. These assays provide a great service to patient care in the hospital.
2. The entire specialized coagulation staff has been trained on the Behring BCS coagulation equipment. It has been decided to obtain two more of these instruments for all routine and specialized coagulation testing. Implementation of this new instrumentation awaits approval of the contract from hospital administration.
3. Ristocetin cofactor and von Willebrand factor antigen assays have been adapted to the BCS instrumentation.

4. All Ecarin clotting time was established for a patient for intraoperative monitoring of hirudin during cardiopulmonary bypass surgery.
 5. The prekallikrein coagulant assay has been established on the BCS instrument.
 6. The dilute russel viper venom time (DRVVT) and tissue thromboplastin inhibition (TTI) time have been established on the BCS instrument.
 7. The chromogenic assays for protein C, antithrombin III, and plasminogen have been established on the BCS instrument, but their full implementation awaits the presence of a back-up BCS instrument in the coagulation laboratory.
- C. Laboratory Growth:
1. University of Michigan Hospitals System.
Overall, there was a 4.9% increase in U of M Hospital laboratory activity in the Coagulation Laboratory from fiscal year '98 to an annualized fiscal year '99. Total gross revenues increase were not made available to me at this writing. There was an across-the-board increase in all categories of tests measured.
 2. M-Labs Activity:
There was 28.6% increase in net M-Labs activity in specialized coagulation testing from fiscal year '98 to '99. In fiscal year '98, combined net patient and client incomes were \$164,614. In fiscal year '99, combined net patient and client incomes were \$211,671. The revenue distribution was equalized over the breath of assays performed in the laboratory.

IV. TEACHING AND RESEARCH ACTIVITIES: Hematology/Flow Cytometry

- A. Received approval from ACGME for 2nd accredited hematopathology fellowship position.
- B. Pathology house officers, hematopathology fellows and fellows from Pediatrics and Hematology/Oncology participated in the following activities:
 1. Daily review of abnormal blood smears, body fluids, joint crystals, bone marrow smears, bone marrow biopsies, lymph node biopsies, splenectomies, lymphomas/leukemias and extramedullary myeloid cell tumors.
 2. Correlation of morphology with cytochemical stains, immunohistochemistry, flow cytometry, gene rearrangement and electron microscopy.
 3. Formal teaching conferences.
 4. Review of cases for the Southwestern Oncology Group.
 5. Weekly review of cases for Lymphoma Conference.
 6. Biweekly review of cases for Leukemia Conference.
 7. Biweekly review of cases for Non-Neoplastic Hematology Conference.
- C. Training and continuing education for medical technologists.
- D. Formal lectures and laboratories for freshman and sophomore medical students.

TEACHING AND RESEARCH ACTIVITIES: Coagulation Laboratory

- A. Pathology House Officers: Residents participated in a twice-a-week sign out rounds of specialized coagulation testing with the laboratory director. Each resident became an

active participant in this activity by actually dictating the report. Pathology residents have been assigned first call for questions and problems related to the Coagulation Laboratory.

- B. Wrote two spectrum articles on coagulation testing to be distributed to M-Labs clients.

V. GOALS FOR 2000-2001: Hematology/Flow Cytometry

- A. Examine feasibility of shifting formal administrative responsibility for bone marrow aspirate interpretation to department of pathology, with concomitant expansion of bone marrow laboratory service.
- B. Critically assess state of automated technology in the hematology laboratory and examine potential for new technologies to increase automation and productivity while adhering to strict regulatory standards.
- C. Examine alternative methods for data archiving (flow cytometry) and physician report generation (hematology/flow cytometry) in effort to improve technologists' efficiency.

GOALS FOR 2000-2001: Coagulation Laboratory

- A. Have the hospital sign the Behring-Dade contract so that two additional BCS instruments can be obtained and full implementation of the BCS system be done.
- B. Assay development.
 - 1. Adapt new chromogenic assays (antithrombin III, protein C, plasminogen)) to new equipment and reagents.
 - 2. Develop a chromogenic assay for prekallikrein.
 - 3. Develop ELISA-based D-Dimer assay using the BCS equipment.
 - 4. Consider developing a chromogenic assay for heparin cofactor II.
 - 5. Consider developing a von Willebrand factor-collagen binding assay.
 - 6. Consider developing a panel of flow cytometry tests for various platelet membrane receptors.
 - 7. Consider upgrading platelet aggregation and secretion studies to include platelet responses to arachidonic acid and γ -thrombin
- C. Teaching.
 - 1. Continue to integrate Pathology Residents more into the operation of the Coagulation Laboratory.
 - 2. Provide Pathology Residents with Hemostasis/Thrombosis synopsis as a teaching tool for this field.
 - 3. Consider developing a fellowship in Clinical Pathology for hemostasis testing.

Bertram Schnitzer, M.D.
Director, Hematopathology

Lloyd M. Stoolman, M.D.
Co-Director, Flow Cytometry

William G. Finn, M.D.
Director, Hematology Laboratory

Alvin Schmaier, M.D.
Director, Coagulation Laboratory

Charles W. Ross, M.D.
Director, Flow Cytometry

HISTOCOMPATIBILITY AND IMMUNOGENETICS LABORATORY

**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

CLINICAL ACTIVITIES:

Clinical activity of the Histocompatibility Laboratory remains stable. The volume of activity makes the Laboratory one of the ten busiest in the country.

DNA-based class I DNA typing joined high resolution Class II DNA typing as our primary technique.

