## DEPARTMENT OF PATHOLOGY AND LABORATORY MEDICINE 2011-2012 ANNUAL REPORT

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#### DEPARTMENT OF PATHOLOGY AND LABORATORY MEDICINE FACULTY AND TRAINEE ROSTER 2011-2012

#### <u>Chair</u>

J. Charles Jennette, M.D., Brinkhous Dist. Professor and Chair

#### **Vice Chairs**

Thomas W. Bouldin, M.D., Professor and Vice Chair for Faculty and Trainee Development Herbert C. Whinna, M.D., Ph.D., Associate Professor and Director of McLendon Clinical Laboratories and Vice Chair for Clinical Services

#### Associate Chair for Administration

Nancy H. Nye

#### **Distinguished Professors**

Joe W. Grisham, M.D. (Kenan Distinguished Professor, Emeritus) Nobuyo N. Maeda, Ph.D. (Robert H. Wagner Distinguished Professor) Marjorie S. Read, Ph.D. (Fred C. & Lelia Owen Prof., Emeritus) Oliver Smithies, D.Phil. (Kay M. & Van L. Weatherspoon Eminent Distinguished Professor) Richard R. Tidwell, Ph.D. (Kenan Distinguished Professor)

#### **Professors**

C. Robert Bagnell, Jr., Ph.D. Dwight A. Bellinger, D.V.M., Ph.D. Debra A. Budwit, M.D. John F. Chapman, Dr.P.H. (9/30/11) Frank C. Church, Ph.D. William B. Coleman, Ph.D. Marila Cordeiro-Stone, Ph.D. Cherie H. Dunphy, M.D. (3/26/12) Rosann A. Farber, Ph.D. William K. Funkhouser, M.D., Ph.D. Peter H. Gilligan, Ph.D. Virginia L. Godfrey, D.V.M., Ph.D. M. David Goodman, M.D. Pamela A. Groben, M.D. Margaret L. Gulley, M.D. Catherine A. Hammett-Stabler, Ph.D. H. Michael Jones, M.D. Kathleen Kaiser-Rogers, Ph.D. David G. Kaufman, M.D., Ph.D. William K. Kaufmann, Ph.D. Hyung-Suk Kim, Ph.D. Joe N. Kornegay, D.V.M., Ph.D. (3/31/12) Susan J. Maygarden, M.D.

Volker R. Nickeleit, M.D. Judith N. Nielsen, D.V.M. Howard M. Reisner, Ph.D. John L. Schmitz, Ph.D. Harsharan K. Singh, M.D. Scott V. Smith, M.D. Michael D. Topal, Ph.D. Karen E. Weck, M.D. Bernard E. Weissman, Ph.D. John T. Woosley, M.D., Ph.D.

#### Associate Professors

Jessica K. Booker, Ph.D. Arlene S. Bridges, Ph.D. Georgette A. Dent, M.D. David Eberhard, M.D., Ph.D. Craig A. Fletcher, D.V.M., Ph.D. Susan C. Hadler, M.D. Tracy M. Heenan, D.V.M. Jonathon W. Homeister, M.D., Ph.D. Masao Kakoki, M.D., Ph.D. Ruth A. Lininger, M.D. Christopher P. Mack, Ph.D. Melissa B. Miller, Ph.D. Joan M. Taylor, Ph.D. Leigh B. Thorne, M.D. Cyrus Vaziri, Ph.D. Monte S. Willis, M.D., Ph.D. Alisa S. Wolberg, Ph.D. Maimoona B. B. Zariwala, Ph.D.

#### Assistant Professors

Araba N. Afenyi-Annan, M.D. (9/30/11) Claudia M. Brady, M.H.S. Megan J. DiFurio, M.D. George Fedoriw, M.D. Adil Hussein Gasim, M.D. Oleg V. Gorkun, Ph.D. (2/29/12) Kevin E. Greene, M.D. Peiqi Hu, M.D. Heike Hunt, M.D. (12/31/11) John P. Hunt, M.D.(1/9/12) Karou Inoue, Ph.D. (7/31/11) Rommel Lu. M.D. Stephanie P. Mathews, M.D. Christopher R. McCudden, Ph.D. (6/29/11) C. Ryan Miller, M.D., Ph.D. Siobhan M. O'Connor, M.D. Komaraiah Palle, Ph.D. (6/30/12) Kumar R. Pandya, Ph.D. (12/31/11) Yara A. Park, M.D. Ashley Rivenbark, Ph.D. Arlin B. Rogers, D.V.M., Ph.D. Lori R, Scanga, M.D., Ph.D. Dennis A. Simpson, Ph.D. Dimitri G. Trembath, M.D., Ph.D. Julia W. Whitaker, D.V.M. Hong Xiao, M.D. Xianwen Yi, M.D., Ph.D.

