

**THE UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL**

Department of Pathology

ANNUAL REPORT



1 JULY 2003 - 30 JUNE 2004

THE UNIVERSITY OF MICHIGAN

MEDICAL SCHOOL

Department of Pathology

ANNUAL REPORT



1 JULY 2003 - 30 JUNE 2004

LIST OF FACULTY

LIST OF FACULTY

<u>Name</u>	<u>Rank</u>	<u>Institutional Affiliation</u>
Abrams, Gerald D.	Professor Emeritus	The University of Michigan
Annesley, Thomas M.	Professor	The University of Michigan
Appelman, Henry, D.	M.R. Abell Professor	The University of Michigan
Baker, James R.	Associate Professor	The University of Michigan
Barr Jr., Mason	Professor ⁺	The University of Michigan
Blaivas, Mila	Clinical Associate Professor	The University of Michigan
Capps, Rodney D.	Assistant Professor	The University of Michigan
Chamberlain, Priscilla	Clinical Instructor II	Veterans Affairs Medical Center
Chensue, Stephen W.	Associate Professor	Veterans Affairs Medical Center
Chinnaiyan, Arul	Assistant Professor	The University of Michigan
Cho, Kathleen R.	Professor*	The University of Michigan
Cooling, Laura	Clinical Assistant Professor	The University of Michigan
D'Amato, Constance J.	Assistant Professor Emeritus	The University of Michigan
Dai, Yiran	Clinical Assistant Professor	The University of Michigan
Davenport, Robertson	Associate Professor	The University of Michigan
de la Iglesia, Felix	Adjunct Research Scientist***	Pfizer
Dressler, Gregory R.	Associate Professor	The University of Michigan
Duckett, Colin	Assistant Professor	The University of Michigan
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 Associate Professor	The University of Michigan
Flint, Andrew	Professor	The University of Michigan
Friedman, Bruce A.	Professor	The University of Michigan
Fullen, Douglas R.	Clinical Assistant Professor	The University of Michigan
Giacherio, Donald	Clinical Assistant Professor	The University of Michigan
Gikas, Paul W.	Professor Emeritus	The University of Michigan
Giordano, Thomas J.	Associate Professor	The University of Michigan
Gordon, David	Professor	The University of Michigan
Greenson, Joel	Professor	The University of Michigan
Headington, John T.	Professor Emeritus	The University of Michigan
Heidelberger, Kathleen P.	Professor Emeritus	The University of Michigan

<u>Name</u>	<u>Rank</u>	<u>Institutional Affiliation</u>
Hogaboam, Cory	Assistant Professor	The University of Michigan
Homeister, Jonathon	Lecturer	The University of Michigan
Inohara, Naohiro	Assistant Research Scientist	The University of Michigan
Johnson, Kent J.	Professor	The University of Michigan
Judd, W. John	Professor	The University of Michigan
Kaldjian, Eric	Adjunct Assistant Professor	Pfizer
Keller, Evan	Assistant Professor##	The University of Michigan
Keren, David F.	Clinical Professor	Warde Medical Laboratories
Killen, Paul D.	Associate Professor	The University of Michigan
Kleer, Celina	Assistant Professor	The University of Michigan
Krueger, Cynthia	Lecturer	The University of Michigan
Kunju, Lakshmi (Priya)	Lecturer	The University of Michigan
Kunkel, Steven L.	Endowed Professor of Pathology Research and Co-Director, Division of General Pathology	The University of Michigan
Lieberman, Andrew P.	Assistant Professor	The University of Michigan
Lieberman, Richard W.	Clinical Assistant Professor+++	The University of Michigan
Lowe, John B.	Professor	The University of Michigan
Lowe, Lori	Clinical Associate Professor	The University of Michigan
Lucas, David	Clinical Associate Professor	The University of Michigan
Lucas, Peter	Lecturer	The University of Michigan
Lukacs, Nicholas	Associate Professor	The University of Michigan
McKeever, Paul E.	Professor	The University of Michigan
McKenna, Barbara J.	Clinical Associate Professor	The University of Michigan
Mellerick-Dressler, Dervla	Assistant Professor	The University of Michigan
Michael, Claire W.	Clinical Associate Professor	The University of Michigan
Midgley, A. Rees	Professor Emeritus	The University of Michigan
Miller, Richard A.	Professor	The University of Michigan
Murphy, Hedwig S.	Assistant Professor	The University of Michigan
Naylor, Bernard	Professor Emeritus	The University of Michigan
Newton, Duane	Clinical Assistant Professor	The University of Michigan
Nunez, Gabriel	Professor	The University of Michigan
Phan, Sem H.	Professor	The University of Michigan
Pierson, Carl L.	Assistant Professor	The University of Michigan
Pu, Robert	Clinical Assistant Profesoor	The University of Michigan

<u>Name</u>	<u>Rank</u>	<u>Institutional Affiliation</u>
Ramsburgh, Stephen R.	Clinical Assistant Professor	The University of Michigan
Rasche, Rodolfo	Clinical Assistant Professor	The University of Michigan
Remick, Daniel G.	Professor	The University of Michigan
Ross, Charles W.	Associate Professor	The University of Michigan
Roulston, Diane	Clinical Associate Professor	The University of Michigan
Ruiz, Robert	Clinical Assistant Professor	The University of Michigan
Schmaier, Alvin	Professor	The University of Michigan
Schmidt, Robert W.	Professor Emeritus	The University of Michigan
Schnitzer, Bertram	Professor	The University of Michigan
Shah, Rajal B.	Clinical Assistant Professor	The University of Michigan
Silverman, Eugene M.	Clinical Associate Professor	The University of Michigan
Smith, Lisa	Clinical Assistant Professor	The University of Michigan
Stoolman, Lloyd M.	Professor	The University of Michigan
Su, Lyndon	Clinical Assistant Professor	The University of Michigan
Thorson, John	Clinical Assistant Professor	The University of Michigan
Till, Gerd O.	Professor	The University of Michigan
Utiger, Cheryl	Clinical Lecturer	The University of Michigan
Valdez, Riccardo	Clinical Assistant Professor	The University of Michigan
Varani, James	Professor	The University of Michigan
Vincenz, Claudius	Research Investigator	The University of Michigan
Ward, Peter A.	Godfrey D. Stobbe Professor and Chairman	The University of Michigan
Warren, Jeffrey S.	Warthin/Weller Professor and Director, Clinical Pathology	The University of Michigan
Wilson, Thomas	Assistant Professor	The University of Michigan

* Joint Appointment, Department of Internal Medicine

** Joint Appointment, Dental School

*** Clinical Appointment, Pfizer

+ Joint Appointment, Department of Pediatrics and Communicable Diseases

++ Joint Appointment, Department of Ophthalmology

+++ Joint Appointment, Department of Obstetrics and Gynecology

Joint Appointment, Department of Urology

Joint Appointment, ULAM and Institute of Gerontology



2003-2004

The Department of Pathology



Faculty, Residents and Fellows
Department of Pathology

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DEPARTMENTAL OVERVIEW



Department of Pathology
University of Michigan

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

**DEPARTMENTAL OVERVIEW
July 2003 – June 2004**

Introduction and Overview

Change within the Department is in view. Early this year (2004), the Dean appointed a search committee to identify a successor for Dr. Ward, who, as of the summer of 2005, will have served as Chair for 25 years. During that time, the clinical activities have more than tripled, the federally funded research support has grown by more than 30-fold, and the teaching activities, which have always been strong, have been enhanced by electronic and digital formats, allowing medical students access in the living quarters to all presentations. The Search Committee in late Spring 2004 screened a series of candidates. Four finalist candidates have been formally interviewed. The hope and expectation is that the process can be brought to a successful conclusion by the turn of the year and that Dr. Ward's successor might take office in the summer of 2005. Substantial issues, especially dealing with space for research and the clinical laboratory system (including both Anatomic and Clinical Pathology) will have to be resolved. The Department currently is in a strong financial and academic position. This should be a strongly positive foundation for the search process.

Faculty recruitment for Pathology diagnostic positions has proceeded carefully and strategically, identifying new areas of diagnostic need. Research recruitments have come to a halt, pending resolution of the space issues and the research directions the next Chair of Pathology would like to pursue.

Teaching Activities

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

For 2003-2004, the Pathology Graduate Program had a total of 19 students enrolled in full time studies. Eight started the year as pre-candidates, with four of them successfully achieving candidacy by the end of the academic year. One student successfully completed the program and was awarded the doctoral degree, while another student had to leave the program and the university due to personal reasons and was awarded the masters degree. Two students transferred to other graduate programs within the university. Four students matriculated into our program from the Program in Biomedical Sciences (PIBS), while two students were affiliated with the Medical Scientist Training Program. One student was funded through a Rackham Merit Fellowship, and was honored in February, 2004 by the Rackham School of Graduate Studies for her achievement in attaining candidacy. The status of Post-doctoral Fellows is described in the section on "Research Activities".

The program had a notable change in curriculum with the modification of Pathology 585 to a new course, "Histopathologic Basis of Disease", with Hedwig S. Murphy, M.D. as course director. Another notable event was the well-attended Annual Pathology Research Symposium held in November, 2003 with Sergio Lira, Ph.D. as keynote speaker. A number of students and select faculty also presented their research during this symposium. Finally, the second bi-annual program retreat was held in June 2004 where a number of issues were discussed. Among the highlights were suggestions for,

- a) improving exposure of the program within PIBS, possibly by inclusion of a pathobiology course in the core PIBS curriculum,
- b) changing the name of the program to increase interest and more accurately reflect the research in the program faculty's labs, and,
- c) several curriculum changes, including the offering of a course to provide training in grantsmanship

Clinical Service Activities

The Anatomic and Clinical Pathology Laboratories continue to provide excellent, full-spectrum service as the UMHS has continued to experience growth in ambulatory care activities and in many major clinical programs. 2003-2004 was marked by new faculty recruitments in molecular diagnostics, bone and soft tissue surgical pathology,

genitourinary pathology and cytopathology. The laboratories continued their trend of more laboratory procedures (approximately 4% each year) operating with a fixed number of staff and a flat budget. Efforts continue to be directed towards more aggressive control of laboratory utilization and the improvement of phlebotomy, central distribution and laboratory operations. In response to pressures to reduce our cost/unit of laboratory service and to improve operating efficiency, a more aggressive plan for laboratory and send-out test utilization has been implemented. Augmentation of the capabilities of the Molecular Diagnostics, Blood Bank, Chemistry, Tissue Typing, Hematology, Microbiology, Cytogenetics, Cytopathology and Surgical Pathology Laboratories was contributory to this process. In 2003-2004, the Laboratories performed more than 3.4 million laboratory diagnostic analyses and handled more than 55,000 surgical pathology cases. The maintenance of high quality service, in the face of increasing complexity of demands, is a testimony to the professionalism of the staff as well as the management capabilities of laboratory directors and senior laboratory personnel. The Laboratories continue to support the M-Labs outreach program. The Laboratories successfully completed the bi-annual College of American Pathologists (CAP) inspection. Maintenance of the delicate balance among quality service, cost-effective testing, utilization control and research and development, which characterizes an academic institution, will be a continuing challenge.

Research Activities

The Department of Pathology's research activities continue to be one of the many strengths of our academic mission. The Department's faculty successfully compete for extramural research support, attract outstanding graduate students and fellows from both the national and international scene, publish in highly visible, peer-reviewed scientific journals, and serve on numerous national and international scientific committees. During the past year, the Department's research efforts increased as reflected by approximately 2 million dollars more spent when compared to the previous year's expenditures. The total research expenditures for 2004 were over \$19 million; this included over \$13.6 million in direct expenditures and \$5.4 million in indirect expenditures. Faculty members in the Department of Pathology hold 86 individual grants from the National Institutes of Health (an increase of 16 funded applications over 02-03, or 19%), 2 Program Projects, 2 MERIT Awards, and 2 training grants. In addition, other support originates from a variety of external non-federal sources including, the American Heart Association, American Lung Association, Kennedy's Disease Fund, The American Cancer Society, The American Federation for Aging Research, the MEDC Life Science Corridor Fund, Muscular Dystrophy Association, National Blood Foundation, Sandler Family Foundation, United Negro College 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 SPOR Program, Breast Cancer Program, Interstitial Lung Disease SCOR, and the acute lung injury SCCOR. This blend of activity underscores the role of Pathology faculty in translational research, especially where DNA-based microarrays and tissue arrays are involved. These studies have resulted in publications dealing with solid tumors and inflammatory diseases. The faculty actively publish in both the clinical and

experimental journals and cover very diverse scientific interests, including clinical pathology, anatomical pathology, and basic cellular and molecular mechanisms of disease. Our faculty members participate in peer review of both the intramural and extramural NIH Programs, and peer review of submitted scientific articles for diverse journals. Another index of the healthy academic research environment in the Pathology Department is the large number of post-doctoral fellows in the different laboratories, as over 40 post-doctoral fellows from many different countries are engaged in research activities and clinical fellowship. These post-doctoral scholars have actively sought positions in the Department of Pathology to enhance their research and clinical careers. Our faculty continue to provide expertise for both internal and external program review, which include serving as ad hoc and permanent members of NIH study sections, serving as committee members for site visit teams, providing expertise on government sponsored special emphasis panels, and organizing or chairing clinical and experimental scientific conferences.

INDIVIDUAL FACULTY REPORTS

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

**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

- A. Freshman Medical Class:
 - 1. Course Director, Lecturer, "Basic Concepts of Disease in Patients and Populations Sequence" - 12 lecture hours.
 - 2. Multidisciplinary Conferences - 2 contact hours.
 - 3. Histopathology Sequence, Sequence Director, Lecturer, Lab Instructor-32 contact hours (8 lectures, 24 lab hours).
- B. Sophomore Medical Class:
 - 1. Pathology Lab Instructor-all sequences. 50 contact hours.
- C. Undergraduate LS&A/Graduate:
 - 1. Biology 224 - 1.5 lecture hours.
- D. Hospital Conferences:
 - 1. Cardiovascular Pathology Case Conference - monthly.
 - 2. Cardiac Pathology teaching conference – monthly.
- E. Post-graduate Medical Education
 - 1. Lecturer – Cardiology Update – Mackinac Island, August 2003.
- F. Community:
 - 1. Organizer, director, and lecturer of "Mini-Med. School", a six-week course for the public, Spring 2004.
- G. Invited Lectures:
 - 1. Keynote Address-UM Medical School White Coat Ceremony, August 2003.
- H. Production of Teaching Materials:
 - 1. Production of CD-Rom and syllabus for Histopathology Lab sequence for M-1.
 - 2. Production of website to accompany M-1 Pathology Lectures.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Pathology of lesions produced by high intensity ultrasound, with Bioengineering staff and students.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL/UNIVERSITY:

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

REGIONAL AND NATIONAL:

- A. Editorial Board, Modern Pathology.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

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

III. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

REGIONAL AND NATIONAL:

- A. Board of Directors, American Association for Clinical Chemistry.
- B. Chair, Clinical Consulting Task Force, American Association for Clinical Chemistry.
- C. Annual Meeting Task Force, American Association for Clinical Chemistry.
- D. Program Coordinating Commission, American Association for Clinical Chemistry.
- E. Chair, NACB Awards Committee.
- F. Chair, NACB/AACC Distinguished Abstracts Program.
- G. House of Delegates, American Association for Clinical Chemistry.
- H. Executive Committee/Journal Management Group, Clinical Chemistry Journal.
- I. Member, Academy of Clinical Laboratory Physicians and Scientists.
- J. Member, National Academy of Clinical Biochemistry.
- K. Member, Association of Clinical Scientists.
- L. Member, American Society for Mass Spectrometry.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES:

- A. "Mass Spectrometry Technology for the 5-10 Year Horizon", Athena Society Meeting, Samos, Greece, September 2003.
- B. "Principles and Clinical Applications of Mass Spectrometry", Gustavus Adolphus College, St. Peter Minnesota, October, 2003.
- C. "Immunosuppressant Drug Monitoring Using LC-MS/MS", Medical College of Ohio, Toledo, Ohio, October, 2003.
- D. "New Technologies for Mass Spectrometric Analyses", Visiting Professor, Washington University, St. Louis, Missouri, December 2003.
- E. "Rapid Analysis of Immunosuppressant Drugs from Whole Blood", Micromass Symposium on Mass Spectrometry and Clinical Applications, Parsippany, New Jersey, March 2004.
- F. "Specimen Preparation for Immunosuppressant Analyses; Balancing Speed, Precision, and Accuracy", Immunosuppressants in Transplantation: Therapy and Testing, Medical University of South Carolina, Charleston, South Carolina, March 2004.
- G. "Clinical Mass Spectrometry", Michigan State University, Lansing, Michigan, April 2004.
- H. "Mass Spectrometry in Clinical Therapeutic Drug Monitoring", Canadian Society of Clinical Chemistry Annual Meeting, London, Ontario, June 2004.
- I. "Immunosuppressant Drug Analysis Using LC/MS", LC/MS Forum, American Association for Clinical Chemistry Annual Meeting, Los Angeles, California, July 2004.
- J. "Calibration and QC Standards for LC/MS", LC/MS Forum, American Association for Clinical Chemistry Annual Meeting, Los Angeles, California, July 2004.

JOURNAL EDITORSHIPS:

- A. Associate Editor, Clinical Chemistry.

EDITORIAL BOARDS:

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

EDITORIAL REVIEW ACTIVITIES:

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

AWARDS:

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

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Annesley, T.M.: Ion suppression in mass spectrometry. Clin. Chem. 2003;49:1041-4.
2. Annesley, T.M., and Clayton, L.T.: A simple, novel extraction protocol for the analysis of immunosuppressants in whole blood. Clin. Chem., 2004;50:in press.

ABSTRACTS:

1. Lake, K.D., Magee, J.C., Stodart, J., McLean, D., Annesley, T.M., and Cibrik, D.: Blinded Neoral C2 monitoring in de novo renal transplant recipients. Amer. J. Transplant. 2004;4(s8):255.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

- A. General surgical pathology – 4 1/2 months.
- B. Gastrointestinal and hepatic pathology services - 4 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 - (2-3 hours per month).
 - 2. Liver Biopsy Conference – 4 hours per year.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

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.

Anaplastic, lymphoma-like carcinoma arising in Barrett's mucosa, with BJ McKenna

Is hyperplasia of the interstitial cells of Cajal a common reaction to intramural masses in the gut?
With Meryem Koker

The apoptotic form of microscopic colitis, with BJ McKenna

Are juvenile-like polyps in adults the same as in children? With Meryem Koker

What is the yield of significant microscopic disease in colorectal biopsies of adult patients with chronic diarrhea and normal endoscopic findings? With BJ McKenna

G cells in the duodenal bulb and their response to therapy. With Wei Xin and Barbara McKenna
Marginal collagenous colitis: does it exist? With BJ McKenna, W Xin, M Anderson and L Evans

The effects of loss of IL-10 and Familial adenomatosis polyposis-like genetic changes on the development of colorectal carcinomas in knock-out mouse models. With Emina Huang.

The prevalence of unsuspected invasive carcinomas in specimens resected for high-grade dysplasia in Barrett's mucosa and the gastric cardia. With Weijian Zhu and members of the Section of Thoracic surgery

The yield of significant microscopic findings in terminal ileal biopsies and their relation to indications for endoscopy and endoscopic findings, with Jon McHugh and Barbara McKenna

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

- 1. Lectures on dysplasia in the gut, the gastrointestinal junction and ulcerative colitis, Rambam Hospital and Technion Institute School of Medicine, Haifa, Israel, July 9, 2003.
- 2. "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, Vancouver, BC, Canada, July 15, 2003
3. "What in the hell is dysplasia?"; "Are there histologic changes that indicate that the refluxate is alkaline rather than acidic?"; "Are cardiac goblet cells a part of multifocal atrophic gastritis?", 7th World Congress, OESO, Paris, France, September 3-4, 2003.
 4. "Changing concepts in Chronic Colitis", Rodger C. Haggitt Gastrointestinal Pathology Society companion meeting, New Orleans, LA, September 17, 2003.
 5. "Tales from the GE Junction" the A James French Society scientific session, Ann Arbor, MI, October 12, 2003
 6. "Just Another Day on the GI Biopsy Service", with B.J McKenna, Annual Meeting, American Society for Clinical Pathology, New Orleans, September 19, 2003; Michigan Society of Pathologists, December 6, 2003
 7. Presentations on small intestinal stromal tumors and minimally differentiated colorectal carcinomas, Diagnostic Problems in Surgical Pathology, Annual meeting, American Society for Clinical Pathology, New Orleans, LA, September 20, 2003.
 8. "Polyps with no names or with obscure names". Rodger C. Haggitt Gastrointestinal Pathology Society companion meeting, Vancouver BC, Canada, March 7, 2004.
 9. Neoplastic diseases of the intestine, sponsored by the American Society of Clinical Pathologists, Santa Fe, NM, April 21, 2004.
 10. Lectures on dysplasia in the gut and gastrointestinal stromal tumors, Rambam Hospital and Technion Institute School of Medicine, Haifa, Israel, June 21, 2004.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Rubenstein J, Sherif A, Appelman H, Chey WD. Ulcerative colitis associated enteritis. Is ulcerative colitis always confined to the colon? J Clin Gastroenterol. 38:46-51, 2004.
2. Lau CD, Simmons M, Syngal S, Bresalier RS, Fortlage L, Normolle D, Griffith KA, Appelman HD, Brenner DE: Dysplasia in Barrett's Esophagus: Implications for Chemoprevention. Cancer, 2004 100(8):1622-27.
3. Appelman HD. Biopsies of the terminal ileum in inflammatory bowel diseases: do they help? Pathology Case Reviews, 9:115-122, 2004.
4. Appelman HD. What is dysplasia in the gut? Accepted for publication in Archiv Path Lab Med. April, 2004.

CHAPTERS AND BOOKS:

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

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

1. Guo G, McKenna BJ, Appelman HD: Serrated adenoma-like mucosa commonly covers colonic submucosal lipomas, *Am J Clin Pathol*, 120:452-3, 2003.
2. El-Zimaity H, Wotherspoon A, deMascarel A, Savio A, Stolte M, Torlakovic E, Younes M, Appelman H, et al: Interobserver variation in the histopathological assessment of MALT/MALT lymphoma. *Mod Pathol*. 17:114A-115A, 2004.
3. Huang EHN, Park J, Appelman HD, et al: Induction of inflammatory bowel disease accelerates adenoma formation in MIN mice. *Gastroenterol*. 126:A-421-2, 2004.
4. El-Zimaity H, Wotherspoon A, Appelman H, et al: Interobserver variation in the histopathologic assessment of MALT/MALT Lymphoma: Towards a consensus. *Gastroenterol*. 126:A-621, 2004

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004

I. CLINICAL ACTIVITIES:

- A. 21 weeks of Surgical Neuropathology Service.
- B. 51 days of Autopsy Service including weekend autopsy calls.
- C. All muscle and nerve biopsies at the UMHS and referred by other hospitals in- and out-of-state throughout the year, including new anti-dystrophy workup (456 muscle biopsies and 104 nerve biopsies). 40% muscle biopsies with EM, 100% nerve biopsies with EM and 18 with teasing. Over 30 cases were tested with antidystrophy antibody (10-15) screen by IPOX.
- D. Diagnostic EM on skin and other tissues for various rare disorders, 14 cases.
- E. Cutting autopsied brains with Pathology House Officers, microscopic evaluation with the residents for the diagnosis.
- F. Consulting on brain, muscle and nerve pathology, intradepartmental cases, VAH and other hospitals in MI and other states. 156 personal consults.

II. TEACHING ACTIVITIES:

- A. Instructed residents, fellows and staff in Neurology, Rheumatology and Pediatrics and students on muscle, nerve and brain biopsies.
- B. Lectures for medical and dental students; M-2 neuropathology labs.
- C. Taught Pathology Residents how to perform and read-out autopsies.
- D. Lectures on muscle, nerve and brain pathology to residents and fellows in Pathology, Neurology, Neurosurgery and Rheumatology.
- E. Conferences on muscle and nerve cases with Neurology Department.
- F. Neuropathology cases review with Pathology Residents.
- G. Weekly and monthly conferences with Neuromuscular staff.
- H. Conferences and lectures for Neurosurgery Residents and staff.
- I. Pediatric Oncology conferences for brain tumor cases.
- J. Tutoring of neurology and pathology residents on Neuropathology – 8 persons.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Collaboration with EMG group (3 papers are being presented this Fall, manuscripts in preparation), neurosurgery (manuscript in preparation), genetics, pediatrics, ophthalmology (Jonathan Trobe, M.D., Christine Nelson, M.D.), rheumatology

(manuscript in preparation), epilepsy and gynecology (Dr. J. Delancey group, pilot study with Daniel Morgan, M.D., completed) on various projects.

- B. MCO Pathology and Neurology – a paper is being presented at the Fall meeting.
- C. National study group (ERSET), part of, for evaluation of temporal lobectomy/hippocampectomy cases.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL:

- A. Member of the Admissions Committee.

INVITED LECTURES:

None

REGIONAL AND NATIONAL:

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

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN PEER REVIEWED JOURNALS:

1. Kocheril SV, Blaivas M, Appelton BE, McCune WJ, Ire RW: Dego's Disease Mimicking Vasculitis. Arthritis Rheum, June 15:51(3):498-500, 2004.
2. Hedera P, Petty EM, Bui M, Blaivas M, Fink JK: The second kindred with distal myopathy linked to chromosome 14q (MPD1): Genetic and clinical analysis. Arch Neurol. 60(9): 1321-5, 2003.
3. *Fewel ME, Blaivas M, Thompson BG: Intradural metastatic pleural mesothelioma presenting with sudden deafness facial palsy, and Brown-Sequard syndrome. Submitted to Neurosurgery.

4. Herschner S, Blaivas M, Gells D: Biopsy of confirmed primary angiitis of the central nervous system with negative MRI and angiography. Resubmitted to Neurology.
5. Lagrange AH, Blaivas M, Gomez-Hassan D, Malow BA: Rasmussen's-like encephalitis presenting as new-onset narcolepsy, cataplexy, and epilepsy in an adult. *Epilepsy Behav.* 4(6):788-92, 2003.

CHAPTER IN BOOKS

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

1. Nolan PC, Blaivas M, Teener JW: Inclusion body myositis with granuloma in muscle biopsy. Presented at the AAEM meeting, Fall 2003.
2. Gruis KL, Teener JW, Blaivas M,. Pediatric macrophagic myofascitis in North America. Abstract to be presented at the 9th International Congress of the World Muscle Society, Goteberg, Swenden, 2004.
3. Gruis KL, Brown DL, Blaivas M. Minicore myopathy with cardioembolic basilar artery thrombosis. Abstract to be presented at the 8th Congress of the European Federation of Neurological Societies (EFNS), Paris, France, 2004.
4. Gruis KL, Teener JW, Blaivas M. Neuropathy associated with non-inflammatory, proliferative vasculopathy. Abstract to be presented at the American Association of Electrodiagnostic Medicine (AAEM), Savannah, Georgia, 2004.
5. Assaly R, Blaivas M et al. IBM subtype in a 25 year old female. Case report. To be presented at the American College of Physicians, Ohio Chapter Scientific Meeting, October, 2004, Columbus, Ohio

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

**ANNUAL DEPARTMENT REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES

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

II. TEACHING ACTIVITIES

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

III. RESEARCH ACTIVITIES

SPONSORED SUPPORT:

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

PROJECTS UNDER STUDY:

- A. Cytokine manipulation of mycobacterial (Th1) and schistosomal (Th2) Ag mediated forms of hypersensitivity granuloma formation.
- B. Regulation and participations of chemokine receptors during Th1 and Th2 immune and inflammatory responses.
- C. Role of chemotactic cytokines in granulomatous inflammation and Th1 and Th2 cell expression.
- D. In vivo regulation of chemotactic cytokine production by leukocytes and stromal cells in the lung.
- E. Dendritic cell recruitment, activation and in vivo migration during innate stages of granuloma formation and Mycobacteria infection.
- F. Role of chemokine receptor 8 (CCR8) in T regulatory function

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

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

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Chensue, S. W. Exposing a killer: pathologists angle for anthrax. Am. J. Pathol. 2003; 163: 1699-702.
- 2. Gyetko M.R, Sud S., Chensue, S. W. Urokinase-deficient mice fail to generate a type 2 immune response following schistosomal antigen challenge. Infect. Immun. 2004; 72:461-7.
- 3. Hashimoto, N, Jin, H., Liu, T, Chensue S.W., Phan S.H. Bone marrow-derived progenitor cells in pulmonary fibrosis. J Clin Invest. 2004, 113:243-52.
- 4. Chiu, B., Freeman, C.M., Stolberg, V.R., Hu, J.S., Komuniecki, E., and Chensue, S. W. The innate pulmonary granuloma: characterization and demonstration of dendritic cell recruitment and function. Am. J. Pathol. 2004, 164:1021-1030.
- 5. Chiu, B., Freeman, C.M., Stolberg, V.R., Hu J.S., Zeibecoglou, K., Lu, B., Gerard, C., Charo, I.F., Lira, S. A. and Chensue, S. W. Impaired lung dendritic cell activation in CCR2 knockout mice. Am. J. Pathol. 2004, In press.

BOOKS AND CHAPTERS IN BOOKS:

- 1. Kunkel S.L., Chensue S.W., Lukacs N., and Hogaboam, C. Cytokine phenotypes serve as a paradigms for experimental immune-mediated lung diseases and remodeling. Am J Respir Cell Mol Biol. 2003 Sep; 29(3 Suppl):S63-6. Review.

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

- 1. Chiu, B-C., Freeman, C.M., Stolberg, V.R., Charo, I.F. and Chensue, S. W. Impaired lung dendritic cell activation in CCR2 knockout mice. Clin. Invest. Med. 27:31C Abs# W9.66.
- 2. Freeman, C.M., Chiu, B-C., Stolberg, V.R., and Chensue, S. W. CCR8 is expressed by an antigen-reactive IL-10 producing CD4+CD25+ T cell population during Th2-mediated granuloma formation in the mouse. Clin. Invest. Med. 27:31C Abs# W

**ARUL M. CHINNNAIYAN, M.D., Ph.D.
ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

- A. Mentor, postdoctoral fellows: Arun Sreekumar, Kajal Sitwala, Manish Bhandari, Jindan Yu, Saravana Dhanasekaran, Rohit Mehra, Eric Albrecht (co-mentored with P.Ward)
- B. Mentor, graduate students: Scott Tomlins (MSTP, Pathology), Qi Cao (Pathology), Jianjun Yu (Bioinformatics), Daniel Rhodes (MSTP, Pathology), Julie Kim (Bioinformatics), Viktoriya Resnick (Bioinformatics), Xiaoyu Jia (Pathology), Ronglai Shen (Biostatistics Masters Student)
- C. Mentor, Undergraduate Students: Shilpa Murthy, CMB Honors Research, Jeff Fielhauer, Biology
- D. Pre-lim Committees:
 - Chair of graduate pre-lim committee for Bioinformatics Graduate Student, Chad Creighton
 - Chair of graduate pre-lim committee for Bioinformatics Graduate Student, Yili Chen.
 - Member of graduate pre-lim committee for Bioinformatics Graduate Student, Viktoriya Resnick.
 - Thesis Committee, Lei Wang, Biochemistry
- E. Instructor, Biochemistry 491
- F. Bioinformatics 511 Luncheon and Seminar
- G. Co-Director, Bioinformatics 511
- H. Cancer Biology Seminar Series, Lecturer, University of Michigan Medical School
- I. Director, Short Course in Cancer Bioinformatics, University of Michigan Medical School

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Molecular Classification of Prostate Cancer", American Cancer Society, RSG-02-179-01-MGO, 07/01/02 – 06/30/06, 15% effort, \$180,000/yr direct costs.
- B. Principal Investigator, "The Role of Polycomb Group Proteins in Prostate Cancer" NIH R01 CA97063 , 07/01/02 – 06/30/07, 20% effort, \$178,000/yr direct costs.

- C. Principal Investigator, “Dysregulation of the Corepressor CtBP in Prostate Cancer”, Department of Defense, PC020322, 1/2/03- 12/31/05, 10% effort, \$125,000/yr direct costs.
- D. Co-Investigator, “Biological Differences between prostate cancer cells that metastasize to the bone versus soft tissue sites”, Department of Defense, DAMD17-02-1-0098 (Pienta), 11/19/01 – 11/18/04, 5% effort, \$141,563/yr direct costs.
- E. Principal Investigator, “A Functional Genomics Approach to Cancer” 07/01/02 – 06/30/06, 0% effort, PEW Charitable Trust, \$55,556/yr direct costs.
- F. Co-Investigator, “Protective Effects of Anti-C5a in Sepsis”, GM61656 (Ward), 12/01/01-11/30/06, 5% effort, \$225,000/yr direct costs.
- G. Co-Investigator, “Functional Genomics Approach to Lethal Metastatic Prostate Cancer”, National Cancer Institute, P50 CA69568 (Pienta), 5/01/03 - 05/31/08, 10% effort, \$144,578/yr direct efforts.
- H. Co-Investigator, “Tissue/Informatics Core of the UM Prostate SPORE, National Cancer Institute, P50 CA69568 (Pienta), 05/01/03- 05/30/08, 2.5% effort, \$253,643/yr direct costs.
- I. Co-Investigator, “Pancreas-Specific Primary Regulatory Targets of Nkx2.2”, NIH, R21 Dk065308 (Mellerick-Dressler), 08/01/03-05/31/05, 2.5% effort.
- J. Principal Investigator, “Discovery of Cancer Biomarkers using High Throughput Multi-Blotting”, GMP Companies, Inc., 12/01/02-11/30/05, 0% effort, \$168, 827/yr direct costs.
- K. Co-Investigator, “Molecular of Dissection of Benign Prostatic Hyperplasia”, Brigham and Women’s Hospital, NIH, U01 AG 22312 (Rubin), 9/30/02-6/30/07, 5% effort, \$120,494/yr direct costs.
- L. Co-Investigator, Brigham and Women’s Hospital (DOD), DAMD17-03-2-0033 (Rubin), 04/01/03-03/31/06, 2.5% effort, \$36,410 direct costs.
- M. Co-Investigator, “Molecular Changes Associated with Prostate Carcinoma (PCa) Bone Metastases”, NIH R01 CA102872-01 (Pienta), 09/24/03-08/31/07, 5% effort, \$173,280 direct costs.
- N. Co-Investigator, “Prostate Cancer Harbinger Genes”, Brigham & Women’s Hospital (NIH Prime) RO1 AG0214104-01 (Rubin), 09/30/02 – 08/31/04, 2.5% effort, \$53,595 direct costs.

PENDING:

- A. Principal Investigator, “Epitomic Biomarkers of Prostate Cancer”, NIH, RFA-CA-04-006, 9/30/04-9/29/09, 10% direct costs, \$452,158/yr direct costs.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Pathology student recruitment activities (lunch, poster session)
- B. Director of the Pathology DNA Microarray Research Lab
- C. Director, Proteomics Initiative

MEDICAL SCHOOL/HOSPITAL:

- A. Member, MSTP Career Advisory Panel
- B. Bioinformatics student interviews
- C. Faculty Candidate Interviews for the Department of Urology and the Cancer Center
- D. MSTP student interviews
- E. Bioinformatics Faculty Search Committee
- F. Co-Director of the U of M Bioinformatics, Proteomics, and Functional Genomics Seminar Series.
- G. Director of Cancer Bioinformatics , Comprehensive Cancer Center

REGIONAL AND NATIONAL:

- A. Ad hoc reviewer for the following Journals: *Nature*, *PNAS*, *Nature Genetics*, *Nature Cancer Reviews*, *Nature Medicine*, *American Journal of Pathology*, *Cancer Cell*, *Journal of Biomedical Informatics*, *Cancer Research*, *Oncogene*, *Neoplasia*, *Cell Death & Differentiation*, *Cytokine*, *Clinical Cancer Research*, *Molecular Diagnosis*, *BMC Cancer*, *Urology*, and the *Journal of Biological Chemistry*.
- B. External grant reviewer for the National Science and Technology Board Biomedical Research Council (Singapore) and the Cancer Society of New Zealand, Inc.
- C. Scientific Review Board, 2003 American Cancer Society, Grants Peer Review
- D. Scientific Review Board, 2003 Department of Defense Prostate Cancer Research Peer Review Program
- E. Scientific Review Board, 2003 Department of Defense Breast Cancer Concept Award Peer Review Program
- F. Research Review Committee, 2003 Mary Kay Ash Charitable Foundation Research Review Committee.
- G. Scientific Review Board, 2004 Genome Canada
- H. Integration Panel, 2004, Department of Defense Prostate Cancer Research Program
- I. External grant reviewer for the National Science and Technology Board Biomedical Research Council (Singapore) and the Cancer Society of New Zealand, Inc.

V. OTHER RELEVANT ACTIVITIES:

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

EDITORIAL BOARDS:

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

PATENTS:

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

INVITED LECTURES/SEMINARS:

- 1. Annual National Cancer Institute SPORE meeting, Invited Speaker and Plenary Session Co-Chair, "The Role of EZH2 in Prostate Cancer", Baltimore, Maryland, Jul 10, 2003.
- 2. AACR Annual Meeting, Invited Speaker, Plenary Session, "The Three B's of Prostate Cancer: Biology, Bioinformatics and Biomarkers", Washington DC, July 12, 2003.
- 3. Genetics, Genomics, and Proteomics Seminar Series, "The Three B's of Prostate Cancer: Biology, Bioinformatics and Biomarkers", Wayne State University, July 21, 2003.
- 4. Invited Speaker, Cancer Biology, Washington University, "The Three B's of Prostate Cancer: Biology, Bioinformatics and Biomarkers", St. Louis, MO, July 29, 2003.
- 5. Moffit Cancer Center, Cancer Center Grand Rounds, "The Three B's of Prostate Cancer: Biology, Bioinformatics and Biomarkers", Tampa, FL, August 8, 2003.
- 6. Shleicher and Schuell, Invited Speaker, "Use of Protein Microarrays to Study Cancer", August 15, 2003.
- 7. 12th Annual American Cancer Society Research Conference, Invited Speaker, "The Three B's of Cancer: Biology, Bioinformatics, and Biomarkers", September 19, 2003.
- 8. SUO/NCI Urologic Oncology Meeting, Invited Speaker, "Gene Expression Analysis in Prostate Cancer", Bethesda, MD December 6, 2003.
- 9. InterProstate SPORE Meeting, Invited Speaker, Immunology Breakout Session, Chicago, Illinois, January 27, 2004.
- 10. UCLA's Genitourinary Oncology Program, Invited Speaker, "Genomic and Proteomic Approaches to Study Prostate Cancer", Los Angeles, CA, February 10, 2004.
- 11. Laura Evans Memorial Breast Cancer Symposium, Invited Speaker, Title TBA, Sun Valley Lodge and Inn in Sun Valley, Idaho February 27, 2004.
- 12. Pew Scholars Meeting, Chalk-Talk on Disease, San Juan, Puerto Rico, March 6, 2004.
- 13. AACR Annual Meeting, Invited Speaker, Educational Session, "Tumor Markers", Washington D.C., March 27, 2004.
- 14. American Society of Investigative Pathologists Annual Meeting, Plenary Session, Invited Speaker, "Bioinformatics approaches to cancer pathology", April 17, 2004.
- 15. Eppley Cancer Center, Invited Speaker, "Genomic and Proteomic Approaches to Study Prostate Cancer", Omaha, Nebraska, April 29, 2004.
- 16. Society of Basic Urological Research Annual Meeting, Invited Speaker, "Functional Genomics Approaches to Prostate Cancer", San Francisco, CA, May 8, 2004.
- 17. Dana Farber Cancer Institute, Invited Speaker, "Integrative Approaches to Cancer: Biology, Biomarkers and Bioinformatics", Boston, MA, May 26, 2004.
- 18. American Society of Clinical Oncology Annual Meeting, Scientific session discussant in the Tumor Biology and Human Genetics Oral Presentation, New Orleans, Louisiana, June 5-8, 2004.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Rios-Doria J, Day KC, Kuefer R, Rashid MG, **Chinnaiyan AM**, Rubin MA, Day ML. (2003). The role of calpain in the proteolytic cleavage of E-cadherin in prostate and mammary epithelial cells. *Journal of Biological Chemistry*, 278(2):1372-9.
2. Xin, W., Rhodes, D.R., Ingold, C., **Chinnaiyan, A.M.**, Rubin, M.A. (2003) Dysregulation of the Annexin Protein Family is Associated with Prostate Cancer Progression. *American Journal of Pathology*, 162(1):255-61.
3. Kuefer, R., Hofer, M.D., Gschwend, J.E., Pienta, K.J., Sanda, M.G., **Chinnaiyan, A.M.**, Rubin, M.A., Day, M.L. (2003) The role of an 80 kDa fragment of E-cadherin in the metastatic progression of prostate cancer. *Clin Cancer Res.*, 9(17):6447-52.
4. Kunju, L.P., Rubin, M.A., **Chinnaiyan, A.M.**, Shah, R.B.(2003) Diagnostic usefulness of monoclonal antibody P504S in the workup of atypical prostatic glandular proliferations. *Am J Clin Pathol*, 120(5):737-45.
5. Peri, S., Deshpande, K.S., **Chinnaiyan, A.M.**, Hamosh, A., Chakravarti, A., Pandey, A. (2003) Development of human protein reference database as an initial platform for approaching systems biology in humans. *Genome Res*, 13(10):2363-71.
6. Kumar-Sinha, C., **Chinnaiyan, A.M.** (2003) Molecular markers to identify patients at risk for recurrence after primary treatment for prostate cancer. *Urology*, 62(1): 19-35.
7. Ghosh, D., Barrette, T.R., Rhodes, D., **Chinnaiyan, A.M.** (2003) Statistical issues and methods for meta-analysis of microarrays in prostate cancer. *Functional Integrative Genomics*, 3(4):180-8. Epub 2003 Jul 22.
8. Albrecht, E.A., **Chinnaiyan, A.M.**, Varambally, S., Kumar-Sinha, C., Barrette, T.R., Sarma, V.J., Ward, P.A. (2004) C5a-induced Gene Expression in Human Umbilical Vein Endothelial Cells. *American Journal of Pathology*, 164(3): 849-59.
9. Knight, P.R., Sreekumar, A., Siddiqui, J., Laxman, B., Copeland, S., **Chinnaiyan, A.M.**, Remick, D. (2004) Development of a sensitive microarray immunoassay and comparison with standard enzyme-linked immunoassay for cytokine analysis. *Shock*, 21(1):26-30.
10. Vivienne Watson J.E., Doggett N.A., Albertson D.G., Andaya A., **Chinnaiyan A.**, Van Dekken H., Ginzinger D., Haqq C., James K., Kamkar S., Kowbel D., Pinkel D., Schmitt L., Simko J.P., Volik S., Weinberg V.K., Paris P.L., Collins C. (2004) Integration of high-resolution array comparative genomic hybridization analysis of chromosome 16q with expression array data refines common regions of loss at 16q23-qter and identifies underlying candidate tumor suppressor genes in prostate cancer. *Oncogene*, Apr 22;23(19):3487-94.
11. Wu M., Wu Z.F., Kumar-Sinha C., **Chinnaiyan A.M.**, Merajver S.D. (2004) RhoC Induces Differential Expression of Genes Involved in Invasion and Metastasis in MCF10A Breast Cells. *Breast Cancer Res Treat.* Mar;84(1):3-12.
12. Rubin M.A., Zerkowski M.P., Camp R.L., Kuefer R., Hofer M.D., **Chinnaiyan A.M.**, Rimm D.L. (2004) Quantitative determination of expression of the prostate cancer protein alpha-methylacyl-CoA racemase using automated quantitative analysis (AQUA): a novel paradigm for automated and continuous biomarker measurements. *Am J Pathol.* 164(3):831-40.

13. Kumar-Sinha C., Shah R.B., Laxman B., Tomlins S.A., Harwood J., Schmitz W., Conzelmann E., Sanda M.G., Wei J.T., Rubin M.A., **Chinnaiyan A.M.** (2004) Elevated alpha-methylacyl-CoA racemase enzymatic activity in prostate cancer. *Am J Pathol.* 164(3):787-93.
14. Hofer M.D., Kuefer R., Varambally S., Li H., Ma J., Shapiro G.I., Gschwend J.E., Hautmann R.E., Sanda M.G., Giehl K., Menke A., **Chinnaiyan A.M.**, Rubin M.A. (2004) The role of metastasis-associated protein 1 in prostate cancer progression. *Cancer Res.* 1;64(3):825-9.
15. Rubin, M.A., Varambally, S., Beroukim, R., Tomlins, S.A., Rhodes, D.R., Paris, P.L., Hofer, M.D., Storz-Schweizer, M., Kuefer, R., Fletcher, J.A., Byrne, J.A., Pienta, K.J. Collins, C., Sellers, W.R., **Chinnaiyan, A.M.** (2004) Overexpression, Amplification and Androgen-regulation of TPD52 in Prostate Cancer. *Cancer Res.* 1;64(11):3814-22.
16. Paris, P.L., Andaya, A., Fridlyand, J., Jain, A.N., Weinberg, V., Kowbel, D., Brebner, J.H., Simko, J., Watson, J.E., Volik, S., Albertson, D.G., Pinkel, D., Alers, J.C., Van Der Kwast, T.H., Vissers, K.J., Schroder, F.H., Wildhagen, M.F., Febbo, P.G., **Chinnaiyan, A.M.**, Pienta, K.J., Carroll, P.R., Rubin, M.A., Collins, C., Van Dekken, H. (2004) Whole genome scanning identifies genotypes associated with recurrence and metastasis in prostate tumors. *Hum Mol Genet.* Jul 1;13(13):1303-13.
17. Nyati, M.K., Maheshwari, D., Hanasoge, S., Sreekumar, A., Rynkiewicz, S.D., **Chinnaiyan, A.M.**, Leopold, W.R., Ethier, S.P., Lawrence, T.S. (2004) Radiosensitization by pan ErbB inhibitor CI-1033 in vitro and in vivo. *Clin Cancer Res*, 10(2): 691-700.
18. Sreekumar, A., Laxman, B., Rhodes, D.R., Bhagavathula, S., Harwood, J., Giacherio, D., Ghosh, D., Sanda, M.G., Rubin, M.A., **Chinnaiyan, A.M.** (2004) Humoral Immune Response to alpha-Methyl-CoA Racemase and Prostate Cancer *Journal of the National Cancer Institute*, 96(11):834-43.
19. Rhodes, D.R., Yu, J., Shanker, K., Deshpande, N., Varambally, R., Ghosh, D., Barrette, T., Pandey, A., **Chinnaiyan, A.M.** (2004) Large scale meta-analysis of cancer microarray data identifies commone transcriptional profiles of neoplastic transformation and progression. *Proceedings of the National Academy of Sciences*, 101(25):9309-14.
20. Ghosh, D.R., **Chinnaiyan, A.M.** (2004) Classification and selection of biomarkers in genomic data using LASSO. The University of Michigan Department of Biostatistics Working Paper Series. <http://www.bepress.com/umichbiostat/paper42>
21. Rhodes DR, **Chinnaiyan A.M.** (2004) Bioinformatics strategies for translating genome-wide expression analyses into clinically useful cancer markers. *Ann N Y Acad Sci*, 1020:32-40.
22. Rhodes D.R., Yu J., Shanker K., Deshpande N., Varambally R., Ghosh D., Barrette T., Pandey A., **Chinnaiyan A.M.** (2004) ONCOMINE: a cancer microarray database and integrated data-mining platform. *Neoplasia*, Jan-Feb;6(1):1-6.
23. Ghosh, D, **Chinnaiyan A.M.** (2004) Covariate adjustment in the analysis of microarray data from clinical studies. *Funct Integr Genomics*, [Epub ahead of print].

