

**THE UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL**

Department of Pathology

ANNUAL REPORT



1 July 2000 - 30 June 2001

THE UNIVERSITY OF MICHIGAN

MEDICAL SCHOOL

Department of Pathology

ANNUAL REPORT



1 JULY 2000- 30 JUNE 2001

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
Annesley, Thomas M.	Professor	The University of Michigan
Appelman, Henry, D.	M.R. Abell Professor	The University of Michigan
Baker, James R.	Associate Professor	The University of Michigan
Barr Jr., Mason	Professor ⁺	The University of Michigan
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
Cooling, Laura	Clinical Assistant 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 Research Scientist***	Pfizer
Dressler, Gregory R.	Associate Professor	The University of Michigan
Elnor, Victor M.	Associate Professor ⁺⁺	The University of Michigan
England, Barry G.	Associate Professor	The University of Michigan
Fantone, Joseph C.	Godfrey D. Stobbe Professor in Pathology Education and Director, Anatomic Pathology	The University of Michigan
Fearon, Eric R.	Professor*	The University of Michigan
Finn, William	Clinical Assistant Professor	The University of Michigan
Flint, Andrew	Professor	The University of Michigan
Friedman, Bruce A.	Professor	The University of Michigan
Fullen, Douglas R.	Clinical Assistant Professor	The University of Michigan
Giacherio, Donald	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

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<u>Name</u>	<u>Rank</u>	<u>Institutional Affiliation</u>
Hogaboam, Cory	Assistant Research Scientist	The University of Michigan
Inohara, Naohiro	Assistant Research Scientist	The University of Michigan
Johnson, Kent J.	Professor	The University of Michigan
Judd, W. John	Professor	The University of Michigan
Kaldjian, Eric	Adjunct Assistant Professor	Pfizer
Keller, Evan	Assistant Professor##	The University of Michigan
Keren, David F.	Clinical Professor	Warde Medical Laboratories
Killeen, Anthony A.	Clinical Associate Professor and Associate Director, Clinical Pathology	The University of Michigan
Killen, Paul D.	Associate Professor	The University of Michigan
Kleer, Celina	Assistant Professor	The University of Michigan
Kunkel, Steven L.	Endowed Professor of Pathology Research and Co-Director, Division of General Pathology	The University of Michigan
Lieberman, Richard W.	Clinical Assistant Professor+++	The University of Michigan
Lowe, John B.	Professor	The University of Michigan
Lowe, Lori	Clinical Associate Professor	The University of Michigan
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.	Professor	The University of Michigan
Ross, Charles W.	Associate Professor	The University of Michigan
Roulston, Diane	Clinical Assistant Professor	The University of Michigan
Rubin, Mark A.	Assistant Professor#	The University of Michigan
Schmaier, Alvin	Professor	The University of Michigan

<u>Name</u>	<u>Rank</u>	<u>Institutional Affiliation</u>
Schmidt, Robert W.	Professor Emeritus	The University of Michigan
Schnitzer, Bertram	Professor	The University of Michigan
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
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.	Godfrey D. Stobbe Professor and Chairman	The University of Michigan
Warren, Jeffrey S.	Warthin/Weller Professor and Director, Clinical Pathology	The University of Michigan
Wilson, Thomas	Assistant Professor	The University of Michigan

* Joint Appointment, Department of Internal Medicine

** Joint Appointment, Dental School

*** Clinical Appointment, Pfizer

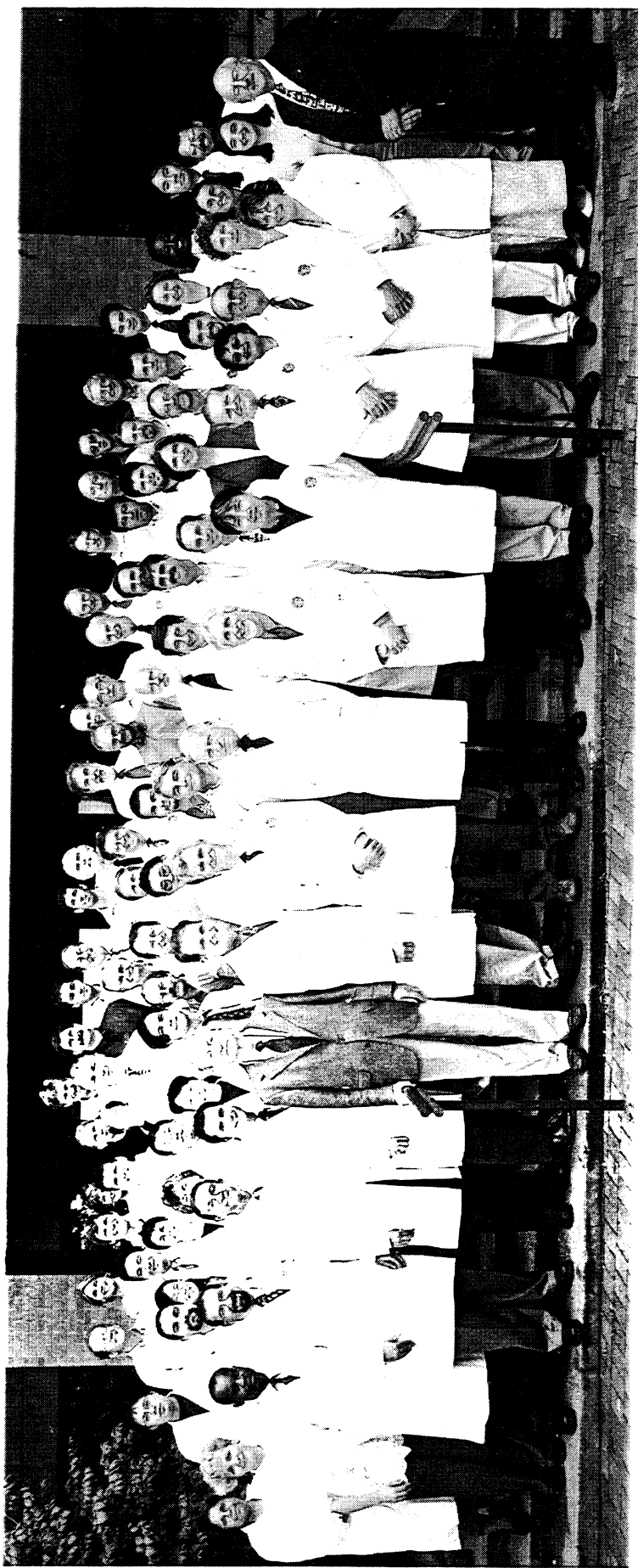
+ Joint Appointment, Department of Pediatrics and Communicable Diseases

++ Joint Appointment, Department of Ophthalmology

+++ Joint Appointment, Department of Obstetrics and Gynecology

Joint Appointment, Department of Urology

Joint Appointment, ULAM and Institute of Gerontology



**Faculty, Residents and Fellows
Department of Pathology
October, 2000**

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DEPARTMENTAL OVERVIEW

DEPARTMENTAL OVERVIEW 2000-2001

Introduction

Much success and considerable innovation are reflected in Departmental activities of the past academic year. In the Spring and Fall of 2000 both the Internal and External Reviews of the Department were completed. The External Reviewers were very impressed with evidence of excellence in teaching, clinical service and research accomplishments of the faculty. They also complemented the Department for its financial success. Availability of additional, flexible space, (especially for research and support functions) was emphasized as an urgent need. This, of course, is also a reflection of the long-standing problem that a considerable amount of space in Medical Science I is dedicated to clinical functions for UMHS. It is possible that major relief will await completion of the new medical research building (approximately 3 years from now). In the meantime, the Department is engaged in vigorous discussions with the Department of Internal Medicine to obtain interim laboratory space in situations in which faculty recruitment is of clear benefit to both departments. The Department has an impressive record of annual increments in revenue derived from diagnostic and research activities. The External Reviewers applauded the Department's plan to continue to expand the depth of expertise in both Anatomic and Clinical Pathology so that there would be fewer areas with only a single faculty member with expertise. The areas of research that will continue to be expanded are: cancer biology, apoptosis and inflammation/immunology. Obviously, all three areas significantly overlap. This emphasis also reflects institutional priorities. The Department has taken an initiative to contribute a Medical Student Scholarship fund to the Medical School, which will allow the indefinite, full tuition scholarship support of one student per year, resulting in a total of four scholarships per year (each to be named after a Pathology faculty member). It should be stressed that the Department has played a major institutional role in developing programs in genomics, bioinformatics and graduate education (PIBS and MSTP programs). Some of these activities, which are based in Pathology, have become magnets for other groups in UMMC. The Department has a maturing scientific relationship with Pfizer (Ann Arbor and worldwide), which is described in greater detail below. Finally, the Department is doing very well chiefly because of its balance of excellence in teaching, service and research.

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. A significant number of undergraduate students complete honors theses under the direction of Pathology faculty.

The Pathology graduate program was successful in recruiting five new students. This represents an increase from our average of two over the past three years. 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). Three students have completed their dissertation work and will be awarded doctoral degrees in 2001.

The Pathology residency and fellowship programs continue to prosper. Applications to the programs increased by approximately 25% this past year reversing a four-year national trend of declining student interest in pathology residency training. The program consists of 27 house officers and fellows. Last year all graduates of the house officer program found desirable positions, in both academia and private practice. Residents were selected for fellowships at several academic centers including; University of Michigan, University of Nebraska, M.D. Anderson Cancer Center, Memorial Sloan Kettering Cancer Center, and Johns Hopkins Hospitals. One resident was awarded a prestigious 2-year Robert Wood Johnson Fellowship in transfusion medicine to be completed at the University of North Carolina.

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. 2000-2001 was marked by several new faculty recruitments and several new initiatives. The laboratories continued their trend of more laboratory procedures (approximately 4%) with a fixed number of staff. Efforts to more aggressively control laboratory utilization were successful as at least \$850,000 in incremental cost was avoided. This success was achieved through proposed operating efficiency, and an aggressive plan for laboratory and send-out test utilization control. The Laboratories continued to reallocate resources needed to meet the continuing and marked increase in clinical activity experienced in 2000-2001. Augmentation of the capabilities of the Molecular Diagnostics, Tissue Typing and Cytogenetics Laboratories was contributory to this process. In 2000-2001 the Laboratories performed more than 3 million laboratory analyses (billable units) 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) inspection in May, 2001. 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.

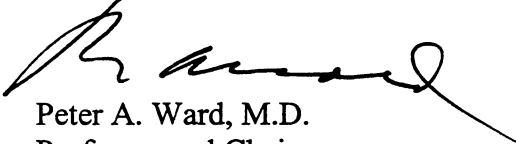
Research Activities

The research activities in the Department of Pathology remain strong underpinnings to support our academic mission. The Department's faculty continue to successfully compete for extramural research support, attract outstanding graduate and post-doctoral fellows from both the national and international scene, publish in highly visible, peer-reviewed scientific journals, and serve on numerous national and international scientific committees. During the past year, the expenditures of active grants and contracts credited to the Pathology Department's research efforts increased by approximately one million dollars when compared to the previous year's expenditures. The total research expenditures for 2000-2001 were over \$12.4 million; this included approximately \$8.83 million in direct expenditures and \$3.5 million in indirect expenditures. Faculty members in the Department of Pathology hold 71 individual grants from the National Institutes of Health, 2 program projects, a MERIT Award, and 7 NIH subcontracts. In addition, other support originates from a variety of external non-federal sources including, the American Heart Association, the Pew Charitable Trusts, American Lung Association, the MEDC Life Science Corridor Fund, and contract grants from nearly a dozen pharmaceutical companies. Many of the Departmental faculty actively participate in the support of institutional initiatives, including the University of Michigan Cancer Center, Urology SPORE Program, Breast Cancer Program, Interstitial Lung Disease SCOR, and the acute lung injury SCOR. This blend of activity underscores the role of Pathology faculty in translational research, especially where DNA-based microarrays and tissue arrays are involved. These studies have resulted in publications dealing with solid tumors and inflammatory diseases. The faculty actively publish in both the clinical and experimental arena and cover very diverse scientific interests, including clinical pathology, anatomical pathology, and basic cellular 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 participates in peer review of NIH grant applications and peer-review of submitted scientific articles for diverse journals. Another index of the healthy academic research environment in the Pathology Department is the large number of post-doctoral fellows in the different laboratories, as over 38 post-doctoral fellows from many different countries are engaged in research activities and clinical fellowship. These post-doctoral scholars have actively sought positions in the Department of Pathology to enhance their research and clinical careers. Our faculty continue to provide expertise for both internal and external program review, which include serving as ad hoc and permanent members of NIH study sections, serving as committee members for site visit teams, providing expertise on government sponsored special emphasis panels, and organizing or chairing clinical and experimental scientific conferences. Finally, the

Department of Pathology Annual Report

Department has a robust research relationship with Pfizer (Ann Arbor and worldwide) as reflected in the Genomic Pathology Laboratory (GPL) which is located in MSRBI. This activity involves investments of resources from both organizations to develop a state-of-the-art laboratory to advance microarray and proteomic programs will be readily available to investigators at both institutions.

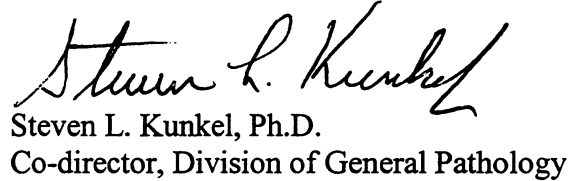
Respectfully submitted,



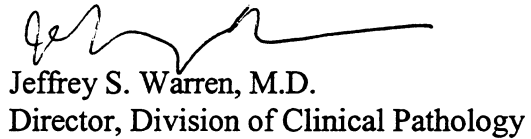
Peter A. Ward, M.D.
Professor and Chairman



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



Steven L. Kunkel, Ph.D.
Co-director, Division of General 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 2000 - 30 JUNE 2001**

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 - 4 contact hours.
 - 3. Pathology 500, Histopathology Sequence, Sequence Director, Lecturer, Lab Instructor-32 contact hours (8 lectures, 24 lab hours).
- B. Sophomore Medical Class:
 - 1. 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.
- F. Hospital Conferences:
 - 1. Cardiovascular Pathology Conference - monthly.
 - 2. Cardiac biopsy review conference-monthly.
- G. House Officers:
 - 1. Training in Surgical and Necropsy Pathology.
- H. Community:
 - 1. Organizer, director, and lecturer of "Mini-Med. School", a six-week course for the public.
- I. Invited Lectures:
 - 1. Keynote Address-UM Medical School White Coat Ceremony, August, 2000.
 - 2. American College of Cardiology, "Cardiology at Big Sky", February, 2001.
 - 3. UM Northern Michigan Summer Conference, June, 2001.
- J. Production of Teaching Materials:

1. Production of CD-Rom and syllabus for Histopathology Lab sequence of Pathology 500.

K. Honors:

1. Elected class marshall, Class of 2001.

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, Sesquicentennial Celebration Committee.
- E. Chair, Medical School Bylaws Committee.

REGIONAL AND NATIONAL:

- A. Editorial Board, Modern Pathology.
- B. Reviewer, Archives of Pathology and Laboratory Medicine and Microbial Ecology in Health and Disease.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000-30 JUNE 2001**

I. CLINICAL ACTIVITIES:

- A. Cytopathology sign-out (in-house Gynecologic & Non-gynecologic cases) (10 months).
- B. Sign-out transfer cytology cases (TC) (6 months).
- C. Performance and interpretation of fine-needle aspirates at Cancer Center Clinic (6 months).
- D. Rapid interpretation of fine-needle aspirations performed by Clinicians and Radiologists (6months).
- 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 Endometrial Carcinoma.
- 2. Expression of Matrix Metalloproteinase in Endometrial Carcinoma.
- 3. Fine-needle aspiration of "Cystic Neck Masses": Diagnostic Accuracy, Cytologic Artifacts and Pitfalls.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

Director, Immunohistochemistry Laboratory.

V. PUBLICATION:

ARTICLES PUBLISHED IN REFEREED JOURNALS:

1. Afify AM and Al-Khafaji BM. Cytologic artifacts and pitfalls of thyroid fine- needle aspiration using ThinPrep: A comparative retrospective review. *Cancer Cytopathol* 93:179-186, 2001.
2. Afify AM, Amy W. Ferguson, Rosa M. Davila, Bruce A. Werness. Expression of CD44S and CD44v5 is more common in Stage III than in Stage I serous ovarian carcinomas. (Accepted in *Applied Immunohistochemistry & Molecular Morphology*)
3. Al-Khafaji BM and Afify AM. Salivary gland fine-needle aspiration using the ThinPrep Technique: Diagnostic accuracy, cytologic artifacts and pitfalls. (Accepted in *Acta Cytologica*)
4. Alaa M. Afify, Basim M. Al-Khafaji, Byungki Kim, and James M. Scheiman. Endoscopic Ultrasound-Guided fine-needle aspiration of the pancreas: Diagnostic utility & accuracy. (Submitted).
5. Alaa M. Afify, Basim M. Al-Khafaji Diagnostic utility of Thyroid Transcription Factor-1 Expression in adenocarcinomas presenting in serous fluids (Submitted).
6. Alaa M. Afify, Basim M. Al-Khafaji, Augusto F. G. Paulino, and Rosa M. Davila. Diagnostic utility of muscle markers in the cytologic evaluation of serous fluids. (Submitted)

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

Scientific Poster/ Abstract Presentations:

1. Diagnostic utility of muscle markers in the cytologic evaluation of serous fluids (Platform).
2. Diagnostic utility of Thyroid Transcription Factor-1 Expression in adenocarcinomas presenting in serous fluids.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

I. CLINICAL ACTIVITIES:

- A. Biochemistry Section, Clinical Pathology Laboratories.
- B. Consultant to Veterans Administration Hospital, Ann Arbor, Michigan.
- C. Laboratory Director, Chelsea Family Practice, M-Care Facility.
- D. Laboratory Director, Briarwood Medical Group, M-Care Facility.
- E. Laboratory Director, Briarwood Family Practice Facility.
- F. Laboratory Director, Chelsea Internal Medicine Associates.
- G. Laboratory Director, West Ann Arbor Health Care Facility.

II. TEACHING ACTIVITIES:

- A. Medical Students:
 - 1. Course Director, Fundamentals of Laboratory Medicine (PTHCLNL.101) Component IV Medical School Curriculum.
 - 2. Lecturer, Minority Students Clerkship in Pathology.
- B. House Officers:
 - 1. Lecturer, Clinical Pathology Grand Rounds.
 - 2. Lecturer, Clinical Pathology Didactic Lecture Series.
 - 3. Daily Sign-out and Interpretation of Laboratory Results.
 - 4. Clinical Pathology Curriculum Committee.
 - 5. Coordinator, Clinical Pathology Block B.

III. RESEARCH ACTIVITIES:

- A. Visiting Scientists, Pfizer Global Research and Development, Ann Arbor Michigan.

IV. 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. NACB/AACC Professional Activities Committee.

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

V. OTHER RELEVANT ACTIVITIES:

JOURNAL EDITORSHIPS:

- A. Associate Editor, Clinical Chemistry.

EDITORIAL BOARDS:

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

EDITORIAL REVIEW ACTIVITIES:

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

INVITED LECTURES:

- 1. Isolation and Identification of a Novel Fosphenytoin Metabolite, Pfizer Global Research Symposium, Novi, Michigan, October, 2000.
- 2. Glucuronidation of Prodrug Reactive Site, Pfizer Research and Development Laboratories, Ann Arbor, Michigan, October, 2000.
- 3. Rave Party Drugs, Hurley Medical Center, Flint, Michigan, March 2001.
- 4. Twenty First Century Technologies in the Clinical Laboratory, Michigan State University, Lansing, Michigan, April, 2001.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Annesley, T.M.: National center for infectious diseases (NCID). Clin. Chem. 2000;46:739.
- 2. 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 2001;41:371-4.
- 3. Roberts, W., Annesley, T., De, B., and Moyer, T.: Free phenytoin measurements by four immunoassays compared to HPLC. Ther. Drug Monitor. 2001;23:148-54.

4. Annesley, T.M., Kurzyniec, S., Nordblom, G.D., Buchanan, N., Pool, W., Reily, M., Talaat, R., and Roberts, W.L.: Glucuronidation of prodrug reactive site: Isolation and characterization of oxymethylglucuronide metabolite of fosphenytoin. Clin. Chem. 2001;47:910-18.

ABSTRACTS:

1. Annesley, T.M., Kurzyniec, S., Nordblom, G.D., Buchanan, N., Pool, W., Reily, M., Talaat, R., and Roberts, W.L.: Glucuronidation of prodrug reactive site: Isolation and characterization of oxyglucuronide metabolite of fosphenytoin. Proc. 10th Analytical Symposium, Novi, 2000.
2. Frank, E.L., Schwartz, E.L., Juenke, J.M., Annesley, T.M., and Roberts, W.L.: Performance characteristics of an automated chemiluminescent phenytoin assay. Clin. Chem. 2001;47:A76.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

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 per month).
 - 2. Liver Biopsy Conference - one hour every other month.
 - 3. Gastrointestinal Biopsy Conference for Gastrointestinal fellows and staff, 9 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 Pennsylvania.
- 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, of Albany Medical Center
- F. Adenomas of the duodenum: are there differences between sporadic and FAP-associated? With Paul Kowalski
- G. Is hyperplasia of the interstitial cells of Cajal a common reaction to intramural masses in the gut? With Neil Bavakaty and Meryem Koker
- H. The apoptotic form of microscopic colitis, with a consortium of pathologists from around the country
- I. The status of the squamous mucosa next to segments of Barrett's esophagus, with WL Lo and Jeffrey Barnett
- J. Are juvenile-like polyps in adults the same as in children? With Meryem Koker

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL AND NATIONAL:

- A. Member, Scientific Advisory Committee, and Board of Directors, International Organization for Statistical Studies of Diseases of the Esophagus, Paris, France.
- B. Central Pathologist, Polyp Prevention Trial, National Cancer Institute, Washington, DC
- C. Member, Editorial Board, Human Pathology.
- D. Member, Editorial Board, Modern Pathology.
- E. Member, Editorial Board, American Journal of Surgical Pathology.
- F. Ad hoc reviewer for American Journal of Pathology, Cancer, Gastroenterology, and American Journal of Gastroenterology.
- G. Member of the 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. Visiting Professor, Department of Pathology, University of Indiana, December, 2000
- 2. Visiting Professor, Department of Pathology, Medical College of Wisconsin, April, 2001

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, Vancouver, BC, Canada, July, 23, 2000
2. "What is the cause and significance of intestinal metaplasia immediately distal to the Z-line?" "Barrett's esophagus is a family of metaplasias." "Do the current data support that an endoscopic-biopsy surveillance program prevents or does not prevent cancer in Barrett's mucosa?" "An updated definition of Barrett's esophagus from the perspective of a pathologist." "What is the acceptable definition of cardia carcinoma?" "What are the histologic criteria for the diagnosis of incipient invasion in Barrett's mucosa with high-grade dysplasia?" 6th World Congress of the International Organization for Statistical Studies on Diseases of the Esophagus (OESO), September 1-6, 2000, Paris, France.
3. "GI biopsy reports, the Good, the Bad and the Ugly", with BJ McKenna. The Ninth Annual Iowa Anatomic Pathology Course, Iowa City IA, September 22, 2000
4. "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, San Diego, CA, Oct 16, 2000; Weekend of pathology, American Society of Clinical Pathologists, Las Vegas NV, Feb 24, 2001
5. "New stuff at the gastric cardia, in Barrett's mucosa and everything in between." Visiting professor grand rounds lecture, Department of Pathology and Laboratory Medicine, Indiana University, Indianapolis, IN, Dec 12, 2000
6. "Pathologic features of GIST", Gastrointestinal Stromal Tumor Workshop, sponsored by the NIH, ASCP and NCI, National Institutes of Health, Bethesda, MD, April 2-3, 2001
7. "Barrett's mucosa, and the gastric cardia", Joint meeting of the Milwaukee Area Pathologists and the Milwaukee Gastrointestinal Society, Milwaukee, WI, April 12, 2001
8. "The pathologist and the inflammatory bowel diseases", Visiting professor lecture, Department of Pathology, Medical College of Wisconsin, Milwaukee, WI, April 13, 2001
9. "Neoplastic diseases of the intestines", half day course, Pathology of the Gastrointestinal Tract, American Society of Clinical Pathologists, Seattle, WA, May 2, 2001
10. Lectures in gastrointestinal pathology on esophagus, gastritis, non-IBD colitis and GI stromal tumors. Eighth Annual Seminar in Pathology. sponsored by United Hospital Center of Clarksburg, WV, Pittsburgh, PA, May 4, 2001
11. "Neoplastic progression in the GI tract: a tribute to Dr. Rodger Haggitt", Annual meeting of the American Gastroenterological Association, Atlanta, GA, May 21, 2000
12. Lectures in esophagogastric and colorectal pathology, Tri-State Pathology Society, 2001 Annual meeting, Orange Beach, AL, May 26, 2001
13. "What's new and cool about Barrett's mucosa and the gastric cardia?", Cecil Krakower Memorial Lecture, Department of Pathology, University of Illinois College of Medicine, Chicago IL, June 6, 2001
14. "The pathologists and GISTS", Department of Pathology and Laboratory Medicine, Albany Medical College, Albany NY, June 13, 2001

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Valdez R, Appelman HD, Bronner MP, Greenson JK. Diffuse duodenitis associated with ulcerative colitis. *Am J Surg Pathol.* 24:1407-1413, 2000
2. Haggitt RC, Appelman HD, Lewin KJ, Riddell RH: Recommendations for the reporting of resected esophageal carcinomas. *Mod Pathol.* 13:1034-1037, 2000
3. Appelman HD, McKenna BJ: Dysplasia in the gut: the diagnosis is harder than it seems. *J Clin Gastroenterol*, Accepted for publication

CHAPTERS AND BOOKS:

1. Kleer CG, Appelman HD: Pathology of Crohn's disease, *Surgical Clinics of North America*, WB Saunders, Philadelphia, 81:13-30, 2001
2. McKenna BJ, Appelman HD, Neoplasms of the small intestine, in Quigley EE and Marsh MN, eds.: *The Small Intestine*, Blackwell Scientific, Cambridge, MA, in press
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. Elderly D, Appelman HD, McKenna BJ: Apoptosis and crypt inflammation in collagenous and lymphocytic colitis. *Mod Pathol.* 14:84A, 2001
2. Lo WYF, Barnett, JL, Appelman HD: Why aren't reflux-type squamous changes next to Barrett's mucosa more common? *Mod Pathol.* 14:91A, 2001
3. McKenna BJ, Elderly D, Odze RD, Brien TP, Appelman HD: Apoptotic colopathy: a new variant of microscopic diarrheal disease? *Mod Pathol.* 14:91A, 2001
4. Tani M, Hinoi T, Caca C, Dunn RL, Cho KR, Fearon ER, Appelman HD, Lucas PC: Reduced CDX2 expression and high-frequency microsatellite instability in anaplastic carcinomas of the colon. *Mod Pathol.* 14:96A, 2001

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

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. 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 visiting pathology fellow from Stanford University Medical School.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Histology of animal models of rheumatoid arthritis with Arthritis and Rheumatology with Blake Roessler.
- B. Rat model in brain tumors growth and treatment, with Neurosurgery Department (Philip Kish, grant application submitted.)
- C. Co-investigator on P.E. McKeever, M.D. grant “Glioma Tissue Markers of Potential Diagnostic and Prognostic Value.”
- D. Evaluation of temporal lobectomy/hippocampectomy cases with Erasmo Passaro, M.D., and the epilepsy group (grant submitted).
- E. Collaboration with EMG group, Radiology (S. Gebarski, M.D.), neurosurgery and pulmonary/internal medicine on various projects.

- F. Supervision of histology/immunohistochemistry projects for residents, fellows and researchers in Neurosurgery, Neurology and Neuroscience labs.
- G. 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. Served as Neuropathologist Expert at the Annual Welsh Neuro-ophthalmology Society Meeting, April 21-22, 2001.
- B. Consulting with outside pathologists, neurologists and family practitioners on muscle and nerve biopsies performance and interpretation, brain biopsies.
- C. Member, American Association of Neuropathologists, IAP, CAP, PNS, and AAN.
- D. Attended International Neuropathology Congress in Birmingham, UK, with poster presentation.
- E. Attended the meeting of American Association of Neuropathologists.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN PEER REVIEWED JOURNALS:

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 gene for the axonal cell adhesion molecule TAX-1 is amplified and aberrantly expressed in malignant gliomas. *Cancer Research* 2001, 61(5):2162-2168.
2. Tuner RS, D'Amato CJ, Chervin RD, Blaivas M: The Pathology of REM sleep behavior with comorbid Lewy body dementia. *Neurology* 2000, 55(11):1730-1732.
3. Gupta S, Blaivas M, Ike RW, Crofford LJ: Polymyositis evolving after rhabdomyolysis associated with HMG Co-A reductase inhibitors: A report of two cases. Accepted to: *J of Clinical Rheumatology*.
4. 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. Accepted to: *Oncology*.

5. 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. Accepted to: Am. J. of Resp. and Critical Care Medicine.
6. McKeever PE, Junck L, Strawderman MS, Blaivas M, Tkaczyk A, Cates MA: Proliferation Index is Related to Patient Age in Glioblastoma. Neurology 2001, 56(9):1216-1218.

* Resident or Fellow

ARTICLES SUBMITTED FOR PUBLICATION:

1. *Fishman S, Blaivas M, Fing JK: Levodopa-carbidopa responsiveness in African-American subject with Machado-Joseph Disease type IV. Resubmitted to: Movement Disorders.

* Resident or Fellow

CHAPTER IN BOOKS:

1. McKeever PE, Blaivas M, Gebarski SS: Chapter in: Diagnosis and Management of Pituitary Tumors. Humana Press, 2001

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

1. Blaivas M, Gebarski S: Complex “embryonal” glio-neuronal tumors in adults defy WHO classification. Presented at the XIVth International Congress of Neuropathology, Birmingham, United Kingdom, September 2-9, 2000.
2. Gebarski S, Blaivas M: Oligoastrocytoma: a germinal matrix neoplasm. Presented at the RSNA Annual Meeting, Chicago, IL, November/December 2000.
3. *Wang J, Blaivas M, Jones MZ, Hoffmann S: Leg Mass in an HIB-Positive Patient FACP. Michigan State University/Kalamazoo Center for Medical Studies, Kalamazoo, MI. Presented at ACP MSU-KCMS meeting, Kalamazoo, MI, September 2000.
4. Junck L, McKeever PE, Strawderman MS, Blaivas M, Tkaczyk A, Cates MA: Proliferation Index is Related to Patient Age in Glioblastoma. Submitted to: Meeting of the Society for Neuro-Oncology, November 2001.

* Resident or Fellow

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

**ANNUAL DEPARTMENT REPORT
1 JULY 2000 - 30 JUNE 2001**

I. CLINICAL ACTIVITIES:

- A. Chief, Pathology and Laboratory Medicine Service (as of March 2001), VA Ann Arbor Healthcare System, responsibilities include, overall laboratory supervision and administration, equipment and methodology evaluation, review and consultation regarding quality management programs, personnel evaluation, counseling and grievance procedures.
- B. Hematology, daily evaluation of pathologist referred blood smears, bone marrow smears, VA Ann Arbor Healthcare System (approx 300 cases/2000).
- C. Surgical/Frozen Section Diagnosis (approx 250 cases/2000)
- D. Surgical Case Diagnosis (4 months in 1999, approx. 1800 cases) VA Ann Arbor Healthcare System.
- E. Autopsy Service, rotational basis, on call 13 weeks/year (staffing 7 cases in 2000).
- F. Special Chemistry/Immunology, daily interpretation of protein electrophoreses and problem ligand studies (approx 1000 cases/2000), VA Ann Arbor Healthcare System.
- G. Blood Bank, consults and investigations, full time as needed, VA Ann Arbor Healthcare System.

II. TEACHING ACTIVITIES:

- A. Pathology house officers, Surgical Pathology/Autopsy supervision and instruction, (5 months/year)
- B. Medical students, Pathology 600 laboratory (28 contact hours)
- C. Graduate students, Immunology 850, (2 contact hours)
- D. Technologists, technicians and hospital staff, ongoing continuing medical education instruction on clinical laboratory topics.
- E. Graduate, undergraduate students, and high school intern research project mentoring.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, Chemokine Determinants of Th1 and Th2 Immune Responses, VA Merit Review Grant, (\$135,000 direct costs annually, 2000-2005).
- B. Principal Investigator, Chemokine Receptor Dynamics in Granuloma Formation, NIH AI43460 (\$115,000 direct costs annually, 1998-2002)

- C. 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. Clinical Executive Board, VA Ann Arbor Healthcare System, voting member
- B. Professional Standards Board, VA Ann Arbor Healthcare System, voting member
- C. Invasive Procedures Committee, VA Ann Arbor Healthcare System, voting member
- D. Information Management Committee, VA Ann Arbor Healthcare System, voting member
- E. Chief of Staff Advisory Committee, VA Ann Arbor Healthcare System, voting member
- F. Blood Utilization Review Committee, VA Ann Arbor Healthcare System, Chairman
- G. Personnel employment and annual evaluations
- H. Anatomic Pathology Quality Assurance evaluation and reporting
- I. Editor, VA Labs 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. Schuster T.G., Hollenbeck B.K., Kauffman C.A., Chensue S.W., Wei J.T. Testicular histoplasmosis. *J. Urol.* 2000, 164(5): 1652.
2. 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.* 2000, 165(3): 1564-1572.
3. Shang X., Qiu, B., Frait, K.A., Hu, J.S., Sonstein, J. Curtis, J.L. Lu, B., Gerard, C. Chensue S.W. Chemokine receptor 1 knockout abrogates natural killer cell recruitment and impairs type-1 cytokines in lymphoid tissue during pulmonary granuloma formation. *Am. J. Pathol.* 2000, 157:2055-2063.
4. Chensue, S.W., Lukacs, N.W., Yang, T.Y., Shang, X., Frait, K.A., Kunkel, S.L., Kung, T., Wiekowski, M.T., Hedrick, J.A., Cook, D.N., Zingoni, A., Narula, S.K., Zlotnik, A., Barrat, F.J., O'Garra, A., Napolitano, M., Lira, S.A. Aberrant in vivo T helper type 2 cell response and impaired eosinophil recruitment in CC chemokine receptor 8 knockout mice. *J. Exp. Med.* 2001, 193:573-584.
5. Tkachuk, A.N., Moormann, A.M., Poore, J.A., Rochford, R.A., Chensue, S.W., Mwapasa, V., Meshnick, S.R. Malaria enhances expression of CC chemokine receptor 5 on placental macrophages. *J. Infect. Dis.* 2001, 183:967-972.
6. Qiu, B., Reich, F., Frait, K.A., Reich, F., Komuniecki, E., and Chensue, S.W. Chemokine expression dynamics in mycobacterial (type-1) and schistosomal (type-2) antigen-elicited pulmonary granuloma formation. *Am J Pathol* 2001, 158: 1503-1515
7. Matsukawa, A., Lukacs, N.W., Hogaboam, C. M., Chensue, S.W., and Kunkel, S.L. Chemokines and their receptors in cell-mediated immune responses in the lung. *Microsc. Res. Tech.* 2001 53: in press.
8. 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.* 2001, in press.

BOOKS AND CHAPTERS IN BOOKS:

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

1. Shang, Xiao-Zhou, Frait, K., Lukacs, N.W., Kunkel, S.L., and Chensue S.W. Role of Eotaxin and MCP-3 in eosinophil mobilization to type-2 hypersensitivity pulmonary granulomas. . *FASEB J.* 2001, 15(4):A356. Abs# 278.11.
2. Murphy, M.E., Chensue, S.W., and Murphy, H.S. Effect of endogenous nitric oxide on vascular endothelial cell cytokines. *FASEB J.* 2001, 15(4):A243. Abs# 217.16.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

- A. Postdoctoral Fellows:
Responsible during the academic year for the following:
1. Rong Wu, M.D.
 2. Donald Schwartz, Ph.D.
 3. Ya-Li Zhai, Ph.D.
 4. Jie Zheng, Ph.D. (5 months)
 5. Amy Ferguson, M.D. (9 months)
- B. Graduate students:
Course Faculty, Pathology 581 – two lecture hours
Course Faculty, Pathology 580/630 – 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. Doctoral Thesis Committee Member for the following graduate students:
Tom Hlaing (Pathology)
Kenute Myrie (Human Genetics)
- G. National:
Course Faculty and Co-organizer: Molecular Biology in Clinical Oncology Workshop.
American Association for Cancer Research, The Given Institute, Aspen, Colorado.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "FHIT Gene Alterations in Cervical Cancer Pathogenesis", NIH RO1 CA81587 (30% effort), September 1, 1998 - August 31, 2002. Final year is twelve month no cost extension.
- B. Principal Investigator, Project 2 ("Molecular Profiling of Ovarian Cancer", 15% effort). NIH: U19 CA84953-03 (Hanash). "Toward a Molecular Classification of Tumors," September 30, 1999 – March 31, 2004.
- C. Principal Investigator, "Oncogene Activation in Ovarian Cancer Pathogenesis", Department of Defense, OCRP OC000105 (15% effort), August 15, 2001 - August 14, 2004.
- D. Co-Investigator (10% effort), "CDX2 Tumor Suppressor Pathway Defects in Colon Cancer", NIH 1R01CA82223-01 (Fearon), 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), June 1 2000 – May 31, 2005.
- F. Co-Investigator, Bioinformatics Pilot Grant (Lubman), University of Michigan, awarded June 2001. No salary support requested for Dr. Cho. Provides partial salary support for Dr. Donald Schwartz, post-doctoral fellow, Cho laboratory.

PENDING:

- A. National Institutes of Health: 1 RO1 CA94172-01 (12/01/01 – 11/30/06). "Molecular Pathogenesis of Ovarian Endometrioid Adenocarcinomas." Role in Project: Principal Investigator (30% effort). (Reviewed by IRG on 06/25/01, priority score 144, percentile score 1.9). Approval for funding pending review by the National Cancer Advisory Board (anticipated Sept. 2001).
- B. Department of Defense: Ovarian Cancer Research Program (OCRP FY01). Program Project. OC010026 (07/01/02 – 06/30/06). "Molecular Mechanisms of Ovarian Carcinogenesis: Therapeutic Implications." Role in Program: Principal Investigator, Overall Program and Ovarian Cancer Resources Core (total of 10% effort). Review anticipated, fall 2001.

PROJECTS UNDER STUDY:

- A. Molecular profiling of ovarian epithelial tumors using 2-D gel approaches and Affymetrix gene chip technologies.
- B. Identification and characterization of novel genes differentially expressed in ovarian carcinomas.
- C. Identification of novel genes amplified in ovarian carcinomas.
- D. Evaluation of the role of Wnt/ β -catenin/Tcf pathway defects in the pathogenesis of ovarian endometrioid adenocarcinomas.
- E. Characterization of genetic alterations in poorly differentiated (anaplastic) colorectal carcinomas.

IV. **ADMINISTRATIVE ACTIVITIES:**

DEPARTMENTAL:

- A. Tuition Selection Committee for selection of meritorious medical student scholarship recipient, 2001

INSTITUTIONAL:

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

REGIONAL AND NATIONAL:

- A. Member, Oral Biology and Medicine 1 Study Section, National Institutes of Health, 1998-2001.
- B. Special Emphasis Panel, Pathology B Study Section, National Institutes of Health/National Cancer Institute, teleconference review of RO1 applications
- C. Special Emphasis Panel, Oncological Sciences IRG, National Institutes of Health/National Cancer Institute, teleconference review of RO1 application (panel chair)
- D. Member, Special Conferences Committee, American Association for Cancer Research, 1999-2002
- E. Co-Organizer, Molecular Biology in Clinical Oncology Workshop, American Association for Cancer Research, 2000.
- F. 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. Member, Editorial Board, *Molecular Diagnostic Pathology*
- F. Member, Editorial Board, *The Women's Oncology Review*
- G. Ad hoc reviewer for *Journal of the National Cancer Institute*, *American Journal of Pathology*, *Biological Signals*, *British Journal of Cancer*

INVITED LECTURES/SEMINARS:

- 1. 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.

2. Molecular Biology of Gynecological Cancers. Molecular Biology in Clinical Oncology Workshop, American Association for Cancer Research, The Given Institute, Aspen, Colorado, July 2000.
3. Cancer Biology Course Lecture: "Cervical Cancer and HPV Oncogenesis". The University of Chicago, Chicago, Illinois, November 2000.
4. Seminar Series for Medical Scientist Training Program Students, "Careers in Academic Medicine- Thinking Outside the Box", Michigan State University, East Lansing, Michigan, November, 2000.
5. The Role of the Fragile Histidine Triad Gene (FHIT) in Cervical Carcinogenesis. Minisymposium on Advances in Molecular Diagnostics and Therapeutics in Cervical Carcinogenesis. 48th Annual Scientific Meeting of the Society for Gynecologic Investigation. Toronto, Canada, March 2001.
6. Molecular Pathogenesis of Gynecologic Tumors, Advanced Molecular Pathology Special Course at the United States and Canadian Academy of Pathology Annual Meeting, Atlanta, Georgia, March 2001.