#### Lecturer

Gayle C. McGhee

#### **Instructor**

Steven Holmes, B.S., M.H.S. April E. Kemper, M.S., M.H.S. Tracie L. Massey, P.A. Vincent J. Moylan, M.S., P.A. (ASCP)

#### **Clinical Faculty (Medical Examiners)**

Sandra C. Bishop-Freeman, Ph.D. Justin O. Brower, Ph.D. Clay Nichols, M.D. Jonathan D. Privette, M.D. Deborah L. Radisch, M.D. Samuel Simmons, M.D. Ruth E. Winecker, Ph.D.

#### **Faculty Emeritus**

Stuart Bentley, M.D. John D. Butts, M.D. John F. Chapman, Dr.P.H. Myra L.Collins, M.D., Ph.D. Robert E. Cross, Ph.D. Frederic G. Dalldorf, M.D. Cora-Jean S. Edgell, Ph.D. James D. Folds, Ph.D. Jonald T. Forman, Ph.D. Joe W. Grisham, M.D. John E. Hammond, Ph.D. William D. Huffines, M.D. (deceased 10/17/11) Susan T. Lord, Ph.D. Nadia N. Malouf, M.D. William W. McLendon, M.D. James Pick, D.V.M. Marjorie S. Read, Ph.D. Kinuko I. Suzuki, M.D.

#### **Jointly Appointed Faculty**

Diane Armao, M.D. (Radiology) Nizar Chahin, M.D. (Neurology) Claire M. Doerschuk, M.D. (Medicine) Ronald J. Falk, M.D. (Medicine) Susan A. Fiscus, Ph.D. (Microbiology) Thomas R. Griggs, M.D. (Medicine) Nigel Key, M.D., Ch.B. (Medicine) Nigel Mackman, Ph.D. (Medicine) Valerie Murrah, D.M.D., M.S.(Dental) Timothy C. Nichols, M.D. (Medicine) Charles M. Perou, Ph.D. (Genetics) Gloria A. Preston, Ph.D. (Medicine) Kathleen W. Rao, Ph.D. (Pediatrics) Harold R. Roberts, M.D. (Medicine) Darrel W. Stafford, Ph.D. (Biology) James Swenberg, D.V.M., Ph.D. (Environmental Sciences and Engineering) Melissa Troester, Ph.D. (Epidemiology) Young E. Whang, M.D., Ph.D. (Medicine) Elizabeth Wilson, Ph.D. (Pediatrics) Daniel Zedek, M.D. (Dermatology)

#### **Adjunct Faculty**

Araba Afenyi-Annan, M.D. William A. Ahrens, M.D. (Carolina Pathology Group) Peter M. Banks, M.D. (Carolinas Medical Center) Gary A. Boorman, D.V.M., Ph.D. (NIEHS) Mark E. Brecher, M.D. (Laboratory Corporation of America) Robert C. Brown, M.D. (Emeritus) Shu Huey Chaing, Ph.D. (State Dept of Health and Human Services) Cherie H. Dunphy, M.D. (Laboratory Corporation of America) Jeffrey Everitt, D.V.M. (GlaxoSmithKline) Thomas Fischer, Ph.D. Dana M. Fowlkes, M.D., Ph.D. (Green Spring Technology) Oleg Gorkun, Ph.D. Delores J. Grant, Ph.D. (North Carolina Central University) Christopher Gregory, Ph.D. (Voyager Pharmaceutical) Heike Hunt, M.D. (Baystate Medical Center) John P. Hunt, M.D. (Baystate Medical Center) Wendell D. Jones, Ph.D. (Constella Health Sciences/Expression Analysis) Scott Kilpatrick, M.D. (Forsyth Medical Center) Suzanne L. Kirby, M.D., Ph.D. Joe N. Kornegay, D.V.M., Ph.D. (Texas A&M University) Myla Lai-Goldman, M.D. (Laboratory Corporation of America, Retired) Chad A. Livasy, M.D. (Carolinas Pathology Group) Roger L. Lundblad, Ph.D. Amil E. Mandal, M.D. (Medical Specialists of St. Augustine) Keith V. Nance, M.D. (Rex Hospital) Thomas M. O'Connell, Ph.D. (LipoScience) William R. Oliver, M.D. (East Carolina University) Richard S. Paules, Ph.D. (NIEHS) Dennis W. Ross, M.D., Ph.D. (Forsyth Medical Center, Retired) Tara C. Rubinas, M.D. (Laboratory Corporation of America) W. Eugene Sanders, M.D. Gary J. Smith, Ph.D. (Roswell Park Cancer Institute) Nobuyuki Takahashi, M.D., Ph.D. (Tohuku University, Sendai, Japan) Paul Wade, Ph.D. (NIEHS) Charles H. Wallas, M.D. Ruth F. Walters, M.D. Douglas C. Wolf, Ph.D., D.V.M. (EPA)

#### **Clinical Fellows**

Kevin A. Alby, Ph.D. (Microbiology)
Laura M. Bender, Ph.D. (Clinical Chemistry)
Elizabeth L. Boswell, M.D. (Surgical Pathology)
Rachel Cianciolo, D.V.M. (Nephropathology)
Steven W. Cotten, Ph.D. (Clinical Chemistry)
Kristy R. Crooks, Ph.D. (Clinical Molecular Genetics)
Christopher J. Gordon, M.D. (Forensic/OCME)
Melissa A. Hayden, Ph.D. (Cytogenetics)
Daniel Kenan, M.D. (Nephropathology)
Andrew P. Laramore, M.D. (Hematopathology)
StaceyO'Neill, M.D. (Molecular Genetics Pathology)
Deborah Spencer, M.D. (Cytopathology)
Dirk P. Stanley, M.D. (Cytopathology)
David L. Zimmerman, M.D. (Forensic /OCME)