BOOKS/CHAPTERS IN BOOKS:

1. None.

ABSTRACTS:

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

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

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. Hongfeng Yu, Ph.D.
2. Ying Liu, Ph.D. (4 months)
3. Malti Kshirsagar, M.D. (6 months)
- B. Graduate students:
1. Neali Hendrix (Dept. of Pathology), faculty mentor, doctoral candidate, PIBS program
2. Albert Levin (Dept. of Epidemiology, School of Public Health), thesis committee member, Ph.D. candidate
Course Faculty, Pathology 581 – three lecture hours
Course Faculty, Pathology 580/630 – two lecture hours
Course Faculty, IMS-I (new curriculum, Dental School) – two lecture hours
- C. Undergraduate students:
Lisa So
- D. House Officers:
Room G sign-out of gynecologic pathology cases; two staff consultation conferences
- E. Interdepartmental:
Multidisciplinary Gynecologic Oncology tumor board – one hour twice per month
- F. National:
Course Faculty and Co-organizer: Molecular Biology in Clinical Oncology Workshop, American Association for Cancer Research, The Given Institute, Aspen, Colorado.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, Project 2 ("Molecular Profiling of Ovarian Cancer", 12.5% effort). NIH: U19 CA84953 (Hanash). "Toward a Molecular Classification of Tumors," September 30, 1999 – March 31, 2004.
- B. Principal Investigator, "Oncogene Activation in Ovarian Cancer Pathogenesis", Department of Defense, OCRP OC000105 (10% effort), August 15, 2001 - August 14, 2004.
- C. Principal Investigator, "Molecular Pathogenesis of Ovarian Endometrioid Adenocarcinomas", NIH RO1 CA94172 (30% effort), February 1, 2002 – January 31, 2007.

- D. Co-Investigator (6% effort), "CDX2 Tumor Suppressor Pathway Defects in Colon Cancer", NIH R01 CA82223 (Fearon), August 15, 1999 – May 31, 2004.
- E. Co-Investigator (10% effort), "The Role of β -Catenin/Tcf Pathway Defects in Cancer." NIH R01 CA85463 (Fearon), June 1 2000 – May 31, 2005.
- F. Co-Investigator (4% effort), "Liquid Proteomics for Marker Screening of Ovarian Cancer", NIH RO1 CA100104 (Lubman), April 15 2003 – April 14, 2008
- G. Principal Investigator (20% effort), "Molecular Markers of Invasion in Cervical Cancer Progression" NIH 1P50CA98252-01 (SPORE in Cervical Cancer, Program PI: T.C. Wu), September 30 2003 – August 31 2008.
- H. Co-Investigator (5% effort), "Markers of Progression to Cervical Cancer in Rural India" NIH 1P50CA98252-01 (SPORE in Cervical Cancer, Program PI: T.C. Wu), September 30 2003 – August 31 2008.
- I. Co-Investigator and mentor for New Investigator (2.5% effort), "Development and Characterization of a Murine Model of Ovarian Endometrioid Adenocarcinoma Induced by Tissue Specific Expression of Oncogenic β -Catenin", Department of Defense, Ovarian Cancer Research Program: DAMD17-OC030117 (R. Wu), February 1 2004 – January 31 2007.

PENDING:

- A. Co-Investigator (2.5% effort), "Molecular Analysis of Breast Cancer Invasion and Metastasis", Department of Defense Breast Cancer Research Program BC044605 (Fearon), 04/01/05 – 03/31/08
- B. Co-Investigator (10% effort), "CDX2 Tumor Suppressor Pathway Defects in Colon Cancer", competing renewal of NIH RO1 CA82223-06 (Fearon), 07/01/04 – 06/30/09
- C. Co-Investigator (5% effort), "Molecular Classifications of Adenocarcinomas", response to SPECS RFA CA-04-015 (Strategic Partnering to Evaluate Cancer Signatures), NIH Number to be assigned (Hanash), 04/01/05 – 03/31/10

PROJECTS UNDER STUDY:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

INSTITUTIONAL:

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

REGIONAL AND NATIONAL:

- A. Special Emphasis Panel, ZRG1 ONC M(04), National Institutes of Health, National Cancer Institute, teleconference review of RO1 application (panel chair), 2004
- B. Integration Panel, Department of Defense, Ovarian Cancer Research Program
- C. Member, Publications Committee, American Association for Cancer Research, 2002-present
- D. Co-Organizer and course faculty member, Molecular Biology in Clinical Oncology Workshop, American Association for Cancer Research, 2000-present
- E. Member, National Comprehensive Cancer Center Panel for establishment of endometrial and cervical cancer treatment guidelines, 1997-present
- F. Member, 2004 Dorothy P. Landon AACR Prize for Translational Cancer Research Selection Committee
- G. Secretary, International Society of Gynecological Pathologists, elected to two year term (2003-2004) renewable for two additional terms, not to exceed six years
- H. Member, Organizing Committee, 10th Biennial International Forum on Ovarian Cancer, Helene Harris Memorial Trust

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 several additional journals

INVITED LECTURES/SEMINARS 2003-2004:

- A. Ovarian Cancer: Insights from Gene Expression Profiling. National Cancer Institute, Bethesda, Maryland, January, 2003.
- B. Molecular Pathology in Oncology: Overview and Selected Applications. Molecular Biology in Clinical Oncology Workshop, American Association for Cancer Research, The Given Institute, Aspen, Colorado, July 2003.
- C. Borderline Ovarian Tumors – Molecular Biologist's Perspective. Borderline Ovarian Tumor Consensus Workshop, National Cancer Institute, Bethesda, Maryland, August 2003.
- D. Ovarian Cancer: Clues to Pathogenesis from Gene Expression Profiling. Pathology Grand Rounds, University of Iowa, Iowa City, Iowa, September 2003.

- E. Role of Wnt Signaling Pathway Defects in Ovarian Cancer Pathogenesis. Invited Seminar, Department of Molecular Pharmacology/Experimental Therapeutics and Tumor Biology Program, Mayo Clinic, Rochester, Minnesota, April 2004.
- F. Molecular Pathology in Oncology: Overview and Selected Applications. Molecular Biology in Clinical Oncology Workshop, American Association for Cancer Research, The Given Institute, Aspen, Colorado, July 2004.

VI. PUBLICATIONS (2003-2004):

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Wu, R., Lin, L., Beer, D.G., Ellenson, L.H., Lamb, B.J., Rouillard, J.-M., Kuick, R., Hanash, S., Schwartz, D.R., Fearon E.R., and Cho, K.R. Amplification and Overexpression of the L-MYC Proto-Oncogene in Ovarian Carcinomas. American Journal of Pathology, 162:1603-1610, 2003.
- 2. Sherman-Baust, C.A., Weeraratna, A.T., Rangel, L.B.A., Pizer, E.S., Cho, K.R., Schwartz, D.R., Shock, T., and Morin, P. J. Remodeling of the extracellular matrix through overexpression of collagen VI contributes to cisplatin resistance in ovarian cancer cells. Cancer Cell, 3:377-386, 2003.
- 3. Schwartz, D.R., Wu, R., Kardia, S.L.R., Levin, A.M., Huang, C.-C., Shedden, K., Kuick, R., Misek, D., Hanash, S., Taylor, J.M.G., Reed, H., Hendrix, N., Zhai, Y., Fearon, E.R., and Cho, K.R. Novel candidate targets of β -catenin/TCF signaling identified by gene expression profiling of ovarian endometrioid adenocarcinomas. Cancer Research, 63:2913-22, 2003.
- 4. Rangel, L.B., Agarwal, R., D'Souza, T., Pizer, E.S., Alo, P.L., Lancaster, W.D., Gregoire, L., Schwartz, D.R., Cho, K.R., and Morin, P.J. Tight junction proteins claudin-3 and claudin-4 are frequently overexpressed in ovarian cancer but not in ovarian cystadenomas. Clinical Cancer Research 9:2567-75, 2003.
- 5. Shedden, K.A., Taylor, J.M.G., Giordano, T.J., Kuick, R., Misek D.E., Rennert, G., Schwartz, D.R., Gruber, S., Logsdon, C., Simeone, D., Greenon, J.K., Cho, K.R., Beer, D.G., Fearon, E.R., and Hanash, S. Accurate molecular classification of human cancers based on gene expression using a simple classifier with a pathologic tree-based framework. American Journal of Pathology 163:1985-95, 2003.
- 6. Rangel, L.B.A., Sherman-Baust, C.A., Wernyj, R.P., Schwartz, D.R., Cho, K.R., and Morin, P.J. Characterization of novel human ovarian cancer-specific transcripts (HOST) identified by serial analysis of gene expression. Oncogene 22:7225-32, 2003.
- 7. Wang, H., Kachman, M.T., Schwartz, D.R., Cho, K.R., and Lubman, D.M. Comprehensive Proteome Analysis of Ovarian Cancers Using Liquid Phase Separation, Mass Mapping and Tandem Mass Spectrometry: A Strategy for Identification of Candidate Cancer Biomarkers. Proteomics 4:2476-95, 2004.
- 8. Sherman ME, Berman J, Birrer MJ, Cho KR, Ellenson LH, Gorstein F, Seidman JD, Current challenges and opportunities for research on borderline ovarian tumors. Human Pathology, 35:961-70, 2004.

BOOKS/CHAPTERS IN BOOKS:

None

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

**ANNUAL DEPARTMENT REPORT
1 JULY 2002-30 JUNE 2003**

I. CLINICAL ACTIVITIES

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

II. TEACHING ACTIVITIES

- A. Resident Education
1. Responsible/Share didactic teaching activities for the following:
 - a. Blood Component Therapy
 - b. Transfusion Reaction Evaluation
 - c. Evaluation and Management of Platelet Refractoriness
 - d. Fundamentals of Clinical Apheresis (with nursing staff)
 - e. Evaluation and Management of Therapeutic Apheresis Requests
 - f. Administrative Issues on-call
 2. Clinical Teaching
Supervision Resident/ Visiting Fellow Activities (12 mo/yr)
 - a. Morning Report
 - b. Transfusion reaction sign-out
 - c. Clinical apheresis requests/patient management
 - d. Special product request evaluation and clinical follow-up
 - e. Case-based informal teaching
 3. Other Clinical Teaching
 - a. Hematology Fellows
 - b. Heme/Onc Nursing Staff (in-service lectures)
 - c. Hematology case conference
 - i. TTP in adolescent patient, role of plasma exchange
 - ii. Management of severe HLA alloimmunization in aplastic anemia
- B. Medical Students
1. Transfusion Medicine. Senior Therapeutics Course, Dept. of Pharmacology
 2. Evaluation and management of platelet refractoriness. Hem/Onc residents, medical students and nursing staff.

III. RESEARCH ACTIVITIES

- A. The Regulation and Biology of Globo-Series Glycosphingolipids
 - 1. Chemical analysis of complex P and Luke related globo-gangliosides
 - 2. Relationship of LKE phenotype on non-globo-glycoconjugates of human RBCs
 - 3. Effect of inflammatory cytokines and retinoic acid on globo- and lacto-family in renal epithelial cells.
 - 4. Molecular basis and regulation of Pk and Luke antigen expression in LKE.
 - 5. Globo/lacto antigens in infectious disease
- B. Clinical Research
 - 1. Factors effecting stem cell collection and engraftment
 - 2. Platelet immunology, role in transfusion therapy

SPONSORED RESEARCH:

Current

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

Pending

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

ADMINISTRATIVE ACTIVITIES

Departmental

- A. Associate Director, Transfusion Medicine

Hospital

- A. Transfusion Subcommittee

V. OTHER RELEVANT ACTIVITIES

INVITED LECTURES AND SEMINARS:

- 1. Invited Lecturer, Internal Medicine Grand Rounds University of Michigan: Basics of Blood Transfusion Therapy. August 2002.
- 2. Invited Lecturer, Internal Medicine Grand Rounds, University of Michigan: Adverse Effects of Transfusion. September 2002.
- 3. Invited Speaker, Canadian Blood Services. Globo- Blood Group System. October 2002.
- 4. Invited Speaker, Canadian Blood Services and University of Toronto, Toronto, CA. Luke, Lewis and Luck. October 2002.

5. Invited Speaker, Carbohydrate Blood Group Workshop, American Association of Blood Banks 56th Annual Meeting, Orlando, FL. A “Globo”-al Perspective on ISBT Collection 209. October 2002.
6. Presenter, American Association of Blood Banks 56th Annual Meeting, Orlando, FL. Identification of two new single nucleotide polymorphisms in FUT3 (Lewis), associated with the Lewis null phenotype in African Americans. October 2002.
7. Presenter, American Association of Blood Banks 56th Annual Meeting, Orlando, FL. A missense mutation in β 3GalT5, the glycosyltransferase responsible for galactosylgloboside and Lewis c synthesis, may be associated with the LKE-Weak phenotype in African Americans. October 2002.
8. Presenter, American Association of Blood Banks 56th Annual Meeting, Orlando, FL. The receptor for shiga toxin is commonly expressed by immature myeloid cells. October 2002.
9. Presenter, American Association of Blood Banks 56th Annual Meeting, Orlando, FL. Increased expression of a *para*-Forssman like glycosphingolipid on LKE-Weak Red Cells. October 2002.
10. Lecturer, Dept. of Surgery Resident Conference, University of Michigan. Basics of hemotherapy. April 2003.
11. Invited Speaker, Immunohematology Reference Laboratory Conference, American Association of Blood Banks, Las Vegas, NV. ABO antigens on human platelets. May 2003.
12. Invited Speaker, Annual Immunohematology Reference Laboratory Conference, American Association of Blood Banks, Las Vegas, NV. Blood and Bugs: the role of blood group antigens and infectious diseases. May 2003.
13. Lecturer, Clinical Pathology Grand Rounds, University of Michigan. Blood and bugs: an unhealthy synergism. May 2003.
14. Invited Speaker, Marion F. Beard Scientific Seminar, American Red Cross, Louisville, KY. Blood and Bugs: the role of blood group antigens and infectious diseases. June 2003.
15. Speaker, Current Topics in Blood Banking, University of Michigan. Working out the bugs; issues in platelet culturing and extended platelet storage. June 2003.
16. Presenter, Invitational Conference on Investigative Immunohematology. Increased autoantibody binding during platelet storage. June 2003.
17. Invited Speaker, Transfusion Medicine Seminar, Delta Blood Banks, Stockton, CA. ABO antigens and human blood platelets. July 2003.
18. Invited Speaker, Transfusion Medicine Seminar, Delta Blood Banks, Stockton, CA. Bugs and Blood: The role of blood group antigens in infectious diseases.

Reviewer

Conn's Current Therapy

Journal of Lipid Research

Journal, Leukemia

Journal, Transfusion

Journal, Thrombosis and Hemostasis

Journal, Thrombosis Research

Scientific Abstracts, American Association Blood Bank 56th Annual Meeting

Professional Memberships

American Association of Blood Banks

Michigan Association of Blood Banks

Education Committee

Specialist in Blood Banking Subcommittee/Course Lecturer

Invitational Conference of Investigative Immunohematology

American Society of Clinical Apheresis

Alpha Omega Alpha

VI. PUBLICATIONS

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

Books/Chapters in Books:

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

Peer-Reviewed Abstracts

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

9. Cooling L, Gu Y, Copeland T. Identification of two new single nucleotide polymorphisms in FUT3 (Lewis), associated with the Lewis null phenotype in African Americans. *Transfusion* 2002;42:S36.
10. Cooling L, Gu Y, Judd WJ, Copeland T. A missense mutation in β 3GalT5, the glycosyltransferase responsible for galactosylgloboside and Lewis c synthesis, may be associated with the LKE-weak phenotype in African Americans. *Transfusion* 2002;42:S32.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

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).

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 Faculty Meeting.
- 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. Executive Committee, Admissions Committee.

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.

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

None.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

A. Cytopathology (16 weeks)

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

B. Surgical Pathology (10 weeks)

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

C. Breast Pathology (10 weeks)

1. Review and Signout of Transfer Breast Cases.
2. Breast Tumor Board

D. On call for intraoperative consultation (5 weeks)

II. TEACHING ACTIVITIES:

A. Fellows, residents and medical school students:

1. Cytopathology:

- a. Introduction to the basic concepts of cytopathology through interaction at the microscope.
- b. Instruction on FNA performance and principles of cytopathology preparations.
- c. Supervision and instruction on rapid assessment of cytology preparations.
- d. Discussion and review of pertinent cytology literature with emphasis on diagnostic applications.

2. Surgical Pathology:

- a. Instruction in surgical pathology diagnostic rooms
- b. Instruction in GU diagnostic room
- c. Instruction in intraoperative consultation

3. Breast Pathology:

- a. Instruction in breast signout and breast tumor board.

4. Monthly cytopathology residents' conference

Weekly cytopathology fellows' conference

- B. Cytotechnologist:
Cytopathology slide conferences.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Cytopathology division quality control and assurance

REGIONAL AND NATIONAL:

- A. Elected member of Quality Control Committee, American Society of Cytopathology
- B. Elected member of Resident In Service Examination Committee, American Society of Clinical Pathology

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

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

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

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

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

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

V. OTHER RELEVANT ACTIVITIES:

- A. Program Committee, Michigan Association of Blood Banks.
- B. Medical Advisory Committee, American Red Cross Southeastern Michigan Region.
- C. Editorial Board, Transfusion.
- D. Consensus Panel Member: Towards an Understanding of TRALI, Toronto, Canada. April 1-2, 2004

VI. PUBLICATIONS:

ARTICLES ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Pealer LN, Marfin AA, Petersen LR, Lanciotti RS, Page PL, Stramer SL, Stobierski MG, Signs K, Newman B, Goodman JL, Chamberland ME, and the West Nile Virus Transfusion Transmission Investigation Team. Transmission of West Nile Virus through blood transfusion—United States, 2002. *N Engl J Med* 2003; 349:1236-1245
2. Reddy P, Davenport R, Ratanatharathorn V, Reynolds C, Silver S, Ayash L, Ferrara JLM, Uberti JP. West Nile virus encephalitis causing fatal CNS toxicity after hematopoietic stem cell transplantation. *Bone Marrow Transplantation*. 2004; 33:109-112.
3. Xin W, Davenport RD, Chang AE, Michael CW. Exaggerated Pigmented Granulomatous Reaction to the Artificial Joint Implant Mimics Metastatic Melanoma. *Diag Cytopathol* 2004; 30:198-200.
4. Davenport RD, Judd WJ, Dake LR. Persistence of Cefotetan on Red Blood Cells. *Transfusion*. 2004; 44:849-852.
5. Davenport RD. Erythropoietic protoporphyria. *Transfusion*. (in press)

ARTICLES SUBMITTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Zhou L, Giacherio D, Cooling L, Davenport RD: Use of B-natriuretic Peptide (BNP) as a Diagnostic Marker in the Differential Diagnosis of Transfusion-Associated Circulatory Overload (TACO). Submitted to *Transfusion*.

BOOKS:

1. Davenport R: Guidelines for the Laboratory Evaluation of Transfusion Reactions. American Association of Blood Banks, Bethesda, MD, 2003.

CHAPTERS IN BOOKS:

1. Davenport RD: Management of transfusion reactions. In: Mintz PD (ed): Practice Guidelines for Transfusion Therapy 2nd ed. AABB Press, Bethesda, MD, in press.

ABSTRACTS AND PRELIMINARY COMMUNICATIONS:

1. Davenport RD, Judd WJ, Dake LR. Persistence of cefotetan on red blood cells. *Transfusion* 2003; 43(9S):1A.
2. Davenport RD, Cooling L, Newman B. Acute pain transfusion reaction associated with transfusion of HLA class II antibodies. *Transfusion* 2003; 43(9S):111A.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

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

MEDICAL SCHOOL/HOSPITALS:

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

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

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

PROJECTS UNDER STUDY:

- A. The identification of co-factors required for Pax protein mediated transcription activation.
- B. The development of novel methods for identifying genes regulated by Pax proteins.
- C. The role of Pax-2 in the initiation and progression of polycystic kidney disease.

- D. The GDNF/RET signaling pathway in the developing kidney.
- E. The role of novel TGF-beta inhibitors in renal development and disease

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

REGIONAL AND NATIONAL:

NIH Study Section, General Medicine B/UDKD, Permanent Member
NCI Program Project, Reviewer, Columbia Univ. Site Visit
NIDDK Special Emphasis Panel, ZDK1 GRB-7
American Journal of Physiology, Editorial Reviews Board
Developmental Dynamics, Editorial Board

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

V. OTHER RELEVANT ACTIVITIES:

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

INVITED LECTURES/SEMINARS:

1. American Society of Nephrology, Annual Meeting, San Diego
2. Dept. of Genetics, University of Nebraska School of Medicine, Omaha
3. 3rd Course on Genetics and Renal Disease, Genoa, Italy
4. Dept. of Pathology, Boston University School of Medicine
5. NIDDK Workshop on Renal Development
6. St. Jude's Children's Research Hospital, Memphis, TN
7. Keystone Meeting on Cell Signaling in Development, Santa Fe

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Cho, E.A., Prindle, M.J. and Dressler, G.R. (2003) The BRCT domain protein PTIP is required for progression through mitosis. *Mol. Cell. Biol.* 23, 1666-1673
2. Brophy, P.D., Lang, K.M. and Dressler, G.R. (2003) The Secreted Frizzled Related Protein SFRP2 Gene is Activated by the Pax2 Transcription Factor. *J. Biol. Chem.* 278, 52401-52405.
3. Cai, Y., Brophy, P., Levitan, I. and Stefano, S. and Dressler, G.R. (2003) Groucho suppresses Pax2 transactivation by inhibition of JNK mediated phosphorylation. *EMBO J.*, 22, 5522-5529.
4. Patel, S. and Dressler, G.R. (2004) Expression of Pax2 in the intermediate mesoderm is regulated by YY1. *Dev. Biol.*, 267, 505-516.

ARTICLES SUBMITTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Lin, J., Cho, E.A., Chen, X., Levitan, I., Patel, S.P., Ullenbruch, M., Phan, S.H., Park, J.P. and Dressler, G.R. (2004) Kielin/Chordin-Like Protein 1, a Novel Enhancer of BMP signaling Mediates Renal Fibrotic Disease.
2. Kim, D. and Dressler, G.R. (2004) Nephrogenic factors promote differentiation of mouse embryonic stem cells into renal epithelia.

BOOK CHAPTERS:

1. Cho, E.A. and Dressler, G.R. (2003) The Formation and Development of Nephrons. In: *The kidney: Normal Development to Congenital Abnormalities* (P. D. Vize, A. S. Woolf, J. B. L. Bard, eds) Academic Press, pp195-210.
2. Dressler, G. R. (2004) Cell Lineages and Stem Cells in the Embryonic Kidney. in *Handbook of Embryonic Stem Cells* (R. Lanza, ed.) Elsevier Science, in press.

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

**ANNUAL DEPARTMENTAL REPORT
JULY 1 2003 – JUNE 30 2004**

I. CLINICAL ACTIVITIES:

None

II. TEACHING ACTIVITIES:

A. Research Mentor:

1. John Wilkinson, Ph.D., Postdoctoral Fellow, 2002 - present.
2. Ezra Burstein, M.D., Lecturer, Department of Internal Medicine 2001 - present.
3. Casey Wright, Ph.D., Postdoctoral Fellow, 2003 - present.
4. Arjmand Mufti, M.D., Fellow, Department of Internal Medicine 2003 - present.
5. Hellan Kang, M.D., Fellow, Department of Internal Medicine 2004 - present.
6. Julie Rumble, Graduate Student, Immunology Program, 2004 - present
7. Rebecca Csomos, Graduate Student, Pathology, 2004 - present.

B. Thesis committee/examiner:

1. Molly Thomas, Pathology Graduate Program
2. Katie Johnson, Immunology Graduate Program
3. Brian Rudd, Pathology

C. Teaching:

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

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

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

Wijmenga and Leo Klomp, University Medical Center, Utrecht, and Dr. George Brewer, University of Michigan..

SPONSORED SUPPORT:

2002 - present	Startup funds from University of Michigan. Funding provided by Department of Pathology, UM Cancer Center and Biomedical Scholars Program (PI).
2003 - 2008	"Prevention of Mammary Cancer in Her-2neu Transgenic Mice," (5%). R01 (P.I. Merajver).
2004 - 2007	"Prostate cancer aggressiveness genes in hereditary prostate cancer," (15%). USARMC Prostate Cancer IDEA Award (Co-PI together with K. Cooney)
2004 - 2007	"XIAP as a molecular target for therapeutic intervention in prostate cancer." (15%). USARMC Prostate Cancer IDEA Award (PI).
2004-2005	"Role of XIAP and AIF in prostate cancer" (0%). NIH/NCI P50 pilot award (PI)
2004 - 2009	"SCF in eosinophilic airway inflammation, "R01 (15%) (NIAID). (PI. Lukacs).

Fellowship awards serving as mentor

2002 - 2004	T32 CA09676-10, NCI Postdoctoral Training Grant to John Wilkinson, Ph.D. "The role of XIAP in the regulation of apoptosis"
2004 - 2006	CDMRP Department of Defense Prostate Cancer Research Program, Postdoctoral Training Award to John Wilkinson, Ph.D. "Role of the XIAP/AIF axis in the development and progression of prostate cancer."
2003 - 2006	American Gastroenterological Association Research Scholar Award to Ezra Burstein, M.D. "Characterization of a novel interacting partner of XIAP."

PENDING:

2004 - 2009	"Control of Apoptosis and Signaling by XIAP," R01 GM067827-01 (NIGMS). (Principal Investigator) (30%).
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IV. ADMINISTRATIVE ACTIVITIES:

1. PIBS International Admissions Committee.
2. Immunology graduate program prelim committee
3. Pathology graduate program prelim committee
3. Scientific Advisory Board, Aegera Therapeutics, 2002
4. Permanent Reviewer, NIH Cellular and Molecular Immunology Study Section
5. Permanent Reviewer, American Cancer Society CCG Study Section, 2004

V. **OTHER RELEVANT ACTIVITIES:**

EDITORIAL AND REVIEWING ACTIVITIES:

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

HONORS AND AWARDS:

Biomedical Scholar Award, University of Michigan, 2002.

INVITED LECTURES/SEMINARS:

- 1. Burnham Institute, La Jolla, CA (2003)
- 2. FASEB-American Society for Investigative Pathology Annual Meeting, San Diego, CA (2003)
- 3. Kansas State University (2003)
- 4. University of Utrecht Medical Center, The Netherlands (2003)
- 5. University of Texas at Austin (2004)
- 6. Gordon Research Conference on Toxicology (2004).

VI. **PUBLICATIONS:**

- 1. Hunter, A.M., Kottachchi, D., Lewis, J., **Duckett, C.S.**, Korneluk, R.G., Liston, P. A novel ubiquitin fusion system bypasses the mitochondria and generates biologically active Smac/DIABLO. *J. Biol. Chem.* **278**:7494-7499 (2003)
- 2. Shin, H, Okada, K, Wilkinson, J.C., Solomon, K.M., **Duckett, C.S.**, Reed, J.C. and Salvesen, G.S. Identification of ubiquitination sites on the X-linked inhibitor of apoptosis protein. *Biochem. J.* **373**:965-971 (2003).
- 3. Burstein, E. and **Duckett, C.S.** Dying for NF- κ B? Control of cell death by transcriptional regulation of the apoptotic machinery. *Curr. Opin. Cell Biol.* **15**: 732-737 (2003).
- 4. Ganesh, L., Burstein, E., Guha-Niyogi, A., Louder, M., Mascola, J., Klomp, L.W.J., Wijmenga, C., **Duckett, C. S.** and Nabel, G.J. The gene product, Murr1 restricts HIV-1 replication in resting CD4+ lymphocytes. *Nature* **426**:853-857 (2003).
- 5. Beltrami, E., Plescia, J., Wilkinson, J.C., **Duckett, C.S.** and Altieri, D.C. Acute ablation of survivin uncovers p53-dependent mitotic checkpoint functions and control of mitochondrial apoptosis. *J. Biol. Chem.* **279**:2077-2084 (2004).

6. Burstein, E., Ganesh, L., Dick, R.D., van De Sluis, B., Wilkinson, J.C., Lewis, J., Klomp, L.W.J., Wijmenga, C., Brewer, G.J., Nabel, G.J. and **Duckett, C.S.** A novel role for XIAP in copper homeostasis through regulation of MURR1. *EMBO J.* **23**:244-254 (2004).
7. Jacob, J., Louis, J.M., Richter, B.W.M., **Duckett, C.S.** and Torchia, D.A. The C-terminal domain, of Viral IAP-associated factor (cVIAF) is a structural homolog of phosducin: resonance assignments and secondary structure of the C-terminal domain of VIAF. *J.Biomol NMR* **82**:197-198 (2004).
8. Steinman, H.A., Burstein, E., Lengner, C., Gosselin, J., Pihan, G., **Duckett, C.S.** and Jones, S.N. An alternative splice form of Mdm2 induces p53-independent cell growth and tumorigenesis. *J. Biol. Chem* **279**:4877-4886 (2004).
9. Lewis, J., Burstein, E., Birkey Reffey, S., Bratton, S.B., Roberts, A.B., and **Duckett, C. S.** Uncoupling of the signaling and caspase-inhibitory properties of XIAP. *J. Biol. Chem.* **279**:9023-9029 (2004).
10. Creagh, E.M, Murphy, B., **Duckett, C.S.** and Martin, S.J. SMAC/Diablo antagonizes XIAP ubiquitin ligase activity to potentiate apoptosis. *J. Biol. Chem.* **279**:29606-29614 (2004).
11. Wilkinson, J. C., Cepero, E., Boise, L.H. and **Duckett, C.S.** Upstream regulatory role for XIAP in receptor-mediated apoptosis. *Mol. Cell. Biol.* **24**:7003-7014 (2004).

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

A. Director, Ligand Assay Laboratory.

II. TEACHING ACTIVITIES:

A. Instructor for Pathology House Offices Laboratory Rotation.

B. Participant, Clinical Pathology Grand Rounds.

C. Graduate Student Advisor for Ph.D. Student Pablo Nepomnaschy

III. RESEARCH ACTIVITIES:

A. OTHER SUPPORT:

ACTIVE

U01 AG12495-11 (McConnell) 12/01/03 - 11/30/08 10%

NIH \$1,062,366 (YR-11)

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

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

5P60 DK20572 (WHHerman) 12/01/02 - 11/30/07 5%

NIH \$1,229,020 Total \$6,071,430

Michigan Diabetes Research and Training Center – Core Facility Lab.

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

SCIENTIFIC COLLABORATIONS:

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

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

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

IV. **SERVICE ACTIVITIES:**

DEPARTMENTAL:

- A. Director, Central Ligand Assay Laboratory.

MEDICAL SCHOOL/HOSPITAL:

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

V. **PUBLICATIONS:**

ARTICLES PUBLISHED AND IN PRESS IN SCIENTIFIC LITERATURE:

1. Flinn, M.V. & England, B.G. (2004). *Are there critical periods in ontogeny of stress response and immune function?* American Journal of Physical Anthropology Suppl. 38, 95-96.
2. Flinn, M.V. & England, B.G. (2004). *Critical periods in ontogeny of stress response and immune function.* American Journal of Human Biology 16, 203.
3. Gauger PG, Mullan MH, Thompson NW, Doherty GM, Matz KA, England BG. *An alternative analysis of intraoperative parathyroid hormone data may improve the ability to detect multiglandular disease.* Archives of Surgery. 139(2):164-9, 2004 Feb.
4. Benghuzzi H. Tucci M. Tsao A. Russell G. England B. Ragab A. *Stimulation of osteogenesis by means of sustained delivery of various natural androgenic hormones.* Biomedical Sciences Instrumentation. 40:99-104, 2004.
5. Cason Z. Benghuzzi H. Tucci M. England B. *TCPL delivery system as a model for E + P replacement therapy in post-ovariectomized adult rats mimicking a postmenopausal condition.* Biomedical Sciences Instrumentation. 39:529-34, 2003.
6. Nepomnaschy PA, McConnell D, Welch K, Strassmann BI and England BG. *Stress and Female Reproductive Function: A study of daily variations in cortisol, gonadotrophins, and gonadal steroids in a Rural Mayan Population.* American Journal of Human Biology. (in press).

ABSTRACTS AND PAPERS AT SCIENTIFIC MEETINGS:

1. Quinlan RJ, Flinn MV, Leone DV, Quinlan MB, Gangestad SJ, Thornhill R, & England BG, *Tradeoffs between indirect parental investment and direct childcare: Long-term effects of household production and breastfeeding duration on children's cortisol levels, fluctuating asymmetry, and growth.* (abstract) Proceedings of the Human Behavior and Evolution Society 2003.
2. Nepomnaschy PA, McConnell D, Welch K, Strassmann BI and England BG (2003) *Stress and Reproduction in a Subsistence Population in Rural Guatemala.* LIFE Spring Academy, Max Planck Institute & The University of Michigan, Ann Arbor, Michigan.
3. Nepomnaschy PA, and England BG (2004) *Reproductive suppression: The critical process of implantation.* LIFE Academy, The University of Michigan, Ann Arbor, Michigan.
4. Nepomnaschy PA, McConnell D, Welch K, Strassmann BI and England BG (2003) *Adrenal and Reproductive Hormone Changes in Parous Mayan Women in Rural Guatemala.* Annual Meeting of the Human Biology Association, Tempe, Arizona.
5. Nepomnaschy PA, Strassmann BI and England BG. (2003) *Psychosocial Stress and Female Reproductive Function in a Rural Mayan Community.* American Anthropological Association, 102nd Annual Meeting, Chicago, Illinois USA.
6. Benghuzzi, HA and England, BG *Long-term sustained delivery of Danazol, T and DHT alters HDL level in castrated rams.* International Conference on Cardiovascular Medicine and Science, July 23-25, 2003, Bethesda, MD, USA, Abstract, International Journal of Cardiovascular Medicine and Science, Vol. 6, No2, pp68, 2003.
7. Adah, F, Benghuzzi, H, Tucci, M, Russell, G, Tsao, A and England, BG, *Sustained Delivery of Statin by Means of TCPL Delivery System and the Effect on Reproductive Hormones,* The 19th

Annual Meeting of the Academy of Surgical Research, October 3rd and 4th, 2003 at the St. Louis Radisson Hotel, St. Louis, MO.

8. Nepomnaschy PA, and England BG (2004) *Reproductive suppression: The critical process of implantation*. 73rd Annual Meeting, American Association of Physical Anthropologists, Tampa, Florida USA.
9. Nepomnaschy PA, McConnell D, Welch K, Strassmann BI and England BG. (2003) *Daily Stress and Female Reproductive Function in a Mayan Population*. Third Biennial Meeting, Society for the Study of Human Development, Cambridge, Massachusetts USA.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003- 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

- A. House Officers:
 - 1. Sign-out of bone marrow biopsies, aspirates, blood smears, and body fluids in Hematology Laboratory.
 - 2. Sign-out of lymph node biopsies and review of hematopathology consultation material.
 - 3. Flow Cytometry sign-out.
- B. Hematopathology teaching:
 - 1. Leukemia conference/biweekly.
 - 2. Lymphoma conference/weekly.
 - 3. Hematology conference/biweekly.
 - 4. Clinical Pathology Grand Rounds.
 - 5. Clinical Pathology Case Conference/weekly.
- C. Medical Students:
 - 1. M-2 Hematology Sequence: Section leader for laboratory sessions (12 hours).
 - 2. M-2 Hematology sequence: "Pathology and Classification of Lymphoma" (Lecture) – 1 hour.
 - 3. M-1 Histopathology Course (24 hours).
- D. Dental and Graduate Students: Pathology 580/630: "Pathology of White Blood Cells" (Lecture) – 1 hour.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Optimization of Clinical Laboratory Hematology Practice.

- B. Gene expression and immunophenotypic profiling of chronic lymphoproliferative disorders.
- C. Utilization management and optimization for clinical laboratories.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

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

DEPARTMENTAL:

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

REGIONAL/NATIONAL:

- A. Co-Editor, Laboratory Hematology (Journal of the International Society for Laboratory Hematology).
- B. Associate Editor, Cytometry Part B: Clinical Cytometry.
- C. Ad hoc Editorial Reviewer: Blood, Human Pathology, Archives of Pathology & Laboratory Medicine
- D. American Society for Clinical Pathology, Check Path Planning Committee (Hematopathology).
- E. College of American Pathologists, Hematology and Clinical Microscopy Resource Committee.
- F. Society for Hematopathology, ASCP Companion Program Committee.
- G. American Society for Clinical Pathology, Hematology Resource Council.
- H. International Society for Laboratory Hematology Program Committee.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

- 1. “Update on Chronic Lymphocytic Leukemia.” Society for Hematopathology companion meeting, American Society for Clinical Pathology annual meeting. New Orleans, LA, September 17, 2003.

2. "Juvenile Myelomonocytic Leukemia." Society for Hematopathology Slide Workshop, Memphis, TN, October 23, 2003.
3. "Chronic Lymphocytic Leukemia." Consultants in Laboratory Medicine, Toledo, OH, March 3, 2004.
4. "Flow Cytometry in the Age of 'Omics'." William Beaumont Hospital, Royal Oak, MI, June 11, 2004.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Kansal R, Ross CW, Singleton TP, Finn WG, Schnitzer B: Histopathologic features of splenic small B-cell lymphomas: a study of 42 cases with a definitive diagnosis by the World Health Organization Classification. *Am J Clin Pathol* 120:335-347, 2003.
2. Brown W, Keeney M, Chin-Yee I, Johnson K, Lantis K, Finn W, Wolfe N, Kaplan S: Validation of body fluid analysis on the Coulter LH 750. *Lab Hematol* 9(3):155-159, 2003.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Finn WG, Sreekumar A, Chinnaiyan A: Trisomy 12-associated chronic lymphocytic leukemia with gene expression profile resembling mantle cell lymphoma.

BOOKS AND CHAPTERS IN BOOKS:

1. Finn WG, Peterson LC (eds.): *Hematopathology in Oncology*. Kluwer Academic Publishers, Boston, 2004.
2. Finn WG: Hematolymphoid system. In: *Yearbook of Pathology and Laboratory Medicine 2004*. Raab SR, Grzybicki DM, Bejarano PA, Bissell MG, Stanley MW, eds. Elsevier, Inc. 2004:259-273.
3. Davis GD, Lantis KL, Finn WG: Laboratory hematology practice: present and future. In: *Hematopathology in Oncology*. Finn WG, Peterson LC, eds. Kluwer Academic Publishers, Boston, 2004;121:167-179. (Cited in *Index Medicus* as Cancer Treat Res 2004;121:167-179.)

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

1. Bakshi NA, Ross CW, Finn WG, Valdez R, Ruiz R, Schnitzer B: Primary bone anaplastic large cell lymphoma (ALCL) in pediatric age group. *Mod Pathol* 2004; 17(suppl 1):239A.
2. Bakshi NA, Finn WG, Valdez R, Ross CE, Schnitzer B: Fascin expression in diffuse large B-cell lymphoma (DLBCL), anaplastic large cell lymphoma (ALCL) and classical Hodgkin lymphoma (CHL). *Mod Pathol* 2004; 17(suppl 1): 239A.
3. Owens SR, Finn WG, Ross CW, Schnitzer B, Valdez R: Type and distribution of small and large intestinal lymphomas. *Mod Pathol* 2004; 17(suppl 1): 264A.

4. Finn WG: Q & A: buffy coat preparation for differential leukocyte counts. CAP Today 18(1):81, 2004.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

- A. Pathology 600 Lectures:
 - 1. Obstructive Lung Disease - November, 2003
 - 2. Pulmonary Neoplasms - November, 2003
 - 3. Pathology of ARDS - November 2003
 - 4. Tissue Reactions to Infectious Agents - November 2003
 - 5. Cardiovascular Pathology Review for Medical Students, October, 2003
 - 6. Pulmonary Pathology Review for Medical Students - November, 2003
 - 7. Gastrointestinal Pathology Review for Medical Students, January, 2004
 - 8. Endocrine Pathology Review for Medical Students, March, 2004
 - 9. Reproductive Pathology Review for Medical Students, April, 2004
 - 10. Musculoskeletal Pathology Review for Medical Students, May, 2004
 - 11. Introduction to Musculoskeletal Pathology, May, 2004
 - 12. Medical Students Question and Answer sessions, October, 2003 - June, 2004
 - 13. USMLE Pathology Review, May and June, 2004
 - 14. Laboratory Instructor, October, 2003 - May, 2004
 - 15. Histology Tutorial for Medical Students, October, 2003 - May 2004
- B. Pathology 630:
 - 1. Respiratory Disease I - October, 2003; April, 2004
 - 2. Respiratory Disease II - November, 2003; April, 2004
- C. Residency Training:
 - 1. Diseases of the Chest I - April, 2004
 - 2. Diseases of the Chest II - April, 2004
 - 3. Diseases of the Chest III - April, 2004
 - 4. Ethics Roundtable Discussion - October, 2003
- E. Other educational activities:
 - 1. M4 student elective mentor, July 2003
 - 2. Participant, Teaching with Technology Institute, May, 2004

3. Center for Research on Learning and Teaching Workshops: "Concept Maps", May, 2004; "Basic Sitemaker", May, 2004; "SiteMaker Database", May, 2004; "Classroom Assessment", May, 2004
4. Radiology - Pathology Correlation elective for M4 students, Course Co-Director, April, 2004
5. Course Director, M-4 Student Pathology Clerkships, 2003-2004
6. Participant, Thoracic Surgery Residents Core Curriculum, 2004

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Learning Pathology in the Context of the Patient, Teaching with Technology Institute, University of Michigan, 2004 -2005
- B. A Murine Model of Graft-Vs-Host Disease Lacrimal Gland Inflammation and Destruction: Histopathology, Immunopathology, and Intervention (Midwest Eye-Banks and Transplantation Center), Victor M. Elner, MD, PhD (Principal Investigator), Andrew Flint, MD (Co-Investigator)
- C. Lung Image Database Consortium (IU01 CA91099-01). Chuck Meyer, PhD (Principal Investigator)
- D. Consultant, Fibroproliferation in Bronchiolitis Obliterans Syndrome, Vibha Lama, MD, Principal Investigator. National Institutes of Health/NHLBI; K23HL077719-01

PROJECTS UNDER STUDY:

- A. Histologic predictors of obliterative bronchiolitis in lung transplant patients
- B. Interactive web-based instruction: effect on examination performance
- C. Clinico-pathologic correlations of interstitial lung diseases
- D. Ophthalmic manifestations of the systemic vasculitides
- E. "Pathology and the Patient", web-based learning and teaching for medical students.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

None

V. OTHER RELEVANT ACTIVITIES:

Member, Admissions Committee, Medical School 2003 - 2004
Reviewer, Journal of Neuro-Ophthalmology 2004

INVITED LECTURES/SEMINARS:

None

VI. PUBLICATIONS:

1. Moroi SE, Hokhale PA, Schteingart MT, Sugar A, Downs CA, Shimizu S, Krafchak C, Fuse N, Elner SG, Elner VM, Flint A, Epstein MP, Boehnke M, Richards JE: Clinicopathologic correlation and genetic analysis in a case of posterior polymorphous corneal dystrophy. *Am J Ophth* 135(4):461-470, 2003
2. Flaherty KR, Mumford JA, Murray S, Kazerooni EA, Gross BH, Colby TV, Travis WD, Flint A, Toews GB, Lynch JP 3rd, Martinez FJ: Prognostic implications of physiologic and radiographic changes in idiopathic interstitial pneumonia. *A J Res and Crit Care Med* 168(5):543-548, 2003
3. Kim N, Trobe JD, Flint A, Keoleian G: Late ipsilateral recurrence of ischemic optic neuropathy in giant cell arteritis. *J Neuro Ophth* 23(2):122-126, 2003
4. Doerr TD, Marentette LJ, Flint A, Elner V: Urokinase-type plasminogen activator receptor expression in adenoid cystic carcinoma of the skull base. *Arch Otolaryngology -Head & Neck Surgery* 129(2):215-218, 2003
5. Flaherty KR, Thwaite EL, Kazerooni EA, Gross BH, Toews GB, Colby TV, Travis WD, Mumford JA, Murray S, Flint A, Lynch JP 3rd, Martinez FJ: Radiological versus histological diagnosis in UIP and NSIP: survival implications. *Thorax* 58(2):143-148, 2003

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

1. Lama VN, Flint A, Smith L, Martinez FJ, Peters-Golden M; Toews GB, Thannickal VJ: Role and origin of myofibroblasts in the pathogenesis of bronchiolitis obliterans in lung transplant recipients. *Am J Resp Crit Care Med*:169:A504, 204

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2001 - 30 JUNE 2002**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

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

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Specificity and sensitivity of NKI-C3 in epithelioid cell tumors of the skin (L. Lowe, M.D. and L. Su, M.D.)
- B. Human telomerase reverse transcriptase expression in melanocytic lesions: an immunohistochemical study on paraffin-embedded tissues (L. Su, M.D.)
- C. BRAF mutations and microsatellite instability in Spitz nevi, atypical Spitz tumors and Spitz-like melanoma (S. Gruber, M.D., J. Poynter, T. Johnson, M.D., J. Elder, M.D.)
- D. University of Michigan (UMMC 2000-0713): Molecular, biochemical and cellular basis of melanoma and other melanocytic lesions: Tissue Bank (T. Johnson, M.D., T. Wang, M.D., J. Schwartz, M.D., J. Voorhees, M.D., A. Dlugosz, M.D., L. Lowe, M.D., L. Su, M.D., C. Bradford, M.D., V. Cimmino, M.D.)
- E. Patient examination with Mela Find™ System developed by Electro-Optical Sciences, Inc., (EOS), 2001 (J. Schwartz, M.D., T. Johnson, M.D., T. Wang, M.D., D. Karimipour, M.D., J. Orringer, M.D., L. Lowe, M.D., L. Su, M.D., C. Bichakjian, M.D., M. Rabe, R.N.)