OTHER:

2000 American Society for Clinical Investigation

2000 American Association of University Pathologists

VI. PUBLICATIONS (2000-2001):

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. 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.
2. 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.
3. 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.
4. Page, C., Huang M., Jin, X., Cho, K., Lilja, J., Reynolds, R.K., and Lin, J. Elevated Phosphorylation of AKT and Stat3 in Prostate, Breast, and Cervical Cancer Cells. *International Journal of Oncology* 17:23-28, 2000.
5. 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* 6:3505-3510, 2000.
6. Wu, R., Connolly, D.C., Ngelangel, 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. *Oncogene* 19:5543-5546, 2000.

7. 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 Reveals Genes Differentially Expressed in Ovarian Cancer. *Cancer Research* 60:6281-6287, 2000.
8. Hough, C.D., Cho, K.R., Zonderman, A.B., Schwartz D.R., and Morin, P.J. Coordinately Up-Regulated Genes in Ovarian Cancer. *Cancer Research* 61:3869-76, 2001.
9. Ferguson, A.W., Katabuchi, H., Ronnett, B.M., and Cho, K.R. Glial Implants in Gliomatosis Peritonei Arise from Normal Tissue, Not from the Associated Teratoma *American Journal of Pathology* 159:51-56, 2001.
10. Giordano, T.J., Shedden, K.A., Schwartz, D.A., Kuick, R., Taylor, J.M.G., Lee, N., Misek, D.E., Greenson, J.K., Kardia, S.L.R., Beer, D.G., Rennert, G., Cho, K.R., Gruber, S.B., Fearon, E.R., and Hanash, S. Organ-Specific Molecular Classification of Primary Lung, Colon, and Ovarian Adenocarcinomas Using Gene Expression Profiles. *American Journal of Pathology* (in press, 2001).

ARTICLES SUBMITTED OR IN PREPARATION:

1. Hinoi, T., Tani, M., Lucas, P.C., Caca, K., Dunn R.L., Macri, E., Loda, M., Appelman, H.D., Cho, K.R., and Fearon, E.R. Loss of CDX2 Expression and Microsatellite Instability are Prominent Features of Large Cell Minimally Differentiated Carcinomas of the Colon. Revised manuscript pending review at American Journal of Pathology, 2001.
2. Wu, R., Zhai, Y., Fearon, E.R., and Cho, K.R. Diverse Mechanisms of β -catenin Deregulation in Ovarian Endometrioid Adenocarcinomas (submitted, 2001).

BOOKS/CHAPTERS IN BOOKS:

1. Cho, K.R. Cervical Cancer. Metabolic and Molecular Bases of Inherited Disease, 8th edition, in Part 4, "Cancer", ed. B. Vogelstein and K. Kinzler, McGraw-Hill, Inc., New York, New York, 2001.
2. Cho, K.R., and Ellenson L.H. Molecular Biology. In Blaustein's Pathology of the Female Genital Tract, 5th edition, ed. Robert J. Kurman, Springer-Verlag, New York, in press.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

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. Occasionally plan and present gross and microscopic Neuropathology for the Neurology Department and 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).
- E. Coordinate and teach Neuropathology in the Radiology/Pathology Senior Elective.

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. International Society of Neuropathology.
- D. Michigan Chapter: Society for Neuroscience.

V. OTHER RELEVANT ACTIVITIES:

INVITED PRESENTATIONS:

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. Archives of Neurology, 2000, 58:265-269.

2. Turner, R.S., D'Amato, C.J., Chervin, R.D., Blaivas, M.: The Pathology of REM sleep behavior disorder with comorbid Lewy body disease. *Neurology*, 2000, 55: 1730-1732.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

I. CLINICAL ACTIVITIES:

- A. Associate Medical Director, Blood Bank and Transfusion Service.
- B. Cytopathology sign-out.

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. M2 Hematology sequence, Blood Transfusion.
- E. Clinical Pathology Grand Rounds, Adverse Effects of Transfusion
- F. Pathology Research Seminar, Pathophysiology of Transfusion Reactions.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Evaluation of Solvent/Detergent-Treated Plasma, Isoagglutinin Depleted, in Normal Healthy Volunteers", V. I Technologies, Inc.

PROJECTS UNDER STUDY:

- A. Pathophysiology of transfusion reactions.
- B. Transfusion risk perception.
- C. Safety of Isoagglutinin-depleted plasma.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

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

V. OTHER RELEVANT ACTIVITIES:

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

VI. PUBLICATIONS:

ARTICLES ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Davenport RD. Nontransfusion hazards of autologous blood donation [letter]. Transfusion 41:152-3, 2001.
- 2. Popovsky MA, Davenport RD. Transfusion-related Acute Lung Injury: Femme Fatale? [editorial] Transfusion 41:312-5, 2001
- 3. Davenport RD. Apheresis Treatment of Recurrent Focal Segmental Glomerulosclerosis after Kidney Transplantation: A Re-analysis of Published Case-Reports and Case-Series. J Clin Apher, in press.

ARTICLES SUBMITTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Fomovskaia G, Fomovaky M, Davenport R, Smith M. FTA-membrane for DNA detection in human blood cells. Submitted to Clinical Chemistry.

ABSTRACTS, AND PRESENTED PAPERS:

- 1. Fomovskaia G, Haddock T, Kubish G, Penezina O, Davenport R. Nageotte chamber method for very low number of leukocytes counting validated for stored red blood cells. Vox Sang 2000;78(suppl 1):P501.
- 2. Judd WJ, Davenport RD, Downs T, Chin S, Hammond D, Pehta JC. In vitro analysis of isoagglutinin depleted ("universal") solvent detergent treated plasma. Vox Sang 2000;78(suppl 1):O097.
- 3. Davenport R, Geohas G, Cohen S, Beach K, Lucchesi K, Pehta J. Phase IV study of PLAS+SD®: hepatitis A (HAV) and parvovirus B19 (B19) safety results. Blood 2000; 96:451a

CHAPTERS IN BOOKS:

- 1. Davenport RD: Hemolytic reactions. In: Popovsky MD (ed.): Transfusion Reactions 2nd ed. AABB Press, Bethesda, MD (in press).
- 2. Davenport, RD: Hemolytic Transfusion Reaction. In: Simon TL, Dzik WH, Snyder EL, Stowell CP, Strauss RG (eds.): Rossi's Principles of Transfusion Medicine 3rd ed. Lippincott Williams and Wilkins, Philadelphia, PA, (in press).
- 3. Davenport RD: Blood Banking. In: Schmaier AH (ed.): Hematology for the Medical Student. Lippincott Williams and Wilkins, Philadelphia, PA, (in press).

4. Davenport RD: Transfusion Therapy In: Schmaier AH (ed.): Hematology for the Medical Student. Lippincott Williams and Wilkins, Philadelphia, PA, (in press).

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000-30 JUNE 2001**

I. CLINICAL ACTIVITIES:

Organizing a Cell Toxicity Laboratory

II. TEACHING ACTIVITIES:

None.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Research activities with intramural support from Dr. Ward.
- 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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

None

MEDICAL SCHOOL/HOSPITAL:

None

REGIONAL AND NATIONAL:

Member, Scientific Advisory Committee, NSF Center for Light Microscopy, Carnegie Mellon University, Pittsburgh, PA
Member, Scientific Advisory Board, Cellomics Inc.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

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 Events (Centre International de Toxicologie, Paris, France, July 2001).
3. RNA expression in the early characterization of hepatotoxicants in high-density DNA microarrays (International CIT Symposium, Paris, France, July 2001).
4. Monitoring Simultaneous Subcellular Events in Vitro by Means of Coherent Multiprobe Fluorescence (IMRA). Ann Arbor, MI July 2001.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. H. Masuda, M.J. Adams, R.C. Secker, E. J. McGuire, J.R. Herman, D. Bailey and F.A. de la Iglesia. Reproductive Toxicology Studies with the Thiazolidinedione Antidiabetic Agent Troglitazone. J. Tox. Sci. In press, 2000.
2. 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.
3. Bulera, S.J., Eddy, S.M., Ferguson, E., Jatkoa, 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. Hepatology, 33: 1239-1258, 2001.
4. Reindel, J.F., Gough, A. W., Pilcher, G.D., Bobrowski, W.F., Sobocinski, G.P., de la Iglesia, F.A. Systemic Proliferative changes and clinical signs in Cynomolgus monkeys administered a recombinant derivative of human epidermal growth factor. Toxicologic pathology 29: 159-173, 2001.
5. Haskins. J.R., Rowse, P., Rahbari, R., de la Iglesia, F.A. Thiazolidinedione toxicity to isolated hepatocytes revealed by coherent multiprobe fluorescent microscopy and correlated with multiparameter flow cytometry of peripheral leukocytes. Archives of Toxicology (In press) 2001.
6. Shi, M.M., Bleavins, M.R., de la Iglesia, F.A. Pharmacogenetic application in drug development and clinical trials. Drug Metabolism and Disposition 29: 591-595, 2001.

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 2001).
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 2001). M.M. Shi,
3. Myrand, S., Bleavins, M.R. and F.A. de la Iglesia. Genotyping for the Functionally Important Human CYP2D6*4 (B) Mutation Using TaqMan Probes. Mol. Pathol. Protocols. (Submitted 2001).

4. Bulera, S.J., Festerling, T.A., de la Iglesia, F.A. Gabapentin Activates MAP kinase In vivo and In vitro in pancreatic acinar cells from Wistar rats: a postulated mechanism for pancreatic acinar cell tumor formation. (submitted, 2001)

BOOKS/CHAPTERS IN BOOKS:

1. Bleavins, M., de la Iglesia, F.A. Oreclinicl immune function testing. An approach using the cynomolgus monkey (*Macaca fasciculata*). In: Towards New Horizons in primate Toxicology. Perspectives for the New Millenium. R. Korte, G.F. Weinbauer, editors. Waxmann Press, Berlin, 2001.
2. De la Iglesia, F.A., J.R. Haskins, G. Feuer. Hepatotoxicity of cardiovascular and antidiabetic drugs. In Drug-Induced Liver Disease, N. Kaplowitz, L. DeLeve (editors). Marcel dekker, New York, (In press, 2001).

**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.
3. Shi, M.M., Sinz, M., Rose, K., Myrand, S., Bleavins, M.R., de la Iglesia, F.A. Human phenol sulfotransferase 1A1*2 genetic polymorphism in type 2 diabetic patients. Am J Human Genetics, 67: suppl 2: abs #2024, 2000.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

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. OTHER SUPPORT:

ACTIVE

U01 AG12495-06 (McConnell) 06/02/99 - 11/30/02

10% NIH

\$371,624

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

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

SCIENTIFIC COLLABORATIONS:

1. 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.

2. University of Mississippi: Hamed Benguzzi, Ph.D. Long-term drug delivery is of considerable research and clinical interest, particularly if the rate and length of delivery time can be accurately controlled. This collaborative effort has focused on the use of immunologically inert biomaterial similar to bone in composition (ceramics) that has proven capable of delivering a wide variety of steroids, protein hormones, therapeutic drugs, vitamins, autocrine and paracrine factors, etc. collectively referred to as *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.
3. University of Missouri: Mark Flinn, Ph.D.: We have monitored several biochemical markers of growth, puberty, stress and immunological function in the salivary excretions of children in a small isolated Caribbean village for approximately 8 years. We have examined several markers in saliva samples obtained from children between the ages of 2 and 21. Samples and a detailed history of relevant physical and emotional events are collected daily over a 2 - 3 month period each year throughout the multiyear study. Salivary levels of adrenal and gonadal steroid hormones provide good estimates of the concentration of biologically active hormone in the peripheral circulation on a twice-daily basis throughout the collection interval. This study has lead to a variety of new insights into the interaction between emotional and environmental stress and normal growth and development in human subjects.
4. University of Michigan: Norman Thompson, M.D. & Paul Gauger, M.D.: The intra-operative determination of circulating levels of parathormone (PTH) allows for the on-site monitoring of PTH levels as an indicator of removal of hypersecreting parathyroid glands. We have developed a cart-mounted analytical system that permits rapid determination (15 min.) of PTH in the O.R. This procedure ensures that all hypersecreting glands are removed before the patient is released from the O.R., thereby greatly reducing the number of repeat surgeries.

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

- A. Director, Central Ligand Assay Laboratory.

MEDICAL SCHOOL/HOSPITAL:

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

V. PUBLICATIONS:

ARTICLES PUBLISHED IN REFEREED JOURNALS:

1. Benghuzzi, Hamed & Barry England. Biocompatibility Of Steroid-HA Delivery System Using Adult Castrated Rams As A Model. Biomed Sci Instrum. 2001; 37: 275-280.

2. Pope, Joseph A., Hamed Benghuzzi, Barry England, & Zelma Cason. Morphometric Analysis Of The Adrenal Compartments Exposed To Sustained Delivery Of Androgens. *Biomed Sci Instrum.* 2001; 37: 155-160.
3. 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. *Biomed Sci Instrum.* 2000;36:221-6.
4. 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. *Biomed Sci Instrum.* 2000;36:171-6.

ABSTRACTS AND PAPERS AT MEETINGS:

1. Benghuzzi, H. & England, B.: Biocompatibility Of Steroid-HA Delivery System Using Adult Castrated Rams As A Model. Abstract accepted for presentation and invited for full length paper at the 38th annual meeting of the Rocky Mountain Bioengineering Symposium, Copper Mountain, CO. April, 2001.
2. Benghuzzi, H. Tsao, A., & England, B.: Sustained Delivery Of DHT From HA Delivery Systems In Adult Rams. 27th Society For Biomaterials. April 24-29, 2001 St. Paul Minnesota.
3. 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. Abstract accepted for presentation and invited for full length paper at the 37th annual meeting of the Rocky Mountain Bioengineering Symposium, Colorado Springs, CO, April, 2001.
4. 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.
5. Leone DV, Quinlan RJ, Quinlan MB, Worthen CC, Flinn MV & England BG . 2001. Duration of breastfeeding, parasite load, growth, fluctuating asymmetry, and cortisol profiles (abstract). *American Journal of Physical Anthropology Supplement 32*: 97-98
6. Pope, J.A., Benghuzzi, H., England, B., & Cason, Z. Morphometric Analysis Of The Adrenal Compartments Exposed To Sustained Delivery Of Androgens. Abstract accepted for presentation and invited for full length paper at the 38th annual meeting of the Rocky Mountain Bioengineering Symposium, Copper Mountain, CO, April, 2001.
7. 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. Abstract accepted for presentation and invited for full length paper at the 37th annual meeting of the Rocky Mountain Bioengineering Symposium, Colorado Springs. CO. April. 2001.
8. Wagner JD, Flinn MV, Gangestad SG, Thornhill R. & England BG. 2001. Testosterone and cortisol response to competition within and between male coalitions (abstract). *American Journal of Physical Anthropology Supplement 32*: 157-158
9. Wagner JD, Flinn MV, Gangestad SG, Thornhill R, & England BG, 2001. Hormone response to competition between male coalitions (abstract). *Proceedings of the Human Behavior and Evolution Society 2001*: 95 [First place poster prize winner]
10. Worthen CC, Flinn MV, Leone DV, Quinlan RJ & England BG 2001. Parasite load, growth, fluctuating asymmetry, and stress hormone profiles among children in a rural Caribbean village (abstract). *American Journal of Physical Anthropology Supplement 32*: 167

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, Maryland, pp ?? - ??, 2000.

INTERVIEWS AND POPULAR PRESS ARTICLES CITING OUR WORK REGARDING HORMONES AND STRESS

1. Small, M.S. "Trouble in Paradise" New Scientist December 16, 2000, p. 34-38.
2. Radio Interview on National Public Radio, Todd Mundt show, September, 2000
3. Small, M.S. "Family Matters" Discover August, 2000, p. 66-71
4. Bloch, N. "Coping with Paradise" Earthwatch June 1999, p. 14-21

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

I. CLINICAL ACTIVITIES:

- A. Autopsy Service.

II. TEACHING ACTIVITIES:

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

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Co-Investigator, "Pulmonary Immune Responses to Inhaled Pathogens". NIH-RO1-HL5531601 (1998-2002)
- B. Principal Investigator, "An Integrated Curriculum for Multiculturalism, Spirituality, and End-of Life Care". Arthur Vining Davis Foundation. (2000-2002).
- C. Co-Investigator, "University of Michigan Integrative Curriculum for Medicine and Allied Health." National Institutes of Health. R25-AT00812-01 (2001-2006).
- D. Co-investigator, "Comprehensive Programs to Strengthen Physicians' Training in Geriatrics." The Donald Reynold's Foundation. (2001-2005).

PROJECTS UNDER STUDY:

- A. Mechanisms of phagocytic cell-mediated tissue injury.
- B. Outcomes measures of undergraduate medical education.
- C. Curriculum development 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 Curriculum Review Group (Chair)

REGIONAL AND NATIONAL:

- A. ALA of Michigan, Grant Review Committee.
- B. USMLE, Step 1 Test Committee.
- C. Pathology Residency Review Committee. ACGME.

V. AWARDS:

Elected to AOA, University of Michigan Chapter of AOA. 2001.

VI. OTHER RELEVANT ACTIVITIES:

- 1. Invited speaker: International Association of Medical Science Educators, 2001, Mayo Clinic, Rochester, Minnesota.

VII. 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; 75: 801-805.
- 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 Med*. 2000; 75: S15-S17.
- 3. Fantone JC, White CB, Woolliscroft JO. University of Michigan Medical School (Description of curriculum, curriculum support and governance, and future directions). *Academic Med*, 2000; 75: S167-S172.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000- 30 JUNE 2001**

I. CLINICAL ACTIVITIES:

- A. Director, Hematopathology Section.
- 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).
 - 5. House Officer Teaching Award, 2001.
- 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.
- C. Medical Students:
 - 1. M-2 Hematology Sequence: Section leader for laboratory sessions (12 hours).
 - 2. M-2 Hematology sequence: "Pathology and Classification of Lymphoma" (Lecture) – 1 hour.
 - 3. M-1 Histopathology Course (24 hours).
 - 4. Medical Student Award for Teaching Excellence, 2000.
- D. Dental and Graduate Students: Pathology 580/630: "Pathology of White Blood Cells" (Lecture) – 1 hour.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Gene expression profiling of chronic lymphoproliferative disorders.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director, Hematopathology Section.
- 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, 2002.
- 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:

- 1. "Biology of Lymphoma Subtypes", Moderator of Platform Session, American Society of Hematology 42nd Annual Meeting, San Francisco, CA, December, 2000.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. 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 31(9):1051-1054, 2000.
- 2. 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. Hum Pathol 32:66-73, 2001.
- 3. Uherova P, Singleton TP, Ross CW, Schnitzer B, Finn WG: The clinical significance of CD10 antigen expression in diffuse large B-cell lymphoma. Am J Clin Pathol 115:582-588, 2001.

4. Valdez R, Finn WG, Ross CW, Singleton TP, Tworek JA, Schnitzer B: Extranodal marginal zone B-cell lymphoma as a cause of the clinicopathologic syndrome of Waldenstrom's macroglobulinemia: a report of six cases. *Am J Clin Pathol* (in press).

ARTICLES SUBMITTED FOR PUBLICATION:

1. Finn WG: Classification of lymphoma. In: *Hematology for the Medical Student*. Schmaier A, and Petruzzelli L, eds. Lippincott Williams & Wilkins.
2. Valdez R, Kroft SH, Ross CW, Schnitzer B, Peterson LC, Singleton TP, Finn WG: Cerebrospinal fluid involvement by mantle cell lymphoma.
3. Uherova P, Ross CW, Finn WG, Singleton TP, Nangia R, Schnitzer B: Peripheral T-cell lymphoma mimicking marginal zone B-cell lymphoma.
4. Nangia R, Singleton TP, Ross CW, Finn WG, Padmore RF, Schnitzer B: "Follicular" Hodgkin's lymphoma: a clinicopathologic study.
5. Hans CP, Finn WG, Singleton TP, Schnitzer B, Ross CW: Utility of anti-CD117 in the flow cytometric analysis of acute leukemia.

BOOKS AND CHAPTERS IN BOOKS:

1. Finn WG: Hematolymphoid system. In: *Yearbook of Pathology and Laboratory Medicine 2001*. Raab SS, Bissell MG, Dabbs DJ, Olson DJ, Silverman JF, Stanley MW, eds. St. Louis, MO: Mosby, Inc., 2001, pp 245-271.
2. Finn WG: Hematolymphoid system. In: *Yearbook of Pathology and Laboratory Medicine 2002*. Raab SS, ed., St. Louis, MO: Mosby, Inc., 2002 (in press).

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

1. Finn WG: Book review: *Interpretation of Diagnostic Tests*, 7th edition, by Jacques Wallach. *Am J Clin Pathol* 115:611, 2001.
2. Finn WG: Book review: *The Handbook of Clinical Pathology*, 2nd edition, by Robert W. McKenna and Joseph Keller. *Am J Clin Pathol* 115:612, 2001.
3. Yang B, Tubbs RR, Hsi ED, Finn WG: Molecular genetic characterization of primary cutaneous B-cell lymphomas (letter – reply). *Am J Surg Pathol* 25:538-539, 2001.
4. Valdez R, Ross CW, Schnitzer B, Nangia R, Finn WG: IgG expression in B-cell chronic lymphocytic leukemia. Poster presentation, United States and Canadian Academy of Pathology Annual Meeting, Atlanta, GA, 2001. *Mod Pathol* 2001; 14(1):181A.
5. Uherova P, Finn WG, Nangia R, Ross CW, Schnitzer B: Peripheral T-cell lymphoma (PTCL) mimicking low grade marginal zone/MALT lymphoma. Poster presentation, United States and Canadian Academy of Pathology Annual Meeting, Atlanta, GA, 2001. *Mod Pathol* 2001; 14(1):181A.
6. Nangia R, Singleton TP, Finn WG, Schnitzer B, Ross CW: CD117 (c-kit) in acute leukemias, chronic myeloproliferative disorders and myelodysplastic syndromes: a paraffin immunohistochemical (IHC) study with flow cytometry (FC) correlation. Poster presentation, United States and Canadian Academy of Pathology Annual Meeting, Atlanta, GA, 2001. *Mod Pathol* 2001; 14(1):173A.

7. Nangia R, Finn WG, Schnitzer B, Ross CW: Refractory anemia with excess blasts in transformation (RAEBt): rare subset with <5% bone marrow blasts. Platform presentation, United States and Canadian Academy of Pathology Annual Meeting. Atlanta, GA, 2001. *Mod Pathol* 2001; 14(1):173A.
8. Mirza I, Yang B, Finn W, MacPherson N, Paproski S, Gascoyne RD, Hsi ED: Primary cutaneous follicular lymphoma (PCFL): clinicopathologic, immunophenotypic and molecular features. Poster presentation, United States and Canadian Academy of Pathology Annual Meeting, Atlanta, GA, 2001. *Mod Pathol* 2001: 14(1):172A.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

I. CLINICAL ACTIVITIES:

- A. Surgical Pathology Rotations, July (3/5), August (1/4), September (1/4), October (1/4), November (1/4), December (1/5), January - June (Sabbatical leave)
- B. Ophthalmic Pathology Service – 52 weeks/year

II. TEACHING ACTIVITIES:

- A. Pathology 600
 - 1. Obstructive Lung Disease - November, 2000
 - 2. Pulmonary Neoplasms - November, 2000
 - 3. Pathology of ARDS - November 2000
 - 4. Tissue Reactions to Infectious Agents - November, 2000
 - 5. Pulmonary Pathology Review for Medical Students November, 2000
 - 6. Gynecologic Pathology Review for Medical Students - April, 2001
 - 7. General Pathology Review for Medical Students - June, 2001
 - 8. Laboratory Instructor, September, 2000 - May, 2001
 - 9. Medical student question and answer sessions, October, 2000 - May, 2001
- B. Pathology 630:
 - 1. Respiratory Disease I - October, 2000
 - 2. Respiratory Disease II - November, 2000
- C. Residency Training:
 - 1. Topics in Medical Ethics I, II, III –2000
 - 2. Consultant's Seminar, September 2000
- D. Other educational activities:
 - 1. M4 student elective mentor, July 2000. January 2001. February 2001
 - 2. University of Michigan New Faculty Orientation. "Teaching Tips". September. 2000
 - 3. Center for Research on Learning and Teaching Workshops: "Tools and strategies for effective online discussions", October, 2000
 - 4. Center for Research on Learning and Teaching Workshops: "Multicultural course transformation", October, 2000
 - 5. Member, M-2 Respiratory Sequence Committee
 - 6. Course Director, M-4 Student Pathology Clerkships
 - 7. Radiology - Pathology Correlation Course Co-Director, April, 2001
 - 8. M1 student mentor, February – May, 2001
 - 9. M2 student mentor, September, 2000 - present
 - 10. Nominated for American Association of Medical Colleges Humanism in Medical Education Award, 2001

11. Center for Research on Learning and Teaching Workshops: "Getting students actively involved in large lecture classes", February, 2001
12. Center for Research on Learning and Teaching Workshops: "Faculty using technology to enhance learning: Tools, techniques and success stories", February, 2001
13. Enriching Scholarship 2001: "What is good teaching?"
14. Enriching Scholarship 2001: "Teaching with technology."
15. "Thoracic Pathology," Department of Surgery, October 2000

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. A Murine Model of Graft-Vs-Host Disease Lacrimal Gland Inflammation and Destruction: Histopathology, Immunopathology, and Intervention (Midwest Eye-Banks and Transplantation Center), Victor M. Elner, MD, PH.D(Principal Investigator), Andrew Flint MD (Co-Investigator)
- B. "Effect of Gamma Interferon Therapy on the Clinical Course of Patients with Idiopathic Pulmonary Fibrosis. Fernando Martinez, MD (Principal Investigator).
- C. "Lung Image Database Consortium (IU01 CA91099-01). Chuck Meyer, PhD (Principal Investigator)

PROJECTS UNDER STUDY:

- A. The separation of usual interstitial pneumonitis from nonspecific interstitial pneumonitis
- B. The cytopathologic features of vitreous fluids
- C. Interactive Teaching in Pathology
- D. Pathology teaching materials production

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

Interviewer of Cytopathology Fellowship Candidate. 2001
Interviewer of Pathology Faculty Candidate, 2001

V. OTHER RELEVANT ACTIVITIES:

- A. Member, Admissions Committee of the University of Michigan Medical School, 1995 - present
- B. Member, Rules Committee, Senate Advisory Committee on University Affairs, 1999 – 2001
- C. Resolution Officer, Office of Student Conflict Resolution, Division of Student Affairs, University of Michigan, 2001

EDITORIAL BOARDS:

None

INVITED LECTURES/SEMINARS:

None.

VI. PUBLICATIONS:

1. King TE, Schwarz M, Brown K, Tooze J, Colby TV, Flint A, Waldron J, Sherniack R. Idiopathic pulmonary fibrosis: Relationship between histopathologic features and mortality. Am J Respir Crit Care Med (in press)
2. Flaherty KA, Toews GB, Lynch III JP, Kazerooni EA, Strawderman III AL, Hariharan K, Flint A, Martinez FJ. Steroids in idiopathic pulmonary fibrosis: Prospective comparative study of varying dosage regimens. Am J Med, 20001; 110:278-82.
3. Martinez FJ, Flaherty KA, Flint A, et al. Histopathological variability in usual and nonspecific interstitial pneumonias. Am J Resp Crit Care (in press).

SUBMITTED PUBLICATIONS:

1. Flaherty KA, Toews GB, Travis WD, Colby T, Kazerooni EA, Gross BH, Jain A, Strawderman III RL, Paine R, Flint A, Lynch III JP, Martinez FJ. Clinical significance of histopathologic classification in patients with suspected idiopathic interstitial pneumonia: Results of a large, well characterized cohort.
2. Flaherty KA, Travis WD, Colby TV, Toews GB, Kazerooni EA, Gross, BH, Jain A, Strawderman III AL, Flint A, Lynch III, JP, Gay S, Martinez FH. Histopathological variability in idiopathic interstitial penumonia: Clinical implications.

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

1. Doerr TD, Marentette LJ, Flint A, Elner V. UPAR expression in adenoid cystic carcinoma of the skull base. AAO-HNSF/ARO Research Forum.
2. Brown RS, Goodman TM, Kison PV, Flint A, Wahl RL. FDG uptake and expression of hetokinase II (HK II) and GLUT-1 in untreated primary human non-small cel lung cancer (NSCLC).
3. Flaherty KA, Toews GB, Lynch III JP, Flint A, Colby TV, Travis WD, Martinez FJ. Rate of change in pulmonary function in patients with UIP and NSIP. Eur Respir J, 2000.
4. Flaherty KA, Kazerooni EA, Gross B, Toews GB, Lynch III JP, Flint A, Colby TV, Travis WD, Martinez FJ. Rate of change in semi-quantitative high resolution computer tomography (HRCT) scores in patients with UIP and NSIP. Eur Respir J, 2000.
5. Martinez FJ, Flaherty KA, Travis WD, Colby TV, Kazerooni EA, Gross BH, Jain A, Strawderman III RL, Flint A, Lynch III JP, Toews GB. Quantifying risk of mortality in idiopathic interstitial pneumonia (IIP). Eur Resp Soc.

6. Flaherty KA, Kazerooni E, Toews G, Colby TV, Travis WD, Gross BH, Flint A, Lynch III JP, Gay S, Martinez FJ. Changes in pulmonary function and semiquantitative HRCT scores in patients with UIP and NSIP. *Am J Resp Crit Care Med*, 2001;103, A983

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000- 30 JUNE 2001**

I. CLINICAL ACTIVITIES:

- A. Director, Pathology Data Systems.
- B. Director, Clinical Support Information Systems, Medical Center Information Technology, University of Michigan Health System (Resigned from position effective May 1, 2001).
- C. Coordinator of strategic planning, Medical Center Information Technology, University of Michigan Health System (effective May 1, 2001).

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

- A. Director of the Nineteenth Annual Symposium on Automated Information Management in the Clinical Laboratory (AIMC), Ann Arbor, Michigan, May 27-29, 1999. Meeting attracted 200 paid registrants and 28 vendors.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. The use Personal Digital Assistants (PDAs) for the transmission of laboratory test results to clinicians.
- B. Evolution of clinical laboratory web portals; e-commerce, and the e-laboratory.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Clinical Laboratory Directors Committee.

HOSPITAL:

- A. Member, CIO Executive Committee (CIOEC).
- B. Chairman, Clinical Support Information Systems Managers' Committee
- C. Compliance officer for the Department of Pathology

UNIVERSITY:

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

V. OTHER RELEVANT ACTIVITIES:

President, Association for Pathology Informatics (API), Bethesda, MD.

INVITED LECTURES AND SEMINARS:

1. Moderator of a series of lectures and panel discussion sponsored by the Washington G2 Report on the use of information technology in the clinical laboratories. Washington, D.C., October 27, 2000.
2. Pushing Test Results into Consumers' Pockets: Analysis of the Mobile Solution. A lecture presented at the 5th annual 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 28, 2000.
3. The Clinical Laboratory Industry as an E-Business: An Integrated and Strategic View of the Future. A lecture presented to the Pathology Department while a visiting professor at Duke University Medical School, Durham, North Carolina, January 4-5, 2001.
4. The Clinical Laboratory Industry as an E-Business: An Integrated and Strategic View of the Future. A lecture presented at the 24th annual Arnold O. Beckman Conference, AACC, Newport Beach, CA, February 11, 2001.
5. How and Why the Clinical Lab Industry Will Thrive as a Healthcare E-Business. A lecture presented as part of an AACC symposium entitled "The Clinical Lab Meets the Internet: Strategies and Solutions" planned and moderated by Bruce Friedman, Miami, FL, February 22, 2001.
6. Information Technology Overview for Lab Managers and Pathologists. A lecture presented at the 2001 Executive War College on Lab and Pathology Management, Seminar on Web-Based Laboratory Informatics Products, Cincinnati, Ohio, May 10, 2001.
7. The Digital and Virtual Department: A Political and Organizational View. A lecture presented as part of a three-day symposium entitled Practical PACS, Ann Arbor, MI, May 17, 2001.
8. A Total Laboratory Solution Employing a Vertical Laboratory Meta-Network. A lecture presented at the 19th annual symposium on Automated Information Management in the Clinical Laboratories (AIMCL), Ann Arbor, Michigan, May 30, 2001.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Friedman, B.A.: The total laboratory solution: A new laboratory e-business model based on a vertical laboratory meta-network. Clin Chem. 2001;1526-1535.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

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

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- 1. Immunohistochemical evaluation of sentinel lymph nodes for micrometastases: patterns of involvement and sensitivity of S100, HMB45 and melan-A immunostains (D. Karimipour, M.D., L. Lowe, M.D., L. Su, M.D., T. Johnson, M.D.)
- 2. S100 A6 protein expression in neurothekeomas (L. Su, M.D.)
- 3. Immunohistochemical quantitation of melanocytes in pigmented basal cell carcinomas
- 4. Sensitivity of melanocytic markers in vitiligo by immunohistochemistry
- 5. Granular cell tumors lack S100 A6 protein expression: an unusual feature for Schwann cell differentiation (N.S. McNutt, M.D., J.A. Reed, M.D., B. Finnerty)

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

None

REGIONAL AND NATIONAL:

A. Ad hoc manuscript reviewer, Journal of Cutaneous Pathology

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

None

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Fullen, D.R., Headington, J.T.: Factor XIIIa-positive dermal dendritic cells and HLA-DR expression in radial versus vertical growth-phase melanomas. J Cutan Pathol 553-558, 1998.
2. Judd, W.J., Fullen, D.R., Steiner, E.A., Davenport, R., Knafl, P.C.: Revisiting the issue: Can the reading for serologic reactivity following 37c incubation be omitted? Transfusion 39: 295-299, 1999.
3. Fullen, D.R., Reed, J.A., Finnerty, B., McNutt, N.S.: S100 A6 expression in fibrohistiocytic lesions. J Cutan Pathol 28: 229-234, 2001.
4. Fullen, D.R., Reed, J.A., Finnerty, B., McNutt, N.S.: S100 A6 preferentially labels type C nevus cells and nevus corpuscles: additional support for Schwannian differentiation of dermal nevi. J Cutan Pathol (in press).

BOOKS/CHAPTERS IN BOOKS:

None

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

1. Fullen, D.R., Headington, J.T.: Factor XIIIa-positive dermal dendritic cells and HLA-DR expression in radial versus vertical growth-phase melanomas. (Poster presentation, United States and Canadian Academy of Pathology, March, 1997)
2. Judd, W.J., Fullen, D.R., Steiner, E.A., Davenport, R., Knafl, P.C.: Omitting the 37c reading. (Platform presentation, American Association of Blood Banks, October, 1997).

3. Fullen, D.R., Reed, J.A., Finnerty, B., McNutt, N.S.: S100 A6 protein expression in fibrohistiocytic lesions. (Platform presentation, American Society of Dermatopathology, November, 1999.)
4. Fullen, D.R., Reed, J.A., Finnerty, B., McNutt, N.S.: S100 A6 preferentially labels type C nevus cells and nevic corpuscles: additional support for Schwannian differentiation of dermal nevi. (Poster presentation, American Society of Dermatopathology, October, 2000)
5. Murphy, M., Fullen, D.R., Carlson, J.A.: Low CD7 expression in benign and malignant cutaneous lymphocytic infiltrates: experience with an antibody reactive with paraffin-embedded tissue. (Poster presentation, American Society of Dermatopathology, October, 2000)

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

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

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

- A. Medical Students
 - 1. Fundamentals of Laboratory Medicine (PTHCLNL.101) 5 contact hours
- B. Pathology House Officers:
 - 1. Clinical Pathology Grand Rounds (2 lectures)
 - 2. Coordinator, Pathology House Officer rotation through Chemistry Lab.
 - 3. Review sign-out and interpretation of electrophoresis results.
 - 4. Review of selected topics in Clinical Chemistry with Block B residents.
- C. Postgraduate:
 - 1. Ph.D. Thesis Committee, Aaron Smith (5/96 to 10/00), Department of Chemistry.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Evaluation of new immunoassay methods for Troponin I and CK-MB.
- B. Clinical Study of 1,25 DihydroxyVitamin D determination by radioimmunoassay (sponsored by Diasorin, Inc.)
- C. Evaluation of meters and data management systems for point of care testing.
- D. Evaluation and implementation of a new line probe technique for measuring extractable nuclear antigens (ENA).
- E. Development of method to monitor serum caffeine levels.
- F. Evaluation of HPLC-MS methods for immunosuppressant drugs Tacrolimus and Sirolimus.

- G. PSA and Percent free PSA levels in an African-American population (Flint Mens Health Study).
- H. Evaluation of an enzymatic method for homocysteine determination.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL /HOSPITAL:

- A. 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

V. PUBLICATIONS:

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

1. Killeen, A.A., Ozturck, C.I., Giacherio, D.A., and Rubenfire, M. Variable expression of Type III hyperlipidemia phenotype in a family with ApoE R136C. Clin Chem 47 (S6) : A103, 2001
2. McBryde, K.D., Kudelka, T. L., Kershaw, D. B., Bienkiewicz, J.C., Mueller, B. A., Giacherio, D.A., and Smoyer, W.E. Clearance of Arginine for urea cycle defects by intermittent hemodialysis. Accepted for presentation at American Society of Nephrology annual meeting, San Francisco, CA.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

I. CLINICAL ACTIVITIES:

- A. Renal Biopsy Service – 10 days.
- B. Autopsy Service – 15 days.

II. TEACHING ACTIVITIES:

- A. Histopathology Lab Section for M1 medical students – 16.5 hours.
- B. Urinary Sequence Lab for M2 medical students – 12 hours.

III. RESEARCH ACTIVITIES:

None.

PROJECTS UNDER STUDY:

None.

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

MEDICAL SCHOOL/HOSPITAL:

- A. Member of Medical School Admissions 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 2000 - 30 JUNE 2001**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

- A. Medical Students:
 - 1. Sequence Co-Coordinator – Component II Endocrine Sequence.
 - 2. Component II Endocrine Sequence - 2 lectures on Endocrine Pathology.
 - 3. Endocrine Pathology Laboratories - preparation of course materials.
 - 4. Component IV Pathology Elective mentor – one month.
- B. House Officers:
 - 1. General Surgical Pathology - 4 months.
 - 2. Endocrine Surgical Pathology - 12 months as needed.
 - 3. Consultation Conferences - four.
 - 4. Molecular Pathology lectures.
 - 5. Endocrine Pathology lectures.
 - 6. Molecular cytology seminary.
- 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.

EXTERNAL:

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

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Co-Principal Investigator, "University of Michigan Endocrine Bank", Millie Schemblechler Adrenal Cancer Research Fund, 1/1/01 to 12/31/01 (\$100,000 direct costs), with Dr. Paul Gauger, Department of Surgery, 5% effort
- B. Co-Investigator, "Great-Lakes-New England Clinical and Epidemiology Center", NCI CA-99-007, 4/1/00 to 03/31/05 (\$4,987,159 total direct costs), with Dr. Dean Brenner, Department of Internal Medicine, 5% effort
- C. Co-Principal Investigator, "Towards a Molecular Classification of Tumors", NCI U19-CA84953, 9/99 to 3/04 (\$951,282/yr direct costs for 4.5 yrs), with S. Hanash, Department of Pediatrics, Pathology Core Director, 20% effort
- D. Co-Principal Investigator, "Proteomics Biomarker Development Laboratory", NCI U01-CA84982, 9/99 to 8/04 (\$304,900/yr direct costs for five years), with S. Hanash, Department of Pediatrics, 10% effort
- E. Director, "Tissue Procurement Contract", Genentech, Inc., 5/99 to 5/2001 (\$92,346 direct costs/year), 10% effort
- F. Principal Investigator, The University of Michigan Comprehensive Cancer Center, Millie Schembechler Adrenal Cancer Research Fund, "Gene Expression Profiles in Adrenal Cortical neoplasms using DNA Microarrays", 8/99 to 8/01 (\$15,000)
- G. Core Director, The University of Michigan Comprehensive Cancer Center, Tissue Procurement Service, 7-98 to present, 10% effort
- H. Core Director, The University of Michigan Comprehensive Cancer Center, Laser Capture Microdissection Core, 1-99 to present

PROJECTS UNDER STUDY:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL and INSTITUTIONAL:

- A. House Officer Candidate Interviews.
- B. Faculty Candidate Interviews.
- C. Sequence Co-Coordinator – Component II Endocrine Sequence
- D. Director, Tissue Procurement Service
- E. Director, Frozen Tumor Bank
- F. Director, Laser Capture Microdissection Core

- G. Medical Institutional Review Board (IRB-Med), full member.
- H. MSTP Career Advisory Panel

NATIONAL:

- A. Editorial Board, *Endocrine Pathology*

V. OTHER RELEVANT ACTIVITIES:

- A. Consultant, Genentech Corporation.
- B. Pathology Consultant, Asterand Corporation.