#### **<u>Co-Chief Residents</u>**

Dana D. Baker, M.D. (PGY IV) Co-Chief Resident Natalie B. Banet, M.D. (PGY IV) Co-Chief Resident Jessica L. Poisson, M.D., Ph.D, (PGY IV) Co-Chief Resident Kimberly J. Woodward, M.D. (PGY IV) Co-Chief Resident

#### **Residents**

Dana D. Baker, M.D. (PGY IV)

Natalie B. Banet, M.D. (PGY IV) Lea L. Bardy, M.D. (PGY III) Gregory D. Bianchi, M.D. (PGY III) Shannon A. Covey, M.D. (PGY II) Daniel L. Duncan, M.D. (PGY II) Kimberly E. Janssen, M.D. (PGY I) Jayson R. Miedema, M.D. (PGY I) Nathan D. Montgomery, M.D. (PGY I) Avani A. Pendse, MBBS, (PGY I) Jessica L. Poisson, M.D. (PGY IV) Brooke Rambally, M.D. (PGY IV) Brooke Rambally, M.D. (PGY II) Olga Speck, M.D. (PGY II) Sara E. Wobker, M.D. (PGY II) Kimberly J. Woodward, M.D. (PGY IV)

#### **Research Associates**

Bakunov, Stanislav A., Ph.D. (Dr. Tidwell) Bakunova, Svetlana M., Ph.D. (Dr Tidwell) Chastain, Paul, Ph.D. (Dr. David Kaufman) Feng Li, Ph.D. (Dr. Smithies) Donald A. Patrick, Ph.D. (Dr. Tidwell) Weihua Tang, M.D. – (Dr. Gulley)

#### **Postdoctoral Research Fellows**

Zhaokang Cheng, Ph.D. – Dr. Joan Taylor Yukako Kayashima, Ph.D. – Dr. Nobuyo Maeda Hind Muallem, Ph.D. – Dr. Margaret Gulley Tan Nguyen-Cao, Ph.D. – Dr. Oliver Smithies Yuliy Rozenberg, Ph.D. – Dr. Oliver Smithies Yuliy Rozenberg, Ph.D. – Dr. Christopher Mack Delisha Stewart, Ph.D. – Dr. Melissa Troester Huili Wang, Ph.D. – Dr. Jonathon Homeister Watanabooyongcharoen, P., Ph.D. (Dr. Herbert Whinna) Yang Yang, Ph.D. – Dr. Cyrus Vaziri Zhigang Zhou, Ph.D. – Dr. Joan Taylor

#### **Graduate Students**

Maria M. Aleman – Dr. Alisa Wolberg Jessica C. Cardenas – Dr. Frank Church Patricia Casbas-Hernandez – Dr. Melissa Troester Dinuka M. DeSilva – Dr. Young Whang David A. Detwiler – Dr. Joe Kornegay Michael L. Durando – Dr. Cyrus Vaziri Meghan E. Free – Dr. Ronald Falk Julia E. Geddings – Dr. Nigel Mackman Kaitlin C. Lenhart – Dr. Joan Taylor Pamela Lockyer – Dr. Cam Patterson Lantz C Mackey – Dr. Jonathon Homeister Adam D. Pfefferle – Dr. Charles Perou Amanda L. Rinkenbaugh – Dr. Albert Baldwin Jessica E. Rodriguez – Dr. Monte Willis Aleeza J. Roth – Dr. Ronald Falk Kristine M. Wadosky – Dr. Monte Willis Bethany L. Walton – Dr. Alisa Wolberg Laura M. Weise Cross – Dr. Christopher Mack

## RESEARCH AND SCHOLARLY ACCOMPLISHMENTS

Over the past year an excellent record of achievement in research has resulted in 259 publications of original papers and book chapters (abstracts not included). Excellence in research and training has attracted outstanding faculty, residents, postdoctoral fellows, and graduate students, has advanced the understanding of disease, and has enhanced the reputation of the department and institution.

## ROBERT C. BAGNELL, Ph.D.

During this reporting period the Dr. Robert Bagnell Laboratory supported research by 343 principal investigators from 42 departments and centers at UNC. The total number of active laboratory clients now stands at 1007. An effort is made to add an additional transmission electron mmicroscope to the laboratory, The Light Microscope course, Pathology 464, is being completely re-imagined and made more suitable to graduate student interests and needs.