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

Director of Histology Laboratory, Department of Pathology

REGIONAL AND NATIONAL:

1. Ad hoc manuscript reviewer, Journal of Cutaneous Pathology
2. Ad hoc manuscript reviewer, Journal of the American Academy of Dermatology

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

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

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Cassarino DS, **Fullen DR**, Sondak VK, Duray PH: Metastatic nevoid melanoma in a 4 ½-year-old child. J Cutan Pathol 30: 647-651, 2003.
2. Su LD, **Fullen DR**, Lowe L, Wang TS, Schwartz JL, Cimmino VM, Sondak VK, Johnson TM: Desmoplastic and neurotropic melanoma. Cancer 100: 598-604, 2004.
3. Sturtz DE, Smith DJ, Calderon MS, **Fullen DR**: Giant folliculosebaceous cystic hamartoma of the upper extremity. J Cutan Pathol 31: 287-290, 2004.
4. Karimipour DF, Lowe L, Su L, Hamilton T, Sondak V, Johnson TM, **Fullen D**: Standard immunostains for melanoma in sentinel lymph node specimens: Which ones are most useful? J Am Acad Dermatol 50: 759-764, 2004.
5. Bogner PN, Su LD, **Fullen DR**: Cluster Designation 5 (CD5) staining of normal and non-lymphoid neoplastic skin. (J Cutan Pathol in press)

BOOKS/CHAPTERS IN BOOKS:

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

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

1. Bogner P, Su L, **Fullen D**: "Detection of CD5 by immunohistochemistry in cutaneous tumors of apocrine and eccrine origin." Poster presentation at the American Society of Dermatopathology 40th annual meeting, October, 2003.

2. Sturtz D, Smith DJ, Calderon M, **Fullen DR**: "Giant folliculosebaceous cystic hamartoma of the upper extremity." Poster presentation at the American Society of Dermatopathology, 40th annual meeting, October, 2003.
3. Zhu W, Su LD, Thomas D, **Fullen DR**: "HTERT expression in melanocytic lesions: an immunohistochemical study on paraffin-embedded tissues." Accepted for poster presentation at the American Society of Dermatopathology 41st annual meeting, October, 2004.
4. **Fullen DR**, Lowe L: "Epidermotropic mucinous adenocarcinoma arising at mucocutaneous stomal anastomosis site." Accepted for poster presentation at the American Society of Dermatopathology 41st annual meeting, October, 2004.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004

I. CLINICAL ACTIVITIES:

- A. Director, Chemistry Laboratory
- B. Sign-out and interpretation of lipoprotein electrophoresis results.
- C. Direct the operation of blood gas/electrolyte analyzers, coagulation testing meters, and hematology analyzers in the Emergency Department and the operating rooms of Main, Mott, and, Kellogg Hospitals.
- D. Direct the workgroup overseeing the quality assurance programs for bedside blood glucose testing in the Medical Center.
- E. Planning group for the 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 Quad Marker Prenatal Screen results from maternal serum testing

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

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

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

5P60 DK20572 (WH Herman, PI) 12/01/02 - 11/30/07 Lab. Co-Director 5% Effort
NIH/NIDDK \$1,229,020 Total \$6,071,430
Michigan Diabetes Research and Training Center – Core Facility Lab.

This grant established a center within the University of Michigan Health System to promote and facilitate multidisciplinary research on diabetes and its related endocrine disorders. The Chemistry Core Lab in the MDRTC performs a variety of Chemistry tests and immunoassays at low cost to support diabetes related research studies.

PROJECTS UNDER STUDY:

- A. Evaluation of HPLC-MS-MS methods for immunosuppressant drugs Tacrolimus, Sirolimus, and Mycophenolic acid
- B. PSA and Percent free PSA levels in an African-American population (Flint Mens Health Study)
- C. Evaluation of EIA assays for extractable nuclear antigens.
- D. Automation of EIA assays for anti-CCP and anti beta-2-glycoprotein I.
- E. Comparison of the utility of BNP and NT-proBNP measurements in heart failure.
- F. Evaluation of a new immunoassay for cyclosporine.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

REGIONAL AND NATIONAL:

- A. Chair, Michigan Section AACC.
- B. Ad hoc reviewer, Clinical Chemistry.
- C. Ad hoc reviewer, Archives of Pathology and Laboratory Medicine

V. OTHER RELEVANT ACTIVITIES:

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

INVITED LECTURES/SEMINARS:

- 1. "B-type Natriuretic Peptide and Heart Failure." Toledo Hospital and Consultants in Laboratory Medicine, Toledo, August 13, 2003.
- 2. "Clinical Utility of Intra-operative PTH Testing." Michigan Section AACC Symposium on Point of Care Testing. Windsor, Ontario, Canada, November 20, 2003.
- 3. "High Sensitivity C-Reactive Protein and Risk for Cardiovascular Disease." Consultants in Laboratory Medicine and ProMedica Health System, Toledo, OH, January 14, 2004.
- 4. "Interferences in Immunoassays" MSCLS Annual Meeting, Lansing, MI. April 7, 2004.

VI. PUBLICATIONS:

ARTICLES PUBLISHED IN REFEREED JOURNALS:

1. Sreekumar A, Laxman B, Rhodes DR, Bhagavathula S, Harwood J, Giacherio D, Ghosh D, Sanda M., Rubin M, and Chinnaiyan A: Protein microarray analysis reveals that prostate cancer patients elicit a humoral immune response to alpha-methylacyl-CoA racemase. Journal of the National Cancer Institute. 96:834-843, 2004

ARTICLES SUBMITTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Zhou L, Giacherio D, Cooling L, and Davenport RD: Use of B-natriuretic peptide (BNP) as a diagnostic marker in the differential diagnosis of transfusion-associated circulatory overload (TACO). (submitted to Transfusion)
2. Laxman B, Sreekumar A, Hofer MD, Rubin MA, Bhagavathula S, Ghosh D, Shah R, Giacherio D, Montie JE, Wei JT, and Chinnaiyan AM: Alpha-methylacyl-CoA racemase as a urine biomarker for the non-invasive detection of prostate cancer. (submitted to Journal of the National Cancer Institute)

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

1. Wang X, Mertz M, Ahmed A, Giacherio D, and Stern S. Resuscitation from combined traumatic brain injury and hemorrhagic shock with racemic vs L-lactated Ringer's. Presented at the Society for Academic Emergency Medicine Regional Meeting, Saginaw, MI. September 19, 2003.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

- A. General Surgical Pathology - three 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 - 3 months.
 - 2. Endocrine Surgical Pathology - 12 months as needed.
 - 3. Consultation Conferences.
 - 4. Molecular Pathology lectures.
 - 5. Endocrine Pathology lectures.
- C. Interdepartmental:
 - 1. Endocrine Conference, Department of Surgery - monthly.
 - 2. Adrenal Cancer Conference - monthly.
 - 3. Lecture to Genetic Counseling Students, "Pathology of Cancer"

EXTERNAL:

- A. Visiting Professor, University of Cincinnati.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. 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 (12 month extension with 10% effort for 6 months)
- B. Core Director, The University of Michigan Comprehensive Cancer Center, Histology/Immunohistochemistry Service, 9-02 to present, 10% effort
- C. Pathology Core Leader, "Proteomics Alliance for Cancer", Michigan Life Sciences Corridor, with G. Omenn (PI), 5% effort (\$2,605,490 direct cost/3 years)
- D. Principal Investigator, "Gene Expression Profiling Studies of Papillary Thyroid Carcinoma", The University of Michigan Comprehensive Cancer Center, Thyroid Cancer Program, 8/1/02 to 7/31/04 (\$50,000 direct costs).
- E. Co-Principal Investigator, "University of Michigan Endocrine Bank", Millie Schembechler Adrenal Cancer Research Fund, 1/1/01 to 6/01/04 (\$350,000 direct costs), with Dr. Paul Gauger, Department of Surgery, 5% effort
- F. 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
- G. 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
- H. Director, "Tissue Procurement Collaboration", Genentech, Inc., 5/99 to 5/2005 (\$700,000 direct costs), 10% effort
- I. Core Director, The University of Michigan Comprehensive Cancer Center, Tissue Procurement Service, 7-98 to present, 10% effort
- J. Core Director, The University of Michigan Comprehensive Cancer Center, Laser Capture Microdissection Core, 1-99 to present
- K. Principal Investigator, "Pfizer Tissue Bank", Pfizer Inc., 1/1/04 to 12/31/06, (\$348,000/yr), 5% effort

PROJECTS UNDER STUDY:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL AND INSTITUTIONAL:

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

NATIONAL:

- A. Editorial Board, *Endocrine Pathology*

V. OTHER RELEVANT ACTIVITIES:

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

INVITED LECTURES/SEMINAR:

- 1. Invited Speaker, “Distinct transcriptional profiles of metastasizing and non-metastasizing adrenal and extra-adrenal paragangliomas uncovered by DNA microarray analysis”, Molecular Differentiation of Benign and Malignant Pheochromocytomas and Neuroblastomas, Cold Spring Harbor Laboratory, Long Island, New York
- 2. Invited Speaker, “Gene Expression Studies of Adrenocortical and Thyroid Tumors”, Laboratory of Pathology, National Cancer Institute, Bethesda, Maryland
- 3. Invited Speaker, “New Diagnostic Tools for Thyroid Cancer Using Gene Expression Profiles”, University of Cincinnati, Cincinnati, Ohio
- 4. Pathology Slide Seminar, “Adrenal Pathology”, University of Cincinnati, Cincinnati, Ohio

VI. PUBLICATIONS:

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

- 1. Dhaini HR, Thomas DG, **Giordano TJ**, Johnson TD, Biermann JS, Leu K, Hollenberg PF, Baker LH. Cytochrome P450 CYP3A4/5 expression as a biomarker of outcome in osteosarcoma. J Clin Oncol 2003;21:2481-2485.

2. **Giordano TJ.** Gene expression profiling of endocrine tumors using DNA microarray analysis: progress and promise. Endo Pathol 2003;14;107-116.
3. Miller CT, Chen G, Gharib TG, Wang H, Thomas DG, Misek DE, **Giordano TJ**, Yee J, Orringer MB, Hanash SM, Beer DG. Increased c-crk proto-oncogene expression is associated with an aggressive phenotype in lung adenocarcinomas. Oncogene 2003;22;7950-7957.
4. Shedden KA, Taylor JMG, **Giordano TJ**, Kuick R, Misek DE, Rennert DR, Gruber SB, Logsdon C, Simeone D, Kardia SLR, Greenson JK, Cho KR, Beer DG, Fearon ER, Hanash S. Accurate molecular classification of human cancer based on gene expression using a simple classifier with a pathologic tree-based framework. Am J Pathol 2003;163;1985-1995.
5. Chen G, Gharib T, Wang H, Huang C-C, Kuick R, Thomas D, Shedden KA, Misek DE, Taylor JMG, **Giordano TJ**, Kardia SLR, Iannettoni MD, Yee P, Hogg PJ, Orringer MB, Hanash SM, Beer DG. Proteins and pathways associated with poor survival in lung adenocarcinoma. Proc Natl Acad Sci USA 2003;100;13537-13542.
6. Beuschlein F, Looyenga BD, Reincke M, **Giordano TJ**, Hammer GD. Clinical impact of recent advances in the biology of adrenocortical cancer. Endocrinologist 2003;13;470-478.
7. Bian X, Lin HJ, **Giordano TJ**, Solomon G, Castle VP, Opipari AW Jr. Chemotherapy-induced apoptosis of S-type neuroblastoma cells requires caspase-9 and is augmented by CD95/Fas stimulation. J Bio Chem 2004;38;10-16..
8. Lin J, Raoof DA, Thomas D, Greenson JK, **Giordano TJ**, Robinson GS, Barve RA, Orringer MB, Beer DG. L-type amino acid transporter-1 overexpression mediates uptake of melphalan in Barrett's adenocarcinoma. Neoplasia 2004;6.
9. Chen G, Wang H, Miller CT, Thomas DG, Gharib TG, Misek DE, **Giordano TJ**, Orringer MB, Hanash SM, Beer DG. Reduced selenium-binding protein 1 expression is associated with poor outcome in lung adenocarcinomas. J Pathol 2004;321-329.
10. Schmalbach CE, Chepeha DB, **Giordano TJ**, Rubin MA, Teknos TN, Bradford CR, Wolf GT, Kuick R, Misek DE, Trask DK, Hanash S: Molecular profiling and the identification of genes associated with metastatic oral cavity/pharynx squamous cell carcinoma. Arch Otolaryngol Head Neck Surg 2004;130;295-302.
11. Hughes DP, Thomas DG, **Giordano TJ**, Baker LH, McDonagh KT. Cell surface expression of epidermal growth factor receptor and her-2 with nuclear expression of her-4 in primary osteosarcoma. Cancer Res 2004;64;2047-2053.
12. Lin J, Raoof DA, Thomas DG, Greenson JK, **Giordano TJ**, Robinson GS, Bournier MJ, Bauer CT, Orringer MB, Beer DG. L-type amino acid transporter-1 overexpression and melphalan sensitivity in barrett's adenocarcinoma. Neoplasia 2004;6;74-84.
13. Eisenhofer G, Bornstein SR, Brouwers FM, Cheung N-KV, Dahia PL, de Krijger RR, **Giordano TJ**, Greene LA, Goldstein DS, Lehnert H, Manger WM, Maris JM, Neumann HPH, Pacak K, Shulkin BL, Smith DI, Tishler AS, Young WF. Malignant pheochromocytoma: current status and initiatives for future progress. Endocrine-Related Cancer.
14. Hong S-H, Misek DE, Wang H, Puravs E, **Giordano TJ**, Greenson JK, Brenner DE, Simeone DM, Logsdon C, Hanash S. An autoantibody-mediated response calreticulin isoforms in pancreatic cancer. Cancer Res.
15. Zhang L, Fu Z., Binkley C, **Giordano TJ**, Burant CF, Logsdon CD, Simeone DM. Raf-1 kinase inhibitory protein inhibits beta-cell proliferation. Surgery.
16. Lin J, Lin L, Thomas DG, Greenson JK, **Giordano TJ**, Robinson GS, Barve RA, Wesihaar FA, Taylor JMG, Orringer MB, Beer DG. Melanoma-associated antigens in esophageal adenocarcinoma: identification of novel MAGE-A10 splice variants. Clin Can Res.

17. Binkely CE, Zhang L, Greenson JK, **Giordano TJ**, Kuick R, Misek D, Hanash S, Logsdon CD, Simeone DM. The molecular basis of pancreatic fibrosis: common stromal gene expression in chronic pancreatitis and pancreatic adenocarcinoma. Pancreas.

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Hong S-H, Misek DE, Puravs E, **Giordano TJ**, Greenson JK, Simeone DM, Brenner D, Logsdon C, Hanash SM. Identification of CLP36 as a tumor antigen that induces an antibody response in pancreatic cancer.
2. Dobbin KK, Beer DG, Meyerson M, Yeatman TJ, Gerald WL, Jacobson JW, Conley B, Buetow KH, Heiskanen M, Simon RM, Minna JD, Girard L, Misek DE, Kuick R, Taylor JMG, Hanash S, Naoki K, Hayes DN, Ladd-Acosta C, Enkemann SA, Viale A, **Giordano TJ**. Inter-laboratory comparability study of cancer gene expression analysis using oligonucleotide microarrays.
3. Chen X, Wang S, Wu N, Sood S, Wang P, Jin Z, Beer DG, **Giordano TJ**, Lin Y, Shih WJ, Lubet RA, Yang CS. Overexpression of 5-lipoxygenase in rat and human esophageal adenocarcinoma, and inhibitory effects of zileuton and celecoxib on carcinogenesis.
4. Hughes PM, Thomas DG, **Giordano TJ**, McDonagh, Baker LH. Constitutive erbB family phosphorylation in osteosarcoma as a target for CI1033 inhibition.
5. Hinoi T, Gesina G, Akyol A, Kuick R, Hanash S, **Giordano TJ**, Gruber SB, Fearon ER. CDX2 regulates expression of ceruloplasmin-related protein hephaestin in intestinal and colonic epithelium.

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

1. **Giordano TJ**, Lizyness M, Kuick R, Sanders D, Thomas D, Misek D, Hanash S, Shulkin B. Transcriptional signature of malignant pheochromocytoma and extra-adrenal paraganglioma. Director's Challenge Investigator's Meeting, November 2003.
2. Lambie, WK, Baker L, **Giordano TJ**, Thomas DG. Identification of c-MET as a marker for distinguishing malignant peripheral nerve sheath tumor from monophasic synovial sarcoma using gene expression profiling. *Mod Pathol* 2004;17;16A.
3. Guo G, **Giordano TJ**, Hanash S, Diamandis EP, Michael CW. Cytologic evaluation of kallikrein 10 as a marker of papillary carcinoma. *Mod Pathol* 2004;17;68A.
4. Lin L, Wang Z, Prescott MS, Albertson DG, Dekken HV, Orringer MB, Glover TW, Thomas DG, **Giordano TJ**, Beer DG. Regional microsatellite instability precedes allelic amplification in chromosomal band 3q26.3-q27 in the development of barrett's adenocarcinomas. *Proceedings of the AACR*, Vol 45, March 2004.
5. Creighton C, Webb C, Misek DE, **Giordano TJ**, Kuick R, Omenn GS, Hanash SM. Delineation of functional networks associated with tumor formation based on analysis of microarray data for lung adenocarcinomas A549 xenografts. *Proceedings of the AACR*, Vol 45, March 2004.
6. Misek DE, Veenstra C, Hinderer Robert, **Giordano TJ**, Beer DG, Hanash SM. Proteomics based identification of tumor antigens that induce an antibody response in esophageal cancer. *Proceedings of the AACR*, Vol 45, March 2004.
7. Mensah-Osman EJ, Thomas DT, **Giordano TJ**, Lizyness M, Hollenberg, P, Baker Laurence. Expression and activity of PXR target genes CYP3A4 and MRD1 in sarcoma tumors predict response to chemotherapeutic agents. *Proceedings of the AACR*, Vol 45, March 2004.

8. Chen G, Wang H, Miller CT, Thomas DG, Gharib TG, Misek DE, **Giordano TJ**, Orringer MB, Hanash SM, Beer DG. Reduced selenium-binding protein 1 expression is associated with poor outcome in lung adenocarcinomas. Proceedings of the AACR, Vol 45, March 2004.
9. Hughes DP, Thomas DG, **Giordano TJ**, McDonagh KT, Baker LH. Activated EGFR and Her-4 in osteosarcoma correlate with apoptosis induced by a pan-erbB inhibitor. Proceedings of the AACR, Vol 45, March 2004.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

- A. Medical Students:
 - 1. GI Pathology Sequence, assisted Dr. Appelman (ten contact hours).
 - 2. GI Pathology Sequence, 2 hours full class lecture
- B. Dental Students:
 - 1. Pathology 630-631 one full class lecture (one contact hour).
- C. House Officers:
 - 1. Surgical pathology diagnosing room instruction for house officers - four months.
 - 2. One didactic lecture on gastrointestinal pathology - April, 2003.
 - 3. Gastrointestinal and hepatic pathology tutoring - four months.
 - 4. Four months consultation conferences.
- D. Interdepartmental:
 - 1. Liver biopsy conference - one hour every 3 months.
 - 2. Multidisciplinary GI tumor board - 1 hour every other week.
 - 3. GI pathology teaching sessions with GI fellows - one hour/month.
 - 4. GI and Liver path teaching to GI and transplant fellows – 2 hours/year

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Co-Investigator R01CA81488-01 (\$4,547,772) “Molecular Epidemiology of Colorectal Cancer”, 20% Salary Support, years 1-4, Stephen Gruber, M.D., Ph.D. Principal Investigator.
- B. Co-Investigator N01-DK-9-2323 (\$1,433,559) “Hepatitis C Clinical Trial”, 7% Salary Support, Anna Lok, M.D. Principal Investigator.
- C. Co-investigator with Hari Conjeevaram M.D., “Study of viral resistance to antiviral therapy of chronic hepatitis c (virahep-c) - clinical centers” (7.5% salary support year 2, 3% years 3 and 4), University of Michigan Grant NIH-NIDDK-01-007

PROJECTS UNDER STUDY:

- A. Study of fatty liver and steatohepatitis with Hari Conjeevaram in Division of Gastroenterology..
- B. NIH study of HCV with Anna Lok in Division of Gastroenterology.
- C. NIH study of the Molecular Epidemiology of Colon Cancer in Israel (grant renewed for 5 more years).
- D. Study of molecular classification of tumors with Stephen Gruber and Thomas Giordano
- E. Study of molecular genetic changes in pancreas cancer with Diane Simione and Craig Logsdon
- F. Study of Yersinia and Crohn's disease with Laura Lamps at the University of Arkansas.
Study of UC dysplasia grading with GI Study Group.
- G. Study of Focally enhanced gastritis with Wei Xin, M.D.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Speaker, USCAP short course on GI pathology, Vancouver, Canada., March 2004.
2. Faculty Member, ASCP Workshop – Surgical Pathology of the Gastrointestinal Tract, Santa Fe, New Mexico, May 2003.
3. Visiting Professor and speaker, Cedars-Sinai Medical Center, October, 2003.
4. Visiting Professor and speaker, Pathology Grand Rounds, Yale University, April, 2004.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Xin W, Brown PI, **Greenson JK**. The clinical significance of focal active colitis in pediatric patients. *Am J Surg Pathol* 27:1134-1138, 2003.
2. Guo G, **Greenson JK**. Histopathology of interval appendectomy specimens: Strong association with granulomatous and xanthogranulomatous appendicitis. *Am J Surg Pathol* 27:1147-1151, 2003.
3. Wai CT, **Greenson JK**, Fontana R, Kalbfleisch J, Marrero J, Conjeevaram H, Lok A. A simple noninvasive index can predict both significant fibrosis and cirrhosis in patients with chronic hepatitis C. *Hepatology* 38:518-526, 2003.
4. Ammori JB, Colletti LM, Zalupski MM, Eckhauser FE, **Greenson JK**, Dimick J, Lawrence TS, McGinn CJ. Surgical resection following radiation therapy with concurrent gemcitabine in patients with previously unresectable adenocarcinoma of the pancreas. *J Gastrointest Surg* 7:766-772, 2003.
5. Ogura Y, Lala S, Xin W, Smith E, Dowds TA1, Chen FF, Zimmermann E, Tretiakova M, Cho JH, Hart J, **Greenson JK**, Keshav S, Nuñez G. Expression of NOD2 in Paneth Cells: A Possible Link to Crohn's Ileitis. *Gut* 52:1591-1597, 2003.
6. Shedden KA, Taylor JM, Giordano TJ, Kuick R, Misek DE, Rennert G, Schwartz DR, Gruber SB, Logsdon C, Simeone D, Kardia SL, **Greenson JK**, Cho KR, Beer DG, Fearon ER, Hanash S. Accurate molecular classification of human cancers based on gene expression using a simple classifier with a pathologic tree-based framework. *Am J Pathol* 163:1985-1995, 2003.
7. Scheiman JM, **Greenson JK**, Lee J, Cryer B. Effect of cyclooxygenase-2 inhibition on human *Helicobacter pylori* gastritis: mechanisms underlying gastrointestinal safety and implications for cancer chemoprevention. *Alimentary Pharmacology & Therapeutics* 17(12):1535-43, 2003.
8. Akintola-Ogunremi O, Pfeifer JD, Tan BR, Yan Y, Zhu X, Hart J, Goldblum JR, Burgart L, Lauwers LY, Montgomery E, Lewin D, Washington K, Bronner M, Xiao S-Y, **Greenson JK**, Lamps L, Lazenby A, Wang HL. Protein expression and gene mutation of c-kit in colonic neuroendocrine carcinomas. *Am J Surg Pathol* 27:1551-1558, 2003.
9. Askari FK, **Greenson JK**, Dick RD, Johnson VD, Brewer G. Treatment of Wilson's Disease with Zinc XVIII. Initial Treatment of the Hepatic Decompensation Presentation with Trientine and Zinc. *Journal of Laboratory & Clinical Medicine* 142(6):385-90, 2003.
10. Lin J, Raoof DA, Thomas DG, **Greenson JK**, Giordano TJ, Robinson GS, Bournier MJ, Bauer CT, Orringer MB, Beer DG. L-type amino acid transporter-1 overexpression and Melphalan sensitivity in Barrett's adenocarcinoma. *Neoplasia* 6:74-84, 2004.

11. Lipkin SM, Rozek LS, Rennert G, Yang W, Chen PC, Hacia J, Hunt N, Shin B, Fodor S, Mark Kokoris⁷, **Greenson JK**, Fearon E, Lynch H, Collins F, Gruber SB. The MLH1 K132H variant is associated with susceptibility to sporadic colorectal cancer. *Nature Genetics* 36:694-9, 2004.
12. Xin W, **Greenson JK**. The clinical significance of focally enhanced gastritis. Accepted to *Am J Surg Pathol*
13. Hong SH, Misek DE, Wang H, Puravs E, Giordano TJ, **Greenson JK**, Brenner DE, Simeone DE, Logsdon CD, Hanash SM. An Autoantibody-Mediated Immune Response to Calreticulin Isoforms in Pancreatic Cancer. Accepted to *Cancer research*.
14. Binkley CE, Zhang L, **Greenson JK**, Giordano TJ, Kuick R, Misek D, Hanash S, Logsdon CD, Simeone DM. The Molecular Basis for Pancreatic Fibrosis: Common Stromal Gene Expression in Chronic Pancreatitis and Pancreatic Adenocarcinoma. Accepted to *Pancreas*.

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Lauwers GY, Goldblum JR, Burgart LJ, Bhan AK, Vauthey JN, **Greenson JK**. Expression Of Neurotrophin Receptors And Ret Protein In Duodenal Gangliocytic Paraganglioma: A Study Of 12 Cases. Submitted to *Am J Surg Pathol*.

BOOKS/CHAPTERS IN BOOKS:

1. **Greenson JK**, Odze RD. Inflammatory Diseases of the Large Intestine, In: *Surgical Pathology of the GI Tract, Liver, Biliary tract, and Pancreas*, First edition. Ed: Robert D. Odze, John R. Goldblum, and James Crawford. Elsevier, Philadelphia, PA. 2004, p. 213-246.
2. **Greenson JK**. Inflammatory/Descriptive Colitides, In: *Gastrointestinal and Liver Pathology*. First Edition. Ed: Montgomery E, Iacobuzio-Donahue C. Elsevier, Philadelphia, PA. In Press.
3. *Sternberg's Diagnostic Surgical Pathology*, Fourth Ed. Edited by Mills SM, Carter D, **Greenson JK**, Oberman HA, Reuter V, and Stoler MH. Lippincott, Williams & Wilkins, Philadelphia, PA. 2004.

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

1. El-Zimaity H, Wotherspoon A, deMarscarel A, Savio A, Stolte M, Torlakovic E, Younes M, Appelman H, Cherian R, Copie-Bergman C, de Jong D, Dixon M, **Greenson J**, Isaacson P, et al. Interobserver variation in the histopathological assessment of MALT/MALT lymphoma. Platform presentation at USCAP meeting 2004, *Mod Pathol* 17:114A, 2004.
2. Schneider EN, Havens JM, Goldblum JR, **Greenson JK**, Shaffer RA, Scott MA, Lamps LW. Molecular Diagnosis of *Campylobacter* infection in cases of focal active colitis. Poster presentation at USCAP meeting 2004, *Mod Pathol* 17:129A, 2004.
3. Xin W, **Greenson JK**. The clinical significance of focally enhanced gastritis. Poster presentation at USCAP meeting 2004, *Mod Pathol* 17:133A, 2004.
4. Huang MY, Chao C, Anderson L, Peterman D, **Greenson JK**, Jacobson, Emick D, Lok AS, Conjeevaram HS. 1-year intense nutritional counseling results in histological improvement in 2/3 of patients with Nonalcoholic steatohepatitis. Platform presentation at DDW meeting 2004, *Gastroenterol* 126:A-683, 2004.
5. Ji B, Simeone DM, Ramachandran V, Arumugam T, Hanash S, Giordano T, **Greenson JK**, Taylor JM, Logsdon CD. CEACAM1 is biomarker for pancreatic cancer. Poster presentation at DDW meeting 2004, *Gastroenterol* 126:A-115, 2004.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Graduate Students:

1. Ph.D. Dissertation Committees, University of Michigan
 - a. Allison Miller (Pathology Graduate Program)
 - b. Betsy Pierce (Graduate Immunology Program)
 - c. Tobias Rodriguez (Graduate Immunology Program)
 - d. Matt Schaller (Graduate Immunology Program)
 - e. Shikha Auora (Graduate Immunology Program)
 - f. Haitao Wen (Pathology Graduate Program)
2. Undergraduate Students
 - a. Jillian Ewing
 - b. James Lee
 - c. Esther Choi
3. PIBS Graduate Student Laboratory Rotations, University of Michigan
 - a. Julie Rumble
 - b. Sudha Natarajan
4. Preliminary Examiner for Ph.D. Program, Pathology and other Graduate Programs, University of Michigan
 - a. Xiaoyu Jia
 - b. Yungfan Man
 - c. Meghan Brennan
 - d. Megan Ballinger (Graduate Immunology Program)
5. Formal Teaching, Dept. of Pathology
 - a. Pathology 581: Inflammation and Sepsis
 - b. Pathology 582: Systemic Inflammatory Responses

B. Postdoctoral Fellows:

1. Claudia Benjamim, Ph.D.
2. Traci Ness, Ph.D.
3. Karen Buckland, Ph.D.
4. Alessia Meneghin, M.D.
5. Ana Coelho, Ph.D.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

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

PROJECTS UNDER STUDY:

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

IV. ADMINISTRATIVE ACTIVITIES:

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

- 1. Center for Scientific Review, ZRG1 IMB (01)
- 2. Fellowship (F32) and R15 Review.
- 3. NIAID, Division of Extramural Affairs, Scientific Review Program
- 4. Special Emphasis Review Panel, RFA HL-04-009
- 5. (Granulomatous Lung Inflammation in Sarcoidosis).
- 6. Member, Graduate Program in Immunology
- 7. Member, Preliminary Examination Committee (Department of Pathology)
- 8. Member, Committee on Student Biomedical Research (CSBR), University of Michigan Medical School.
- 9. Facilitator for Thematic Poster Discussion, Interstitial Lung Diseases: Pathogenesis and Therapeutic Implications. American Thoracic Society 2004 Meeting

INVITED LECTURES/SEMINARS:

1. 'Chemokines and pulmonary fibroblasts: a fibrotic combination. Chemokines: latest advances and clinical outcomes. Cambridge, MA.
2. 'Weighing the pros and cons of pulmonary allergic responses to *Aspergillus fumigatus*.' American Society for Microbiology, New Orleans, LA.
3. 'Inflammation'. Symposium on Extracellular Matrix (SIMEC), Angra De Reis, Rio de Janeiro, Brazil

PATENTS

Treatment of liver disease and injury with ELR-CXC chemokines.

Filed August 9, 1999.

Awarded April 13, 2004.

Docket Number: 4100.000980.

Serial Number: **09/632,531**

US Patent Number: 6,719,969

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICAITON IN REFERRED JOURNALS.

1. Neff S.B., Neff T.A., Kunkel S.L., Hogaboam C.M. *Alterations in cytokine/chemokine expression during organ-to-organ communication established via acetaminophen-induced toxicity. Exp. Mol. Pathol.*, 75(3): 187-93, 2003.
2. Benjamin C. F., Hogaboam C.M., Lukacs N.W., Kunkel S.L. *Septic mice are susceptible to Aspergillosis. Am. J. Pathol.*, Dec; 163(6): 2605-17, 2003.
3. Ajuebor M.N., Zagorski J., Kunkel S.L., Strieter R.M., Hogaboam C.M. *Contrasting roles for CXCR2 during experimental colitis. Exp. Mol. Pathol.*, Feb; 76(1): 1-8, 2004.
4. Hogaboam C.M., Takahashi K., Ezekowitz R.A.B., Kunkel S.L., Schuh J.M. *Diminished airway hyperresponsiveness but not airway remodeling in mannose-binding-lectin-A-deficient mice during chronic fungal asthma. J Leukoc Biol.* May; 75(5): 805-14. Epub 2004 Feb 03.
5. Hildebrandt G.C., Duffner U.A., Olkiewicz K.M., Corrión L.A., Willmarth N.E., Williams D.L., Clouthier S., Hogaboam C.M., Reddy P.R., Moore B.B., Liu C., Yanik G., Cooke K.R. *A critical role for CCR2: MCP-1 interactions in the development of idiopathic pneumonia syndrome after allogeneic bone marrow transplantation. [Epub ahead of print], 2003. Blood*, Mar 15; 103 (6): 2417-26, 2004.
6. Kolodsick, J.E., Toews G.B., Jakubzick C., Hogaboam C.M., Moore T.A., McKenzie A., Wilke C.A., Chrisman C.J., Moore B.B. *Protection from FITC-induced fibrosis in IL-13 deficient, but not IL-4 deficient mice results from impaired collagen synthesis by fibroblasts. J. Immunol.*, Apr 1; 172(7): 4068-76, 2004.
7. Jakubzick C., Choi E.S., Kunkel S.L., Evanoff H., Martinez F.J., Puri R.K., Flaherty K.R., Toews G.B., Colby T.V., Kazerooni E.A., Gross B.H., Travis W.D., Hogaboam C.M. *Augmented pulmonary IL-4 and IL-13 receptor subunit expression in Idiopathic Interstitial Pneumonia. J. Clin. Pathol.*, 57: 477-486, 2004.

8. Jakubzick C., Choi E.S., Kunkel S.L., Evanoff H., Martinez F.J., Puri R.K., Flaherty K.R., Toews G.B., Colby T.V., Kazerooni E.A., Gross B.H., Travis W.D., Hogaboam C.M. *Human pulmonary fibroblasts exhibit altered IL-4 and IL-13 receptor subunit expression in Idiopathic Interstitial Pneumonia*. **Am. J. Pathol.**, 164: 1989-2001, 2004.
9. Choi E.S., Jakubzick C., Kunkel S.L., Evanoff H., Martinez F.J., Puri R.K., Flaherty K.R., Toews G.B., Colby T.V., Kazerooni E.A., Gross B.H., Travis W.D., Hogaboam C.M. *Enhanced Monocyte Chemoattractant Protein-3/CC chemokine Ligand-7 in Usual Interstitial Pneumonia*. **Am. J. Resp. Crit. Care Med.**, in press, 2004.
10. Ajuebor M.N., Swain M.G., Hogaboam C.M. *The role of CCL3/MIP-1 α in experimental colitis*. **Eur. J. Pharmacol.**, in press, 2004.
11. Ren X., Carpenter A., Hogaboam C.M., Colletti L.M. *Stem cell factor restores hepatocyte proliferation in TNF-receptor-1 knockout mice following 70% hepatectomy*. **Hepatology**, in press, 2004.
12. Jakubzick C., Matsukawa A., Wen H., Keller M., Kunkel S.L., Hogaboam C.M. *Role of CCR4 ligands, CCL17 and CCL22, during Schistosoma mansoni egg-induced pulmonary granuloma formation in mice*. **Am. J. Pathol.**, in press, 2004.
13. Ajuebor M.N., Hogaboam C.M., Le T., Proudfoot A.E.I., Swain M.G. *CCL3/MIP-1 α is pro-inflammatory in murine T cell-mediated hepatitis by recruiting CCR1-expressing IFN- γ producing CD4 (+) T cells to the liver*. **Eur. J. Immunol.**, in press, 2004.
14. Ramos C.D.L., Canetti C.A., Souto J.T., Silva J.S., Hogaboam C.M., Ferreira S.H., Cunha F.Q. *MIP-1 α /CCL3 acting on the CCR1 receptor mediates neutrophil migration in immune inflammation via sequential release of TNF- α and LTB $_4$* . **J. Leukoc. Biol.**, in press.
15. Ness T.L., Carpenter K.J., Ewing J.L., Hogaboam C.M., Kunkel S.L. *CCR1 and CCL5 interactions exacerbate innate immune responses during sepsis*. **J. Immunol.**, In press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Ajuebor M.N., Aspinall A.I., Zhou F., Le T., Yang Y., Sidobre S., Kronenberg M., Hogaboam C.M., Swain M.G. *Lack of chemokine receptor CCR5 promotes murine fulminant liver failure by preventing the apoptosis of IL-4-producing CD1d-restricted NKT cells*. **J. Clin. Invest.**, submitted.
2. Zhou F., Ajuebor M.N., Beck P., Le T., **Hogaboam C.M.**, Swain M.G. *CD154 expressing CD4+ T cells drive murine T cell mediated hepatitis via a novel cytokine-apoptotic cascade*. **J. Clin. Invest.**, submitted.
3. Benjamim C.B., Lundy S., Lukacs N.W., **Hogaboam C.M.**, Kunkel S.L. *Reversal of long-term sepsis-induced immunosuppression through intrapulmonary dendritic cell therapy*. **Nat. Med.**, submitted.
4. Lin N.J., Schuh J.M., **Hogaboam C.M.** *Maintenance of airway hyperresponsiveness in chronic asthma may be mediated by Th2-independent mechanisms*. **J. Allergy Clin. Immunol.**, submitted.
5. Matsukawa A., Maeda T., Sano G., Lukacs N.W., **Hogaboam C.M.**, Kunkel S.L., Lira S.A. *Absence of CC chemokine receptor 8 enhances innate immunity during septic peritonitis*. **J. Immunol.**, submitted.
6. Moore B.B., Kolodsick J.E., Thannickal V.J., Cooke K., **Hogaboam C.M.**, Wilke C.A., Toews G.B. *CCR2-mediated recruitment of fibrocytes to the alveolar space following fibrotic injury and their differentiation into effector fibroblasts*. **J. Immunol.**, submitted.

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

Chapters:

1. Schuh J.M., Hogaboam, C.M. *The innate and acquired pulmonary immune response to Aspergillus fumigatus.* In: **Fungal Immunology from an Organ Perspective.** Ed: G. Huffnagel, P. Fidel. In press, 2004.

Abstracts:

1. Benjamim C.F., Wen H., Hogaboam C., Lukacs N.W., Kunkel S.L., *Severe sepsis accelerates the formation of Th2 S. mansoni egg formation.* **FASEB J.** 18(4): A382.9, 2004.
2. Jakubzick C., Choi E.S., Carpenter K.J., Kunkel S.L., Evanoff H., Martinez F.J., Flaherty K.R., Toews G.B., Colby T.V., Travis W.D., Hogaboam C.M. *Enhanced CCL7 expression in usual interstitial pneumonia.* **Am J Respir Crit Care Med** 169:A706, 2004.
3. Moore B.B., Thannickal V.J., Hogaboam C., Toews G.B. *IL-13 α 1 expression and function on effector fibroblasts in fluorescein isothiocyanate-induced lung fibrosis.* **Am J Respir Crit Care Med** 169:A741, 2004.
4. Pierce B., Carpenter K.J., Jakubzick C., Kunkel S.L., Flaherty K.R., Martinez F.J., Hogaboam C.M. *A Novel Murine Model of Human IIP.* **Am J Respir Crit Care Med** 169, A862, 2004.

**JONATHON HOMEISTER, M.D.
RESEARCH INVESTIGATOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

None.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Title of grant" (Training Grant), Grant Number (5%), \$235,013/year (\$2,693,183/ten years), June 1, 1996 -May 31, 1997.
- B. Principal Investigator, "Lung Injury by Oxygen Metabolites", NIGMS-NIH-5-R37-GM-29507 (20%), \$262,568/year (\$1,271,378/five years), July 1, 1996 - June 30, 1997.

PENDING:

- A. Co-Investigator, "The Role of Cytokines and Adhesion Molecules in Thermal Injury", (5%), \$178,772/year (\$1,384,651/five years), with G.O. Till, Principal Investigator.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

None.

MEDICAL SCHOOL/HOSPITAL:

None.

UNIVERSITY OF MICHIGAN:

None.

REGIONAL AND NATIONAL:

None.

INVITED LECTURES/SEMINARS:

1. Invited Lecturer, "The Selectins in Animal Models of Acute Inflammation", in Symposium on Glycoconjugates and Contract Structures of the Cell Surface in Bonn, Germany, July 11-16, 1995.

VI. PUBLICATIONS:

BOOKS/CHAPTERS IN BOOKS:

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

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

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

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

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

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

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

PENDING SUPPORT:

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

PROJECTS UNDER STUDY:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

REGIONAL AND NATIONAL:

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

V. INVITED LECTURES AND SEMINARS

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

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Bednarski, J.J., Warner, R.E., Rao, T., Leonetti, F., Yung, R., Richardson, B.C., Johnson, K.J., Ellman, J.A., Opipari, A.W., Jr. Glick, G.D. Attenuation of autoimmune disease in Fas-deficient mice by treatment with a cytotoxic benzodiazepine. *Arthritis and Rheumatism*. 2003. 148(3):757-66.
2. Warner, R.L., Bhagavathula, N., Kamalakar, C.N., Lateef, H., Younkin, E., Johnson, K.J., Varani, J.: Matrix metalloproteinases in acute inflammation: induction of MMP-3 and MMP-9 in fibroblasts and epithelial cells following exposure to pro-inflammatory mediators in vitro. *Experimental and Molecular Pathology*. 2004. 76:189-195.
3. Saluja, M., Johnson, K.J., Bhat, S., Lange, L., Holzman, L., McCune, J.: Class V Lupus Nephritis: Correlation of membranous glomerular ultrastructural changes with disease severity and outcome in lupus patients initiating cyclophosphamide therapy. *Lupus*. In Press.
4. Jock, C.A., Paulauskis, J.D., Baker, D., Olle, E., Bleavins, M.R., Johnson, K.J. Heard, P.L.: Influence of matrix application timing on spectral reproducibility and quality in SELDI-TOF-MS. *Biotechniques*. In Press
5. Warner, R.L., Lukacs, N., Shapiro, S.D., Varani, J., Johnson, K.J.: Role of metalloelastase in a model of allergic lung responses induced by cockroach allergen. *American J. Pathology*. In Press
6. Glovsky, M.M., Ward, P.A., Johnson, K.J.: Complement determinations in human disease. *Annals of Allergy, Asthma and Immunology*. In Press
7. Warner, R.L., Winter, H.C., Speyer, C.L., Varani, J., Goldstein, I.J., Murphy, H.S., Johnson, K.J.: Marasmius oreades lectin induces renal thrombotic microangiopathic lesions. *Exp. Mol. Pathol.* In Press

ARTICLES SUBMITTED FOR PUBLICATION:

1. Warner, R.L., Younkin, E., Johnson, K.J., Varani, J.: Matrix metalloproteinase production by lung parenchymal cells. Submitted for publication.
2. Warner, R.L., Winter, H.C., Varani, J., Goldstein, I.J., Johnson, K.J.: Marasmius Oreades lectin induces kidney injury as a model of glomerular microangiopathic hemolytic anemia. Submitted for publication.
3. 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.
4. 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*.
5. 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.

6. J.D., Myc, A., Cao, Z., Johnson, K.J., Wright D.C., Brisker, J., and Baker, J.R.: Prevention of influenza A virus infection by non-ionic surfactant nanoemulsions in a murine model. Submitted for publication.
8. Heard, P.L., Bleavins, M.R., Johnson, K.J., Shi, M. and de la Iglesia, F.A.: Induction of Alanine Aminotransferase Gene Expression by Tacrine in Hep G2 Cells. Submitted for publication.
7. Fligiel, S.E.G., Standiford, T., Fligiel, H.M., Strieter, R.W., Tashkin, D., Warner, R.S., Johnson, K.J., Varani, J.: Matrix metalloproteinases (MMPs) and MMP inhibitors in acute lung inflammation. Submitted for publication.
8. Varani, J., Bhagavathula, N., Scherzer, H., Fay, K., Boitano, A.E., Glick, G. D., Johnson, K.J., Kang, S., Opipari, A.W.: A novel benzodiazepine selectively inhibits keratinocyte proliferation and reduces retinoid-induced epidermal hyperplasia in organ-cultured human skin. Submitted for publication.
9. Ren, X., Olle, E.W., McClintock, S., Warner, R.L., Caprenter, A., Johnson, K.J., Colletti, L.: MMP-9 as an important factor in hepatic regeneration following partial hepatectomy. Submitted for publication.
10. Olle, E.W., Skeekumar, S., Warner, R.L., McClintock, S., CHinnaiyan, A.M., Paulauskis, J.D., Bleavins, M.R., Anderson, T., Johnson, K.J.: Development of a pseudo-two color antibody array: An internally controlled microarray. Submitted for publication.
11. Patel, A., O'Toole, J., Normal, S., Shah, R., Johnson, K., Luan, F., Cibrik, D.: Treatment of BK nephropathy with intravenous immunoglobulin. Submitted for publication.
12. Fligiel, SEG., Standiford, T., Fligiel, H., Strieter, R.W., Tashkin, D., Warner, R.L., Johnson, K.J., Varani, J.: Matrix metalloproteinases (MMP's) and MMP inhibitors in acute lung inflammation. Submitted for publication.
13. Fligiel, SEG., Tashkin, D., Fligiel, H., Standiford, T., Johnson, K.J., Varani, J.: Matrix metalloproteinases (MMP's) and MMP inhibitors in chronic, habitual smokers of tobacco, marijuana and cocaine. 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.
5. Atlas of Rheumatology, Edited by Hunder. Current Medicine. In Press

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

1. Cibrik, D.M., Johnson, K.J., Delnomdedieu, M.: Visual 3D NMR spectroscopy of urine from renal transplant patient. ATC Meeting, 2003.