INVITED LECTURES/SEMINAR:

- A. Invited Speaker, Arthur Purdy Stout Memorial Lecture, "Follicular Lesions of the Thyroid", Annual Meeting of the American Society of Clinical Pathology / College of American Pathologists, San Diego, CA
- B. Invited Speaker, "Pathogenesis of Adrenal Cortical Carcinoma", International Academy of Pathology, Nagoya, Japan
- C. Pathology Department Research Seminar, "Pathogenesis of Adrenal Cortical Carcinoma".

VI. PUBLICATIONS:

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

1. Pawlik TM, Richards ML, Burney R, Giordano TJ, Thompson NW. Intravaginal Parathyroid Adenoma: Report of Two Cases. In press: World J Surg.
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. Scheingart DE, Giordano TJ, Benitez R, Burdick M, Starkman MN, and Strieter RM. Overexpression of CXC-chemokines by an adrenocortical carcinoma: A novel clinical syndrome.
4. Brichory F, Beer D, le Naour F, Giordano T, and Hanash S. Proteomics-based identification of PGP9.5 as a tumor antigen that induces a humoral immune response in lung cancer.
5. Giordano TJ, Shedden KA, Schwartz DR, Kuick R, Taylor JMG, Lee N, Misek DE, Greenson JK, Kardina SLR, Beer DG, Rennert G, Cho KR, Gruber SB, Fearon ER, Hanash S. Organ-specific molecular classification of primary lung, colon and ovarian adenocarcinomas using gene expression profiles. In press: *Am. J. Pathol.*

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Richards ML, Thompson NW, Giordano TJ. Spontaneous infarction of a parathyroid adenoma in primary hyperparathyroidism.
2. Bretz JD, Mesozi E, Giordano TJ, Thompson NW and Baker, JR Jr. Inflammatory cytokine regulation of TRAIL-mediated apoptosis in thyroid epithelial cells.

3. Beer DG, Kardia SLR, Huang C-C, Misek DE, Lin L, Chen G, Gharib TG, Giordano TJ, Thomas DG, Lizyness ML, Kuick R, Taylor JMG, Iannettoni MD, Orringer MB, Hanash S. Gene expression profiles define a high-risk group among patients with stage I lung adenocarcinoma.
4. Koch CA, Vortmeyer AO, Diallo R, Poremba C, Giordano TJ, Sanders D, Bornstein SR, Chrousos GP, Pacak K. Survivin: a novel neuroendocrine marker for pheochromocytoma.

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

1. Thomas D, Baker L, and Giordano T. Tissue microarray blocks: an efficient method for screening soft tissue and bony sarcomas. Presented at the 2000 Meeting of the Walther Cancer Institute
2. Thomas D, Giordano T, Sanders D, and Baker L. Her2/neu expression in osteosarcomas and other bony sarcomas. Presented at the 2000 Meeting of the Walther Cancer Institute.
3. Thomas D, Baker L, and Giordano T. Tissue microarray blocks: an efficient method for screening soft tissue and bony sarcomas. Presented at the 2000 Meeting of the Connective Tissue Oncology Society.
4. Thomas D, Giordano T, Sanders D, and Baker L. Her2/neu expression in osteosarcomas and other bony sarcomas. Presented at the 2000 Meeting of the Connective Tissue Oncology Society.
5. Koch CA, Vortmeyer AO, Poremba C, Giordano TJ, Sanders D, Chrousos GP, and Pacak K. Survivin: a novel neuroendocrine marker for pheochromocytoma. Presented at the 11th International Congress of Endocrinology.
6. Gruber SB, Sprecher B, Misek D, Kuick R, Tomsho L, Kardia S, Taylor J, Giordano T, Greenson J, Rennert G, Hanash S, and Fearon E. Integrated genomic and proteomic analysis of colorectal cancer. Presented at the 2000 American Cancer Society Schilling Conference.
7. Gruber SB, Rennert G, Bonner JD, Sprecher B, Lee N, Misek D, Kuick R, Tomsho L, Kardia S, Taylor J, Giordano T, Greenson J, Hanash S, and Fearon E. Integrated epidemiologic, genomic and proteomic approach to colorectal cancer. Presented at the 2000 Meeting of the Society of Epidemiological Research.
8. Thomas D, Giordano T, Sanders D, and Baker L. Her2/neu expression in osteosarcomas and other bony sarcomas. Presented at the 2000 Fall Cancer Research Symposium, University of Michigan Comprehensive Cancer Center.
9. Schteingart DE, Giordano TJ, Benitez R, Burdick M, Strieter RM. An animal model of human adrenocortical carcinoma. Presented at the 2001 Meeting of the Endocrine Society.
10. Tan LC, Thomas DG, Sanders D, Mataverde P, Baker L, Giordano TJ and Kleer CG. Detection of telomerase catalytic component (hTERT) in invasive and in situ lobular carcinomas. Presented at the 2001 Annual Meeting of the United States and Canadian Academy of Pathology.
11. Thomas DG, Sanders D, Mataverde P, Lizyness M, Baker L, and Giordano TJ. Laser capture microdissection (LCM) and RT-PCR of telomerase components from formalin fixed paraffin sections of solid tumors. Presented at the 2001 Annual Meeting of the United States and Canadian Academy of Pathology.
12. Giordano TJ. Co-chair, Proffered Papers Section in Techniques, 2001 Annual Meeting of the United States and Canadian Academy of Pathology.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

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 - April, 2000.
 - 3. Gastrointestinal and hepatic pathology tutoring - six months.
 - 4. Five 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.
 - 4. GI and Liver path teaching to GI and transplant fellows – 3 hours/year

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Co-Investigator R01CA81488-01 (\$4,547,772) “Molecular Epidemiology of Colorectal Cancer”, 20% Salary Support, years 1-4, Stephen Gruber, M.D., Ph.D. Principal Investigator.

- B. Co-Investigator N01-DK-9-2323 (\$1,433,559) "Hepatitis C Clinical Trial", 7% Salary Support, Anna Lok, M.D. Principal Investigator.
- C. Co-investigator in GI Study Group awarded \$15,955.00 grant for a workshop on "Reproducibility of the diagnosis of dysplasia in ulcerative colitis."
- D. Co-investigator with Hari Conjeevaram M.D., "Study of viral resistance to antiviral therapy of chronic hepatitis c (virahep-c) - clinical centers" (7.5% salary support year 2, 3% years 3 and 4), University of Michigan Grant NIH-NIDDK-01-007

PROJECTS UNDER STUDY:

- A. Study of Small cell carcinomas of the colon with GI Study Group
- B. Study of fatty liver and steatohepatitis with Hari Conjeevaram in Division of Gastroenterology..
- C. NIH study of HCV with Anna Lok in Division of Gastroenterology.
- D. NIH study of the Molecular Epidemiology of Colon Cancer in Israel.
- E. Study of molecular classification of tumors with Stephen Gruber and Thomas Giordano
- F. Study of etiology of pancreas cancer with David Garabrandt, School of Public Health.
Study of Yersinia and Crohn's disease with Laura Lamps at the University of Arkansas.
Study of UC 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.
Reviewer, Modern Pathology
Reviewer, Cancer Research
Webmaster, Hans Popper Hepatopathology Society.
Education Committee member, USCAP.
President, Gastrointestinal Pathology Society.

Judge for Resident Abstract competition, Hans Popper Hepatopathology Society
Editorial Board member, The Online Journal of Digestive Diseases

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Invited Participant, International Panel Study of Inflammatory Bowel Disease, Nottingham, England, July 2000
2. Moderator, Gastrointestinal Pathology Companion Meeting at IAP, Nagoya, Japan, Oct. 2000.
3. Chairperson of Proffered Papers, GI Pathology Section, IAP Meeting, Nagoya, Japan, Oct. 2000
4. Co-director of USCAP course entitled "Infectious Diseases of the GI tract," March, 2001.
5. Invited Panelist, Gastrointestinal Pathology Specialty Conference, USCAP Meeting, March 2001.
6. Invited Speaker, GI Pathology Society Companion Meeting at USCAP Meeting, Atlanta, March 2001.
7. Faculty Member, ASCP Workshop - Surgical Pathology of the Gastrointestinal Tract, Seattle, Washington, May 2001.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Valdez R, Bronner M, Appelman HD, Greenson JK: Diffuse Duodenitis Associated with Ulcerative Colitis. *Am J Surg Pathol* 24:1407-1413, 2000.
2. 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 Pathol* 32:379-388, 2001.
3. 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 Pathol* 32:368-378, 2001.
4. Lamps LW, Madhusudhan KT, **Greenson JK**, Pierce RH, Massoll NA, Dean PJ, Scott MA. The Role of *Yersinia enterocolitica* and *Yersinia pseudotuberculosis* in Granulomatous Appendicitis: A Histologic and Molecular Study. *Am J Surg Pathol* 25:508-15, 2001.
5. Schenk M, Schwartz AG, O'Neal E, Kinnard M, **Greenson JK**, Fryzek JP, Ying GS, Garabrant, DH. Familial Risk of Pancreas Cancer. *The Journal of the National Cancer Institute*. 93:640-644;2001.
6. Bavikatty NR, Goldblum JR, Nielsen S, Abdul-Karim FW, **Greenson JK**. Florid Vascular Proliferation of the Colon Related to Intussusception and Mucosal Prolapse: Potential Diagnostic Confusion with Angiosarcoma. Accepted in *Modern Pathology*
7. Giordano TJ, Shedden KA, Schwartz DR, Kuick R, Taylor JMG, Lee N, Misek DE, **Greenson JK**, Kardia SLR, Beer DG, Rennert G, Cho KR, Gruber SB, Fearon ER, Hanash S. Organ-specific molecular classification of primary lung, colon and ovarian adenocarcinomas using gene expression profiles. Accepted to *Am J pathol*.

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Resnick MB, Herzog Y, Brodzky A, **Greenson JK**, Eldar S, Gluzman-Poltorak Z, Newfeld G, Tzafrir C. Neuropilin-2 is a Novel Neuroendocrine Marker Expressed in Pancreatic Islet Cells and Islet Cell Tumors. Submitted to Modern Pathology.
2. Montgomery E, Bronner MP, **Greenson JK**, Haber MM, Hart J, Lamps LW et al. Are Ulcers a Marker for Invasive Carcinoma in Barrett's Esophagus (BE)? Data from a Diagnostic Variability Study with Clinical Follow-up. Submitted to Am J Gastroenterol.
3. Chiles MC, Madhusudhan KT, **Greenson JK**, Pierce RH, Scott MA, Dean PJ, Lamps LW. Yersinia Enterocolitica DNA is Detected in Crohn's Disease. Submitted to Am J Surg Pathol.
4. Quallich LD, Haftel HM, Greenson JK, Fontana RJ. Is it Crohn's disease? Severe systemic granulomatous reaction to sulfasalazine in a patient with rheumatoid arthritis : A case report and review of the literature. Submitted to Am J Gastroenterology

BOOKS/CHAPTERS IN BOOKS:

1. Inflammatory Diseases of the Colon, in Surgical Pathology of the Gastrointestinal Tract, Liver, Biliary tract, and Pancreas. Edited by Robert D. Odze, John R. Goldblum, and James Crawford. Harcourt Health Sciences.

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

1. Chiles MC, Madhusudhan KT, **Greenson JK**, Pierce RH, Scott MA, Dean PJ, Lamps LW. Yersinia Enterocolitica DNA is Detected in Crohn's Disease. Poster Presentation at USCAP Meeting 2001. Modern Pathol 14:82A, 2001.
2. Bavikatty NR, Goldblum JR, Nielsen S, Abdul-Karim FW, **Greenson JK**. Florid Vascular Proliferation of the Colon Related to Intussusception and Mucosal Prolapse: Potential Diagnostic Confusion with Angiosarcoma. Poster Presentation at USCAP meeting 2001. Modern Pathol 14:81A, 2001.
3. Hart J, Wang HL, Yang XJ, Kuan SF, Goldblum J, Burgart L, Lauwers G, Lewin D, Montgomery E, Washington K, Bronner M, Xiao SY, **Greenson JK**, Lamps L, Lazenby A. Immunohistochemical Evaluation of TTF-1 and CK 7 and 20 Expression in 54 Colorectal Neuroendocrine Carcinomas. Poster Presentation at USCAP meeting 2001. Modern Pathol 14:86A, 2001.
4. Wang HL, Goldblum J, Burgart L, Lauwers G, Lewin D, Montgomery E, Washington K, Bronner M, Xiao SY, **Greenson JK**, Lamps L, Lazenby A, Hart J. Biological Behavior and Molecular Pathology of Colorectal Neuroendocrine Carcinomas (CNCs). Platform Presentation at USCAP meeting 2001. Modern Pathol 14:98A, 2001.
5. Wang HL, Kuan SF, Goldblum J, Burgart L, Lauwers G, Lewin D, Montgomery E, Washington K, Bronner M, Xiao SY, **Greenson JK**, Lamps L, Lazenby A, Hart J. Do Colorectal Neuroendocrine Carcinoma Arise From Preexisting Adenoma? Poster Presentation at USCAP meeting 2001. Modern Pathol 14:98A, 2001.
6. Resnick MB, Cohen T, Newfeld G, **Greenson JK**. Neuropilin-2 is a Novel Neuroendocrine Marker Expressed in Pancreatic Islet Cells and Islet Cell Tumors. Poster Presentation at USCAP meeting 2001, Modern Pathol 14:202A, 2001.
7. Greenson JK, (Book Review) An Atlas of Gastrointestinal Endoscopy and Endoscopic Biopsies. Am J Surg Pathol 25:555;2001.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 -30 JUNE 2001**

60% Appointment
2 months, retirement furlough
2 months extended sick leave
8 months active consultancy, heart transplant service and pediatric pathology

I. CLINICAL ACTIVITIES:

- A. Pediatric Necropsies, ad hoc consultant.
- B. Pediatric Surgical Consultation Cases, intra and extra mural, 3x a wk., eight months.
- C. Heart biopsy service, regular back-up for Dr. Gerald Abrams.
- D. Teratology Unit, histology, ad hoc 8 months as necessary.
- E. 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.), ad hoc, as consultant.

II. TEACHING ACTIVITIES:

- A. House Officers in Pathology, as consultant on Pediatric cases in surgical reading rooms, eight months.
- B. House Officers in Pathology, gross and microscopic supervision of pediatric necropsies, ad hoc as consultant.

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.

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. Still in progress.
- 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.

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. Pediatric Cardiology Accepted for publication.
2. Jasty R, van Golen C, Lin H-J, Solomon G. Heidelberger K, Polverini P, Opipari A, Feldman E, Castle VP: Bcl-2 and N-Myc co-expression increases IGF-IR and features of malignant growth in neuroblastoma cell lines. Neoplasia (In press).

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

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. Christin Carpenter
 - b. Esther Choi
- B. Postdoctoral Fellows:
 - 1. Kate Blease, Ph.D.
 - 2. Jane Schuh, Ph.D.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

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.

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.

Co-investigator, *Monokine gene expression/regulation in lung injury.* R01 HL31237 (10%), \$200 000 per annum, 4/01/00 - 3/31/05.

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.

Co-investigator, *Specialized Centers of Research - Pathobiology of Fibrotic Lung Disease.* P50 HL56402-04 Tissue Core (5%), \$1 300 000 per annum, 09/01/97 - 08/30/01.

Principal Investigator, Specialized Centers of Research - Pathobiology of Fibrotic Lung Disease. Project 1: Chemokines and chemokine receptors in IPF. P50 HL56402-04 (20%), 185 917 per annum for Project 1, 12/01/01-11/30/06.

Principal Investigator, Role of CXCR4 During Allergic Airway Fibrosis.
Research Contract from AnorMED, Inc. 23, 135.00 per annum, 02/16/01 - 02/16/02.

Co-investigator, Monocyte/Macrophage Signals in Lung Granuloma.
R01 (15%), \$250 000.00 per annum, 07/01/01 - 06/30/06

Principal Investigator, Caspase Inhibition in the Context of Experimental CLP-induced Sepsis. Research Contract from Idun Pharmaceuticals, \$22,081.00 per annum, 07/01/01-06/30/02.

PENDING SUPPORT:

Principal Investigator, Therapeutic Targeting of RANTES/CCL5 during Chronic Fungal Asthma. R01 (45%), 175 000 per annum, 04/01/02 – 03/31/07.

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.
 3. University of Michigan. Office of the Vice President for Research.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS

1. American Society for Cell Biology, San Francisco, CA. Dec. 9-12, 2000. Title: '*Chemokine biology during chronic airway disease*'.
2. Transatlantic Airway Conference, Key Biscayne, FL. Jan 23-27, 2001. Title: '*Mechanisms of Airway Remodeling*'.
3. Aventis Pharmaceuticals, Bridgewater, N.J. Feb. 15-18, 2001. Title: '*Role of Chemokines in Chronic Fungal Asthma*'.
4. ASPET Short Course, Pharmacology of Inflammation: Basic Mechanisms and Therapeutic Treatments. Orlando, FL. March 29-April 4, 2001. Title: '*Cytokines in health and disease: the quest for the ultimate balance*'.
5. Department of Pathology (University of Michigan). April 23, 2001. Title: '*Role of chemokines and chemokine receptors in allergic disease*'.
6. Cystic Fibrosis Foundation, ABPA Consensus Conference, Bethesda, MD. June 12-13, 2001. Title: '*Animal Models of ABPA*'.
7. World Asthma Meeting, Chicago, IL. July 12-July 15, 2001. Title: '*Chemokines*'.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICAITON IN REFERRED JOURNALS.

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. *Inflamm. Res.*, 49(6): 297-304, 2000.
2. 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.*, 165: 1564-1572, 2000.
3. 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.*, 165: 1603-1611, 2000.
4. Bone-Larson C.L., Hogaboam C.M., Steinhauser M.L., Oliveira S.H.P., 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. Dependence on MCP-1. *Am. J. Pathol.*, 157: 1177-1186, 2000.

5. Steinhauer 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.*, 68 (11): 6108-6114, 2000. (Profiled by Reuters Health Information Services (Dec. 12, 2000)).
6. 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* 177: 8-20, 2000.
7. Matsukawa A., Hogaboam C.M., Lukacs N.W., Kunkel S.L. Chemokines and innate immunity. *Rev Immunogenet.* 2(3): 339-58, 2000.
8. Blease K., Lukacs N.W., Hogaboam C.M., Kunkel S.L. Review: chemokines and their role in airway hyperreactivity. *Respir. Res.* 1: 54-61, 2000.
9. 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 progression from acute to chronic colitis in the rat. *J Immunol.* 166(1): 552-558, 2001.
10. Blease K., Mehrad B., Standiford T.J., Lukacs N.W., Kunkel S.L., Hogaboam C.M. Anti-fungal and airway remodeling roles for murine MCP-1/CCL2 during pulmonary exposure to *Aspergillus fumigatus* conidia. *J. Immunol.*, 166(2): 1832-1842, 2001.
11. Matsukawa A., Kaplan M.H., Hogaboam C.M., Lukacs N.W., Kunkel S.L. Pivotal role of Signal Transducer and Activator of Transcription (Stat) 4 and Stat6 in the innate immune response during sepsis. *J. Exp. Med.*, 193: 679-688, 2001.
12. Blease K., Jackubzick C., Westwick J., Lukacs N., Kunkel S.L., Hogaboam C.M. Therapeutic effect of IL-13 immunoneutralization during chronic experimental fungal asthma. *J. Immunol.*, 166 (8): 5219-5224, 2001.
13. Matsukawa A., Lukacs N.W., Hogaboam C.M., Chensue S.W., Kunkel S.L. III. Chemokines and Other Mediators, 8. Chemokines and their receptors in cell mediated immune responses in the lung. *Microsc. Res. Tech.* 53 (4): 298-306, 2001.
14. Oliveira S. H. P., Hogaboam C. M., Berlin A., Lukacs N. W. SCF-induced airway hyperreactivity is dependent on leukotriene production. *Am. J. Physiol. (Lung Cell Mol Physiol)* 280: L1242-L1249, 2001.
15. Reardon C., Sanchez A., Hogaboam C.M., McKay D.M. Tapeworm infection reduces the epithelial ion transport abnormalities in murine dextran-sulfate sodium-induced colitis. *Infect. Immun.*, 69(7): 4417-4423, 2001.
16. Lukacs N.W., Hogaboam C.M., Chensue S.W., Blease K., Kunkel S.L. Type 1/Type 2-cytokine paradigm and the progression of pulmonary fibrosis. *Chest.* 120 (1): S5-8, 2001.
17. Lukacs N.W., Tekkanat K.K., Hogaboam C.M., Berlin A., Miller A., Evanoff H., Lincoln P., Maassab H. Respiratory Syncytial Virus predisposes mice to augmented allergic airway responses via IL-13-mediated mechanisms. *J. Immunol.*, 167(2): 1060-1065, 2001.

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., Steinhauer 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- α and signal transducer activator of transcription-3 during liver regeneration. *FASEB J.*

3. Blease K., Kunkel S.L., Jakubzick C., Puri R.K., Hogaboam C.M. Interleukin-13 fusion cytotoxin ameliorates chronic fungal asthma. *J. Immunol.*
4. Blease K., Schuh J., Jakubzick C., Lukacs N.W., Kunkel S.L., Joshi B.H., Puri R.K., Kaplan M., Hogaboam C.M. Stat6-deficient mice develop airway hyperresponsiveness and airway remodeling during chronic fungal-induced asthma. *Am. J. Pathol.*

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

1. Lukacs N.W., Oliveira S.H.P., Hogaboam C.M. SCF-induced chemokine production, allergic airway inflammation and airway hyper-reactivity. *In: Mast Cells and Basophils. Academic Press, Chapter 38, pages 609-621, 2000.*
2. Kunkel S.L., Phan S.H., Lukacs N.W., Hogaboam C.M., Chensue S.W Chemokine/cytokine biology during the evolution of fibrotic disease. *In: Progress in Inflammation Research. Ed: M.J. Parnham. Birkhauser Verlag, Basel, 2000.*
3. Mohamed H.H., Hogaboam C.M., Lukacs N.W., Bone-Larson C.L., Hayes P.C., Colletti L.M., Strieter R.M., Kunkel S.L., Simpson K.J. Circulating concentrations of CXC chemokines in acetaminophen induced fulminant hepatic failure. *Hepatology 32: (4) 153, Part 2, 2000.*
4. Bone-Larson C.L., Hogaboam C.M., Chen S-C., Lira S.A., Kunkel S.L. Enhanced liver regeneration in CXCR3-deficient mice after partial hepatectomy. *FASEB J., 15(4): A217.7, 2001.*
5. Ajuebor M.N., Hogaboam C.M., Kunkel S.L., Zagorski J., Wallace J.L. Involvement of the CXCR2/KC axis in the mediation of acute colonic inflammation. *FASEB J., 15(4): A529.1, 2001.*

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

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
- B. Co-Principal Investigator, "Mechanisms of MMP Involvement in Acute Lung Injury" NIH
- C. Principal Investigator, "Mechanisms of Vasculitis", Pfizer

PROJECTS UNDER STUDY:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

REGIONAL AND NATIONAL:

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

V. INVITED LECTURES AND SEMINARS:

- 1. Invited Main Speaker – 5 Ali Conference, Tokyo, Japan.
- 2. Invited Speaker- Mechanisms of Human Vasculitis, Milan, Italy.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. 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. Free Rad. Biol. Med., 2000; 29:8-16.

2. Shanley, T.P., Davidson, B.A., Nader, N.D., Bless, N., Vasi, N., Ward, P.A., Johnson, K.J., and Knight, P.R.: Role of macrophage inflammatory protein-2 in aspiration-induced lung injury. *Critical Care Medicine*. 2000;28(7):2437-2444.
3. Rich, P.B., Reickert, C.A., Sawada, S., Awad, S.S., Lynch, W.R., Johnson, K.J., Hirschl, R.B.: Effect of rate and inspiratory flow on ventilator-induced lung injury. *J Trauma*. 2000;49:903-11.
4. Yung, R., Ray, D., Eisenbraun, J., Deng, C., Attwood, J., Eisenbraun, M., Johnson, K., Miller, R., Hanash, S., and Richardson, B.: Unexpected effects of a heterozygous DNMT1 null mutation on age-dependent DNA hypomethylation and autoimmunity. *J. Gerontology:Biological Sciences*. 2001;56(6)B268-B276.
5. Warner, R.L., Beltran, L., Younkin, E.M., Lewis, C.S., Weiss, S.J., Varani, J., and Johnson, K.J.: Role of stromelysin 1 and gelatinase B in experimental acute lung injury. *Am J of Respir Cell and Mol Biol*, 2001;24:537-544.
6. Warner, R.L., Lewis, C.S., Beltran, L., Younkin, E.M., Varani, J., and Johnson, K.J.: The role of metalloelastase in immune complex-induced acute lung injury. *Am J of Pathol*. 2001;158:2139-2144.
7. Varani, J., Hattori, Y., Dame, M.K., Schmidt, T., Murphy, H.S., Johnson, K.J., Wojno, K.J.: Matrix metalloproteinases (MMPs) in fresh human prostate tumour tissue and organ-cultured prostate tissue: levels of collagenolytic and gelatinolytic MMPs are low, variable and different in fresh tissue versus organ-cultured tissue. *Br J Cancer*. 2001;84:1076-83.
8. O'Shea, S., Johnson, K., Clark, R., Sliwkowski, M.X., Erickson, S.L.: Effects of in vivo heregulin beta1 treatment in wild-type and ErbB gene-targeted mice depend on receptor levels and pregnancy. *Am J Pathol*. 2001;158:1871-80.

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, 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.
5. 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.
6. 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.
7. Yung, R., Kaplan, M., Ray, D., Schneider, K., Ru-Ran, M., Johnson, K.J., and Richardson, B.: Common Effector functions of autoreactive Th1 and Th2 cells suggest a mechanism for tolerance abrogation and autoantibody induction. Submitted for publication.
8. Yung, R., Kaplan, M., Ray, D., Schneider, K., Ru-Ran, M., Johnson, K.J. and Richardson, B.: Autoreactive murine Th1 and Th2 cells kill syngeneic macrophages and induce autoantibodies. 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. 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.
2. Okechukwu, C.N., Meier-Kriesche, H.U., Killen, P.D., Johnson, K.J., Armstrong, D., and Kaplan, B.: Histologic evolution of acute rejection by era. Submitted to AST Meeting, 2000.
3. Varani, J., Dame, M., Johnson, K.J., and Wojno, K.J.: Elaboration of matrix metalloproteinases by fresh human prostate tissue and by prostate tissue in organ culture. Experimental Biology 15(4):475.12, 2001.
4. Warner, R.L., Lukacs, N.W., Lewis, C.S., Varani, J., and Johnson, K.J.: Role of matrix metalloproteinases in a model of allergic inflammation in mice. Experimental Biology 15(4):50.1, 2001.
5. Burmeister, W., Varani, J., Bleavins, M., Dame, M., and Johnson, K.J.: Effects of three matrix metalloproteinase inhibitors (PD-159879, PD-166793 and marimastat) on proliferation of fibroblasts from human, marmoset, cynomolgus monkey, and rat. Experimental Biology, 15(4):131.11, 2001.
6. Johnson, K.J., Warner, R.L., Beltran, L., Younkin, E.M., Lewis, C.S., and Varani, J.: Role of stromelysin-1 and gelatinase B in experimental acute lung injury. Experimental Biology, 15(4):71.5, 2001.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

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 "100 Years of Human Blood Groups".
- 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. Pathology Residents:
 - 1. Provided instruction in immunohematology to house-officers during their Blood Bank Rotation (over 200 contact hours).
- F. Current Topics in Blood Banking Conference. Towsley Center for Continuing Medical Education:
 - 1. Program Director - Planned and coordinated the June, 2001 Current Topics in Blood Banking Symposium and Preconference Workshops.
 - 2. Presented Workshop entitled: "When the Urine is Red, or Not."
 - 3. Presented talk entitled: "Immune Hemolysis."
 - 4. Presented talk entitled: "Controversies in Immunohematology. "

III. RESEARCH ACTIVITIES:

- 1. Judd WJ, Dake L. PEG adsorption of autoantibodies results in loss of concomitant alloantibodies. *Transfusion* 2000;40(S):28.

2. Judd WJ, Davenport RD, Succhi M. An "enzyme-only" IgG C3-binding alloanti-C causing an acute hemolytic transfusion reaction. *Transfusion* 2000; 40(S):119.
3. Judd WJ, Downs T, Davenport RD, Hammond D, Sing C, Pehta JC. In vitro analysis of isohemagglutinin-depleted solvent detergent plasma. Presented at the International Society for Blood Transfusion Meeting, Vienna, Austria, July 2000.
4. Steiner EA, Judd WJ, Combs MR, et al. Prenatal antibody titers by the gel test. Submitted for presentation at the Annual Meeting of the American Association of Blood Banks, San Antonio, TX, October, 2001.

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. 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. If we do nothing else right it should be ABO/Rh typing. Annual Meeting of the Michigan Association of Blood Banks. Detroit, MI, September 2000.
2. The blood bank of the future. Annual Meeting of the Michigan Association of Blood Banks. Detroit, MI, September 2000.
3. Serological Artifacts. *Transfusion Medicine Symposium*. DiaMed Ch, Cressier, Switzerland, September 2000,
4. Carbohydrate antigens of the red cell membrane. DiaMed Ch, Cressier, Switzerland, September 2000,
5. The clinical insignificance of a positive direct antiglobulin test. DiaMed Ch, Cressier, Switzerland, September 2000,

6. Application of special methods in antibody identification. DiaMed Ch, Cressier, Switzerland, September 2000,
7. Blood groups and disease. DiaMed Ch, Cressier, Switzerland, September 2000,
8. Approaches to antibody identification. MABB Seminar on: Antibody Identification – Is it auto? Is it allo? Royal Oak, MI, October 2000.
9. Application of special methods in immunohematology. MABB Seminar on: Antibody Identification – Is it auto? Is it allo? Royal Oak, MI, October 2000.
10. Clinical insignificance of a positive direct antiglobulin test. AABB Annual Meeting, Washington, DC. November 2000.
11. Transfusing in the face of coldreactive autoantibodies. AABB Annual Meeting, Washington, DC. November 2000.
12. Meet the Expert. American Association of Blood Banks Annual Meeting, Washington, DC, November 2000.
13. Antibody detection to identification using tubeless techniques. American Association of Blood Banks Annual Meeting, Washington, DC, November 2000.
14. Impact of 3rd generation antibody detection methods on the Transfusion Service. Kentucky Association of Blood Banks Annual Meeting, Lexington, KY, March 2001.
15. Issues in implementing an electronic crossmatch. University of Texas Teleconference Center, San Antonio, TX, February 2001.

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

1. 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* 2001;41:371-4.
2. Judd WJ. Practice guidelines for prenatal/perinatal immunohematology revisited. **Transfusion: Accepted.**
3. Judd WJ. Pretransfusion testing practices: *Amer J Clin Pathol*: Accepted.
4. Judd WJ, Dake L. PEG adsorption of autoantibodies causes loss of concomitant alloantibody. *Immunohematology*: Accepted
4. Lee S, Russo DCW, Reiner AP, Lee JH, Sy MY, Telen MJ, Judd WJ, Simon P, Rodrigues MJ, Chabert T, Poole J, Jovanovic-Srzentic S, Levene C, Yahalom V, Redman CM. Molecular defects underlying the Kell null phenotype. *J Biol Chem*: Accepted.

CHAPTERS IN BOOKS:

1. Judd WJ. Pretransfusion testing. In: McClatchey KD, ed. *Clinical laboratory medicine*, ed 2. Baltimore: Lippincott, Williams and Wilkins. Accepted.
2. Judd WJ. Red cell immunology and compatibility testing. *Rossi's Principles of Transfusion Medicine*, ed 3. Baltimore: Lippincott, Williams and Wilkins. Accepted.

**ERIC KALDJIAN, M.D.
ADJUNCT ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY
PFIZER**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

I. CLINICAL ACTIVITIES:

II. TEACHING ACTIVITIES:

III. RESEARCH ACTIVITIES:

Tumor profiling:

- A. Expression profiling of human kidney cancer. Pfizer in-house support, collaboration with UM Pathology (Mark Rubin).
- B. Expression profiling of cancer cell lines and tumor xenografts
- C. Expression profiling of rodent cancer

Toxicities of matrix metalloproteinase inhibitors in rat joints.

Molecular organization of the lymph node reticular network.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

MEDICAL SCHOOL/HOSPITAL:

- A. Member, Sesquicentennial Celebration Committee

UNIVERSITY OF MICHIGAN:

REGIONAL AND NATIONAL:

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

HONORS AND AWARDS

PATENTS:

INVITED LECTURES/SEMINARS:

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Kaldjian, E.P., Gretz, J. E., Anderson, A. O., Sun, D., Shaw, S. Spatial and molecular organization of lymph node T cell cortex: A labyrinthine cavity bounded by an epithelium-like monolayer of fibroblastic reticular cells anchored to basement membrane-like extracellular matrix. *Int Immunol* (accepted for publication for Oct 2001)

BOOKS/CHAPTERS IN BOOKS:

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

1. Gieseg M., Rubin M., Cody T., Kaldjian E.P. Expression profiling renal tumors as a first step in the evaluation of tumor models. *AACR Oncogenomics*, January, 2001.
2. Sobocinski G., Shaw S., Anderson A.O. and Kaldjian E.P. Immunohistochemical localization of extra-cellular matrix proteins of the lymph node reticular network. *USCAP Annual Meeting*, March 2001.
3. Gieseg M., Rubin M., Cody T., and Kaldjian E.P. Discrimination of chromophobe and clear-cell renal cell carcinomas by mRNA expression profiling. *USCAP Annual Meeting*, March 2001.
4. Shah R, Kaldjian E.P., Gieseg M., Figurski J., Redman B.J. and Rubin M. Epidermal growth factory receptor expression is up-regulated in clear cell renal carcinoma: immunohistochemical tissue array confirmation of cDNA expression analysis. *USCAP Annual Meeting*, March 2001.
5. Sun, X., Develaraja, R., Renkiewicz, R., Qiu, L., Cody, T., Kaldjian, E.P., Welgus, H., and Baragi, V. Effects of Broad Spectrum Matrix Metalloproteinase Inhibitor, Marimastat on Growth Plate Chondrocytes. *First International Conference on Growth Plate*, May 2001.

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 2000 – 30 JUNE 2001

I. TEACHING ACTIVITIES:

- A. Post-doctoral Fellows: Jin-Lu Dai, M.D., Pete Smith, D.V.M.
- B. Graduate Students: Jian Zhang, M.D., Jill Murtha, D.V.M., Zheng Fu.
- C. Undergraduate Students: Avni Patel, Richard Prebish, Mary Whitney, Kara Deboer, Brian Adams, Bobbi Terelli, Bora Hong
- D. Director, ULAM Post-doctoral Fellow Training Grant
- E. Institute of Gerontology Training Grant
- F. Immunology Training Program
- G. Committees, Henli Chen and Maya Williams
- H. PIBS Admissions Committee Immunology Representative

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-15904), "Ethanol-mediated osteoporosis and interleukin-6". (Keller,PI) 3/1/98-2/28/03 \$748,000 direct cost; \$260,200 indirect cost)
- 2. National Institute of Aging (R01-AG-15904-S1), Supplement for "Ethanol-mediated osteoporosis and interleukin-6." (Keller, PI) 12/15/98-12/14/00 \$116,000 direct cost; \$56,000 indirect cost)
- 3. National Institute of Aging (R01-AG-11970), "Interleukin-6 and Osteoporosis" (Keller; PI), 5/1/95-4/30/01 Current & final two years \$630,600 direct cost; \$204,000 indirect cost.

4. 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).
5. U. Michigan Cancer (Center Summer Student Research Grant) "Role of interleukin-6 in prostate cancer bone metastases." (Dai; PI: Keller:Mentor) \$2,500.
6. Parke-Davis Pharmaceuticals, (Gift) Bone Biology Research Development; \$50,000.
7. National Institute of Aging. (R01) "Aging, gene expression and oxidative stress" (Keller; PI) 12/01/99-11/30/04 (\$135,000 annual directs)
8. Dept. of Defense PC991111 "Interleukin-6 and prostate cancer progression" (Keller; Role: PI) 10/01/99-09/28/02 (\$69,000 annual directs)
9. U. Michigan BMRC (Basic Science Program Project Planning Grant) "The biology of prostate cancer skeletal metastases." (Keller; Role: PI), 08/01/99-07/30/00 (\$10,000)
10. U. Michigan BMRC, Equipment Grant for PCR Realtime cyclers. (Keller, PI) (\$48,000)
11. U. Michigan SPORE in Prostate Cancer. "Role of AKT kinase in androgen-independent prostate cancer, Z. Fu Student Award. (Keller; Role: PI Mentor) 08/01/00-07/31/01 (\$5,000 annual direct costs).
12. U. Michigan SPORE in Prostate Cancer. "Role of osteoprotegerin in prostate cancer, J. Zhang Student Award. (Keller; Role: PI Mentor) 08/01/00-07/31/01 (\$5,000 annual direct costs).
13. U. Michigan SPORE in Prostate Cancer Summer Student Award (Student: Mary Whitney) (Keller Role: PI Mentor) \$5,000.
14. U. Michigan SPORE in Prostate Cancer Summer Student Award (Student: Zheng Fu) (Keller Role: PI Mentor) \$5,000.
15. UROP Summer Student Award (Student: Mary Whitney) (Keller Role: PI Mentor) \$2,500.

CONSULTANT ACTIVITY:

1. Pfizer Inc. Bone Biology, Contact, Vijaykumar Baragi, PhD.
2. Immunex, Seattle Washington, Prostate cancer skeletal metastasis

III. ADMINISTRATIVE ACTIVITIES:

ULAM:

- A. Director of Training Grant
- B. Chair, Jody C. Ungerleider Memorial Award Committee

MEDICAL SCHOOL/HOSPITAL/UNIVERSITY:

- A. Rackham Student Appeals Committee
- B. Associate Director, Connective Tissue Oncology Program (Cancer Center)
- C. Steering Committee, Program in Comparative Integrative Genomics (Physiology Dept.)
- D. PIBS Admissions Committee: Immunology Representative.
- E. Colony for Aged Rodents Advisory Committee
- F. Director, Transgenic and Mutant Rodent Core

REGIONAL AND NATIONAL:

A. Editorial Reviews:

1. *Hormone and Metabolic Research*
2. *Urology*
3. Clinical Cancer Research
4. *Journal of Clinical Investigation*
5. *The Prostate*

B. Grant Reviews

1. External Scientific Grant Reviewer, VA Merit Review Board, Department of Veterans Affairs
2. Ad hoc reviewer, U.S. Army Osteoporosis Grants
3. Ad hoc reviewer, EVMS Institutional Grants
4. American Federation for Aging Research
5. Office of Vice President for Research, U.M.
6. NIH: Special Emphasis Panel, NIA Claude Pepper Center Reviews
7. NIH: NIAAA: Special Emphasis Panel, Microarray based research on alcohol's effects on behavior, nervous system function and organ pathophysiology.
8. Department of Defense Section C Review Panel: Osteoporosis Grants
9. NIH: Caloric restriction Special Emphasis Panel
10. American Kennel Club Canine Research Grants
11. Department of Defense Pathology B: Prostate Cancer Grants
12. Chair, Biology of Aging Symposia. The second international conference on aging and geriatrics. Washington DC.

OTHER RELEVANT ACTIVITIES:

A. Memberships:

1. Director, Bone metabolism core, Program in Comparative Integrative Genomics
2. Michigan Comprehensive Cancer Center
3. Faculty, Graduate Program in Cellular and Molecular Biology
4. Faculty, Graduate Program in Immunology
5. Multipurpose Arthritis and Musculoskeletal Disease Center
6. Co-Director, Program in Connective Tissue Oncology, U.M. Cancer Center
7. Director, Nathan Shock Center Mutant & Transgenic Rodent Core

IV. **INVITED LECTURES/SEMINARS:**

1. "Skeletal Metastasis in Prostate Cancer." Invited seminar. Dept. of Urology. Kanazawa University, Japan, October 2000."
2. "Skeletal Metastasis in Prostate Cancer." Invited seminar. Dept. of Immunology. Tianjin Medical University, Tianjin, China, October 2000."

3. "Aging and cytokines." Invited seminar. Vaccines 2000 International Conference. Institute of Advanced Studies Geriatrics and Gerontology. Washington, D.C., October, 2000.
4. "Inflammatory cytokines." Invited seminar. Anemia in Geriatrics Summit Meeting. Sponsored by Amgen. Puerto Rico. February 2001.
5. "The Biology of Skeletal Metastases" Invited seminar. Eastern Virginia Medical School, Norfolk, VA. March 2001.
6. "The Biology of Skeletal Metastases" Invited seminar. American College of Veterinary Internal Medicine. Denver, CO, May 2001.
7. "Prostate Cancer Skeletal Metastasis: Gene Array Analysis and Murine Models." Invited Seminar. Midwestern Bone Biology and Cancer Meeting, Indiana University, Bloomington, IN. May 2001.
8. "Targeting Prostate Cancer Skeletal Metastasis." Invited Seminar. Immunex Corporation. Seattle, WA. June 2001.
9. "Use of Gene Array to Identify A Prostate Cancer Metastasis Suppressor Gene." Guanxi Medical University, Nanning, China. June 2001.
10. "The Biology of Aging." Invited seminar. Second International Conference on Aging. Washington, D.C. October, 2001.