## DWIGHT A. BELLINGER, D.V.M., Ph.D.

Dr. Bellinger's research interests remain in the area of hematology and cardiovascular disease. They have used a swine model for studying atherosclerosis for many years. They are using their colony of familial hypercholesterolemic pigs to study the role of hyperlipidemia and insulin resistance on atherosclerosis, wound healing and renal disease. Grant funds continue for the maintenance of the hemophilia A and B and von Willebrand disease dogs at the FOBRL as a National Resource. These dogs continue to be an effective model to test various gene therapies and other strategies to correct these inherited bleeding disorders. Studies using this model have resulted in human trials.

## JESSICA K. BOOKER, Ph.D.

Dr. Booker's research draws from her expertise in clinical molecular genetics and instrumentation to collaborate with colleagues on a diverse range of projects. Current projects include the identification and characterization of novel *BRCA1* and *BRCA2* mutations, including silent and missense sequence variants that result in truncated proteins. As Scientific Director of the Clinical Molecular Genetics Laboratory, Dr. Booker works closely with the research analysts and clinical fellows as they develop new assays for acquired and inherited diseases. New assays currently under development include PML-RAR $\alpha$ , skewed X-inactivation, PIK3CA, quantitative NPM1, and custom sequencing as requested by clinicians. Assays being redesigned for improved efficiency or sensitivity include automated nucleic acid extraction, EBV, and a Fragile X methylation assay that will ultimately eliminate the need for Southern blotting. Dr. Booker is actively involved in the NCGENES project investigation the clinical implementation of next-generation sequencing.

### THOMAS W. BOULDIN, M.D.

For the coming year, Dr. Bouldin will continue to be very heavily involved in all aspects of diagnostic neuropathology, providing service for surgical neuropathology, the nerve biopsy service, and ophthalmic pathology.

### CLAUDIA M. BRADY, M.H.S.

Claudia Brady's current clinical activities include instructing PGY1 through PGY4 pathology residents and second year Pathologists' Assistant students from Duke University in the Gross Room. Training includes preparation of biopsy specimens through dissection, examination, and dictation of larger and more complex surgical excisions. Emphasis is placed on thoroughness including acquiring all relevant clinical information about the case prior to dissection, proper triage, prioritization of caseload, and efficiency without compromising quality. Ms. Brady enjoys all levels of PGY pathology residents and medical students on all benches in Surgical Pathology also trains all levels of PGY pathology residents and medical students on all benches in Surgical Pathology. She believes with the current faculty PAs providing all the training for the residents, they will develop good habits and mentality with a methodical approach to their patients; the surgical pathology specimen that they handle.

## ARLENE S. BRIDGES, Ph.D.

Dr. Bridges' current research activities involve translational drug development. Primary research activities involve analysis of antiparasitic agents (in collaboration with Dr. Richard R. Tidwell, Director of the UNC Consortium for Parasitic Drug Development), anti-HIV agents (in collaboration with Dr. Ron Swanstrom, Director of the UNC Center for AIDS Research), and anticancer nanoparticles (in collaboration with Dr. Joseph DeSimone, Director of the Carolina Center for Cancer Nanotechnology Excellence). As Director of the ADME Mass Spectrometry Center, Dr. Bridges' role is to provide study design assistance, bioanalytical support and data interpretation to preclinical and clinical studies conducted by not only these three research groups, but to other scientists at UNC and beyond. Last year, one goal was to acquire new mass spectrometers to meet the growing demand and to replace existing aging equipment. She recently re-submitted a Shared Instrumentation Grant to the NIH and is awaiting her score. She has also negotiated with the Schools of Pharmacy and Medicine to purchase a new high-end mass spectrometer for the Center. The Center received from the SOM and SOP a new AB SCiex 5600 Triple TOF mass spectrometer. Finally her goal of increasing interest in the ADME Mass Spectrometry Center is ongoing. The recent publication of a marketing flyer in conjunction with NC TraCS and the updates to the Center website have already helped generate new users. New collaborators with off-campus include Agile Sciences and the Hamner Institute. Dr. Bridges' goals for the coming year are three-fold. First, she hopes to continue to increase interest in the ADME Mass Spectrometry Center with continued marketing. Second, she hopes to continue to acquire new equipment, either by donation, lease-purchase, or instrumentation grants. Third, she hopes to encourage more users to cite the use of the Core in their publications and grant proposals.

## DEBRA A. BUDWIT, M.D.

Dr. Debra Budwit is co-investigator of a study ecaluating the follow-up and management strategies for patients less than 30 years of age with a diagnosis of cervical intraepithelian neoplasia 2 (CIN2). Patient accrual will end this year at which time study data will be reviewed and analyzed. She also engages in clinicopathologic studies of interest in the areas of breast and gynecologic pathology, with multiplemanuscripts in progress for which completion is anticipated during the coming year.