2. Rem X.M., Johnson, K.J., Senior, R.M., Shipley, J.M., Carpenter, A., Colletti, L.: MMP-9 is important for hepatic regeneration. *American College Surgery*. 2003.
3. Warner, R.L., Nerusu, K., Bhavarathula, N., McClintock, S., Johnson, K.J., Varani, J.: Alveolar wall damage and neutrophil transmigration is defective in stromelysin-1-deficient mice. *Experimental Biology*. 15 (5)866.10. 2003
4. Warner, R.L., McClintock, S., Varani, J., Johnson, K.J.: Macrophage cytokine production is defective in stromelysin-1-deficient mice. *Experimental Biology*. 15(5). 866.11. 2003.
5. Bagnoli, P., Tredici, S., Bull. J.L., Brant, D.O., Johnson, J., Costantino, M.L., Hirschl. R.B.: Preliminary histological results of repeated induced collapse of rabbit airways during total liquid ventilation. *ESAO Conference* 2004.
6. Warner, R.L., Winter, H.C., Speyer, C.L., Varani, J., Goldstein, I.J., Murphy, H.S., Johnson, K.J.: Marasmius oreades lectin induces renal thrombotic microangiopathic lesions: A model of hemolytic uremic syndrome. *Faseb J*. 2004.
7. McClintock, S., Ren, X., Olle, E., Warner, R.L., Colletti, L., Senior. R.M., Shipley, J.M., Carpenter, A., Johnson, K.J.: MMP-9 as an important factor in hepatic regeneration following partial hepatectomy. *Faseb J*. 2004

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003- 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

Resident Training/Contact Hours

- A. Clinical Pathology Grand Rounds:
 - 1. Program Director (CME Accredited Program 10016)
- B. Anatomical pathology Conferences:
 - 1. Program Coordinator (CME Accredited Program 10004)
- C. Core-Lecture Series in Blood Banking for 1st-year Pathology House Officers:
 - 1. Program Coordinator
 - 2. Presented lectures on:
 - a) Pretransfusion testing 4 hours
 - b) Prenatal/perinatal testing 4 hours
 - c) Immune hemolysis 4 hours
 - d) Antibody identification 4 hours
- D. Clinical Pathology Case Study Conference (CME Accredited Program 10021)
 - 1. Program Coordinator
 - 2. Participant 40 hours
- E. Management Lecture Series
 - 1. Developed/coordinated series of 8 lectures on laboratory management issues relative to Pathology Residents
- F. Ethics
 - 1. Departmental liaison, GME ethics program
 - 2. Incorporated four 1-hour sessions on ethical issues into the Residency Training Program
- G. Resident/Fellow Training
 - 1. Provided instruction in immunohematology to six house-officers during their Blood Bank Rotation (over 200 contact hours)
 - 2. Provided instruction in immunohematology to five haematology/oncology fellows (28 hours).
 - 3. Lan Zhou, MD, PhD, Blood Bank Fellow
- H. Current Topics in Blood Banking Conference, Towsley Center for Continuing Medical Education:

1. Program Director – Planned and coordinated the June, 2004 Current Topics in Blood Banking Symposium and Preconference Workshops 11.5 hours
2. Presented Workshop entitled: Prenatal-Perinatal Testing. 3.5 hours
3. Presented talk entitled: Validating your life away.
4. Moderated afternoon session on Controversies/New Horizons
5. Moderated Ask the Experts sessions

III. RESEARCH ACTIVITIES:

- A. Lectin studies, with Irwin Goldstein, PhD.
- B. Davenport RD, Judd WJ, Dake LR. Persistence of cefotetan on red blood cells. *Transfusion* 2003;43(S):1.
- C. Principal Investigator, field trial on automated blood typing system (Ortho Clinical Diagnostics).
- D. Sturgeon JK, Whelchel SD, Chance N, Mann N, Judd WJ, Barker C, Lori S, Sturgill K, Weinheimer M. Use of Reader SATM for serological consultation with a Immunohematology Reference Laboratory. *Transfusion* 2003;43(S):93.
- E. Judd WJ, Cooling L. Novel application of the gel test: detection of microbial-induced hemagglutination. *Vox Sang* 2004;87(S3):76-7.
- F. Dake LR, Judd WJ, Davenport RD. On a much higher incidence of anti-c in R1R1 patients with anti-E. Abstract accepted for poster presentation.

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

- A. Blood Bank Daily Rounds.
- B. Weekly Blood Bank Communication Meetings.
- C. Monthly Clinical Pathology Faculty Meetings.
- D. CP Resident's Training Committee

REGIONAL/NATIONAL/INTERNATIONAL:

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

V. **OTHER RELEVANT ACTIVITIES:**

INVITED LECTURES:

1. Validating your life away. Blood group serology, 2004. Durham, UK, April 2004.
2. P, p-fimbrae, piliation and polyagglutination. University of Lund, Sweden, April 2004.

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

1. Loganathan D, Winters H, Judd WJ, Petryniak J, Goldstein IJ. Immobilized *Marasmius oreades* agglutinin: use for binding and isolation of glycoproteins containing the xenotransplantation or human type B epitopes. *Glycobiology* 2003;13:955-60.
2. Judd WJ. International forum: current status of immunoprophylaxis with anti-D immunoglobulin. *Vox Sang* 2003;329-30.
3. Davenport RD, Judd WJ, Dake LR. Persistence of cefotetan on red blood cells. *Transfusion* 2004;44:849-52.

CHAPTERS IN BOOKS:

1. Practice guidelines for prenatal/perinatal testing. Bethesda, MD: American Association of Blood Banks, in press.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003-30 JUNE 2004**

I CLINICAL ACTIVITIES

- A. General Surgical pathology: Twelve weeks
- B. Genito-Urinary Pathology Subspecialty service : Eighteen weeks
- C. Genito- Urinary Pathology Transfer (TS) cases : Twenty six weeks
- D. Genito-Urinary Pathology Consultation service: Five weeks
- E. Urology Tumor Board : Biweekly, 12 months
- F. Rapid warm autopsies coverage for advanced prostate cancer: 24/7 availability, 12 months

II TEACHING ACTIVITIES

- A. Medical Students:
 - 1. M-2 GU Pathology Lab Sequence: 2 hours lab session
- B. House Officers and GU Fellow:
 - 1. Surgical Pathology Diagnosing Room Teaching for House Officers : Twelve weeks
 - 2. GU Pathology Diagnosing Room Teaching for HO & Fellow: Eighteen weeks
 - 3. GU Pathology TS/Consult cases Teaching for GU fellow : Twenty six weeks
 - 4. Didactic Lecture on Testicular tumors for House Officers : One, Sep'03
- C. Interdepartmental:
 - 1. GU Pathology teaching sessions with Urology Residents : One hour/bimonthly

III RESEARCH ACTIVITIES

SPONSORED SUPPORT

- 1. Co-Investigator- 2/2004, University of Michigan Grant- Bladder Cancer (Tissue Blood/ Urine/Data) Bank. (P.I. Cheryl T Lee)
- 2. Co-Investigator- 4/18/2004, University of Michigan Grant -Clinical Characterization Of Uroplakin Expression in Human Bladder Cancer. (P.I. Cheryl T Lee)
- 3. Co-Investigator-6/24/2004, University of Michigan Grant- Characterization of Neoadjuvant Paclitaxel, Carboplatin and Gemcitabine Response in Locally Advanced Bladder Cancer. (P.I Cheryl T Lee)

PENDING SUPPORT

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

IV PROJECTS UNDER STUDY

- A. Comparison of monoclonal P504S and polyclonal antibody to Alpha Methylacyl Co A Racemase in the work-up of Atypical Prostatic Glandular Proliferations in Prostate needle biopsies: A Prospective Study
- B. Papillary Renal Carcinoma: Focus on Morphologic Sub typing and correlation with Clinicopathologic and Immunohistochemical parameters.
- C. Role of image-guided core biopsy in renal masses: Evaluation of adequacy, sensitivity and accuracy of diagnosis.
- D. Significance of positive proximal urethral margin in radical prostatectomy: does the presence of benign prostate glands make a difference?
- E. Minimally Invasive Radical Prostatectomy: Initial experience and evaluation of clinicopathologic parameters
- F. Characterization of protein expression and frequency of Uroplakin (UP-1a, UP1b, UPII and AU1) in human bladder cancer.
- G. Co-Investigator- Characterization of Neoadjuvant Paclitaxel, Carboplatin and Gemcitabine Response in locally advanced bladder cancer.
- H. Evaluation of Stathmin as a Marker of Metastatic Prostate cancer using tissue micro-arrays.
- I. Use of tissue micro arrays to identify biomarkers in renal carcinomas treated with interleukin- 2.

V ADMINISTRATIVE ACTIVITIES

DEPARTMENTAL

- A. Faculty Candidate interviews

VI PUBLICATIONS

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS

- 1. Kunju Lakshmi, Rubin Mark, Chinnaiyan Arul and Shah Rajal. Diagnostic Usefulness of Monoclonal Antibody P504S in the Work-up of Atypical prostatic glandular proliferations. Am J Clin Pathol 2003;120;737-45
- 2. Shah Rajal, Kunju Lakshmi, Shen Ronglai, Leblanc Michelle, Zhou Ming and Rubin Mark. Usefulness of Basal Cell Cocktail (p63 + 34betaE12) in Diagnosis of Atypical Prostate Glandular Proliferations. Am J Clin Pathol, In Press.

ARTICLES SUBMITTED FOR PUBLICATION

- 1. Kunju Priya L, Lee Cheryl, Montie James and Shah Rajal. Utility of Cytokeratin 20 and MIB-1 as Markers of Urothelial Dysplasia. Submitted to Am J Clin Pathol, Aug 2004.

PRESENTATIONS

1. Cytokeratin 20 and Ki-67 as Markers of Urothelial Dysplasia. Platform Presentation at United States and Canadian Academy of Pathology, Vancouver, March 2004.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO EDITOR

1. LP Kunju , M Snyder, C Lee, J Montie and RB Shah. Cytokeratin 20 and Ki-67 as markers of Urothelial Dysplasia. Mod Pathol 17 (1): 681, Jan 2004
2. M Snyder, R Mehra, LP Kunju, J Montie and RB Shah. Utility of a Novel Immunohistochemical Panel (PSA, high Molecular Weight Cytokeratin and/or p63) in the Differentiation of Poorly Differentiated Prostate Adenocarcinoma from Urothelial Carcinoma

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

None

II. TEACHING ACTIVITIES:

- A. Host Defense Sequence, First Year Medical School
- B. Case Reports First Year Medical Students
 - 1. Grand rounds: Pediatrics
- C. Academic Advisor, Immunology graduate program
- D. Operating committee Graduate Program in Immunology
- E. 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/serve on thesis committee the following postdoctoral fellows, graduate students, medical Students and undergraduates:
 - Fellows: Jane Schuh, Claudia Benjamim, Ana Steven Lundy, Traci Ness, Ana Lucia
 - Graduate Students ; Hiatal Chen, Claudia Jakubzick
 - Undergraduate Students: Ester Choi, Ted Martens, Jillian Ewing, Susan Lewis, Harriet Weber, Laura Westwick
- P. Doctoral Thesis Committee Member/Orals Committee for the following graduate students: Haital Wen (Pathology), Chinh Tran (Immunology), Andrea Waite (CMDDB), Anavelys Ortiz-Suarez (CMB) Tina Yee (Micro/Immunology), John Marrow (MSTP, Neuroscience)

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 (pending priority score 138)
- D. SCOR Occupational and Immunological Lung Disease, P50HL-46487 Principal Investigator for Project 3
- E. SCCOR Acute Lung Injury, P50HL60289, Principal Investigator Project 3.

PROJECTS UNDER STUDY:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL/UNIVERSITY:

- A. Member, Committee on medical student research
- B. Medical school admission interview committee
- C. Medical scientist training program interviewer
- D. Member MMP Microbiology Molecular mechanisms in Microbial Pathogenesis Training Program
- E. Member, Research Council of the Office of the Vice President for Research
- F. Member, Michigan cancer center
- G. Grant reviewer, Biomedical Research Council
- H. Member, Advisory Committee Cancer Center Animal Core
- I. Associate Dean for Interdisciplinary Programs, Rackham Graduate School
- J. CMB Advisory Committee
- K. Dean's Research Advisory Board
- L. Medical School Space master Plan Steering Committee
- M. Medical School Communications Advisory Committee
- N. Member, Advisory committee on Medical School appointments, promotions, and tenure
- O. Member, Human Research Coordinating Council
- P. Member, Dean's Task Force on Rodent Populations
- Q. Committee of associate chairs for research

- R. Member, LCME Self-Study group
- S. Associate Dean, Rackham Graduate School
- T. Interim Dean Rackham Graduate School
- U. Member, search committee for Chair of Microbiology/immunology
- V. Member, search committee Chair of Biomaterial Sciences (Dental School)
- W. Member, search committee for Chair of Pathology Department
- X. Member, search committee faculty recruit ULAM
- Y. Member PEERS accreditation team for OVPR

REGIONAL AND NATIONAL

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

V. OTHER RELEVANT ACTIVITIES:

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

INVITED LECTURES AND SEMINARS:

1. Keynote Speaker, Anti-inflammatory Effects of Macrolides, Tokyo, Japan, July 2003.
2. Plenary Lecturer, 6th World Congress on Inflammation, Vancouver, Canada, August 2003
3. Invited Speaker, Immunology lecture series, University of Cincinnati, September, 2003
4. Grand Rounds Presenter; Lilly Lecture Series, Indianapolis, IN, October 2003
5. Invited Speaker, Science Lecture Series, Gryphon Sciences, San Francisco, CA, Nov 2003
6. Invited Speaker, Association of University Pathologists, Cozumel, Mexico, Feb 2004
7. Keynote Speaker, Inflammation Research Association, Boston, MA Feb 2004
8. Plenary Lecturer, Society of Medicines Research, London, UK, March 2004
9. Invited Speaker, Novartis, Horsham, England, March 2004.
10. Invited Speaker, COPD: The Important Questions, Marbella, Spain, April 2004,
11. Invited Lecturer, Wayne State University, Detroit, MI, April 2004
12. Invited Speaker, Innate Immunity and Vaccine Development, Annessey, France, June 2004,

VI. PUBLICATIONS

ARTICLES PUBLISHED IN REFEREED JOURNALS

1. Jakubzick, CJ, Choi, ES, Joshi, BH, Keane, MP, Kunkel SL, Puri, RK, Hogaboam, CM. Therapeutic attenuation of pulmonary fibrosis via targeting of IL-4 and IL-13 responsive cells. *J. Immunol* 2003; 171:2684-2693.
2. Stamatovic SM, Keep RF, Kunkel SL, Andjelkovic AV. Potential role of MCP-1 in endothelial cell tight junction 'opening': signaling via Rho and Rho kinase. *J Cell Sci.* 2003 Nov 15;116(Pt 22):4615-28.
3. Schuh JM, Blease K, Kunkel SL, Hogaboam CM. Chemokines and cytokines: axis and allies in asthma and allergy. *Cytokine Growth Factor Rev.* 2003 Dec;14(6):503-10.
4. Ness TL, Hogaboam CM, Strieter RM, Kunkel SL: Immunomodulatory role of CXCR2 during experimental septic peritonitis. *J Immunol.* 2003 Oct 1;171(7):3775-84.
5. Kunkel SL, Chensue SW, Lukacs N, Hogaboam C. Cytokine phenotypes serve as a paradigms for experimental immune-mediated lung diseases and remodeling. *Am J Respir Cell Mol Biol.* 2003; 29:S63-6.
6. Neff SB, Neff TA, Kunkel SL, Hogaboam CM. Alterations in cytokine/chemokine expression during organ-to-organ communication established via acetaminophen-induced toxicity. *Exp Mol Pathol.* 2003 Dec;75(3):187-93.
7. Gharaee-Kermani M, McCullumsmith RE, Charo IF, Kunkel SL, Phan SH. CC-chemokine receptor 2 required for bleomycin-induced pulmonary fibrosis. *Cytokine.* 2003 Dec 21;24(6):266-76.
8. Varma MR, Varga AJ, Knipp BS, Sukheepod P, Upchurch GR, Kunkel SL, Wakefield TW, Henke PK. Neutropenia impairs venous thrombosis resolution in the rat.. *J Vasc Surg.* 2003 Nov;38(5):1090-8.
9. Benjamim CF, Hogaboam CM, Kunkel SL. Septic mice are susceptible to pulmonary aspergillosis. *Am J Pathol.* 2003 Dec;163(6):2605-17.
10. Benjamim CF, Hogaboam CM, Kunkel SL. The chronic consequences of severe sepsis. *J Leukoc Biol.* 2004 [Epub ahead of print]
11. Jakubzick C, Choi ES, Kunkel SL, Evanoff H, Martinez FJ, Puri RK, Flaherty KR, Toews GB, Colby TV, Kazerooni EA, Gross BH, Travis WD, Hogaboam CM. Augmented pulmonary IL-4 and IL-13 receptor subunit expression in idiopathic interstitial pneumonia. *J Clin Pathol.* 2004 May;57(5):477-86.
12. Ye, Ping, Kazanjian, P., Kunkel, SL, Kirschner, DE. Lack of good correlation of serum CC-Chemokine levels with human immunodeficiency virus-1 disease stage and response to treatment. *J Lab Clin Med.* 2004 May;143(5):310-9
13. Ajuebor MN, Zagorski J, Kunkel SL, Strieter RM, Hogaboam CM. Contrasting roles for CXCR2 during experimental colitis. *Exp Mol Pathol.* 2004 Feb;76(1):1-8
14. Hogaboam CM, Takahashi K, Ezekowitz RA, Kunkel SL, Schuh JM. Mannose-binding lectin deficiency alters the development of fungal asthma: effects on airway response, inflammation, and cytokine profile.. *J Leukoc Biol.* 2004 May;75(5):805-14
15. Henke PK, Varga A, De S, Deatrick CB, Eliason J, Arenberg DA, Sukheepod P, Thanaporn P, Kunkel SL, Upchurch GR Jr, Wakefield TW. Deep Vein Thrombosis Resolution Is Modulated by Monocyte CXCR2-Mediated Activity in a Mouse Model. *Arterioscler Thromb Vasc Biol.*

- 2004 Apr 22 [Epub ahead of print]
18. Jakubzick C, Choi ES, Carpenter KJ, Kunkel SL, Evanoff H, Martinez FJ, Flaherty KR, Toews GB, Colby TV, Travis WD, Joshi BH, Puri RK, Hogaboam CM. Human pulmonary fibroblasts exhibit altered interleukin-4 and interleukin-13 receptor subunit expression in idiopathic interstitial pneumonia. *Am J Pathol*. 2004 Jun;164(6):1989-2001.
 19. Choi ES, Jakubzick C, Carpenter KJ, Kunkel SL, Evanoff H, Martinez FJ, Flaherty KR, Toews GB, Colby TV, Kazerooni EA, Gross BH, Travis WD, Hogaboam CM. Monocyte Chemoattractant Protein-3/CC Chemokine Ligand-7 in Usual Interstitial Pneumonia. *Am J Respir Crit Care Med*. 2004 Jun 10 [Epub ahead of print]
 20. Thomas MS, Kunkel SL, Lukacs NW. Regulation of cockroach antigen-induced allergic airway hyperreactivity by the CXCR3 ligand CXCL9. *J Immunol*. 2004 Jul 1;173(1):615.

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

**DEPARTMENT OF PATHOLOGY
1 JULY 2003 – 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

- A. Graduate students and postdoctoral fellows:
 - 1. Responsible during the current academic year for teaching activities for the following:
 - a. Monzy Thomas, Ph.D. (postdoctoral fellow)
 - b. Zhigang Yu, M.D. (postdoctoral fellow)
 - c. Christopher Pacheco (thesis student)
 - 2. Rotating graduate student
 - a. Jennifer Plane, Neuroscience Graduate Program
 - 3. Thesis committee member
 - a. Valerie Drews, Neuroscience Graduate Program
 - b. Jennifer Harrell, Pharmacology Graduate Program
 - 4. Preliminary examination committee member
 - a. Meghan Brennan, Pathology Graduate Program
 - b. Yunfang Min, Pathology Graduate Program
 - c. Xiaoyu Jia, Pathology Graduate Program
- B. Lecturer on neurodegenerative disease, pathology house officers
- C. Lecturer and laboratory instructor, M2 Pathology, Neuroscience Sequence
- D. Instructor, Pathology/Radiology elective for M4 students
- E. Course director and instructor, Pathology 858
- F. Member, Neuroscience Graduate Program
- G. Member, Pathology Graduate Program

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, Paul Beeson Career Development Award in Aging Research, NIH and American Federation for Aging Research, K08 AG024758, "Modifiers of polyglutamine toxicity", 75%, \$200,000/yr (\$600,000/5 yr), 8/1/04 – 5/31/07

- B. Principal Investigator, Muscular Dystrophy Association, "Altered androgen receptor function in Kennedy's disease", 5%, \$73,409/yr (\$219,000/3 yr), 7/1/02 – 6/30/05
- C. Principal Investigator, Kennedy's Disease Association, "A knock-in mouse model of Kennedy's disease", 0%, \$23,810/yr, 3/1/04 – 2/28/05
- D. Principal Investigator, Nathan Shock Center of Excellence in Aging Mutant and Transgenic Rodent Core, "A knock-in mouse model of Kennedy's disease", 0%, \$22,584/2 yr, 7/1/03 – 6/30/05
- E. Principal Investigator, Biomedical Research Council University of Michigan, "Early death of mutant males in a knock-in mouse model of Kennedy's disease", 0%, \$30,000/yr, 7/1/04 – 6/30/05
- F. Principal Investigator, Atorvastatin Research Award, Pfizer, "Understanding the neuropathology of Niemann-Pick C through mouse models", 0%, \$45,000/yr (\$90,000/2 yr), 7/1/04 – 6/30/06
- G. Core Principal Investigator, Michigan Alzheimer's Disease Research Center, NIH, P50 AG08671, 15%, "Neuropathology Core", \$47,034/yr, 6/1/99 – 5/31/05
- H. Principal Investigator, Muscular Dystrophy Association, "A knock-in mouse model of Kennedy's disease", 5%, \$90,000/yr (\$270,000/3yr), 7/1/04 – 6/30/07
- I. Sponsor/Mentor, (Christopher Pacheco, Principal Investigator), NIH, F31 NS51143, "Understanding Niemann-Pick C with cell and mouse models", 0%, \$41,076/yr (\$164,304/4yr)

PROJECTS UNDER STUDY

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

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

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

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

III. RESEARCH ACTIVITIES:

SOFTWARE DEVELOPMENT:

PathView Image Database – Software Disclosure (U of Michigan 2000)
Profiler, Tissue Microarray & Genomics DB Module (under PathView) – Disclosure July 2002
Diagnostic Hierarchy – schema development in MS Access, with link to Oracle 8i

SPONSORED SUPPORT:

None

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Member, Pathology Bioinformatics, Department of Pathology.

MEDICAL SCHOOL/HOSPITAL:

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

UNIVERSITY OF MICHIGAN:

None.

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

- 1. “Clinical Impact of Bethesda System Guidelines,” James A. French Society, Campus Inn, Ann Arbor, October 2003.
- 2. Three hours, clinical pathologic correlation lectures. 39th Annual Northern Michigan Summer Conference. Shanty Creek, Michigan. June 21-23, 2004.

VI. PUBLICATIONS:

ARTICLES PUBLISHED IN REFEREED JOURNALS:

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

BOOKS/CHAPTERS IN BOOKS:

None.

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

PUBLICATIONS (non-peer reviewed):

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

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004

I. CLINICAL ACTIVITIES:

- A. Dermopathology Service – 12 months.
- B. Dermopathology Consultation Service (including MLabs and Veterans Administration Hospital) – 12 months.

II. TEACHING ACTIVITIES:

- A. Medical Students:
 - 1. Lecturer, MS II Dermatology Sequence (2 hours full class lecture)
 - 2. Dermopathology laboratory director and instructor, MS II Dermatology Sequence (2 contact hours)
 - 3. Dermopathology, Pathology Clerkship, MS I and MS IV students (4 students).
- B. House Officers:
 - 1. Dermopathology sign-out (Pathology and Dermatology Residents).
 - 2. Review of dermatopathology consultation material.
 - 3. Dermopathology teaching conference (weekly-twice monthly).
- C. Diagnostic Conference, Department of Dermatology (weekly).
- D. Director of Diagnostic Conference, Department of Dermatology – (2 hours/month)
- E. Hospital Conferences:
 - 1. Multidisciplinary Melanoma Conference (twice monthly).
- F. Honors:
 - 1. Listed in *Best Doctors in America 2003-2004*
 - 2. *Token of Appreciation from Medical Students (TAMS) AWARD*, awarded by The University of Michigan Medical School Class of 2004

III. RESEARCH ACTIVITIES:

Sponsored Support:

Patient Examination with MelaFind™ system developed by Electro-Optical Sciences, Inc. (EOS). 2001 Jennifer L. Schwartz, M.D., Timothy M. Johnson, M.D., Timothy S. Wang, M.D., Darius J. Karimipour, M.D., Jeffrey S. Orringer, M.D., Lori Lowe, M.D., Lyndon Su, M.D., Doug Fullen, M.D., Christopher Bichakjian, M.D., Mitzi Rabe, R.N. (Study ongoing through 2004) \$5,750.

Projects under Study:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director, Dermatopathology Service, Department of Pathology, University of Michigan
- B. Member, Advisory Committee on Appointments, Promotions, and Tenure (ACAPT), Department of Pathology, University of Michigan
- C. Member, Residency Review Committee, Department of Dermatology, University of Michigan
- D. Coordinator, QA/QC program (Mohs surgery slides), Cutaneous Surgery and Oncology Program, Department of Dermatology, University of Michigan
- E. Member, Multidisciplinary Melanoma Program, University of Michigan Comprehensive Cancer Center
- F. Member, Search Committee, University of Michigan Health System, Pathology/Radiology Billing Manager (12/2003-2/2004)
- G. Interviewer, Pathology House Officer Candidates

REGIONAL AND NATIONAL:

- A. **Editorial Board, *Cancer*, Skin Section Editor**
- B. Editorial Board, *Journal of the American Academy 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, *The American Journal of Dermatopathology*
- G. Ad hoc manuscript reviewer, *Journal of Cutaneous Pathology*
- H. Ad hoc manuscript reviewer, *Dermatologic Surgery*
- I. Ad hoc manuscript reviewer, *Human Pathology*

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Basic Self-Assessment in Dermatopathology, faculty, American Academy of Dermatology Annual Meeting, Washington DC, February 2004.
2. Advanced Self-Assessment in Dermatopathology, faculty, American Academy of Dermatology Annual Meeting, Washington DC, February 2004.
3. "The Conundrum of Melanocytic Terminology: Atypical Nevi and Atypical Junctional Melanocytic Hyperplasia," invited seminar, Topics in Pathology, Pathology and Laboratory Medicine, VAAHS and University of Michigan Medical School, February 2004.
4. "The Conundrum of Melanocytic Terminology: Atypical Nevi and Atypical Junctional Melanocytic Hyperplasia. What you need to know to manage your patient," invited seminar, Dermatology Foundation: Clinical Symposia, Amelia Island, Florida, March, 2004.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Pacella SJ, **Lowe L**, Bradford C, Marcus BC, Johnson TM, Rees R: The utility of sentinel lymph node biopsy in head and neck melanoma in the pediatric population. *Plast Reconstr Surg* 112: 1257-1265, 2003.
2. Altman JF, **Lowe L**, Redman B, Esper P, Schwartz JL, Johnson TM, Haefner HK: Placental metastasis of maternal melanoma. *J Am Acad Dermatol* 49: 1150-1154, 2003.
3. Wechter ME, Reynolds KR, Haefner HK, **Lowe L**, Gruber SB, Schwartz JL, Johnston CM, Johnson TM: Vulvar melanoma: Review of diagnosis, staging and therapy. *Journal of Lower Genital Tract Disease* 8: 58-69, 2004.
4. Su LD, Fullen DR, **Lowe L**, Wang TS, Schwartz JL, Cimmino VM, Sondak VK, Johnson TM: Desmoplastic and neurotropic melanoma. Analysis of 57 cases, including 33 cases with lymphatic mapping and sentinel lymph node biopsy. *Cancer* 100: 598-604, 2004.
5. DuBay D, Cimmino V, **Lowe L**, Johnson TM, Sondak VK: Low recurrence rate after surgery for dermatofibrosarcoma protuberans: A multidisciplinary approach from a single institution. *Cancer* 100: 1008-1016, 2004.
6. Wechter ME, Gruber SB, Haefner HK, **Lowe L**, Schwartz JL, Reynolds KR, Johnston CM, Johnson TM: Vulvar melanoma: a report of 20 cases and review of the literature. *J Am Acad Dermatol* 50: 554-562;2004.
7. Karimipour DJ, **Lowe L**, Su L, Hamilton T, Sondak V, Johnson TM, Fullen D: Melanoma sentinel lymph node biopsy: utility and sensitivity of standard immunostains. *J Am Acad Dermatol* 50: 759-764, 2004.
8. Sondak VK, Taylor JMG, Sabel MS, Wang Y, **Lowe L**, Grover AC, Chang AE, Yahanda AM, Moon J, Johnson TM: Mitotic rate and younger age are predictors of sentinel lymph node positivity: Lessons learned from the generation of a probabilistic model. *Ann Surg Oncol* (in press)

9. Rosi YL, **Lowe L**, Kang S: Treatment of hidradenitis suppurativa with Infliximab in a patient with Crohn's disease. *Journal of Dermatologic Treatment* (in press)

ARTICLES SUBMITTED FOR PUBLICATION:

1. Sabel MS, Griffith K, Sondak VK, **Lowe L**, Cimmino V, Chang AE, Johnson TM: Predictors of non-sentinel lymph node positivity in patients with a positive sentinel node for melanoma. *Ann Surg Oncol* 2004.
2. Cho S, **Lowe L**, Hamilton TA, Fisher GJ, Voorhees JJ, Kang S: Long term treatment of photoaged human skin with topical retinoic acid improves epidermal cell atypia and thickens collagen band in the papillary dermis. *Arch Dermatol* 2004.
3. Schmalbach CE, **Lowe L**, Teknos TN, Johnson TM, Bradford CR: Reliability of sentinel lymph node mapping with biopsy for identifying regional spread of head and neck Merkel cell carcinoma. *Arch Otolaryngol* 2004.

CHAPTERS IN BOOKS:

1. Marder W, Lath V, Crofford L, **Lowe L**, McCune WJ: Systemic lupus erythematosus, scleroderma and myositis. In: Hunder G (ed): *Atlas of Rheumatology*, 4th edition (Philadelphia, PA: Current Medicine LLC, 2004). (in press).
2. **Lowe L**: Deposition Disorders: Fitzpatrick JE, Morelli J (eds): *Dermatology Secrets in Color* (Philadelphia, PA: Elsevier, 3rd edition, 2004), in press.

ABSTRACTS, BOOK REVIEWS, PRELIMINARY COMMUNICATIONS, PANEL DISCUSSIONS:

1. Borschel GH, Johnson TM, **Lowe L**, Brown DL: Total peripheral margin control of facial atypical junctional melanocytic hyperplasia using the "square" technique. American Society of Plastic Surgery Annual Meeting, San Diego, California, October, 2003.
2. Schmalback, **Lowe L**, Teknos TN, Johnson TM, Bradford CR: Reliability of sentinel lymph node mapping with biopsy for identifying regional spread of head and neck Merkel cell carcinoma. 6th International Conference on Head and Neck Cancer, Washington D.C., August 2004.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

- A. Surgical pathology - 24 weeks
- B. Bone and soft tissue pathology consultation – 12 months

II. TEACHING ACTIVITIES:

- A. Medical/Dental Students
 - 1. Pathophysiology 540 (dental students)- 3 class lecture hours
 - 2. Pathophysiology, Connective Tissue Unit (Wayne State University medical students), Course Director and 3.5 class lecture hours
- B. House Officers
 - 1. Surgical pathology sign-out – 24 weeks
 - 2. Bone and soft tissue pathology elective – 5 house officers, 1month each
 - 3. Lectures in bone pathology – 2 hours
 - 4. Consultant conferences – 2 hours

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. RTOG 0330, A pilot phase II study of pre-operative radiation therapy and thalidomide (IND 48832; NSC 66847) for low grade primary soft tissue sarcoma or pre-operative MAID/thalidomide/radiation therapy for high/intermediate grade primary soft tissue sarcoma of the extremity or body wall. Study chair: Burton L. Eisenberg, M.D.
- B. Primary versus radiation-associated craniofacial osteosarcoma: biologic and clinicopathologic comparisons. First author: Jonathan McHugh, M.D., PGY3
- C. Immunohistochemical study comparing useful and new markers in MPNST, synovial sarcoma, and Ewing's sarcoma. First author: Stephen Olsen, M.D., PGY4
- D. Multiplex RT-PCR/capillary electrophoresis to detect and genotype characteristic translocations from formalin-fixed soft tissue tumor specimens. Principle investigator: John Thorson, M.D.

PENDING:

- A. S0346, Phase II study of trastuzumab (NSC-688097), celecoxib or the combination in treatment of recurrent synovial sarcoma (SWOG trial). Study coordinator: Laurence Baker, M.D.
- B. Radomized trial of neoadjuvant adriamycin/ifosfamide vs. gemcitabine/taxitol in high grade soft tissue sarcoma (U of M trial). Principal investigator: Mark Zalupski, M.D.

IV. ADMINISTRATIVE ACTIVITIES:

REGIONAL AND NATIONAL:

- A. Abstract Review Board, Bone and Soft Tissue Pathology, United States and Canadian Academy of Pathology

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Bone and Soft Tissue Specialty Conference, What is New in Pathology of Osteochondroma? United States and Canadian Academy of Pathology, March 9, Vancouver.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Lucas DR, Pass HI, Madan SA, Adsay VA, Wali A, Tabaczka P, Lonardo F. Sarcomatoid mesothelioma and its histologic mimics: a comparative immunohistochemical study. *Histopathology* 42:270-9, 2003.
2. Lonardo F, Pass HI, Lucas DR. Immunohistochemistry frequently detects c-kit expression in pulmonary small cell carcinoma and may help select clinical subsets for a novel form of chemotherapy. *Appl Immunohistochem Mol Morphol*. 11:51-5, 2003.
3. Miller PR, Johnson SC, Lucas DR, Nasser S. Post-arthroplasty hip dysfunction: Imaging and intervention. *The Radiologist* 10:39-54, 2003.
4. Lucas DR, Al-Abbadi M, Tabaczka P, Hamre MR, Weaver DW, Mott MJ. c-kit expression in desmoid fibromatosis: comparative immunohistochemical evaluation of two commercial antibodies. *Am J Clin Pathol* 119:339-345, 2003
5. Zhang H, Lucas DR, Pass HI, Che M. Disseminated malignant solitary fibrous tumor of the pleura. *Path Int* 54:111-5, 2004
6. Zalupski M, Rankin C, Lucas D, Muler J, Ryan J. Adjuvant therapy of osteogenic sarcoma, a phase II trial: Southwest Oncology Group Study 9139 *Cancer* 100(4):818-25, 2004.
7. Mendelson S, Wooley P, Lucas D, Markel D, The effect of hyaluronic acid on a rabbit model of full-thickness cartilage repair. *Clin Ortho* 1(424), 266-271, 2004
8. Hamre M, Severson R, Chuba P, Thomas R, Lucas DR, Mott MP. Second malignant neoplasms (SMNS) after primary sarcomas of childhood and adolescence. (In Press)
9. Kraybill W, Spiro I, Harris J, Ettinger D, Trotti A, Lucas D, Blum R, Eisenberg B, RTOG 95-14: Phase II study of neoadjuvant chemotherapy and radiation therapy compared with radiation therapy in the management of high-risk, high-grade soft tissue sarcomas of the extremities and body wall. *J Clin Oncol* (In Press)

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

1. Ali-Fehmi R, Silva E, Sakr W, Lucas D, Che M, Dey J, Adsay V. The challenge in distinguishing metastatic ovarian and pancreatobiliary carcinomas in the abdomen and the morphologic criteria for their distinction. *Mod Pathol* 16, 180A, 2003.
2. Chitlur MB, Devarahally SS, Severson RK, Lucas DR, Ravindranath Y, Hamre MR. Concurrent cancers in childhood and adolescence. *Pediatr Res* 53: 300A
3. Al-Abbadi MA, Saleh HA, Lucas DR, Tabaczka PM. Differential expression of her-2/neu receptor of invasive mammary carcinoma between caucasian and African American patients in the Detroit metropolitan area. Correlation with Overall Survival and Other Prognostic Factors. *Mod Pathol* 17(Sup. 1), 21A, 2004
4. Al-Abbadi MA, Washington TA, Tekyi-Mensah E S, HA Saleh, DR Lucas, CA Briston. Fine needle aspiration of lymph nodes as an initial diagnostic tool: retrospective and prospective study of 160 cases combining cytomorphology and immunophenotypic analysis by flow cytometry with emphasis on a specific technique for optimal cellular procurement. *Mod Pathol* 17(Sup. 1), 61A, 2004

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

- A. Sign-out of breast pathology transfer cases and extramural breast pathology consultation cases; 20 weeks
- B. Review of breast pathology cases for multidisciplinary breast care clinic; 20 weeks
- C. Pathology representative, weekly interdisciplinary Breast Care Conference; 20 weeks

II. TEACHING ACTIVITIES:

- A. Medical Students (M2):
M2 Pathology Laboratory Instructor (Respiratory, Bone/Soft Tissue sequences); 18 hours
- B. House Officers:
Instruction of breast pathology fellow; 20 weeks

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

CURRENT:

- A. Principal Investigator, "NF-kB Signaling and the Molecular Pathogenesis of MALT Lymphoma" (Mentored Career Development Award), K08 CA094920-02 (80%), National Institutes of Health, \$684,500 (total direct costs), 7/1/02 – 6/30/07.

PROJECTS UNDER STUDY:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

- A. Career Advisory Panel, Medical Scientist Training Program

V. **OTHER RELEVANT ACTIVITIES:**

Member, Michigan Comprehensive Cancer Center

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Degnim, A.C., Griffith, K.A., Sabel, M.S., Hayes, D.F., Cimmino, V.M., Diehl, K.M., Lucas, P.C., Snyder, M.L., Chang, A.E. and Newman, L.A. (2003) Clinicopathologic features and metastasis in nonsentinel nodes of breast carcinoma patients. **Cancer** 98:2307-2315
2. Lucas, P.C., McAllister-Lucas, L.M. and Nunez, G. (2004) NF- κ B signaling in lymphocytes: a new cast of characters. **J. Cell Sci.** 117:31-39
3. Longo, K.A., Wright, W.S., Kang, S., Gerin, I., Chiang, S-H., Lucas, P.C., Opp, M.R., and MacDougald, O.A. (2004) Wnt10b inhibits development of white and brown adipose tissues. **J. Biol. Chem.**, 279:35503-35509

ARTICLES SUBMITTED FOR PUBLICATION:

1. Williams, J., Lucas, P.C., Griffith, K., Choi, M., Fogoros, S., Hu, Y.Y., and Liu, J.R. (2004) Expression of Bcl-x_L in ovarian carcinoma is associated with chemoresistance and recurrent disease. Submitted

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

1. McAllister-Lucas, L.M, Kuffa, P., Siu, K., Lucas, P.C., Inohara, N., and Nunez, G (2003) Purification of a Bimp3-binding complex: A novel method for identifying critical lymphocyte signaling proteins. **14th Annual Pediatric Research Symposium**, University of Michigan.
2. McAllister-Lucas, L.M, Kuffa, P., Siu, K., Lucas, P.C., Inohara, N., and Nunez, G (2004) Purification of a Bimp3-binding complex: A novel method for identifying critical lymphocyte signaling proteins. **Doris Duke Charitable Foundation Clinical Research Symposium**, Cold Spring Harbor Laboratories.
3. Koker, M., Lucas, P.C., Griffith, K., Sabel, M., Newman, L., Rubin, M.A., and Kleer, C.G. (2004) Tumor characteristics predictive of sentinel lymph node metastases in patients with breast cancer. **Modern Pathology**, 17:37A.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 – 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

DEPARTMENTAL:

- A.
 - 1. Neuroscience Sequence, Neuropathology for Second Year Medical Students. Prepared two laboratories and two lectures on brain tumors; toxic, metabolic, demyelinating and infectious diseases. Taught four laboratories.
 - 2. Senior medical student Neuropathology electives.
- B. House Officers:
 - 1. Brain cutting, sampling, microscopic examination and special stain instruction of pathology House Officers.
 - 2. Individual instruction of Pathology House Officers on neurosurgical biopsy material, 28 weeks.
 - 3. Review all neurosurgically removed material in the hospital in CME-approved monthly conference, 27 weeks.
 - 4. Invited presentations of neuropathologic observations at various clinical conferences and CPC conferences.
 - 5. Pathology Resident's Tuesday AP Conference rotated with other faculty.
 - 6. One month House Officer Electives.
 - 7. Pathology Resident's Monday Special Conferences rotated with other faculty.
 - 8. Autopsy call.
 - 9. Pathology Gross Conference.
- C. Review laboratory techniques with UMMC Histologists.
- D. Other Faculty: Brain Tumor Board, CPC, and other joint clinical conferences.

REGIONAL AND NATIONAL:

Faculty, "New Methods of Brain Tumor Analysis": 41st Annual AFIP Kenneth M. Earle Memorial Neuropathology Review, Armed Forces Institutes of Pathology, Rockville, Maryland, 2003.

III. RESEARCH ACTIVITIES:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL AND NATIONAL:

- A. Editorial Board, Journal of Histochemistry and Cytochemistry.
- B. Editor, Histochemical Society Newsletter.
- C. Primary Review Pathologist, Children's Cancer Study Group CCG 9897 nationwide study of childhood low grade gliomas.
- D. Reviewer for the following journals:
 - 1. Journal of Neuropathology and Experimental Neurology.
 - 2. Journal of Histochemistry and Cytochemistry.
 - 3. American Journal of Pathology.

4. Archives of Pathology and Laboratory Medicine.
- E. Member, Brain Tumor/EMF Study Scientific Advisory Panel, National Cancer Institute, Jonathan Samet, Chairman.
- F. Member, Review Panel, Program for Treatment of Malignant Brain Tumors, National Cancer Institute, William Jewell, Chairman.
- G. Member, Review Panel, Molecular Markers of Glioma Initiation and Progression, National Cancer Institute, Susan Naylor, Chairwoman.
- H. M-Labs Neuropathology Services.

V. OTHER RELEVANT ACTIVITIES:

PROFESSIONAL ORGANIZATIONS:

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

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Xin W, Rubin MA, **McKeever PE**.: Differential expression of cytokeratin 8 and 20 differentiate between craniopharyngioma and Rathke cleft cyst. Arch Pathol Lab Med 126:1174-8, 2002.
2. Valdez R, **McKeever PE**, Finn WG, Ross CW, Schnitzer B.: Composite germ cell tumor and high-grade B-cell lymphoma arising in the sella turcica: a report of one case. Human Pathol 33:1044-7, 2002.
3. Youkilis AS, Park P, **McKeever PE**, Chandler WF.: Parasagittal ependymoma resembling falcine meningioma. Am. J. Neuroradiol: 22: 1105-8, 2001.
4. Song DK, Boulis NM, **McKeever PE**, Quint DJ.: Angiotropic large cell lymphoma with imaging characteristics of CNS vasculitis. Am. J. Neuroradiol.: 23: 239-42, 2002.
5. Jain R, Mukherji SK, Garton H, Gujar S, **McKeever PE**, Robertson P.: Imaging findings of childhood primary intracranial squamous cell carcinoma. Am. J. Neuroradiol 24:109-111, 2003.

6. Lin PT, Bijwaard K, **McKeever PE**.: Adult peripheral primitive neuroectodermal tumor of the cauda equina diagnosed by a combined immunohistochemical and molecular genetic analysis. (in preparation)
7. Hassan AS, Trobe JD, **McKeever PE**, Gebarski SS: Linear magnetic resonance enhancement and optic neuropathy in primary angitis of the central nervous system. *Journal of Neuro-Ophthalmology* 23: 127-31, 2003.
8. Lin PT, Bijwaard K, **McKeever PE**.: Adult peripheral primitive neuroectodermal tumor of the cauda equina diagnosed by a combined immunohistochemical and molecular genetic analysis. (in preparation).
9. **McKeever PE**, Junck L, Li L, Mena H, Tkaczuk A, Yan M.: Block age affects MIB-1 proliferation indices. (in preparation).

BOOKS/CHAPTERS IN BOOKS:

1. McKeever PE: New Methods of Brain Tumor Analysis. In: *Kenneth M. Earle Memorial Neuropathology Review*. Armed Forces Institute of Pathology, Washington, D.C., 2003, pp.1-54.
2. McKeever PE: Glial cell pathology. In: *Encyclopedia of Neuroscience, Elsevier Science, 3rd edition*. Smith BH and Adelman A, eds., (in press).
3. McKeever PE, Blaivas M, Gebarski SS: In: *Pituitary Tumors, Chapter 23*. Thapar K, Kovacs K, Scheithauer BW, Lloyd RV (Eds). The Humana Press Inc., Totowa, New Jersey, 2000. (in press).
4. McKeever PE: Laboratory methods of brain tumor analysis. In: *Principles and Practice of Neuropathology*. Nelson JS, Mena H, Parisi J, Schochet S (Eds). Oxford, New York 2003, pp. 272-297.
5. McKeever PE: Immunohistochemistry of the nervous system. In: *Diagnostic Immunohistochemistry*. Dabbs DJ (Ed). Churchill Livingstone, 2002, pp.559-624.
6. McKeever PE, Boyer P: The brain, spinal cord, and meninges. In: *Diagnostic Surgical Pathology, 4th edition*. Sternberg SS, Antonioli DA, Carter D, Mills SE, Oberman HA (Eds). Lippincott, Philadelphia (in press).

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

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

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- 1. Co-Investigator (Principle Investigator: E-J Wamsteker, M.D.) ASGE Endoscopic Research Award (\$25,000) "Approaches to improve the cytologic diagnosis of pancreatobiliary malignancy by ERCP", 0% effort, American Society for Gastrointestinal Endoscopy.
- 2. Co-Investigator/Project Pathologist (Primary investigator: Daniel F. Hayes, M.D.), 0% effort, Daniel F. Hayes Breast Cancer Gift Fund, "A Pilot Study to Determine the Feasibility of Splitting Ductal Lavage Samples". (Phase I)
- 3. Co-Investigator/Project Pathologist (Primary investigator: Daniel F. Hayes, M.D.), 0% effort, Daniel F. Hayes Breast Cancer Gift Fund, "Investigation of surrogate biomarkers of breast cancer risk and evidence of chemopreventive agent activity using ductal lavage samples."