V. **AWARDS/HONORS:**

1. Abstract selected for Plenary Poster Session, American Society Bone and Mineral Research Annual Meeting, Toronto, 2000.

VI. **PUBLICATIONS:**

PUBLISHED ARTICLES:

1. 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. 6:1969-1977, 2000.
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. 164:800-805, 2000.
3. Dai J, Lin D, Zhang J, Habib P, Smith P, Murtha J, Fu Z, Yao Z, Qi Y, Keller ET. Chronic alcohol ingestion induces osteoclastogenesis and bone loss through interleukin-6 in mice. J Clin Invest. 106:887-895, 2000.
4. Morris MD, Tarnowski CP, Timlin A, Carden A, Dreier JL, Ignelzi MA Jr., Lin DL, Keller ET. Raman imaging as a probe of chemical and biomechanical properties of bone tissue. Proc. SPIE. 3918, 151-158, 2000.
5. Smith PC, Hobish A, Lin DL, Culig Z, Keller ET. Interleukin-6 and prostate cancer progression. Cytokine and Growth Factor Rev. 12:33-40, 2001.
6. Keller ET, Zhang J, Yao Z, Qi Y. The impact of chronic estrogen deprivation on immunologic parameters in the ovariectomized rhesus monkey (*Macaca mulatta*) model of menopause. J Repro Immunol. 50:41-55, 2001.
7. Yao Z, Zhang J, Dai, J, Keller ET. Ethanol activates NF κ B DNA binding and p56lck protein tyrosine kinase in human osteoblast-like cells. Bone, 28:167-173, 2001.

8. Lin DL, Tarnowski CP, Patel AH, Rohn E, Morris MD, Keller ET. The bone metastatic LNCaP-derivative C4-2B prostate cancer cell line induces mineralization *in vitro*. *Prostate*, 47:212-221, 2001.
9. Harada S, Keller ET, Fujimoto N, Koshida K, Namiki M, Matsumoto T, Mizokami A. Longterm exposure of tumor necrosis factor- α causes hypersensitivity to androgen and anti-androgen withdrawal phenomenon in LNCaP prostate cancer cells. *Prostate*, 46:319-326, 2001.
10. Zhang J, Dai J, Smith P, Qi Y, Lin D, Strayhorn C, Mizokami A, Fu Z, and Keller ET. Osteoprotegerin inhibits prostate cancer-induced osteoclastogenesis and prevents prostate tumor growth in the bone of mice. *J Clin Invest*, 107:1235-1244, 2001.

ARTICLES ACCEPTED FOR PUBLICATION:

1. Zhang J, Johnston G, Stebler B, Keller ET. Oxidative stress-mediated activation of NF κ B and the interleukin-6 promoter requires NF κ B-inducing kinase activity. *Antioxidant Redox Signaling*, In Press.
2. Richard V, Lairmore MD, Green PL, Feuer G, Erbe RS, Albrecht B, Keller ET, Dai J, Rosol TJ. Humoral hypercalcemia of malignancy: SCID/beige mouse model of adult T-cell lymphoma (ATL) associated with human T-cell lymphotropic virus infection. *American Journal of Pathology*, In Press.
3. Smith PC and Keller ET. Anti-interleukin-6 monoclonal antibody induces regression of human prostate cancer xenografts in nude mice. *Prostate*, In Press.
4. Lin DL, Keller ET. Interleukin-6 induces androgen receptor activity through up-regulation of receptor expression in prostate cancer cells. *Clin Cancer Res*, In Press.

ABSTRACTS:

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* 2000.
2. Keller ET, Lin D, Dai J, Habib P, Zhang J, Murtha J, Smith P, Fu Z. Alcohol promotes bone loss through interleukin-6 induced osteoclastogenesis. *American Society for Bone and Mineral Research Annual Meeting*, Toronto, 2000.
3. Lin D, Zhang J, Dai J, Keller ET. Alcohol induces interleukin-6 secretion from primary human osteoblasts and bone marrow stromal cells *in vitro*. *American Society for Bone and Mineral Research Annual Meeting*, Toronto, 2000.
4. Zhang J, Devalaraja R, Dai J, Baragi V, Keller ET. Osteoprotegerin (OPG) and anti-interleukin-6 (IL-6) antibody inhibit osteoclastogenesis induced by prostate cancer cells *in vitro*. *American Society for Bone and Mineral Research Annual Meeting*, Toronto, 2000.
5. Dai JL, Zhang J, Keller ET. BMP-7 is expressed in prostate carcinoma and down regulated by PTHrP *in vitro*. *American Association for Cancer Research Annual Meeting*, New Orleans, 2001.
6. Fu Z, Keller ET. Identification of Raf kinase inhibitor protein (RKIP) as a metastasis suppressor gene in prostate cancer skeletal metastasis. *American Association for Cancer Research Annual Meeting*, New Orleans, 2001.

7. Lin DL, Tarnowski CP, Zhang J, Rohn E, Patel AH, Morris MD, Keller ET. Osteotropic prostate cancer cells develop an osteoblastic phenotype, including hydroxyapatite production. American Association for Cancer Research Annual Meeting, New Orleans, 2001.
8. Smith PS and Keller ET. Anti-Interleukin-6 Monoclonal Antibody Inhibits Prostate Cancer Growth In Vivo. American Association for Cancer Research Annual Meeting, New Orleans, 2001.
9. Zhang J, Dai JL, Qi Y, Strayhorn C, Lin DL, Fu Z, Keller ET. Osteoprotegerin (OPG) inhibits prostate cancer cells induced osteoclastogenesis and prevents the establishment of prostate cancer skeletal metastasis in mice. American Association for Cancer Research Annual Meeting, New Orleans, 2001.
10. Zhang J, Dai JL, Keller Et. Anti-human OPG antibody sensitizes prostate cancer cells to TRAIL-mediated apoptosis in vitro. American Association for Cancer Research Annual Meeting, New Orleans, 2001.
11. Zhang J, Dai J, Lin D, Habib P, Smith P, Murtha J, Fu Z, Yao Z, Qi Y, Keller ET. Osteoprotegerin abrogates chronic alcohol ingestion-induced bone loss in mice. American Society for Bone and Mineral Research Annual Meeting, Phoenix, AZ, 2001.
12. Dai J, Zhang J, Lin D, Keller ET. Prostate cancer cells induce osteoblastogenesis through bone morphogenetic proteins. American Society for Bone and Mineral Research Annual Meeting, Phoenix, AZ, 2001.
13. Lin D, Zhang J, Dai J, Keller. Alcohol induces interleukin-6 secretion from primary human osteoblasts and bone marrow stromal cells in vitro. American Society for Bone and Mineral Research Annual Meeting, Phoenix, AZ, 2001.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

- A. M2 Pathology Lecture - Renal Sequence (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 (7 hours).
- F. Renal Pathology for Nephrology Fellows Lectures (9 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, "The Glomerular Podocyte", NIH RO1-DK46073, (10% Effort) \$225,000 direct costs/year, 4/1/02-3/30/95.
- B. Co-Investigator, "Mouse Models of of Diabetic Nephropathy and Neuropathy", RFA-DK-01-009, 5% Effort, \$545,421 direct costs/year, 9/30/01-9/30/06.

PROJECTS UNDER STUDY:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

- A. Faculty recruitment, Departments of Internal Medicine, Pediatrics.
- B. Component II Curriculum development, M2 Urinary System.
- C. 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. Kidney International.
 - 2. Journal of Clinical Investigation.
 - 3. Journal of American Society of Nephrology.

V. INVITED LECTURES AND SEMINARS:

None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. 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:

None

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

- 1. Brophy PD, Mills M, White SC, Killen P, Gregory MJ, Smoyer WE: Presentation and Clinical Course of Pediatric Membranous Lupus Nephritis. J Amer Soc Nephrol, 2001

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

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: Bone Marrow Transplant, Pediatric Oncology
- 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:
Fellows: Drs., Emma Campbell, Kate Blease, Kim Tekkanat, Akihiro , Matsukawa, Sandra Oliveira, Jane Schuh, Allison Johns, Steven Lundy, Traci Ness, Robert Edwards
Graduate Students (MSTP): Sara Cheng (MSTP), Cindi Bone-Larsen, Claudia Jakubzick, Molly Thomas
Medical Students: Matt Steinhauser
Undergraduate Students: Joe Barber, Rob Schrader, Matthew Slenderbrook, Ester Choi, Kristin Carpenter
- P. Doctoral Thesis Committee Member/Orals Committee for the following graduate students: Brian Lane (CMB), Joyce J. Lai (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), Tina Yee (Micro/Immunology)
- Q. Oral preliminary examination committee Allison Miller (Pathology) (Pathology) Jennifer A. Kennell (CMB)
- R. Facilitator CIC SROP Conference Research Roundtable

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

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

PROJECTS UNDER STUDY:

- A. Role of cytokines in acute inflammation
- B. Regulation of chemokine gene expression
- C. Macrophage-lymphocyte interactions in the initiation, maintenance, and resolution of chronic inflammation
- 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
- G. Chair, Medical School Selection Tuition Selection 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, U of M Multi-Purpose Arthritis Center
- K. Member, Human Research Coordinating Council

- L. CMB Advisory Committee
- M. Dean's Research Advisory Board
- N. Medical School Space master Plan Steering Committee
- O. Medical School Communications Advisory Committee
- P. Member, Advisory Committee on Medical School Appointments, Promotions, and Tenure
- Q. Member, Human Research Coordinating Council (IRB review process)
- R. Member, Dean's Task Force on Rodent Populations
- S. Distinguished Faculty Lectureship Award (2001)
- T. Faculty Min-Medical School

REGIONAL AND NATIONAL:

- A. Associate Editor, Journal of Clinical Investigation
- B. 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. Co-Chair 2002 International Chemokine Conference
- J. Member, Advisory Board XIth International Vascular Biology Meeting
- K. 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
- L. Grant Reviewer, The Arthritis Society
- M. Grant Reviewer, Veterans Administration
- N. National Institutes of Health Study Section, Lung Biology and Pathology
- O. Elected American Society for Clinical Investigation

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

Invited Speaker, International Symposium on Chemokines, Horsham, England September 2000

Invited Speaker, American Association of Pharmaceutical Societies, Satellite meeting on experimental models of disease. October, 2000

Invited Speaker, Arthur Atsunobu Hirata Memorial Lecture in Immunology, University of Kansas, November 2000

Visiting Professor, National Center for Biotechnology, University of Madrid, Madrid Spain, Nov 2000

Invited Speaker, Emerging trends in the use of animal models in cardiopulmonary disease, San Francisco, CA March 2001

Invited Speaker, Psychoneuroimmunology Research Society Symposium, Orlando Fl March 2001

Invited Speaker, Experimental Biology 2001, Orlando, Fl, March 2001

Invited speaker, session chair. William Harvey Lecture Series, Chemokines and Chemokine Receptors, Porto, Portugal, April 2001

Invited Speaker, First World Association of Sarcoidosis and other Granulomatous Disease Conference, Venice Lido, Italy, June 2001

Visiting Professor, Department of Pathology McMaster University, June 2001

VI. PUBLICATIONS:

ARTICLES PUBLISHED IN REFEREED JOURNALS:

1. Blease, K., Lukacs, N.W., Hogaboam, C.M., Kunkel, S.L. Chemokines and their role in airway hyper-reactivity. *Respiratory Research*. 2000; 1:54-61.
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 response to *Aspergillus* in CCR2^{-/-} mice. *J. Immunol.* 2000; 165: 2603-1611.
3. Steinhäuser, M.L., Hogaboam, C.M., Matsukawa, A., Strieter, R.M., Kunkel, S.L. The chemokine C10 promotes disease resolution and survival in an experimental model of bacterial sepsis. *Infection Immunity*. 2000;68:6108-6114.
4. Matsukawa, A., Hogaboam, C.M., Lukacs, N.W., Kunkel, S.L. Chemokines and innate immunity. *Rev Immunol* 2000; 2:339-358.
5. Frank, S.M., Kluger, M.J., Kunkel, S.L. Elevated thermostatic set-point in postoperative patients. *Anesthesiology*. 2000, 93:1426-1431.
6. Biedermann T., Kneilling M., Mailhammer, R., Maier, K., Sander, C.A., Kollias, G., Kunkel S.L., Hultner, L., Rocken, M. Mast cells control neutrophil recruitment during T cell mediated delayed-type hypersensitivity reactions through tumor necrosis factor and macrophage inflammatory protein 2. *J. Exp Med* 2000, 192:1441-1452.
7. Bone-Larson C.L., Hogaboam, C.M., Steinhäuser, M.L., Oliveria, S.H., Strieter, R.M., Kunkel, S.L. Novel protective effects of stem cell factor in a murine model of acute septic peritonitis. Dependence on MCP-1. *Am. J. Pathol.* 2000; 157:1177-1186.
8. Blease, K., Kunkel, S.L., Hogaboam, C.M. Acute inhibition of nitric oxide exacerbates airway hyperresponsiveness, eosinophilia, and CC chemokine generation in a murine model of fungal asthma. *Inflamm Res* 2000;49:297-304.
9. Bian, Z.M., Elner, S.G., Yoshida, A., Kunkel, S.L., Su, J., Elner, V.M. Activation p38, ERK1/2, and NIK pathways is required for IL-1 beta and TNF alpha-induced chemokine expression in human retinal pigment epithelial cells. *Exp. Eye Res.* 2001; 73:111-121.
10. Fife, B.T., Kennedy, K.J., Paniagua, M.C., Lukacs, N.W., Kunkel, S.L., Luster, A.D., Karpus, W.J. CXCL10 (IFN-gamma inducible protein-10) control of encephalitogenic CD4⁺ T cell accumulation in the central nervous system during experimental autoimmune encephalomyelitis. *J. Immunol.* 2001; 166:7616-7624.
11. Bian, Z.M., Elner, V.M., Yoshida, A., Kunkel, S.L., Elner, S.G. Signaling pathways for glycated human serum albumin-induced IL-8 and MCP-1 secretion in human RPE cells. *Invest Ophthalmol Vis Sci* 2001;42:1660-1668.
12. Yoshida, A., Elner, S.G., Bian, Z.M., Kunkel, S.L., Lukacs, N.W., Elner, V.M. Differential chemokine regulation by Th2 cytokines during human RPE-monocyte co-culture. *Invest Ophthalmol Vis Sci*. 2001;42:1631-1638.
13. 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. *Miocr Res Tech* 2001; 53:298-306.

14. Blease, K., Jakubzick, C., Westwick, J., Lukacs, N., Kunkel, S.L., Hogaboam, C.M. Therapeutic effect of IL-13 immunoneutralization during chronic experimental fungal asthma. *J. Immunol.* 2001; 166:5219-5224.
15. Matsukawa, A., Kaplan, M.H., Hogaboam, C.M., Lukacs, N.W., Kunkel, S.L. Pivotal role of signal transducer and activator of transcription (STAT)4 and Stat 6 in the innate immune response during sepsis. *J. Exp. Med.* 2001;193:679-688.
16. Chensue, S.W., Lukacs, N.W., Yang, T.Y., Shang X., Frait, K.A., Kunkel, S.L., Kung, T., Wiekowski, M.T., Hedrick, J.A., Cook, D.N., Zingoni, A., Narula, S.K., Zlotnik, A., Barrat, F.J., O'Garra, A., Napolitano, M., Lira, S.A. Aberrant in vivo T helper type 2 cell response and impaired eosinophil recruitment in CC chemokine receptor 8 knockout mice. *J. Exp. Med.* 2001; 193:573-584.
17. Koch, A.E., Volin, M.V., Woods, J.M., Kunkel, S.L., Connors, M.A., Harlow, L.A., Woodruff, D.C., Burdick, M.D., Strieter, R.M. Regulation of angiogenesis by the CXC chemokines interleukin-8 and epithelial neutrophil activating peptide 78 in the rheumatoid joint. *Arthritis Rheum.* 2001; 44:31-40.
18. Barton, C.C., Barton, E.X., Ganey, P.E., Kunkel, S.A.L., Roth, R.A. Bacterial lipopolysaccharide enhances aflatoxin B1 hepatotoxicity in rats by a mechanism that depends on tumor necrosis factor alpha. *Hepatology* 2001; 33:66-73.
19. Cheng, S.S., Lai, J.J., Lukacs, N.W., Kunkel, S.L. Granulocyte-macrophage colony stimulating factor up-regulates CCR1 in human neutrophils. *J. Immunol.* 2001; 166:1178-1184
20. 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 progression from acute to chronic colitis in the rat. *J. Immunol.* 2001;166:552-558.
21. Blease, K., Mehrad, B., Lukacs, N.W., Kunkel, S.L., Standiford, T.J. Hogaboam, C.M. Antifungal and airway remodeling roles for murine monocyte chemoattractant protein-1/CCL2 during pulmonary exposure to *Aspergillus fumigatus* conidia. *J. Immunol.* 2001, 166:1832-1842.
22. Lukacs, N.W., Hogaboam, C.M., Chensue, S.W., Blease, K. Kunkel, S.L. Type1/type2 cytokine paradigm and the progression of pulmonary fibrosis. *Chest* 2001, 120:1s

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

I. CLINICAL ACTIVITIES:

- A. Gynecologic Pathology Consultation - twelve months.
- B. Gynecologic Oncology Semimonthly Tumor Planning Conference - twelve months.
- C. Autopsy service – five months (6 weeks, 3 weekends).
- D. Gynecologic Oncology – Colposcopy Clinic, one half day/week, twelve months.
- E. Placental Pathology – twelve months

II. TEACHING ACTIVITIES:

- A. Residents:
 - 1. Sign-out - Gynecologic Pathology, Placentas, and Autopsy cases.
 - 2. Review cases and supervise presentation of semimonthly Gynecologic Oncology Tumor Planning Conference – twelve months.
 - 3. Instruction in the Gross Examination, frozen section diagnosis, and processing of Gynecologic Surgical specimens and Placentas, July 2000.
 - 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, “Blue Book” Online guide to Gynecologic Oncology, and other resources
 - 9. Morbidity and Mortality Conferences – Internal Medicine, General Surgery, and Obstetrics & Gynecology
- B. University of Michigan Medical Students:
 - 1. M2, Obstetrics & Gynecology Sequence: Five hours Gynecologic Pathology lectures; preparation of examination questions.
 - 2. M2, Obstetrics & Gynecology Sequence: Laboratory instruction.
 - 3. M2 resource web page in Gyn Pathology (<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.
 - 5. M3 – Teaching during weekly Colposcopy Clinic
- C. Michigan State University Medical Students
 - 1. M2, Obstetrics & Gynecology Sequence: Two hours Gynecologic Pathology lectures; preparation of examination questions.
- D. Ob/Gyn Residents and Gynecologic Oncology Fellow:
 - 1. Semimonthly Tumor Planning Conference – twelve months.
 - 2. Colposcopy clinic staff – one-half day per week (twelve months).
 - 3. Operating Room Instruction – approximately one-half day per week
 - 4. Lectures in Gynecologic Pathology to Gyn Oncology Service – two/year
 - 5. Gyn Pathology Rotation for 3rd year Gyn Oncology Fellow – one month

- E. Dental Students
 - 1. Pathology 631, Fall 2000. 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%, completed June 2001.
- B. BioSampleX Proposal: To Create a Tissue Bank Serving Biotechnology Research Companies Supported by the Oxford Bioscience Venture Capital Group
BioSampleX, Inc.
11/01/00 - 10/31/02
\$250,060

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 2000. "Gynecologic Pathology Reporting for the General Pathologist".
2. The 9th Annual Primary Health Care of Women, December 2000 at Towsley Center. "Highlights in Gynecologic Pathology: Clinical Pathologic Correlation of Selected Cases at the University of Michigan".
3. Automated Information Management in the Clinical Laboratory (AIMCL) 2001. "Innovations in Digital Imaging Technology in the Pathology Laboratory".

VI. PUBLICATIONS:

ARTICLES PUBLISHED IN REFEREED JOURNALS:

1. Smith YR, Haefner HK, **Lieberman RW**, Quint EH. Comparison of Microscopic Examination and Human Papillomavirus DNA Subtyping in Vulvar Lesions of Premenarchal Girls. J Pediatr Adolesc Gynecol (2001) 14:81-84.

ARTICLES SUBMITTED TO REFEREED JOURNALS:

1. Feters MD, **Lieberman RW**, Abrahamse PH, Shanghvi RV, Sonnad SS. Cost Effectiveness Of Papanicolaou Screening For Vaginal Cancer After Hysterectomy For Benign Disease. Submitted to JAMA, June 2001.
2. Heller DS, Haefner H, Hameed M, **Lieberman RW**. Hidradenitis Suppurativa: Immunohistochemical Evaluation of Apocrine & Eccrine Involvement. Submitted to J Lower Genital Tract Disease, June 2001.

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 2000 - 30 JUNE 2001**

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

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. "Glycoconjugate function in mammals". Source of award: Howard Hughes Medical Institute
- B. Program Project - Project #2 Principal Investigator, "Carbohydrate-dependent adhesion of normal and tumor cells", NIH - CA71932 (25% effort), \$732,109/five years direct cost, 07/08/96 - 06/31/02
- 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, Biomedical Scholars Program Committee
- D. Chair, Biomedical Scholars Program Committee
- E. Member, Microarray and Microchip Technology Advisory Committee
- F. Member, Department of Pathology's Internal Review Committee
- G. Member, Department of Pathology's Graduate Program Committee
- H. Member, University of Michigan Technology Transfer Committee
- I. 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 the European Journal of Biochemistry
- D. Consulting Reviewer for Proceedings of the National Academy of Sciences USA, Journal of Cell Biology, Journal of Experimental Medicine, Biochemistry, Journal of Immunology, Glycoconjugate Journal, Cell, Nature Genetics, Immunity, Nature Immunology, Blood, and Transfusion
- E. 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. Glycosylation loci that determine selectin-dependent leukocyte trafficking events. Department of Molecular and Cell Biology, Boston University Goldman School of Dental Medicine, Center for Advanced Biomedical Research. Boston. September 2000.
- 2. Leukocyte-endothelial cell adhesion events determined by mammalian glycosylation pathways. Cardiovascular Research Center Symposium. Department of Cardiology, University of Michigan Medical School. September 2000.
- 3. Molecular approaches to understanding mammalian glycosylation. Glycoconjugates in Biological Systems. Karolinska Institute. Stockholm, Sweden. October 2000.
- 4. Glycosylation loci that determine selectin-dependent leukocyte trafficking events. Oklahoma Medical Research Foundation. Oklahoma City, OK. November 2000.
- 5. Requirements for selectin ligands for lymphocyte trafficking to lymph nodes and sites of inflammation. The Scripps Research Institute. La Jolla, CA. March 2001.

VII. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Weninger W, Ulfman LH, Cheng G, Lowe JB, and von Andrian UH. Specialized contributions by $\alpha(1,3)$ -fucosyltransferase-IV and FucT-VII during leukocyte rolling in dermal microvessels. *Immunity* 12:665-676, 2000.
2. Williams DA, Tao W, Yang F, Kim C, Gu Y, Mansfield P, Levine JE, Petryniak B, Derrow CW, Harris C, Jia B, Zheng Y, Ambruso D, Lowe JB, Atkinson SJ, Dinauer MC, and Boxer L. A dominant negative mutation of the hematopoietic-specific Rho GTPase, Rac 2, is associated with a human phagocyte immunodeficiency. *Blood* 96:1646-1654, 2000.
3. 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. *J Biol Chem* 275:31353-31360, 2000.
4. Misra AK, Ding Y, Lowe JB, and Hindsgaul O. A concise synthesis of the 6-O- and 6'-O-sulfated analogues of the sialyl Lewis X tetrasaccharide. *Bioorg Med Chem Lett* 10:1505-1509, 2000.
5. Pykari M, Toivonen S, Natunen J, Niemela R, Salminen H, Aitio O, Ekstrom M, Parmanne P, Valimaki M, Alais J, Auge C, Lowe JB, Renkonen O, and Renkonen R. The acceptor and site specificity of $\alpha(1,3)$ -fucosyltransferase V. High reactivity of the proximal and low of the distal Gal β 1-4GlcNAc unit in i-type polylactosamines. *J Biol Chem* 275:40057-40063, 2000.
6. Lowe JB. Glycosylation, Immunity, and Autoimmunity. *Cell* 104:809-812, 2001.
7. Domino SE, Zhang L, and Lowe JB. Molecular cloning, genomic mapping, and expression of two *Secretor* blood group $\alpha(1,2)$ -fucosyltransferase genes differentially regulated in mouse uterine epithelium and gastrointestinal tract. *J Biol Chem* 276:23748-23756, 2001.
8. Homeister JH, Thall AD, Petryniak B, Maly P, Rogers CE, Smith PL, Kelly RJ, Gersten KM, Askari S, Cheng G, Smithson G, Marks RM, Misra A, Hindsgaul O, von Andrian UH, and Lowe JB. The $\alpha(1,3)$ fucosyltransferases Fuc-TIV and Fuc-TVII exert collaborative control over selectin-dependent leukocyte recruitment and lymphocyte homing. *Immunity* 15:115-126, 2001.
9. Yeh J-C, Hiraoka N, Petryniak B, Nakayama J, Ellies LG, Rabuka D, Hindsgaul O, Marth JD, Lowe JB, and Fukuda M. Novel sulfated lymphocyte homing receptors and their control by a new core 1 extension $\beta(1,3)$ -N-acetylglucosaminyltransferase. *Cell* 105:957-969, 2001.
10. Smithson G, Rogers CE, Smith PL, Scheidegger EP, Petryniak B, Myers JT, Kim DSL, Homeister JW, and Lowe JB. Fuc-TVII is required for Th1 and Tc1 lymphocyte selectin ligand expression and recruitment in inflammation, and together with Fuc-TIV regulates naïve T cell trafficking to lymph nodes. *J Exp Med* 2001. in press.

ARTICLES SUBMITTED OR IN PREPARATION:

1. Smith PL, Rogers CE, Myers JM, Petryniak B, and Lowe JB. Dysregulated expression of selectin ligands on fetal thymocytes in mice with a targeted disruption of the Gal β 2 GalNAc transferase locus. In preparation.
2. 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.
3. Erdmann I, Scheidegger EP, Koch F, Burg G, Lowe JB, and Kundig TM. Fucosyltransferase-VII deficient mice lacking functional E-, P-, and L-selectin ligands show defective CD4+ and CD8+ T cell migration into the skin but normal extravasation into visceral organs. In preparation.

BOOKS AND CHAPTERS IN BOOKS:

1. 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, 2000.
2. Lowe JB. Red Cell Membrane Antigens. pp. 314-361, IN *The Molecular Basis of Blood Diseases, 3rd Edition*. Stamatoyannopoulos G, Nienhuis AW, Majerus PW, and Varmus H (eds.). W. B. Saunders Company, Orlando, Florida, 2001.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001

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 (4 students).
- B. House Officers:
 - 1. Dermatopathology sign-out.
 - 2. Review of dermatopathology consultation material.
 - 3. Dermatopathology teaching conference/weekly.
- C. Diagnostic Conference, Department of Dermatology (weekly).
- D. Director of Diagnostic Conference, Department of Dermatology – (monthly)
- E. Hospital Conferences:
 - 1. Multidisciplinary Melanoma Conference (twice monthly).
- F. Honors:
 - 1. Recognition in *The National Registry of Who's Who*, 2001 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: Vernon Sondak, 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. Immunohistochemical evaluation of sentinel lymph nodes for micrometastases: patterns of involvement and sensitivity of S100, HMB45 and melan-A immunostains (D. Fullen, D. Karimipour, L. Su, and T. Johnson)

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

REGIONAL AND NATIONAL:

- A. Member, Dermatopathology Test Committee, American Board of Pathology.
- B. Member, Dermatopathology Test Committee, American Board of Dermatology.
- C. Member, North American Melanoma Pathology Study Group.
- D. Member, American Medical Women's Association Mentorship Program
- E. Member, American Academy of Dermatology's Minority Medical Student Mentor Program
- F. Ad hoc manuscript reviewer, Journal of Cutaneous Pathology.
- G. Ad hoc manuscript reviewer, The American Journal of Dermatopathology.
- H. Ad hoc manuscript reviewer, Journal of the American Academy of Dermatology.
- I. Ad hoc manuscript reviewer, Archives of Dermatology.
- J. Ad hoc manuscript reviewer, Dermatologic Surgery
- K. 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, Washington, DC, March, 2001.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Bowen GM, Chang A, Lowe L, Hamilton T, Patel R, Johnson TM: Solitary melanoma confined to the dermal/subcutaneous tissue: evidence for revisiting the staging classification. Arch Dermatol 136:1397-1399, 2000.
- 2. Quin J, Lowe L, Mertz M: The effect of a new tissue-adhesive wound dressing on the healing of traumatic abrasions. Dermatol 201:343-346, 2000.
- 3. Johnson TM, Yahanda AM, Sondak VK, Cimmino V, Lowe L: Melanoma: Role of lymphatic mapping and sentinel nodal biopsy. Curr Probl in Dermatol 13:119-122, 2001.

4. Anderson KW, Lowe L, Su LD, Baker SR, Johnson TM: A staged excision approach for lentigo maligna and lentigo maligna melanoma of the head and neck: The "square" procedure. *Arch Facial Plast Surg* (in press).
5. Su LD, Lowe L, Bradford CR, Johnson TM, Yahanda AI, Sondak VK: Immunostaining for cytokeratin 20 improves detection of micrometastatic Merkel cell carcinoma in sentinel lymph nodes. *J Am Acad Dermatol* (in press).
6. Guitart J, Lowe L, Piepkorn M, Prieto VG, Rabkin MS, Ronan SG, Shea CR, Tron VA, White W, Barnhill RL: Histologic characteristics of thin metastasizing melanomas: A case-control study of 43 cases. *Arch Dermatol* (in press).
7. Altman JF, Lowe L, Redman B, Esper P, Schwartz JL, Johnson TM, Haefner HK: Placental metastasis of maternal melanoma. *J Am Acad Dermatol* (in press).
8. Fader DJ, Lowe L: Concomitant CO₂ and hair laser ablation for the treatment of in situ squamous cell carcinomas. *Dermatol Surg* (in press).

BOOKS/CHAPTERS IN BOOKS:

1. Lowe, L.: Deposition Disorders: Fitzpatrick, J.E., Aeling, J. (eds): *Secrets of Dermatology* (Philadelphia, PA: Hanley and Belfus, Inc., 2nd edition, 2001), pp 106-111.

ABSTRACTS, BOOK REVIEWS, PRELIMINARY COMMUNICATIONS, PANEL DISCUSSIONS:

1. 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.
2. Ratner D, Lowe L, Johnson TM, Fader DJ: Perineural spread of basal cell carcinomas treated with Mohs. American Society for Dermatologic Surgery – American College of Mohs Micrographic Surgery and Cutaneous Oncology Combined Meeting, November, 2000.
3. Sheng H, Goich S, Wang A, Lowe L, Sasaki H, Dlugosz A: Induction of multiple types of skin tumors in mice overexpressing an activated Gli2 mutant. Society for Investigative Dermatology Annual Meeting, May, 2001.

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

**ANNUAL DEPARTMENT REPORT
1 JULY 2000-30 JUNE 2001**

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

- A. Pathology 585, Lecturer, Inflammation section, Summer, 2000, 2001
- B. Pathology 580, Dental School. Lectures on Inflammation, cytokines and Immunology
- C. Pathology 581, Graduate Students. Lectures on Inflammation and Immune responses.
- D. Pathology 643, Course Director, Immune mechanisms of Disease, Fall, 2000.
- E. Post-doctoral fellows- Kim Tekkanat, Alison John, Steve Lundy, Kavita Ramen
- F. Graduate Students- Allison Miller, Molly Thomas
- G. Visiting Scientist- Akihiro Matsukawa

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

Active

- A. Principal Investigator, "Role of C-C chemokines in eosinophil airway inflammation", R-29 FIRST Award, 5/1/96-4/30/01, National Institutes of Health.
- B. Principal Investigator, "SCF and mast cells in allergic airway inflammation", NIH R01. 9/1/99-8/30/03
- C. Principal Investigator, "Cockroach allergen-induced airway inflammation" NIH Program Project, Project IV with P.A. Ward, M.D., Program Director 3/1/99-2/28/04.
- D. 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. Towes, 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 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:

-Section Editor

Journal of Immunology

-ASIP Program Committee for Experimental Biology 2000-present

-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. Role of chemokines in RSV-induced airway responses. Chemokine Gordon Conference. NH, July 23rd, 2000.
- 2. The role of chemokines in eosinophilia and allergic airway inflammation. Imperial College, London, U.K. Dec. 4th, 2000.

3. Chemokines and airway inflammation. British Society of Immunology, Harrogate, U.K. Dec. 6th, 2000.
4. Chemokines in allergic airway inflammation and eosinophil activation. University of Sheffield. Program for Immunological research. Sheffield, UK. Dec. 8th, 2000.
5. The role of SCF in initiation and maintenance of allergic airway responses. Bayer Corp. Berkley, CA. Dec. 20th, 2000.
6. The role of chemokines in allergen and viral-induced airway inflammation. Wayne State University, Detroit, MI. March 13, 2001.
7. Pathobiology course on Inflammation. Exp. Biol. 2001. Orlando, Florida. Session Chair. March 31, 2001.
8. Cytokine and chemokines in allergen and viral-induced lung inflammation. National Institute of Aging. Baltimore, MD. June 19, 2001.
9. The role of cytokines and chemokines in asthma. Anormed Inc. Annual Meeting. Seattle, WA. July 27th, 2001.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Lukacs, N.W. Migration of helper T lymphocyte subsets into inflamed tissues. *J. Allergy and Clin Immunol.* 106:264-270, 2000.
2. Cheng, S.S., J.J. Lai, N.W. Lukacs, and S.L. Kunkel. Granulocyte-macrophage colony stimulating factor up-regulates CCR1 in human neutrophils. *J. Immunol.* 166:1178-1184, 2001.
3. Tekkanat, K.K., H.F. Maassab, D.S. Cho, J.J. Lai, M.H. Kaplan, and N.W. Lukacs. IL-13-induced airway hyperreactivity and mucous production during respiratory syncytial virus (RSV) infection. *J. Immunol.* 166(5):3542-3548, 2001.
4. Lukacs, N.W., M.M. Glovsky, and P.A. Ward. Complement-dependent immune complex-induced bronchial inflammation and hyperreactivity. *Am. J. Physiol.- Lung* 280:512-518, 2001.
5. Chensue, S.W., N.W. Lukacs, T. Yang, X. Shang, K.A. Frait, S.L. Kunkel, M.T. Wiekowski, J.A. Hedrick, D.N. Cook, A. Zingoi, S.K. Narula, M. Napolitano, and S.A. Lira. Aberrant Th2 cell function and impaired eosinophil recruitment in CCR8 knockout mice. *J. Exp. Med.* 193: 573-584, 2001.
6. Teixeira, M.M. A. Talvani, W.L. Tafuri, N.W. Lukacs, and P.G. Hellewell. Eosinophil recruitment into sites of delayed-type hypersensitivity reactions in mice. *J. Leuk. Biol.* 69:353-360, 2001.
7. Guo, RF, AB Lentsch, RL Warner, M. Huber-Lang, JV Sarma, T Hlaing, MM Shi, NW Lukacs, and PA Ward. Regulatory effects of eotaxin on acute lung inflammatory injury. *J. Immunol.* 166:5208-5218, 2001.
8. Blease, K, C Jakubzick, J Westwick, N Lukacs, SL Kunkel, and CM Hogaboam. Therapeutic effect of IL-13 immunoneutralization during chronic experimental fungal asthma. *J. Immunol.* 166:5219-5224, 2001.
9. Matsukawa, A, MH Kaplan, CM Hogaboam, NW Lukacs, and SL Kunkel. Pivotal role of signal transducer and activator of transcription (stat)4 and stat6 in the innate immune response during sepsis. *J Exp. Med.* 193:679-688, 2001.

10. Oliveira, S.H.P., S.L. Kunkel, R.M. Strieter, and N.W. Lukacs. Stem cell factor stimulates murine mast cells to produce CC chemokines and express CC chemokine receptors. *Inflam. Res.* 50:168-174, 2001.
11. Oliveira, S.H.P., C.M. Hogaboam, and N.W. Lukacs. SCF-induced airway hyperreactivity is dependent upon leukotriene production. *Amer. J. Physiol.-Lung* 280(6):L1242-9, 2001.
12. Fife BT, Kennedy KJ, Paniagua MC, Lukacs NW, Kunkel SL, Luster AD, Karpus WJ. CXCL10 (IFN-gamma-Inducible Protein-10) Control of Encephalitogenic CD4(+) T Cell Accumulation in the Central Nervous System During Experimental Autoimmune Encephalomyelitis. *J Immunol.* 166(12):7617-7624, 2001.
13. Yoshida A, Elner SG, Bian ZM, Kunkel SL, Lukacs NW, Elner VM. Differential chemokine regulation by th2 cytokines during human rpe-monocyte coculture. *Invest Ophthalmol Vis Sci.* Jun;42(7):1631-8, 2001.
14. Blease K, Mehrad B, Lukacs NW, Kunkel SL, Standiford TJ, Hogaboam CM. Antifungal and airway remodeling roles for murine monocyte chemoattractant protein-1/CCL2 during pulmonary exposure to *Aspergillus fumigatus* conidia. *J Immunol.* 2001 166(3):1832-42
15. Andr  Klein; Andr  Talvani; Patr cia M.R. Silva; Marco A. Martins; Tim N.C. Wells; Amanda Proudfoot; N.W. Lukacs & Mauro M. Teixeira. SCF-induced leukotriene B₄ production cooperates with eotaxin to mediate the recruitment of eosinophils during allergic pleurisy in mice. *J. Immunol.* 167: 524-531.
16. Tekkanat, K.K., Hussein Maassab, David Cho, Joyce Lai, Aaron A. Berlin, Mark H. Kaplan, and Nicholas W. Lukacs. Role of IL-12 and STAT4 in regulation of airway inflammation and hyperreactivity in RSV infection. *Am. J. Pathol.* (In Press)
17. N.W. Lukacs, K.K. Tekkanat, A. Berlin, C.M. Hogaboam, A. Miller, H. Evanoff, P. Lincoln, and H. Maassab. Respiratory syncytial virus predisposes mice to augmented allergic airway responses via IL-13-mediated mechanisms. *J. Immunol.* 15;167(2):1060-5.
18. N.W. Lukacs, D. M. Prosser, S. A. Lira, D. N. Cook. Requirement for the chemokine receptor CCR6 in allergic pulmonary inflammation. *J. Exp. Med.* (In Press).

BOOKS/CHAPTERS IN BOOKS:

1. Matsukawa, A., C.M. Hogaboam, N.W. Lukacs, and S.L. Kunkel. 2000. Chemokines and Innate Immunity. *Reviews in Immunogenet.* 2:339-358.
2. Bone-Larson, C.L., K.J. Simpson, L.M. Coletti, N.W. Lukacs, S.C. Chen, S. Lira, S.L. Kunkel, and C.M. Hogaboam. 2000. The role of chemokines in the immunopathology of the liver. *Immunol. Rev.* 177:8-20.
3. Lukacs, N.W. and K.K. Tekkanat. 2000. Role of chemokines in asthmatic airway inflammation. *Immunol Rev.* 177:21-30.
4. Lukacs, N.W., T. Standiford, C.M. Hogaboam, and S.L. Kunkel. 2001. Regulation of Lung Inflammation: Chemokines and Immunity. IN- *Acute Lung Injury*. ED- H. Wong and T. Shanley. Marcel Dekker. (In Press).
5. Matsukawa A, Lukacs NW, Hogaboam CM, Chensue SW, Kunkel SL. III. Chemokines and other mediators, 8. Chemokines and their receptors in cell-mediated immune responses in the lung. *Microsc Res Tech.* 53(4):298-306, 2001.
6. Lukacs, N.W., S.H.P. Oliveira and C.M. Hogaboam. SCF-induced chemokine production, allergic airway inflammation and airway hyperreactivity. IN-*Mast cells and basophils*. ED- B. Marone, LM Lichtenstein, SJ Galli. Academic Press. PP.609-617.