TEACHING ACTIVITIES:

Members of the Laboratory were involved in the teaching activities of the Laboratory and were effective in their work. The laboratory was involved in the instruction of pathology residents, allergy fellows, renal fellows and postdoctoral candidates from the Department of Hematology. Dr. James Baker stepped down as Laboratory Director and become a Laboratory Consultant. Dr. Baker has continued to play an active role in the Laboratory and in ASHI. Ms. Cynthia Schall, the Laboratory Supervisor, was involved in teaching review courses at ASHI, Henry Ford Hospital, and the University of Michigan. She also oversaw the activities for residents in the Laboratory.

NEW GOALS:

The goal for the Laboratory is to continue address the demand for more complex services from the transplant programs. The transplant programs have become more active in their clinical and basic research activities.

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

CLINICAL IMMUNOPATHOLOGY LABORATORY

**DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 1999- 30 JUNE 2000**

I. OVERVIEW:

The Immunopathology Laboratory performed more than 60,000 analyses in 1999-00. Anthony A. Killeen, M.D., Ph.D. and John Lowe, M.D. provided invaluable service to the laboratory in the interpretation of protein electrophoresis studies. Kent Johnson, M.D., Paul Killen, M.D., Ph.D., and Dr. Killeen 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 complement assays, and in the measurement of plasma viscosity.

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 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 participated in the department-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**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000****I. CLINICAL ACTIVITIES:**

Accommodating increased specimen volumes and implementing new testing methods to meet the requirements of the clinical services were the primary issues addressed during the year. Requests for *Chlamydia trachomatis* / *Neisseria gonorrhoeae* DNA, CMV antigenemia, EBV antibody and VZV shell vial culture all increased > 20% compared to last year's volume. Overall, the volume increased 8%. To meet the clinical needs of our hepatitis patients, qualitative and quantitative HCV molecular tests were evaluated and implemented. Amplified products are shared with Molecular Diagnostics to provide HCV genotyping results. Due to changing nosocomial antimicrobial resistance, Microbiology implemented additional testing methods to detect ESBL-producing isolates and cooperated with Infection Control Services to provide patient surveillance cultures in targeted patient care units to determine the rate of vancomycin- resistance in enterococci. Test utilization data was reviewed and, as a result of low test volume, several tests were discontinued (e.g., mycoplasma/ureaplasma culture) or modified (e.g., dermatophyte screening, anaerobe identification). Much effort was applied to the Millennium project (computer upgrade); this effort will be intensified during the next year.

II. RESEARCH ACTIVITIES:

Several clinical investigations were completed during the fiscal year, two of which resulted in poster presentations at national meetings. The recovery rate of fecal parasites was assessed comparing two different collection kits, one of which is composed of a single vial contained no mercury salts. The results allowed us to switch to the new vial. We also evaluated a new media for the isolation of *Haemophilus influenzae* from the sputum of CF patients and subsequently added this media to our culture setup. Studies comparing a new CMV DNA blood assay with the standard antigenemia assay were successfully completed. Preliminary studies on antifungal susceptibility testing were conducted which will be expanded. We successfully completed a multiyear project with School of Public Health investigators to assess the incidence of sexually transmitted diseases present in a select patient population in Indonesia by performing molecular diagnostic tests on collected specimens. We also cooperated with the pulmonary research team and with various infectious disease section investigators to collect, test and ship isolates for new antimicrobial clinical investigations.

III. TEACHING ACTIVITIES:

All laboratory personnel continue to provide periodic instruction to Pathology House Officers and Infectious Disease Fellows and residents on diagnostic procedures used in the Microbiology/Virology Laboratories. Infectious Disease Laboratory rounds are held each weekday during which staff members and assigned Pathology House Officers interact with ID team members to answer questions, demonstrate laboratory diagnostic procedures and discuss interesting findings.

Numerous in-service education programs were held during the course of the year with individual technologists and Pathology House Officers giving presentations to staff members.

IV. PROFESSIONAL DEVELOPMENT:

Both supervisors and most Sr. Technologists attended one or more regional and national scientific meetings during the year and presented their posters at these meetings. Several other staff members attended regional meetings of interest. In addition, the Laboratory subscribed to two audioconference programs which provided a total of 15 conferences during the year that were available to all staff members and Pathology House Officers as part of our ongoing CME program.

Carl L. Pierson, Ph.D., Director
Clinical Microbiology/Virology Laboratories

PHLEBOTOMY SERVICES AND CENTRAL DISTRIBUTION

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 1999 - 30 JUNE 2000

Fiscal year 2000 continued to challenge Phlebotomy Services and Central Distribution. Staff have been involved in several projects having institutional implications, including:

- a. CIS Project:
Phlebotomy and Central Distribution staff have been involved in designing the new order entry system for the university hospital. Meetings were held with IBM project developers to outline current process and needs of the areas.
- b. ICD-9 Code Project
Shellie Campbell, Outpatient Phlebotomy Supervisor is intricately involved in institutional efforts to get improved compliance in the providing of appropriate ICD-9 codes for ordered pathology tests. Shellie and her staff has been involved in monitoring compliance rates and providing feedback to service users. Shellie is responsible for providing the institutional task force with feedback on pathology issues.
- c. Pathology Y2K Operational Contingency Plan:
Y2K planning for the pathology department required extensive involvement of Central Distribution and Phlebotomy Services. An elaborate plan was developed to ensure Pathology and Radiology service levels for critical tasks to patient care units would meet service needs. Central Distribution and Phlebotomy Services staff were critical components of the plan that would facilitate the collection, documentation, testing, and result reporting of pathology and radiology results in the event that Y2K problems appeared. Staff were supportive and were involved in a dress rehearsal of the process prior to December 31, 1999 to evaluate the plan. Staff also volunteered for on-call coverage in case the situation warranted additional assistance.
- d. Newborn Screen Testing Protocol:
Central Distribution was involved in developing a process for documenting test results in the Cerner LIS for newborn metabolic disorder screening tests. The process involved developing protocols for ordering, transporting and resulting tests being performed by the Michigan Department of Community Health. This assures the consistent availability of test results to clinicians.
- e. Millennium Testing/Validation:
Staff is currently involved in testing and validating the new Cerner LIS software. Collection lists and orders entry processes are areas of concentration. Testing, a validation plan, and educational materials for staff training are being generated.
- f. Mental Health Program Support:
Inpatient Phlebotomy has expanded phlebotomy service support for the University of Michigan Hospitals and Health Centers mental health program. The support was expanded from 2 days of phlebotomy service at offsite locations to 2 additional days at locations in Ypsilanti, Michigan.

Operationally, Central Distribution and Phlebotomy Services have been impacted by increased test volumes (see below) and significantly by staff turnover. Management has been successful in motivating staff to handle the increased volumes with current staff. Efforts have also been made to minimize staff turnover and loss the detrimental loss of departmental expertise. These efforts have included developing a new training relationship between Central Distribution and the Inpatient Training Supervisor (Marie Moorhouse). This effort is expected to streamline the training process and allow for a more effective training program as a result of involving staff level preceptors in the training of new staff. A high priority for the coming year will be to address the issues related to retention of trained staff.

Outpatient Phlebotomy Services:

Outpatient phlebotomy services continued to provide services at two blood drawing stations in the Taubman Center and at one blood drawing station in the Cancer/Geriatric Center. Service was expanded in the Taubman Center to support the later clinic hours on Monday evenings until 8:00 PM. In addition, the supervisors and staff are directly involved in monitoring and coaching facility service users on the appropriate ICD-9 codes submitted in order to optimally bill for service provided.

Outpatient patient volumes have increased 5% (6495 patients) over fiscal year 1999.

	III. Outpatient Phlebotomy Test Volumes		
	FY 1999	FY 2000	% Change
<i>Cancer/Geriatric Center</i>	40647	41324	1.67%
<i>Taubman Drawing Stations</i>	87763	93581	6.63%
TOTAL	128410	134905	5.06%

In addition to this added volume, the number of pediatric patients seen in the Taubman Drawing Stations increased 6% (467 patients) over fiscal year 1999. The number of patients drawn through an indwelling catheter also increased in the Cancer/Geriatric Center Drawing Station nearly 8% (328 patients), over fiscal year 1999. This volume of patients-a total of 795 -may not appears significant at first glance, but both pediatric and indwelling catheter draws are much more time consuming and contribute to lower staff productivity.

Inpatient Phlebotomy Services:

Inpatient Phlebotomy Services continue to be responsible for specimen collection and specimen transport in Mott Children's Hospital and the University Hospital.

Calculated patient draws have increased nearly 5.5% (6936 patients) over fiscal year 1999.

INPATIENT PHLEBOTOMY VOLUMES			
	FY 1999	FY 2000	% Change
<i>Inpatient Phlebotomy</i>	126645	133581	5.48%

This additional volume was supported with existing staff. Inpatient Phlebotomy staff are also responsible for covering the phlebotomy responsibility for the UMHHS Mental Health program. Staff have also been involved in enhancing the audit trail for specimens being transported from the Mott Children's Hospital operating room. They are responsible for better documenting accountability for specimen pickup from the location.

Central Distribution:

Central Distribution continues to be a critical area, related to the receipt of specimens by Department of Pathology laboratories. Specimen volumes continue to increase and specimen handling duties have become more demanding. The increase in Send Out Laboratory volumes are a clear indication of overall volume demands in Central Distribution.

SEND OUT LABORATORY TEST VOLUMES			
	<i>FY 1999</i>	<i>FY 2000</i>	<i>% Change</i>
<i>Mayo Medical Laboratories</i>	25411	30444	19.81%
<i>Miscellaneous Laboratories</i>	4144	5687	37.23%
TOTAL	29555	36131	22.25%

Send Out test volumes have increased 22% over fiscal year 1999. This increased volume has been handled by current staffing levels.

A relatively high employee turn over rate of nearly 40% continues to plague the department. Significant effort will be addressing this issue which negatively impacts the departments ability to improve service levels.

-Harry Neusius

GENERAL PATHOLOGY

**ELECTRON MICROSCOPY SERVICE
DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

We have successfully transitioned virtually all of the diagnostic electron microscopy cases to digital images, an evolutionary process with multiple steps. The first was the installation of the new electron microscope with the digital camera. Once this had been installed, there was the necessary learning curve by the staff to understand how to manipulate the digital images for optimal clarity and quality. All of the images were printed for review by the pathologist. The next step was the installation of the network hardware, and allocation of sufficient network space for the digital images. At the present time, the cases are placed on the network for diagnosis by the pathologist and virtually no cases are printed. We have successfully negotiated with the manufacturer to obtain additional copies of the image viewing software at no charge. This will be installed for the pathologists who routinely use electron microscopy.