4. Co-Investigator/Project Pathologist (Primary investigator: Daniel F. Hayes, M.D.), 0% effort, Daniel F. Hayes Breast Cancer Gift Fund, "A pilot study to correlate change in mammographic density and to determine safety of tetratrismolyhdate chemoprevention in women at high risk for breast cancer."
5. Co-Investigator/Project Pathologist (Primary Investigator: Lisa Newman, M.D.) "Feasibility Study of Evaluating Breast Cancer patients with Ductal Lavage" 0% effort
6. Co-Investigator/Project Pathologist (Principle investigator: David Reisman, M.D.) American Lung Association, "Loss of BRG1 and BRM in non-small cell lung cancer-An alternate mechanism to disrupt the retinoblastoma pathway", 5% effort (\$35,000/year-direct cost).
7. Co-Investigator/Project Pathologist. (Primary Investigator: Gustavo R. Rosania) Development of microanalysis methods for studying transport and secretory functions of mammary epithelia." (Pending)
8. Co-Investigator/Project Pathologist. (Primary Investigator: Gustavo R. Rosania) "Develop laboratory analysis protocols to study shed vesicles originating from healthy and pathologic mammary epithelia." (Pending)
9. Co-Investigator. (Primary Investigators: Gregory Kalemkerian & David Reisman) Studying genomic profiles of advanced lung, and head and neck cancers that will correlate with response to chemotherapy." 5% effort (Pending)

PROJECTS UNDER STUDY:

1. Establish DNA ploidy analysis by Chromavision.
2. Establish immunostaining protocol for ThinPrep slides.
3. Diagnostic pitfalls in pulmonary cytopathology. Three review articles, in progress.
4. Sturm C, Michael CW. Cytologic features of microglandular hyperplasia.
5. Dai Y, Michael CW. Application of Beta Catenin and Cyclin D1 in mesothelial lesions.
6. Li Q, Michael CW. The differential diagnosis of malignant mesothelioma, adenocarcinoma and squamous cell carcinoma: Back to morphology.
7. Michael CW, Abati A. The diagnosis of malignant mesothelioma in effusions: Reappraisal of morphologic criteria.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

None.

REGIONAL AND NATIONAL:

Member, Editorial Board, Diagnostic Cytopathology
Reviewer, Diagnostic Cytopathology.
Reviewer, Cancer Cytopathology.
Reviewer, Journal of Clinical Pathology
Reviewer, Medical Science Monitor
Secretary, Papanicolaou Society of Cytopathology.
Member, American Society of Clinical Pathologists, Non-Gynecologic Star Program
Member, American Society of Cytopathology, Scientific Committee

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "Cytopathology of the Lung. Differential Diagnosis and Diagnostic Pitfalls". **Workshop**, American Society of Clinical Pathology, October, 2003.
2. "The interpretation of cytologic specimens prepared by the ThinPrep technique". **Short Course**, United States and Canadian Academy of Pathology. Vancouver, Canada. March , 2004.
3. "Cytopathology of the Lung. Differential Diagnosis and Diagnostic Pitfalls". **Workshop**, M-Lab Symposium, May, 2004

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Xin W, Davenport R, Chang D, Michael CW. The Exaggerated Pigmented Granulomatous Reaction to the Artificial Joint Implant Mimics Metastatic Melanoma. *Diagn cytopathol*, 2004; 30:198-200.
2. Anca M. Avram, , Christine Sturm, Claire W. Michael, Craig A. Jaffe, and James C. Sisson. Cryptococcal Thyroiditis and Hyperthyroidism. *Thyroid* 2004;14:471-474.
3. Michael CW, Richardson PH, Boudreaux CW. Pulmonary lymphoma of the MALT type: report of a case with cytological, histological, immunophenotypical correlation, and review of the literature (in press, *Annals of Diagnostic Pathology*).
4. Abdul-karim F, Michael CW, Kosciak RL, Cheng L. Cytopathology, Book chapter in "Essentials of anatomic Pathology" edited by Cheng L and Bostwick DG. Humana press Totowa, New Jersey. 6 (1-63), second edition, 2004.
5. Liu W, Michael CW. Malignant mesothelioma versus adenocarcinoma in serous fluids: The everlasting challenge. *Check Sample, American Society of Clinical pathology* (in press).
6. Ruffin MT, Bailey BM, Normelle DP, Michael CW, Bjeniasz ME, Kmak DC, Unger ER, Brenner DE. Low dose topical delivery of All-Trans Retinoic acid for CINII and III Cancer Epidemiology: Biomarkers and prevention. (in press)

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Afify A, Stern R, Michael CW. Differentiation of mesothelioma from adenocarcinoma in serous effusions: The role of hyaloromic acid and CD44 localization. (Diagn cytopathol)

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

1. Guo G, Giordano TJ, Hanash S, Diamandis EP, and Michael CW. Cytologic evaluation of Kallikerin 10 as a marker of papillary thyroid carcinoma. Mod Path, 2004;17:69A.
2. Zhu W, Michael CW. How important is on-site adequacy assessment for thyroid FNA? An evaluation of 883 cases. ASC, Nov 2004.
3. Pu, R, Bedrossian CW and Michael CW. Performance and cost analysis of immunohistochemistry stains on ThinPrep versus cellblock preparations in diagnosing adenocarcinoma in serous effusions. ASC, Nov, 2004.

**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 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Graduate students:

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

B. Postdoctoral Fellows:

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

C. In Lab:

1. Gonzalo Garcia, Ph.D.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, R. A. Miller, "Laboratory for Anti-Geric Testing, Evaluation and Research," NIH/NIA U01-AG022303-02, \$302,572. direct costs/year, 7/03-6/08.
- B. Principal Investigator, R. A. Miller, "Wild Derived Mouse Stocks: New Models for Aging Research." NIH/NIA R01-AG13711-07, \$175,000 direct costs/year, 9/1/00 – 8/31/05.
- C. Principal Investigator, R. A. Miller, "Genetic Control of Longevity in Mice." NIH/NIA R01-AG11687-10, \$291,292 direct costs/year, 9/1/93-11/30/03.
- D. Principal Investigator, R. A. Miller, "Activation Defects in T Cells of Aged Mice," NIH/NIA R01-AG19619-04, \$250,000 direct costs/year, 9/30/00 – 8/31/05.
- E. Principal Investigator, R. A. Miller, "Genetics of Age-Sensitive Traits in Mice," NIH/NIA P01-16699-05, direct costs/year 5: \$637,739, 5/1/99 – 4/30/04. Core A (Administrative), R. A. Miller, \$31,575. Core C (Animal), R. A. Miller, \$26,671. Project 1 (Immunology), R. A. Miller, \$60,486.
- F. Program Director, R. A. Miller, "Research Training in Experimental Immunology," NIH T32-AI-07413-11 (5%), \$312,412 direct costs/year, 9/15/98 – 8/31/08.
- G. Principal Investigator, J. Halter, "Claude D. Pepper Older Americans Independence Center," NIH P30-AG08808, \$919,621 direct costs/year, 9/1/99-8/31/04. R. A. Miller serves as (a) Director, Core Facility for Aged Rodents, direct costs/year \$95,602; (b) Director, Research Development Core, \$60,154 direct costs/year); and (c) Project Director, "Weight Gain Trajectory and Life Span in Mice", \$103,510 direct costs/year).
- H. Principal Investigator, J. Faulkner, "Nathan Shock Center of Excellence in the Basic Biology of Aging," NIH P30-AG13283-08, \$139,000 direct costs/year, 9/1/95 – 6/30/05. R. A. Miller directs the Gene Expression Profiling Core and the Laboratory for Anti-Geric Testing.
- I. Principal Investigator, Andrzej Bartke, Southern Illinois University, "Gene expression and Biomarkers in Dwarf Mice," SIU Subcontract 02-17, component of R01-AG19899-01, \$32,894 direct costs/year, 9/1/01 – 8/31/06
- J. Principal Investigator, R. Buffenstein, "Mechanisms of Aging in the Long-Lived Naked Mole Rat." CCNY Subcontract., component of R01-AG022891-01, \$25,237 direct costs/year, 9/30/03-8/31/08. R. A. Miller subcontract for gene expression studies.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director, Experimental Immunology Training Program

MEDICAL SCHOOL/HOSPITAL:

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

- E. Associate Director for Research, Geriatrics Center

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

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

HONORS AND AWARDS:

- A. None.

INVITED LECTURES/SEMINARS:

2003

1. University of Michigan, Geriatrics Resident Training Course, Ann Arbor, MI. "Introduction to the Biology of Aging." July 8.
2. University of Michigan, Pathology Department Seminar Series, Ann Arbor, MI. "New Animal Models for Aging Research." September 15.
3. University of Michigan Bone Research Center Symposium, Ann Arbor, MI. "Genetic Analysis of Aging and Disease in Mice." October 15.
4. American College of Rheumatology 67th Annual Meeting, Orlando, FL. "Biology of Aging: Why Do Joints Last Just About 80 Years?" October 26.
5. Longevity Consortium Annual Meeting, Santa Monica, CA. "Extending Human Life Span: Scientific Prospects and Political Obstacles." November 6.
6. American College of Veterinary Pathology, Banff, Alberta, Canada. "Not Your Father's Aging Rodent: New Mouse Models for Aging Research." November 17.
7. University of Iowa Center on Aging, Iowa City, Iowa. "Are There Genes for Aging?" December 9.

2004

1. Yale University Department of Genetics, New Haven, CT. "Not Your Father's Aging Rodent: New Models for Aging Research.." January 13.
2. University of Michigan School of Medicine, Darwinian Medicine Interest Group, "Are There Genes for Aging?" January 15.

3. University of Colorado Institute for Behavioral Genetics, Boulder, CO. "Genetic Analysis of Aging and Disease in Mice." February 13.
4. University of Illinois, Champaign, IL. "Genetic Analysis of Aging and Disease in Mice." February 22.
5. Oakwood Hospital, Detroit, MI. Medical Grand Rounds: "Are There Genes for Aging?" March 19.
6. Annual Meeting, American Society of Investigative Pathologists, Washington, DC. "Genetics of Aging in Mice: Are We Getting Anywhere?" April 20.
7. New Jersey Medical School, Newark, NJ. Conference on "Creating Old People," "The Genetic Toolbox: Why Some Species Live Longer than Others." April 30.
8. NIA Workshop on Timing of Aging Processes, Bethesda, MD. "Early predictors of life expectancy in mice: when does aging begin?" May 6.
9. NIA Workshop on New Uses for Survival Data, Bethesda, MD. "Survivor Data: A Consumer's Report." May 11.
10. University of Michigan Nathan Shock Center for the Biology of Aging Annual Meeting. "Not Your Father's Aging Rodent: New Models for Aging Research." May 25.
11. Annual Meeting of American Aging Association (AGE), Tampa, FL. "Genetics and Gene Expression Studies of Aging Mice." June 5.
12. Great Lakes Science Writers Briefing, Ann Arbor, MI. "Extending Human Life Span: Scientific Prospects and Political Obstacles." June 14.
13. University of Pittsburgh School of Medicine, Pittsburgh, PA. "Aging and Cancer in a Segregating Mouse Population. June 17.
14. Annual Meeting of the Endocrine Society, New Orleans, LA. "Genetics and Gene-Expression Analyses of Hormone-Mutant Mice." June 19.
15. In Search of the Fountain of Health, New York Academy of Sciences, New York. "Perspectives on Longevity Research." June 23.
16. Nathan Shock Center Symposium on Array Research., Seattle, WA. "'We Don't Need No Stinkin' T-tests' - A Cynic's Guide to the Microarray Literature." June 24.
17. American Association for the Advancement of Science, Washington, DC. SAGE-Crossroads Webcast on Aging and Policy Issues. July 6.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Garcia, G. G. and R. A. Miller. 2003. Age-related defects in CD4+ T cell activation reversed by glycoprotein endopeptidase. *European Journal of Immunology* 33:3464-3472.
2. Xu, S., N. Yi, D. Burke, A. Galecki, and R. A. Miller. 2003. An EM algorithm for mapping binary disease loci: application to fibrosarcoma in a four-way cross mouse family. *Genetical Research* 82:127-138.
3. Wolf, N., A. Galecki, R. D. Lipman, S. Chen, M. Smith-Wheelock, D. Burke, and R. A. Miller. Quantitative trait locus mapping for age-related cataract severity and synechia prevalence using four-way cross mice. *Invest. Ophthalmology and Visual Science*, in press.

4. Ortiz-Suarez, A., and R. A. Miller. 2003. Antigen-independent expansion of CD28^{hi} CD8 cells from aged mice: cytokine requirements and signal transduction pathways. *J. Gerontol. Biol. Sci.* 58A: 1063-1073.
5. Harper, J. M., A. T. Galecki, D. T. Burke, S. L. Pinkosky, and R. A. Miller. 2003. Quantitative trait loci for insulin-like growth factor-I, leptin, thyroxine, and corticosterone in genetically heterogeneous mice. *Physiological Genomics* 15:44-51.
6. Miller, R. A. 2004. "Accelerated Aging": A Primrose Path to Insight? *Aging Cell* 3:47-51.
7. Miller, R. A. 2004. Rebuttal to Hasty and Vijg, "Accelerated aging by mouse reverse genetics: a rational approach to understand longevity." *Aging Cell* 3:53-54.
8. Miller, R. A. 2004. Roy Walford: a tribute. *Experimental Gerontology* 39:917-918.
9. Harper, J. M., A. T. Galecki, D. T. Burke, and R. A. Miller. 2004. Body weight, hormones and T-cell subsets as predictors of lifespan in genetically heterogeneous mice. *Mechanisms of Ageing and Development* 125:381-390.
10. Volkman, S. K., A. T. Galecki, D. T. Burke, **R. A. Miller**, and S. A. Goldstein. Quantitative trait loci that modulate femoral mechanical properties in a genetically heterogeneous mouse population. *J. Bone and Mineral Research*, in press.
11. Lipman, R., A. Galecki, D. T. Burke and R. A. Miller. Genetic loci that influence cause of death in a heterogeneous mouse stock. *J. Gerontol. Biol. Sci.*, in press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Berger, S. B, and R. A. Miller. A glycoprotein endopeptidase enhances cytokine production by CD4 T cells of old and young mice. Submitted.
2. Labrie, J. E., III, D. T. Burke, A. T. Galecki, R. A. Miller, and R. M. Gerstein. Bone marrow B cell populations in aged mice are influenced by genetic polymorphisms and correlated with T cell subset variations. Submitted.
3. Vergara, M., M. Smith-Wheelock, J. M. Harper, R. Sigler, and R. A. Miller. Hormone-treated Snell dwarf mice gain weight and become fertile but remain long-lived. Submitted.
4. Wisser, K. C., J. A. Schauerte, D. T. Burke, A. Galecki, S. Chen, R. A. Miller, and A. Gafni. Mapping tissue-specific genes correlated with age-dependent changes in protein stability and function. Submitted.
5. Hanlon, P., A. Lorenz, Z. Shao, J. Harper, S. Volkman , S. Goldstein, A. T. Galecki, R. A. Miller, and D. T. Burke. Identification of genetic interactions among mouse QTL using a random walk approach. Submitted.
6. Garcia, G. G. and R. A. Miller. Age-associated changes in glycosylation of CD43 and CD45 on mouse CD4 T cells. Submitted.

BOOKS/CHAPTERS IN BOOKS:

1. Miller, R. A. 2003. The biology of aging and longevity. In: Principles of Geriatric Medicine and Gerontology, 5th Edition, W. R. Hazzard et al., eds., McGraw-Hill, Inc., NY, Chapter 1, pp 3 – 15.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

- A. 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
- B. Graduate students:
 - 1. Course Director, Pathology 585, Lecture and Laboratory course for Graduate students (20 hrs)
 - 2. Laboratory Instructor, pathology 600 (M2 pathology course)

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator: "Hormones and Dendritic Cells" VERAM 12/03-12/04 (25,000).
- B. Co-Investigator "Gender-specific T cell homing and autoimmunity" (B. Richardson, Internal Medicine, PI) NIH RO1AI42753 12/98 - 11/03 (\$1,609,959)
- C. Co-Investigator, "Molecular Mechanisms of Lung Host Defense" (J Curtis, PI) Research Enhancement Award Program (REAP) Veteran's Administration 10/01/98-09/30/03 (\$1,350,000)
- D. Co-investigator, "Metabolic imaging of Renal and Prostate Cancer using C-11 Acetate" (S. Snyder, PI) RO1-CA089448-01 12/01/01-11/31/04 (\$1,801,214)
- E. Co-Investigator. "Lung Injury by Oxygen Metabolites" NIH/NIGMS R37 GM29507. National Institute of Health (Peter A. Ward, PI). 07/01/01 - 06/30/06 (\$1,123,824).

PROJECTS UNDER STUDY:

- A. Endothelial cell responses in inflammation
 - 1. The enzyme source of endothelial cell oxidants
 - 2. The role of endothelial cell derived oxidants in signaling and cell injury
 - 3. Repertoire of endothelial cell derived cytokines and their role in inflammation
- B. Gender-specific effects of hormones on T cells and endothelial cells in autoimmunity
 - 1. Effect of estrogen on endothelial cell estrogen receptor expression
 - 2. The role of estrogen in endothelial cell adhesion molecule expression and lymphocyte homing
- C. Gender-specific effects of hormones on dendritic cells in autoimmunity
 - 1. Effect of estrogen on antigen presentation by dendritic cells
 - 2. Role of estrogen in the autoimmune response to antigen

IV. ADMINISTRATIVE ACTIVITIES:

MEMBERSHIP IN PROFESSIONAL SOCIETIES

American Association for the Advancement of Science (1991-present)
New York Academy of Science (1991-present)
American Society for Investigative Pathology (Fellow, 1995-present).
American Society of Clinical Pathologists (Fellow, 1995-present)
American Association of University Women (199-present)
The A. James French Society of Pathologists (1996-present)
Society for Experimental Biology and Medicine (2000-present)
The Oxygen Society (2001-present)
Society for Free Radical Research International (2001-present)
The Nitric Oxide Society (2001v)
American Heart Association (1997-present)

DEPARTMENTAL

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

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL AND NATIONAL:

- A. Manuscript Review for
 - 1. Clinical Immunology and Immunopathology
 - 2. Biochemical pharmacology
 - 3. Shock

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

V. OTHER RELEVANT ACTIVITIES:

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

VI. PUBLICATIONS:

BOOKS/CHAPTERS IN BOOKS:

1. Murphy, H. S., J. Varani and P. A. Ward. Biology of Endothelial Cells: Role of the Endothelium in Lung Inflammation. Middleton's Allergy: Principles and Practice. N. F. Adkinson. Mosby St Louis. 2003.
2. Murphy, H.S., Ward, P.A. Inflammation. In Pathology. E. Rubin (ed) Lippincott-Raven New York 2004
3. H.S. Murphy, J.Varani and P.A.Ward. Neutrophil-mediated endothelial cell injury. Perspectives in Lung Endothelial Cell Barrier Function. C. Patterson (ed). Elsevier. 2004

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Hattori, Y, K C. Nerusu, N Bhagavathula, M. Brennan, N Hattori, H. S. Murphy, L Su, T. S. Wang, T. M. Johnson, J. Varani. Vascular expression of matrix metalloproteinase-13 (Collagenase-3) in basal cell carcinoma. Experimental & Molecular Pathology. 74(3):230-7, 2003
2. Speyer, C L., R.L.Warner, J.V. Sarma, B.C.Chiu. M. E. Murphy, I. J. Laudes, S. Chensue, H. S. Murphy, P.A. Ward. Regulation of Chemokine Expression by Inducible Nitric Oxide Synthase. Am. J Pathol 163(6):2319-28, 2003

3. Robey, T.C., Valimaa, T., Murphy, H.S., Mooney, D.J., Weatherly, R.A The use of internal "Knitted-type" stents in a rabbit tracheal reconstruction model. Arch. Otolaryng (Accepted for publication)
4. Montgomery, J. S., B. K. Hollenbeck, P. C. Fisher, H. S. Murphy, W. Underwood. Benign Paratesticular Schwannoma. J. Urology (accepted for publication).
5. Murphy, H. S., Q. Sun, B. A. Murphy, S. W. Chensue, B. C. Richardson, R. Yung. Tissue Specific Estradiol Enhancement of Endothelial Cell Dependent Lymphocyte Recruitment. Microvasc. Res. 2004.
6. Park, P, Gala, V C, Choksi, V R, Murphy, H S, Ramnath, S. Well-circumscribed, Minimally Enhancing Glioblastoma Multiforme of the Trigone: Case Report and Review of the Literature. Surgical Neurology (Accepted for publication).
7. Grimmer, J.F. Gunnlaugsson, C.B, Alsberg, E, Murphy, H.S., Kong, H, Mooney, D.R., Weatherly, R.A. Tracheal Reconstruction Using Tissue-Engineered Cartilage. Arch Otolaryngol Head and Neck Surg (Accepted for publication.)
8. T-H. Chun, F. Sabeh, H. S. Murphy, K. McDonagh, E. D. Allen, S.J. Weiss. MTI-MMP-dependent Neovessel formation within the confines of the 3-dimensional extracellular matrix. Genes & Development (Accepted for publication.)
9. R. L. Warner, H. C. Winter, C. L. Speyer, J. Varani, I.J. Goldstein, H. S. Murphy, K. J. Johnson, Marasmus oreades lectin induces renal thrombotic microangiopathic lesions: A model of hemolytic uremic syndrome. Am. J. Pathol. (Accepted for publication.)
10. Dame, M. K. S Yu, R Garrido, W Bobrowski, J E McDuffie, H. S. Murphy, M Albassam, J Varani. A stepwise method for the isolation of endothelial cells and smooth muscle cells from individual canine coronary arteries. In Vitro Cellular and Developmental Biology-Animal. 39:402-406, 2003.

SUBMITTED PUBLICATIONS

1. Toung, J., H. S. Murphy, M.E. P. Prince. Parotid Lipoma: A case report. (Submitted for publication.)
2. Piotrowski, M. Bessette, R., Cutler, D., Kachalia, A., Murphy, H.S., Roseborough, J. W., Saint, S., Underwood, W., Chensue, S. learning to Improve Safety: False Positive Pathology Report Results in Wrongful Surgery. Joint Comm J. Quality and Safety (submitted for publication).

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

1. H.S. Murphy, Q. Sun, B.A. Murphy, B.C. Richardson. Estradiol Enhances Antigen Presentation by Spleen Dendritic Cells. Keystone Symposium, 2003.
2. J Grimmer, E Alsberg, H.S.Murphy, H Kong, D. J. Mooney R. Weatherly, Tracheal Reconstruction in Rabbits using Polyglycolic-Acid (PGA) Mesh Embedded with Alginate-Encapsulated Chondrocytes. American Academy of Otolaryngology 2003.
3. H.S. Murphy, Q. Sun, B.A. Murphy, B.C. Richardson. Estradiol Enhances Antigen Presentation by Spleen Dendritic Cells. 2nd Annual Pathology Symposium, University of Michigan. 2003.
4. HS Murphy, Q Sun, BA Murphy, D Ray, BC Richardson. Estradiol Upregulates MHCII and Enhances Antigen Presentation by Dendritic Cells. FASEB Journal 18:A427.2004

5. HC Winter, C Speyer, J J Varani, I J Goldstein, H S Murphy, K J Johnson. Marasmius oreades lectin induces renal thrombotic microangiopathic lesions: A model of hemolytic uremic syndrome. FASEB Journal 18:A1188. 2004
6. H.S. Murphy, Q. Sun, B.A. Murphy, D. Ray, B.C. Richardson. Estradiol Upregulates MHCII and Enhances Antigen Presentation by Dendritic Cells. Keystone Symposium, Immune Evasion. 2004.
7. Choksi, V.R., Park, P, Kaza, A, Murphy, HS, Ramnath, S.Minimally Enhancing Glioblastoma Multiforme of the Trigone American Society of Neuroradiology. 2004
8. M E. Murphy, Sun, Q., Richardson, B.C., Murphy, H.S. Estrogen Enhances IL-4 Mediated MCP-1 Exoression in Endothelial Cells. FASEB Summer Research Conference: Steroid Hormone Receptors: Integration of Plasma Membrane- and Nucelar-Initiated Signaling in Hormone Action. 2004

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

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

III. RESEARCH ACTIVITIES:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Advisory Committee on Appointments and Promotions.

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

- 1. A series of 12 lectures on cytopathology (History of Cytopathology, Non-neoplastic entities seen in routine cytologic specimens, Cytopathology of Mesothelioma) given at All India Institute of Medical Sciences, Delhi, Tata Memorial Hospital, Mumbai (Bombay), Armed Forces Medical

- College, Pune, University of Belgaum, Belgaum, University of Madras, Madras, and University of Pondicherry, Pondicherry, India, November-December, 2003-2004.
2. Naylor, B.: a). Cytopathology of serous fluids, b). Cytology of mesothelioma, c). Transthoracic fine needle aspiration cytology, c) History of cytopathology. Lectures, Cytotechnology Training Program, Wayne State University, Detroit, Michigan, 20034

HONORS AND AWARDS:

Shiran Mehtaji Oration, Indian Academy of Cytologists, Pune, India, November 2003.

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,

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

- A. Associate Director, Clinical Microbiology/Virology Laboratories.
- B. Co-Coordinator, Infectious Disease Microbiology Laboratory Rounds.
- C. Technical Consultant - M-Labs.
- D. New clinical test development, verification and implementation.

II. TEACHING ACTIVITIES:

- A. Instructor, Pathology House Officer Microbiology/Virology Program.
- B. Coordinator, Clinical Microbiology/Virology In-service Program.
- C. Instructor, Infectious Disease Laboratory Rounds.
- D. Coordinator, Clinical Microbiology Journal Club
- E. Preceptor for M-4 elective in Pathology.
- F. Preceptor for Pharmacy Resident rotation in Clinical Microbiology and Virology.
- G. Lecturer, Epidemiology 680, "Hospital Epidemiology," School of Public Health
- H. Lecturer, Clinical Microbiology, Wm. Beaumont Hospital Medical Technology Program
- I. Clinical Pathology Grand Rounds, UM Dept. of Pathology.
 - 1. "Introduction to molecular methods in clinical microbiology." Grand Rounds presentation, Clinical Pathology Division, Department of Pathology, University of Michigan Medical Center. 2/20/04.
 - 2. "Application of molecular methods in clinical microbiology—Case Presentations." Grand Rounds presentation, Clinical Pathology Division, Department of Pathology, University of Michigan Medical Center. 3/19/04.
- J. Continuing Education Lecturer, UM Dept. of Pathology.
 - 1. "Why is Flu such a big deal?" Continuing Education Seminar, Department of Pathology, University of Michigan Medical Center. 01/07/04.
 - 2. "Why is Flu such a big deal?" Brown-bag lunch seminar for Medical Technology students, Department of Pathology, University of Michigan Medical Center. 03/24/04.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. "Role of EBV and malaria co-infection in the pathogenesis of endemic Burkitt's lymphoma," Principal Investigator: Rosemary Rochford, UM School of Public Health.

- B. "Serologic response to EBV infection in the presence and absence of malaria endemicity," Principal Investigator: Duane Newton, Dept. of Pathology, University of Michigan.
- C. Co-investigator (20% effort); R01 NIH Grant AI057853-01A1, Principal Investigator: Arnold S. Monto, MD, Project Title: Comparative Study of Influenza Vaccines in Adult

PROJECTS UNDER STUDY:

- A. "Real-Time" PCR for the rapid diagnosis of infectious diseases:
 - HSV
 - HCV
 - HBV
 - EBV
 - BK virus
 - Enterovirus
 - Bordetella pertussis*
- B. Use of the HandyLab bedside PCR device for detecting *Streptococcus agalactiae* during pregnancy.
- C. Use of rapid antigen detection tests for the diagnosis of Parainfluenza and Adenovirus infections in pediatric patients.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL/NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

PROFESSIONAL ORGANIZATIONS:

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

INVITED LECTURES/ SEMINARS:

- 1. "West Nile virus in the U.S. and Michigan." Providence Hospital Infectious Diseases Symposium, Southfield, MI. 8/20/03.
- 2. "Flu, RSV, and SARS—Are you ready for winter respiratory virus season?" Michigan Branch Fall Meeting, South Central Association for Clinical Microbiology, East Lansing, MI. 10/07/03.
- 3. "West Nile virus in the U.S. and Michigan." Department of Biology Seminar Series, Central Michigan University, Mt. Pleasant, MI. 1/15/04.
- 4. "COBAS TaqMan HCV Test (RUO) and MagNA Pure." Roche Diagnostics Technology Symposium, Clearwater Beach, FL. 04/26/04.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Pealer, L.N., et al for the **West Nile Virus Transmission Investigation Team**. 2003. Transmission of West Nile virus through blood transfusion in the United States in 2002. *New England Journal of Medicine* 349:1236-45.

BOOKS/ CHAPTERS IN BOOKS:

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

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

- 1. **D.W. Newton**. "Laboratory Methods for Detection of West Nile Virus," *Advance for Laboratory Professionals*, Sept. 2004 issue.
- 2. R.E. Hankerd and **D.W. Newton**. 2004. Assessment of the performance characteristics of Roche COBAS TaqMan HCV Test for determination of HCV viral loads. Poster presented at the 20th Annual Clinical Virology Symposium and Annual Meeting of the Pan American Society for Clinical Virology, Clearwater, FL.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

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
- F. Supervise Undergraduate Research Opportunities Program (UROP) student projects

III. RESEARCH ACTIVITIES:

- A. Principal Investigator, "Mechanisms of pulmonary fibrosis," NIH, R37, HL28737 MERIT Award.
- B. Principal Investigator, "Myofibroblasts in pulmonary fibrosis," NIH, 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. Bone marrow precursor cells as extrapulmonary sources of lung fibroblasts
- C. Molecular regulation of the α -smooth muscle actin, telomerase reverse transcriptase and FIZZ1 promoter and gene expression.
- D. Myofibroblast differentiation and its regulation by cytokines.
- E. Microarray analysis of lung gene expression in lung fibrosis.
- F. Induction and regulation of telomerase expression in lung fibrosis.
- G. Role of eosinophils in pulmonary fibrosis.
- H. Characterization of FIZZ1 and its role in myofibroblast differentiation

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL AND NATIONAL:

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

INVITED LECTURES/SEMINARS:

- Invited Speaker, "Role of fibroblast phenotypes in fibrotic lung disease", Schering-Plough Research Institute, NJ, 2003
- Invited Speaker, "Fibroblasts and pulmonary fibrosis", McMaster University, Hamilton, Ontario, Canada, 2003
- Invited Speaker, "Molecular regulation of the α -smooth muscle actin gene in myofibroblast differentiation", 2nd FIRI Meeting on "Mechanisms of Wound Healing and Fibrotic Diseases in the Aged" Centro Studi Cappuccini - San Miniato (Pisa), Italy, 2003
- Invited Speaker, "Myofibroblasts- where do they come from and what regulates their survival?", Post graduate course, American Thoracic Society Annual Meeting, Orlando, FL, 2004
- Featured Speaker, "Insights into mechanisms of fibrosis from animal models", Mini-Symposium on "Molecular and cellular mechanisms of pulmonary fibrosis", American Thoracic Society Annual Meeting, Orlando, FL, 2004
- Invited Speaker, "Toward a fibroblast ontology in pulmonary fibrosis", Tulane University Center for Gene Therapy, New Orleans, LA, 2004

V. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Yang, Y., Zhe, X., Phan, S.H., Ullenbruch, M., and Schuger, S.: Involvement of SRF Isoforms in Myofibroblast Differentiation During Bleomycin-Induced Lung Injury. *Am. J. Respir. Cell Mol. Biol.* 2003; 29:583-590.
2. Gharaee-Kermani, M., McCullumsmith, R.E., Charo, I.F., Kunkel, S.L., and Phan, S.H.: CC-Chemokine receptor 2 required for bleomycin-induced pulmonary fibrosis. *Cytokine* 2003; 24:266-276.
3. Huaux, F., Liu, T., McGarry, B., Ullenbruch, M., Xing, Z., and Phan, S.H.: Eosinophils and T-lymphocytes possess distinct roles in bleomycin-induced lung injury and fibrosis. *J. Immunol.* 2003; 171:5470-5481.
4. Schramm, C.M., Puddington, L., Wu, C., Guernsey, L., Gharaee-Kermani, M., Phan, S.H., Thrall, R.S.: Chronic inhaled ovalbumin exposure induces antigen-dependent but not antigen-specific inhalational tolerance in a murine model of allergic airway disease. *Am. J. Pathol.* 2004; 164:295-304.
5. Hashimoto, N., Jin, H., Liu, T., Chensue, S.W., and Phan, S.H.: Bone marrow derived progenitor cells in pulmonary fibrosis. *J. Clin. Invest.* 2004; 113:243-252.
6. Liu, T., Dhanasekaran, S.M., Jin, H., Tomlins, S.A., Chinnaiyan A.M., and Phan, S.H.: Induction of FIZZ-1 expression in lung injury and fibrosis. *Am. J. Pathol.* 2004; 164:1315-1326.
7. Barbarin, V., Arras, M., Misson, P., Delos, M., McGarry, B., Phan, SH, Lison, D., and Huaux, F.: Characterization of the effect of interleukin-10 (IL-10) on silica-induced lung fibrosis in mice. *Am. J. Respir. Cell Mol. Biol.* 2004; 31 78-85.

BOOKS/CHAPTERS IN BOOKS/REVIEWS:

1. Gharaee-Kermani, M., **Phan, S.H.**: Role of fibroblasts and myofibroblasts in idiopathic pulmonary fibrosis, in, Lynch, J. (Ed.) *Idiopathic pulmonary fibrosis*. Marcel Dekker, New York, 2003; Chapter 20, pp 501-563.

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

1. Hu B, Wu Z, Jin H, Hashimoto N, Liu T, Phan SH: Interleukin-1 β suppression of myofibroblast differentiation is mediated by CCAAT/enhancer-binding protein β isoforms. *Am. J. Resp. Crit. Care Med.* 2004;169:A660
2. Liu T, Jin H, Ullenbruch M, Hu B, Hashimoto N, Moore B, McKenzie A, Phan SH: Regulation of FIZZ1 expression in bleomycin-induced lung fibrosis: role of IL-4/IL-13 and mediation via Stat6. *Am. J. Resp. Crit. Care Med.* 2004;169:A744
3. Hashimoto N, Ullenbruch M, Jin H, Phan SH: Altered lung fibroblast chemokine receptor expression and responsiveness to cognate ligands in bleomycin-induced lung fibrosis. *Am. J. Resp. Crit. Care Med.* 2004;169:A300

4. Gharraee-Kermani M, McGarry B, Ullenbruch M, Jin H, MCCullumsmith R, Kunkel SL, Charo I, Phan SH: Derangement in lung fibroblast TGF β signaling in CCR2 deficient mice accompanies reduced lung fibrosis. Am. J. Resp. Crit. Care Med. 2004;169:A301
5. Huaux F, Liu T, McGarry B, Ullenbruch M, Phan SH: Complex regulation of pulmonary fibrosis by eosinophils. Clin. Invest. Med. 2004;27:100D

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

- A. Cytology sign out 20 weeks (from September 2003 to June 2004)
- B. Cytology consultation for TC cases, M-lab cases, etc
- C. Fine needle Aspirations performance at Cancer Center Clinic and hospital wards
- D. On site evaluation for specimen adequacy at Taubman Endocrine Clinic, Medical Procedure Unit, Ultrasound and CT-guided aspirations performed by clinical colleagues
- E. Daily surgical pathology consensus conference participation

II. TEACHING ACTIVITIES:

- A. Medical students, Residents, and Fellows:
 - 1. Responsible during the current academic year for teaching activities for the following:
 - a. At daily sign out sessions
 - b. Teaching of FNA performance at clinic
 - c. Two 1-hour lectures on cytopathology
 - d. Weekly interesting case conference
 - f. Monthly cytopathology conference
- B. Cytotechnologist:
 - Slide conference (1 hour each X 2)

III. RESEARCH ACTIVITIES:

PATHOLOGIC FEATURES OF BREAST CANCER ASSOCIATED WITH COMPLETE RESPONSE TO NEOADJUVANT CHEMOTHERAPY: IMPORTANCE OF FRESH TUMOR NECROSIS. Robert T. Pu, Anne F. Schott, David E. Sturtz, Kent A. Griffith, and Celina G. Kleer (submitted).

IRB MED#2004-0374 (Approved): Methylation profiling of tumor suppressor genes of different tumors and its potential clinical application.

PENDING:

GU SPORES pilot grant application: Gene Methylation Profiling of Prostate Cancers of Different Disease Outcomes (not funded).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Interviewing Resident, Fellow, and Faculty candidates (8-10)

V. **OTHER RELEVANT ACTIVITIES:**

HONORS AND AWARDS

- A. F. Stephen Vogel Award from USCAP at 2004 Annual Meeting, Vancouver, Canada

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. **Pu, R.T.**, Laitala, L.E., Alli, P.M., Fackler, M.J., Sukumar, S., and Clark, D.P. (2003) Methylation profiling of benign and malignant breast lesions and its application to cytopathology. **Modern Pathology** 16(11):1095-1101.

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

1. **Robert Pu**, Bedrossian C and Michael, CW. Performance and cost analysis of immunohistochemistry stains on ThinPrep (TP) versus cell block (CB) preparations in diagnosing adenocarcinoma in serous effusions (accepted for 52nd Annual ASC meeting 2004).
2. **Robert Pu**, Zong-Mei Sheng, Douglas Clark, and Timothy O'Leary. Gene methylation profiling of mesothelioma using real-time methylation-specific-PCR. (2003) Abstract presented at 51st Annual Scientific Meeting (#149).

**STEPHEN RAMSBURGH, M.D.
ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

- A. General Surgical Pathology – 25 weeks

II. TEACHING ACTIVITIES:

- A. Graduate students:
1. M2 Pathology Lab – 70 hours
 2. Applied Clinical Anatomy Musculoskeletal System – 4 hours
 3. Applied Clinical Anatomy Head and Neck – 4 hours
 4. M-2 Lecture Breast Disease – 5 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
 5. Surgical Pathology Elective for senior level residents – 60 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:

1. *Surgical Pathology: A Reference* (publication pending)

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

None

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

- A. Coordinator, Biweekly Pathology Gross Conference.
- B. Lectures to Pathology House Officers in Anatomic and Clinical Pathology.
- C. Pathology 600, Provided written critiques of student autopsy write-ups (168).
- D. Laboratory Instructor, Pathology 600 (M2 pathology course), year long
- E. Thesis Committee - Erin Gatza, Department of Immunology
- F. Mentored research of Stewart Wang, M.D., Ph.D. (Department of Surgery), Grace Su, M.D., (Department of Medicine), Jean Nemzek, D.V.M. (Unit for Lab Animal Medicine), Postdoctoral fellows, Hong Yan Xiao, M.D., Ekram El Laban, M.D.
- G. Graduate Students – Laura McKinley, Department of Pathology, Devin Horton, Program in Cell and Molecular Biology, Sudha Natarajan, Department of Pathology

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 – 2003. 10% effort
- D. Co-Investigator, "Inflammation and the Host Response to Injury", GM-99-007, Ronald Tompkins, M.D. Principal Investigator Mass. General Hospital. Protein Analysis and Cell Biology Core, \$613,115, 2001 – 2006, 5% effort.
- E. Co-Investigator, "Inflammation and the Host Response to Injury", GM-99-007, Ronald Tompkins, M.D. Principal Investigator Mass. General Hospital. Protein Analysis and Cell Biology Core, \$613,115, 2001 – 2006, 10% effort.
- F. Co-Investigator, "Can Paraxonase be Used to Treat Endotoxemia and Sepsis", Life Sciences Initiative, Bert LaDu Principal Investigator, \$150,000, 2001-2004. 2% effort
- G. Co-Investigator, NIH HD040112, "Neuroimmunology/Cytokine Alterations In Vulvodinia" Principal Investigator, Barbara Reed, \$375,000, 2000 – 2003

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL AND NATIONAL:

- A. Executive Committee, Michigan Association of Medical Examiners.
- B. Deputy Medical Examiner for Washtenaw County.
- C. Member, American Society of Investigative Pathology Education Committee
- D. Member, Michigan Coalition on Donation
- E. Publications Committee, International Cytokine Society
- F. Awards Committee, Shock Society
- G. Organizer, Shock Society Young Investigator's Research Forum
- H. Organizer, Shock Society Fun Run 2004
- I. Member, Michigan Association of Medical Examiners, Shock Society, American Association of Immunologists, A. James French Society, American Society of Investigative Pathologists, United States-Canadian Academy of Pathology.

V. OTHER RELEVANT ACTIVITIES:

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

INVITED LECTURES/SEMINARS:

- 2003 Organizer and Moderator, Magic Bullets for the Treatment of Sepsis Shock Society meeting
- 2003 Faculty Forum Speaker, Camp Michigan
- 2003 Keynote Speaker, State University of New York at Buffalo, Research Day, *The Inflammatory Response of Sepsis*
- 2003 Invited speaker, Keystone Symposium on Sepsis, Lake Tahoe, California
- 2003 Chair, Experimental Biology Poster Discussion Session
- 2003 Expert Panel Discussion, Michigan Association of Medical Examiners
- 2003 Member Panel Discussion, American Association of Medical Colleges Annual Meeting, Washington D.C., *Disabilities in Medical School*
- 2004 International Sepsis Forum, Oak Island Resort, Canada, *Acute Pancreatitis, Models, Markers, and Mediators*

VI. PUBLICATIONS:

ARTICLES PUBLISHED

- 1. Xiao H, Kovics R, Jackson V, Remick DG: Effects of platelet inhibitors on propyl gallate-induced platelet aggregation, protein tyrosine phosphorylation, and platelet factor 3 activation. *Blood Coagul Fibrinolysis* 15: 199-206., 2004.
- 2. Woodford NL, Call DR, Remick DG, *et al.*: Model of angiogenesis in mice with severe combined immunodeficiency (SCID) and xenoengrafted with Epstein-Barr virus-transformed B cells Endothelial barrier dysfunction caused by LPS correlates with phosphorylation of HSP27 in vivo. *Comp Med* 54: 209-15., 2004.
- 3. Nemzek JA, Xiao HY, Minard AE, Bolgos GL, Remick DG: Humane endpoints in shock research. *Shock* 21: 17-25., 2004.
- 4. McKinley L, Kim J, Bolgos GL, Siddiqui J, Remick DG: Reproducibility of a novel model of murine asthma-like pulmonary inflammation. *Clin Exp Immunol* 136: 224-31, 2004.

5. Knight PR, Sreekumar A, Siddiqui J, Laxman B, Copeland S, Chinnaiyan A, Remick DG: Development of a sensitive microarray immunoassay and comparison with standard enzyme-linked immunoassay for cytokine analysis. *Shock* 21: 26-30., 2004.
6. Hirano S, Rees RS, Yancy SL, Welsh MJ, Remick DG, Yamada T, Hata J, Gilmont RR: Endothelial barrier dysfunction caused by LPS correlates with phosphorylation of HSP27 in vivo. *Cell Biol Toxicol* 20: 1-14., 2004.
7. Copeland S, Siddiqui J, Remick D: Direct comparison of traditional ELISAs and membrane protein arrays for detection and quantification of human cytokines. *J Immunol Methods* 284: 99-106., 2004.
8. Zeng X, Dai J, Remick DG, Wang X: Homocysteine mediated expression and secretion of monocyte chemoattractant protein-1 and interleukin-8 in human monocytes. *Circ Res* 93: 311-20., 2003.
9. Xing L, Remick DG: Relative cytokine and cytokine inhibitor production by mononuclear cells and neutrophils. *Shock* 20: 10-6., 2003.
10. Trout D, Weissman DN, Lewis D, Brundage RA, Franzblau A, Remick D: Evaluation of hypersensitivity pneumonitis among workers exposed to metal removal fluids. *Appl Occup Environ Hyg* 18: 953-60., 2003.
11. Steinstraesser L, Burghard O, Nemzek J, Fan MH, Merry A, Remick DI, Su GL, Steinau HU, Wang SC: Protegrin-1 increases bacterial clearance in sepsis but decreases survival. *Crit Care Med* 31: 221-6., 2003.
12. Siddiqui J, Remick DG: Improved sensitivity of colorimetric compared to chemiluminescence ELISAs for cytokine assays. *J Immunoassay Immunochem* 24: 273-83., 2003.
13. Remick DG, Bolgos GE, Siddiqui J: Inflammatory status in sepsis alters efficacy of interleukin-18 binding protein therapy. *Crit Care Med* 31: 2096-101., 2003.
14. Remick DG: Cytokine therapeutics for the treatment of sepsis: why has nothing worked? *Curr Pharm Des* 9: 75-82., 2003.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003- 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

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

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Immunophenotypic profiling of hematolymphoid neoplasms by flow cytometry and immunohistochemistry.
- B. Pathology reviewer for therapeutic trials in systemic mastocytosis.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

REGIONAL/NATIONAL:

- A. Resident In-Service Examination (RISE) Committee, American Society for Clinical Pathology.
- B. American Society for Clinical Pathology, CheckPath Expert Review Panel, Hematopathology.
- C. Manuscript reviewer, Archives of Pathology and Laboratory Medicine.
- D. Manuscript reviewer, Clinical Cytometry.
- E. Manuscript reviewer, Human Pathology
- F. Program Committee, Clinical Cytometry Society National Meeting.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

- 1. “Applications of flow cytometry in diagnosis of hematolymphoid neoplasia”, lecture to fellows and staff, division of Hematology/Oncology, Providence Hospital, Southfield, MI.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Kansal R, Ross CW, Singleton TP, Finn WG, Schnitzer B: Histopathologic features of splenic small B-cell lymphomas: a study of 42 cases with a definitive diagnosis by the World Health Organization Classification. Am J Clin Pathol 120:335-347, 2003.

ARTICLES SUBMITTED FOR PUBLICATION:

- 1. Kaminski MS, Tuck M, Estes J, Kolstad A, Ross CW et al. Tositumomab and iodine I 131 tositumomab (BEXXAR® Therapeutic Regimen) as initial therapy for follicular B-cell lymphoma.

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

- 1. Bakshi NA, Ross CW, Finn WG, Valdez R, Ruiz R, Schnitzer B: Primary bone anaplastic large cell lymphoma (ALCL) in pediatric age group. Mod Pathol 2004; 17(suppl 1): 239A.
- 2. Bakshi NA, Finn WG, Valdez R, Ross CW, Schnitzer B: Fascin expression in diffuse large B-cell lymphoma (DLBCL), anaplastic large cell lymphoma (ALCL) and classical Hodgkin lymphoma (CHL). Mod Pathol 2004; 17(suppl 1): 239A.