7. Lukacs, N.W. Role of chemokines in the pathogenesis of asthma. *Nature Review of Immunology*.
8. Lukacs NW, Hogaboam C, Chensue SW, Blease K, Kunkel SL. Type 1/type 2 cytokine paradigm and the progression of pulmonary fibrosis. *Chest*. 2001. 120(1 Suppl):S5-8.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 – 30 JUNE 2001**

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. 46% increase in personal cases over last year.
- 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": 39th Annual AFIP Kenneth M. Earle Memorial Neuropathology Review, Armed Forces Institutes of Pathology, Rockville, Maryland, 2001.
- 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. Characterization of Rosai-Dorfman disease in brain with Drs. Michael Boland and Karin Muraszko.
- B. Viral vectors in glioma therapy with Drs. Julian Hoff and Brian Ross.
- C. 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 Residency Training. 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. Vortmeyer AO, Huang SC, Koch CA, Governale L, Dickerman RD, McKeever PE, Oldfield EH, Zhuang Z. Somatic von Hippel-Lindau gene mutations detected in sporadic endolymphatic sac tumors. *Cancer Research* 60:5963-5, 2000.
2. McKeever PE, Junck L, Strawderman MS, Blaivas M, Tkaczyk A, Cates MA, Yan, M, Li L.: Proliferation index is related to patient age in glioblastoma. *Neurology* 56: 1216-1218, 2001.
3. Lin PT, Bijwaard K, McKeever PE. Adult peripheral primitive neuroectodermal tumor of the cauda equina diagnosed by a combined immunohistochemical and molecular genetic analysis. (in preparation)
4. McKeever PE, Junck L, Li L, Mena H, Tkaczky A, Yan M, Blaivas M. Block age affects MIB-1 proliferation indices. (in preparation).
5. Xin W, Rubin MA, McKeever PE. Differential expression of cytokeratin 8 and 20 differentiate between craniopharyngioma and Rathke cleft cyst. (in preparation)
6. Valdez R, McKeever PE, Finn WG, Ross CW, Schnitzer B. Composite germ cell tumor and high-grade B-cell lymphoma arising in the sella turcica: a report of one case. (in preparation)

BOOKS/CHAPTERS IN BOOKS:

1. McKeever PE: Glial cell pathology. In: Smith BH and Adelman A, eds.: *Encyclopedia of Neuroscience*, Elsevier Science, 3rd edition (in press).
2. McKeever PE, Blaivas M, Gebarski SS: Pituitary Tumors. Chapter 23 In: Thapar K, Kovacs K, Scheithauer BW, Lloyd RV (Eds): *The Humana Press Inc., Totowa, New Jersey*, 2000. (in press).
3. McKeever PE: Laboratory methods. In: Nelson JS, Parisi J, Schochet S (Eds): *Principles and Practice of Neuropathology*, Oxford, New York (in press).
4. McKeever PE: The nervous system. In: Dabbs DJ (Ed): *Comprehensive Diagnostic Immunohistochemistry*, Harcourt Brace & Co., Orlando (in press).
5. McKeever PE: The nervous system. In: Kohen E (Ed): *Fluorescent Probes in Oncology*, Imperial College Press, London (in press).
6. McKeever PE: New Methods of Brain Tumor Analysis. Kenneth M. Earle Memorial Neuropathology Review. Armed Forces Institute of Pathology, Washington, D.C., 2001, pp.1-54.

**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.
2. Junck L, McKeever PE, Blaivas M, Tkaczuk A: The shorter survival of older patients with glioblastoma is partly due to more rapid tumor cell proliferation. World Federation on Neuro-Oncology First Quadrennial Meeting/Society for Neuro-Oncology Sixth Annual Meeting, Washington D.C., 2001.
3. Xin W, Rubin MA, McKeever PE: Differential expression of cytokeratin 8 and 20 distinguish craniopharyngioma from Rathke cleft cyst. ASCP Meetings, 2001.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

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, as needed.
- D. Necropsy Service - four weekends.

II. TEACHING ACTIVITIES:

- A. Medical School Students:
 - 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.
 - 5. Anatomic Pathology Conference: 2/year-Review of Cytopathology
- C. Other Education Activities:
 - Cytotechnologists - Cytopathology Conferences.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

Co-Investigator 1 U01 CA68291-01 (\$8,798.00-direct cost) "Retinoids and Intermediate Biomarkers for CIN II and III", 9% effort, National Institute of Health.

PROJECTS UNDER STUDY:

- 1. Abdul-Karim F, Michal CW. Cytopathology in "Essentials of Anatomic Pathology" edited by Liang Cheng. (Near completion.)
- 2. Michael CW, Collin B, Georgy B, Elhosseiny A. The cytologic spectrum and diagnostic pitfalls of apocrine lesions of the breast. (Manuscript near completion)
- 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. (Manuscript near completion.)

4. 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. (Manuscript near completion.)
5. Liu J, Michael CW. Fibroadenoma versus ductal carcinoma in breast aspirates: The grey zone. (Manuscript near completion.)
6. Michael CW, Collins B, Flint A. The cytologic classification of pulmonary neuroendocrine tumors: How far can we go?
7. Bavikatty N, Michael CW. The use of immunoperoxidase stains in separating squamous cell carcinoma from mesothelioma and adenocarcinoma in effusions. (Manuscript near completion.)
8. McConnell J, Silverman E, Michael CW. Psammoma bodies on pap smears: Differential diagnosis and diagnostic pitfalls. (Manuscript near completion.)
9. 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.
10. Fine needle aspiration of squamous lesions; Diagnostic features and pitfalls.
11. Performance of routine immunostains performed on cell blocks prepared by different methods.
12. Dai Y, Michael CW. Application of B-Catenin and Cyclin D1 in mesothelial lesions.

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. Chair, Research Task Force, Papanicolaou Society of Cytopathology.
- D. Member, Quality Control Committee, Papanicolaou Society of Cytopathology.
- E. Chair, Committee of Public Information, American Society of Cytopathology.
- F. Member, Task Force for Patient Advocacy, American Society of Cytopathology.
- G. Member, Abstract review committee, United States and Canadian Academy of Pathology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "The cervical smear and new technology." Breast and Cervical Cancer Control Program, Travis City, MI, Sept. 20, 2000.
2. "Cytopathology in the new millennium." Detroit Medical Center, Detroit, MI. February 6, 2001.
3. "The interpretation of cytologic specimens prepared by the ThinPrep technique." Short Course, United States and Canadian Academy of Pathology, Atlanta, GA. March 3-9, 2001.
4. "Pitfalls in pulmonary cytology." Ohio Society of Cytology. April 28, 2001.
5. "The interpretation of cytologic specimens prepared by the ThinPrep technique." Ohio Society of Cytology. April 28, 2001.
6. "The interpretation of cytologic specimens prepared by the ThinPrep technique." Saint Joseph Mercy Hospital, Ann Arbor, MI. May 16, 2001.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Michael CW, McConnell J, Pecott J, Afify AM, Al-Khafaji B. Comparison of the ThinPrep and AutoCyte liquid based to preparations in non-gynecologic specimens. Diagn Cytopathol (in press).
2. Tworek JA, Michael CW. Parotid gland mucosa associated lymphomas and their cytologic mimics. Seminars in Diagnostic Pathology, 2001;18:147-150.
3. Michael CW, Buschman B. Can true papillary neoplasm of the breast and their mimickers be accurately classified by cytology. Cancer Cytopathol (in press).

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Bavikatty N, Michael CW. The cytologic features of small cell carcinoma on ThinPrep. Diagn Cytopathol.
2. Akdas-Barkan G, Rubin M, Michael CW. Comparison of ThinPrep and conventional smears in the diagnosis of fine needle aspirates of melanoma. Diagn Cytopathol
3. Hammoud M, Haefner H, Michael CW, Ansbacher R. Atypical glandular cells of undetermined significance: Histologic findings and proposed management. A J of Obstetrics and Gynecology.

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

1. Liu J, Michael CW. Fibroadenoma versus ductal carcinoma in breast aspirates: The grey zone. Acta Cytol 2000, 44(5);886
2. Michael CW, Collins B, Flint A. The cytologic classification of pulmonary neuroendocrine tumors: How far can we go? Acta Cytol 2000, 44(5);902.
3. Akdas-Barkan G, Rubin M, Michael CW. Evaluation of fine needle aspiration of melanoma using ThinPrep versus conventional smears. Modern Pathology, 2001, 14(1);49A

4. Elsheikh TM, Cramer HM, Michael CW, Henry MR, and Bernacki EB. Salivary gland neoplasms with basaloid cell features: FNA cytologic-histologic correlation of 48 cases. *Modern Pathology*, 2001, 14(1);51A
5. Michael CW. Book review. "Color Atlas of Cancer Cytology." *Am J Clin Path*

**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 2000 - 30 JUNE 2001**

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 502, Research Responsibility Course, 12 hours.
2. Program Director, "Experimental Immunopathology Training Grant."
3. Ph.D. Dissertation Committees, University of Michigan:
 - a. Pamela Bennett-Baker
 - b. Wannee Asavaroengchai
 - c. Meera Nathan
 - d. Tyler Sisk
 - e. Tania Gourley
 - f. Yadira Hernandez
 - g. John Erb-Downward
4. Ph.D. Dissertation Advisor:
 - a. Anavelys Ortiz-Suarez
 - b. Scott Berger
5. Undergraduate students:
 - a. Ashwin Pamidi

B. Postdoctoral Fellows:

1. James Harper

C. In Lab:

1. Igor Dozmorov, Ph.D.
2. Gonzalo Garcia, Ph.D.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, R. A. Miller "Activation Defects in T Cells of Old Mice", NIH/NIA R01-AG-19619 (8%), \$250,000 direct costs/year, 9/30/00 - 8/31/05.
- B. Principal Investigator, R. A. Miller, "Genetics of Age-Sensitive Traits in Mice", NIH/NIA P01-16699-03 (20%), \$634,394 direct costs/year, 4/1/99 – 3/31/04. Core A (Administrative), R. A. Miller, \$28,196. Core C (Animal), R. A. Miller, \$58,411. Project 1 (Immunology), R. A. Miller, \$56,975.
- C. Principal Investigator, R. A. Miller, "Genetic Control of Longevity in Mice", NIH R01-AG-11687-06 (8%), \$119,174 direct costs/year, 9/1/93 - 11/30/03.
- D. Principal Investigator, R. A. Miller, "Wild Derived Mouse Stocks: New Models for Aging Research," NIH/NIA R01-AG13711-04A1 (5%), \$175,000 direct costs/year, 9/1/00 - 8/31/05.
- E. Principal Investigator, J. Faulkner, "Nathan Shock Center of Excellence in the Basic Biology of Aging", NIH P30-AG13283-06, \$89,400 direct costs/year, 9/1/95 – 6/30/00. R. A. Miller directs the Gene Expression Profiling Core, 10% effort.
- F. Principal Investigator, J. Halter, "Claude D. Pepper Older Americans Independence Center", NIH P30-AG08808-12 (15%), \$849,650 direct costs/year, 9/1/99 - 8/31/04. R. A. Miller serves as (a) Director, Core Facility for Aged Rodents (5% effort; \$102,310 current year direct costs); (b) Director, Research Development Core (10% effort; \$59,283 current year direct costs); and (c) Project Director, "Weight Gain Trajectory and Life Span in Mice" (5% effort; \$95,888 current year direct costs).
- G. Program Director, R. A. Miller, "Research Training in Experimental Immunopathology", NIH T32-AI-07413-07 (5%), \$244,353 direct costs/year, 9/15/98 – 8/31/03.
- H. Principal Investigator, R. A. Miller, "Summer Training Courses in Experimental Aging Research", NIH/NIA R13-AG12917-09 (0%), \$33,566 direct costs/year, 4/1/98 - 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, Research Development Core, Nathan Shock Center
- G. Operating Committee, Immunology PhD program
- H. Associate Director, Nathan Shock Center for Aging

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

- A. Journal of Gerontology: Biological Sciences.
- B. Aging: Clinical and Experimental Research
- C. Mechanisms of Ageing and Development
- D. Experimental Gerontology

HONORS AND AWARDS:

- A. None.

INVITED LECTURES/SEMINARS:

2000

1. Annual Longevity Assurance Gene Consortium Meeting, Galveston, TX. "Genetics of Longevity in Mice." July 16 – 19.
2. Genetics of Aging III, Bar Harbor, ME. "QTL Mapping of Longevity and Disease-Resistance in Mice." August 6 – 9.
3. Workshop on Transgenic Mice in Aging Research, San Antonio, TX. "Use of Natural Variation to Guide Transgenic Research in Aging." September 15 – 16.
4. Medical Staff Grand Rounds, Oakwood Hospital, Dearborn, MI. "Are There Genes for Aging?" September 29.
5. Biomarkers of Aging: From Rodents to Man, Canyon Ranch, Tucson, AZ. "Biomarkers of aging in heterogeneous mice." October 5 – 8.
6. Conference on Death and Its Enemies, University of Michigan, Ann Arbor, MI. "Extending Life: Scientific Prospects." December 1.
7. Institute of Gerontology, University of Michigan, Ann Arbor. "New Animal Models for Aging Research." December 7.

2001

1. Immunology Program, Tufts University School of Medicine. "Signal Transduction Defects in Aging T Cells." January 18.
2. Department of Veterinary Pathology, Michigan State University. "New Animal Models for Research on Aging." February 2.
3. 2nd International Meeting on Aging and Immunity, Cordoba, Spain. "Genetic and Biomarker Analysis of Immune Aging in Mice." March 23 – 25.
4. University of Michigan School of Nursing. "New Animal Models for Aging Research." April 11.
5. NIH "Science and the Public Health" Seminar Series, Bethesda, MD. "Biology of Aging and Longevity: Evidence from the Laboratory and the Jungle." April 17.

6. International Longevity Center conference on Anti-Aging Medicine, Tucson, AZ. "Hope From Bottles: Rising Expectations of Longevity." May 3 – 6.
7. Summer Training Course in Aging Research, San Antonio, TX. "Animal Models for Aging" and "Introduction to Aging Research." June 2 – 7.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Eisenbraun, M. D., A. Tamir, and R. A. Miller. 2000. Altered composition of the immunological synapse in an anergic, age-dependent memory T cell subset. *J. Immunology* 164:6105-6112.
2. Tamir, A., M. D. Eisenbraun, G. G. Garcia, and R. A. Miller. 2000. Age-dependent alterations in the assembly of signal transduction complexes at the site of T cell/APC interaction. *J. Immunol.* 165:1243-1251.
3. Dozmorov, I., A. Bartke, and R. A. Miller. 2001. Array-based expression analysis of mouse liver genes: effect of age and of the longevity mutant Prop1^{df}. *J. Gerontol. Biol. Sci.*, 56A: B72-B80.
4. R. A. Miller 2001. Biomarkers of aging: prediction of longevity using age-sensitive T cell subset determinations in a middle-aged, genetically heterogeneous mouse population. *J. Gerontol. Biol. Sci.* 56A:B180-B186.
5. Flurkey, K., J. Papaconstantinou, R. A. Miller, and D. E. Harrison. 2001. Life span extension and delayed immune and collagen aging in mutant mice with defects in growth hormone production. *Proc. Natl. Acad. Sci. USA* 98:6736-6741.
6. Yung, R., D. Ray, J. K. Eisenbraun, C. Deng, J. Attwood, M. D. Eisenbraun, K. Johnson, R. A. Miller, S. Hanash, and B. Richardson. 2001. Unanticipated effects of a heterozygous Dnmt1 null mutation on age-dependent DNA hypomethylation and autoimmunity. *J. Gerontol. Biol. Sci.*, in press.
7. Garcia, G. G., and R. A. Miller. 2001. Single-cell analyses reveal two defects in peptide-specific activation of naïve T cells from aged mice. *J. Immunol.* 166:3151-3157.
8. Warner, H. R. D. Ingram, R. A. Miller, N. L. Nadon, A. G. Richardson. 2000. Workshop report: program for testing biological interventions to promote healthy aging. *Mechanisms of Ageing and Development* 155: 199 – 208.
9. Miller, R. A., A. Galecki, and R. J. Shmookler-Reis. 2001. Interpretation, design and analysis of gene array expression experiments. *J. Gerontol. Biol. Sci.* 56A: B52-B57.
10. Miller, R. A., 2001. New paradigms for research on aging and late-life illness. *Mechanisms of Ageing and Development* 122: 130- 132.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Jackson, A. U., A. T. Galecki, C. Chrisp, D. T. Burke, and R. A. Miller. Mouse loci associated with life span exhibit sex-specific and epistatic effects. Submitted.
2. Miller, R. A. and C. Chrisp. An index of age-sensitive immune status that predicts longevity for young and middle-aged mice destined to die of multiple forms of neoplasia. Submitted.
3. Qiu, B., X. Shang, K. A. Frait, J. Hu, E. Komuniecki, R. A. Miller and S. W. Chensue. Differential effects of aging on cytokine and chemokine responses during Type-1 (mycobacterial) and Type-2 (Schistosomal) pulmonary granulomatous inflammation in mice. Submitted.

4. Miller, R. A., C. Chrisp, A. U. Jackson, A. T. Galecki, and D. T. Burke. Coordinated genetic control of neoplastic and non-neoplastic diseases in mice. Submitted.

BOOKS/CHAPTERS IN BOOKS:

1. Miller, R. A. Genetics of increased longevity and retarded aging in mice. 2001. Handbook of the Biology of Aging, 5th Edition; E. J. Masoro and S. N. Austad, editors; Academic Press, NY. Chapter 14, pp. 369 – 395.
2. Miller, R. A. 2000. Biology and genetics of aging and longevity. In: Kelley's Textbook of Internal Medicine, 4th Edition; H. David Humes et al., editors, Lippincott Williams and Wilkins, Philadelphia, PA. Chapter 15, pages 108 – 118.
3. Miller, R. A. 2001. Biomarkers and genetics of aging in mice. In: Cells and Surveys; C. E. Finch, J. W. Vaupel, and K. Kinsella, eds, National Academy Press, Washington, DC. Chapter 8, pp 180 – 212.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

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
- B. House Officers
 - 1. Pathology house officers, Autopsy supervision and instruction (13 weeks /year)
 - 2. Pathology house officers, Surgical Pathology supervision and instruction, (5 months/year)
 - 3. Lecture and Case presentations at weekly Urologic Pathology Conferences
- C. Graduate students:
 - 1. Course Director, Pathology 585, Lecture and Laboratory course for Medical Illustration Graduate students (15 hrs)
 - 2. Laboratory Instructor, pathology 600 (M2 pathology course)
- D. Undergraduate students:

III. RESEARCH 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. Co-investigator, "Metabolic imaging of Renal and Prostate Cancer using C-11 Acetate" RO1-CA089448-01 12/00 -11/03 (\$750,000)

- E. Co-Investigator. 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)

PROJECTS UNDER STUDY:

- A. Endothelial cell responses in inflammation
 - 1. The enzyme source of endothelial cell oxidants
 - 2. The role of endothelial cell derived oxidants in signaling and cell injury
 - 3. Repertoire of endothelial cell derived cytokines and their role in inflammation
- B. Gender-specific effects of hormones on T cells and endothelial cells in autoimmunity
 - 1. Effect of estrogen on endothelial cell estrogen reception expression
 - 2. The role of estrogen in endothelial cell adhesion molecule expression and lymphocyte homing
- C. Role of prostate endothelial cells in malignancy

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Autopsy Quality Assurance Review
- B. Chief, Histopathology and Electron Microscopy Services

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL AND NATIONAL:

- A. Manuscript Review for
 - Clinical Immunology and Immunopathology
 - Biochemical pharmacology
 - Shock
 - Free Radical Biology and Medicine
 - American Journal of Pathology
 - Microvascular Research
- B. Membership in National organizations
 - American Association for the Advancement of Science (1991)
 - New York Academy of Science (1991)
 - American Society for Investigative Pathology (Fellow,1995)
 - 1996 Institutional Liason to University of Michigan
 - American Society of Clinical Pathologists (Fellow, 1995)
 - American Association of University Women (1995)
 - The A. James French Society of Pathologists (1996)

Society for Experimental Biology and Medicine (2000)
The Oxygen Society (2001)
Society for Free Radical Research International (2001)
The Nitric Oxide Society (2001)

V. OTHER RELEVANT ACTIVITIES:

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

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. 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* (accepted for publication).
2. 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.* 126:985-91, 2000 Aug
3. Murphy, H.S. Yu, C. Quddus, J. Functional Expression of NAD(P)H Oxidase in Lung Microvascular Endothelial Cells. *Biochem. Biophys. Res. Comun.* 278(3):584-589, 2000
4. Varani J, Hattori Y, Dame M, Schmidt T, Murphy HS, Johnson K and Wojno K. Matrix metalloproteinases (MMPs) in fresh human prostate tumor tissue and organ-cultured prostate tissue: Levels of collagenolytic and gelatinolytic MMPs are low, variable and different in fresh tissue versus organ-cultured tissue *Brit. J Cancer* 84:1076-1083
5. Robey, T.C., Valimaa, T., Murphy, H.S., Mooney, D.J., Weatherly, R.A The use of internal "Knitted-type" stents in a rabbit tracheal reconstruction model. *Arch. Otolaryng* (accepted for publication).

SUBMITTED PUBLICATIONS:

1. Warner R., Kang S., Murphy H.S. Varani J. Skin inflammation due to ultraviolet radiation is associated with induction of nitric oxide. (Submitted for publication).
2. Hattori, Y., Hattori N., Murphy, H.S., Su, L., Johnson, T. M. and Varani, J. Expression of MMP-13 (Collagenase-3) in microvascular endothelial cells of human skin and basal cell carcinoma of the skin. (submitted for publication).

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

1. Murphy, H.S., Yu, C. functional Expression of p47 Component of NADPH Oxidase in Endothelial Cells. *J Mol Cell Cardiol.* 32: A32.2000.

2. Murphy, H.S., Yu, C., Dame, M., Warner, R., Varani, J. NO-Induced HSP-70 Expression in Endothelial Cells. *J Mol Cell Cardiol.* 32: A48 2000.
3. 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. Frank Lamberson Lectureship. Univ. of Mich. 2000.
4. Robey, T., Valimaa, T. Murphy, H.S., Tormala, P., Mooney, D.J., Weatherly, R.A. Bioabsorbable PLLA stents and their use in a rabbit tracheal reconstruction model. *Am Soc Ped. Otolaryn. Meeting*, May , 2001.
5. Murphy, M.E., Chensue, S. W., Murphy, H.S. Effect of Endogenous Nitric Oxide on Vascular Endothelial Cell Cytokines. *FASEB J* 15:217, 2001
6. Murphy, B.A., Yu, C., Richardson, B.C., Murphy, H.S. Effect of Estrogen on Adhesion Molecules of Spleen Endothelial Cells. *FASEB J* 15: 526, 2001
7. Murphy, B.A., Yu, C., Richardson, B.C., Murphy, H.S. Effect of Estrogen on Spleen Dendritic Cells in Short-term Culture. *FASEB J* 15:272, 2001
8. Laudes, I.J., Huber-Lang, M., Speyer, C., Albrecht, E., Chu, J, Murphy, H.S., Riedemann, N., Sarma, V., Ward, P.A. C5a receptor expression on rat endothelial cells. *FASEB J* 15:926, 2001.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

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

III. RESEARCH ACTIVITIES:

- A. History of cytopathology.
- 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
Associate Editor
Editorial Advisory Board
North American Review Board
- C. International Academy of Cytology:
International Board of Cytopathology, Member
- D. Awards Committee, American Society of Cytopathology

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

- 1. Naylor, B.: Dr. George N. Papanicolaou: His life and his legacy. Lecture, 3rd Panhellenic Congress on Tumor Markers, Athens, Greece, December, 2000.

2. Naylor, B.: Papanicolaou: His life and his legacy. Lecture, Hygeia Hospital, Athens, Greece, December, 2000.
3. Naylor, B.: Lecturer: a. Cytology of serous effusions: Technical matters and diagnostic problems, b. Fine needle aspiration of lung, c. Non-neoplastic entities in routine cytologic specimens, d. The century for cytopathology: A history of the development of cytopathology in the 20th Century. Cytology Education Seminar, Marmara University, Istanbul, Turkey, December, 2000.
4. 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, 2001.
5. Naylor, B.: Tumors on zooplankton. Research Seminar, Department of Pathology, University of Michigan, February, 2001.
6. Bartziota, E., Naylor, B., Schneider, V., and Tasca, L.: In Romania it's the "Méthode Babes - Papanicolaou". Kasumasa Masabuchi Award Lecture, 14th International Congress of Cytology, Amsterdam, Netherlands, May, 2001.
7. Michael, C.W. and Naylor, B.: Amyloid in cytologic specimens. Poster presentation, 14th International Congress of Cytology, Amsterdam, Netherlands, May 2001.
8. Naylor, B.: The Century for Cytopathology. Lecture, Volker Schneider Cytology Laboratory, Freiberg, Germany, June, 2001.

HONORS AND AWARDS:

Kasumasa Masabuchi Lifetime Achievement in Clinical Cytology Award of the International Academy of Cytology, May 2001.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Omair, M., Naylor, B., Jude, D.J., Quddus, J., Beals, T.F., and Vanderploeg, H.A.: Histology of herniations through the body wall and cuticle of zooplankton from the Laurentian Great Lakes. J Invertebrate Pathol., 2001, 77:103-108.

BOOKS/CHAPTERS IN BOOKS:

None.

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

None.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000- 30 JUNE 2001**

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 to sophomore class in system sequences. (two contact hours)
- B. Daily case review with pathology house officer assigned to blood bank.
- C. Postgraduate course, "Current Topics in Blood Banking", Planning Committee.
- D. Lectures on Transfusion Medicine presented to Pathology and Hematology/Oncology House Officers.
- E. Seminars and lectures on Pathology of Breast to Pathology House Officers.
- F. Presentation of consultation slide conferences (2) on pathology of the breast to pathology house officers.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Microinvasive carcinoma of the breast (with L. Pierce)
- B. Correlation of histopathology and molecular pathology with prognosis of cystosarcoma phyllodes (with C. Kleer)
- C. Phase II evaluation of primary chemotherapy with doxorubicin/doetaxel 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. Liason 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

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

INVITED LECTURES/PAPERS/SEMINARS:

- 1. Chair of meeting on Universal Leukoreduction of Cellular Blood Components. University Health System Consortium. Chicago, IL. October 23-24, 2000.

2. Oberman, HA. Impact of universal leukoreduction in a large University Hospital. University Health System Consortium. Chicago, IL. October 23-24, 2000.
3. A forty year perspective on the diagnosis and resultant management of breast cancer. Breast Care Center Forum. University of Michigan. May 16, 2001.
4. Problem solving in the blood bank. Workshop. Current Topics in Blood Banking. 28th annual symposium. University of Michigan. June 6, 2001.
5. Oberman HA, Goldman EB. Legal aspects of transfusion medicine. Current Topics in Blood Banking. 28th annual University of Michigan. June 7, 2001.
6. Oberman, HA. Leukoreduction of cellular blood components. Current Topics in Blood Banking. 28th annual University of Michigan. June 8, 2001.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS

1. Kleer CG, Giordano TJ, Braun T, Oberman HA. Pathologic, immunohistochemical and molecular features of benign and malignant phyllodes tumors of the breast. *Mod. Pathol.* 2001; 14:185-190.
2. Ratko TA, Cummings JP, Oberman HA, et al. Evidence-based recommendations for the use of leukoreduced cellular blood components. *Transfusion.* 2001;41: (in press)

TEXTBOOKS, CHAPTERS IN TEXTBOOKS:

1. Fibroadenomas, adenomas, cystosarcomas and hamartomas (Chapter 4). *Atlas of Pathology of the Female Breast.* Current Medicine. Philadelphia, PA. (in press)

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

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. 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
 - 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.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

Co-investigator for “Predicting response to therapy and early detection of recurrent oral cancer” (NIH 89570), Thomas E. Carey (principal investigator).

Co-investigator for "Evaluating Neck Dissection Specimens" (U-M, Faculty Group Practice Plan, Academic Award – September 2001), Douglas Chepeha, M.D. (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.
- D. Reviewer, Head & Neck

V. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Snyder ML, Paulino AFG. Melan-A as a useful diagnostic immunohistochemical stain for the diagnosis of primary sinonasal melanomas. *Head & Neck* (in press).
2. Afenyi-Annan A, Paulino AFG. Pathologic quiz case: abnormal uterine bleeding. *Arch Pathol Lab Med* (in press).
3. Pfeifle R, Paulino AF, Helman J. Schwannoma of the tongue. *Oral Surg Oral Med Oral Path* (in press).
4. Kowalski PJ, Paulino AFG. Proliferation index as a prognostic marker in hemangiopericytoma of the head and neck. *Head & Neck* 2001;23:492-496.
5. 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* 2000;175:1721-1725.
6. Snyder ML, Paulino AFG. Pathologic quiz case: an unusual salivary gland tumor. *Arch Pathol Lab Med* 2000;124:1559-1560.
7. Paulino AFG, Singh B, Shah JP, Huvos AG. Basaloid squamous cell carcinoma of the head and neck. *Laryngoscope* 2000;110:1479-1482.
8. Baker LH, Biermann JS, Hayes CW, McGinn CJ, Paulino AFG, Sondak VK. The multidisciplinary approach to sarcoma: the University of Michigan comprehensive cancer center experience. Princeton, NJ, Bristol-Myers Squibb Company, 2000.
9. Folpe AL, Goodman ZD, Ishak KG, Paulino AFG, Taboada EM, Meehan SA, Weiss SWW. Clear cell myomelanocytic tumor of the falciform ligament/ligamentum teres: a novel member of the perivascular epithelioid clear cell family of tumors. *Am J Surg Pathol* 2000;24:1239-1246.

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

1. Afenyi-Annan A, Rubin MA, Paulino AFG. Expression of CD44 in Ewing's sarcoma. Poster at the EORTC meeting, April 2001.
2. Afenyi-Annan A, Paulino AFG. Post-chemotherapy tumor necrosis in Ewing's sarcoma: the Huvos and Picci grading systems revisited. Poster at the EORTC meeting, April 2001.
3. Afenyi-Annan A, Mucci NR, Rubin, MA, Paulino AFG. Evaluation of biomarkers in Ewing's sarcoma using tissue microarray. Poster at the USCAP meeting, March 2001.
4. Afify AM, Al-Khafaji BM, Paulino AFG, Davila RM. Diagnostic utility of muscle markers in the cytologic evaluation of serous fluids. Presented at the USCAP meeting, Mar 2001.
5. Snyder ML, Paulino AFG. Melan-A as a useful diagnostic immunohistochemical stain for the diagnosis of primary sinonasal melanomas. Presented at the international conference on head and neck cancer, July 2000.
6. Kowalski PJ, Paulino AFG. Proliferation index as a prognostic marker in hemangiopericytoma of the head and neck. Poster at the international conference on head and neck cancer, July 2000.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

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

PROJECTS UNDER STUDY:

- A. Mechanisms of lung injury and fibrosis.
- B. Cytokine regulation of fibroblast function.
- C. 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 and regulation 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, Program in Biomedical Sciences Admissions Committee.

REGIONAL AND NATIONAL:

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

INVITED LECTURES/SEMINARS:

- Invited Speaker/Consultant "Pathophysiology of pulmonary fibrosis", Schering-Plough, NJ, 2000
- Visiting Professor, University of Pittsburgh, Pittsburgh, PA, 2001
- Visiting Professor, University of Texas Health Science Center, Tyler, TX, 2001

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

- 1. 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.
- 2. 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; 23:460-465.
- 3. Roy, S.G., Nozaki, Y., and Phan, S.H.: Regulation of α -smooth muscle actin gene expression in myofibroblast differentiation from rat lung fibroblasts. Int. J. Biochem. Cell Biol. 2001; 33:723-744.
- 4. Gharaee-Kermani, M., Nozaki, Y., Hatano, K., and Phan, S.H.: Lung interleukin-4 gene expression in a murine model of bleomycin-induced pulmonary fibrosis. Cytokine 2001; in press.

BOOKS/CHAPTERS IN BOOKS/REVIEWS:

1. Gharaee-Kermani, M., Phan, S.H.: Role of cytokines and cytokine therapy in wound healing and fibrotic diseases. *Curr. Pharmaceutical Design*. 2001; 7:125-133.

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

1. Nozaki Y, Shimamoto K, Nishiwaki K, Shimokata K, Phan SH, Hasegawa Y: Analysis of human alveolar fibroblasts in idiopathic pulmonary fibrosis. *Am. J. Resp. Crit. Care Med*. 2001;163:A423
2. Peters-Golden M, Bailie M, Marshall T, Wilke C, Phan SH, Toews G, Moore B: Protection from bleomycin-induced fibrosis in 5-lipoxygenase deficient mice is associated with reduced lung leukocyte numbers and increased macrophage generation of interferon- γ . *Am. J. Resp. Crit. Care Med*. 2001;163:A424
3. Gharaee-Kermani M, Huaux F, Ullenbruch M, McGarry B, Weiss SJ, Phan SH: The role of estrogen in pulmonary fibrosis. *Am. J. Resp. Crit. Care Med*. 2001;163:A713
4. Liu T, Ullenbruch M, Phan SH: Regulation of lung fibroblast telomerase expression by bFGF and IL-4. *Am. J. Resp. Crit. Care Med*. 2001;163:A944
5. Huaux FA, McGarry B, Ullenbruch M, Phan SH: Reduced pulmonary responses to silica particles in monocyte chemotactic protein-1 receptor CCR2 deficient mice. *The Toxicologist* 2001;60:423

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

I. CLINICAL ACTIVITIES:

A. General Surgical Pathology – 33 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:

Resident Teaching Award - 2000

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 2000 - 30 JUNE 2001**

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 at least one week a month.
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 (17th Symposium in October 2001), a one day-long event with lectures and case presentations for pathologists (most are M-Labs clients). CME credits are provided. Held twice a year (October/April).
- C. Sign-out in cytopathology, with residents, fellow and, occasionally with medical students.
- D. In-service teaching to laboratory staff at 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:

Ongoing collaborative study with Department of Radiology (Lawrence Kuhn, M.D.) and Hematology/Oncology (Valerie Castle, M.D.) on "Detection of Lymph Node Metastasis Using Ultrasound".

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. M-Labs Network for M-care members. Coordinating M-Labs QA activities with D. Moss; monthly review of occurrence reports.
- B. Medical Director of the University of Michigan Health Service Laboratory, and Forest Health Medical Center in Ypsilanti.
 - C. Active medical staff member at 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. Referee for the Hematology Survey, College of American Pathologists (CAP)
- B. Inspector, for the CAP Accreditation Program. Performed two inspections.
- C. 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 2000 - 30 JUNE 2001**

I. CLINICAL ACTIVITIES:

- A. Director, Autopsy Service.
- B. Director, Electron Microscopy Service
- C. Supervision of Autopsies-11 weeks, signed out 85 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 600 (M2 pathology course), year long
- J. Thesis Committee - Andrew Merry, Kellie Breen, Department of Physiology
- K. Directed research of Michael O'Reilly, M.D. (Department of Anesthesiology), Stewart Wang, M.D., Ph.D. (Department of Surgery), Susan Stern, M.D., (Department of Emergency Medicine), Grace Su, M.D., (Department of Medicine), Jean Nemzek, D.V.M. (Unit for Lab Animal Medicine), Postdoctoral fellows. Jiyou Kim, Ph.D., Liyu Xin, M.D., Ph.D.
- L. Visiting physician, Steven Kamiza, M.D.
- M. Medical Students – David Newcomb
- N. Graduate Students – Andrew Merry, Kellie Breen, Laura McKinley
- O. Undergraduate Students - 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, 1990-2004. 30% effort
- B. Principal Investigator, "Regulation of IL-8 gene expression: four years, GM50401 \$870,822, 1995- 2004. 20% effort
- C. Principal Investigator, "Chemokines in the Pathogenesis of Asthma", ES09589, project #3, \$1,180,00, 1998 – 2002. 10% effort
- D. Principal Investigator, "Training Med School Faculty to Tackle Malaria in Malawi", TW 00908, \$12,000, 2000-2001
- E. Co-Investigator, "Inflammation and the Host Response to Injury", GM-99-007, Ronald Tompkins, M.D. Principal Investigator Mass. General Hospital. Budget for Animal Core and Protein Analysis Core \$1,226,223. 2001 – 2006. 15% effort
- F. Co-Investigator, "Can Paraxonase be Used to Treat Endotoxemia and Sepsis", Life Sciences Initiative, Bert LaDu Principal Investigator, \$150,000, 2000-2003. 2% effort
- G. Co-Investigator, NIH HD040112, "Neuroimmunology/Cytokine Alterations In Vulvodynia" Principal Investigator, Barbara Reed, \$375,000, 2000 – 2003

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director - Autopsy Service.
- B. 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
- F. Member, Paul W. Gikas Scholarship Selection Committee

MEDICAL SCHOOL/HOSPITAL:

- A. Member, Medical School Admissions Committee
- B. Member, Executive Committee, Medical School Admissions Committee

- C. Member, Biomedical Research Council Undergraduate Research Council
- D. Advisory Committee on, Appointments and Promotions and Tenure, Instructional Tract, 1997 – 2001
- E. Chair, Advisory Committee on, Appointments, Promotions and Tenure, Instruction Tract, 1999 – 2001.
- F. University Committee on Use and Care of Animals, 1997 – 2001
- G. Chair, University Committee on Use and Care of Animals, 1998 - 2001
- H. Reviewer, Biomedical Research Council grants
- 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. Chair, NIH Special Emphasis Panel, Feb 2001
- E. Chair, NIH Special Emphasis Panel, June 2001
- F. Member, Michigan Coalition on Donation
- G. Publications Committee, International Cytokine Society
- H. Awards Committee, Shock Society
- I. Organizer, Shock Society Young Investigator's Research Forum
- J. 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. Reviewer:
 - 1. Journal of Immunology, reviewed 7 papers .
 - 2. Journal Leukocyte Biology, reviewed 1 paper
 - 3. American Journal of Pathology, reviewed 2 papers.
 - 4. Shock, reviewed 10 articles.
 - 5. Journal of Clinical Investigation, reviewed 4 articles
 - 6. American Journal of Physiology, reviewed 1 article.
 - 7. American Journal of Respiratory Cell and Molecular Biology, reviewed 1 article
 - 8. American Journal of Respiratory and Critical Care Medicine, reviewed 3 articles
 - 9. Cellular Immunology, reviewed 4 articles
 - 10. Kidney International, reviewed 3 articles
 - 11. Immunological Investigations, reviewed 1 article
 - 12. Lung, reviewed 1 article

13. European Journal of Immunology, reviewed 1 article
14. Grant Reviewer, VA, reviewed 1 grant

INVITED LECTURES/SEMINARS:

- 2000 Visiting Professor, Washington University School of Medicine, Department of Surgery, St. Louis, MO, *Sepsis, Nothing Works, But Have We Learned Anything?*
- 2000 Visiting Professor, Cleveland Clinic Foundation, Department of Immunology Cleveland, Ohio, *Too Much Is Never Enough, The Inflammatory Response to Sepsis*
- 2000 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*
- 2000 Visiting Professor, Oklahoma University Health Sciences Center, Oklahoma City, Oklahoma, *The Immunopathology of Sepsis, Why doesn't anything work?*
- 2000 Invited Speaker, Experimental Biology, Molecular Analysis of Lung Injury Minisymposium, *Genetic Redundancy and the Inflammatory Response*
- 2001 Visiting Professor, Institute Mario Negri, Milan, Italy, *Using the Inflammatory Response to Sepsis to Guide Therapy*
- 2001 Invited presentation, Esperion Therapeutics, Ann Arbor, Michigan *The Immunopathology of Sepsis*

VI. PUBLICATIONS:

ARTICLES PUBLISHED

1. Cooper, P. J., D. Fekade, D. G. Remick, P. Grint, J. Wherry, and G. E. Griffin. Recombinant human interleukin-10 fails to alter proinflammatory cytokine production or physiologic changes associated with the Jarisch-Herxheimer reaction J Infect Dis. 2000, 181:203-9.
2. Su, G.L., R.D. Klein, A. Aminlari, H. Y. Zhang, L. Steintraesser, W.H. Alarcon, D.G. Remick, and S.C. Wang. Kupffer cell activation by lipopolysaccharide in rats: role for lipopolysaccharide binding protein and toll-like receptor 4 Hepatology. 2000. 31:932-6
3. Nemzek, J. A., D. R. Call, S. J. Ebong, D. E. Newcomb, G. L. Bolgos, and D. G. Remick. 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.
4. Remick, D. G., D. E. Newcomb, G. L. Bolgos, and D. R. Call. Comparison of the mortality and inflammatory response of two models of sepsis: lipopolysaccharide vs. cecal ligation and puncture 2000, Shock. 13:110-6.
5. Kronfol Z, Remick D.G: Cytokines and the Brain: Implications for Clinical Psychiatry. Am J Psychiatry 2000, 157: 683-694
6. De Plaen IG, Tan XD, Chang H, Wang L, Remick DG, Hsueh W: Lipopolysaccharide activates nuclear factor kappaB in rat intestine: role of endogenous platelet-activating factor and tumour necrosis factor. Br J Pharmacol 2000, 129: 307-314
7. Remick DG, Call DR, Ebong SJ, Newcomb DE, Nybom P, Nemzek JA, Bolgos GE. Combination immunotherapy with soluble tumor necrosis factor receptors plus interleukin 1 receptor antagonist decreases sepsis mortality. Critical Care Medicine 2001, 29: 473-481

8. Call DR, Nemzek JA, Ebong SJ, Bolgos GR, Newcomb DE, Remick DG. Ratio of local to systemic chemokine concentrations regulates neutrophil recruitment. *American Journal of Pathology* 2001, 158: 715-721
9. Nemzek JA, Siddiqui J, Remick DG, Development and optimization of cytokine ELISAs using commercial antibody pairs 2001. *J Immunol Methods*. 255: 149-57
10. Call DR, Nemzek JA, Ebong SJ, Bolgos GR, Newcomb DE, Wollenberg GK Remick DG Differential local and systemic regulation of the murine chemokines KC and MIP2. 2001 *Shock* 278-284
11. Stern SA, Wang X, Mertz M, Chowanski ZP, Remick DG, Kim HM, Dronen SC Under-resuscitation of near-lethal uncontrolled hemorrhage: effects on mortality and end-organ function at 72 hours. *Shock* 2001, 15: 16-23
12. Mosher B, Dean R, Harkema J, Remick D, Palma J and Crockett E: Inhibition of kupffer cells reduced cxc chemokine production and liver injury. *J Surg Res* 2001, 99:201-210
13. Steinstraesser L, Klein RD, Aminlari A, Fan MH, Khilanani V, Remick DG, Su GL and Wang SC: Protegrin-1 enhances bacterial killing in thermally injured skin. *Crit Care Med* 2001, 29:1431-1437
14. Steinstraesser L, Fohn M, Klein RD, Aminlari A, Remick DG, Su GL and Wang SC: Feasibility of biolistic gene therapy in burns. *Shock* 2001, 15:272-277

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

1. S.Ebong, S.Goyert, J.Nemzek, J.Kim, G.Bolgus, and D.Remick. Immunopathologic Alterations in CD14-Deficient Murine Sepsis *Exp Biol*, San Diego CA 2000
2. Nemzek, S.Ebong, G.Bolgus, and D.Remick. Effects of keratinocyte growth factor on acute lung injury in two-hit model *Exp Biol*, San Diego CA 2000
3. Remick, Genetic redundancy and the inflammatory response *Exp Biol*, San Diego CA 2000
4. 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. 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. 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 2000- 30 JUNE 2001

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. Clinical Pathology Grand Rounds (one lecture).
 - 5. Clinical Pathology Case Conference/weekly.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Immunophenotyping in acute and chronic leukemias.
- B. Radioimmunotherapy for B-cell lymphoma.
- C. Gene expression profiling of chronic lymphoproliferative disorders.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director, Clinical Flow Cytometry Laboratory.
Coordinator, CP resident teaching program.
- B. Clinical Pathology Incentive Distribution Committee.
- C. Pathology Faculty Incentive Committee.
- D. Interviewer of residency candidates.