We are presently in the position of being able to eliminate all prints from processing the cases. This will result in significant savings of commodities since we will not need to purchase film, photochemicals or photographic paper. Another important consideration is a substantial time savings since the electron microscopy staff will no longer require time in the darkroom to develop and process the photographic prints. As originally outlined five years ago, we believe that we will be able to accommodate the increased workload with no increase in personnel.

The commodity savings can be roughly estimated based on the volume of work performed. The average number of prints which are generated per case is approximately 16, at cost of \$1.50 per print. This results in a commodity cost saving of approximately \$13,300 per year ($\$1.50/\text{print} \times 16 \text{ prints/case} \times 555 \text{ cases}$ which go all the way to prints).

In the past five years there has been a 46 percent increase in the number of cases processed by the electron microscopy lab (an additional 243 cases per year compared to 1994-95). Despite this increase there has been no increase in the number of staff assigned to the electron microscopy service, and as detailed above there should be an actual reduction in the commodity costs. This highlights the wise investment by the Department in the new electron microscope with its state-of-the-art digital technology.

The construction of electron microscopy lab was completed this year. With the termination of these renovations and the new digital electron microscope, the Department is well positioned to accommodate the service needs for the future.

The table below indicates the volume of cases processed by the electron microscopy service during the past academic year. The % increase is relative to the 1994-95 year.

	94-95	95-96	96-97	97-98	98-99	99-00	% increase
Nerve/Muscle	252	275	308	258	275	290	15%
Renal	256	276	333	320	349	379	48%
Other	23	43	20	55	100	105	356%

Department of Pathology Annual Report

Total	531	594	661	669	724	774	46%
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This is a breakdown of the cases. Inside cases are from University Hospital patients while outside cases are from outside the hospital. Prints indicate that the specimen was processed completely, all the way to generating the prints.

	Inside	Outside	Submitted	Prints	% processed
Renal	176	202	379	330	87%
Nerve/Muscle	174	116	290	120	41%

Daniel G. Remick, M.D.
Director, Electron Microscopy Service

M-LABS**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000****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 two hospitals and to the University of Michigan Health Service. MLabs is the primary reference laboratory and provides full esoteric laboratory testing to another 11 hospitals in Michigan and northern Ohio. MLabs does esoteric testing for a regional medical laboratory and a local pharmaceutical firm. MLabs also now provides daily courier service and receives laboratory testing from 23 Integrated Health Associates' practices, 52 MCare physician offices/clinics, 7 UMHS physician office acquisitions, and a nearby correctional facility.

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".
 - Clinical trials for clinical research organizations and pharmaceutical firms.
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 FY2000, MLabs added 12 new physician offices and specialty service practices to our client list. The majority of these were related to our contract to provide coverage to M-Care patients. Some were for specialty services, and a few were UMHS acquired practices.
- A new hospital full reference laboratory account.
- One contract for a university health service was terminated.
- MLabs submitted 3 proposals to prospective major clients during FY2000. Of these, one was rejected, one was accepted, and one is pending.

IV. BILLING ACTIVITY:

- Net billings for anatomic pathology increased by 20.5% and those for clinical pathology increased by 21.8%. Total combined billing increased by 21.4%.

V. MANAGED CARE ACTIVITIES:

In the last three years, MLabs has contracted with M-Care 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 M-Care over its previous fee for service contracts for these lab services.

In FY2000, MLabs has engaged in negotiations with M-Care to develop a full-risk outpatient lab agreement for all groups and products to become effective 9/1/2000 (current target date).

MLabs continues to manage the M-Care/MLabs agreement for Medicare HMO Program (Senior Plan). Five subcontracts are in place.

We prepare quarterly QA reports on lab services for M-Care's QA department and have conducted a Physician Satisfaction Survey for MLabs subcontracted providers and reported the results to M-Care. We assist M-Care with resolution of laboratory service issues.

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 70 member laboratories located in Michigan. At the end of FY99, JVHL had contracts for laboratory services with 10 managed care organizations, including Select Care, and a subcontract with MLabs for MCare work. In FY2000, JVHL, in association with GLN, successfully bid on the outpatient laboratory work for the state-wide Blue Care Network HMO contract. The contract has been signed and the services are being successfully delivered to BCN enrollees.

MLabs is represented on JVHL's Executive committee, QA committee, operations committee and its "elab's" committee, and on the GLN steering committee as well as on the marketing, operations, and medical staff committees of these 2 networks.

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 make our services run smoothly, particularly in the area of phlebotomy. 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 will continue our efforts to try to obtain esoteric laboratory testing from the two hospital laboratory networks (JVHL and GLM) to which we belong. Other areas of potential growth are laboratory work from clinical trials.

IX. IMPEDIMENTS:

Serving the burgeoning physician office market has reduced the ability of MLabs marketing personnel to provide services to our hospital clients and markedly reduced our ability to investigate and solicit business from prospective new markets. Additional personnel will be required to reestablish growth of revenue-producing markets.

As 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. 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 1999- 30 JUNE 2000

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, emerging technology allowing for detailed gene expression studies of cell lines, animal models, and tissues (including pathologic specimens). With the recent 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 a year 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 10K human cDNA chip containing over 4500 known named genes and numerous ESTs (expressed sequence tags). Similarly, we have produced an 8K rat

cDNA chip and are in the process of establishing a 5K mouse cDNA chip. All cDNA microarrays have undergone validation and quality control and are currently being functionally tested using samples obtained from various labs including those of Dr. Peter Ward (Pathology); Dr. Mark Rubin (Pathology), Dr. Steven Ethier (Cancer Center) and Dr. Chinnaiyan. DNA microarray projects currently underway involve profiling global gene expression in apoptosis, inflammation, sepsis, prostate cancer, and breast cancer.