3. Owens SR, Finn WG, Ross CW, Schnitzer B, Valdez R: Type and distribution of small and large intestinal lymphomas. *Mod Pathol* 2004; 17(suppl 1): 264A.
4. Ross CW, Roulston D, Valdez R, Finn WG, Schnitzer B: Congenital myelodysplastic syndrome in an infant with Down Syndrome, evolving to acute myelogenous leukemia. Society for Hematopathology/European Association for Hematopathology 2003 Workshop. Reactive and Neoplastic Disorders in Pediatric Hematopathology. Impact of Molecular, Cytogenetic, and Flow Cytometric Methodologies on Diagnosis and Treatment, Case 110.
5. Finn WG, Ross CW, Valdez R, Schnitzer B: Juvenile myelomonocytic leukemia. Society for Hematopathology/European Association for Hematopathology 2003 Workshop. Reactive and Neoplastic Disorders in Pediatric Hematopathology. Impact of Molecular, Cytogenetic, and Flow Cytometric Methodologies on Diagnosis and Treatment, Case 111.
6. Valdez R, Ross CW, Finn WG, Schnitzer B: Infectious mononucleosis. Society for Hematopathology/European Association for Hematopathology 2003 Workshop. Reactive and Neoplastic Disorders in Pediatric Hematopathology. Impact of Molecular, Cytogenetic, and Flow Cytometric Methodologies on Diagnosis and Treatment, Case 91.
7. Schnitzer B, Valdez R, Finn WG, Ross CW: ALK-positive large B-cell lymphoma. Society for Hematopathology/European Association for Hematopathology 2003 Workshop. Reactive and Neoplastic Disorders in Pediatric Hematopathology. Impact of Molecular, Cytogenetic, and Flow Cytometric Methodologies on Diagnosis and Treatment, Case 109.
8. Valdez R, Roulston D, Ross CW, Finn WG, Schnitzer B: Anaplastic large cell lymphoma, T-cell phenotype, small cell variant. Society for Hematopathology/European Association for Hematopathology 2003 Workshop. Reactive and Neoplastic Disorders in Pediatric Hematopathology. Impact of Molecular, Cytogenetic, and Flow Cytometric Methodologies on Diagnosis and Treatment, Case 93.
9. Valdez R, Lowe L, Ross CW, Finn WG, Schnitzer B: Juvenile xanthogranuloma, early proliferative phase. Society for Hematopathology/European Association for Hematopathology 2003 Workshop. Reactive and Neoplastic Disorders in Pediatric Hematopathology. Impact of Molecular, Cytogenetic, and Flow Cytometric Methodologies on Diagnosis and Treatment, Case 92.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

- A. Director, Clinical Cytogenetics Laboratory

II. TEACHING ACTIVITIES:

- A. House Officers and Fellows
 - 1. Rotations in Cytogenetics
 - a. Pathology residents (N=7)
 - b. Hematopathology fellow (N=1)
 - c. Maternal Fetal Medicine fellows (N=2)
- B. Clinical Cytogenetics teaching
 - 1. Abnormal Cytogenetics Case Conference (Biweekly) for technologists, residents, fellows, and faculty
 - 2. Leukemia Conference (Biweekly)
 - 3. Pediatric Genetics Post-clinic Conference (Weekly)
 - 4. Joint Genetics Conference (Monthly)
 - 5. Pediatric Tumor Conference
 - 6. Clinical Pathology Grand Rounds:
"The Autosomes and Constitutional Abnormalities" 2/6/04
 - 7. Invited speaker, HG641 Applied Clinical Genetics
"Clinical Cytogenetics"

III. RESEARCH ACTIVITIES:

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director, Clinical Cytogenetics Laboratory
- B. Interviewer
 - 1. Hematopathology Fellow Candidates
 - 2. Hematopathology Faculty Candidates
 - 3. Pathology Chair Candidates

UNIVERSITY OF MICHIGAN:

- A. Interviewer
 - 1. Clinical Genetics Residency/Fellowship Candidates
- B. Clinical Track Faculty Discussion Group (with Associate Dean of Medical School)

REGIONAL AND NATIONAL:

- A. American Board of Medical Genetics
 - 1. Board questions for 2005 ABMG Exam
 - 2. Maintenance of Certification Committee

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

VI. PUBLICATIONS:

ABSTRACTS:

- 1. Heerema, N.A., W. Sanger, B. Hirsch, M.E. Magenis, L. McGavran, S. Patil, K. Rao, **D. Roulston**. Importance of review for cooperative group cytogenetic studies, a report from the Children's Oncology Group (COG). 38th Biennial American Cytogenetics Conference April 22-25, 2004 *Cytogenetic and Genome Research*.

CASE REPORTS:

- 1. Valdez, R., **D. Roulston**, C.W. Ross, W.G. Finn, B. Schnitzer. Congenital myelodysplastic syndrome characterized by del(13q) in infant twins with Down syndrome. Society for Hematology/European Association for Haematopathology 2003 Workshop, Oct 23-25 2003, Memphis TN
- 2. Ross, C.W., **D. Roulston**, R. Valdez, W.G. Finn, B. Schnitzer. Fatal outcome in a pediatric anaplastic large cell lymphoma, small cell variant, with the t(2;5) associated with favorable prognosis. Society for Hematology/European Association for Haematopathology 2003 Workshop Oct 23-25 2003, Memphis TN

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 – 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

- A. Consultant, pediatric surgical pathology, full time
- B. Consultant, pediatric autopsy pathology, full time
- C. Consultant, Teratology histopathology, full time
- D. Medical Director, Special Studies Laboratory (see separate report)
- E. Pathology co-ordinator, Children's Oncology Group cases

II. TEACHING ACTIVITIES:

- A. Medical Students
 - 1. M2 Pathology Laboratory (~50 hours)
 - 2. M4 Pathology Elective (~8 hours)
- B. Pathology House Officers:
 - 1. Pathology Teaching Conferences, Hirschsprung disease (1 hour)
 - 2. Pediatric Pathology Case Review (2-3 hours per week)
 - 3. Pediatric Autopsy Pathology cases and signout (variable)
 - 4. Pediatric Surgical Pathology Cutting Manual Revision (ongoing)
- C. Interdepartmental:
 - 1. Teratology histology signout (1.5 hours per week)
 - 2. Pediatric GI Pathology Case Conference (2 hours per month)
 - 3. Pediatric GI Pathology Teaching Conference (2 hours per month)
 - 4. Pediatric Hematology Oncology Tumor Board (2 hours per month)
 - 5. Pediatric Surgery, Radiology, Pathology Conference (1.5 hours per month)
 - 6. Pathology contributor for Pediatric Surgery, Radiology, Pathology Conference teaching case web presentations, Pediatric Surgery internal website (www.surgery.med.umich.edu/i/peds/Internal_site.htm)
 - 7. Pediatric Pulmonology Conference (1 hour per month)
 - 8. Pediatric Morbidity & Mortality Conference (1 hour per quarter)
 - 9. Pediatric Hematology Oncology Fellow Pathology Tutorials (variable)
 - 10. Pediatric Hematology Oncology Wednesday Morning Teaching Conference (variable)

III. RESEARCH ACTIVITIES:

- A. Series report on radiology-pathology correlation in pediatric myofibroma with Dr. Hernandez of Pediatric Radiology (manuscript submitted)
- B. Case study of fetal lymphocytic thyroiditis with Dr. Mason Barr of Teratology (manuscript in preparation)

- C. Case study of massive fetal intracranial hemangiopericytoma with Dr. Mason Barr of Teratology (manuscript in preparation)

IV. ADMINISTRATIVE ACTIVITIES:

- A. Mott Executive Committee

V. PUBLICATIONS:

- 1. Lau JJ, Trobe JD, Ruiz RE, Cho RW, Wechsler DS, Shah GV, Gebarski SS. Metastatic neuroblastoma presenting with binocular blindness from intracranial compression of the optic nerves. J Neuroophthalol. 24(2):119, 2004.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

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

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

None.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITALS:

- A. Director of Hematopathology Fellowship Training Program

REGIONAL AND NATIONAL

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

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARD:

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

INVITED LECTURES/SEMINARS:

- 1. "A Practical Approach to Diagnostic Hematological Problems," ASCP Educational Course, Lectures given included a) Classification of Non-Hodgkin's Lymphomas. b) Hodgkin's Disease; c) Extranodal Lymphomas. Las Vegas, NV, November 2003.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Kansal R, Ross CW, Kroft SH, Singleton TP, Finn WG, Schnitzer B: Histopathology of splenic small B-cell lymphomas: A study of 54 cases classified by flow cytometric immunophenotypic analysis or lymph node biopsy. Am J Clin Pathol 120:335-347, 2003.
- 2. Schnitzer B, Valdez R: Hodgkin lymphoma. Clinical, morphologic, immunophenotypic and molecular characteristics. Cancer Treat Res 121:259-290, 2004.

ARTICLES SUBMITTED FOR PUBLICATION:

BOOKS AND CHAPTERS IN BOOKS:

- 1. Hsi ED, Schnitzer B. Benign Lymphadenopathies. In Jaffe ES, Harris NL, Vardiman J (eds). Diagnostic Hematopathology. Harcourt Health Sciences, 2004.

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

1. Ross CW, Roulston D, Valdez R, Finn WG, Schnitzer B: Congenital myelodysplastic syndrome in an infant with Down's Syndrome, evolving to acute myelogenous leukemia. Society for Hematopathology/European Association for Hematopathology 2003 Workshop. Abstract Book. Reactive and Neoplastic Disorders in Pediatric Hematopathology. Impact of Molecular, Cytogenetic, and Flow Cytometric Methodologies on Diagnosis and Treatment 2003. Case 110.
2. Finn WG, Ross CW, Valdez R, Schnitzer B: Juvenile myelomonocytic leukemia. Society for Hematopathology/European Association for Hematopathology 2003 Workshop. Abstract Book. Reactive and Neoplastic Disorders in Pediatric Hematopathology. Impact of Molecular, Cytogenetic, and Flow Cytometric Methodologies on Diagnosis and Treatment 2003. Case 111
3. Valdez R, Ross CW, Finn WG, Schnitzer B: Infectious mononucleosis. Society for Hematopathology/European Association for Hematopathology 2003 Workshop. Abstract Book. Reactive and Neoplastic Disorders in Pediatric Hematopathology. Impact of Molecular, Cytogenetic, and Flow Cytometric Methodologies on Diagnosis and Treatment 2003. Case 91.
4. Schnitzer B, Valdez R, Finn WG, Ross CW: ALK-positive large B-cell lymphoma. Society for Hematopathology/European Association for Hematopathology 2003 Workshop. Abstract Book. Reactive and Neoplastic Disorders in Pediatric Hematopathology. Impact of Molecular, Cytogenetic, and Flow Cytometric Methodologies on Diagnosis and Treatment 2003. Case 109.
5. Valdez R, Roulston D, Ross CW, Finn WG, Schnitzer B: Anaplastic large cell lymphoma, T-cell phenotype, small cell variant. Society for Hematopathology/European Association for Hematopathology 2003 Workshop. Abstract Book. Reactive and Neoplastic Disorders in Pediatric Hematopathology. Impact of Molecular, Cytogenetic, and Flow Cytometric Methodologies on Diagnosis and Treatment 2003. Case 93.
6. Valdez R, Lowe L, Ross CW, Finn WG, Schnitzer B: Juvenile xanthogranuloma, early proliferative phase. Society for Hematopathology/European Association for Hematopathology 2003 Workshop. Abstract Book. Reactive and Neoplastic Disorders in Pediatric Hematopathology. Impact of Molecular, Cytogenetic, and Flow Cytometric Methodologies on Diagnosis and Treatment 2003. Case 92.
7. Bakshi NA, Ross CW, Finn WG, Ruiz R, Valdez R, Schnitzer B: Primary bone anaplastic large cell lymphoma (ALCL) in pediatric age group. Mod Pathol 17:239A, 2004.
8. Bakshi NA, Finn WG, Valdez R, Ross CW, Schnitzer B: Fascin expression in diffuse large B-cell lymphoma (DLBCL), Anaplastic large cell lymphoma (ALCL) and Classical Hodgkin lymphoma (CHL) Mod Pathol 17:339A, 2004.
9. Owens SR, Finn WG, Ross CW, Schnitzer B, Valdez R: Type and distribution of small and large intestinal lymphomas. Mod Pathol 17:264A, 2004.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

- A. Room #1 and 2 General Surgical Pathology sign-out, 8 weeks/year
- B. GU surgical subspecialty sign-out, 18 weeks/year
- C. Genitourinary transfer cases (TS), 26 weeks/year
- D. GU consultation service, daily, 12 months
- E. Participation in Urology Tumor Board and Grand Rounds, biweekly, 12 months
- F. Rapid warm autopsies for men with advanced prostate cancers, 24/7 availability 12 months
- G. Backup coverage of Nephropathology service, 1-2 weeks/year

II. TEACHING ACTIVITIES:

- 1. Residents didactic Monday evening Anatomic Pathology Lectures, 2/year
- 2. Residents Wednesday Consultation Conferences, 2/year
- 3. GU clinical pathology resident teaching, daily, 18 weeks
- 4. General surgical pathology resident teaching, 8 weeks
- 5. GU fellow (Matthew Snyder) teaching, 12 months
- 6. Post doctoral fellow (Rohit Mehra), 12 months
- 7. Urology resident pathology lectures, monthly, 12 months
- 8. M2-Renal Sequence and Reproductive Sequence Lectures, 3/year

III. RESEARCH ACTIVITIES:

- 1. Director, Tissue core, Prostate SPORE (assumed responsibility June, 2004), 2 months
- 2. Co-director for Prostate Cancer SPORE Tissue Core, 10 months
- 3. Translational research/pathology consultant for Genitourinary research, 12 months

IV. SPONSORED SUPPORT:

- 1. University of Michigan Prostate SPORE (Specialized Program for Research Excellence) Tissue Core Grant (Director (from June, 2004), Co-director (7/03-5/04) tissue core, 20% salary support)- P50 CA69568 (PI, Pienta-07/01/03-05/31/08)
- 2. Analysis of 8p loss in Human Prostate Cancer- Co Investigator, Ro1, 5RO1 CA 60948-08, (JA Macoska, PI), 4/01/01-3/31/05-5% salary support
- 3. DAMD17-01-1-0076 (M.J. Imperiale) 7/1/01-6/30/04, Co-investigator, 5% salary support. Role of the Human Polyomavirus, BKV, in Prostate Cancer-Co-investigator Department of Defense/USAMRMC

4. Erb Signaling in Prostate Cancer Progression- Co Investigator, DRDA 1234, UMCC 1234; CRC 1234 E

V. **ADMINISTRATIVE ACTIVITIES:**

DEPARTMENTAL:

1. GU fellowship coordination.
2. House officer, GU fellowship and faculty Candidate Interviews.
3. Director, Prostate SPORE tissue core laboratory

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Zhou M, **Shah R**, Shen Ronglai and Rubin MA. Basal Cell Cocktail (34 β E12+p63) improves the detection of Prostate Basal Cells. *Am J Surg Pathol*, Vol. 27, No. 3, 2003
2. Kunju Lakshmi, Rubin Mark, Chinnaiyan Arul and **Shah Rajal**. Diagnostic Usefulness of the Monoclonal Antibody P504S in the Work Up of Atypical Glandular Proliferations - *Am J Clin Pathol*, Vol 120, No.5, November 2003: 737-745
3. Skitzki Joseph, **Shah Rajal**, Francis Isaac and Chang Alfred. Hepatic Angiomyolipoma: An Unusual Liver Tumor. *Contemporary Surgery* Vol 59, No8/August 2003
4. Chandan Kumar-Sinha, **Rajal B. Shah**, Bharathi Laxman, Scott A. Tomlins, Jason Harwood, Werner Schmitz, Ernst Conzelmann, Martin G. Sanda, John T. Wei, Mark A. Rubin, and Arul M. Chinnaiyan. *American Journal of Pathology*, 2004 Mar; 164(3): 787-93. PMID: 14982833
5. Kalikin Linda, Schneider Abraham, Thakur Melissa, Fridman Yaron, Griffin Laura, Dunn Rodney, Rosol Thomas, **Shah Rajal B.**, Rehemtulla Alnawaz, MaCauley and Pienta Kenneth. In Vivo Visualization of Metastatic Prostate Cancer and Quantitation of Disease Progression in Immunocompromised Mice. *Cancer biology and therapy*, Vol 2, Issue 6, November/December 2003, 656-660
6. **Shah Rajal**, Kunju Lakshmi, Shen Ronglai, LeBlank Michele and Rubin Mark. Utility of Basal Cell Cocktail (p63+34 β E12) in the Diagnosis of Atypical Prostate Glandular Proliferations. Utility of Basal Cell Cocktail (p63+34 β E12) in the Diagnosis of Atypical Prostate Glandular Proliferations. *Am J Clin Pathol*, In Press.
7. Das Dweepanita, **Shah Rajal** and Imperial Michael. Detection and Expression of Human BK Virus Sequences in Neoplastic Prostate Tissues. July 19, *Oncogene*, 2004

VII. **PRESENTATIONS:**

1. "Recent changes in the Staging and Classification of Genitourinary Cancers-an update". Genitourinary Oncology Conference, The University of Michigan Hospitals, January 15, 2004
2. "Prostate SPORE Tissue Core Info structure- University of Michigan Experience"- The Cleveland Clinic Foundation Delegation, January 15, 2004
3. "Interpretation of Prostatic Pathology: Critical Issues and Emerging Markers."-Guest Speaker, Association of Pathologist and Microbiologist, Gujarat Chapter, India, 31st January, 2004

4. "The Varied Morphological and Immunophenotypic Spectrum of Hormone Refractory Metastatic Prostate Cancer: Lesson From A Rapid Autopsy Program". 93rd annual United and Canadian Academy of Pathology Meeting, Vancouver, BC, Canada, March, 2004

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

1. **Shah RB**, Mehra R, Zhou M, Chinnaiyan A. M., Harwood J, Pienta K. J., and Rubin M.A. The Varied Morphological and Immunophenotypic Spectrum of Hormone Refractory Metastatic Prostate Cancer: Lesson From A Rapid Autopsy Program University of Michigan School of Medicine, Ann Arbor, MI and Brigham and Women's Hospital, Harvard Medical School, Boston, MA. *Modern Pathol*, 17(1): 177A, Jan 2004
2. Matthew Snyder, Rohit Mehra, Lakshmi Priya Kunju, James Montie+, and **Rajal B. Shah**. Departments of Pathology and Urology+, University of Michigan, Ann Arbor, MI. Utility of a Novel Immunohistochemical (IHC) Panel (PSA, High Molecular Weight Cytokeratin and/or p63) in the differentiation of Poorly differentiated Prostate Adenocarcinoma (PCa) from Urothelial Carcinoma (UC). *Modern Pathol*, 17(1):178A, Jan 2004
3. L.P. Kunju, MD, M. Snyder, C. Lee, J. Montie and **R.B. Shah**, MD, University of Michigan, Ann Arbor, MI. Cytokeratin 20 and Ki- 67 as Markers of Urothelial Dysplasia. *Modern Pathol*, 17(1): 163A, Jan 2004

IX. PROJECTS SUBMITTED FOR PUBLICATION:

1. **Shah RB**, Mehra R, Zhou M, Chinnaiyan A. M., Harwood J, Pienta K. J., and Rubin M.A. Androgen Independent Metastatic Prostate Cancer is a Heterogeneous group of Diseases: Lesson From A Rapid Autopsy Program University of Michigan School of Medicine, Ann Arbor, MI and Brigham and Women's Hospital, Harvard Medical School. Submitted for publication, *Cancer Research*.
2. α -methylacyl-CoA racemase (AMACR) as a urine biomarker for the non-invasive detection of prostate cancer. Submitted for the publication.
3. Development of a Non-T7 Based Whole Transcriptome Amplification Method for Gene Expression Profiling. Submitted for publication (2004).
4. Treatment of BK Nephropathy with Intravenous Immunoglobulin. Submitted for the publication (2004)
5. The metastasis suppressor gene Raf kinase inhibitor protein (RKIP) and prognosis in prostate cancer. Submitted for publication (2004)

X. PROJECTS UNDER STUDY

1. Role of Image guided core needle biopsies in the management of renal mass lesions: Evaluation of adequacy, sensitivity and accuracy of the diagnosis.
2. Comparison of Monoclonal Antibody (P504S) and Polyclonal Antibody to α -Methylacyl-CoA Racemase in work-up of atypical prostate needle biopsies.
3. Use of tissue micro arrays to identify markers associated with response to interleukin-2 in renal cell carcinoma.

4. Papillary renal cell carcinoma: Emphasis on the histological typing and its correlation with clinicopathologic and immunohistochemical parameters.
5. Stathmin as a biomarker for metastatic prostate cancer: evaluation using tissue microarrays
6. Minimally invasive radical prostatectomy: Initial experience and evaluation of clinicopathologic parameters.
7. Significance of positive proximal urethral margin in staging radical prostatectomy: does the presence of benign prostate glands make a difference?
8. Erb(EGFR) signaling in the progression of prostate cancer.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

- A. Surgical Pathology Coverage of M-Labs cases, including most cases from:
 - 1. University of Michigan Health Service, non-dermatology cases, Ann Arbor, Michigan.
 - 2. Forest Health Medical Center, Ypsilanti, Michigan.
 - 3. Other various clients including numerous satellite sites and University acquired practices.
- B. Rotation with other staff pathologists:
 - 1. Coverage at the University Hospitals of weekend autopsy call.
- C. Clinical Pathology consults for M-Labs clients.
- D. Surgical Pathology "Quickie" Anatomic Pathology consults for pathologists at M-Labs client hospitals and others.

II. TEACHING ACTIVITIES:

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

III. RESEARCH ACTIVITIES:

None.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Michigan Health Corporation representative to Joint Venture Hospital Labs (JVHL).
- B. Director, M-Labs:
 - 1. Provide leadership for and participate in planning, marketing, and implementation of M-Labs programs.
 - 2. Growth. In FY 2004, M-Labs added 7 new physician offices and specialty service practices to our client list. These now number in 150 offices. The majority of these are related to our contract to provide coverage to M-Care patients. There were no new full reference laboratory accounts. No contracts for services were terminated.
This fiscal year, gross billings for clinical pathology services increased by 26% and gross billing for anatomic pathology services increased by 9%.

M Labs submitted 3 proposals to prospective new clients during FY2004. All are still pending.

The Department of Pathology rejected business opportunities to provide dermatopathology services to 3 dermatology practices.

3. Managed Care Activities

We have begun negotiations for a new capitation rate, to begin 1 January 2005, for our contract of 4/1/01 with M Care to provide outpatient lab services for all groups and products for M Care's commercial and Medicare products. M-Labs prepares quarterly QA reports on lab services for M Care QA department and have conducted a Physician Satisfaction Survey for M-Labs subcontracted providers and reported the results to M Care. We assist M Care with resolution of laboratory service issues. We are actively engaged in contracting for delivery of HEDIS data for M Care to assist them in meeting requirements of the NCQA.

4. Networks. MLabs is a member of 2 laboratory networks, Great Lakes Laboratory Network (GLN) which consists of 28 hospital laboratories, predominantly in the western and northern parts of Michigan, and Joint Venture Hospital Laboratories (JVHL) which has grown to include 10 equity members and 120 participating member laboratories located in Michigan. JVHL has contracts for laboratory services with 16 managed care organizations including BCN.

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

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

C. Member Department of Pathology Incentive Committee.

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

V. **OTHER RELEVANT ACTIVITIES:**

I have retired from the University of Michigan as of July 1, 2004.

VI. **PUBLICATIONS:**

None

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004

I. CLINICAL ACTIVITIES:

A. Assistant Director, Cytogenetics Laboratory

II. TEACHING ACTIVITIES:

A. House Officers and Fellows

1. Rotations in Cytogenetics
 - a. Pathology Residents (N=6)
 - b. Maternal/Fetal Medicine Fellows (N=2)
 - c. Genetics Fellow (N=1)
 - d. Hematology/Oncology Fellows (N=1)

B. Clinical Cytogenetics

1. Abnormal Cytogenetics Case Conference (Biweekly)--- technologists, residents, and fellows
2. Leukemia Conference (Biweekly)
3. Hematology Conference (Biweekly)
4. Pediatric Genetics Post-clinic Conference (Weekly)
5. Joint Genetics Conference (Monthly)
6. Clinical Pathology Grand Rounds
 - a. "Cytogenetics II: The X and Y chromosomes and sex chromosome abnormalities" 03/13/04

III. RESEARCH ACTIVITIES:

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

PROJECTS UNDER STUDY:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

V. PUBLICATIONS:

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

1. Lama VN., Smith LR, Flint A., Golden MP., Martinez FJ, Thannickal VJ. **in preparation.** Role and origin of myelofibroblasts in Bronchiolitis Obliterans in post-lung transplantation.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Research mentor (200+ contact hours)

- 1. **Rughi Okuyama, M.D., post-doctoral fellow (4/02-present) and Ronald Craig, PhD, Research Associate (1/91-present):** Mechanisms and clinical ramification of donor T-cell trafficking during active cellular immunotherapy for metastatic cancer. Identified the vascular selectins as the principle vascular adhesion receptors required for effector T-cell entry into subcutaneous murine melanomas. Showed that selectin- and, to a minor extent, $\alpha 4$ -integrin-mediated trafficking of host and donor lymphocytes into tumors initiates anti-tumor activity. Developed high-resolution imaging techniques that show the entry and accumulation of anti-tumor effector cells in individual metastatic lesions in the lung varies markedly. Consequently, the entry of circulating cells into tumors limits the therapeutic response even in highly susceptible tumors.
- 2. **Randall Knibbs, Ph.D., Research Scientist (1/94-present)** - Dr. Knibbs studies the trafficking and priming efficiency of cultured dendritic cells that overexpress lymph node homing receptors. Initial studies show that homing-receptor transduced dendritic cells are significantly better than control DC in a murine T-cell lymphoma treatment model. In separate studies, the synergy between peptide-pulsed dendritic cells and adoptive immunotherapy is under investigation.
- 3. **Undergraduate and graduate research assistants:** Mentored four undergraduate students in the laboratory participating in work/study programs and one graduate student.

B. Co-director, lecturer and seminar leader, M2 Hematology Sequence (16 contact hours+20 hours administration/development)

- 1. Authored the 7th generation of The Virtual Microscope-Hematopathology Interactive Syllabus (<http://141.214.6.12/virtualheme99>). Unique software provides access to interactive case-presentations and high-resolution "virtual slides" covering the pathophysiology, diagnosis and treatment of the hematologic malignancies. This award-winning "active" learning experience captures the essentials of the in-class laboratory exercises thus provides students with a flexible tool for preview and review.
- 2. Teaching performance metrics
 - i. Lecture rating: 4.57/5 (mean for all faculty in sequence: 4.12).
 - ii. Laboratory rating: 4.54/5 (mean for all faculty in sequence: 4.26).

- iii. Student comments (Class 2006)
- a. Dr. Stoolman's web page is awesome. It is a very helpful and reliable source of information for disorders of the blood. It was very user-friendly and helped a great deal in explaining the important points for each disorder. I liked the cases that went along with the various disorders-they helped me to understand the clinical presentations better. Dr. Stoolman was a very good teacher as well. He was interesting and respectful to the students.
 - b. The lab sessions, course review and website were all great.
 - c. Thank you for the great web tools. They were the basis for my organizational scheme for the WBC neoplasms.
 - d. I like how Stoolman tries to help students understand the concepts in so many ways. I especially like his PowerPoint modules.
 - e. This instructor had very clear slides and he enlarged them to make it easier for us to read which showed that he really cared about us understanding the material. Slide pictures were also very relevant and helpful. I also appreciated all the extra work that this instructor put into the on-line PowerPoint's, on labs and the unknowns.
 - f. He made the lab very clear and understandable. The web-based lab review and unknown PowerPoint slides were excellent tools for consolidating the lab portion of the course. Overall, I think that one of the most helpful lectures of the course was [Dr. Stoolman's] overview of MPD, MDS and Leukemias since it let us know where we were headed for the next series of lectures.
 - g. I thought this professor made his objectives very clear. I liked the lab web page and the unknowns. They really helped me study. The websites were excellent and were very helpful in reviewing the diseases.
 - h. Dr. Stoolman goes above and beyond the call of duty with his web-page. It is a great source of information.
 - i. Excellently organized and great webpage.
 - j. Dr. Stoolman's labs were really helpful. He reinforced didactic material and shared some very useful handouts with us. His presentation style is really clear and while he seems pretty open to questions, he tended to anticipate them and address problem areas for us as well. Perhaps he fostered a sense that we knew the material better than we did; I don't know... thanks a lot--I had pretty much given up on lab, and I'm glad I stuck around for the Stoolman sessions.
 - k. Dr. Stoolman is one of the best teachers I have had here at the medical school. He is very clear and thorough and I really learned a lot from his sessions!!! thanks Dr. Stoolman!
 - l. Great use of technology; the stuff on the webpage was very helpful.
 - m. I really learned a lot about the Leukemias from lab.
 - n. Probably the most beneficial lab sessions for me were the sections covered by Stoolman.
 - o. It was very clear Dr. Stoolman put a LOT of time and effort into preparing for his presentations. It showed. His were among the clearest and easiest

to assimilate. In fact, in an otherwise dismal sequence with very haphazard material presentation and disjointed lessons, Dr. Stoolman's material really stood out as some of the only coherent presentations.

- p. He was really good; well-organized, thorough, had a good sense of humor, etc. It was helpful.

C. Lecturer and Seminar leader M1 Host Defense Sequence (4 contact + 30 development)

1. Lectured and developed computer-based courseware for lecture syllabus and case presentations.
2. Teaching performance metrics
 - i. Lecture rating: 4.5/5 (mean for all faculty in sequence: 4.31).
 - ii. Student comments (Class 2007)
 - a. Dr. Stoolman's classroom presentation was the most technologically advanced of the series and that increased the effectiveness of his presentation.
 - b. The visuals kept me awake. Also the visuals added to the lecture, reinforcing important points. It was also helpful to hear certain important points clearly re-emphasized.
 - c. Dr. Stoolman made a real effort to keep students interested in the material. The time he spent preparing his presentation must have been enormous, and I appreciate the effort very much.
 - d. The use of animation and movies in the PowerPoint presentation for his lecture made the material more relevant and understandable for the students. It provided a more comprehensive understanding of the material than would sheer words on a page that might describe the same processes. Moreover, the animation was so engrossing that it kept all the students' attention for the entire lecture. It was a lasting impression.
 - e. Dr. Stoolman did a great job at giving a review of previous material and his PowerPoint presentation was very interesting/informative.
 - f. Audiovisuals and presentation were immaculate. He seemed very lucid and clear. I enjoyed his presentation.
 - g. The movies were excellent. The repetition was excellent (really driving home what we needed to know). I really appreciated Dr. Stoolman's lectures and the time he put into his presentation.
 - h. Dr. Stoolman had excellent animated slides that really demonstrated his points well.
 - i. Engaging and interesting presentations, with good audiovisuals.
 - j. Excellent PowerPoint animations!
 - k. The movies that he used were very good and gave me another way to digest and understand the information that was presented.
 - l. Best AV presentation I've likely ever seen. Kept the lecture interesting and helped us to really see how things happen.
 - m. I really liked how Dr. Stoolman used animations in his presentation. Not only did it lighten the mood and make it more fun to learn, but it also enabled us to grasp and visualize the material better. He also made sure to stress the key points so that we would know what is most important.

- n. Great PowerPoint slides. Although a simpler method could have got the point across, the animations helped to stick the material in my head.
- o. Dr. Stoolman's animations were creative and clearly must have required much effort and time to produce. I appreciated his desire to put together a lecture that students would enjoy.
- p. The A/V slides were excellent...well done!
- q. Incredible audiovisuals and that helped liven things up.
- r. Very interesting stories what with the historical perspective and all. Excellent presentation style which is captivating and energized and makes lots of otherwise complicated pathways interesting.
- s. The movies really augmented the lecture.
- t. Dr. Stoolman did an OUTSTANDING job on his slides. The animation and sound effects made the lecture very interesting and made the material easier to understand.
- u. Excellent presentation. Needs to teach the other profs. how to use PowerPoint.
- v. The audiovisuals were very nice: they were fun and engaging.
- w. We had only one lecture with Dr. Stoolman but his PowerPoint presentation was very interactive with innovative video clips and illustrations that helped to understand the material better. His oral presentation was concise and to the point and was easy to follow along and understand the material he presented. He also covered the material at an appropriate pace.
- x. This information was vital to understanding the whole sequence. Dr Stoolman's lecture was very helpful and had a good broad base of information that was a helpful framework for the other information in the sequence.
- y. Professor Stoolman's slides were very entertaining, and the movies he presented kept my attention. He was very clear and organized and easy to follow.

D. Author, Pathology Laboratory Course for Dental Students (20 hours administration/development)

- 1. 7th generation of The Virtual Microscope- Interactive web-based syllabus for General and Organ systems pathology for dental students. URL=<http://141.214.6.12/cyberscope631/>. This award-winning site incorporates several hundred, high resolution (1900 X 1300 pixel) photographs of gross and microscopic specimens into an interactive laboratory syllabus.
- 2. *The Virtual Microscope Website now serves as the primary histopathology teaching modality for Dental Students. The platform allowed the Department to meet the teaching requirements of the revised dental curriculum while reducing faculty effort by ~50%.*

E. Resident Teaching: (30 contact hours)

- 1. Flow cytometry service, case sign-out (3 months)
- 2. Autopsy service, weekend coverage

III. **RESEARCH ACTIVITIES:**

- A. Principal Investigator (Kevin McDonagh, co-investigator)- Retroviral transgene induction of homing receptors on dendritic cells used for active immunotherapy: impact on trafficking, antigen priming and tumor suppression. University of Michigan Comprehensive Cancer Center Innovation Award Program., \$50,000 (direct); July 2003-June 2004.
- B. Principal Investigator (Kevin McDonagh, co-investigator)- Lymphoma/leukemia therapies using dendritic cells engineered to overexpress lymph-node homing receptors. The Leukemia & Lymphoma Society Translational Research Program. \$130,000 (direct + indirect, annual); Oct 2003-Sept 2006.
- C. Principal Investigator- T Cell Trafficking in Adoptive Cellular Immunotherapy; NIH, R01CA73059, 30% effort, \$196,000 (annual, direct); April 2001 -Mar 2006
- D. Principal Investigator- Research Training in Translational Tumor Immunology; NIH/NCI, T32 CA 88784, 5% effort (no salary support), \$321,306 (annual, direct); supports 2 pre-doctoral students and 4 post-doctoral students; Feb 2001-Jan 2006.
- E. Co-investigator on Project 2 and Co-director of the Immunology Core (with J. Mule, B. Redman and A.E. Chang, Surgical Oncology Division, University of Michigan)- Cellular Vaccines for Cancer Immunotherapy, NIH P01CA59327, 15% effort, \$1,000,000 (annual, direct); June 2001-April 2006.
- F. Co-investigator (with B. Redman and A. E. Chang, Surgical Oncology Division, University of Michigan)- T-Cell Therapy of Human Renal Cell Cancer; NIH R01CA69102, \$250,000 (annual, direct), 10% effort, April 2001 -Mar 2006.
- G. 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.
- H. Co-investigator (with B. Richardson, Rheumatology Division, University of Michigan)-“Gender specific T-cell homing and autoimmunity”; NIH, R01AI42753, 0% effort, \$187,000 (annual, direct); Apr 1998-Mar 2003.
- I. Trainer on three funded pre-/post-doctoral training grants: Translational Immunology (L. Stoolman, PI); Surgery Oncology Research (A.E. Chang, PI) and Immunopathology (R. Miller, PI).

IV. **ADMINISTRATIVE ACTIVITIES:**

- A. **Faculty Director, Medical Student Portal Project:** (30 contact hours + 200 hours administration/development)
 - 1. Initiated and co-directed (with Chris Chapman, Assistant Media Manager LRC) the development of Web-based Course Design, Management and Delivery Platform for the Medical School Curriculum. This application uses the C-Tools Platform developed by the Media Union at the University of Michigan. The project is a collaborative effort involving staff from the LRC, MSIS and the Media Union. The C-Tool Platform allows faculty to collaborate on course design, manage schedules, deliver electronic documents, disseminate announcements and conduct asynchronous and real-time discussions with students

- over the Web. The Medical Student Portal was successfully launched, on-time and on-budget, for the M1-students beginning August of 2003 (Class of 2007).
2. Convened working group to monitor and address operational problems, plan for revisions. Provided hands-on training for faculty, staff and students. Chaired long-range planning sessions.
- B. **Faculty Director, High Resolution Slide Scanning Initiative** (200 hours administration/development)
1. Negotiated the purchase of slide scanning hardware and software. The purchase was supported through an NCI Director's Challenge Grant and the Department of Pathology.
 2. This initiative creates a core laboratory, based in Pathology, that generates diagnostic quality, high resolution images of tissue sections (400X magnification, true-color optical scans; file sizes 10-60 GB uncompressed per image) that can be viewed, annotated and analyzed online. The system combines an automated slide scanner and a server cluster with 2-terabytes of RAID-5 storage capacity (initially). These images will supplement tissue sections/microscopes in teaching venues, complement traditional microscopic approaches in resident/fellow training and foster research collaborations that involve faculty at multiple centers. Applications in continuing medical education, diagnostic telepathology and basic research utilizing tissue sections are possible as well.
- C. **Principal Investigator- Research Training in Translational Tumor Immunology;** NIH/NCI, T32 CA 88784, 5% effort (no salary support), \$321,306 (annual, direct); supports 2 pre-doctoral students and 4 post-doctoral students; Feb 2001-Jan 2006.
- D. **Director of Research Flow Cytometry Laboratory and Co-Director of Clinical Flow Cytometry Laboratory-** Negotiated the purchase of four FC-500 flow cytometry instruments, including the acquisition and LIS interface software. Three instruments for the Clinical Flow Cytometry Laboratory, one instrument for general research in the Department of Pathology. Managed the operation of the research flow cytometry instrument for the Department of Pathology.
- E. **Member, Graduate Student Administrative Committee, Immunology Training Program**
- F. **Co-Director, M2 Hematology Sequence** - see educational activities.

V. **OTHER RELEVANT ACTIVITIES:**

EDITORIAL ACTIVITIES:

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

VI. PUBLICATIONS:

ARTICLES IN PEER REVIEWED PUBLICATIONS:

1. John, A. E., N. W. Lukacs, A. A. Berlin, A. Palecanda, R. F. Bargatze, **L. M. Stoolman**, and J. O. Nagy. 2003. Discovery of a potent nanoparticle P-selectin antagonist with anti-inflammatory effects in allergic airway disease. *FASEB Journal*.17(15):2296-8
2. Mo, R. R., J. K. Eisenbraun, J. Sonstein, R. A. Craig, J. L. Curtis, **L. M. Stoolman**, J. Chen, and R. L. Yung. 2003. CD49d overexpression and T cell autoimmunity. *Journal of Immunology*. 171(2):745-53.
3. R.N. Knibbs, M.. Dame, M.R. Allen, Y. Ding, W.J. Hillegas, J. Varani, **L.M. Stoolman**. Sustained high yield production of recombinant proteins on transiently-transfected COS-7 cells grown on trimethylamine coated microcarrier beads. 2003. *Biotechnology Progress*. 19:9.
4. Skitzki, J., R. A. Craig, R. Okuyama, R. N. Knibbs, K. McDonagh, A. E. Chang, and **L. M. Stoolman**. 2004. Donor cell cycling, trafficking, and accumulation during adoptive immunotherapy for murine lung metastases. *Cancer Research*.64(6):2183-91.
5. Sabel, M. S., J. Skitzki, **L. Stoolman**, N. K. Egilmez, E. Mathiowitz, N. Bailey, W. J. Chang, and A. E. Chang. 2004. Intratumoral IL-12 and TNF-alpha-loaded microspheres lead to regression of breast cancer and systemic antitumor immunity. *Annals of Surgical Oncology*.11(2):147-56.

BOOK CHAPTERS:

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

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

1. **Stoolman, Lloyd M**; Skitzki, Joseph; Okuyama, Ryugi; March, Christopher A; Knibbs, Randall N; Craig, Ronald A. Donor cell cycling, trafficking, accumulation and clinical activity during adoptive immunotherapy [Meeting] *FASEB Journal*. 18(4-5). 2004. Abst. 85.14.
2. John, Alison E.; Lukacs, Nicholas W.; Berlin, Aaron A.; Palecanda, Aiyappa; Bargatze, Robert F.; **Stoolman, Lloyd M.**; Nagy, Jon O.. Discovery of a potent nanoparticle P-selectin antagonist with anti-inflammatory effects in allergic airway disease. [Article] *FASEB Journal*. 17(15). December 2003. 2296-2298.
3. Skitzki, Joseph J.; Craig, Ron A.; Knibbs, Randall N.; Chang, Alfred E.; **Stoolman, Lloyd M.** The trafficking of infused, cultured tumor-draining lymph node cells (TDLN) into tissues is required for their continued proliferation and clinical activity during adoptive immunotherapy for metastatic cancer. [Meeting] *Proceedings American Association for Cancer Research Annual Meeting*. 44 July 2003. 1158.
4. **LM Stoolman**. 1998-2004 (updated annually). The Virtual Microscope- Interactive web-based syllabus for medical student (M2) Hematopathology laboratory. URL=<http://141.214.6.12/virtualheme99/>.

5. **LM Stoolman.** 1998-2004 (updated annually). The Virtual Microscope- Interactive web-based syllabus for General and Organ systems pathology for dental students (D2). URL=<http://141.214.6.12/cyberscope631/>.
6. **LM Stoolman.** 1999-2004 (updated annually). Hematopathology Unknown Exercises. Powerpoint-based exercise containing high resolution, annotated images and imbedded questions used by Medical Students (Hematology Sequence, year 2).
7. **LM Stoolman.** 1999-2004 (updated annually). Leukocyte Pathophysiology and Leukocyte Trafficking. Powerpoint lecture outlines including high-resolution images, video clips and animations used by Medical Students (Host Defense Sequence, year 1), Dental Students (General Pathology Course, year 1) and Graduate Students (Pathology 581).

**JOHN THORSON, M.D., PH.D.
CLINICAL ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

- A. Director, Molecular Diagnostics Laboratory
- B. Clinical Immunology Laboratory; sign out of cases (4 weeks/year)

II. TEACHING ACTIVITIES:

- A. House Officers:
 - 1. Coordinator, Pathology House Officer rotation through Clinical Molecular Diagnostics Laboratory
 - 2. Review of selected topics in Molecular Diagnostics with Block D residents
- B. Clinical Pathology Grand Rounds:
 - 1. "Molecular Diagnostics" (2/13/04)
 - 2. "Pharmacogenomics" (3/12/04)
- C. Lecturer, Clinical Concepts in Medical Genetics course (HG 649)
- D. Medical Technologists – 1 hour continuing education lecture

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

PROJECTS UNDER STUDY:

- A. DNA-based multiplex real time PCR assay for detection and characterization of BCRABL translocation breakpoints in clinical samples
- B. High throughput multiplex PCR assays for detection of BCL2 and BCL1 translocations in formalin fixed tissue specimens
- C. Fluorescent multiplex RT-PCR/capillary electrophoresis assays for the detection of tumor specific chimeric transcripts in soft tissue tumors
- D. DNA methylation profiling of prostate tumors

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Clinical Assistant Professor of Pathology
- B. Director, Molecular Diagnostics Laboratory

V. OTHER RELEVANT ACTIVITIES:

- A. Consultant to Consultants in Laboratory Medicine, Toledo, OH

EDITORIAL BOARDS:

- A. Ad hoc reviewer, Thrombosis and Haemostasis

PROFESSIONAL MEMBERSHIPS

- A. American Society of Clinical Pathologists
- B. College of American Pathologists
- C. United States and Canadian Academy of Pathology
- D. Academy of Clinical Laboratory Physicians and Scientists
- E. American Association for Clinical Chemistry
- F. Association for Molecular Pathology
- G. American Society of Human Genetics

INVITED LECTURES/SEMINARS:

1. "Update on the treatment and monitoring of chronic myelogenous leukemia". Consultants in Laboratory Medicine, Toledo OH, June 9, 2004.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Valdez R, Thorson J, Finn WG, Schnitzer B, Kleer CG. Lymphocytic mastitis: A Clinicopathologic, Immunophenotypic, and Molecular Evaluation of Eleven Cases. *Mod Pathol* 2003;16(3):223-228.
2. Si MW, Thorson JA, Lauwers GY, DalCin P, and Furman, J. 2004. Hepatocellular lymphoepithelioma-like carcinoma associated with Epstein Barr virus: a hitherto unrecognized entity. *Diag Mol Path* (in press).

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

1. Weigelin HC, Lucas DR, Ruiz RE, Howard JK and Thorson JA. "Multiplex RT-PCR/capillary electrophoresis to detect and genotype characteristic translocations from formalin-fixed soft tissue tumor specimens" Accepted for poster presentation at the Association for Molecular Pathology 2004 annual meeting, November 10-13, 2004.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

- A. None.

II. TEACHING ACTIVITIES:

- A. Mentor for students who worked in my laboratory over the past year, including five post-doctoral fellows, one pathology graduate student, one medical student, two SPH graduate students, three undergraduate students and two high school students.
- B. Thesis mentor for Ashish Lal (MPH degree), School of Public Health
- C. Thesis mentor for Ian Hortch (MPH degree), School of Public Health
- D. Course director – Pathology 581. Tissue, cellular and molecular basis of disease.
- E. Instructor – Pathology 581 – Tissue, cellular and molecular basis of disease.
- F. Instructor – Interdisciplinary Dental School course.
- G. Instructor – Pathology 582 – Tissue, cellular and molecular basis of disease
- H. Instructor – Pathology 553 – Cancer Biology

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, “Retinoids for Diabetic Foot Ulcers.” NIH DK59169.
- B. Principal Investigator, “MMP-3 and acute lung injury.” NIH NHLBI 70979
- C. Principal Investigator (subcontract to UofM), “Novel therapeutic approach to psoriasis” NIH AR 44767.
- D. Principal Investigator, “Topical approach to treatment of psoriasis” NIH 50330
- E. Principal Investigator (subcontract to UofM), “Co-polymer–microcarrier culture system for human influenza vaccine production” H1H AI 50315.
- F. Principal Investigator (subcontract to UofM), “Non-irritating retinoids for treatment of aging” NIH AR49621.

PROJECTS UNDER STUDY:

- A. The biology of collagen destruction and repair in diabetic skin.
- B. Role of MMP-3 in acute and chronic lung injury.
- C. Synthetic PPAR-g ligands for treatment of psoriasis.

- D. Topical PPAR-g ligands for treatment of psoriasis.
- E. The development of a microcarrier-based protocols for production of human influenza vaccine.
- F. Development of a non-irritating retinoid for replacement of RA in therapy of skin aging.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

- A. Member of Medical School Institutional Review Board (IRBMED) (B2).
- B. Member, Program in Biomedical Sciences (PIBS) Curriculum Committee
- C. Member, Program in Biomedical Sciences (PIBS) Admissions Committee
- D. Member, Program in Biomedical Sciences (PIBS) Steering Committee
- E. Member, Medical School Committee on Summer Research Opportunities.
- F. Member, University of Michigan Cancer Center Basic Research Committee.
- G. Member, Cancer Biology Research Training Grant Scientific Steering Committee.
- H. Member, Department of Dermatology Research Training Grant Steering Committee.

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, July 30, 2003.