REGIONAL/NATIONAL:

- A. Central pathology reviewer, multicenter study of I¹³¹ anti-B1 radioimmunotherapy for B-cell lymphoma, Corixa Pharmaceutical.
- B. Pathology reviewer, Zenarestat clinical trial, Pfizer Pharmaceutical.
- C. Hematology Council Member, Commission on Continuing Education, American Society of Clinical Pathologists.
- D. Manuscript Reviewer, American Society of Clinical Pathologists Check Sample Program.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Skacel M, Ross CW, Hsi ED. A reassessment of primary thyroid lymphoma: high-grade MALT-type lymphoma as a distinct subtype of diffuse large B-cell lymphoma. *Histopathology* 37:10-18, 2000.
2. Kaminski MS, Estes J, Zasadny KR, Francis IR, Ross CW, Tuck M. et al. Radioimmunotherapy with iodine (131)I tositumomab for relapsed or refractory B-cell non-Hodgkin lymphoma: updated results and long-term follow-up of the University of Michigan experience. *Blood* 96(4):1259-66, 2000.
3. 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* 31:1051-1054, 2000.
4. 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. *Hum Pathol* 32:66-73, 2001.
5. Uherova P, Singleton TP, Ross CW, Schnitzer B, Finn WG. The clinical significance of CD10 antigen expression in diffuse large B-cell lymphoma. *Am J Clin Pathol* 115:582-588, 2001.
6. Valdez R, Finn WG, Ross CW, Singleton TP, Tworek JA, Schntizer B. Extranodal marginal zone B-cell lymphoma as a cause of the clinicopathologic syndrome of Waldenstrom's macroglobulinemia: a report of six cases. *Am J Clin Pathol* (in press).

ARTICLES SUBMITTED FOR PUBLICATION:

1. Nangia R, Singleton TP, Ross CW, Finn WG, Padmore RF, Schnitzer B. Follicular Hodgkin's lymphoma: a clinicopathologic study.

2. Valdez R, Kroft SH, Ross CW, Schnitzer B, Singleton TP, Peterson LC, Finn WG. Cerebrospinal fluid involvement by mantle cell lymphoma.
3. Uherova P, Ross CW, Finn WG, Singleton TP, Nangia R, Schnitzer B. Peripheral T-cell lymphoma mimicking marginal zone B-cell lymphoma.
4. Hans CP, Finn WG, Singleton TP, Schnitzer B, Ross CW. Utility of anti-CD117 in the flow cytometric analysis of acute leukemia.

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

1. Ross CW. The revised European-American classification of lymphoid neoplasms (REAL classification). Michigan Oncology Journal, Fall 2000.
2. Nangia R, Finn WG, Schnitzer B, Ross CW. Refractory anemia with excess blasts in transformation (RAEBt): rare subset with <5% bone marrow blasts. Mod Pathol 2001; 14:173A
3. Nangia R, Singleton TP, Finn WG, Schnitzer B, Ross CW. CD117 (c-kit) in acute leukemias, chronic myeloproliferative disorders and myelodysplastic syndromes: a paraffin immunohistochemical (IHC) study with flow cytometry (FC) correlation. Mod Pathol 2001; 14:173A.
4. Uherova P, Finn WG, Nangia R, Ross CW and B Schnitzer. Peripheral T-cell lymphoma (PTCL) mimicking low grade marginal zone/MALT lymphoma. Mod Pathol 2001;14:181A.
5. Valdez R, Ross CW, Schnitzer B, Nangia R, Finn WG. IgG expression in B-cell chronic lymphocytic leukemia. Mod Pathol 2001; 14:181A.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

I. CLINICAL ACTIVITIES:

- A. Director, Clinical Cytogenetics Laboratory

II. TEACHING ACTIVITIES:

- A. House Officers and Fellows
1. Rotations in Cytogenetics
 - a. Pathology (N=6)
 - b. Genetics (N=3)
 - c. Hematology/Oncology (N=1)
- B. Medical Students
1. Fundamentals of Laboratory Medicine (PTHCLNL 101)
Component IV Medical School Curriculum. (2 days, N=4)
Genetic Counselors (Human Genetics 644 – Interdisciplinary Care)
Lecture and Interactive Training in Clinical Cytogenetics – 2 hours
Clinical Cytogenetics teaching
 2. Abnormal Cytogenetics Case Conference (Biweekly)
for technologists, residents, fellows, and faculty
 3. Leukemia Conference (Biweekly)
 4. Pediatric Genetics Post-clinic Conference (Weekly)
 5. Joint Genetics Conference (Monthly - 1 case presentation)
 6. Clinical Pathology Grand Rounds
 - a. “Introduction to Clinical Cytogenetics.” 3/2/01

III. RESEARCH ACTIVITIES:

- A. Cytogenetic and FISH analysis for “A Phase II Study of Oral Tetrathiomolybdate (TM), an Inhibitor of Angiogenesis, for the Treatment of Multiple Myeloma.” (GCRC Protocol), M01-RR00042, with Harry Erba, M.D., Ph.D. Principal Investigator.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director, Clinical Cytogenetics Laboratory
- B. Interviewer
1. Pathology Residency Candidates
 2. Hematopathology Fellow Candidates
 3. Hematopathology Faculty Candidates
 4. Molecular Pathology Fellow Candidate
 5. Cytogenetics Fellow Candidate

UNIVERSITY OF MICHIGAN:

- A. Interviewer
 - 1. Human Genetics Faculty Candidates
 - 2. Clinical Genetics Residency Candidates

REGIONAL AND NATIONAL:

- A. Assistant Editor: *Genes, Chromosomes & Cancer*
- B. Peer-Reviewer, *Leukemia, Genes, Chromosomes & Cancer*
- C. Children's Oncology Group (COG)
 - 1. Cytogenetics Review Committee Member
 - 2. Participate as an Approved Laboratory for patients requiring cytogenetics studies (Leukemia and Solid Tumor protocols)
- D. Southwest Oncology Group (SWOG)
 - 1. Participate as an Approved Laboratory for cytogenetics studies (Leukemia Protocols)

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Gao Q, Horwitz M, Roulston D, Hagos F, Zhao N, Freireich EJ, Golomb HM, Olopade OI. 2000. Susceptibility gene for familial acute myeloid leukemia associated with loss of 5q and/or 7q is not localized on the commonly deleted portion of 5q. Genes, Chromosomes & Cancer 28:164-172.
- 2. Dickstein JJ, Davis EM, Roulston D. Localization of the Chromosome 22 Breakpoints in Two Cases of Acute Megakaryoblastic Leukemia (AML- M7) with the t(1;22)(p13;q13). Cancer Genet. Cytogenet, In Press

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001

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 - 08/01/01-07/31/02 - NIH - \$107,972 - 30% Effort Tissue and Serum Core Resource for Prostate Cancer (Prostate SPORE grant)
- B. Co- Histopathology/Immunohistochemistry Core Investigator - 5P30 CA46952 - 6/00-05/31/06 - NIH - \$64,850 - 10% Effort
- C. Principal Investigator - 99-3397 - 05/31/00-05/31/01 - NIH/NCI - \$236,859 - 20% Effort - Development of Tissue Microarray Technology for the Prostate SPORE.
- D. Principal Investigator - CA69568 - 08/01/00-07/31/02 - 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).
- E. Principal Investigator – SPORE Faculty Development Award – 08/1/00-07/31/01 – 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.
 - F. 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.
 - G. Co-Investigator – R01 CA79596-01A1 – 07/01/99-06/30/04 – NIH/NCI - \$186,666 – 5% Effort – Genetic Analysis of Hereditary Prostate Cancer Families.
 - H. Co-Investigator – R01 CA82419 – 04/01/00-03/31/04 – NIH/NCI - \$157,000 – 5% Effort – Modulating Tolerance for Prostate Cancer Antigen Vaccines. (P.I. K. Conney)
 - I. Co-Investigator – CA-69568 – 08/01/00-07/31/01 – NIH/NCI - \$70,000 – 5% Effort – Prostate Elasticity Imaging - A New Technology for Early Detection and Monitoring of Prostate Pathology. (P.I. M. Sanda)
 - J. Co- Investigator – DOD – 7/01/01-6/30/04 – 5% Effort – Role of the Human Polyomavirus, BKV, in Prostate Cancer.
 - K. Co-Investigator – 2R01 CA60948 – 04/01/01-03-31-05 – NIH – \$630,000 – 5% Effort (P.I. Macoska) - Analysis of 8p Loss in Human Prostate Cancer.
 - L. Co-Investigator – 01/01/01-06/30/02 – UM Bioinformatics Program - \$75,000 – 0% Effort – A Bioinformatics Approach to Cancer Profiling” (P.I. Chinnaiyan)

PENDING SUPPORT:

- A. Co-Investigator-Life Sciences Corridor Fund- 38-6006309-DNS 073133571- \$789,450 - 5% effort - 1/1/01-1/1/04 - "Development of a Bio-Chip-based protein microarray platform for human disease"
- B. Co- Investigator - 9-9-070 – 07/01/00-6/30/02 – NIH/NCI – 5 % Effort – Quick Trials for Prostate Cancer Therapy.
- C. Co-Investigator - 00-3917 – 01/01/01-12/31/03 – 10% Effort – (PI Prim Reddy) - \$31,115 – “CaM-BP68: A Prognostic Indicator of Prostate Cancer
- D. Co-Investigator – 01/01/02-12/31/05 – American Cancer Society - \$1,199,439 – 10% Effort – Molecular Classification of Prostate Cancer (P.I. Chinnaiyan)
- E. Principal Investigator – 01/01/02-12/31/05 – NIH - \$1,144,576 – 20% Effort – Analysis of Prostate Cancer Progression by cDNA Arrays
- F. Co-Investigator – 09/01/01-8/31/02 – R13 CA94453-01 - \$5,000 – 0% Effort – Tissue Microarray Informatics Standards Workshop

ONGOING RESEARCH:

- A. 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).
- B. 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.)

- C. 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).
- D. Characterization of E-Cadherin in prostate carcinoma in collaboration with Dr. Mark Day (Urology)
- E. Gene profiling of early neoplastic alterations in the prostate by cDNA expression arrays in collaboration with Dr. Arul Chinnaiyan (Funded through SPORE Faculty Development Award)
- F. Locally advanced prostate cancer: a clinical and molecular characterization of hormone sensitive prostate tumor cases from Ulm, Germany in collaboration with Dr. Arul Chinnaiyan (Pathology and Urology) and Prof Hautman (Ulm).

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)
- G. 2001-present American Urological Association, Affiliate member

DEPARTMENTAL:

Director of Urologic Pathology
GU Pathology Fellowship Supervisor

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
- D. Executive committee member for Prostate Cancer SPORE (U of M)

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, BioTechniques, Archives of Pathology and Laboratory Medicine
- C. USCAP Abstract Review Board (2000-2003)-Genitourinary Section

- D. Department of Defense Prostate Cancer Molecular Biology Study Section, July 6-8, 2000
- E. Santa Fe Institute, Complexity Workshop, January 15th – 16th, 2001
- F. NCI sponsored Prostate Cancer Pathology Committee for Common Data Elements
- G. CaP Cure “Think Tank” in Molecular Imaging of Prostate Cancer, Aug 2001

EXTRAMURAL INVITED PRESENTATIONS:

- A. Plenary Presentation, "High-Density Tissue microarrays-The University of Michigan Prostate SPORE experience", 8th SPORE Investigators Workshop, Chantilly, Va., July 9-10, 2000
- B. “Development of high throughput tissue microarrays for prostate cancer research:” The prostate SPORE experience.” Ann Arbor, MI, 9/18/00.
- C. Invited Guest Lecturer, "Interpretation of Prostate Needle Biopsies with Carcinoma", ARTP (French Urologic Society) 9th Scientific Meeting, Paris, France, 9/28/00.
- D. “Application of Tissue Microarrays for Evaluation of Prostate Cancer Biomarkers.” Yale University, Haven, CT. Grand Rounds, 10/26/00.
- E. Guest Professor, “Prostate Cancer Outcomes Research: The Critical Role of the
- F. Pathologist from Gross Pathology to cDNA Expression Array Analysis. Memorial Sloan Kettering Cancer Center, Department of Pathology, 12/14/00.
- G. Invited Seminar and Speaker, “Prostate Pathology in the Post-Genomic Era.” Lausanne University, Dept. of Pathology, Lausanne, Switzerland. 1/8-9/01.
- H. “Relationship Database to Handle High-Density Tissue Microarray Data for Clinical and Pathology Studies: The Michigan SPORE (CA69568) Model”, United States and Canadian Academy of Pathology Annual Meeting, Platform Presentation, Atlanta, GA, March 2001.
- I. “Lack of Association Between Prostate Carcinoma Nuclear Grading and Prostate Specific Antigen Recurrence Following Radical Prostatectomy”, United States and Canadian Academy of Pathology Annual Meeting, Platform Presentation, Atlanta, GA, March 2001.
- J. “Correlation of Human Papillomavirus Detection with p53, p27, and Ki-67 Protein Expression in Penile Carcinoma Using Tissue Microarray Technology”, United States and Canadian Academy of Pathology Annual Meeting, Platform Presentation, Atlanta, GA, March 2001.
- K. “Using High-Density cDNA Microarrays to Define a Molecular Signature for Prostate Cancer”, United States and Canadian Academy of Pathology Annual Meeting, Platform Presentation, Atlanta, GA, March 2001.
- L. “Prostate Cancer Outcomes Research: The Critical Role of the Pathologist from Gross Pathology to cDNA Expression Array Analysis”. University of Pittsburgh, Pittsburgh, PA, Diagnostic Pathology Conference, 4/5/01.
- M. Grand Rounds, “Prostate Cancer Outcomes Research: Combining cDNA and Tissue Microarray Analysis”, Mayo Clinic, Rochester, MN, 5/10/01.
- N. Seminar Speaker, “Prostate Cancer Outcomes Research: Combining cDNA and Tissue Microarray Analysis”, Genentech, San Francisco, CA, 5/17/01.
- O. Course Director and Invited Speaker, “Fundamental Elements of the TMA Infostructure” , University of Michigan, 19th Annual AIMCL 2001, May 30 to June 1, 2001.

- P. Seminar Speaker, University of Wuppertal, Departments of Urology and Surgery, Germany, June 2001.
- Q. Seminar Speaker, University of Ulm, Departments of Urology and Surgery, Germany, June 2001.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Zhang X, Lee C, Ng PY, Rubin M, Shabsigh A, Buttyan R. Prostatic Neoplasia in Transgenic Mice with Prostate-directed Overexpression of the C-myc Oncoprotein. *Prostate* 2000, 43(4): 278-85.
2. 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. *J Natl Cancer Inst.* 2000, 92(11):937-939.
3. 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?" *Eur Urology* 2000, 38(1): 79-84.
4. 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. *Urology* 2000, 55(6):904-908.
5. Hollenbeck BK, Bassile N, Wei JT, Montie JE, Hayasaka S, Taylor JMG, Rubin MA. Whole-Mounted Radical Prostatectomy Specimens Do Not Increase Detection of Adverse Pathologic Features: *J Urol* 2000, 164(5):1583-86.
6. 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? *Am J Surg Pathol* Vol. 24(12)1634-40.
7. 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. *Urology* 2000 Vol. 56(15)721-5.
8. Rubin MA, Mucci NR, Manley S, Sanda M, Cushenberry E, Strawderman M, Montie JE, Bassily NH. Predictors Of Gleason Pattern 4/5 Prostate Cancer On Radical Prostatectomy: Can High Grade Tumor Be Predicted Preoperatively? *J of Urol.* 2001 Vol. 165(1)114-8.
9. Mucci. N. R. Rubin. M. A. Strawderman, M. S. Montie, J. E. Smith, D. C. Pienta. K. J. Expression of nuclear antigen Ki-67 in prostate cancer needle biopsy and radical prostatectomy specimens. *J Natl Cancer Inst.* 2000, Vol. 92(23)1941-2.
10. Renaud EJ, Liu D, Pipe SW, Rubin MA, Teitelbaum DH. Inferior vena cavectomy for nonexcisable Wilms' tumor thrombus. *J Pediatr Surg* 36(3):526-9, 2001.
11. Rashid MG, Sanda MG, Vallorosi CJ, Rios-Doria J, Rubin MA, Day ML. Post-translational Truncation and Inactivation of Human E-Cadherin Distinguishes Prostate Cancer from Matched Normal Prostate. *Cancer Research* 2001, 61(2):489-92.
12. Kim HL, Vander Griend DJ, Yang X, Benson DA, Dubauskas Z, Yoshida BA, Chekmareva MA, Ichikawa Y, Sokoloff MH, Zhan P, Karrison T, Lin A, Stadler WM, Ichikawa T, Rubin MA, Rinker-Schaeffer CW. Mitogen-activated Protein Kinase 4 Metastasis Suppressor Gene Expression is Inversely Related to Histological Pattern in Advancing **Human Prostatic Cancer**. *Cancer Research* 2001, 61:2833-2837.

13. 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. *Cancer Research* 2001, 61:2390-2394.
14. Ficazzola MA, Faiman M, Gitlin J, Woo K, Melamed J, Rubin MA, and Walden PD. Antiproliferative B-cell Translocation Gene 2 Protein is Down-Regulated Post-Transcriptionally as an Early Event in Prostate Carcinogenesis. *Carcinogenesis* 2001, 22(8):1271-1279.
15. Rubin MA, Mucci NR, Figurski J, Smith D, Pienta KJ, Day ML. E-Cadherin Expression in Prostate Cancer: A Broad Survey Using High Density Tissue Microarray Technology. *Human Pathology* 2001, 32(7):690-697.
16. Moskalik AP, Rubin MA, Wojno KJ, Bree R, Rubin JM, Fowlkes JB, Montie JE, Manley S, Carson PL. Analysis of 3-D Ultrasound Doppler Quantitative Measures for the Discrimination of Prostate Cancer. *Urol* - In press.
17. Chaib H, Cockrell EK, Rubin M, Macoska JA. Profiling and Verification of Gene Expression Patterns in Normal and Malignant Human Prostate Tissues by cDNA Microarray Analysis. *Neoplasia* 2001, 3(1):43-52.
18. Shah R, Mucci NR, Macoska JA, Rubin MA. Postatrophic Hyperplasia of the Prostate Gland: Neoplastic Precursor or Innocent Bystander? *Am J Pathol* 2001, 158:1767-1773.
19. Bova GS, Parmigiani G, Epstein JI, Wheeler TM, Mucci NR, Rubin MA. Web-based Tissue Microarray Visual Image Data Analysis: Initial Validation Testing Through Prostate Cancer Gleason Grading. *Human Pathology* 2001, 32(4):417-427.
20. Rubin MA, Mucci NR, Figurski J, Pienta KJ, Day ML. E-Cadherin Expression in Prostate Cancer: A Broad Survey Using High Density Tissue Microarray Technology. *Hum Pathology* 2001, 32(7):690-697.
21. Spencer SL, Rubin MA, Hussain H, Wolf, Jr. JS. Complete Transurethral Resection of Bladder Endocervicosis. *J Urol* - In press
22. Seifman BD, Rubin MA, Williams L, Wolf, Jr. JS. The Functional Effects of Unilateral Laser Papillectomy in the Pig. *Urology* - In press.
23. Dhanasekaran SM, Barrette TR, Ghosh D, Shah R, Varambally S, Kurachi K, Pienta K, Rubin MA, and Chinnalyan AM. Delineation of Prognostic Biomarkers in Prostate Cancer. *Nature* 2001, 412: 822-826.
24. Rubin MA, Kleter B, Zhou M, Ayala G, Cubilla AL, Quint WG, Pirog EC. Detection and typing of Human Papillomavirus (HPV) DNA in penile carcinoma – evidence for multiple independent pathways of penile carcinogenesis. *Am J Pathol* – in press.
25. Manley S, Mucci NR, de Marzo A, Rubin MA. Relational Database Structure To Manage High-Density Tissue Microarray Data and Images for Pathology Studies Focusing on Clinical Outcome: The Prostate SPORE Model. *Am J Pathol* 2001 – In press.
26. Zhou M, Hayasaka S, Taylor JMG, Shah R, Proverbs-Singh T, Manley S, Rubin MA. Lack of Association between Prostate Carcinoma Nuclear Grading and Prostate Specific Antigen Recurrence Following Radical Prostatectomy. *J Urology* – in press.

*Equal Contribution

ABSTRACTS:

1. Seifman BD, Williams AL, Rubin MA, Wolf, Jr. JS. The Functional Effects of Unilateral Endoscopic Laser Papillectomy. *AUA* 2000 (1036).

2. 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).
3. 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).
4. 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).
5. 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).
6. 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).
7. 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. AACR, 2000 (4536).
8. 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. AACR, 2000 (1543).
9. Seifman BD, Williams AL, Rubin MA, Wolf, Jr. JS. The Functional Effects of Unilateral Laser Endoscopic Papillectomy. J of Urol 163 (4) 2000 232:1036.
10. 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).
11. 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. J of Urol 163 (4) 2000 190:847.
12. 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. J of Urol 163 (4) 2000 7:31.
13. 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. J of Urol 163 (4) 2000 37:160.
14. Afenyi-Annan, A, Mucci NR, Rubin MA. Evaluation of Biomarkers in Ewing's Sarcoma Using Tissue Microarray. Modern Pathol 2001, 14(1):9A
15. Kowalski, PJ, Rubin MA, Kleer CG. Reduced or Absent E-Cadherin Expression Predicts Early Metastases in Breast Cancer. Modern Pathol 2001, 14(1):29A
16. Akdas-Barkan G, Rubin MA, Michael CW. Evaluation of Fine Needle Aspirations of Melanoma Using ThinPrep Versus Conventional Smears. Modern Pathol 2001, 14(1):49A
17. Chinnaiyan AM, Dhanasekaran S, Mucci NR, Pienta KJ, Rubin MA. Using High-Density cDNA Microarrays to Define a Molecular Signature for Prostate Cancer. Modern Pathol 2001, 14(1):105A

18. DeMarzo AM, Mucci NR, Cushenberry E, Rubin MA. Association of p27^{Kip1} Protein Expression and Formalin-Fixation: Optimal Fixation Times Determined Using High-Density Tissue Microarray. *Modern Pathol* 2001, 14(1):106A
19. Proverbs-Singh T, Mucci NR, Strawderman M, Rubin MA. Prostate Carcinoma Biomarker Analysis using Tissue Microarrays: Optimization of a Tissue Sampling Strategy for Proliferation Labeling Index. *Modern Pathol* 2001, 14(1):120A
20. Rubin MA, Figurski J, Mucci NR, Manley S, Day ML. E-cadherin Expression in Clinically Localized and Hormone Refractory Prostate Carcinoma by Use of High-Density Tissue Microarrays: Lack of Correlation with Tumor Progression. *Modern Pathol* 2001, 14(1):122A
21. Sanda M, Manley S, Rubin, MA. Surgical Margin Status Adds Predictive Value to Prostate Cancer Staging: Single Institution Study of 1050 Radical Prostatectomy Cases. *Modern Pathol* 2001, 14(1):122A
22. Shah R, Kaldjian E, Gieseg M, Figurski J, Redman BJ, Rubin MA. Epidermal Growth Factor Receptor Expression is Up-Regulated in Clear Cell Renal Carcinoma: Immunohistochemical Tissue Array Confirmation of cDNA Expression Analysis. *Modern Pathol* 2001, 14(1):123A
23. Shah R, Amin A, Macoska J, Rubin MA. Molecular Profiling to Distinguish Flat Urothelial Carcinoma In-Situ from Reactive Changes after BCG Therapy. *Modern Pathol* 2001, 14(1):123A
24. Zhou M, Shah R, Proverbs-Sing T, Mucci NR, Manley S, Rubin MA. Lack of Association Between Prostate Carcinoma Nuclear Grading and Prostate Specific Antigen Recurrence Following Radical Prostatectomy. *Modern Pathol* 2001, 14(1):131A
25. Zhou M, Pirog EC, Proverbs-Sing T, Mucci NR, Kleter B, Ayala G, Cubilla AL, Quint WGV, Rubin MA. Correlation of Human Papillomavirus Detection with p53, p27, and Ki-67 Protein Expression in Penile Carcinoma Using Tissue Microarray Technology. *Modern Pathol* 2001, 14(1):131A
26. Manley S, Mucci NR, DeMarzo A, Rubin MA. Relational Database to Handle High-Density Tissue Microarray Data for Clinical and Pathology Studies: The Michigan Prostate SPORE (CA69568) Model. *Modern Pathol* 2001, 14(1):234A
27. Mucci NR, Manley S, Bova S, Rubin MA. A High Throughput Tissue Microarray Process: Improvements in Preparation, Digital Imaging, and Review. *Modern Pathol* 2001, 14(1):234A

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

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 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. Children's Cancer Study Group: Review of in-house cases of lymphoma cases.
- C. Member, Hematology Workshop Review Committee, American Society of Clinical Pathologists.
- D. Hematology Planning Committee, American Society of Clinical Pathologists.
- E. Bylaws Committee, Society for Hematopathology.
- F. Chair, Hematology Check-Path Committee, American Society of Clinical Pathologists.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARD:

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

INVITED LECTURES/SEMINARS:

- 1. "A Practical Approach to Diagnostic Hematological Problems," ASCP Educational Course, Lectures given included a) Reactive Lymphadenopathies: Diagnosis and Differential Diagnosis; b) Non-Hodgkin's Lymphomas and their Differential Diagnosis; c) Hodgkin's Disease; d) Differential Diagnosis of Hodgkin's Disease; e) A Practical Approach to Diagnosis and Classification of Lymphomas and Leukemias by Immunohistochemistry, Flow Cytometry and Molecular Genetic Analysis; f) Extranodal Lymphomas and, g) Acute Lymphoblastic Leukemias, Chicago, IL, November, 2000.
- 2. Real/WHO Classification of Non-Hodgkin's Lymphomas, "Interesting Lymphoid Lesions". Slide Seminar, Visiting Professor, Muncie Medical Center, Muncie, IN, December, 2000.
- 3. "Reactive Lymphadenopathies." Tutorial on Neoplastic Hematopathology. Department of Laboratory Medicine and Pathology, Cornell University, Miami, Florida, February, 2001.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Bavikatty NR, Ross CW, Finn WG, Schnitzer B, Singleton TP: Anti CD10 immunoperoxidase staining of paraffin-embedded acute leukemias: Comparison with flow cytometric immunophenotyping. Human Pathol 31:1051-1054, 2000.

2. Finn WG, Singleton TP, Schnitzer B, Ross CW, Stoolman LM: Adhesion molecule expression in CD10-negative chronic B-cell leukemias: Comparison with CD5-positive B-cell chronic lymphocyte leukemia. *Human Pathol* 32:66-73, 2001.
3. Uherova P, Singleton TP, Ross CW, Schnitzer B, Finn WF: The clinical significance of CD10 antigen expression in diffuse large B-cell lymphoma. *Am J Clin Pathol* 115:582-588, 2001.
4. Izban KF, Ergin M, Huang Q, Qin J, Martinez RL, Schnitzer B, Ni H, Nickoloff BJ, Alkan S: Characterization of NF-kB expression in Hodgkin's disease. Inhibition of constitutively expressed NF-kB results in spontaneous caspase-independent apoptosis in Hodgkin and Reed-Sternberg cells. *Mod Pathol* 14:297-310, 2001.
5. Yegappan S, Schnitzer B, His ED: Follicular lymphoma with marginal zone differentiation: Microdissection demonstrates the t(14;18) in both the follicular and marginal zone components. *Mod Pathol* 14:191-196, 2001.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Valdez R, Finn WG, Ross CW, Singleton TP, Tworek JA, Schnitzer B: Extranodal marginal zone lymphoma as a cause of the clinicopathologic syndrome of Waldenstrom's macroglobulinemia. A report of six cases. *Am J Clin Pathol*.
2. Uherova P, Ross CW, Finn WG, Singleton TP, Nangia R, Schnitzer B: Peripheral T-cell lymphoma (PTCL) mimicking low grade marginal zone MALT lymphomas. *Mod Pathol*.
3. Nangia R, Singleton TP, Ross CW, Finn WG, Padmore RF, Schnitzer B: Follicular Hodgkin's lymphoma. A histopathologic study. *Am J Clin Pathol*.
4. Hans CP, Ross CW, Singleton TP, Schnitzer B, Finn WG. Utility of anti-CD117 in the flow cytometric analysis of acute leukemia. *Mod Pathol*.

BOOKS AND CHAPTERS IN BOOKS:

1. Reactive Lymphadenopathies. In: Knowles, D. (ed). *Neoplastic Hematopathology*, 2nd Ed. Williams & Wilkins, 2001.

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

1. Nangia R, Singleton TP, Finn WG, Schnitzer B, Ross CW: CD119 (c-kit) in acute leukemias, chronic myeloproliferative disorders and myelodysplastic syndromes: A paraffin immunohistochemical (IHC) study with flow cytometry (FC) correlation. *Mod Pathol* 14:173A, 2001.
2. Nangia R, Finn WG, Schnitzer B, Ross CW: Refractory anemia with excess blasts in transformation (RAEBt): Rare subset with <5% bone marrow blasts. *Mod Pathol* 14:173A, 2001.
3. Uherova P, Finn WG, Ross CW, Schnitzer B: Peripheral T-cell lymphoma (PTCL) mimicking low grade marginal zone MALT lymphomas. *Mod Pathol* 14:181A, 2001.
4. Valdez R, Ross CW, Schnitzer B, Nangia R, Finn WF: IgG expression in B-cell chronic lymphocytic leukemia. *Mod Pathol* 14:181A, 2001.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001

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. Forest Health, Ypsilanti, Michigan.
 - 4. Other various clients including numerous satellite sites and University acquired practices.
- B. Autopsy Coverage for Trillium Hospital, Albion, Michigan, and Forest Health, Ypsilanti, 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 Forest Health.
- F. Clinical Pathology consults at Trillium Hospital 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 interesting cases.
- B. Sign out some M-Labs and University of Michigan autopsies with residents.
- C. In-service teaching to laboratory staffs at Trillium Hospital.

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 2000, 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 was terminated.
This fiscal year, net billings for clinical pathology services increased by 14.7% and net billing for anatomic pathology services increased by 10.0%. Total combined billings increased by 13.3% over our last fiscal year.
MLabs submitted 2 proposals to prospective new clients during FY2000. Both were rejected.
 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 have successfully renegotiated with MCare a full-risk outpatient lab agreement for all groups and products which became effective 4/1/2001.
MLabs continues to manage the MCare/MLabs agreement for Medicare HMO Program (Senior Plan). Nine subcontracts are in place. Five are pending.
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.
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. This contract was implemented this fiscal year.
MLabs coordinates the Pathology Department's issues concerning contractual obligations to JVHL and GLN. These include such items as BCN critical value list and HEDIS reporting.
- C. Member Department of Pathology Incentive Committee.
 - D. Member, University of Michigan Networking Leads Committee.
 - E. Department of Pathology representative to Managed Care Committee.
 - F. Director, Laboratory at Trillium Hospital, Albion, Michigan.
 - G. Chair, Tissue/Transfusion and Infection Control Committees, Trillium Hospital.

- H. Member, Surgical and Medicine/Family Practice Committees, Trillium Hospital.
- I. Member, Peer Review Committee, Forest Health.
- J. Plan and review Laboratory QA and CQI at Trillium Hospitals.
- K. Review Quality Control of Clinical Pathology tests at Trillium Hospital.

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 2000 - 30 JUNE 2001

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

- A. Research mentor:
 - 1. Nobuhiro Takeshita, M.D., post-doctoral fellow (April 1998-present) and Ronald Craig, PhD, Research Associate: 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, conducted jointly with Dr. Craig, indicates that T-lymphoblasts grown from tumor-draining lymph node cells expressing binding sites for the adhesion receptor P-selectin (so-called Plig^{high} cells) are 10-100 fold more potent than cells derived from unfractionated populations against pulmonary and subcutaneous tumor implants. As few as 1×10^6 cultured Plig^{high} cells completely suppress pulmonary metastases generated by infusion of 3×10^5 murine sarcoma cells. The potency of the cultured Plig^{high} cells exceeds that reported for all previous forms of adoptive immunotherapy in the murine sarcoma model. Recent studies indicate that the Plig^{high} T-cells are responsible for tumor suppression in active immunotherapy as well. During the current year, these studies produced three manuscripts (1 in press, 1 submitted, 1 in preparation). In addition, Dr. Stoolman's R01 supporting this work was renewed and several projects based on the results were funded as part of a new R01 and P01 (Drs. L.M. Stoolman and A.E. Chang, co-investigators).
 - 2. Randall Knibbs, Ph.D., Research Scientist (January, 1994-present) - Dr. Knibbs conducted toxicologic and functional studies on several novel inhibitors of the selectin family under an NIAID funded SBIR contract from Ligocyte, Inc. (project coordinated by Jon Nagy, PhD at Ligocyte and Lloyd Stoolman, MD at the University of Michigan). In addition, Dr. Knibbs and Melissa Allen in the laboratory developed adenoviral transfection vectors containing a gene-segment encoding murine L-selectin. This vector successfully conferred high levels of L-selectin expression in the HELA cell line. The vector will now be used to test the hypothesis that tumor-antigen pulsed, cultured murine dendritic cells expressing high levels of L-selectin will traffic more efficiently to lymph nodes and confer higher levels of tumor immunity in murine models. Finally, Dr. Knibbs participated in several collaborative

projects investigating selectin ligand structure and function. These collaborative studies resulted in six manuscripts (submitted or in preparation) during the current year.

3. Graduate research assistants: Mentored two Ph.D. and one MD/ Ph.D. candidates during laboratory rotations.
 4. Undergraduate research assistants: Mentored two undergraduate students in the laboratory participating in work/study programs.
- C. Director, General Pathology Laboratory Course for Dental Students (Pathology 631) and co-director, General Pathology Lecture Course (Pathology 630): The 4th generation Virtual Microscope Pathology Laboratory Interactive Syllabus was deployed for the course (<http://141.214.6.12/cyberscope631/>). In addition, complete high resolution digital “maps” of selected microscopic slides were added to the site employing a new image server from the Bacus Laboratories, Inc. These “Websites” cover a larger area of the tissue sections (20-50%) than the single high resolution images currently in use. They can be zoomed and panned thus simulate the viewing experience through the microscope more accurately than previously possible. It is anticipated that this technology will initially supplement and, eventually, replace the glass slide sets currently employed in the classroom.
- 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 4th 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.
- 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); April 2001 -Mar 2005 (RENEWED).
- B. Co-investigator on Project 2 and Co-director of the Immunology Core (with A.E. Chang, Surgical Oncology Division, University of Michigan)- Cellular Vaccines for Cancer Immunotherapy, NIH P01CA59327, 15% effort, \$1,000,000 (annual, direct); June 2001-April 2006 (NEW).
- C. Co-investigator (with A. E. Chang, Surgical Oncology Division, University of Michigan)- T-Cell Therapy of Human Renal Cell Cancer; NIH R01CA69102, \$250,000 (annual, direct), 10% effort, (NEW, award pending).
- D. 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, June 1999-

- April 2001. Co-investigator (with B. Richardson, Rheumatology Division, University of Michigan)- “Gender specific T-cell homing and autoimmunity”; NIH, R01AI42753, 10% effort, \$187,000 (annual, direct); Apr 1998-Mar 2003.
- 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.
- 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.
- G. Trainer on three funded pre-/post-doctoral training grants: Translational Immunology (J. Mule, PI); Surgery Oncology Research (A.E. Chang, PI) and Immunopathology (R. Miller, PI).

IV. ADMINISTRATIVE ACTIVITIES:

- A. Director of Research Flow Cytometry Laboratory and Co-Director of Clinical Flow Cytometry Laboratory- managed the development of new software to interface clinical flow cytometry instruments with the Laboratory Information System (Cerner Milleneum). Participated in the consolidation of Clinical Flow Cytometry and Hematology Laboratories. Managed the operation of the research flow cytometry 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, Medical School Curriculum Review Group
- D. Member, Learning Resources Center Oversight Committee
- E. Member, Medical School InfoTech Committee
- F. Member, Medical School and MD/PhD Admissions Committees
- G. Member, Pathology/Immunology Graduate Program Admissions Committee
- H. Participant, Retreat on Medical School Sequence II Content
- I. 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. Journal of Experimental Medicine.
- E. American Journal of Pathology.
- F. Journal of Immunology (Associate Editor).

VI. PUBLICATIONS:

ARTICLES IN PEER REVIEWED PUBLICATIONS:

1. K. Tanigawa, K. Phillips, N. Takeshita, R.A. Craig, R.N. Knibbs, A.E. Chang and **L.M. Stoolman**. 2001. Journal of Immunology. Tumor-specific responses in lymph nodes draining murine sarcomas are concentrated in cells expressing P-selectin binding sites (in press).
2. Finn WG, Singleton TP, Schnitzer B, Ross CW, **L.M. Stoolman**. 2001. Human Pathology: 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. 32: 66 (2001).
3. **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)
4. M. Jutila, S. Kurk, L. Turk, R. Knibbs, **L.M. Stoolman**: L-selectin can serve as an E-selectin ligand on human T-cells. (submitted)
5. A. Matsukawa, N.W. Lukacs, C.M. Hogaboam, R.N. Knibbs, D.C. Bullard, S.L. Kunkel and **L.M. Stoolman**: Mice Genetically Lacking Endothelial Selectins are Resistant to the Lethality in a Murine Model of Septic Peritonitis. (submitted)
6. Wusi Maki, William G. Telford, Randall N. Knibbs, **Lloyd M. Stoolman** and Sam T. Hwang: CC chemokine receptor-6 (CCR6) co-localizes with CD18 and enhances adhesion to activated endothelial cells in CCR6-transduced Jurkat T cells. (submitted)
7. Jeffrey L. Curtis, Joanne Sonstein, Ronald A. Craig, Jill Todt, Randall N. Knibbs, Timothy Polak, Daniel C. Bullard, and **Lloyd M. Stoolman**: Altered Lung Lymphocyte Recruitment in response to intratracheal particulate antigen challenge in mice lacking endothelial selectins is subset specific. (in preparation)
8. N. W. Lukacs, R.N. Knibbs, A. Johns, **L.M. Stoolman**: E- and P-selectin molecules are involved in the inflammatory responses during allergen-induced airway hyperactivity. (in preparation)
9. Daniel, Myers DVM, Dianna Farris LVT, Angela Hawley MS, Shirley Wroblewski BS, Amy Chapman BS, **Lloyd Stoolman MD**, Randy Knibbs PhD, Robert Strieter MD, Thomas Wakefield MD: Selectins and Interleukin-10 Influence Acute Thrombus Formation in a Mouse Model of Venous Thrombosis. (in preparation)

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

1. **LM Stoolman**, Michael Lougee, Douglas Gibbs and Tom Peterson. 2000/2001. 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.**
2. **LM Stoolman**, Michael Lougee, Douglas Gibbs, Tom Peterson and Gerald Abrams. 2000/2001. 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. New this year are high resolution digital “maps” covering 20-50% of the microscopic section. These “webslides” emulate glass slides more precisely than single photographs. The features are as described above. **1999 Computerworld-Smithsonian Award Finalist.**
 3. **LM Stoolman**. 2000/2001. Hematopathology Unknown Exercises. Interactive, CD-based excercises for medical student (M2) Hematopathology laboratory. CD-based publication used in M2-Heme sequence.
 4. **LM Stoolman**. 2000/2001. 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 2000 - 30 JUNE 2001**

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-4 per year)
 - 5. Anatomic Pathology Core Conference – (2 per year)
 - 6. Anatomic Pathology Consultation Conference – (2 per year)
- C. Diagnostic Conference, Department of Dermatology – (weekly)

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Pathogenesis of nephrogenic fibrosing dermopathy. (Dr. Leslie Crofford, Dr. Richard Swartz, Dr. Lori Lowe)
- B. Role of sentinel lymph node biopsy for borderline melanocytic proliferations. (Dr. Timothy Johnson, Dr. Vernon Sondak, Dr. Lori Lowe, Dr. D. Fullen)

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Co-director, Dermatopathology Service

REGIONAL AND NATIONAL:

- A. Ad hoc manuscript reviewer, Journal of Cutaneous Pathology
- B. Ad hoc manuscript reviewer, International Journal of Dermatology

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

- A. Invited speaker, "Interstitial mycosis fungoides, a variant of mycosis fungoides resembling granuloma annulare and inflammatory morphea", American Society of Dermatopathology 37th Annual Meeting, October 2000.