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.

During the first year of operation, the personnel of the Pathology Microarray Laboratory have:

1. Obtained the expertise required to produce and analyze cDNA microarrays
2. Identified and assembled the infrastructure necessary to produce high-density microarrays.
3. Established several databases and a web site (<http://www.pathology.med.umich.edu/achinnaiyanlab/>) to handle microarray data.
4. Processed over 10,000 human cDNA clones and 8,000 rat cDNA clones for the generation of a 10K human cDNA chip and an 8K rat cDNA chip.
5. In collaboration with various laboratories at the University, generated RNA samples and labeled cDNA probes for analysis on microarrays.
6. Developed and validated a biochip-based protein microarray system for the large-scale analysis of antibody and protein levels in cell lines, body fluids, and tissues.

III. FUTURE GOALS:

The future goals of the Pathology Microarray Lab in the next calendar year include:

1. Supporting the research funding applications of Pathology faculty.
2. Publishing data using microarray technology in peer-reviewed journals to establish the Department in the fast moving field of genomics/proteomics.
3. Construct a 5K mouse cDNA chip so that tissues from mouse models can be profiled.
4. Expand the rat and human DNA chips to include additional cDNA clones
5. Develop and utilize protein microarray technology to answer biologically important questions
6. Train post-doctoral fellows and students in making and using micorarrays.

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. Arun Sreekumar, a Research Fellow, was involved in developing the protein microarray platform. Ralph Fenn, an M4 medical student, did a research rotation in the lab where he began to construct a 5K mouse cDNA chip.

Nick Kannan, an undergraduate student, rotated through the lab and gained experience in basic cell and molecular biology.

Arul M. Chinnaiyan, M.D., Ph.D.
Director, Pathology Research Microarray Laboratory

PATHOLOGY DATA SYSTEMS

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 1999 - 30 JUNE 2000

The following is a list of some of the major accomplishments of Pathology Data Systems (PDS) personnel during the past academic year, July 1999 through June 2000:

Installation of Cerner PathNet V.500 (Millennium)

- After an extended software development period caused by the complexity of the new client-server architecture and the complexity/volume of our clinical laboratories, we are not ramping up for the Millennium go-live which will take place at the end of this calendar year or in early 2001.
- This new system will provide multiple strategic advantages for the laboratories, not the least of which will be enhanced functionality and the storage of test results in a relational Oracle database, which will allow easy replication to test results to multiple other distributed clinical databases such as the CDR.

Y2K Efforts

- An extraordinary amount of energy during the latter months of 1999 were devoted to remediation of the Cerner Classic system (the currently installed LIS) to a Y2K-ready status. In addition to these efforts, additional work was required to ensure that the LIS would be able to exchange data with various other hospital information systems with which it was interfaced. As a result of all of these efforts, we entered the new year and millennium with little or no disruption to hospital and lab work processes.

Near-Total Elimination of Hardcopy Laboratory Report Printing

- As a result of the wide availability of test results on PathNet and on the Clinical Data Repository/CareWeb, to which test results are replicated from PathNet, and a desire by the health system leadership to move to a paperless electronic medical record system, printing of the “purple” outpatient and the “pink” inpatient hardcopy medical record reports was terminated on April 21, 2000. The only hardcopy reports remaining are the white outpatient reports delivered directly to physicians in clinics for their review. The elimination of most hardcopy lab reports has resulted in substantial savings in terms of the cost of paper, labor, and computer cycles for the print jobs within PDS.

Personnel Cutbacks and Budgetary Reduction in Pathology Data Systems

- Due to a deficit in the UMHS operating budget, a decision was made to reduce the MCIT and the PDS operating budget by 20%. In order to accommodate to a budget cut of this magnitude, MCIT was completely reorganized during the Spring of 2000, resulting in a number of RIFs. A substantial number of open positions were also given up within MCIT. PDS had to reorganize itself and cut back on some services in order to respond to the 20% cut

in personnel. Extreme efforts were taken to cushion the labs from major disruptions in work flow as a result of these cutbacks.

MCIT Reorganization

- As a result of the MCIT reorganization, Ancillary Information Systems (the organizational unit to which Pathology Data Systems previously belonged) has been renamed Clinical Support Information Systems. This latter business unit has been expanded from the previous ancillary systems (Pathology, Radiology, Radiation Oncology, Pharmacy) by the addition of the Office of Clinical Affairs (OCA), Graduate Medical Education (GME), Telemedicine, Medical Information Systems (MIS), Food and Nutrition Services (FANS), and Social Work.
- Bruce Friedman has been appointed as the director of renamed Clinical Support Information Systems and Steve Gendler has been appointed as the Manager of the new unit. Both will continue to manage Pathology Data Systems as part of their large range of duties.

Ancillary Desktop Software Image Distribution

- MCIT has mounted a major effort to standardize the software “image” that is loaded on PCs distributed throughout the enterprise. This will help to lower the maintenance costs for these devices.
- Steve Gendler and others in PDS have been very active in this enterprise effort, using SMS software to assist in the automated distribution of the standardized software image to workstations distributed throughout the health system. The software “image” developed and adopted by the ancillary information systems has been adopted as one of the major images to be distributed throughout the health system.