## FRANK C. CHURCH, Ph.D.

The research area of Frank Church, Ph.D. is concerned with proteases and their inhibitors in human biology and in various disease processes focused in the area of hemostasis –thrmbosis, vascular biology and cancer biology. For more than 20 years they have performed structure to activity studies with heparin-binding serpins (serine protease inhibitors) and the serine protease throbin, where they were involved in identifying the heparin-binding sites in thrombin, antithrombin, heparin cofactor II and protein C inhibitor, and the role of thrombomodulin to accelerate thrombin inhibition by protein C inhibitor. They are using mouse models of vascular and tissue injury (saphenous vein thrombosis and IVC stasis models, and cutaneous wound healing model) to understand the link between senescense (p16<sup>ink4a</sup>), aging obesity, diabetes, wound healing, and venous thrombosis. HUVEC, THP-1, and HepG2 cells are being used to study the mechanism relating aging obesity to pro promote thrombosis. They are characterizing the Tidwell Library of di-cationic compounds ("pentaminidine like") for potential therapeutic anticoagulant activities. Separately, they study signaling systems supported by PAI-1 in breast cancer cell motility, how breast adipocytes modulate PAI-1 expression, and how these interactions contribute to changes in the breast tumor microenvironment.

## WILLIAM B. COLEMAN, Ph.D.

Dr. Coleman's laboratory is focused on elucidation of epigenetic mechanisms underlying human breast cancer development by examining breast cancers that exhibit high rates of gene silencing due to hypermethylation defects (which are ER-negative) and those that lack methylationdependent gene silencing (which are ER-positive). They found that ER-negative breast cancers exhibit a hypermethylation defect characterized by overexpression of DNMT3b protein and elevated DNMT activity leading to concurrent aberrant methylation of numerous genes, and that this group significantly corresponds (~70%) to the basal subtype of breast cancer. Recent efforts have characterized the role of several microRNAs in the post-transcriptional regulation of DNMT3b. Ongoing efforts will continue to examine the molecular basis for the hypermethylation defect and investigate strategies for targeting the epigenome in the treatment of these breast cancers.

## MARILA CORDIERO-STONE, Ph.D.

Dr. Cordeiro-Stone's research program is focused on molecular mechanisms underlying the responses of human cells to DNA damage induced by solar radiation. Normal human fibroblasts and melanocytes, as well as various melanoma cell lines, are used as experimental model

systems. Cultured cells are exposed to UVB and UVA wavelengths represented in ambient sunlight and their responses compared at the levels of DNA replication and repair, the intra-S checkpoint, and induced mutagenesis. Such comparison is possible through the determination of actual densities of induced DNA lesions as more accurate indices of molecular dose than the incident fluence of radiation. The etiology of skin melanomas and carcinomas are strongly connected to sun exposure, but the mechanistic roles of short (UVB) or longer (UVA) wavelengths are not clearly understood. This information is essential for the development of guidelines aiming at skin cancer prevention. Studying the function(s) of proteins involved in the regulation of DNA replication and the network of pathways that protect the human genome from genotoxic effects of DNA damage is essential for a better understanding of the pathogenesis of skin cancers with an environmental etiology.

### **GEORGETTE A. DENT, M.D.**

Dr. Dent's research is focused on the role that enrichment activities play in the career development of medical students. She is particularly interested in the impact of international programs and graduate study in public health on educational outcomes. She is collaborating with the recently established School of Medicine Office of International Activities to investigate the impact of international service and research programs on medical student education. A manuscript describing some of this work was published in *Academic Medicine* last year. In collaboration with the School of Public Health, she is investigating the impact of training in public health on physician practice patterns and career satisfaction. A preliminary report of this work was published in the April 2008 volume of *Academic Medicine*. Goals for the future include extending the physician survey to additional alumni using social media.

## MEGAN J. DiFURIO, M.D.

Dr. DiFurio's areas of subspecialty interest include cytopathology, and gynecologic and breast surgical pathology. She has provided clinical services as well as participated in clinicopathologic and translational research projects in these areas over the past year. Dr. DiFurio presented an abstract on a strategy for improving Pap test unsatisfactory rates at the annual American Society of Cytopathology meeting in November 2010 and participated with the Division of Gynecologic Oncology at UNC in a round table journal club discussion which has recently been accepted for publication in the American Journal of Obstetrics and Gynecology. Other current research projects include the following: (1) collaboration with Dr. Bae-Jump in Division of Gynecologic Oncology in the study of the effects of obesity and anti-diabetic medications (e.g., Metformin) on development of ovarian carcinoma in a mouse gene knock-out model, (2) collaboration with Dr. Van Le in Division of Gynecologic Oncology in the study of the optimal size of margins in women with squamous cell carcinoma of the vulva, (3) collaboration with Dr. Rahangdale in the Department of OB/GYN and Dr. Smith in the School of Public Health in the collection and archiving of cytology and biopsy materials from women with cervical dysplasia with the future hope of looking for factors to help predict which women will go on to develop invasive cervical carcinoma, (4) collaboration with Dr. Brewster on the Division of Gynecologic Oncology in the study of the possible presence of microbiotic organisms ion the upper GYN tract and the possible relationship to carcinogenesis, and (5) collaboration with Dr. Hackman in the Department of Otolaryngology/Head and Neck Surgery in the study of the accuracy of ultrasound guided FNA

in detecting persistent disease in lymph nodes of patients with head and neck squamous cell carcinoma after definitive chemotherapy. In the next year, Dr. DiFurio hopes to continue with these research interests especially expanding her work in the area of cervical and vulvar neoplasia. She is also looking forward to continuing to help Dr. Lininger to expand the gynecologic and breast pathology outside consultation service. Other goals include continuing to provide at least 4 lectures/slide teaching sessions for the pathology residents and fellows and becoming more involved in the Reproductive Medicine course for the UNC Medical Students.