VI. PUBLICATIONS:

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

1. 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. *J Cutan Pathol* 28(7):351-355, 2001.
2. Cowper, S.E., Robin, H.S., Steinberg, S.M., Su, L.D., Gupta, S., LeBoit, P.E.: Scleromyxoedema-like cutaneous disease in renal-dialysis patients. *Lancet* 356(9234):1000-1001, 2000.
3. Su, L., Duncan, L.: Lymphoma- and leukemia-associated atypical CD30+ reactive cutaneous T-cell infiltrates. *J Cutan Pathol* 27:249-254, 2000.
4. 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: a pathogenic trigger of epitope spreading. *Arch Dermatol* 136:652-656, 2000.
5. 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. *J Cutan Pathol* 27(8):392-399, 2000.
6. Romero, J.B., Rasmussen, J.E., Su, L.: Multiple light yellow papules: pseudoxanthoma elasticum-like papillary dermal elastolysis. A case report. *Arch Dermatol* 136(6):791-792, 794-795, 2000.
7. Sachs, D., Su, L., Dlugosz, A.: Verrucous annular ulcerated hip plaques. Diagnosis: superficial granulomatous pyoderma form of pyoderma gangrenosum. A case report. *Arch Dermatol* 136(10):1263-1268, 2000.
8. 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. *J Cutan Pathol* (In press)
9. Cowper, S.E., Su, L.D., Bhawan, J., Robin, H.S., Leboit, P.E.: Nephrogenic Fibrosing Dermatopathy. *Am J Dermatopathol* (In press)

10. Su, L.D., Lowe, L., Bradford, C.R., Yahanda, A.I., Johnson, T.M., Sondak, V.K.: Immunostaining for cytokeratin 20 improves detection of micrometastatic Merkel cell carcinoma in sentinel lymph nodes. *J Am Acad Dermatol* (In press)
11. Anderson, K.W., Johnson, T.M., Lowe, L., Su, L., Baker, S.R.: A staged excision approach for lentigo maligna and lentigo maligna melanoma of the head and neck: the "square" procedure. *Arch Facial Plast Surg* (In press)
12. 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*)

ABSTRACTS AND PRESENTED PAPERS:

1. Gupta S., Su, L.D., Crofford, L.J.: A novel fibrosing cutaneous disorder in hemodialysis patients: a series of three patients. (Abstract presented at the ACR 64th Annual Scientific Meeting 2000 and published in *Arthritis and Rheumatism* 43(9) Suppl.:S320, 2000)

BOOKS/CHAPTERS IN BOOKS:

1. Fazel, N., Wilczynski, S., Lowe, L., Su, L.: Clinical, histopathological and molecular aspects of cutaneous human papillomavirus infections. *Dermatologic Clinics* 17(3):521-536, 1999.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

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. Co-Investigator, "Mechanisms and Prevention of Lung Injury Caused by Mustard Gas" (U.S. DOD)
B. Co-Investigator, "Liquid Ventilation in ARDS" (NIH HL-54224)
C. Co-Investigator, "Lung Injury Produced by Oxygen Metabolites", (NIH GM-29507).
D. Senior Mentor, "Training Grant in Burn, Trauma and Wound Healing Research" (NIH)

PENDING SUPPORT:

- A. Mechanism and Prevention of Lung Injury Caused by Mustard Gas (II) (U.S. DOD)

PROJECTS UNDER STUDY:

- A. Lung injury caused by 2-chloroethylethyl sulfide.
B. Pathomechanisms of ischemia-reperfusion injury.
C. Pathophysiologic role of complement activation products in secondary lung injury

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Interviewed candidates for faculty and postdoctoral positions

- B. Participation in undergraduate research program

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL AND NATIONAL:

None

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

Invited speaker, Meeting on Half-Mustard Gas, Washington, DC, October 20, 2000

EDITORIAL BOARDS:

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

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Younger JG, Sasaki N, Waite MD, Murray HN, Saleh EF, Ravage ZA, Hirschl RB, Ward PA, Till GO. Detrimental effects of complement activation in hemorrhagic shock. J. Appl. Physiol. 90: 441-446, 2001
- 2. Younger JG, Sasaki N, Delgado J, Ko AC, Nghiem TX, Waite MD, Till GO, Ward PA. Systemic and lung physiological changes in rats after intravascular activation of complement. J. Appl. Physiol. 90: 2289-2295, 2001

3. McClintock SD, Till GO, Ward PA. Protection from 2-chloroethylethyl sulfide-induced lung injury in the rat. *FASEB J.* (submitted)

BOOKS AND CHAPTERS IN BOOKS:

None

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

1. Younger J, Sasaki N, Nghiem T, Hirschl RB, Till GO, Ward PA. Lung inflammation and function in a model of complement-mediated acute injury. Society for Academic Emergency Medicine, Annual Meeting 2000
2. Younger J, Sasaki N, Nghiem T, Hirschl RB, Till GO, Ward PA. Physiological manifestations of systemic activation of complement. Society for Academic Emergency Medicine, Annual Meeting 2000
3. Younger JG, Sasaki N, Till GO, Ward PA. Role of complement activation in circulatory collapse: Studies with cobra venom factor hemorrhagic shock. *Immunopharmacology* 49:22, 2000
4. Younger JG, Sasaki N, Nghiem T, Till GO, Ward PA. Systemic hemodynamic and metabolic effects of intravascular complement activation with CVF. *Shock (Suppl.)* 13:A57, 2000
5. Hultquist D, Mack C, Massey V, Quandt K, Seekamp A, Schlafer M, Till GO, Xu F. Flavin reductase-catalyzed reactions protect tissues from peroxidative damage. *The Peroxidase Superfamily II of Animal and Human Enzymes: Biochemical Basis and Clinical Application.* September 3-8, 2000, Vienna, Austria
6. Hultquist DE, Mack CP, Massey V, Seekamp A, Schlafer M, Till GO. A role for cytoplasmic NADPH reductase in protecting heart, lung, and muscle from peroxidative damage. second Mid-Eastern Regional Meeting on Medical Sciences. Jerusalem, March 25-30, 2001
7. McClintock SD, Till GO, Ward PA. Protection from half-mustard gas-induced acute lung injury in the rat. *FASEB J.* 15: A245-A245, 2001
8. Till GO. Book review in *Arch. Pathol. Lab. Med.* 125:710–710, 2001. "Therapeutic Interventions in the Complement System" Edited by . Lambris JD and Holers VM. Humana Press, 2000.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

I. CLINICAL ACTIVITIES:

- A. None.

II. TEACHING ACTIVITIES:

- A. Mentor for students who worked in my laboratory over the past year, including five post-doctoral fellows, one pathology graduate student, one medical student, three undergraduate students and two high school students.
- B. Course director – Pathology 581. Tissue, cellular and molecular basis of disease.
- C. Instructor – Pathology 581 – Tissue, cellular and molecular basis of disease.
- D. Instructor – Pathology 600 – Pathology course for dental students.
- 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, University of Michigan Minority Student Research Opportunities Program. Five students from under-represented minority groups studied in my laboratory during the past year.
- K. Member, University of Michigan Student Research Opportunities Program.
- L. Member, Cancer Biology Training Grant Steering Committee.
- M. 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, "Retinoids for Diabetic Foot Ulcers," NIH DK59169.
- C. Principal Investigator, "Co-polymer - Trimethylamine microcarriers for high-density cell growth under serum-free conditions," HHS CA74595.
- D. Principal Investigator on Project 10, "Retinoic Acid and Cells of the Skin," Johnson and Johnson Corporation.
- E. 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 biology of collagen destruction and potential repair in diabetic skin
- C. The development of substrates for optimum growth of cells in large scale culture.
- D. Biological basis of photoaging and natural aging in skin.
- E. 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, Department of Pathology and Laboratory Medicine, MD Anderson Cancer Center, March 16, 2001.
2. Invited speaker, Johnson & Johnson Retinoid Symposium, Philadelphia PA, June 6-8, 2001.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. 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.
2. Ellis CN, Zeigler ME, Chi Y, Varani J, Fisher GJ, Pershadsingh HA, Benson CG, Kurtz TW. Troglitazone improves psoriasis and normalizes models of proliferative skin disease. *Arch. Dermatol.* 136:609-616, 2000.
3. Varani J, Warner RO, Gharaee-Kermani M, Phan SH, Kang S, Chung J, Wang Z-Q, Datta SH, Fisher GJ, Voorhees JJ. Vitamin A antagonizes elevated collagen-degrading matrix metalloproteinase and stimulates collagen accumulation in naturally-aged human skin. *J. Invest. Dermatol.* 114:480-489, 2000.
4. 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.* 114:177-182, 2000.
5. Warner RL, Bless NM, Lewis CS, Younkin E, Beltran L, Guo RF, Johnson KJ, Varani J. Time-dependent inhibition of immune complex-induced lung injury by catalase: Relationship to alterations in macrophage and neutrophil matrix metalloproteinase expression. *Free. Rad. Biol. Med.* 29:8-16, 2000.
6. Warner RL, Lewis CS, Beltran L, Varani J, Johnson KJ. Immune complex-induced lung injury in MMP-3 and MMP-9 gene-deleted mice: Evidence for two separate mechanisms of action. *Amer. J. Respir. Cell. Molecular Biol* (in press).
7. Varani J, Hattori Y, Dame MK, Murphy HS, Johnson KJ, Wojno KJ. Elaboration of matrix metalloproteinases by human prostate tissue in organ culture: Relationship to invasion in culture and to tumor spread. *Brit. J. Cancer* 84:1076-1083, 2001.
8. Riser B.L., Varani J., Cortes P., Yee J., Dame M.K., Sharba A.K. Cyclic mechanical strain on mesangial cells up-regulates intracellular adhesion molecule 1 (ICAM-1) and leukocyte adherence: Possible role in hypertension-induced nephropathy. *Amer. J. Pathol.* 158:11-18, 2001.
9. Varani J, Spearman D, Perone P, Fligiel SEG, Datta SC, Wang ZQ, Shao Y, Kang S, Fisher GJ, Voorhees JJ. Inhibition of type I procollagen synthesis by damaged collagen in photoaged skin and by collagenase-degraded collagen in vitro. *Amer. J. Pathol* 158:931-942, 2001.
10. Lewis C, Warner RL, Varani J, Johnson KJ. The role of metalloelastase in immune complex-induced acute lung injury. *Amer. J. Pathol.* 158:2135-2144, 2001

11. Moon SE, Dame MK, Remick DR, Elder JT, Varani J. Induction of matrix metalloproteinase-1 (MMP-1) during epidermal invasion of the stroma in human skin organ culture: Keratinocyte stimulation of fibroblast MMP-1 production. *Brit. J. Cancer* (in press).
12. Varani J, Zeigler ME, Dame MK, Kang S, Fisher GJ, Voorhees JJ, Stoll SW, Elder JT. HB-EGF activation of keratinocyte ErbB receptors mediates epidermal hyperplasia following retinoid treatment: A prominent side effect of retinoid therapy. *J. Invest. Dermatol* (in press).
13. Zeigler ME, Chi Y, Tumas D, Bodary S, Tang H, Varani J. Anti-CD11a ameliorates disease in the human skin – SCID mouse transplant model: Comparison with Cyclosporin A and clobetasol propionate. *Lab. Invest.* (in press).
14. Varani J, Fligiel SEG. Human squamous epithelial cell invasion under in situ conditions in a human skin organ culture model. *Histology & Histopath.* (in press).
15. Varani J, Petryniak J, Takagaki M, Dame MK, Petryniak B, Goldstein IJ. Differential expression of an a-galactosyl – containing trisaccharide on high- and low-malignant murine sarcoma cells: Identification and regulation. *Clin. Exp. Metastasis* (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* 1:17-28, 2000.
2. Varani J, Mezick J. Retinoids and skin repair. In: *Mechanisms and Treatment of Aging*. Marcell-Dekker (in press).

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

1. Varani J, Zeigler ME. Regulation of matrix metalloproteinase expression in organ-cultured human skin. *Keystone symposium on Signaling-2000*, 81:2000.
2. Varani J, Warner RO, Gharaee-Kermani M, Phan SH, Kang S, Chung J, Wang Z-Q, Datta SH, Fisher GJ, Voorhees JJ. Vitamin A antagonizes elevated collagen-degrading matrix metalloproteinase and stimulates collagen accumulation in naturally-aged human skin. *J. Invest. Dermatol.* 114:641, 2000.
3. Varani J. Expression of matrix metalloproteinases in fresh human prostate tissue and following organ culture. *Exp. Biol.* 2001.
4. Warner RO, Lewis CS, Beltran L, Varani J, Johnson KJ. Immune complex-induced lung injury in MMP-3 and MMP-9 gene-deleted mice: Evidence for two separate mechanisms of action. *Exp. Biol.* 2001.
5. Johnson KJ, Lewis C, Warner RO, Beltran L, Varani J. The role of metalloelastase in immune complex-induced acute lung injury. *Exp. Biol.* 2001.
6. Zeigler ME, Bhagavathula N, Varani J. (2001) MAPK signaling mediates properties of collagen-stimulated epidermal keratinocytes. *AACR Proceed.* 42,147, 2001.
7. Varani J, Zeigler ME, Dame MK, Kang S, Fisher GJ, Voorhees JJ, Stoll SW, Elder JT. HB-EGF activation of keratinocyte ErbB receptors mediates epidermal hyperplasia following retinoid treatment: A prominent side effect of retinoid therapy. *J. Invest. Dermatol.* 2001.
8. Moon SE, Dame MK, Remick DR, Elder JT, Varani J. Induction of matrix metalloproteinase-1 (MMP-1) during epidermal invasion of the stroma in human skin organ culture: Keratinocyte stimulation of fibroblast MMP-1 production. *J. Invest. Dermatol.* 2001.

9. Fligiel SEG, Perone P, Varani J. Collagen destruction induced by metalloproteinase (MMP) treatment in vitro is similar to dermal collagen damage in photodamaged skin: An ultrastructural analysis. *J. Derm. Pathol.* 2001.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

- A. Graduate students:
Johannes Bauer, Student of the "Freie Universitaet in Berlin, Germany"
Michael Zeidler, Student of the "Freie Universitaet in Berlin, Germany"
- B. 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: "CD40 Signal transduction", NIH HD33881, \$677,079 / 4 years August 1, 1996 – July 31 , 2000.

PENDING:

- A. Principal Investigator: "Study of Death receptors in Neuronal Systems". \$1,839,087 / 5 years December 1, 2001 – November 30, 2006

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. Weber, C.H., Vincenz, C.: The death domain superfamily: a tale of two interfaces. TIBS (2001), in press.
2. Zetoune, F.S., Murthy, A.R., Shao, Z., Hlaing, T., Zeidler, M.G., Li, Y., Vincenz, C.: A20 inhibits NF- κ B activation downstream of multiple MAP3 kinases and interacts with the I κ B signalosome. Cytokine (2001) in press.
3. Wang, X., Bauer, J. H., Li, Y., Shao, Z., Zetoune, F. S., Cattaneo, E., and Vincenz, C.: Characterization of a p75NTR apoptotic signaling pathway using a novel cellular system. J. Biol. Chem. (2001). In press.
4. Weber, C.H., Vincenz, C.: A docking model of key components of the DISC complex: death domain superfamily interactions redefined. FEBS letters (2001), 492, 171-176.
5. Hlaing, T., Guo, R.F., Dilley, K.A., Loussia, J.M., Morrish, T.A., Shi, M.M., Vincenz, C. Ward, P.A.: Molecular cloning and characterization of DEFCAP-L and -S. two isoforms of a novel member of the mammalian Ced-4 family of apoptosis proteins. J. Biol. Chem. (2001) 276, 9230-9238.

6. Kratchmarova, I., Sosinowski, T., Weiss, A., Witter, A., Vincenz, C., Pandey, A.: Characterization of promoter region and genomic structure of the murine and human genes encoding Src like adapter protein. *Gene*(2001), 262: 267-273.

BOOKS/CHAPTERS IN BOOKS:

1. Claudius Vincenz. Death receptors and apoptosis: Deadly signaling and evasive tactics. *Cardiovascular Disease* (2001). 19, 31-43.

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

1. Keystone meeting on apoptosis: January 2001, Keystone, CO. Characterization of the p75^{NTR} apoptotic signaling pathway using a novel cellular model.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

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 (2000-01):
1. Ren-Feng Guo, M.D.
 2. Neils Reidemann, M.D.
 3. Ines Laudes, M.D.
 4. Cecelia Speyer, Ph.D.
 5. Eric Albrecht, Ph.D.
- B. Graduate students
1. Tommy Hlaing
- C. UROP Undergraduate Students:
1. Kari Dilley, Junior
 2. Jennifer Loussia, Sophomore
 3. Stephanie McGuire, Senior
 4. Vishalee Padgaonkar, Senior
- D. Research mentoring of two Research Scientists (Drs. Younger and Vincenz)
- 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%), \$227,536/year, 6/1/96-5/31/06.
- B. Principal Investigator, "Lung Injury by Oxygen Metabolites", NIGMS-NIH-GM-29507 (20%), \$204,700/year (\$1,123,824/four years), 7/1/01-6/30/06.
- C. Principal Investigator, "Inflammatory Cells and Lung Injury", NHLBI-PO1-HL-31963 (25%), \$246,249/year (Proj. I) \$816,953 (all projects), 07/01/99 -02/29/04.
- D. Principal Investigator, "Rational Design of Adhesion Blocking Anti-Inflammatories" (LigoCyte) (10%), \$124,878/year; 06/15/00-06/14/01.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Chair, Department of 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.
- D. Geriatric Center Executive Committee.
- E. Howard Hughes Medical Institute Dean's Advisory Committee.
- F. Internal Medicine Advisory Committee for the University of Michigan George M. O'Brien Renal and Urologic Center.
- G. Michigan Eye Bank Research Review Committee.
- H. Undergraduate Research Opportunity Program, University of Michigan.
- I. University of Michigan Cancer Center Executive Committee.

UNIVERSITY OF MICHIGAN:

- A. Senate Advisory Committee on University Affairs, 1998 – present.
- B. 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.
 - a. Chair and member, 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

“Gold Headed Cane Award”, ASIP, Orlando, Florida (April 2001)

INVITED LECTURES/SEMINARS:

- 1. Invited Speaker, “Leukocyte Recruitment and the Inflammatory Response”, 2nd Symposium on Vascular Biology, Munster, German, October 7, 2000.
- 2. Invited Speaker, “Regulation of Lung Inflammation”, Lovelace Respiratory Research Institute, Sante Fe, New Mexico, October 5, 2000.
- 3. Invited Speaker, “The Role of Complement in Sepsis”, University of Texas-Institute of Molecular Medicine, Houston, TX, February 9, 2001.
- 4. Invited Speaker, “Role of Complement in Sepsis”, IX Congress of Medicine, Monterrey, Mexico, March 14, 2001.
- 5. ASPET Short Course Presentation, “Molecular Mechanisms of Leukocyte Recruitment”, Experimental Biology, Orlando, FL, March 31, 2001.
- 6. Invited Speaker, “Regulation of the Inflammatory Response”, Baylor College of Medicine, Houston, TX, June 6, 2001.
- 7. Invited Speaker for Distinguished Scientist Seminar, “Role of Complement in Sepsis”, University of South Alabama, Mobile, AL. June 17, 2001.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS

- 1. 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. *Critical Care Medicine*, 2000;2437-2444.
- 2. Lentsch, A.B., Ward, P.A.: The NFkappaBb/IkappaB system in acute inflammation. *Archivum Immunologiae et Therapiae Experimentalis*. 2000;48(2):59-63.

3. Martinez-Mier, G., Toledo-Pereyra, L.H., McDuffie, J.E., Warner, R.L., and **Ward, P.A.**: P-selectin and chemokine response after liver ischemia and reperfusion. *J of the Amer Coll of Surg.* 2000;191:395-402.
4. Guo, R.F., Huber-Lang, M., Wang, X., Sarma, V., Padgaonkar, V.A., Craig, R.A., Riedemann, N.C., McClintock, S.D., Hlaing, T., Shi, M.M., and **Ward, P.A.**: Protective effects of anti-C5a in sepsis-induced thymocyte apoptosis. *J Clin Invest.* 2000;106:1271-1280.
5. Mulligan, M.S., McDuffie, J.E., Shanley, T.P., Guo, R.F., Sarma, J.V., Warner, R.L., and **Ward, P.A.**: Role of RANTES in experimental cardiac allograft rejection. *Exp Mol Pathol.* 2000;69:167-174.
6. Martinez-Mier, M.G., Toledo-Pereyra, Bussell, S., Gauvin, J., Vercruysse, G., Arab, A., Harkema, J.R., Jordan, J.A., and **Ward, P.A.**: Nitric oxide diminishes apoptosis and p53 gene expression after renal ischemia and reperfusion injury. *Transplantation.* 2000;70:1431-1436.
7. Martinez-Mier, G., Toledo-Pereyra, L.H., **Ward, P.A.**: Adhesion molecules in liver ischemia and reperfusion. *J Surg Res.* 2000;94:185-194.
8. Huber-Lang, M., Sarma, V.J., Lu, K.T., McGuire, S.R., Padgaonkar, B.A., Guo, R.F., Younkin, E.M., Kunkel, R.G., Ding, J., Erickson, R., Curnutte, J.T., and **Ward, P.A.**: Role of C5a in multi-organ failure during sepsis. *J Immunol* 2001;166:1193-1199.
9. Lukas, N.W., Glovsky, M.M., and **Ward, P.A.**: Complement-dependent immune complex-induced bronchial inflammation and hyperreactivity. *Am J Physiol:Lung Cell Mol Physiol.* 2001;280:L1-L7.
10. Younger, J.G., Sasaki, N., Waite, M.D., Murray, H.N., Saleh, E.F., Ravage, Z.A., Hirschl, R.B., **Ward, P.A.**, and Till, G.O.: Detrimental effects of complement activation in hemorrhagic shock. *J Appl Physiol.* 2001;90:441-446.
11. Shanley, T.P., Davidson, B.A., Nader, N.D., Bless, N., Vasi, N., **Ward, P.A.**, Johnson, K.J., and Knight, P.R.: Role of macrophage inflammatory protein-2 in aspiration-induced lung injury. *Critical Care Medicine.* 2000;28(7):2437-2444.
12. Guo, R.F., Lentsch, A.B., Warner, R.L., Huber-Lang, M., Sarma, J.V., Hlaing, T., Shi, M.M., Lukacs, N.W., and **Ward, P.A.**: Regulatory effects of eotaxin on acute lung inflammatory injury. *J Immunol.* 2001 166(8):5208-5218.
13. Huber-Lang, M.S., Sarma, J.V., McGuire, S.R., Lu, K.T., Guo, R.F., Padgaonkar, V.A., Younkin, E.M., Laudes, I.J., Riedemann, N.C., Younger, J.G., and **Ward, P.A.**: Protective effects of anti-C5a peptide antibodies in experimental sepsis. *FASEB J.* 2001 15(3):568-570.
14. Hlaing, T., Guo, R.F., Dilley, K.A., Loussia, J.M., Morrish, T.A., Shi, M.M., Vincenz, C., and **Ward, P.A.**: Molecular cloning and characterization of DEFCAP-L and -S, two isoforms of a novel member of the mammalian Ced-4 family of apoptosis proteins. 2001. *J Bio Chem.* 276(12):9230-9238.
15. Younger, J.G., Sasaki, N., Waite, M.D., Murray, H.N., Saleh, E.F., Ravage, Z.A., Hirschl, R.B., **Ward, P.A.**, and Till, G.O.: Detrimental effects of complement activation in hemorrhagic shock. *J Appl Physiol.* 2001 90(2):441-446.
16. Younger, J.G., Sasaki, N., Delgado, J., Ko, A.C., Nghiem, T.X., Waite, M.D., Till, G.O., and **Ward, P.A.**: Systemic and lung physiological changes in rats after intravascular activation of complement. *J Appl Physiol.* 2001 90:2289-2295.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

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-August 2000.
- 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" journal club series: pathology residents, M4 students (41 contact hours).
- B. "Current Management Problems for Pathology Residents" series: pathology residents (14 contact hours).
- C. Clinical Pathology Grand Rounds:
 - 1. "Cases and Images in Immunopathology" (12/8/00).
 - 2. "Amyloidosis" (12/15/00).
- D. Immunopathology signout: pathology residents, M-4 medical students, EMU medical technology students (three times/week; 26 weeks/year).
- E. Immunopathology component of Block B (Clinical Pathology); ad hoc topical reviews: pathology residents (68 contact hours).
- F. M-1 Host Defense sequence: "Autoimmunity and tumor immunology" (5/18/01); (1 contact hour); Case Studies (5/17/01; 5/18/01); (2 contact hours).
- G. 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); (6/1/96-6/30/01).
 - 3. Melanie Hoekstra (Undergraduate; University of Michigan; UROP); (6/11/01 – 8/15/01).
 - 4. Rachna Arora (Undergraduate; University of Michigan) ; (6/11/01-8/15/01).

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.

PROJECTS UNDER STUDY:

- A. Role of cellular redox status and neutrophil-derived mediators in MCP-1-mediated pulmonary granulomatous vasculitis.
- B. Modulation of proinflammatory endothelial and smooth muscle cell functions by erythropoietin, reactive oxygen intermediates, and reactive nitrogen intermediates.
- C. Pathophysiologic role of oxidants in uremia and its complications (collaboration with Rajiv Saran, M.D., Department of Internal Medicine, University of Michigan Medical School).
- D. Ischemia-reperfusion injury in perinatal rat brain (collaboration with Faye Silverstein, M.D., Departments of Pediatrics and Neurology, University of Michigan Medical School).
- 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. 1998-2001.
- D. Member, Professional Billing Compliance Committee, 1999-present.
- E. Member, Operations Improvement Committee, 2000-present.
- F. Dean's Advisory Committee (ad hoc substitute for Dr. Peter Ward), 1994-present.
- G. Clinical Council (ad hoc substitute for Dr. Peter Ward), 1996-present.

DEPARTMENTAL:

- A. Interviewer of Pathology Residency Candidates, 1989-present.
- B. Interviewer of Pathology Graduate Program Candidates, 1990-present.
- C. Chairman, Laboratories Communications Committee, 1993-present.
- D. Chairman, Department of Pathology Quality Assurance Committee, 1993-present.

- E. Clinical Associate and Advisory Committee for Medical Technology Program, Eastern Michigan University, 1993-present.
- F. Chairman, Category Risk II Faculty Salary Planning Committee, Department of Pathology, 1996-present.

REGIONAL AND NATIONAL:

- A. Ad hoc referee for:
 - 1. American Journal of Pathology.
 - 2. Laboratory Investigation.
 - 3. Human Pathology.
 - 4. Journal of Applied Physiology.
 - 5. Lung.
 - 6. Blood.
 - 7. Journal of Laboratory and Clinical Medicine.
 - 8. Pediatric Research.
 - 9. Journal of Leukocyte Biology.
 - 10. American Review of Respiratory Disease.
 - 11. Chest.
 - 12. Journal of Pharmacology and Experimental Therapeutics.
 - 13. Circulation.
 - 14. Ophthalmology.
 - 15. American Journal of Respiratory Cell and Molecular Biology.
 - 16. Clinical Immunology and Immunopathology.
 - 17. Circulation Research.
 - 18. Journal of Immunology.
 - 19. Surgery.
 - 20. Reviews of Infectious Diseases.
 - 21. Infection and Immunity.
 - 22. Experimental Lung Research.
 - 23. Journal of Rheumatology.
 - 24. Clinical Infectious Diseases.
 - 25. Journal of Clinical Investigation.
 - 26. Cytometry.
 - 27. Biological Signals.
 - 28. Metabolism.
 - 29. Molecular Medicine Today.
 - 30. American Journal of Respiratory and Critical Care Medicine.
 - 31. The Cancer Journal.
 - 32. British Journal of Pharmacology.
 - 33. Kidney International
- B. Member, Test Committee for Clinical Pathology, American Board of Pathology, 1999-present.
- C. Member, Council for Diagnostic Immunology and Molecular Pathology, American Society of Clinical Pathologists, 1998-present.

- D. Ad hoc Reviewer; Clinical Trials Review Committee; National Institutes of Health (NHBLI); Bethesda, MD; September 27-28, 2000.

V. **INVITED LECTURES/SEMINARS:**

1. Warren JS: Mechanisms of pulmonary granuloma formation. Festschrift in Honor of Larry Roth. Indiana University, Indianapolis, IN, June 14, 2001.

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Miller MJ, Gomez HF, Snyder RJ, Stephens EL, Czop RM, Warren JS: Detection of Loxosceles venom in lesional hair shafts and skin: application of a specific immunoassay to identify dermonecrotic arachnidism. *Am J Emerg Med* 18:626-628, 2000.
2. 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* 165:295-305, 2000.
3. Gomez HF, Miller MJ, Waggener MW, Warren JS: Antigenic cross-reactivity of venoms from medically important North American Loxosceles spider species. *Toxicon* 39:817-824, 2001.
4. Desai A, Lankford HA, Warren JS: Homocysteine augments cytokine-induced chemokine expression in human vascular smooth muscle cells: implications for atherogenesis. *Inflammation* 25:79-86, 2001.
5. Desai A, Lankford HA, Warren JS: Loxosceles deserta spider venom induces the expression of vascular endothelial growth factor (VEGF) in keratinocytes. *Inflammation* (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).

BOOKS/CHAPTERS IN BOOKS:

1. Warren JS, Ward PA: The inflammatory response, in Beutler E, Lichtman MA, Coller BS, Kipps TJ and Seligsohn U (eds.) Williams' Hematology, 6th Edition, McGraw-Hill, New York, NY, 2001, pp. 67-77.
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 2000 - 30 JUNE 2001**

I. CLINICAL ACTIVITIES:

- A. None

II. TEACHING ACTIVITIES:

- A. Mentor, postdoctoral fellow: John R. Vance, Ph.D.
- B. Mentor, graduate students: Paul DeRose (MSTP, rotation), Heidi Rottschaefer (PIBS, rotation), Yayi Chang, (Pathology, rotation), Sarah Sutter (PIBS, rotation)
- C. Mentor, undergraduate student: Anthony Iacco
- D. Path 581, 2 lectures
- E. Path 582, 1 lecture, 1 discussion section (2 hours)
- F. Member, thesis committees: Tammy Morrish (Human Genetics), Jonathan Rios-Doria (CMB)
- G. Member, preliminary examination committee: Jonathan Rios-Doria (CMB)
- H. Member, Cellular and Molecular Biology Training Program

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.
- D. Principal Investigator, "End Processing in DNA Double-Strand Break Repair", NIH/NCI 1 R01 CA90911-01 (27%), \$166,000/current year (\$601,750/four years), 4/1/2001-3/31/2005.

PENDING:

- A. Principal Investigator, "Probing the mechanisms of gemcitabine action using a yeast genomic approach", University of Michigan Comprehensive Cancer Center Munn Research Grant (0%, no salary support), \$15,000/year (\$15,000/one year), 9/1/2001-8/31/2002.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Faculty candidate interviews: Andy Lieberman, Todd Kroll
- B. Pathology student recruitment activities (lunch, poster session)

MEDICAL SCHOOL/HOSPITAL:

- A. Member, MSTP Career Advisory Panel
- B. Faculty candidate interviews: Vivian Chang (Human Genetics), Robert Marciniak (Human Genetics)
- C. PIBS student interviews and recruitment dinners
- D. MSTP student interviews
- E. Member, InCyte EST resource evaluation team

UNIVERSITY OF MICHIGAN:

- A. Member, faculty panel for CMB program site visit
- B. Grant review, University of Michigan Biomedical Research Council

REGIONAL AND NATIONAL:

- A. Grant review, NIH/NCI program project grant site visit team
- B. Manuscript review, Neoplasia

V. OTHER RELEVANT ACTIVITIES:

- A. Biological Sciences Scholars Program, University of Michigan
- B. Pew Scholars Program in the Biomedical Sciences, Pew Charitable Trusts
- C. Member, Michigan Comprehensive Cancer Center

EDITORIAL BOARDS:

- A. None

HONORS AND AWARDS

A. None

PATENTS:

A. None

INVITED LECTURES/SEMINARS:

1. "What to do with broken chromosomes: Enzymatic processing of DNA ends", Cancer Biology Research Seminar, University of Michigan, November, 2000.
2. "Pathways of DNA double-strand break repair", Pew Scholars Meeting, Costa Rica, March 2001.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Vance JR, **Wilson TE**. Uncoupling of 3' phosphatase and 5' kinase functions in budding yeast: Characterization of *S. cerevisiae* DNA 3' phosphatase (TPP1). *J. Biol. Chem.* 276: 15073-81 (2001).
2. Vance JR, **Wilson TE**. Repair of DNA strand breaks by the overlapping functions of lesion-specific and non-specific DNA 3' phosphatases. *Mol Cell Biol.* in press.

ARTICLES SUBMITTED OR IN PREPARATION:

1. Karathanasis E, **Wilson TE**. Factors affecting the outcome of competition between homologous and nonhomologous repair of DNA double-strand breaks. *In preparation.*

BOOKS/CHAPTERS IN BOOKS:

1. 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. Yeast Genetics and Molecular Biology, Genetics Society of America, Seattle, WA, July 2000.
2. Vance JR, **Wilson TE**. Identification of a 3' phosphatase activity from *S. cerevisiae*. Presented at the National Academy of Sciences Colloquium "Links Between Recombination and Replication", Irvine, California, November 2000.

SECTION REPORTS

ANATOMIC PATHOLOGY

AUTOPSY SERVICE

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 2000 - 30 JUNE 2001

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. By having all cases completed within this time frame, the clinicians can be assured that results will be available for when they wish to speak with the families. Most cases were completed in 60 days and virtually all were finished within 90 days for the 2000-01 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
2000-2001	84	99	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 2000-01 year is listed below.

Medicine 22%
Surgery 24%
Pediatrics 22%
Other services 24%

Hospital total 23%

III. Conferences

We continue to present our cases at several different conferences. Pathology regularly participates in the weekly Death and Complications conference in the Department of Surgery. We also make presentations at the monthly Morbidity and Mortality conference in the Department of Internal Medicine. A new, monthly conference has been initiated in the Department of Internal Medicine where 4 autopsies are presented each month. In contrast to the usual M&M conference where most of the presentation deals with the clinical story, the emphasis for this conference is on the autopsy findings and histopathology.

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

V. College of American Pathologists Inspection

The Autopsy Service was inspected in 2001 by the College of American Pathologists. For the first time in recent memory, there were no deficiencies noted. This performance may be credited to everyone who has worked diligently to complete their autopsies on time.

VI. Statistics

This covers the time period July 1, 2000 to June 30, 2001.

Total number of autopsies performed	325
Hospital autopsies	294
Medical examiner autopsies	31

Daniel G. Remick, M.D.

CYTOPATHOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY

ANNUAL REPORT

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Total gynecologic specimens for the year were 48,847, representing a 2.2% increase over the previous year (47,756). Non-gynecologic specimens numbered 6,116; a 4.2% increase from last year. Fine needle aspirations totaled 1,476 for the current year, representing a 7.6% increase over the previous fiscal year (1,371). Of these aspirates, the cytopathologists have performed or attended a total of 829 aspirates, presenting an 18% increase from last year (698). The laboratory achieved the turnaround time for non-gynecologic specimens within 24-48 hours; however, the turnaround time for the Papanicolaou smears suffered this year and approached 5 weeks. This was a result of the continuing increase in number of Papanicolaou smears accessioned in conjunction with the loss of one cytotechnologist. Corrective actions have been taken to improve the turnaround time through out-sourcing of the backlogged pap smears, recruitment of additional cytotechnologists and creating an evening shift.

Ms. Kristin Kearn has joined our laboratory, and assumed her responsibilities as the chief cytotechnologist in March. Jenise Felan was re-appointed as Vice President, and Mr. Brian Smola, as Web Chairman for the Michigan Society of Cytology.

Our laboratory received high compliments from the College of the American Pathology Accreditation. Although, the laboratory was criticized for being very crowded and limited in space.

Our fellowship program continued to be highly successful. Dr. Neil Bavikatty completed his training with distinction, and Dr. Jing Liu received her added qualification in cytopathology in August of 2000. Our cytopathology fellowship received full accreditation from the American Board of Pathology.

The department continues its active role in assessing the new technology and the preparing the laboratory for implementation of the ThinPrep technology effective July 2001.

The Cytopathology Section had excellent representation at national and international meetings with several posters presented. Drs. Naylor and Michael presented a poster at the International Academy of Cytology. Dr. Naylor received a recognition award in cytopathology in Amsterdam. Dr. Michael presented a short course at the USCAP National Meeting, and a national teleconference sponsored by the American Society of Cytology. Dr. Afify had a platform presentation and poster presentation at the USCAP National Meeting.

Ms. Kristin Kearn continued the development and testing of the V500 Program in Cytopathology. At this stage, we are testing the billing and troubleshooting of the program.

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

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

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

	1998-1999	1999-2000	2000-2001
ID	5,865	6,246	6,947
MD	4,401	6,153	6,381
TD	1,228	1,275	1,486
DP	595	796	876
MISC			87
TOTAL	12,089	14,470	15,777

Once again, the Dermatopathology Service has seen a significant increase in volume. Dermatopathology cases represented approximately 30% of total surgical pathology accessions. Overall, there has been a 4% increase in MD cases, a 10% increase in consultation cases, an 11% increase in ID cases and a 17% increase in TD cases. The total number of cases for 2000-2001 was 15,777, a 9% increase when compared to the previous year. The clinical service load seen by each faculty member of the Dermatopathology Service, Dr. Su, Dr. Fullen, and Dr. Lowe, is substantial and exceeds any other surgical pathologist in the Department. In addition, we have continued to be productive in scholarly activities and academic pursuits.

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 and Dr. Douglas Fullen actively participate in 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 remains the largest melanoma program in the United States. Accordingly, the volume of difficult pigmented lesions seen by our service is substantial, as are the numbers of wide local excisions, biopsies, and sentinel lymph node biopsies generated by this

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

Lori Lowe, M.D.
Director
Dermatopathology Service

NEUROPATHOLOGY SERVICE
DEPARTMENT OF PATHOLOGY
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1 JULY 2000 – 30 JUNE 2001

Dr. Mila Blaivas, Ms. Constance J. D'Amato, and Dr. Paul E. McKeever contributed to the Neuropathology Service. Ms. D'Amato retired this year. We anticipate the arrival of Dr. Andrew P. Lieberman this year.

I. CLINICAL ACTIVITIES:

1. There were over 1200 neurosurgical cases examined this year. There were many personal consult cases. (M.B. = 103)
2. The Diagnostic Unit of the Neuropathology Core Laboratory of the MADRC processed 58 dementia brain cases. Of these 58 brains, 35 were MADRC cases, 16 were neurology hospital patients, and 7 were from the Michigan Dementia Postmortem Network Program.
3. There were 315 muscle biopsies, 30% with electron microscopy. There were 82 peripheral nerve biopsies. There were 5-teased fiber preparations and 80 with electron microscopy. 16 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 150 difficult neuro-oncology cases.

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 the following Continuing Medical Education accredited conferences: periodic conferences for Neurology; monthly Rheumatology Pathology Grand Rounds and occasional CPC conferences; monthly conferences where all biopsies are presented and interpreted; a weekly conference where abnormal brains are examined (including two or three weeks per month for dementia cases) with all clinicians invited; weekly nerve and muscle conferences; monthly nerve and muscle biopsy conferences. We provided individual instruction on autopsies and biopsy material; Neuropathology 858, an 8-hour laboratory course; bi-monthly conferences with Neuroradiology, Neurosurgery and Neuroradiology House Staff and every third month a microscopic conference for dementia brain cases. Weekly seminars are provided to neurological and neurosurgical house staff on clinico-pathological correlations.
4. Electives: Pathology, Neurosurgery, and Neurology Residents chose elective rotations in the Neuropathology Section.