Adoption of the Remedy Help Desk System in Pathology

- As part of the standardization of work processes, PDS and Pathology have adopted the Remedy system for the generation of trouble-tickets to document calls coming into the Help Desk about computer, information system, and networking problems.
- The adoption of this enterprise-wide system is critical for gauging hot-spots and high-maintenance information systems on the basis of the complaints that are documented in the Remedy system. This is also a more organized way to address customer complaints.

Planning for the Clinical Information System (CIS)

- UMHS has begun a huge effort, in collaboration with IBM, to develop initially an order-entry and result-reporting system that will evolve into a electronic medical record (EMR). This is called the CIS (clinical information system) project. During the latter part of 1999, a broad range of laboratory personnel were very active in participating in the CIS planning process for the labs, developing highly detailed flow diagrams of lab processes, including lab test ordering and result reporting, which will eventually be automated.
- The first process to be automated under the CIS will be inpatient pharmacy, starting with the physician order and culminating in the passing of medications to patients, documented by having the nurse check the patient identification and the name of the medication by scanning a bar code on both the patient ID wrist band and on the medication being administered.
- Neither Pathology or Radiology will have interfaces built initially from the CIS system to the back-end radiology or pathology information systems, although the physicians will be

presented with a computer screen for ordering both radiology procedures and lab tests. Initially, lab and radiology orders generated by computer screen selections will generate hardcopy requisitions, albeit printed rather than hand-written as before.

- Following the successful deployment of end-to-end pharmacy ordering and documentation of passing of medications to patients, both pathology and radiology processes will be totally automated in the second phase of CIS with electronic interfaces being built between the CIS and the pathology and radiology information systems.

Study of New Cross-Departmental Inexpensive Data Storage Systems

- PDS personnel are actively studying the possibility of installing relatively inexpensive data storage that could be utilized and managed cooperatively by multiple departments.
- Such storage, often referred to as a Storage Area Network (SAN) will be a marked improvement from the current system with little accommodation to inexpensive archival storage for data that are not actively being used.

Educational Activities

- The eighteenth annual Symposium on Automated Information Management in The Clinical Laboratory (AIMCL) was presented at the Towsley Center on May 31, June 1-2, 2000. There were 28 vendors in attendance at the meeting and more than 300 paid registrants.
- The meeting for the first time attracted an international contingent, with more than 30 registrants from abroad.
- This post-graduate CME meeting is the most important of its kind in the country relating to laboratory computing with a special focus on clinical pathology and laboratory management.

Bruce A. Friedman, M.D.
Laboratory Director

**ANN ARBOR VA HEALTH SYSTEM
PATHOLOGY AND LABORATORY MEDICINE SERVICE**

**DEPARTMENT OF PATHOLOGY - UNIVERSITY OF MICHIGAN
ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

INTRODUCTION:

The VA Ann Arbor Healthcare System (VAAHS) is a tertiary health care provider for veterans partnered with the University of Michigan. 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 VAAHS Pathology and Laboratory Medicine Service maintains a close relationship with the University Department of Pathology at every level. All pathologists in the VAAHS have medical school appointments and participate in university activities in a manner similar to other departmental sections. Recruitment for VAAHS 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 Chief, Pathology and Laboratory Medicine Service at the VAAHS is a voting member of the Dean's Committee. The VAAHS laboratory was inspected in 2000 and retains full accreditation by the College of American Pathologists. The VAAHS was inspected by the JCAHO in 1997 and is currently fully accredited. The medical center's Decentralized Hospital Commuter System (*Vista*) is recognized as the most fully integrated medical information system. It combines all of the clinical management of the patient and is moving toward a totally computerized patient medical record by 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 major reorganization thrusts are underway at the VAAHS. 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). This includes 23,000 sq. ft for the complete relocation of Pathology and Laboratory Medicine. 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 is moving 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, decrease in fee basis (send-out) testing to nonVA clinical labs and an increase in the workload in Ann Arbor VAAHS's anatomic pathology and the clinical labs.

ANATOMICAL PATHOLOGY:

- A. **Surgical Pathology:** 5,029 surgical cases have been accessioned and reported during this period of time. This continues 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. Morbidity and Mortality Conferences are held jointly by Pathology and Medicine Service. Weekly Urology Case Review Conference is held by Dr. Murphy. The residents assigned to autopsy and surgical pathology are primary presenters in these 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 review and analysis of frozen sections, amended diagnoses, surgical appropriateness, turnaround times and follow-up of positive diagnoses, within the medical center. The surgical and cytology readout stations are fully integrated into a hospital digital imaging system. Routine images are captured on cases of interest. These are particularly useful in presentations to clinical teams reviewing specimens from their patients with the pathology staff and residents.
- B. **Autopsy Pathology:** 30 autopsies were performed during this year that is a rate of approximately 23% of in-patient deaths. Assigned residents perform the autopsies, prepare the pathologic diagnosis, and present the case in conference to the staff pathologists and other residents. The resident cuts and otherwise prepares the tissue for the preparation of slides and then reviews them and makes a microscopic diagnosis. These steps are supervised by staff pathologists who permit a gradual increase in independence for the resident with increased experience. Several autopsies performed at the VAAHS are also presented at the extended Gross Conference at the University. The Department of Veterans Affairs has issued a new 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. The VAAHS has participated in the last two national VA Autopsy Conferences, to learn mechanisms to more fully realize the values from autopsies and increase the number of next of kin who grant permissions for autopsy.
- C. **Cytology:** 2245 cases were examined and diagnosed during this period. This is a slight decrease over the last reporting year. Nearly all of the cytology specimens are of a diagnostic type, with very few screening cytologies. Although there is not a formal rotation in cytology within the VAAHS the cytological material is readily available and is used as correlative information for surgical and autopsy pathology. This laboratory is a VA "Center of Excellence" in cytology. They process and report all of the cytology specimens from one neighboring VA and the GYN cases from another.