2. Invited speaker: Molecular Design International. Memphis, TN. Nov. 6, 2003.
3. Invited speaker: Zymogenetics, Inc. Seattle, WA. Nov. 19, 2003.
4. Invited speaker: Breast Cancer Program Symposium. Karmanos Cancer Center, Detroit, MI, April 16, 2004.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Hattori Y, Nerusu K, Bhagavathula N, Brennan M, Hattori N, Murphy HS, Su L, Wang TS, Johnson TM, Varani J. Vascular expression of matrix metalloproteinase-13 (collagenase-3) in basal cell carcinoma. *Exp. Molec. Pathol.* 74:230-237, 2003.
2. Chakrabarty S, Radjendirane V, Appelman H, Varani J. Extracellular calcium and calcium sensing receptor function in human colon carcinoma: Promotion of E-cadherin expression and suppression of b-catenin/TCF activation. *Cancer Res.* 63: 67-71 2003.
3. Fligiel SEG, Varani J, Datta SH, Kang S, Fisher GJ, Voorhees JJ. Collagen degradation in aged/photoaged skin in vivo and after exposure to MMP-1 *in vitro*. *J. Invest. Dermatol.* 120:842-848, 2003.
4. Brennan M, Bhatti H, Nerusu KC, Bhagavathula N, Kang S, Varani J, Voorhees JJ. Matrix metalloproteinase-1 is the major collagenolytic enzyme responsible for collagen damage in UV-irradiated human skin. *Photochem. Photobiol.* 78:43-48, 2003.
5. Varani J, Fligiel SEG, Zhang J, Aslam MN, Lu Y, Dehne L, Keller ET. Separation of retinoid-induced epidermal and dermal thickening from skin irritation. *Arch. Dermatol. Res.* 295:255-262, 2003.
6. Dame M, Xinwen J, Garrido R, Bobrowski W, MuDuffie E, Murphy H, Albassam M, Varani J. A stepwise method for the isolation of endothelial cells and smooth muscle cells from individual canine coronary arteries. *In Vitro Cell. Develop. Biol.* 39:402-406, 2003.
7. Bhagavathula N, Nerusu K, Ellis CN, Chittiboyina A, Avery MA, Christopher Ho CI, Benson SC, Pershadsingh HA, Kurtz TW, Varani J. Rosiglitzone inhibits biological responses in keratinocytes and signaling events that underlie responsiveness. *J. Invest. Dermatol.* 122:130-139, 2004.
8. Warner RL, Bhagavathula N, Nerusu K, Lateef H, Younkin E, Johnson KJ, Varani J. Matrix metalloproteinases (MMPs) in acute inflammation: Induction of MMP-3 and MMP-9 in fibroblasts and epithelial cells following exposure to pro-inflammatory mediators *in vitro*. *Exp. Molec. Pathol.* 76:189-195, 2004.
9. Varani J, Schuger L, Leonard C, Fligiel SEG, Kang S, Fisher GJ, Voorhees JJ. Reduced fibroblast interaction with intact collagen as a mechanism for depressed collagen synthesis in photoaged skin. *J. Invest. Dermatol.* 122:1471-1479, 2004.
10. Warner RL, Winger HC, Speyer CL, Varani J, Goldstein IG, Murphy HS, Johnson KJ. Marasmius oreades lectin induces renal thrombotic microangiopathic lesions. *Exp. Molec. Pathol* 77:77-84, 2004.
11. Warner RL, Likacs NW, Shapiro SD, Bhagavathula N, Nerusu KC, Varani J, Johnson KJ. Role of metalloproteinase in a model of allergic lung responses induced by cockroach allergen. *Amer. J. Pathol.* (in press) 2004.

12. Varani J, Kelley EA, Perone P, Lateef H. Retinoid-induced epidermal hyperplasia in human skin organ culture: Inhibition with soy extract and soy isoflavones. *Exp. Molec. Pathol.* 77: 176-183, 2004.
13. Varani J, Lateef H, Fay K, Elder JT. Antagonism of epidermal growth factor receptor tyrosine kinase ameliorates the psoriatic phenotype in organ-cultured skin. *Skin Pharm. Physiol.* (in press) 2004.
14. Lateef H, Stevens MJ, Varani J. All-trans retinoic acid suppresses matrix metalloproteinase activity and increases collagen synthesis in diabetic human skin in organ culture. *Amer. J. Pathol.* 165:167-174, 2004.
15. Varani J. Growth factors, intracellular signaling and skin hyperplasia. *J. Clin. Ligand Assay.* (in press) 2004.
16. Aslam MH, Fligiel H, Lateef H, Fisher GJ, Ginsburg I, Varani J. PADMA 28: A multicomponent herbal preparation with retinoid-like dermal activity but without epidermal effects. *J. Invest. Dermatol.* (in press) 2004.
17. Fligiel SEG, Standiford T, Fligiel SEG, Strieter RW, Tashkin D, Warner RL, Johnson KJ, Varani J. Matrix metalloproteinases (MMPs) and MMP Inhibitors in acute lung inflammation. (Submitted for publication), 2004.
18. Fligiel SEG, Tashkin D, Fligiel H, Standiford T, Johnson KJ, Varani J. Matrix metalloproteinases (MMPs) and MMP Inhibitors in chronic, habitual smokers of tobacco, marijuana and cocaine. (Submitted for publication), 2004.
19. Lateef H, Stevens M, Varani J. Topical pretreatment of diabetic rats with all-trans retinoic acid improves healing of subsequently-induced superficial wounds. *Diabetes* (in press), 2004.
20. Bhagavathula N, Nerusu KC, Fisher GJ, Liu G, Landolfi N, Voorhees JJ, Varani J. Amphiregulin and epidermal hyperplasia: Amphiregulin is required to maintain the psoriatic phenotype of human skin grafts on SCID mice. *Amer. J. Pathol.* (in press). 2004.
21. Varani J, Bhagavathula N, Nerusu KC, Sherzer H, Fay K, Boitano AE, Glick GD, Johnson KJ, Kang S, Opipari AW, jr. A novel benzodiazepine selectively inhibits keratinocyte proliferation and reduces retinoid-induced epidermal hyperplasia in organ-cultured human skin. *J. Pharmacol. Exp. Therapeut.* (in press) 2004.
22. Chakrabarty S, Wang H, Cnaff L, Hendy GN, Appelman H, Varani J. Calcium sensing receptor in human colon carcinoma: Interaction with Ca^{2+} and 1,25-dihydroxyvitamin D3. *Cancer Res* (in press) 2004.

BOOKS AND CHAPTERS IN BOOKS:

1. Varani J. Organ-cultured skin as a model for squamous epithelial cell invasion. *Frontiers in Bioscience* (in press).
2. Murphy H, Varani J, Ward PA: The Biology of Endothelial cells. *Allergy: Principals and practices*. Sixth Edition. E. Middleman, et al, eds. Mosbey, St. Louis, MO.
3. Murphy H, Varani J, Ward PA. Endothelial cell injury by neutrophils: Pathophysiology. *Perspectives in Lung Endothelial Barrier Function* (in press).
4. Varani J, Stevens MJ, Lateef H. Repair of connective tissue deficits in diabetic skin. *Current. Diabetes Rev.* (in press) 2004.

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

1. Dame MK, Yu X, Garrido R, Bobrowski W, McDuffie JE, Albassam M, Varani J. A method for the isolation of endothelial cells and smooth muscle cells from individual canine coronary arteries. Pfizer Technical Report. 2003.
2. Bhagavathula N, Kumar C, Bhagavathula S, Nerusu K, Chinnaiyan A, Varani J. Rosiglitazone – mechanisms of action in hyperproliferative disorders of skin. AACR 2004 (abs).
3. Varani J, Schuger L, Leonard C, Fligiel SEG, Kang S, Fisher GJ, Voorhees JJ. Reduced fibroblast interaction with intact collagen as a mechanism for depressed collagen synthesis in photoaged skin. *J. Invest. Dermatol.* 2004.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

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 (2003-04):
1. Jayne Reuben, Ph.D.
 2. Hungwei Gao, Ph.D.
 3. Laslo Marco Hoesel
- B. Graduate students
1. Stephanie McGuire, 3rd Year Medical Student
 2. Kurt Bernacki, 1st Semester Medical Student
 3. Vaishalee Padgaonkar, 4th Year Medical Student
 4. Daniel Rittirsch, Visiting 4th Year Medical Student (Ulm, Germany)
 5. Michael Fleirl, Visiting 4th Year Medical Student (Ulm, Germany)
- C. UROP Undergraduate Students:
1. Nick Rancilio
 2. Matthew Pianko
 3. Brandon Baugh
- D. Undergraduate students:
1. Lecture, College Honors Seminar 250 (LS&A), three hours.
 2. Jeff Crawford, 1st Year Undergrad (Calvin College)
 3. Eddie Martinez, 1st Year Undergrad (U. of Mich.)

III. RESEARCH ACTIVITIES

SPONSORED SUPPORT

- A. Principal Investigator, "Lung Immunopathology" (Training Grant) HL07517, \$227,536/yr., (5%) 06/01/96 - 05/31/06
- B. Principal Investigator, "Inflammatory Cells and Lung Injury" NIH/NHLBI PO1-HL31963, \$246,249 /yr. (25%) \$816,953/yr (all projects) 03/01/99 - 02/29/04
- C. Principal Investigator; "Lung Injury by Oxygen Metabolites (MERIT) RO1- GM29507 NIH/NIGMS, (20%) \$204,700/yr, 07/01/01 - 06/30/05
- D. Principal Investigator, "Protective Effects of Anti-C5a in Sepsis," NIH/NIGMS RO1-GM61656, (20%) \$204,700/yr; 01/01/02 - 05/31/07

- E. Principal Investigator, "Mechanisms and Prevention of Lung Injury Caused by Exposure to Mustard Gas" DAMD 17-03-2-0054 USAMRMC, \$1,932,000 total, (5%), 08/15/03 – 08/14/05

IV. ADMINISTRATIVE ACTIVITIES

DEPARTMENTAL:

- A. Chair, Department of Pathology.

MEDICAL SCHOOL/HOSPITAL:

- A. Medical School Executive Committee
- B. Clinical Chairs Council.
- C. Conflict of Interest Committee.
- D. Conflict of Interest and Commitment Committee
- E. Faculty Group Practice Committee
- F. Technology Transfer Committee.
- G. Geriatric Center Executive Committee.
- H. Michigan Eye Bank Research Review Committee.
- I. Undergraduate Research Opportunity Program, University of Michigan.
- J. University of Michigan Cancer Center Executive Committee.

UNIVERSITY OF MICHIGAN:

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

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES

EDITORIAL BOARDS

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

INVITED LECTURES/SEMINARS:

- 1. Invited Lecturer, Immunology Seminar: “Role of Complement in Sepsis”; University of Iowa, Iowa City, IA; October 8, 2003.
- 2. Invited Speaker, “Mechanisms of lung inflammatory reactions and oxidant pathways involved in damage to endothelial cells”; Multiple Organ Failure Meeting, Tokyo, Japan; October 25, 2002.
- 3. Invited Participant, Atorvastatin Research Awards Summit Meeting, Phoenix, AZ; January 30 – February 1, 2003
- 4. Invited Speaker, “Complement Activation and C5aR in Sepsis”, 6th World Congress on Trauma, Shock, Inflammation and Sepsis, Munich, Germany; March 2-6, 2004.
- 5. Invited Participant, 2nd ERS Lung Science Conference, Taormina, Italy; March 26-28, 2004
- 6. Invited Speaker, “Endotoxin challenge in the rodent”, International Sepsis Forum Shock Conference, Halifax, Nova Scotia; June 2, 2004

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS

- 1. Guo, R.F., Riedemann, N.C., Bernacki, K.D., Sarma, J.V., Laudes, I.J., Reuben, J.S., Younkin, E.M., Neff, T.A., Paulauskis, J.D., Zetoune, F.S., and **Ward, P.A.**: Neutrophil C5a receptor and the outcome in a rat model of sepsis. *FASEB J. Express*; article 10.1096/fj.02-0009fje, published online August 1, 2003
- 2. Guo, R.F., Riedemann, N.C., Bernacki, K.D., Sarma, J.V., Laudes, I.J., Reuben, J.S., Younkin, E.M., Neff, T.A., Paulauskis, J.D., Zetoune, F.S., and **Ward, P.A.**: Neutrophil C5a receptor and the outcome in a rat model of sepsis. *FASEB J.* 2003 17:1889-1891.
- 3. Riedemann, N.C., Guo, R.F., and **Ward, P.A.**: The enigma of sepsis. *J. Clin. Invest.* 2003 112: 460-467.
- 4. Younger, J.G., Shankar-Sinha, S., Mickiewicz, M., Brinkman, A.S., Valencia, G.A., Sarma, J.V., Younkin, E.M., Standiford, T.J., Zetoune, F.S., and **Ward, P.A.** Murine complement interactions with *Pseudomonas aeruginosa* and their consequences during pneumonia. *Am. J. Respir. Cell Mol. Biol.* 2003 29:432-438.
- 5. Riedemann, N.C., Guo, R.F., and **Ward, P.A.**: Conceptual perspectives: a key role of C5a/C5aR activation for the development of sepsis. *J. Leukoc.Biol.* Dec. 2003 74(6):966-970.
- 6. Riedemann, N.C., Guo, R.F., Bernacki, K.D., Reuben, J.S., Laudes, I.J., Neff, T.A., Gao, H., Speyer, C., Sarma, J.V., Zetoune, F.S., and **Ward, P.A.**: Regulation by C5a of neutrophil activation during sepsis. *Immunity*, 2003 19:193-202.

7. Anaya-Prado, R., Toledo-Pereyra, L.H., Guo, R.F., Reuben, J., **Ward, P.A.**, Walsh J. The attenuation of hemorrhage-induced liver injury by exogenous nitric oxide, L-arginine, and inhibition of inducible nitric oxide synthase. *J. Invest. Surg.* 2003;16(5):247-261.
8. **Ward, P.A.**: Acute lung injury: how the lung inflammatory response works. *Eur Respir J Suppl.* 2003 Sep;44:22s-23s.
9. Speyer, C.L., Neff, T.A., Warner, R.L., Guo, R.F., Sarma, J.V., Riedemann, N.C., Murphy, M.E., Murphy, H.S., and **Ward, P.A.**: Regulatory effects of iNOS on acute lung inflammatory responses in mice. *Am J Pathol.* 2003 163(6):2319-2328.
10. **Ward, P.A.**, Riedemann, N.C., Guo, R.F., Huber-Lang, M., Sarma, J.V., and Zetoune, F.S.: Anti-complement strategies in experimental sepsis. *Scand J Infect Dis*, 2003 35(9):601-603.
11. Huber-Lang, M., Weiss, M., Sarma, J.V., and **Ward, P.A.**: To be critical for the critically ill. *Lancet*, 2003 362(9399):1945.
12. Guo, R.F., Riedemann, N.C., and **Ward, P.A.**: Role of C5a-C5aR interaction in sepsis. *SHOCK*, 2004 21(1):1-7.
13. **Ward, P.A.**: The dark side of C5a in sepsis. *Nature Reviews-Immunology*. 2004 4:133-142.
14. Riedemann, N.C., Guo, R.F., Hollman, T.J., Gao, H., Neff, T.A., Reuben, J.S., Speyer, C.L., Sarma, J.V., Wetsel, R.A., Zetoune, F.S., and **Ward, P.A.**: Regulatory role of C5a in LPS-induced IL-6 production by neutrophils during sepsis. *FASEB J.* 2004 18:370-372, Epub 2003 Dec 19.
15. **Ward, P.A.**, Sarma, V., Rittirsch, D., Zetoune, F., Brueckner, U., and Huber-Lang, M.: Changes in the C5L2 receptor during experimental and clinical sepsis. *Molec Immunol*, 2004 41:323-324.
16. Zetoune, F., Rittirsch, D., Huber-Lang, M., and **Ward, P.A.**: Changes in the C5L2 C5a receptor during sepsis. *Molec Immunol*, 2004 41:331.
17. Albrecht, E.A., Chinnaiyan, A.R., Varambally, S., Kumar-Sinha, C., Barrette, T.R., Sarma, J.V., and **Ward, P.A.**: C5a-induced gene expression in human umbilical vein endothelial cells. *Am J. Path.* 2004 164:849-859.
18. Laudes, I.J., Guo, R.F., Riedemann, N.C., Speyer, C., Craig, R., Sarma, J.V., and **Ward, P.A.**: Disturbed homeostasis of lung ICAM-1 and VCAM-1 during sepsis. *Am J. Path.* 2004 164(4):1435-1445.
19. Gao, H., Guo, R.F., Speyer, C.L., Reuben, J., Neff, T.A., Hoesel, L.M., Riedemann, N.C., McClintock, S.D., Sarma, J.V., Van Rooijen, N., Zetoune, F.S., and **Ward, P.A.**: Stat3 activation in acute lung injury. *J Immunol.* 2004 172:7703-7712.
20. Riedemann, N.C., Guo, R.F., Gao, H., Lei, S., Hoesel, M., Hollmann, T.J., Wetsel, R.A., Zetoune, F.S., and **Ward, P.A.**: Regulatory role of C5a on macrophage migration inhibitory factor (MIF) release from neutrophils. *J Immunol.* 2004 173(2):1355-1359.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

- A. Director, Division of Clinical Pathology/Clinical Laboratories, May 1993-present.
- B. Director, Clinical Immunopathology Service; September 1989-present.
- C. Microbiology Laboratory; review of peripheral blood parasite smears; July 1996-present.
- D. Molecular Diagnostics Laboratory; signout of cases (3 weeks/year); July 1997-2003.
- E. Molecular Diagnostics Laboratory; Interim Director, August 2002-June 2003.
- F. Sendout Laboratory; Director, August 2002-present.

II. TEACHING ACTIVITIES:

- A. "Current Topics in Immunopathology" journal club series: pathology residents, M4 students (41 contact hours).
- B. "Current Management Problems for Pathology Residents" series: pathology residents (13 contact hours).
- C. Clinical Pathology Grand Rounds:
 - 1. "Cases and images in immunopathology" (11/14/03).
- D. Immunopathology signout: pathology residents, M-4 medical students, medical technology students (three times/week; 48 weeks/year).
- E. Immunopathology component of Block B (Clinical Pathology); ad hoc topical reviews: pathology residents (67 contact hours).
- F. Supervision of Research activities for:
 - 1. Anjali Desai, Ph.D. (Research Investigator); (6/15/96-present).
 - 2. Kevin Coles (2003 UM graduate); (5/03-6/04).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

PROJECTS UNDER STUDY:

- A. Role of cellular redox status and neutrophil-derived mediators in MCP-1-mediated pulmonary granulomatous vasculitis.
- B. Modulation of proatherogenic endothelial and smooth muscle cell functions by erythropoietin, reactive oxygen intermediates, and reactive nitrogen intermediates.
- C. Role of erythropoietin in accelerated atherogenesis in ApoE (-/-) mice with drug-induced chronic renal disease.
- D. Measurement of NO production by endothelial cells using a chemical sensor. (Collaboration with Michael Meyerhott, Ph.D., Department of Chemistry, University of Michigan).
- E. Pathophysiologic role of oxidants in uremia and its complications (collaboration with Rajiv Saran, M.D., Department of Internal Medicine, University of Michigan Medical School).

- F. Ischemia-reperfusion injury in perinatal rat brain (collaboration with Faye Silverstein, M.D., Departments of Pediatrics and Neurology, University of Michigan Medical School).

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL:

- A. Member, Operations Improvement Committee, University of Michigan Health System 2000-2003.
- B. Member, Professional Billing Compliance Committee, University of Michigan Medical School 1999-present.
- C. Dean's Advisory Committee (ad hoc substitute for Dr. Peter Ward), 1994-present.
- D. Clinical Council (ad hoc substitute for Dr. Peter Ward), 1996-present.

DEPARTMENTAL:

- A. Interviewer of Pathology Residency Candidates, 1989-present.
- B. Interviewer of Pathology Graduate Program Candidates, 1990-present.
- C. Chairman, Laboratories Communications Committee, 1993-present.
- D. Chairman, Department of Pathology Quality Assurance Committee, 1993-present.
- E. Clinical Associate and Advisory Committee for Medical Technology Program, Eastern Michigan University, 1993-present.
- F. Chairman, Category Risk II Faculty Salary Planning Committee, Department of Pathology, 1996-present.

REGIONAL AND NATIONAL:

- A. Ad hoc referee for:
 - 1. American Journal of Pathology.
 - 2. Laboratory Investigation.
 - 3. Human Pathology.
 - 4. Journal of Applied Physiology.
 - 5. Lung.
 - 6. Blood.
 - 7. Journal of Laboratory and Clinical Medicine.
 - 8. Pediatric Research.
 - 9. Journal of Leukocyte Biology.
 - 10. American Review of Respiratory Disease.
 - 11. Chest.
 - 12. Journal of Pharmacology and Experimental Therapeutics.
 - 13. Circulation.
 - 14. Ophthalmology.
 - 15. American Journal of Respiratory Cell and Molecular Biology.
 - 16. Clinical Immunology and Immunopathology.
 - 17. Circulation Research.
 - 18. Journal of Immunology.
 - 19. Surgery.
 - 20. Reviews of Infectious Diseases.
 - 21. Infection and Immunity.
 - 22. Experimental Lung Research.
 - 23. Journal of Rheumatology.
 - 24. Clinical Infectious Diseases.

25. Journal of Clinical Investigation.
26. Cytometry.
27. Biological Signals.
28. Metabolism.
29. Molecular Medicine Today.
30. American Journal of Respiratory and Critical Care Medicine.
31. The Cancer Journal.
32. British Journal of Pharmacology.
33. Kidney International
- B. Member, Test Committee for Clinical Pathology, American Board of Pathology, 1999-present.
- C. Member, Council for Diagnostic Immunology and Molecular Pathology, American Society of Clinical Pathologists, 1998-present.
- D. Member, Diagnostic Immunology Resource Committee, College of American Pathologist, 2000-present.
- E. President, Michigan Society of Pathologists, 2003.
- F. Member, Committee on Self-Assessment, American Society of Clinical Pathology, 2003.

V. INVITED LECTURES/SEMINARS:

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

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

ARTICLES SUBMITTED FOR PUBLICATION:

1. Desai A, Lankford H, Warren JS: Nitric oxide suppresses erythropoietin-induced monocyte chemoattractant protein-1 in endothelial cells: Implications for atherogenesis in chronic renal failure. *J Pharm Exp Therapeutics* (submitted).
2. Desai A, Zhao Y, Warren JS: Erythropoietin and EPO mimetic peptide-1 exert anti-apoptotic activity and upregulate bcl-2 expression in human umbilical vein endothelial cells (submitted).

BOOKS/CHAPTERS IN BOOKS:

1. Warren JS, Ward PA: The inflammatory response, in Beutler E, Lichtman MA, Collier BS, Kipps TJ and Seligsohn U (eds.) *Williams' Hematology*, 6th Edition, McGraw-Hill, New York, NY, (in press).
2. Warren JS: Leukocyte functional assays by flow cytometry, in Keren DF, McCoy JP, Carey JL, and Hanson CA (eds.) *Flow Cytometry and Clinical Diagnostics*, 3rd Edition, ASCP Press, Chicago, IL, (in press).

3. Warren JS: Immunodeficiency disease, in McClatchey KD (ed.) Clinical Laboratory Medicine, 2nd Edition, Lippincott Williams and Wilkins, Philadelphia, PA, (in press).
4. Warren JS: Immunopathology, in Rubin E (ed.) Pathology 4th Edition, Lippincott-Williams and Wilkins, Philadelphia, PA, (in press).
5. Warren JS, Ward PA: The inflammatory response, in Lichtman MA, et. al. (eds.) Williams Hematology, 7th Edition, McGraw-Hill, New York, NY, (in press).

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

1. Desai A, Zhao Y, Lankford HA, Warren JS. Human recombinant erythropoietin (EPO) upregulates bcl-2 expression in human umbilical vein endothelial cells. Experimental Biology, Washington, DC (abstract), April 17-21, 2004.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. CLINICAL ACTIVITIES:

- A. Assistant Director of the Molecular Diagnostics laboratory. Performed signout coverage in the director's absence and provided technical consultation and assistance in the implementation of new procedures.

II. TEACHING ACTIVITIES:

- A. Mentor, postdoctoral fellows: Rajashree Deshpande, Anandi Srinivasan, Leana Topper
- B. Mentor, graduate student fellows: Phil Palmbo (MSTP, CMB), James Daley (CMB)
- C. Mentor, rotation student: Scott Leiser (PIBS)
- D. Mentor, undergraduate students: Monica Heger, Renee Vander Laan
- E. Member, thesis committees: Tammy Morrish (Human Genetics), Jonathan Rios-Doria (CMB), Marc Prindle (CMB), Anne Casper (Human Genetics), Sandra Durkin (Human Genetics), Hui-Min Tseng (University of Texas Health Science Center at San Antonio, Molecular Medicine Program)
- F. Member, preliminary examination committee: Natalie Whitfield (CMB, chair), Fred Derheimer (CMB), Brandi Thompson (CMB).
- G. Member, Cellular and Molecular Biology Training Program
- H. Path 581, 2 lectures
- I. Path 582, 1 lecture, 1 discussion section
- J. Path 850, Coursemaster, research seminar series for graduate students
- K. Two week full-time course in molecular biology and DNA repair, University of Michigan Postdoctoral Research Training Program

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Disposition of DNA Double-Strand Breaks Among Multiple Pathways of Repair", Pew Scholars Program in the Biomedical Sciences (8%), \$60,000/year (\$240,000/four years), 7/1/2000-6/30/2004.
- B. Principal Investigator, "End Processing in DNA Double-Strand Break Repair", NIH/NCI 1 R01 CA90911-01 (27%), \$145,250/current year (\$601,750/four years), 4/1/2001-3/31/2005.
- C. Mentor, "Role of APC-Binding Protein BIM1 on Chromosome Dynamics", NIH NRSA 5 F32 GM064204-04, Leana Topper, Ph.D., postdoctoral fellow, 11/2002-8/2004.

PENDING:

- A. Principal Investigator, "Systematic Genetics Analysis of Yeast NHEJ", NIH/NCI 1 R01 CA102563-01A1 (30%), \$157,500/current year (\$787,500/five years), 8/1/2004-7/31/2009. *Funded, will begin after report period.*

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Pathology student recruitment activities (lunch, poster session)
- B. Chair and organizer, Pathology Research Seminar Series
- C. Member, Pathology Graduate Program Curriculum Committee

MEDICAL SCHOOL/HOSPITAL:

- A. Member, MSTP Career Advisory Panel
- B. MSTP student interviews
- C. Faculty candidate interviews/recruitment.

UNIVERSITY OF MICHIGAN:

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

REGIONAL AND NATIONAL:

- A. None.

V. OTHER RELEVANT ACTIVITIES:

- A. Manuscript review, Genetics, MCB, Biochemistry
- B. Biological Sciences Scholars Program, University of Michigan
- C. Pew Scholars Program in the Biomedical Sciences, Pew Charitable Trusts
- D. Member, Michigan Comprehensive Cancer Center

EDITORIAL BOARDS:

- A. None

HONORS AND AWARDS

- A. None.

PATENTS:

A. None

INVITED LECTURES/SEMINARS:

1. "Multiple mechanisms for repairing 3' blocking lesions in DNA: the replication connection." Graduate Center for Toxicology, University of Kentucky, Lexington, Kentucky, September 29, 2003.
2. "Nonhomologous end-joining: lessons from simple organisms." Norris Comprehensive Cancer Center, Department of Pathology, University of Southern California, Los Angeles California, January 26, 2004.
3. "Piecing together the mechanism of nonhomologous end-joining" Pew Scholars Program/Latin Fellows Program Annual Meeting, Rio Grande, Puerto Rico, March 8, 2004.
4. "Repairing broken chromosomes - from microbes to man." Siteman Cancer Center Cancer Biology Course, Washington University School of Medicine, St. Louis, Missouri, April 20, 2004.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Deshpande R, Wilson TE. Identification of DNA 3' phosphatase active site residues and their differential role in DNA binding, Mg²⁺ coordination and catalysis. *Biochemistry*, 43:8579-89 (2004).

ARTICLES SUBMITTED OR IN PREPARATION:

1. Della M, Palmboos PL, Tseng HM, Tonkin LM, Daley JM, Topper LM, Pitcher RS, Tomkinson AE, Wilson TE, Doherty AJ. Mycobacterial Ku and Ligase proteins constitute a two-component NHEJ repair machine. *Science*, submitted.
2. Daley JM, Wilson TE. Rejoining of DNA double-strand breaks as a function of overhang length. *Mol. Cell. Biol.*, submitted.
3. Karumbati AS, Wilson TE. Abrogation of the Chk1-Pds1 checkpoint leads to tolerance of persistent single-strand breaks. *EMBO J.*, submitted.
4. Nonhomologous End Joining in Yeast. *Annual Review of Genetics*. Book chapter, due March, 2005.

BOOKS/CHAPTERS IN BOOKS:

1. None

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

1. Karumbati AS, Wilson TE. Suppressors of the slow growth phenotype of *apn1 tpp1 rad1* yeast: unexpected phenotypes of DNA damage checkpoint mutants. Genetics Society of America conference "Yeast Genetics and Molecular Biology", Seattle, Washington, July 2004.
2. Palmbo PL, Daley JM, Topper LM, Tonkin LM, Della M, Doherty AJ, Wilson TE. Reconstitution of bacterial nonhomologous end-joining (NHEJ) in yeast: a living test tube to study DNA repair. Genetics Society of America conference "Yeast Genetics and Molecular Biology", Seattle, Washington, July 2004.

SECTION REPORTS

ANATOMIC PATHOLOGY

AUTOPSY SERVICE

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 2003 - 30 JUNE 2004

I. Timely Completion of Autopsy Reports:

The autopsy service continues to emphasize timely completion all our autopsy reports. This has required active management of the autopsy late list and individually contacting both house officers and faculty when their cases are older than 30 days. Additionally, with the new incoming house officers we have made a strong statement that autopsies should be completed within 30 days. The table below lists the autopsy completion time for different years. Since January 1, 2004, we have started a new initiative where any autopsy older than 45 days is closely tracked until it is finished. This close tracking is accomplished by paging the house officer each day that their case is not complete. Since adopting this protocol on January 1, 2004, there has only been a single autopsy later than 60 days.

Time Interval	% completed in 60 days	% completed in 90 days	# of Autopsies
1995-96	40	58	541
1996- 97	64	89	565
1998-99	96	100	350
1999-2000	91	100	295
2000-2001	84	99	295
2001-2002	85	99	293
2003-2004	94	99	306

II Autopsy Reporting on Careweb

Starting January 1, 2004, autopsy results have been available on Careweb. The front page from the autopsy report, the clinicopathological diagnosis, is placed on Careweb. Coupled with the improved turnaround time, this has significantly improved the utility of the autopsy service by providing timely feedback in an easily accessible manner.

III Conferences:

We continue to present our cases at several different conferences. Pathology regularly participates in the weekly Death and Complications conference in the Department of Surgery. We also make presentations at the monthly Morbidity and Mortality conference in the Department of Internal Medicine. A continuing monthly conference in the Department of Internal Medicine has 4 autopsies presented each month. In contrast to the usual M&M conference where most of the presentation deals with the clinical story, the emphasis for this conference is on the autopsy findings and histopathology. This conferences run primarily by the first year pathology residents who have completed their autopsies. At the request of the Department of Emergency Medicine, we also making presentations twice a year to their house officers.

IV Autopsy percentage:

We continue to determine the autopsy rate by clinical service in the hospital. The total number of deaths, number of cases and autopsy percentage for the 2002-03 year are listed below. This information as they shared with both the clinical chairs as well as the residency program directors of the University of Michigan.

	# of deaths	# of cases	% of deaths
Medicine	476	110	23%
Surgery	277	44	16%
Pediatrics	120	42	35%
Other services	46	12	26%
Total Hospital	919	208	23%

Hospital total 23%

V Medical Examiner Cases:

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

VI Statistics:

This covers the time period July 1, 2003 to June 30, 2004.

Total number of autopsies performed	314
Hospital autopsies	240 (includes 37 brain only)
Medical examiner autopsies	74

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

CYTOPATHOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY

ANNUAL REPORT

1 JULY 2003 – 30 JUNE 2004

Total gynecologic specimens for the year were 48,020; a 5.5% decrease from last year. (Botsford Hospital is now doing their own ThinPreps.) Non-gynecologic specimens numbered 7,002, a 6.2% increase from last year. Fine needle aspirations totaled 1,572 for the current year, a 2.9% increase from last year. The laboratory continued to achieve the turnaround time for non-gynecologic specimens within 24-48 hours, and the turnaround time for the cervical smears have improved to an average of 3 working days.

Mrs. Linda Luchansky joined our department as a laboratory assistant on July 14, 2003, and Ms. Linda Dawson joined as a new cytotechnologist on September 1st, 2003. At this time, we are approximately 96% converted to ThinPrep in gynecologic specimens. An amended report combining the original cytologic diagnosis and the HPV test by the Diogene method has been constructed through the Cerner program, and we continue to work with Cerner to construct a system that will enable automatic flagging of ASCUS cases and automatic ordering of the HPV testing. A proposal for a reflexive HPV testing for ASCUS cases was submitted for consideration by the ECCA.

The fine needle aspiration service at the Taubman Center was coordinated to assist with ultrasound guided thyroid aspirates performed by the Endocrinology Service. These patients are scheduled on Tuesday and Friday afternoons. Negotiations with the Cancer and Geriatric Center regarding the relocation of the fine needle aspiration clinic to Multiprocedure Room 4 from our current dedicated FNA room is ongoing.

Our fellowship program continued to be highly successful. Drs. Lennart Tan and Guangming Guo completed their training with distinction. Dr. Robert Pu was successfully recruited and joined our faculty in cytopathology effective in September of 2003.

The Cytopathology Section had excellent representation at national meetings with workshops and posters presented by the cytology faculty and fellows. Dr. Robert Pu received the F. Stephen Vogel Award at the 94th Annual USCAP Meeting at Vancouver, Canada (2004).

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

DERMATOPATHOLOGY SERVICE
DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 – 30 JUNE 2004

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

Clinical Service

The clinical service volume is as follows:

	2001-2002	2002-2003	2003-2004
ID	7,205	6,811	6343
MD	7,248	9,663	9514
TD	1,691	1,698	1568
DP	1,244	1,336	1577
MISC	126	145	172
TOTAL	17,514	19,653	19,174

The Dermatopathology Service continues to be a high volume service, with greater than 19,000 cases signed out this year. The consult service experienced an 18% growth in volume. The clinical service load seen by each faculty member of the Dermatopathology Service, Dr. Su, Dr. Fullen, and Dr. Lowe, is substantial, with greater than 6,000 cases each.

We continue our active involvement in the University of Michigan Multidisciplinary Melanoma Clinic (MDMC) and Tumor Board (bi-weekly). This remains the largest melanoma program in the United States. Accordingly, the volume of difficult pigmented lesions seen by our service is substantial, as are the numbers of wide local excisions, biopsies, and sentinel lymph node biopsies generated by this busy clinic, all of which directly impact on Dermatopathology. In addition, we have a very visible role in Cutaneous Lymphoma Conference and Tumor Board.

Education

The Dermatopathology Service continues its extensive and committed involvement with residency and medical student education in the both the Departments of Pathology and Dermatology. Teaching activities include daily instruction at the microscope during signout, weekly formal didactic sessions, weekly diagnostic conference, and active participation in the MSII Dermatology Core Sequence and

Dermatopathology Laboratory. Dr. Lyndon Su and Dr. Douglas Fullen also actively participate in formal dermatopathology didactic sessions for our pathology residents.

Scholarly Activities

During this academic year, two of the Dermatopathology faculty successfully participated in the promotions process. Dr. Lyndon Su's promotion to Clinical Associate Professor will be effective September 1, 2004. Dr. Lori Lowe's promotion to Clinical Professor will also become effective September 1, 2004. Dr. Lowe is the 8th woman to achieve the rank of Clinical Professor at the University of Michigan. We continue to be highly productive in scholarly activities and academic pursuits with numerous publications individually and/or collectively in well-respected peer reviewed journals. In addition, we have all actively participated at national meetings, either as invited speaker(s) and/or abstract/poster presentations.

Goals for 2004-2005

The Dermatopathology Service remains committed to the search and recruitment of an additional faculty member. In addition, we are in the process of establishing a Dermatopathology Fellowship program.

Respectfully submitted,

Lori Lowe, M.D.
Director
Dermatopathology Service

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

Dr. Mila Blaivas, Ms. Constance J. D'Amato, Dr. Andrew Lieberman and Dr. Paul E. McKeever contributed to the Neuropathology Service. Ms. D'Amato is active emeritus.

I. CLINICAL ACTIVITIES:

1. There were over 1200 neurosurgical cases examined this year. There were many personal consult cases. (M.B. = 135)
2. The Diagnostic Unit of the Neuropathology Core Laboratory of the MADRC processed 74 dementia brain cases. Of these 74 brains, 63 were MADRC cases, 6 were neurology hospital patients, and 5 were from the Michigan Dementia Postmortem Network Program.
3. There were 434 muscle biopsies, 40% with electron microscopy. There were 110 peripheral nerve biopsies. There were 17-teased fiber preparations and 100 with electron microscopy. 18 skin or non-muscle/nerve tissue examined with electron microscopy. 23 muscle biopsies were examined with 10-14 anti-dystrophy antibodies in the IPOX laboratory.
4. There were over 300 University Hospital brains examined.
5. The Brain Tumor Board of the University of Michigan Cancer Center and Hospitals, supported weekly by a neuropathologist, reviewed neuropathology and clinical aspects of more than 150 difficult neuro-oncology cases.

II. TEACHING ACTIVITIES:

1. Medical Students: This year the neuropathology faculty taught in the eight weeks Neuroscience Sequence for our second year medical school curriculum. There were fourteen hours of neuropathology taught: six hours of lecture and eight hours in the laboratory.
2. Dental Students: 4 lectures.
3. House Officers, Graduate Students, Postgraduate and other students and faculty: These included the following Continuing Medical Education accredited conferences: periodic conferences for Neurology; monthly Rheumatology Pathology Grand Rounds and occasional CPC conferences; monthly conferences where all biopsies are presented and interpreted; a weekly conference where abnormal brains are examined (including two or three weeks per month for dementia cases) with all clinicians invited; weekly nerve and muscle conferences; monthly nerve and muscle biopsy conferences. We provided individual instruction on autopsies and biopsy material; Neuropathology 858, an 8-hour laboratory course; bi-monthly conferences with Neuroradiology, Neurosurgery and Neuroradiology House Staff and every third month a microscopic conference for dementia brain cases. Weekly seminars were provided to neurological and neurosurgical house staff on clinico-pathological correlations.

4. Neuropathology 858, an evening course, given in the Fall, was taught by Dr. Lieberman and Ms. D'Amato.
5. Electives: Senior Medical Students, Pathology, Neurosurgery, and Neurology Residents were offered elective rotations in the Neuropathology Section.

III. RESEARCH ACTIVITIES:

1. Dr. Andrew Lieberman and Ms. D'Amato provided neuropathology support for MADRC. Dr. Lieberman was co-director of the Neuropathology core of MADRC.
2. Dr. Blaivas is working on the histology of animal models and human application in genetic treatment of rheumatoid arthritis with the Arthritis and Rheumatology Section with Blake Roessler; Neurology, Neuro-oncology, Genetics, Gynecology, and Pulmonary/Internal medicine on various projects.
3. Dr. McKeever and associates were determining differences in gene product expression in brain tumors. They assessed the predictive value of markers in brain tumor specimens. He is finishing publications from a NIH funded project studying the prognostic potential of MIB-1 proliferation marker on brain tumors. He was the study pathologist for a multi-institutional study of treatments of low-grade astrocytoma for the Children's Cancer Group.
4. Dr. Lieberman's laboratory studies the mechanisms of neurodegeneration in Kennedy's disease, a disorder affecting motor neurons of the brain stem and spinal cord. He is using cell culture and animal models to determine how the causative mutation leads to neuronal dysfunction and death. He is the principal investigator on grants from the NIH and Muscular Dystrophy Association, that support his work.
5. University of Michigan Cancer Center faculty and staff with clinical research interests in brain tumors met and generated a number of project considerations with Pathology, Neurosurgery, Nuclear Medicine, Neuropathology, Neurology and Neuroradiology collaborations.
6. Collaboration with Neurology, Michigan State University, The Alzheimer's Association, Spectrum Health, and Wayne State University has established a registry for Alzheimer's disease and other dementias and degenerative diseases.

CLINICAL PATHOLOGY

DIVISION OF CLINICAL PATHOLOGY**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

The Clinical Laboratories have continued to provide excellent, full-spectrum service (more than 800 different laboratory analyses) as the UMHS has continued to expand both its volume and scope in ambulatory care activities and experienced growth in several major clinical programs. Substantial effort has again been directed towards aggressive laboratory utilization control, the improvement of test ordering, laboratory logistics, achievement of compliance with HCFA-mandated rules on documentation of test-ordering indications, and achievement of compliance with federal rules related to FDA approval of testing methods. Superimposed upon these efforts has been further development of computer links with M-Labs clients. In 2003-04 the Clinical Laboratories performed more than 3-4 million billable analyses (10 million individual measurements), supported a wide array of clinical and research programs, and added or replaced more than 40 testing methods. The maintenance of high quality services by the Clinical Laboratories, in the face of increasing complexity of demands, is testimony to the professionalism of the staff and the management capabilities of the laboratory directors and senior laboratory personnel. The Clinical Laboratories successfully completed the biannual College of American Pathologists self-inspection in May, 2004. Maintenance of the delicate balance among quality service, cost effective testing, utilization control, and the research and development which characterizes an academic institution, will be a continuing challenge.

A major achievement was the continuing pursuit of an aggressive utilization management program. More than \$980,000 in direct laboratory cost avoidance and test utilization control was realized in 2003-04. This was made possible through educational meetings with each clinical department chairman, a series of extra-departmental educational presentations, publication of on-line (CareWeb) cost data, and, most effectively, direct utilization control policies and interventions.

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

Faculty and laboratory staff participated in a wide variety of intramural and extramural educational programs during 2003-04. For instance, the AIMCL (informatics) course in Las Vegas was again well attended, making it the most visible courses of its kind in the United States. The May AIMCL course brought together leaders from a variety of institutions and laboratory information technology fields to discuss the future of clinical pathology practice. These programs, along with the M-Labs educational programs, are prominent examples of educational outreach activities. The revised clinical pathology residency training format, which organizes pathology residents into teams that rotate through four blocks of clinical laboratories that are grouped according to "relatedness of discipline", was

again updated in 2003-04. In keeping with a thematic approach, the 2003-04 version solidified the four rotation blocks and places greater emphasis on molecular diagnostics, coagulation, informatics, and management. The continued high quality of trainees in the Hematopathology Fellowship program has enhanced the service, educational, and academic missions of the Hematopathology group and the Department.

The academic achievements of faculty members within the Clinical Pathology Division have been outstanding. As a group, the CP faculty had approximately 100 articles published in peer-reviewed journals. Most faculty members played highly visible leadership roles in national organizations, courses, symposia, as well as on editorial boards, examining committees, and research review study sections; an illustration of their high levels of recognition throughout the United States (see individual reports). Numerous faculty members received extramural funding that supported a variety of scholarly activities (see individual reports).

The Clinical Pathology Division will continue to face new challenges. In addition to its ongoing academic enterprises, educational issues, leadership and development in quality assurance, and laboratory resource utilization in the context of the hospital cost efficiency program, the Division plans to continue its attention to informatics and the clinical molecular diagnostics program. Achievement of these objectives will require the continued commitment, professionalism, and hard work of the faculty, laboratory staff, administration, and house officers.

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

**UNIVERSITY HOSPITALS BLOOD BANK
AND TRANSFUSION SERVICE**

**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

PATIENT CARE:

Blood component utilization increased relative to the previous year by 6.7% overall with approximately 104,800 total components dispensed. Red Blood Cell utilization approximated 31,000 units, representing a slight decline from the previous year. Platelet Concentrate utilization was approximately 51,000, which is increased. Increased overall utilization represents increased clinical activity. The medical staff continues efforts to assure appropriate use of blood components.

Hematopoietic progenitor cell processing activity was comparable to the previous year with 458 total units processed. Most patients are continuing to reach the collection target in one procedure.

The transfusion and apheresis activity was also similar to the previous year with 1471 patient encounters. There were 564 therapeutic apheresis procedures and 356 hematopoietic progenitor cell collections performed. The proportion of progenitor cell collections and therapeutic apheresis procedures has remained steady. LDL apheresis is experiencing slow and steady growth with 49 procedures performed.

The Blood Bank successfully implemented automated type and screen testing using the Ortho ProView device. Automated testing has significantly decreased the turn-around time for pretransfusion testing. The University of Michigan is current a national leader in the use of this technology. Margaret Stoe was instrumental in implementation of automation.

Screening of Platelet Concentrates for bacterial contamination by pH testing was implemented. Phyllis Gruszczynsk was instrumental in this effort. The rate of false-positive tests has been less than 1%, which is lower than was expected based on validation studies. The Blood Bank continues to explore options for the improvement of bacterial screening.

The Blood Transfusion Policies and Standard Practices was revised and updated. Significant changes and additions were made to transfusion guidelines for the aid to clinicians ordering transfusions.

EDUCATIONAL ACTIVITIES:

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

The 30th annual postgraduate course, "Current Topics in Blood Banking", was held on June 2-4, 2004. The course, under the direction of Mr. Judd, attracted over 100 technologists and physicians from throughout the United States. It continues to be one of the most popular postgraduate courses in the country devoted to blood bank topics. The Blood Bank and Transfusion Service medical and technical staffs were instrumental in planning, organizing and presenting this program.

PROFESSIONAL ACTIVITIES:

Members of the Blood Bank and Transfusion Service medical and technical staffs were active at the regional and national levels. Suzanne Butch served on committees of the American Association of Blood Banks, the Michigan Association of Blood Banks, ICCBBA, the American Society for Clinical Laboratory Science, the Michigan Society for Clinical Laboratory Science, and the National Certifying Agency of Clinical Laboratory Personnel. Suzanne Butch also was chosen to present the Karen Tiegerman Memorial Lecture at the Massachusetts Association of Blood Banks Annual Meeting. LouAnn Dake was a member of the AABB Immunohematology Reference Laboratories Accreditation Program Unit Committee, and presented at programs of the Michigan Association of Blood Banks and the Immunohematology Reference Laboratory Conference. Phyllis Gruszczynski worked extensively with the department recruitment committee and has participated in several site visits to schools. Terry Downs was Co-chair of the Michigan Association of Blood Banks Spring Workshop. Dr. Davenport served on the Editorial Board of TRANSFUSION, and was a Consensus Panel member of the international conference Towards an Understanding of TRALI, held in Toronto, Canada, April 1-2, 2004. Ms. LouAnn Dake, Sandra Hoffmann, Suzanne Butch, and Margaret Stoe participated in assessment activities for the American Association of Blood Banks. Sheryl Woloskie, RN became the first person at our facility to be certified by the ASCP as a Hemapheresis Practitioner. Margaret Stoe was elected President of the Michigan Association of Blood Banks.