5. A Pathology Fellow from Stanford University Medical School spent a month on the Neuropathology service.

III. RESEARCH ACTIVITIES:

1. Dr. Margaret Jones, Ms. D'Amato and Dr. Blaivas provided neuropathology support for MADRC. Ms. D'Amato was Core Coordinator of the Diagnostic Neuropathology Core of MADRC. She has also been working with several 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; 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; Quantitative evaluation of temporal lobectomy. hippocampectomy cases with Dr Erasmo Passaro's group; Collaboration with EMG group, Radiology (S. Gebarski, M.D.), Neurology, Neuro-oncology, Genetics and Pulmonary/Internal medicine 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 study of treatments of low-grade astrocytoma 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, Spectrum Health, and Wayne State University has established a registry for Alzheimer's disease and other dementias and degenerative diseases.

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

**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
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INTRODUCTION

Immunoperoxidase has seen a 13.2% increase in average slides stained per day as well as the addition of 21 new antibodies in the past year. A new frozen section panel of antibodies has been added to aid in the diagnosis of muscular dystrophies. Muscle histochemistry continues to grow and the laboratory has taken on several new clients and this is reflected in the 23.8% increase in caseload. Immunofluorescence continues to increase for the renal and heart specimens.

CLINICAL IMMUNOHISTOCHEMISTRY

Year-end figures show that the average number of slides stained per day has increased from 113.5 slides/day to 128.5 slides/day representing a 13.2% increase over last year. Twenty-one new antibodies have been added to the menu of antibody stains including a-Synuclein, Merosin, B-Amyloid Precursor Protein, Tau, a-Sarcoglycan, B-Sarcoglycan, G-Sarcoglycan, D-Sarcoglycan, Dystrophins 1,2,&3, Calpain, Spectrin, TTF1, p27, B-Dystroglycan, BCL6, CD21, MNF-116, PGP 9.5 and Tyrosinase. Additionally, our lab supported and helped the research immunohistochemistry laboratory between 7/2000 and 9/2000. During this period 1327 slides were processed and stained in our laboratory.

With the loss of one FTE in August 2000 and the ever-increasing workload we have made efficiency the top priority. All antibodies have successfully been automated as of this year. Starting in May 2001, the Histology laboratory has been helping (when time permits) to enter the requested immunohistochemical cases in the computer during the evening so that the labels can be generated the next day. An additional FTE, from the other laboratory (Electron Microscopy Lab) was assigned to help our laboratory (2 days/week), she helps in immunofluorescence staining, preparing the slides, and helps other staff to complete their work. Additionally, the Herceptest has been eliminated from the Dako Autostainer which has decreased the number of runs needed per day on this machine and reduces the cost.

Although all of these measures have helped to ease the loss of one FTE, the permanent solution to keep up with the continuous increase in the number of the cases and the demand for new antibodies should be recruitment of a full-time FTE.

As in the past, we have continued to score 100% on the biannual Immunohistochemistry CAP testing. We were able to give the inspector some advice on an antibody that was sub-optimal in their laboratory.

IMMUNOFLUORESCENCE

Under the direction of Drs. Killen, Johnson and Gordon this laboratory continues to stain skin, heart and renal biopsies using the automated Ventana ES immunostainer. The caseload has remained steady in all areas. There were over 424 renal biopsies and 192 skin and heart biopsies. This is comparable to last year (447 and 210 respectively).

NEURAL AND MUSCULAR STUDIES

This service under the direction of Dr. Blaivas has developed many new diagnostic tools this year. A panel of 11 frozen section antibodies has been added for the diagnosis of muscular dystrophies. Three new special stains that were obtained from the Mayo Clinic have been added for muscular disease diagnosis. All of these new tests have increased our recognition as a lab and this is evident by the number of new clients that have been added recently. The case load for this service has increased from 255 muscles last year to 313 this year (23.8%).

CONCLUSION

The clinical load in all services continues to increase in the year 2001. Our future goals are the establishment of In Situ hybridization in the lab and continuing with quality improvement and increased efficiency.

SURGICAL PATHOLOGY SERVICE

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 2000 - 30 JUNE 2001

The volume of specimens processed in the Surgical Pathology Division continues to grow at an unprecedented rate, having experienced a 6.5% increase in volume compared to last year. This year, the Division saw 38,882 in-house surgical specimens, 3957 personal consults, and 11,380 M-Lab cases. This represents a 33.7% increase over the past 4 years.

Remarkably, the histology laboratory has managed to keep up with this volume of work without increasing the number of FTEs. Ms. Kathy Smieszny is to be congratulated for her superb managerial skills during this time period. We have been fortunate in retaining many of our best technicians by adjusting their salaries to once again be competitive with neighboring hospitals.

Construction is scheduled to begin in July of 2001 for the new and enlarged gross room/frozen section area. 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. We hope to hire one or two pathology assistants once this room is completed. This will lessen the burden of grossing and tissue procurement on the residents assigned to room I.

Our surgical pathology fellowship program has endured recent changes in funding for house officer slots. Currently, we can only take residents for their fifth year and can no longer take board eligible or board certified candidates. Not surprisingly this has meant a shift towards the vast majority of our fellows pursuing careers in community practice rather than academic pathology.

Despite our dramatically increasing service commitments, the Surgical Pathology Division has maintained its productivity at national and international meetings. At this year's USCAP meeting, our faculty presented over 30 abstracts, directed a short course, and moderated or spoke at numerous companion meetings and subspecialty conferences. Our faculty also taught several courses at the annual ASCP meeting and presented in several workshops at the IAP meeting in Nagoya, Japan. In addition to these accomplishments, the level of NIH funding among the surgical pathology faculty has remained at incredibly high levels.

As my tenure as director of surgical pathology draws to a close, I would like to thank my colleagues for all of their hard work and dedication over the past 4 1/2 years.

Joel K. Greenson, M.D.
Director, Surgical Pathology

CLINICAL PATHOLOGY

DIVISION OF CLINICAL PATHOLOGY

**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
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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 and experienced growth in several major clinical programs. Substantial effort has been directed towards aggressive laboratory utilization control, the improvement of test ordering, laboratory logistics, achievement of compliance with HCFA-mandated rules on documentation of test-ordering indications, and achievement of compliance with federal rules related to FDA approval of testing methods. Superimposed upon these efforts has been further development of computer links with M-Labs clients and ongoing software conversion to the Cerner Millennium product. In 2000-01 the Clinical Laboratories again performed more than 3 million billable analyses (5 million individual measurements), supported a wide array of clinical and research programs, and added or replaced more than 30 testing methods. The maintenance of high quality services by the Clinical Laboratories, in the face of increasing complexity of demands, is testimony to the professionalism of the staff and the management capabilities of the laboratory directors and senior laboratory personnel. The Clinical Laboratories successfully completed the biannual College of American Pathologists onsite in May, 2001. Maintenance of the delicate balance among quality service, cost effective testing, utilization control, and the research and development which characterizes an academic institution, will be a continuing challenge.

A major initiative was achievement of a more aggressive utilization management program. More than \$850,000 in direct laboratory cost avoidance and test utilization control was realized in 2000-01. This was made possible through educational meetings with each clinical department chairman, a series of extra-departmental educational presentations, publication of on-line (CareWeb) cost data, and, most effectively, direct utilization control policies and interventions.

Finally, the Clinical Laboratories have continued to respond to the change in scope and organization of UMHS patient care activities. In contrast to the early 1990s when 70% of laboratory testing volume came from inpatient services and 30% from ambulatory patients, the split is now 40:60 in the opposite directions. The laboratories currently support more than 30 UMHS-owned regional satellite facilities as well as many more patients who are M-Care subscribers. These shifts have substantially increased our focus to informatics, logistics, and cost-containment.

Faculty and laboratory staff participated in a wide variety of intramural and extramural educational programs during 2000-01. For instance, the 28th annual Blood Bank/Transfusion Medicine course and the ASMCL course were again well attended, making them among the most visible courses of their kinds in the United States. The May AIMCL course brought together leaders from a variety of institutions and laboratory information technology fields to discuss the future of clinical pathology practice. These programs, along with the M-Labs educational programs, are prominent examples of educational outreach activities. The revised clinical pathology residency training format (July, 1993),

which organizes pathology residents into teams that rotate through three blocks of clinical laboratories that are grouped according to “relatedness of discipline”, was again updated in 2000-01. In keeping with a thematic approach, the 2000-01 version solidified the four rotation blocks and places greater emphasis on molecular diagnostics, coagulation, informatics, statistics, and management. The continued high quality of trainees in the Hematopathology Fellowship program has enhanced the service, educational, and academic missions of the Hematopathology group and the Department. The Department added a second slot in the Hematopathology Fellowship program and added a Blood Bank/Transfusion Medicine fellow. Outstanding new faculty were recruited in Cytogenetics (Diane Roulston, Ph.D.) and Blood Bank/Transfusion Medicine (Laura Cooling, M.D.).

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
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This year marks the retirement of Dr. Harold Oberman as Medical Director of the Blood Bank and Transfusion Service. Dr. Oberman has been the Director of the Blood Bank at the University of Michigan since 1964. Under his leadership it is achieved national recognition as a leader in the field of transfusion medicine.

PATIENT CARE:

Blood component utilization remained relatively unchanged from the previous year with approximately 110,000 total components dispensed. Red Blood Cell utilization approached 30,000 units with the majority being used in surgery. Platelet Concentrate utilization was approximately 50,000. Blood usage was stable despite increases in activity of major blood using clinical activities including cardiovascular surgery, trauma/burn, and hematology/oncology. This reflects the successful efforts of the medical staff to control costs in these areas.

Hematopoietic progenitor cell processing activity was comparable to the previous year with over 400 procedures performed. The trend toward use of peripheral blood progenitor cells over bone marrow continued. The Hematopoietic Progenitor Cell laboratory is maximized in space and personnel utilization, and will not be able to accommodate expansion of clinical programs without additional resources.

The transfusion and apheresis activity was also similar to the previous year. The number of peripheral blood progenitor cell collections stable, but the number of donors collected increased. This is due to improved mobilization of progenitor cells and better timing of collections. Dr. Cooling performed a study of autologous progenitor cell collects, the results of which will further improve the efficiency of collections. The Transfusion and Apheresis Service introduced red cell exchange for sickle cell disease. This procedure will improve outcome and decrease hospital stays for selected patients in sickle cell crisis. Increase therapeutic apheresis activity was experienced in the areas of vascular heart transplant rejection, post-transplant recurrence of focal segmental glomerulosclerosis, and cryoglobulinemia.

In the national trend toward prestorage leukocyte reduction of all cellular blood components has continued. This was reflected in a greater use of leukocyte-reduced red cells and platelets at UMHS. While the trend toward universal leukocyte reduction has been driven largely by blood centers and regulatory agencies, there is considerable debate within the field of transfusion medicine as to its appropriateness. The Blood Bank and Transfusion Service has continued a long-standing policy of providing leukocyte-reduced blood components to patients with established indications, while endeavoring to contain costs associated with provision of blood components.

The Blood Banks staff worked closely with the Office of Clinical Affairs and nursing services to implement informed consent for blood transfusion. The newly adopted policies on informed consent improve communication with patients regarding to rescind benefits transfusion, as well as better documentation of patient consent.

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 and crossmatched apheresis 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. Ms. Butch and Ms. Stoe were served on the Blood Transfusion Process Improvement Team, which was chaired by Dr. Davenport.

EDUCATIONAL ACTIVITIES:

Members of the Blood Bank medical and technical staffs participated in Pathology house officer teaching, Hematology fellow teaching, M2 and M4 medical students teaching, the transfusion component of nursing orientation, and many interdepartmental conferences.

The 28th annual postgraduate course, "Current Topics in Blood Banking", was held on June 6-8, 2001. 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. The Blood Bank and Transfusion Service medical and technical staff were instrumental in planning, organizing and presenting this program.

Aside from the lectures and presentations noted in the individual faculty reports of Mr. Judd and Drs. Davenport, Cooling, and Oberman; Mrs. Stoe, Mrs. Dake, Mrs. Hoffman, Ms. Bensette, Ms. Downs, Ms. Gruszczynski, Mr. Rohrkemper, 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 on a variety of technical and management topics.

PROFESSIONAL ACTIVITIES:

Dr. Laura Cooling joined the medical staff as Assistant Medical Director. She brings a wide range of experience to the Blood Bank and Transfusion Service, and is making considerable contributions at patient care and education.

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 served on committees of the American Association of Blood Banks, the Michigan Association of Blood Banks, ICCBBA, the American Society for Clinical Laboratory Science, the Michigan Society for Clinical Laboratory Science, and the National Certifying Agency of Clinical Laboratory Personnel. Ms. Dake was a member of the AABB Immunohematology Reference Laboratories Accreditation Program

Unit Committee, and presented at programs of the Michigan Association of Blood Banks and the Immunohematology Reference Laboratory Conference. Dr. Davenport served the American Association of Blood Banks on the Scientific Section Coordinating Committee, the Editorial Board of TRANSFUSION, and the Annual Meeting Program Planning Committee. Ms. Butch and Ms. Stoe served as Assessors for the American Association of Blood Banks. Ms. Stoe was elected to the Executive Board of the Michigan Association of Blood Banks.

RESEARCH ACTIVITIES:

Faculty research activities are documented in individual reports of Dr. Oberman, Dr. Davenport, Dr. Cooling, and Mr. Judd.

The Transfusion and Apheresis Service provided crucial support in leukocyte collection for General Clinical Research Center clinical research protocols. Ms. Woloskie was particularly involved in these studies. The Transfusion and Apheresis Service also participated in a multi-center clinical trial in the evaluation of Solvent/Detergent-Treated Plasma, Isoagglutinin Depleted.

Robertson D. Davenport, M.D.
Associate Medical Director,
Blood Bank and Transfusion Service

CLINICAL CYTOGENETICS LABORATORY

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 2000 - 30 JUNE 2001

Overview

The laboratory had a 14% increase in volume this year, with approximately 2400 samples processed overall. About 1340 bone marrow and solid tumor samples, 530 prenatal, and 550 constitutional genetics samples were processed. Most notable was that the number of bone marrow samples received remained at the same level as first experienced in January 2000, when the average weekly volume increased by 35-40%.

This was the laboratory's first year under the direction of Diane Roulston, Ph.D., who began in August 2000. Dr. Thomas Glover (University of Michigan, Departments of Human Genetics and Pediatrics) continued to provide invaluable expertise and sign-out coverage of constitutional genetics cases. Analysis and sign-out of a fraction of the bone marrow samples were covered by another consultant, Dr. Ramesh Babu of Penrose-St. Francis Hospital, Colorado Springs, CO.

Clinical Services

By far the most significant procedural change made last year was in the technology used for karyotyping. An automated karyotyping system (Cytovision) was purchased, which allowed conversion to digital imaging, both for standard karyotyping and for fluorescence in situ hybridization (FISH). A new fluorescence microscope that interfaces with the karyotyping system allows for enormously increased capabilities in the types of DNA probes employed and quality of the results. In order to house the computer network cables, and to provide space for the components of the Cytovision system, major renovations were made in one section of the laboratory space. This allowed us to create a room that can be darkened for the FISH microscope, and to have desk space for the system's microscopes, CPU's, monitors and keyboards and for the six technologists who continuously use the system. The conversion allowed us to discontinue use of the darkroom for all routine work. The technologists are to be commended for their rapid training and implementation of the new system.

The laboratory had its first CAP inspection under new directorship, and no deficiencies were noted. To achieve this end, all laboratory protocols were reviewed and revised. Turn-around times were brought into compliance. A new FISH protocol section was written, and reports were designed according to ACMG and CAP standards. The quality control program was thoroughly upgraded. The Laboratory Supervisor, Beth Cox, is to be commended for her initiative and perseverance that enabled us to pass this milestone.

Education

Residents and fellows from several departments came to the laboratory for rotations. Six residents in Pathology, three residents in Pediatric Genetics, and one fellow from Hematology/Oncology rotated through. The Pathology and Genetics residents gave brief talks for the technologists in areas relevant to the case work in the laboratory. This contributed to the requirements for continuing education for the

certified technologists. A course in laboratory medicine for medical students brought four students to the laboratory for part of a day, and four students from the genetic counseling Master's degree program visited and watched procedures.

Future Plans

The primary goal for next year is to cover the analysis and sign-out of all cases in house. To this end, we plan to hire an additional cytogeneticist in order to assist with triage and sign-out of the bone marrow samples. Also, there is a need for development of sub-telomeric FISH testing, which can detect molecular-level deletions that are associated with certain types of birth defects. With the new FISH system, this testing is within reach.

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

**COMBINED HEMATOLOGY LABORATORY
(HEMATOLOGY, BONE MARROW, FLOW CYTOMETRY, COAGULATION)**

**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 2000-30 JUNE 2001**

I. HEMATOLOGY AND BONE MARROW LABORATORIES:

CLINICAL ACTIVITIES:

- A. The laboratory began planning for a reorganization of space to optimize operations in the bone marrow and flow cytometry areas.
- B. Operation of the Coulter STKS hematology analyzer in the Taubman Center hematology laboratory was discontinued. Blood samples defined for the Taubman Center laboratory are now processed in the main hematology laboratory. This change will reduce maintenance costs and reagent costs, and will free technologist time for operations in the main laboratory, while maintaining a high level of clinical service.
- C. Continued improvements in software for the Coulter GenS hematology analyzer have resulted in a further reduction in the number of manual differential counts performed, despite a 6% increase in complete blood count (CBC) sample volume.
- D. The laboratory is currently working with Central Distribution to implement a criterion urinalysis instrument in the Emergency Department (ED). This will decrease turnaround times and eliminate the potential for duplicate charges for urinalysis done in the ED, and will eliminate redundancy of work in the main hematology laboratory.
- E. The hematopathology section enthusiastically welcomed Dr. Riccardo Valdez as its newest member, while bidding farewell to Dr. Rina Nangia, with many thanks for her significant contributions over the last two years.
- F. Test volumes continue to increase in the hematology laboratory despite the presence of at least one vacant 40-hour position at all times due to a shortage of qualified medical technologists to fill open positions. A summary of clinical test volume is as follows:

Test	Volume Fiscal 2001	Change from Previous year
Complete blood counts (with or without automated differential counts)	335,093	+6%
Manual Differential Counts	42,443	-9%
Urinalysis	49,685	+2.5%
Body Fluid Cell Counts and Differential Counts	6,248	-5%
Erythrocyte Sedimentation Rates	15,970	+38%
Reticulocyte Counts	5,336	+10%
Bone Marrow Aspirates	1,731	+7%
Bone Core Biopsies	1,799	+9%

Other Special Testing (osmotic fragility, Heinz body., inulin screen, etc.)	1,621	+13%
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II. FLOW CYTOMETRY

The Clinical Flow Cytometry section processed about 6100 specimens, a volume increase of 9% from the previous year. The percentage change in volume (relative to 1999-00) is listed below for each of the major test categories:

<u>Test Category</u>	<u>Change from 1999-00</u>
Immunodeficiency monitoring	+16%
CD34 stem cell counts	+0%
Chronic leukemia/lymphoma phenotyping	+20%
Acute leukemia phenotyping	+13%
T-cell subset monitoring in organ transplant recipients	-84%
Antiplatelet antibody testing	-9%

M-Labs referrals continue to comprise a substantial part of the work volume, including 26% of all acute leukemia immunophenotyping panels, 52% of all chronic leukemia/lymphoma panels, and 46% of all immunodeficiency monitoring.

Attending staff continue to triage all requests for leukemia/lymphoma immunophenotyping, with cancellation of unwarranted requests. Of the 2425 specimens submitted for leukemia/lymphoma immunophenotyping, pathologist review lead to cancellation of 829 of these requests.

Antiplatelet antibody testing by flow cytometry was discontinued in favor of an alternative methodology. Leukemia and lymphoma profiles are the most labor-intensive tests offered by the laboratory, and test volumes continue to show substantial growth.

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 decision was made to purchase and implement Behring BCS coagulation equipment in the routine and specialized coagulation laboratories. In February 01, the decision was made to go live with these instruments by the Summer of 01. At present, the BCS activation date is planned for 8/28/01. The entire specialized coagulation staff has been trained on the Behring BCS coagulation equipment. A number of routine coagulation personnel have also been

trained in this equipment. It has been decided to have two of these instruments in routine coagulation area and 1 instrument in the specialized coagulation testing area.

2. In preparation for the go live date, all assays have been re-established in the BCS instrumentation. These include the PT, APTT, fibrinogen, antithrombin, plasminogen, protein C activity, von Willebrand factor activity and antigen, tissue thromboplastin inhibition assay, all specific coagulation factor assays (XII, XI, IX, VIII, X, II, VII, V, prekallikrein, and high molecular weight kininogen). Normal ranges and between instrument variability has been worked out for all these assays.
3. The antifactor Xa assay has been established on the BCS using a single low molecular weight standard from the World Health Organization (WHO). This approach simplifies the standard curve for all the different low molecular weight heparins.
4. An attempt at "autoverification" of specialized coagulation testing was performed at the institution in January of 2001. There were some glitches in the computer program that resulted in a wrong patient value being transmitted electronically. This error resulted in a pediatric patient getting a dose of heparin when none was indicated. Fortunately, no ill consequence befell the patient. The program was suspended indefinitely.
5. The Coagulation laboratory has finally implemented an electronic records of the dictations of the specialized coagulation reports. These reports now appear regularly on CareWeb.

C. Laboratory Growth:

1. University of Michigan Hospitals System and M-Labs combined.

Overall, there was an 8.6% increase in coagulation laboratory activity in from fiscal year '00 to an annualized fiscal year '01. The largest increase in laboratory testing was in performance of anti-factor Xa assays. There was a 110% increase from 249 to 523 assays reflecting the increase use of low molecular weight heparins in patient care. There was a 61% increase in D-Dimer assays reflecting the abolition of the fibrin split product assay and increase use of the assay for diagnosis of DVT. There was a 15.9% increase in testing for the tissue thromboplastin inhibition assay (695 assays to 805 assays) reflecting increased awareness in antiphospholipid syndromes. Other assays that had a big increase in requests include prothrombin time (13%) and activated partial thromboplastin time (6.7%). We have noted a decrease in requests for the thrombin clotting time reflecting less use of this assay to monitor standard heparin and, probably, less use of standard heparin in in-patient management. Overall, the laboratory performed 195,982 individual assays with \$6,188,124 generated charges for University of Michigan health systems.

MLabs activity has also increased with a total of 5939 specialized tests being performed and \$280,090 in revenue generated for the medical system. If one excludes the number of routine coagulations tests (i.e., PT, APTT, fibrinogen, D-Dimer) performed for the U of Michigan health systems, the total number of specialized tests performed in the coagulation laboratory is 11,164 tests. MLabs accounts for 35% of all specialized coagulation testing and 16% of specialized coagulation testing revenue. Thus MLabs activity is an important segment of the specialized coagulation testing performed in this institution.

IV. TEACHING AND RESEARCH ACTIVITIES: Hematology/Flow Cytometry

- A. The hematopathology section continues to be academically productive. Members of the section published several papers in peer-reviewed journals, presented papers in poster and platform sessions at the USCAP and ASCP meetings, were invited as lecturers or moderators at several national meetings, participated as members or chairs of national committees, served on Editorial Boards, and will present several cases at the upcoming biennial Society for Hematopathology Slide Workshop.
- B. The hematopathology fellowship officially expanded to include two ACGME-accredited positions. We welcomed Drs. Patricia Uherova and Milind Valenkar as the new fellows for the 2001/2002 academic year.
- C. 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.
- D. Training and continuing education for medical technologists.
- E. 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. Published two spectrum articles on coagulation testing to be distributed to M-Labs clients

V. GOALS FOR 2001-2002: Hematology/Flow Cytometry

- A. Reallocate space within the laboratory for more efficient operations.
- B. Continue to work with vendors to develop paperless archiving systems for hematology and flow cytometry.
- C. Continue phasing out operations in the Taubman Center hematology laboratory.

GOALS FOR 2001-2002: Coagulation Laboratory

- A. Full implementation of the BCS equipment
- B. Assay development.
 - 1. Develop quantitative D-Dimer assay on the BCS for DVT diagnosis
 - 2. Develop a chromogenic assay for prekallikrein
 - 3. Improve range of testing of platelet function assays.
 - 4. Develop new methodology for lupus anticoagulant testing
 - 5. New antigen assays for total and free Protein S and Protein S activity
- 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.

William G. Finn, M.D.
Director, Hematopathology

Bertram Schnitzer, M.D.
Director, Hematopathology Fellowship Program

Charles W. Ross, M.D.
Director, Flow Cytometry

Lloyd M. Stoolman, M.D.
Co-Director, Flow Cytometry

Alvin Schmaier, M.D.
Director, Coagulation Laboratory

HISTOCOMPATIBILITY AND IMMUNOGENETICS LABORATORY

**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

CLINICAL ACTIVITIES:

Clinical activity of the Histocompatibility Laboratory remains stable, making the Laboratory one of the ten busiest in the United States.

DNA-based class I HLA and class II HLA typing, are the primary techniques. Dr. Riccardo Valdez joined the faculty as a hematopathologist and will devote a portion of his professional effort in the area of histocompatibility and immunogenetics. The goal is for Dr. Valdez to gain ASHI certification as a laboratory director.

TEACHING ACTIVITIES:

Ms. Cynthia Schall, the Laboratory Supervisor, and other members of the Laboratory were involved in the teaching activities of the Laboratory and were effective in their work. Laboratory personnel were involved in the instruction of pathology residents, allergy fellows, renal fellows and postdoctoral candidates from the Department of Hematology. Dr. Baker has continued to serve as a consultant and plays an active role in ASHI. Cynthia Schall was again 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 which have become more active in their clinical and basic research activities. Dr. Valdez joined the faculty as a hematopathologist and now devotes a portion of his professional effort in the area of histocompatibility and immunogenetics. Dr. Valdez will continue to develop his expertise in tissue typing and will participate in the teaching programs.

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

CLINICAL IMMUNOPATHOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY

ANNUAL REPORT

1 JULY 2000- 30 JUNE 2001

I. OVERVIEW:

The Immunopathology Laboratory performed more than 65,000 analyses in 2000-01. 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 the analysis of antibodies to extractable unclear antigens, and in the measurement of several individual analytes previously measured by nephelometry.

III. RESEARCH AND DEVELOPMENT:

The Laboratory supported clinical studies of the effects of cytotoxic/immunosuppressive drugs on IgG, IgA and IgM as well as IgG subclass concentrations in lupus patients and in serum banking in conjunction with Dr. Joseph McCune (Department of Medicine, University of Michigan). Several commercially-financed methods and instrument evaluations were also carried out. These studies involved a new method for detection of antibodies to extractable nuclear antigens and antineutrophil cytoplasmic antibodies.

IV. QUALITY ASSURANCE:

The laboratory actively participated in the Division-wide utilization management program.

V. TEACHING/PROFESSIONAL:

Residents, M4 medical students, and medical technology students from Eastern Michigan University rotated through the laboratory. Clinical Pathology Grand Rounds included immunopathology presentations by Dr. David Keren (Warde Medical Laboratory, Ann Arbor), and Dr. Warren (see individual faculty report). Drs. Warren and Keren continued a weekly series of didactic sessions entitled "Current Topics in Immunopathology". Other professional activities of faculty and staff in the laboratory are summarized under individual reports.

Jeffrey S. Warren, M.D.
Director, Clinical Immunopathology Laboratory

GENERAL PATHOLOGY

**ELECTRON MICROSCOPY SERVICE
DEPARTMENT OF PATHOLOGY - ANNUAL REPORT
1 JULY 2000 - 30 JUNE 2001**

We have successfully transitioned 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. At first, all 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 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.

In the past 6 years there has been a 43 percent increase in the number of cases processed by the electron microscopy lab (an additional 230 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 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	00-01	% increase
Nerve/Muscle	252	275	308	258	275	290	323	28%
Renal	256	276	333	320	349	379	372	45%
Other	23	43	20	55	100	105	66	187%
Total	531	594	661	669	724	774	761	43%

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 final digital images for diagnosis.

	Inside	Outside	Submitted	Images	% processed
Renal	178	194	372	276	74%
Nerve/Muscle	120	203	323	115	36%

The electron microscopy lab has also begun to assist with nerve teasing. This is a labor intensive effort which frequently requires 8 hours of time. Nerve teasing is done in order to prepare the tissue for optimal examination by the neuropathologist. During the past year 3 nerve teases were performed.

Additionally, the technical personnel from the electron microscopy suite have begun to spend up to 2 days per week assisting in the immunohistochemistry lab. We are carefully tracking the turnaround time in the EM suite to ensure that we are not negatively impacted by this loss of personnel, and we will also monitor the amount of overtime that needs to be completed in order to process the EM cases in a timely manner. We are hoping that the improved efficiency of the digital imaging system will allow us to both accommodate the 43% increase in workload as well as the nerve teasing and assisting in immunohistochemistry.

Daniel G. Remick, M.D.
Director, Electron Microscopy Service

M-LABS**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001****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 90 physician offices/clinics 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 MCare 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 2 proposals to prospective new clients during FY2000. Both of these were rejected.
- Two business opportunities were rejected by MLabs because the Department of Pathology could not provide the services which were requested.

IV. BILLING ACTIVITY:

- Net billings for anatomic pathology increased by 10.0% and those for clinical pathology increased by 14.7%. Total combined billing increased by 13.3%.

V. MANAGED CARE ACTIVITIES:

In the last three years, MLabs has contracted with MCare for provision of outpatient lab services, first to its Medicare members, and later for members enrolled in MCare's commercial and Medicaid products. MLabs subcontracted much of the work to MCare's provider hospital labs with benefits to hospitals and patients. These contracts are capitated, which will result in considerable savings to MCare over its previous fee for service contracts for these lab services.

In FY2001, MLabs has successfully renegotiated with MCare, the terms and conditions of the new MCare/MLabs agreement for MCare HMO, POS, Grad Care and Medicare HMO (Senior Plan) and its implementation April 1, 2001. Nine new subcontracts are in place; 5 subcontracts pending. MLabs provides ongoing management of the agreement for which it receives compensation from MCare.

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.

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 on the GLN steering committee as well as on the marketing, operations, and medical staff committees of these 2 networks. MLabs coordinates all of Departmental issues pertaining to contractual obligations to JVHL and GLN, eg. Blue Care Network critical values and HEDIS reporting.

VII. PROSPECTS:

Looking ahead, we foresee an increasingly competitive market for outreach and esoteric laboratory testing. We are already experiencing fierce competition in the hospital reference laboratory market from increasingly consolidated large independent laboratories with a national presence who offer a broad range of esoteric testing at extremely competitive prices. Purchasing agreements among groups of hospitals and affiliations/consolidations among groups of hospitals may also dictate their use of reference laboratories other than MLabs.

In the next few years, MLabs will focus its efforts on maintaining and increasing its existing hospital client base. This will require some reduction in our pricing, some broadening of our test menu, and continued efforts to interface the Department of Pathology's information system with client hospital information systems. We may also enter into arrangements with client hospitals where we would provide some management of their outreach programs.

Our recently much increased physician office client base will require efforts to continue to make our services run smoothly. In addition to the managed care work contracted to MLabs, we will focus our efforts on obtaining the discretionary (pull-through) laboratory work from these physician clients.

MLabs plans to increase our efforts significantly in marketing specialty (niche) areas such as dermatopathology, renal pathology, cytogenetics, molecular diagnostics, neuropathology, hematopathology, and flow cytometry. We 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:

As other hospital labs develop increasingly complex testing capabilities, the University of Michigan Clinical Laboratories must be increasingly innovative to bring more complex testing in-house in order to have a sufficient menu of complex testing to successfully compete in the hospital reference laboratory market. Investment in additional resources, personnel and space will be necessary if MLabs is to be able to accommodate the increased demand for esoteric testing where we have special expertise. So far, recently, additional resources have not been made available stifling growth in these areas. In addition, cost constraints have worked to reduce the scope and frequency of esoteric testing. If this trend continues, it would produce a downward spiral of reduction in volume leading to increased unit costs, leading and reduction in volume, etc.

Prepared by Eugene M. Silverman, M.D.

PATHOLOGY RESEARCH MICROARRAY LABORATORY**DEPARTMENT OF PATHOLOGY****ANNUAL REPORT****1 JULY 2000- 30 JUNE 2001****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). The first 10K human chip was produced in May of 2000. 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 to handle microarray data (<http://www.pathology.med.umich.edu/achinnaiyanlab/>).
- 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.

In the second year of operation, the Pathology Microarray Lab has achieved the following milestones:

- 1) To establish the Department as a leader in the field of genomics/proteomics the Pathology Microarray Lab had several publications accepted in pre-eminent journals including:

Chinnaiyan, A. M., Huber-Lang, M., Kumar, C., Barrette, T.R., Shankar, S. Sarma, V.J., Ward, P.A. (2001). Molecular Signatures of Sepsis: Multiorgan Gene Expression Profiles of Systemic Inflammation. *American Journal of Pathology*, In Press.

Dhanasekaran, S.M., Barrette, T.R., Mucci, N.R., Shah, R., Kurachi, K., Pienta, K., Rubin, M.A., Chinnaiyan, A.M. (2001) Delineation of Prostate Cancer Biomarkers, *Nature*, In Press.

Sreekumar, A., Nyati, M.K., Varambally, S., Barrette, T.R., Ghosh, D., Lawrence, T.S., Chinnaiyan, A.M. (2001). Profiling of Cancer Cells Using Protein Microarrays: Discovery of Novel Radiation-Regulated Proteins, *Cancer Research*, In Press.

- 2) The Pathology Microarray Lab has supported the following grant applications by providing preliminary gene expression analyses:

R21/R33, Gene Expression Analysis of Human Prostate Cancer by use of Laser Capture Microdissection and cDNA microarrays, P.I. M. Rubin

ACS Beginning Investigator Grant , Molecular Classification of Prostate Cancer, P.I. A. Chinnaiyan

Bioinformatics Pilot Research Grant , A Bioinformatics Approach to Cancer Profiling, P.I. A. Chinnaiyan

R01, Protective Effects of anti-c5a in Sepsis, P.I. P. Ward

R01, Lung Injury by Oxygen Metabolites, P.I. P. Ward

Microarray Supplement, Sepsis Profiling, P.I. P. Ward

U of M SPORE in Prostate, P.I. K. Pienta

P01, Program Project on Prostate Cancer Bone Metastases, P.I. E. Keller

- 3) The Pathology Microarray Lab can now produce 20K human cDNA arrays, 10K rat cDNA arrays, and 5K mouse cDNA arrays
- 4) A protein microarray platform is being optimized for use with clinical specimens and cell lines.

III FUTURE GOALS:

The future goals of the Pathology Microarray Lab in the next calendar year include:

1. Continue to support the research funding applications of Pathology faculty.
2. Continue to publish data using microarray technology in peer-reviewed journals to establish the Department in the fast moving field of genomics/proteomics.
3. Expand the rat, mouse, human DNA chips to include additional cDNA clones. Ultimately, we would like to develop a chip that can monitor the entire expressed genome.
4. Develop and utilize protein microarray technology to answer biologically important questions
5. Train post-doctoral fellows and students in making and using microarrays.
6. Develop a unified bioinformatics platform for the analysis of DNA microarray, tissue microarray, protein microarray and clinical/pathology data.
7. Position our resources and expertise such that we can take advantage of opportunities in the emerging field of "clinical genomics".

IV. TEACHING/PROFESSIONAL:

Terry Barrette, the Laboratory manager, has played an important role in setting up our microarray database and data analysis programs. 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. Scott Lesser, 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

**ANN ARBOR VA HEALTH SYSTEM
PATHOLOGY AND LABORATORY MEDICINE SERVICE**

**DEPARTMENT OF PATHOLOGY - UNIVERSITY OF MICHIGAN
ANNUAL DEPARTMENTAL REPORT
1 JULY 2000 - 30 JUNE 2001**

INTRODUCTION:

The Ann Arbor VA Healthcare System (AAVAHS) is a University of Michigan affiliated tertiary health care provider for veterans. It is one of three tertiary medical centers in the Veterans Integrated Service Network (VISN) #11 serving the veteran population of Michigan, and portions of Ohio, Indiana and Illinois. The AAVAHS Pathology and Laboratory Medicine Service maintains a close relationship with the University Department of Pathology at every level. All pathologists in the AAVAHS have medical school appointments and participate in university activities in a manner similar to other departmental sections. Recruitment for AAVAHS 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 AAVAHS laboratory was inspected in 2000 and retains full accreditation by the College of American Pathologists. The AAVAHS was inspected by the JCAHO in 1999 and is currently fully accredited. The medical center's Decentralized Hospital Computer System (*Vista*) is recognized as the most fully integrated medical information system. It combines all of the clinical management of the patient and has shifted to a computerized patient record system (CPRS) in year 2000. Data storage for all components of pathology and the clinical laboratories contains full patient information for 1 ½ decades. Digital images of selective patient surgical, cytopathology, autopsy and ultrastructural specimen are stored as part of the patient medical record and are accessible to clinicians within minutes of case review.

Two major reorganization thrusts are underway at the AAVAHS. 1) The facility is refocusing its mode of healthcare delivery, downsizing inpatient care and greatly expanding its ambulatory care. In keeping with this change, a substantial capital improvement program is ongoing. Completed to date are Research Building, two additional parking structures and a 340,000 sq. ft. clinical addition. This building is attached to the existing hospital and provides space for ambulatory care, new surgical suites, post surgical recovered unit, vascular cath facilities, four intensive care units and a floor for diagnostic services (Pathology, Clinical Labs, Radiology and Nuclear Medicine). Pathology and Laboratory Medicine occupies 23,000 sq. ft on the third floor of the clinical addition. The previous structure is currently under complete remodeling to allow for current standards of inpatient privacy. Also included will be administrative offices, and additional research space. Current discussions concern a complete functional restructuring of the clinical labs. 2) The VISN 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, equipment

standardization, VISN-wide reagent contracting, decreased cost of referred (send-out) testing to nonVA clinical labs and an increase in the workload in Ann Arbor AAVAHS's anatomic pathology and the clinical labs.

ANATOMICAL PATHOLOGY:

- A. **Surgical Pathology:** 5,155 surgical cases have been accessioned and reported during year 2000 and 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 AAVAHS 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 AAVAHS 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:** 2265 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 AAVAHS 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:** 309 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 AAVAHS 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 AAVAHS 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 856,255 clinical pathology procedures were performed in the laboratory. In Chemistry there were 706,316; in Hematology 88,702; in Urinalysis 11,744, in Microbiology 28,158, and in Blood Bank 21,275. These figures represent productivity (billable) rather than weighted test numbers. A formal clinical pathology rotation has not been available for pathology residents although the residents may participate or observe clinical pathology procedures when this activity is appropriate in relation to their other rotations. Drs. Chensue, Utiger and Chamberlain oversee the clinical laboratory and make available interesting and pertinent clinical laboratory information available to residents as desired. Clinical Pathology 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 AAVAHS 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.

RESEARCH:

The specific efforts of the pathology staff are included on individual reports. Dr. Stephen Chensue has strong funded research programs. He also participates in cooperative studies with other investigators at the University of Michigan. Dr. Murphy carries a full investigative program. She and Dr. Chensue have research laboratories in Research Building 31 of the AAVAHS. All staff participate in various clinical studies and collaborate with a variety of investigators. The laboratory in general serves the AAVAHS research program by providing considerable technical support for clinical research and in some cases for more basic research in both anatomic and clinical pathology.

ADMINISTRATION:

Dr. Chensue was appointed as Chief of Service in March 2001. The staff pathologists at the VAMC serve in various capacities involving administrative tasks for the University of Michigan, such as the Resident Selection Committee, the Medical Student Admissions Committee, Graduate student testing and thesis committees, teaching faculty of the second year medical students as well as other graduate course in the medical, dental schools and the school of public health. At the AAVAHS, 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 AAVAHS. 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 pathologists.

SUMMARY:

The AAVAHS Pathology and Laboratory Medicine Service considers the practice of high quality medicine and the appropriate care of the veteran patients as its first and highest responsibility. There is close supervision of resident activities as they are involved with patient care. All staff members are privileged and evaluated in accordance with their training, experience, continuing education and participation in quality improvement activities. Within the service there is an extensive quality improvement program that integrates with that of the hospital as a whole. The Pathology and Laboratory Medicine Service has maintained accreditation by the College of American Pathologists since the early 1960's. The Blood Bank maintains approval by the federal Food and Drug Administration. The partnership with the University of Michigan serves to strengthen and improve the quality of patient care to our veterans. The teaching effort involving both residents and medical students is of benefit to the two institutions. The newly constructed Clinical Addition now houses: Ambulatory Care, Surgical Suites, the Intensive Care Units, Nuclear Medicine, Radiology and the full Clinical and Anatomic Pathology laboratories.

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