- D. Electron Microscopy: 295 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 VAAHS research investigators. An elective rotation is available for pathology residents in electron microscopy. In other rotations the electron microscope findings are used to complement surgical or cytopathology diagnoses. This VAAHS is a "Center of Excellence" in electron microscopy and serves as consultant to other VA Medical Centers, to the University of Michigan Medical Center and to other hospitals by contract.

CLINICAL PATHOLOGY:

During the period of this report 877,266 clinical pathology procedures were performed in the laboratory. In Chemistry there were 719,183; in Hematology 92,787; in Urinalysis 12,135, in Microbiology 29,090, and in Blood Bank 24,571. These figures represent productivity (billable) rather than weighted test numbers. Each of these numbers has increased slightly during this year, with the exception of the hematology procedures. 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 and Chamberlain oversee the clinical laboratory and make available interesting and pertinent clinical laboratory information available to residents as desired. Clinical Pathology data is available to pathology residents via computer for their information in surgical pathology, autopsy pathology, and elective rotations.

EDUCATION AND TEACHING:

In surgical pathology the staff pathologists provide one-to-one mentoring during the surgical sign out time. In addition, there is a surgical pathology conference approximately every other week and an autopsy conference with the entire staff following each autopsy. Residents join in continuing educational activities in histopathology and cytopathology from the AFIP, CAP, and ASCP. Because of the closeness of various sections of the laboratory there is frequent consultation among the pathologists and the residents are involved throughout. Since the VAAHS is physically close to the University, the residents are expected to attend the appropriate teaching conferences at the University as well. The staff contribute to the laboratory and lecture portions of the second year medical students at the University of Michigan. The VA staff also 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 Dr. Beals and Dr. Chensue have made presentations at international pathology conferences. Dr. Chensue prepared a CD training program for transfusion reactions.

RESEARCH:

The specific efforts of the pathology staff are included on individual reports. Dr. Stephen Chensue has a strong funded research program. 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 the Research Building of the VAAHS. All staff participate in various clinical studies and collaborate with a variety of investigators. The laboratory in general

serves the VAAHS 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. Beals serves as Chief of Service. 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, and the 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 VA Medical Center the pathology staff members serve on all major committees involved with institutional policies and procedures. Dr. Beals has been designated by the National Veterans Administration to oversee anatomic pathology within Department of Veterans Affairs Medical Centers. He has been instrumental in developing policies and procedures related to anatomic pathology within the Department of Veterans Affairs. Dr. Beals has been permanently appointed Director of Pathology for the VA nationally. He is also the Chief Consultant Officer for the Diagnostic Service Strategic Healthcare Group. In this capacity serving as the leader of the Veteran Health Administration National Headquarters' administrative oversight of: Pathology, Clinical Laboratories, Radiology and Nuclear Medicine.

The VA's National Cytopathology Proficiency Program's administrative offices are located in the VAAHS. 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. It has entered its fifth year with more than 721 circulating glass cytology smears and 401 participating pathologist.

SUMMARY:

The Department of Veterans Affairs Medical Center 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 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.

Ted F. Beals, M.D.
Chief, Pathology and Laboratory Medicine Service
Ann Arbor VA Health System

UNIVERSITY OF MICHIGAN/PFIZER JOINT COLLABORATIVE RESEARCH PROGRAM

**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

The Department of Pathology for several years has enjoyed a close professional relationship with the Drug Safety Evaluation Department at Pfizer Global Pharmaceutical Research Division in Ann Arbor. This Department was headed by Dr. Felix De la Iglesia who holds a faculty appointment in the Department. Dr. De la Iglesia is a world expert on hepatic injury as well as morphometric analysis of cellular injury. For several years we have collaborated scientifically with Dr. de la Iglesia and his colleagues and these efforts resulted in several publications.

These scientific interactions have been greatly expanded recently in the context of increased collaborations between the University and Pfizer. Pfizer and the University of Michigan, Department of Pathology entered into a formal agreement with Pfizer and colleagues to enhance joint research interests. One good example is the organization of the Genomic Pathology Research Laboratory. Other examples include combined positions for postdoctoral fellowship programs as well as providing research opportunities for individuals at both institutions. Currently, there is one Parke-Davis postdoctoral fellow in the Department and several fellows from the Department collaborate with Pfizer colleagues including working at the Pfizer Laboratories. In terms of faculty interactions, there are scientific collaborations with Pfizer and the Department of Pathology dealing with models of inflammation and the regulation of the inflammatory response. There are also collaborations dealing with the mechanisms of apoptosis and DNA alteration in diseases such as SLE as well as morphometric evaluation of tissue injury. These interactions were mutually beneficial and have provided both groups with expertise that was not otherwise available at only one or the other of the two institutions. These collaborations have been mutually reinforcing as demonstrated by joint seminars between the two laboratories and joint efforts in recruitment of postdoctoral fellows and minority graduates.