## CHERIE H. DUNPHY, M.D.

Dr. Dunphy's research involves the development of distinguishing markers of diffuse large B-cell lymphoma, double-hit lymphomas, and Burkitt lymphoma by full gene expression profiling with extrapolation of immunohistochemical markers and correlation with clinical outcomes. She has established several collaborations:

- 1. with Dr. Ken Young, Wisconsin, regarding gene expression profiling of diffuse large B-cell lymphoma.
- 2. with Dr. Sandeep Dave, Duke University, regarding gene expression profiling of diffuse large B-cell lymphoma and Burkitt lymphoma.
- 3. with Dr. Kristy Richards, UNC, regarding diffuse large B-cell lymphoma.
- 4. with Dr. Kristy Richards, UNC, and Matthew Breen, NC State University, regarding FISH of dog lymphomas.

Dr. Dunphy will continue to work as an author/editor on several projects:

- 1. Editorship/Authorship of E-Medicine Pathology textbook for liquid and solid Hematopathology/Hermatology;
- 2. Authoring and editing textbook entitled Frozen Section: Lymph Node;
- 3. Authoring Chapter regarding Hematopathology for Medical School textbook;
- 4. Authoring and editing textbook entitled An Atlas of Neoplastic Hematopathology;
- 5. Analysis of the Significance of CD200 Expression in Plasma Cell Dyscrasias; and
- 6. Authoring and editing Mini-Series Topic of Myeloproliferative Neoplasms and Myelodysplastic/Myeloproliferative Overlap Neoplasms: Current Diagnosis and Therapy Authoring and Editing of Topics recently presented at the Society for Hematopathology Symposium at USCAP, 2010 entitled: Atypical and Reactive Lymphoid Proliferations Mimicking Malignant Lymphoma to be published in Seminars of Diagnostic Pathology.

## DAVID EBERHARD, M.D., Ph.D.

Dr. Eberhard's laboratory space has been under renovation since his 4/17/2011 start date (He has a temporary office in the interim). The lab should be ready for use in September 2011. He has been purchasing equipment for the new lab and is posting job requirements for a Research Associate laboratory manager and a Research Technician. His ongoing activities include: "Director of Pre-Clinical Molecular Pathology" for the Cancer Genomics efforts in the Lineberger Cancer Center, develop pathology QA and tumor sample workflow (LIMS and physical sample workflow) within the LCCC, participate in clinical trial protocol development, advise in clinical development of new assays, and nanostring analysis core service. His plans and goals include: continuing and expand ongoing activities described above. Implement BSP LIMS

and digital pathology for sample QA, initiate original and collaborative research focusing on solid tumor heterogeneity and how it relates to response and recurrence after therapy, digital pathology analytic approaches to define and quantitative heterogeneity, methods to facilitate molecular and genomic analyses of tumor cell subpopulations.

## ROSANN A. FARBER, Ph.D.

Dr. Farber plans to write and submit a manuscript on work previously completed by members of her lab on instability of CG- and AT-repeat sequences in normal fibroblasts and mismatch-repair-deficient cancer cell lines.

## **GEORGE FEDORIW, M.D.**

Dr. Fedoriw's research, in collaboration with Dr. Sarantopoulos (Department of Medicine), is primarily focused on further defining the role of the B cell activating factor (BAFF) in chronic graft versus host disease (cGVHD) after allogeneic bone marrow transplantation. Findings from his work were recently presented a Keystone meeting in spring of 2011. He has also investigated pathways of B cell activation in HIV associated lymphomas (funded through the UNC Center for AIDS Research), and is working to identify relevant B cell subsets in human cGVHD (funded through the NC TraCS Institute). Dr. Fedoriw also actively provides research support for collaborators in the Lineberger Cancer Center and the School of Pharmacy. His goals for the upcoming year include applying for additional funding for independent research work.

## CRAIG A. FLETCHER, D.V.M., Ph.D.

As Director of DLAM and Assistant Dean of Animal Research Resources, he continues to provide oversight of veterinary and husbandry care for the research animals at UNC as his primary function. He will continue to develop DLAM's processes and metrics that embrace and move forward the university's research goals. In addition, he is also collaborating with Dr. Julia Whitaker and Dr. Sheryl Moy to study the effect of caging environment on mouse reproduction and behavior. He will also continue to pursue his research on the role of genetic variants in regulating systemic inflammation and platelet activation in the development of atherosclerosis. Thus far, his research collaboration has performed a comprehensive genetic screen of 4 genes (*CX3CL1, CX3CR1, CXCR3* and *PF4*), and report *PF4* locus variants associated with the modulation of serum PF4 and TNF $\alpha$  levels. The next step will be to understand the relationships between the PF4 variants and their control of vascular reactivity and inflammation.