RESEARCH ACTIVITIES:

Faculty research activities are documented in individual reports of Dr. Davenport, Dr. Cooling, and Mr. Judd. The Transfusion and Apheresis Service provided crucial support in leukocyte collection for General Clinical Research Center clinical research protocols.

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

CLINICAL CYTOGENETICS LABORATORY

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 2003 - 30 JUNE 2004

Overview

The laboratory had a 14.2% increase in the number of samples processed this year (N=3218) compared to last fiscal year, with a total of 2711 cytogenetics and 466 FISH studies performed (+8.3% and +68.8% respectively). An additional 41 samples were cultured for send-out biochemical or molecular genetic testing.

Thomas Glover, Ph.D. (Professor, Department of Human Genetics) continued to provide invaluable expertise and sign-out coverage of constitutional genetics cases. Lisa R. Smith, Ph.D. served as Assistant Director. One full-time technologist was hired following a departure and one new full-time technologist position was filled.

Clinical Services

The number of samples sent for cytogenetic analysis increased in both major sections of the laboratory, both for constitutional and oncology studies. The constitutional blood samples saw a dramatic increase as of January 2004. The second half of the fiscal year had a 41% increase in sample number over the first half (N=+121). We determined that these increases were caused by increases in faculty staffing in Pediatrics, including Genetics, Endocrine, and Neurology sections. This occurred at the same time that we were understaffed by one FTE due to an extended medical leave. To accommodate the increase, in addition to requesting overtime, we began to send some samples out to Mayo Medical Laboratories in May. Nineteen blood samples were sent out for cytogenetic analysis. The year-end total showed a 14.9% increase in the number of blood samples (N=+92) over last fiscal year. The prenatal diagnosis samples had a slight increase, at +1.5% with a 6.8% increase in amniocentesis samples offset by a -15.7% decline in chorionic villus samples (N=+24 and -17, respectively). Tissue samples for karyotyping, including skin biopsies and products of conception, declined by -6.0% (N=-7). The tissue culture service for fibroblasts to send out for biochemical and molecular genetic studies leveled off (N= -2, -4.7%) after three years of increases.

For neoplasias, the number of bone marrow samples increased significantly (N=+117, +9.4%). The solid tumors had a slight increase (N=+3, +4.8%). Much of this gain can be attributed to the addition of MLabs client Botsford Hospital in July 2003, which submitted 89 samples over the year. Submissions from this one client comprised a significant fraction of MLabs oncology samples (35.6%). MLabs samples accounted for a higher fraction of the labor-intensive oncology samples this year (16.8%) over last year (+2.8%). In response to the dramatic increase in constitutional blood samples and substantial incremental increases in oncology samples from in-house, two MLabs clients were discontinued in June 2004.

The number of FISH tests increased for both constitutional and oncology FISH. Constitutional FISH increased by 17.1% (N=+25), while oncology FISH increased by 50% (N=+65) over last year. The increase in oncology FISH testing is due to increasing demand for BCR/ABL fusion gene monitoring following Gleevec therapy. In addition, we began Subtelomeric FISH testing after long-standing demand from several departments. The initial frequency of submissions for subtelomeric FISH was at expected levels, however, with the increase in constitutional blood samples came a concomitant increase in requests for subtelomeric FISH. As was done for constitutional blood karyotyping, we sent out six subtelomeric FISH samples to accommodate the volume. A total of 100 subtelomeric FISH tests were performed in house.

Education

A total of 10 residents and fellows from several departments came to the laboratory for rotations. Seven Pathology residents, one Hematopathology fellow, and two fellows from Maternal Fetal Medicine rotated through the laboratory. The Pathology residents and Ob-Gyn fellows gave brief talks for the technologists in areas relevant to the case work in the laboratory, making a much-appreciated contribution to continuing education.

Future Plans

As a consequence of the increased demand for both standard cytogenetics and FISH testing, we added one new full-time technologist position, and if increases continue, we expect that another position will be necessary.

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

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

**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 2003-30 JUNE 2004**

Overview

The 2003-2004 academic year saw continued growth, development, innovation, and academic leadership in the combined hematopathology laboratories. We continued our goal toward laboratory automation with the purchase of three new Beckman-Coulter LH755 hematology analyzers and a Beckman-Coulter 1500 automation line, with necessary laboratory renovations and installation of the automation line scheduled for winter 2004-2005. We continued our tradition of leadership in the optimization of laboratory operations by expanding our coagulation autoverification initiative, implementing new coagulation assays, and expanding the services offered by our bone marrow laboratory staff. We made significant progress toward improving flow cytometry operations with the purchase of three new Beckman-Coulter FC500 five-color flow cytometers and automated prep instrumentation, with ongoing projects designed to markedly improve our ability to analyze, interpret, and report the results from samples received for flow cytometric analysis. Meanwhile, clinical volumes continue to increase at a steady pace.

For details, section-specific reports are as follows:

I. Coagulation Laboratory (Dr. Alvin Schmaier)

Several changes were made in the operating procedures in the Coagulation Laboratory. First, we revised our assay for antithrombin from an anti-factor Xa to an anti-thrombin (IIa) based test. This change resulted in a tighter normal range. Since there was a tighter reference range using thrombin (IIa) than factor Xa, we evaluated the anti-IIa assay against a new anti-Xa assay for antithrombin. The reference range for the anti-Xa assays was slightly wider (85-123%) than the anti-IIa assays (92-122%). We chose to use the anti-IIa antithrombin assays. Second, we changed our free protein S antigen assay from an electroimmunodiffusion assay to immunoturbidometric assay performed on the Dade-Behring BCS. Third, the D-Dimer assay study to assess its ability to screen for DVT was completed. A value of D-Dimer > 3.0 has a 64% sensitivity, 76% specificity, and 70% accuracy to predict that a patient has a proximal DVT in the right patient setting. The data are currently being analyzed as to the negative predictability of the test, i.e., in the proper clinical setting, a negative D-Dimer excludes the diagnosis of DVT to what degree. Fourth, we have instituted autoverification of normal fibrinogen levels. Fifth, we are currently proceeding with the development of a protein C coagulant assay to replace the protein C amidolytic assay since the former is a more global screen of protein C activity. Sixth, we have continued our evaluation of the Platelet Function Analyzer (PFA) as an assay to assess platelet dysfunction. To date, only 20 patient samples have been recruited for study. Seven out

of 20 patients were normal; 13/20 patients had abnormal platelet function. Patients with mild platelet function defects (aspirin-like, ADP and epinephrine defects, or epinephrine alone) do not appear to have PFA defects. However individuals with more profound platelet function defects (2/13), appear to have abnormal closure times. This investigation will continue to increase the number of patients studied before we can institute the assay as part of our diagnostic armamentarium. Last, we are currently evaluating an antithrombin antigen LIA assay as a replacement of the radial immunodiffusion technique. If successful, this assay change will make the antithrombin antigen assay fully automated on the BCS rather than the manual assay currently in use. This change should improve turnaround time and reduce technologist time.

II. Hematology and Bone Marrow Laboratories (Dr. William Finn)

We continued our ambitious goal of pre-analytical automation in the main hematology laboratory with the purchase and deployment of three Beckman Coulter LH755 hematology analyzers and slidemakers. Our plan is to extend this deployment to include automated slide stainers, and the installation of an automated Beckman Coulter 1500 line, to include a 2000 sample "stockyard" that will allow for not only the automated feeding and analysis of blood samples, but for the automated retrieval and testing of previously analyzed samples when additional testing is needed. Currently, we are making excellent progress on the automation project, in cooperation with the Department of Pathology, the University, and Beckman-Coulter. We currently are working with a timeline that includes demolition and renovation of a portion of the hematology laboratory with planned completion by February 2005, followed by line installation in March 2005.

We continue to refine our hematology verification and slide review criteria. As a result of this continued optimization, we achieved a 36% decrease in manual differential counts and a 4% decrease in manual slide reviews. We also continue to review our test menu, and we discontinued tests that are obsolete or for which there is little or no remaining clinical demand.

Microscopic urinalysis was discontinued as an orderable test. Based upon data generated and reviewed in our laboratory, microscopic urinalysis is now performed only on samples for which the macroscopic analysis shows results that indicate the potential for a meaningful microscopic abnormality. This revision in policy reduced microscopic urinalyses by 13%.

Test ordering and sample labeling began in the Cancer Center infusion center allowing us to transfer one technologist from the Cancer Center laboratory to the bone marrow differential count project. This change also reduced turnaround times. The change was a result of a suggestion from our staff and implemented by Pathology Data Systems.

In the bone marrow laboratory, we instituted a new system of differential counting of bone marrow samples by the medical technologists in the laboratory. This began as a pilot project with training of selected staff, and training continues to expand. Technologists and pathology residents are working cooperatively on a day-to-day basis in the performance of these differential counts.

Meanwhile, test volumes continue to increase relentlessly. There was an increase of 14% in complete blood counts (CBCs) ordered, an increase of 6% in body fluid analyses, an 18 % increase in bone marrow aspirates and biopsies, and an 18% increase in erythrocyte sedimentation rate orders.

Flow Cytometry Laboratory (Drs. Charles Ross and Lloyd Stoolman)

The laboratory is in the process of major upgrades, having purchased three Beckman-Coulter FC500 five-color flow cytometers and automated PrepPlus instruments. The laboratory staff have all been trained on the new instruments, and they have done outstanding work designing and building appropriate protocols and panels into the new instruments. Day-to-day use of this new technology is being phased-in at the time of this report, with full deployment planned for the upcoming academic year. The new technology will substantially enhance our data-analysis, reporting, and storage capabilities, with substantial increases in the efficiency of these functions predicted.

We continue to evaluate and improve our approach to clinical flow cytometry. We are updating our interfaces to the laboratory databases and lab information system, with continuing discussions on the most appropriate approach to sample analysis, interpretation, and reporting. A new mast cell panel was designed in cooperation with Dr. Cem Akin, who joined the faculty this year and is very active in the treatment of patients with systemic mast cell disease. Additional panels have been evaluated for monitoring of the expanding multiple myeloma patient base, and we are actively evaluating an expansion of our acute leukemia panel to include immunophenotypic markers of myelodysplasia.

The volume of immunodeficiency monitoring assays performed in the laboratory increased 3% from last year. The volume of CD34 stem cell counts was unchanged. Attending staff continue to triage all requests for leukemia/lymphoma immunophenotyping, with cancellation of unwarranted requests. Leukemia/lymphoma immunophenotyping, the most labor intensive testing performed in the laboratory, continued to increase (by 20% for the chronic leukemia/lymphoma panel, and by 25% for the acute leukemia panel). MLabs referrals comprise 25% of all acute leukemia analyses, 49% of chronic leukemia/lymphoma analyses, and 28% of immunodeficiency monitoring requests.

III. Academic and Educational Efforts

The faculty (Drs. Finn, Ross, Schmaier, Schnitzer, Stoolman, Valdez) and staff of the combined hematopathology laboratories continue to be active participants in the national and international hematopathology scene, with our faculty continuing to serve as faculty to national courses, numerous national and international committees, invited lectureships, editorial boards, etc, and continuing to publish numerous articles in peer-reviewed journals.

We continue to have two ACGME accredited fellowship positions. We were thankful for the dedicated service of last year's fellows, Drs. Nasir Bakshi and Scott Owens, and we welcome this year's fellows, Drs. Maurice Grant and Ajay Rawal.

We continue to be very active participants in all aspects of resident and medical student education, with our faculty teaching numerous small group sessions and lectures. Drs. Schmaier and Stoolman continue to serve as director and co-director, respectively, of the second year medical school hematology sequence, and Dr. Valdez continues his distinguished service on the Medical School admissions committee.

William G. Finn, M.D.
Clinical Associate Professor of Pathology
Director, Hematopathology
Associate Director, Clinical Pathology

CLINICAL IMMUNOPATHOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY

ANNUAL REPORT

1 JULY 2003- 30 JUNE 2004

I. OVERVIEW:

The Immunopathology Laboratory performed more than 70,000 analyses in 2003-04. John Lowe, M.D. and John Thorson, M.D., Ph.D. provided invaluable service to the laboratory in the interpretation of protein electrophoresis studies. Kent Johnson, M.D., and Paul Killen, M.D., Ph.D., also provided invaluable coverage of anti-neutrophil cytoplasmic antibody (ANCA) and anti-GBM studies.

II. CLINICAL SERVICES:

Integration of clinical immunopathology testing into the Chemistry Section has been fully realized. New procedures were implemented in the protein electrophoresis area, in the analysis of antibodies to extractable nuclear antigens, and in the measurement of several individual analytes previously measured by nephelometry.

III. RESEARCH AND DEVELOPMENT:

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

IV. QUALITY ASSURANCE:

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

V. TEACHING/PROFESSIONAL:

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

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

CLINICAL MICROBIOLOGY / VIROLOGY LABORATORIES

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 2003 - 30 JUNE 2004

Dr. Newton assumed directorship of the laboratory from Dr. Pierson on July 1, 2003 when Dr. Pierson began his first year of a 2-year, 50% appointment. Dr. Newton was previously the Assistant Director of the Clinical Microbiology/Virology Laboratories.

I. CLINICAL ACTIVITIES:

The Laboratory continued to experience significant increases in test volume with an approximately 7% increase compared to that of FY 2003, with a total testing volume approaching 300,000 tests. Interestingly, the greatest % increases were seen in several molecular tests which are the most complex and costly assays performed in the laboratory.

Molecular diagnostics continues to be a major growth area of the laboratory. Two automated instruments for specimen extraction have been incorporated into the laboratory and have replaced very labor-intensive manual procedures for nucleic acid extraction for CT/NG and HCV amplified testing. Work continues in the lab to automate the specimen extraction procedures for additional nucleic acid amplification tests. New real-time PCR tests have been implemented (HCV viral loads) or are about to be implemented (HSV qualitative test from CSF) in the lab. The incorporation of the new HCV viral load assay has improved our efficiency and decreased our turn around time for reporting these results. We have also begun evaluation of a new test for EBV viral load assessment by real-time PCR in order to bring this test in-house rather than sending it out.

Through a great deal of cooperation between the supervisors, senior clinical technologists, and bench technologists, evaluations of laboratory workflow and organization have occurred and are ongoing with the aim to increase laboratory efficiency. Concomitant with this, we have begun reviewing systems for automated bacterial identification and susceptibility testing to determine whether these systems offer significant improvements in these areas. Following completion of site visits, we plan to bring in appropriate systems for hands-on evaluation.

In collaboration with Pharmacy, Infectious Diseases and Infection Control, we have generated several unit- and hospital-specific antibiograms to more closely track trends in antimicrobial resistance throughout the hospital and health system. These are being used to assess the appropriateness of antibiotic usage and determine whether changes in therapeutic recommendations or antibiotic formulary are required.

The laboratory received an on-site refresher course from MDCH on the bacterial and viral agents of bioterrorism, and several members of the laboratory also were certified in the packaging and shipping of biological hazardous materials. The supervisory staff was also successful in hiring several new medical technologists to fill open positions.

II. RESEARCH ACTIVITIES:

The additional faculty depth in the laboratory has allowed for increased participation in a variety of research projects with collaborators from within UM, other universities, and with industry.

- The protocols for automated specimen extraction and real-time PCR for HCV viral load assessment were developed in collaboration with Roche Diagnostic, and we were able to present our results at an international meeting in April 2004. The success of this project has led to further collaborations with this company.
- In collaboration with Binax, Inc., our laboratory is participating in a clinical trial of rapid antigen detection tests for adenovirus and parainfluenza virus in samples from pediatric patients.
- We have established collaborations with investigators in the UM School of Public Health and have participated in research projects through performing EBV serologic testing and influenza virus testing, and have provided additional support through training of SPH researchers in fluorescent microscopy, viral culture and molecular diagnostics.
- Dr. Newton is a co-investigator on an recently awarded 1.2 million dollar NIH grant with Dr. Arnold Monto at UM SPH, and will be providing 20% effort to provide technical expertise in influenza virus molecular diagnostics.
- The Laboratory is cooperating with a local company to evaluate a real-time PCR method for the direct bedside detection of group B Streptococcus in urogenital specimens. Clinical evaluation of the system is expected to begin in 2004.
- We are collaborating with MDCH on a project for surveillance of MRSA in Michigan.
- We are a clinical study site for two projects evaluating the in vitro activity of newly developed antibiotics—both projects are sponsored by pharmaceutical companies.
- We are collaborating with multiple hospitals around the country on an NIH project evaluating emerging antibiotic resistance in Group A streptococci.
- We are evaluating the performance of a new test to detect Aspergillus antigens in serum of immunocompromised patients, which can potentially be used to predict risk for developing disseminated disease.
- The Laboratory responded to numerous IRB-approved requests from clinical services for specific laboratory data to fulfill research goals.

III. TEACHING ACTIVITIES:

All laboratory personnel continued to provide instruction to Pathology House Officers and Infectious Disease Fellows and residents on diagnostic procedures used in the Microbiology/Virology Laboratories. Several laboratory preceptorships for medical students, pharmacy students, and Pharm.D. residents were also provided during the year. Infectious Disease Laboratory rounds were held each weekday during which staff members and assigned Pathology House Officers interacted with ID team members to answer questions, demonstrate laboratory diagnostic procedures and discuss interesting findings. Numerous in-service education programs were held during the course of the year with individual technologists and Pathology House Officers giving presentations to staff members.

IV. PROFESSIONAL DEVELOPMENT:

Both supervisors and most of our Sr. Technologists attended one or more regional or national scientific meetings during the year. Several other staff members attended regional scientific meetings of interest. In addition, the Laboratory subscribed to two audioconference programs which provided a total of 10 conferences during the year that were available to all staff members and Pathology House Officers as part of our ongoing CME program. Monthly inservice programs were provided by Pathology residents and faculty.

V. GOALS FOR FY 2005

1. Continue process and efficiency improvements to accommodate an expected increase in test volume.
2. Expand our menu of nucleic acid tests to support the diagnostic needs of our clinical services, e.g., EBV viral load, enterovirus PCR, BK virus PCR.
3. Continue our transition to automated specimen extraction for appropriate nucleic acid amplification tests.
4. Continue our assessment of automated bacterial identification and susceptibility systems.
5. Continue our evaluation of the rapid NA amplification method for the detection of group B Streptococcus in urogenital specimens.
6. Assess current and future laboratory space and architectural requirements.
7. Assist in the selection of a new Laboratory Information System.

Respectfully submitted,

Duane Newton, Ph.D. Director

Carl L. Pierson, Ph.D., Co-Director

Clinical Microbiology/Virology Laboratory

MOLECULAR DIAGNOSTICS LABORATORY

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 2003 - 30 JUNE 2004

Overview

The Laboratory had an 8% increase in volume relative to the same period in the previous year. Several state-of-the-art pieces of analytical equipment were acquired, which have allowed the Laboratory to expand its test menu and streamline its operation.

Clinical Services

The Laboratory currently employs one full time supervisor, five full time technologists, one of whom functions as a research and development technologist, and two part time technologists. All staff members are cross-trained in all areas of the laboratory.

Tom Wilson, M.D., Ph.D., began an active role as Assistant Director of the Laboratory, providing assistance with assay development. Both Dr. Wilson and Jeffrey Warren, M.D., provided assistance with sign out responsibilities for the laboratory. Charles Ross, M.D., and William Finn, M.D. both participated actively in the work-up and result interpretation of cases in molecular hematology.

The Laboratory saw an increase in annual volume to approximately 7,850 tests during the 2003-4 academic year. The growth in test volume was spread relatively equally across the testing menu.

Average turn around times for the Laboratory were 4-5 total days, decreased from an average of 5-6 total days during the previous year. This was in part due to an increased efficiency in the operation of the laboratory afforded by the application of updated technology.

During the past academic year, the Laboratory acquired several new analytical instruments, including an ABI 3100 16-channel capillary electrophoresis instrument, an ABI PRISM 7900 real time PCR instrument, a Roche LightCycler real time PCR instrument, a Tecan Evo automated robotic pipettor, and two additional ABI 9700 PCR machines. This influx of state-of-the-art technology has had, and will continue to have, a significant impact on the operation of the Laboratory, both in terms of efficiency of operation and in the ability to add new assays to the Laboratory's test menu.

A variety of new assays were developed and/or validated for clinical use by the Laboratory during the past year. These include 1) an assay to detect mutations in the *FLT3* gene, which are associated with a subset of acute myeloid leukemias 2) an RT-PCR assay to detect chimeric transcripts resulting from the t(x;18) translocation characteristic of synovial sarcomas, and 3) the use of capillary electrophoresis to analyze microsatellite markers for the assessment of bone marrow engraftment status. In addition, the Laboratory has validated and is currently making use of procedures to extract both DNA and RNA from formalin fixed, paraffin embedded tissue specimens. This has allowed an expansion in the number and types of specimens upon which the Laboratory can perform molecular testing.

Education

Educational activities of the Laboratory included the training of Medical Technology students from Wayne State University and Eastern Michigan University, each of whom completed their CLS/MT Clinical Training in the Laboratory during a one-week rotation. Training included DNA and RNA extractions, polymerase chain reaction, Southern analysis, and an overview of all testing performed in the Laboratory.

Several senior level Pathology residents spent time in the laboratory during their CP Block D rotations, gaining an overview of all testing performed in the laboratory and participating in the review, interpretation and sign out of cases.

Future Plans/Research and Development

It is anticipated that the laboratory will be moving to a new location near the north campus within the next 3 to 6 months. This move will result in incremental square footage, thereby alleviating a significant blockade to the expansion of the laboratory's activities.

Priorities for the next academic year will be 1) the migration of many currently performed assays to the recently acquired state-of-the-art instrumentation and 2) the development and validation of additional tests to be included on the Laboratory's menu of assays.

Assays developed in-house to detect the chimeric, translocation specific transcripts that characterize alveolar rhabdomyosarcomas (*PAX3/FKHR*, *PAX7/FKHR*) and desmoplastic small round cell tumors (*EWS/WT1*) are currently being validated and will be available within the next month. A similar assay targeting the chimeric transcripts found in Ewing's sarcomas is currently in development.

Validation of an in-house developed PCR-based assay for T-cell receptor gene rearrangements is nearly complete and this assay will be available on a clinical basis within the next month. Following this, a similar assay for B-cell receptor gene rearrangements will be implemented. Both of these assays will be applicable to either fresh or formalin fixed tissue. In addition, a novel multiplex real time PCR assay for detecting *BCL2/IGH* translocations, which characterize follicular lymphomas, is currently being developed.

Several quantitative real time PCR assays to assess gene expression levels are being developed in consultation with the hematology/oncology and bone marrow transplant services, targeting the current and expected future needs of these groups. These include assays for *BCR/ABL*, *PML/RARA*, and *TEL/AML1*.

Discussions with the Medical Genetics service have identified a group of genes for which DNA sequence analysis has significant clinical implications. These include *MECP2* (Rett syndrome), *UBE3A* (Angelman syndrome), *PTPN11* (Noonan syndrome), and *P57KIP2* (Beckwith Weideman syndrome). Development and implementation of the techniques required for this type of analysis is expected to begin within the next few months.

John A. Thorson, M.D., Ph.D.
Director, Molecular Diagnostics Laboratory

GENERAL PATHOLOGY

M-LABS

**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 2003 - 30 JUNE 2004**

I. MISSION:

MLabs is the University of Michigan Health System's reference laboratory program, established in 1985. MLabs offers the high quality reference laboratory services and other resources of the Department of Pathology laboratories to hospitals, clinics, other institutions, and physician offices. MLabs mission is to ensure that the Department of Pathology laboratories: (1) remain financially strong, (2) receive sufficient laboratory specimens for teaching, training and research programs, and (3) to encourage increased productivity of the laboratory staff.

II. CURRENT STATUS:

Since its origin, the MLabs program has experienced continuous growth, most notably since 1994 at which time the University Hospital chose to increase resources devoted to it. Gross billings have increased fourfold in the last four years.

MLabs currently provides full anatomic pathology coverage and esoteric clinical laboratory services to one hospital and to the University of Michigan Health Service. MLabs is the primary reference laboratory and provides full esoteric laboratory testing to another 13 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 approximately 100 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".
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 FY2004, MLabs added 7 new physician offices and specialty service practices to our client list. The majority of these were related to our contract to provide coverage to M-Care patients. Some were for specialty services, and a few were UMHS acquired practices.
- No hospital full reference laboratory accounts.
- Two contracts for services were terminated, both for Cytogenetics testing.
- MLabs submitted 3 proposals to prospective new clients during FY2004. All are pending
- Business opportunities were rejected by MLabs because the Department of Pathology could not provide the services which were requested. Three dermatology practices requested dermatopathology. These requests were denied.

IV. BILLING ACTIVITY:

- Gross billings for anatomic pathology increased by 9 % and those for clinical pathology increased by 26%.

V. MANAGED CARE ACTIVITIES:

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

For FY2004, we have begun negotiations for our third contract with M Care to provide outpatient laboratory services for all groups and products for M Care's commercial and Medicare products. M Labs prepares quarterly QA reports on lab services for M Care's QA department and have conducted a Physician Satisfaction Survey for M Labs subcontracted providers and reported the results to M Care. We assist M Care with resolution of laboratory service issues. We are actively engaged in

contracting for delivery of HEDIS data for M Care to assist them in meeting requirements of NCQA and other certifying entities.

VI. NETWORK ACTIVITY:

In the past several years, hospitals throughout the country have been forming networks in order to cope with the evolving demands of a changing health care system including intense cost cutting by third party payors, reduction in inpatient laboratory testing, competition from commercial laboratories, and carve out of outpatient laboratory services (to large independent labs) from managed care contracts. The formation of laboratory networks gives hospital labs the geographic coverage which allows them to successfully compete in a managed care environment as well as to decrease unit costs and increase revenue streams through outreach activities.

MLabs has been positioning itself to deal with an increase in managed care testing by playing a key role in two laboratory networks. Great Lakes Laboratory Network (GLN) consists of 28 hospital laboratories, predominantly in the western and northern parts of Michigan; Joint Venture Hospital Laboratories (JVHL) has grown to include 9 equity members including UMHS, and 72 participating member laboratories located in Michigan. JVHL has contracts with 14 managed care organizations including Blue Care Network. M Labs is represented on the Executive Committee.

VII. PROSPECTS:

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

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

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

MLabs plans to increase our efforts significantly in marketing specialty (niche) areas such as dermatopathology, renal pathology, cytogenetics, molecular diagnostics, neuropathology, hematopathology, and flow cytometry. We currently provide laboratory listing to 2 University Health Systems. We are working with a third health system to set up their laboratory and do their esoteric testing.

IX. IMPEDIMENTS:

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

Prepared by Eugene M. Silverman, M.D.

Pathology Research Microarray Laboratory

**DEPARTMENT OF PATHOLOGY
ANNUAL REPORT**

1 JULY 2003- 30 JUNE 2004

I. OVERVIEW:

The Pathology Research Microarray Laboratory was established in 1999-2000 as part of the larger Microarray Network at the University of Michigan Medical School. This array facility is in addition to the one in the Cancer Center, which is largely devoted to genetic analysis of solid tumors from humans. DNA microarray analysis is a powerful technology allowing for detailed gene expression studies of cell lines, animal models, and tissues (including pathologic specimens). With the sequencing of the entire human genome, it may soon be possible to monitor gene expression on a comprehensive, global scale as opposed to focusing on one gene at a time. Not only will this technology have an obvious application in the basic sciences, it has the potential of impacting the treatment and diagnosis of patients. As Pathology is a discipline comprised of both scientific investigation and clinical diagnosis, it is imperative that the Department play a role in the use and development of this technology. Clinical Pathology, in particular, has the opportunity of utilizing microarray technology to develop novel diagnostic and prognostic biomarkers.

The Pathology Research Microarray Laboratory functions to support the current and future research activities of the Department as well as Interdepartmental Programs. The primary focus of this facility is in three areas important in the study of human pathology including 1) inflammation, 2) apoptosis/cell death and 3) cancer. These studies are accomplished using characterized animal models as well as with human specimens and cell lines.

II. RESEARCH AND DEVELOPMENT:

While DNA microarray analysis is a potent technique to explore complex and interlocking systems, it is clear that this technology is in its infancy and that there are formidable problems in dealing with the multitude of data generated. Dr. Arul Chinnaiyan has carefully developed our Research Microarray Laboratory, beginning 2 years ago when he visited the Brown and Botstein laboratories at Stanford in order to talk with experts and determine the best microarray system to meet our needs. Our microarray methodology is based primarily on techniques learned at the 1999 Cold Spring Harbor Workshop on DNA Microarrays attended by Dr. Chinnaiyan and taught by Drs. Joseph DeRisi (UCSF), Michael Eisen (Stanford), and Patrick Brown (Stanford), all of whom are renowned experts in the field.

Beginning October of 1999, the Lab has been assembling the equipment, clone sets, and supplies necessary to produce high-density cDNA microarrays including a robotic arrayer, microarray scanner, PCR machines, and liquid handling instrumentation. The Lab has

successfully generated a 20K human cDNA chip, 10K rat cDNA chip and a 5K mouse cDNA chip.

During this reporting period the following investigators have utilized the Microarray facilities:

1. Dr. Peter Ward (Pathology), studies on sepsis and c5a.
2. Dr. Sem Phan (Pathology), studies using in vivo fibrosis models.
3. Dr. Dan Remick (Pathology, protein microarrays), sandwich antibody microarrays.
4. Dr. William Finn (Pathology), Profiling of hematologic malignancies (CLL and MCL).
5. Dr. Kenneth Pienta (Internal Medicine), gene expression mediated by PAR1.
6. Dr. Marc Lippman (Internal Medicine), Gene expression mediated by ErbB family members.
7. Dr. Andrew Lieberman (Pathology), gene expression mediated by androgen receptor variants.
8. Dr. Mark Rubin (Brigham Woman's Hospital Pathology), prostate cancer profiling
9. Dr. Sofia Merajver (Internal Medicine) Gene expression mediated by Rho family members.
10. Dr. Steven Ethier (Radiation Oncology) Gene expression mediated by FGFR family inhibitors.
11. Dr. Joseph Holoshitz (Internal Medicine) Gene expression of studies in identical twins with and without rheumatologic disease.
12. Dr. Kent Johnson (Pathology) and Pfizer Corporation- Development of antibody microarrays.
13. Dr. Donna Livant (Radiation Oncology) Gene expression mediated by PHSCN.
14. Dr. Paul Harari (Univ. of Wisconsin, Radiation Oncology) Gene expression mediated by Tarceva.
15. Dr. Celina Kleer (Pathology) Gene expression mediated by WISP.
16. Dr. Theodora Ross (Internal Medicine) Gene expression mediated by HIF1.
17. Dr. Chinnaiyan (Pathology and Urology). Gene expression profiles of prostate cancer and benign prostatic hyperplasia. Gene expression mediated by EZH2 and AMACR. Development of protein microarray technologies for antibody microarrays and antigen microarrays for humoral immune response.

In addition to establishing DNA microarrays in the laboratory, a large effort has also been placed on devising a system to monitor protein levels and activity in a high-throughput fashion. While various genome scale methodologies to identify variations in DNA and RNA exist, an analogous "biochip" to explore protein function has been difficult to implement for various reasons. In this Lab we plan to establish a platform for the massively parallel analysis of protein levels, interactions, and function. One area for which we will implement both DNA and protein microarray technology is the development of novel cancer and inflammation biomarkers. Dr. Dan Remick and Dr. Kent Johnson are both working with the Microarray Lab in order to fabricate and test protein/antibody microarrays for their respective areas of interest.

The following manuscripts include data made possible by the Microarray Lab:

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3. Kuefer, R., Hofer, M.D., Gschwend, J.E., Pienta, K.J., Sanda, M.G., **Chinnaiyan, A.M.**, Rubin, M.A., Day, M.L. (2003) The role of an 80 kDa fragment of E-cadherin in the metastatic progression of prostate cancer. *Clin Cancer Res.*, 9(17):6447-52.
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5. Peri, S., Deshpande, K.S., **Chinnaiyan, A.M.**, Hamosh, A., Chakravarti, A., Pandey, A. (2003) Development of human protein reference database as an initial platform for approaching systems biology in humans. *Genome Res*, 13(10):2363-71.
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10. Vivienne Watson J.E., Doggett N.A., Albertson D.G., Andaya A., **Chinnaiyan A.**, Van Dekken H., Ginzinger D., Haqq C., James K., Kamkar S., Kowbel D., Pinkel D., Schmitt L., Simko J.P., Volik S., Weinberg V.K., Paris P.L., Collins C. (2004) Integration of high-resolution array comparative genomic hybridization analysis of chromosome 16q with expression array data refines common regions of loss at 16q23-qter and identifies underlying candidate tumor suppressor genes in prostate cancer. *Oncogene*, Apr 22;23(19):3487-94.
11. Wu M., Wu Z.F., Kumar-Sinha C., **Chinnaiyan A.M.**, Merajver S.D. (2004) RhoC Induces Differential Expression of Genes Involved in Invasion and Metastasis in MCF10A Breast Cells. *Breast Cancer Res Treat.* Mar;84(1):3-12.
12. Rubin M.A., Zerkowski M.P., Camp R.L., Kuefer R., Hofer M.D., **Chinnaiyan A.M.**, Rimm D.L. (2004) Quantitative determination of expression of the prostate cancer protein alpha-methylacyl-CoA racemase using automated quantitative analysis (AQUA): a novel paradigm for automated and continuous biomarker measurements. *Am J Pathol.* 164(3):831-40.
13. Kumar-Sinha C., Shah R.B., Laxman B., Tomlins S.A., Harwood J., Schmitz W., Conzelmann E., Sanda M.G., Wei J.T., Rubin M.A., **Chinnaiyan A.M.** (2004) Elevated alpha-methylacyl-CoA racemase enzymatic activity in prostate cancer. *Am J Pathol.* 164(3):787-93.

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19. Rhodes, D.R., Yu, J., Shanker, K., Deshpande, N., Varambally, R., Ghosh, D., Barrette, T., Pandey, A., **Chinnaiyan, A.M.** (2004) Large scale meta-analysis of cancer microarray data identifies commone transcriptional profiles of neoplastic transformation and progression. *Proceedings of the National Academy of Sciences*, 101(25):9309-14.
20. Ghosh, D.R., **Chinnaiyan, A.M.** (2004) Classification and selection of biomarkers in genomic data using LASSO. The University of Michigan Department of Biostatistics Working Paper Series. <http://www.bepress.com/umichbiostat/paper42>
21. Rhodes DR, **Chinnaiyan A.M.** (2004) Bioinformatics strategies for translating genome-wide expression analyses into clinically useful cancer markers. *Ann N Y Acad Sci*, 1020:32-40.
22. Rhodes D.R., Yu J., Shanker K., Deshpande N., Varambally R., Ghosh D., Barrette T., Pandey A., **Chinnaiyan A.M.** (2004) ONCOMINE: a cancer microarray database and integrated data-mining platform. *Neoplasia*, Jan-Feb;6(1):1-6.
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The Pathology Microarray Lab has supported the following grant applications by providing preliminary gene expression analyses:

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

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

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

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

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

DOD grant, Biological Differences between prostate cancer cells that metastasize to the bone versus soft tissue sites, P.I. K. Pienta

Breast Cancer Research Foundation, “Transcriptome Analysis of the EGFR Receptor in Breast Cancer, The Breast Cancer Foundation”, PI M. Lippman

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

RO1, The Role of Polycomb Group Proteins in Prostate Cancer, P.I. Chinnaiyan

Glue Grant, U54 GM64351 Inflammation and the Host Response to Injury; P.I. D. Remick

Department of Defense, DOD PC020322 (Chinnaiyan)
Pfizer Sponsored Research Agreement (Ward)

GMP Sponsored Research Agreement (Chinnaiyan)

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

III FUTURE GOALS:

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

1. Continue to support the research funding applications of Pathology faculty with preliminary data and bioinformatics expertise.
2. Continue to publish data using microarray technology in peer-reviewed journals to establish the Department in the fast moving field of genomics/proteomics.
3. Expand the rat, mouse, human DNA chips to include additional cDNA clones. Ultimately, we would like to develop a chip that can monitor the entire expressed genome.
4. Develop and utilize protein microarray technology to answer biologically important questions.
5. Train post-doctoral fellows and students in making and using 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. In September of 2003, Dr. Kumar accepted a position as Senior Scientist at the Institute of Bioinformatics, Bangalore India where he setting up their Microarray capabilities. Sooryanaryana Varambally, previously a post-doctoral fellow in the lab was promoted to Research Investigator. Arun Sreekumar, a Research Fellow, was involved in developing the protein microarray platform. Other postdoctoral fellows in the Department of Pathology that have received training in DNA or protein microarrays include: Saravana Dhanasekaran, Ira Maine (mentored by M. Rubin), Atreya Dash (mentored by M. Rubin), Monzy Thomas (mentored by A. Lieberman), Eric Albright (mentored by P. Ward), and Thomas Neff (mentored by P. Ward). Similarly the following medical and graduate students received training in microarrays, microarray analysis and or QRT-PCR: Dan Rhodes (MSTP), Scott Tomlins (MSTP), Qi Cao (Pathology), Jianjun Yu (Bioinformatics), Chad Creighton (Bioinformatics), Patrick Lester (Pathology), Julie Kim (Bioinformatics), Viktoriya Resnick (Bioinformatics), Xiaoyu Jia (Pathology) Smita Lakhota (Graduate Student, Indian Institute of Sciences), and Ronglai Shen (Biostatistics Masters Student).

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 2002 - 30 JUNE 2003**

INTRODUCTION:

The VA Ann Arbor VA Healthcare System (VAAAHS) is a University of Michigan affiliated tertiary health care provider for veterans. It is one of three tertiary medical centers in the Veterans Integrated Service Network (VISN) #11 serving the veteran population of Michigan, and portions of Ohio, Indiana and Illinois. The VAAAHS Pathology and Laboratory Medicine Service maintains a close relationship with the University Department of Pathology at every level. All pathologists in the VAAAHS have medical school appointments and participate in university activities in a manner similar to other departmental sections. Recruitment for VAAAHS pathologists is a joint activity and candidates are selected on the basis of academic performance and potential as well as professional competence similar to any departmental candidate. There are four full-time pathology staff positions. Two and 1/2 resident training positions in the Department's program are supported with funds from the Department of Veterans Affairs. All residents serve monthly rotations in Surgical Pathology, Autopsy Pathology, and a number of arranged electives including Diagnostic Electron Microscopy and special study programs in Surgical Pathology, Cytopathology and Digital Imaging. The VAAAHS laboratory was inspected in 2002 and retains full accreditation by the College of American Pathologists. The VAAAHS was inspected by the JCAHO and is currently fully accredited. The medical center's Decentralized Hospital Computer System (*VistA*) is recognized as the most fully integrated medical information system. It combines all of the clinical management of the patient and has shifted to a computerized patient record system (CPRS) in year 2000. Data storage for all components of pathology and the clinical laboratories contains full patient information for 1 ½ decades. Digital images of selective patient surgical, cytopathology, autopsy and ultrastructural specimen are stored as part of the patient medical record and are accessible to clinicians within minutes of case review.

Two ongoing reorganizational thrusts are underway at the VAAAHS. 1) The facility is refocusing its mode of healthcare delivery, downsizing inpatient care and greatly expanding its ambulatory care. In keeping with this change, a substantial capital improvement program is ongoing. Completed to date are Research Building, two additional parking structures and a 340,000 sq. ft. clinical addition. This building is attached to the existing hospital and provides space for ambulatory care, new surgical suites, post surgical recovered unit, vascular cath facilities, four intensive care units and a floor for diagnostic services (Pathology, Clinical Labs, Radiology and Nuclear Medicine). Pathology and Laboratory Medicine occupies 23,000 sq. ft on the third floor of the clinical addition. The previous structure is currently under complete remodeling to allow for current standards of inpatient privacy. Also included will be administrative offices, and additional research space. Current discussions concern a complete functional restructuring of the clinical labs. 2) The VISN continues efforts toward an integrated health delivery system. Diagnostic Services will be a target for networking/consolidation among the current 8 independent facilities. This will result in additional sharing of service

responsibilities, equipment standardization, VISN-wide reagent contracting, decreased cost of referred (send-out) testing to nonVA clinical labs and an increase in the workload in VAAAHs's anatomic pathology and the clinical labs. Ann Arbor is currently performing all surgical pathology for the Battle Creek/Grand Rapid facilities. The VISN has added an additional outpatient facility in Flint which is serviced by the Ann Arbor laboratory. A recent CARES review was implemented by the VA Secretary in order to project veteran medical care needs for the next two decades and based upon that review the VAAAHs will likely be facing increasing demand and expansion of services.

ANATOMICAL PATHOLOGY:

- A. **Surgical Pathology:** 5,648 surgical cases were accessioned and reported during year 2002 continuing a steady increase over the prior reporting periods. The resident assigned to surgical pathology, usually a first year resident, acts as coordinator of the section and in that capacity has the opportunity to examine all of the specimens grossly and microscopically under close one-to-one mentoring by the staff pathologists. The resident interacts with the clinical teams. Weekly Urology Case Review Conference is held by Dr. Murphy. The residents assigned to autopsy and surgical pathology are primary presenters in clinical conferences. The residents obtain a broad educational experience and aid in providing high quality medical care. There is an extensive quality improvement program within Anatomical Pathology including regular consultations with the Armed Forces Institute of Pathology, University of Michigan, and other outside consultants. There is extensive quality assurance review and analysis of frozen sections, amended diagnoses, surgical appropriateness, turnaround times and follow-up of positive cancer diagnoses. The surgical and cytology readout stations are fully integrated into a hospital digital imaging system. Images are captured on cases of interest and when needed for documentation purposes. These are particularly useful in presentations to clinical teams reviewing specimens from their patients with the pathology staff and residents.
- B. **Autopsy Pathology:** 33 autopsies were performed during this year that is a rate of approximately 24% of in-patient deaths. Assigned residents perform the autopsies, prepare the pathologic diagnosis, and present the case in conference to the staff pathologists and other residents. The resident cuts and otherwise prepares the tissue for the preparation of slides and then reviews them and makes a microscopic diagnosis. These steps are supervised by staff pathologists who permit a gradual increase in independence for the resident with increased experience. Several autopsies performed at the VAAAHs are also presented at the extended Gross Conference at the University. The Department of Veterans Affairs maintains a policy to recognize the value of the autopsy and to encourage increased utilization. There is an expectation that all facilities will obtain permission to perform autopsies on at least 30% of their in-house deaths.
- C. **Cytology:** 2,363 cases were examined and diagnosed during this period. This is a slight increase over the last reporting year. Most of the cytology specimens are of diagnostic type, however the VAAAHs performs all PAP screening cytologies for the northern tier of VISN 11. Although there is not a formal rotation in cytology within the VAAAHs the cytological material is readily available and is used as correlative information for surgical and autopsy pathology. This laboratory is a VA "Center of Excellence" in cytology.

- D. **Electron Microscopy:** 60 electron microscopy cases were processed. Ultrastructural diagnosis is provided through sharing agreements with several Michigan hospitals. Some of the University of Michigan pathology specimens are processed and reported. The unit also serves several VAAHS research investigators. An elective rotation is available for pathology residents in electron microscopy. In other rotations the electron microscope findings are used to complement surgical or cytopathology diagnoses. This VAAHS is a "Center of Excellence" in electron microscopy and serves as consultant to other VA Medical Centers, to the University of Michigan Medical Center and to other hospitals by contract.

CLINICAL PATHOLOGY:

During the period of this report 1,088,933 clinical pathology procedures were performed in the Ann Arbor and its affiliated Toledo outpatient laboratory. In Chemistry there were 776,838; in Hematology 99,026; in Urinalysis 13,672, in Microbiology 25,786 and in Blood Bank 19,754. The Toledo unit performed 94,603 tests. These figures represent productivity (billable) rather than weighted test numbers. A formal clinical pathology rotation has not been available for pathology residents although the residents may participate or observe clinical pathology procedures when this activity is appropriate in relation to their other rotations. Drs. Chensue, Utiger and Chamberlain oversee the clinical laboratory and make available interesting and pertinent clinical laboratory information available to residents as desired. Clinical Pathology and medical historical data is available to pathology residents via CPRS for their information in surgical pathology, autopsy pathology, and elective rotations.

EDUCATION AND TEACHING:

In surgical pathology the staff pathologists provide one-to-one mentoring during the surgical sign out time. In addition, there is a surgical pathology conference approximately every other week and an autopsy conference with the entire staff following each autopsy. Residents join in continuing educational activities in histopathology and cytopathology from the AFIP, CAP, and ASCP. Because of the closeness of various sections of the laboratory there is frequent consultation among the pathologists and the residents are involved throughout. Since the VAAHS is physically close to the University, the residents are expected to attend the appropriate teaching conferences at the University as well. The staff contribute to the laboratory and lecture portions of the second year medical students at the University of Michigan. The VA staff also participate in other ad hoc lectures and in a moderate number of seminars for the resident staff, most often given at the University of Michigan. Both Drs. Chensue and Murphy have made presentations at international pathology conferences. Through his research program Dr. Chensue also mentors post-doctoral fellows and graduate students.

RESEARCH:

The specific efforts of the pathology staff are included on individual reports. Dr. Stephen Chensue has strong funded research programs. He also participates in cooperative studies with other investigators at the University of Michigan. Dr. Murphy carries a full investigative program. She and

Dr. Chensue have research laboratories in Research Building 31 of the VAAAHs. All staff participate in various clinical studies and collaborate with a variety of investigators. The laboratory in general serves the VAAAHs research program by providing considerable technical support for clinical research and in some cases for more basic research in both anatomic and clinical pathology.

ADMINISTRATION:

Dr. Chensue was appointed as Chief of Service in March 2001. The staff pathologists at the VAMC serve in various capacities involving administrative tasks for the University of Michigan, such as the Resident Selection Committee, the Medical Student Admissions Committee, Graduate student preliminary exam and thesis committees, teaching faculty of the second year medical students as well as other graduate course in the medical, dental schools and the school of public health. At the VAAAHs, the pathology staff members serve on all major committees involved with institutional policies and procedures.

The VA's National Cytopathology Proficiency Program's administrative offices are located in the VAAAHs. All VA pathologists privileged in cytopathology are required to participate in a 16 glass slide comprehensive proficiency review annually. This is the largest comprehensive cytopathology proficiency program in the nation.

SUMMARY:

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

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