These interactions are expected to continue and to increase in the future in view of the integration of the former Parke-Davis Laboratories into the Pfizer global research initiatives. This industrial-academic partnership represents an important model for collaborative experimental research that will be jointly and intellectually beneficial. This collaboration also provides an important opportunity for University graduates and fellows to the needs of the pharmaceutical industry.

Felix A. de la Iglesia, M.D.

Peter A. Ward, M.D.

FINANCE AND ADMINISTRATION

DIVISION OF FINANCE AND ADMINISTRATION

**DEPARTMENT OF PATHOLOGY - UNIVERSITY OF MICHIGAN
ANNUAL DEPARTMENTAL REPORT
1 JULY 1999 - 30 JUNE 2000**

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 four 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 Finance and Administration
Beverly J. Smith, Administrative Assistant, Personnel and Payroll functions

Clinical Faculty Offices & Surgical Pathology Transcription, University Hospitals:

Deborah Day Jansen, Administrative Coordinator
Paulette Dozier, Office Manager, Surgical Pathology Transcription
Yolande Salwoski, Office Manager, Clinical Faculty Offices

B. OFFICE OF ACADEMIC AND BUSINESS AFFAIRS - MEDICAL SCHOOL:

David R. Golden, Clinical Department Associate
Michael Hulbert-Shearon, Student Services Assistant
John E. Harris, Financial Analyst
Catherine A. Niemiec, Administrative Assistant

C. OFFICE OF THE CHAIRMAN

Laura D. Blythe, Staff Assistant
Janice M. Kitley, Executive Secretary

D. PATHOLOGY PHOTOGRAPHY AND IMAGING CENTER:

Mark V. Deming, Senior Photographer
Elizabeth Horn, Photographer

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 2000.

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. Mr. Morrow assisted with the planning, development and implementation of the Operations Improvement Program (expense reduction) for the Pathology Laboratories as mandated by Hospital and Health Centers Administration and the Operations Improvement Group. For Fiscal Year 2000, we were required to develop payroll reductions in the amount of \$787,460.

Administrative Coordinator: This individual, Mrs. Deborah Day Jansen, assists with the coordination of intra and inter laboratory activities for the anatomic and clinical pathology laboratories which include coordination of required proficiency tests; coordination of inspections required for continuing certification or licensure by the JCAH, CAP and MDPH; serving as departmental representative on the Safety Committee, Disaster Committee and as United Way Chairperson. In addition, the Administrative Coordinator acts as the liaison with the Hospital for renovation projects and coordinates the publication of the Pathology Laboratories Handbook (including on-line version) and 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 unit collected through her innovated marketing techniques. Mrs. Jansen also manages the Surgical Transcription Unit and has assumed responsibility for the Faculty Office Suite in the Hospitals. During this fiscal year we experienced turnover within the surgical transcription group and this event, coupled with increased activity has caused a delay in processing surgical pathology reports.

Billing Coordinator: This individual, Ms. Nancy Coray, is responsible for processing and auditing all laboratory charges (gross charges of approximately \$155,001,852), 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 effective 08/01/00 resulting in changes to our Health Quest Billing System, timeliness of charges should improve dramatically.

Administrative Assistant: This individual, Mrs. Beverly Smith, oversees the clerical support staff assigned to the Administrative Support Center and coordinates personnel and payroll paperwork for all Pathology Laboratories staff (approximately 407 FTEs). The Administrative Assistant 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, personnel and payroll paperwork 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 the payroll and personnel issues for staff in the Medical School (approximately 134 FTEs) including our House Officer Program (24 FTEs), Post Doctoral Fellows (39 FTEs), as well as supervising the staff in the Pathology Education Office.

OFFICE OF THE CHAIRMAN:

In addition to providing support to the Chairman, Mrs. Janice Kitley 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 faculty appointments, payroll, and personnel issues, and travel and dues reimbursements.

PATHOLOGY PHOTOGRAPHY AND IMAGING UNIT:

Mr. Mark Deming is the photographer assigned to this service. He is responsible for a variety of photography and imaging services including those requested by our clinical and research faculty and house officer staff. A major renovation including installation of a fire door and card swipe security system was completed in FY 2000. The renovation will allow us to move to digital photography.

SUMMARY OF FINANCIAL DATA:

1. Grants and Contracts and Other Accounts:

266 active grants, contracts and other accounts

Department of Pathology Annual Report

Total Extramural Direct Expenditures:	\$7,953,225
Indirect Extramural Research Expenditures:	<u>\$3,611,872</u>
Total Sponsored Projects:	\$11,565,097

2. Faculty Group Practice Plan - Pathology:

Number of charge entries:	136,396
Gross Billings - Anatomic and Clinical Pathology:	\$18,378,610
Collections	\$ 6,795,037
Part A Payment:	\$ 2,579,000
M-Labs Net Transfer:	\$ 926,000

3. All Fund Expenditures – Medical School

Compensation & Benefits	\$14,417,456
Commodities & Other Costs	<u>\$ 9,818,624</u>
Total	\$24,236,080*

4. Pathology Laboratories:

Number of billed tests reported to MECON:	2,589,480
Total Gross Revenue - Pathology Laboratories:	\$155,001,852
Total Direct Expenses Pathology Laboratories:	\$ 44,861,569

*Includes General Fund, Extramural Funds, FGP Professional Fee Income, Gift, etc.

Respectfully submitted,

Eugene J. Napolitan
Administrator