### WILLIAM K. FUNKHOUSER, M.D., Ph.D.

Dr. Funkhouser collaborates as a funded Pathologist with the Baric research group on lung morphologic changes in SARS respiratory virus vaccination models in mice. Dr. Funkhouser collaborates with Dr. Olshan in Public Health Epidemiology on followup studies derived from the 5 year funded CHANCE study on risk factors for head and neck carcinoma in the state of North Carolina. Dr. Funkhouser collaborates with Dr. Hayes at the LCCC on projects related to inter-observer reproducibility of morphologic diagnosis of non-small cell lung carcinoma (NSCLC) and molecular subsets of the different types of NSCLC. These projects are attempting to define more accurate criteria for making the diagnoses of the different types of NSCLC, and identifying molecular subsets with statistically different natural histories or responses to therapies. Dr. Funkhouser collaborates with Dr. Coleman of the DPLM on two projects. The first is to define molecular methods for determination of neoplastic clonalityunique to each neoplasm in a given individual. Such a method would allow distinction of two morphologically similar neoplasms from one another, e.g. distinguishing a solitary pulmonary metastasis from a new lung carcinoma. The second is a technical project, with a goal of creating a durable, reusable solid phase cDNA library in a microscale bioreactor.

## PETER H. GILLIGAN, Ph.D.

There are two areas that will be pursued in the coming year. Studies to understand the microbiome of chronic lung disease in cystic fibrosis patients are ongoing. In the coming year, the focus of the work will be the role of anaerobic bacteria and on viruses in this process. The second area of investigation will be in the development of novel diagnostics for the detection of *Clostridium difficile* infections. Novel amplification technologies to detect *C. difficile* toxin genes will be evaluated.

## VIRGINIA L. GODFREY, D.V.M., Ph.D.

Dr. Godfrey will continue to provide collaborative pathology evaluations for colleagues in the Medical School faculty, particularly members of the Lineberger Comprehensive Cancer Center. Recent and continuing projects include morphologic evaluations of: 1) pig models of atherosclerosis and Type II diabetes (Nichols), 2) Brg 1 mutant mice (Bultman), 3) dog models of hemophilia (Nichols), and 4) mouse models of choline deficiency (Ziesel). She will assist in characterization of new mouse models through the interactions with the National Gnotobiotic Rodent Resource (B Sartor), the Mutant Mouse Regional Resource Center (MMRRC) at UNC (Magnuson), and the Collaborative Cross (Pardo Manuel de Villena).

### MICHAEL DAVID GOODMAN, M.D.

Dr. David Goodman has participated in medical and dental student, pathology resident and house staff education as directed by the department chairman during the year July 1, 2011 to June 30, 2012. These activities have included presentation of formal lectures, laboratory section leadership and gross autopsy conference attendance. Additionally, he has attended interdisciplinary clinical care conferences and sentinel event meetings as required. Dr. Gooman is currently a part-time faculty member with a 16% FTE position. He continues to emphasize autopsy service with associated resident autopsy training and hospital quality assurance. He will assist in medical student instruction as needed in laboratory sessions (pulmonary, general and urinary sections). He plans to continue to actively attend department functions in support of the department's mission.

### KEVIN G. GREENE, M.D.

Dr. Greene is currently a subinvestigator in a clinical trial, and associated extension study, evaluating the efficacy and safety of everolimus in liver transplant recipients. He is also currently

collaborating with a radiation oncologist to create digital 3D reconstructions of liver tissue to evaluate the relationship between tumor and radioactive isotope beads. Additional similar projects are anticipated for next year.

## PAMELA A. GROBEN, M.D.

Dr. Groben enjoys collaborating with colleagues on translational research projects and projects that require her surgical pathology skills. She is currently working with Nancy Thomas from Dermatology looking at cutaneous melanoma. She reviews slides on melanomas and other melanocytic lesions, record the histologic features and use laser capture micro-dissection to acquire melanoma cells in small lesions so that mutations for BRAF mutations and DNA-methylation profiles can be determined. (See Thomas, "Tandem BRAF mutations in primary invasive melanoma", 2007; Thomas, "Number of nevi and early life UV exposure are associated with BRAF-mutant melanoma", 2007; Thomas, "Relationship between germline MC1R variants and BRAF-mutant melanoma in a North Carolina population based study", 2010; and Conway, "DNA-methylation profiling distinguishes malignant melanoma from benign nevi", 2011 in the publication section). Several studies are ongoing and histologic review and laser capture to acquire DNA continues to be a requirement.

# MARGARET L. GULLEY, M.D.

Dr. Margaret L. Gulley's research is aimed at 1) understanding the molecular basis of Epstein-Barr virus (EBV)-related malignancies, and 2) developing novel laboratory tests to assist in diagnosis and management of affected patients. In the past year there has been substantial progress towards these goals. They are validating two gene expression profiling systems to apply in paraffin embedded tissue, blood, plasma, serum and other specimen types. They used well-characterized paraffin embedded cell lines for analytic validation, and they are currently collecting data on primary specimens from patients with cancer, precursor lesions, and nonneoplastic controls to demonstrate clinical utility in categorizing disease using patterns of RNAs (coding and non-coding). In work of a more general nature, they teamed with researchers campus-wide to improve biobanking services for local investigators. They validated novel molecular assays for use in clinical trials and in routine patient care. This work builds on basic science discoveries and translates them to the clinical realm, reinforcing the important role of pathologists in advancing medical practice using modern molecular tools. In the coming year, they seek more funding for assay validation projects and clinical trials to gather clinical evidence of efficacy. They will continue to maximize productivity of local clinical investigators by making tissue/lab/pathologist resources available for team science.

## SUSAN C. HADLER, M.D., M.S.

Dr. Susan Hadler's efforts in the Medical School are centered around teaching and curriculum. She is involved in teaching 1<sup>st</sup>, 2<sup>nd</sup> and 4<sup>th</sup> year medical students in multiple courses, as well as Pathology and Toxicology graduate students and Physical Therapy graduate students. She serves on a number of medical school curriculum related committees. Her efforts in the Dental School are also centered on teaching; she teaches 1<sup>st</sup> year dental students in multiple courses. She also serves on the Dental School's admissions committee.

## CATHERINE A. HAMMETT-STABLER, Ph.D.

Dr. Hammett-Stabler's focus is in the improvement of clinical laboratory support of pain management and addiction. During the past year, she has systematically determined previously undocumented cross-reactivity of the immunoassay-based drug screens used by the MCL Core Laboratory for commonly prescribed or abused drugs (or their metabolites). In addition, she continues collaborations with Drs. Robert Aris and Margaret Gourlay. Her work with Dr. Aris investigates the uptake, metabolism, and mechanism of action of immunosuppressant drugs by and within human tracheobronchial epithelial cells. The work with Dr. Gourlay continues assessing the relationship between osteoporosis and various biomarkers. Work conducted this past year suggests the previously reported association between higher concentrations of follicle stimulating hormone (FSH) and lower bone mineral density (BMD) reflects an indirect effect of body composition (lean vs fat mass) on FSH, not a direct effect of FSH on BMD.

### TRACY M. HEENAN, D.V.M.

The Office of Animal Care and Use, Directed by Tracy Heenan will continue to provide excellent service to animal research community, ensuring humane animal care and use, facilitating the application review process, providing exemplary training of research personnel, and conducting fair and thorough investigations of animal welfare concerns and noncompliance while still working to establish rapport with researchers and fostering animal research. The necessity of providing fair and thorough customer service is one of Office of Animal Care and Use (OACU) guiding principles. With escalating compliance-related responsibilities, such as increased investigator-managed animal facilities as well as offsite facilities, it will most likely be necessary to add an additional T/C Coordinator position in the next five years. OACU, like everyone on campus, has had to plan for budgetary cuts. The office has made monumental strides in reducing the amount of paper as well as the associated costs by moving to an electronic review process. The office continues to find new ways to eliminate the voluminous paper copies of meeting information. Members review applications and the 1000 plus page semi-annual facility report electronically. The office has fully implement the position responsible for Grant Application/IACUC Application congruency. IACUC applications are being compared with grant applications and faculty training is ongoing. This will be a process requiring cooperation and buy-in from research faculty. During the next several years the office will continue to educate and advise faculty, students, research personnel, IACUC, Division of Laboratory Animal Medicine (DLAM) personnel, and Department of Environment Health and Safety (EHS) representatives regarding proper animal care and use policies and practices. The Director will continue to serve as an integral link between the IACUC and the Office of the Vice Chancellor for Research (VCR), DLAM, EHS, and the University Employee Occupational Health Clinic and will work to enhance all levels of communication between these groups.

### STEVEN HOLMES, M.H.S.

Steven Holmes' area of expertise is in surgical pathology and gross anatomy. With this knowledge I am able to fulfill my role as an instructor to residents, medical students, prospective applicants and Pathologists' Assistant students. My instruction includes but not limited to

indentifying and proper orientation of specimens as well as proper conduct and safety training in the laboratory. These skills are needed for handling simple biopsies up to complex surgical resections. Due to the high volume of specimens, my training also includes proper time management without adversely affecting patient care. Within the past few years I've able to become a more confident teacher. This confidence stems from a year at private practice and years as an instructor/recruiter at Duke University Medical Center. In the upcoming year, I envision an even more hands on role with the departmental staff regarding staff instruction through laboratory bench work, conference planning and via meetings. I also plan to take a more active role in the frozen section room and learn the connection amongst the other labs with surgical pathology. Throughout the year, the growth, maturation, and improved skill level of residents in the surgical pathology laboratory is a reflection of my success as a clinical instructor.

## JONATHON W. HOMEISTER, M.D., Ph.D.

The research of Jonathon Homeister, M.D., Ph.D. has two major goals. The first is to utilize leukocyte lineage-specific transgenic gene expression and leukocyte lineage-specific gene targeting in murine experimental models to investigate  $\alpha(1,3)$ -fucosyltransferase (FUT) gene function in the development of atherosclerotic cardiovascular disease. They are using these mice and other mice made deficient in FUT-IV and FUT-VII in all tissues to define a role for the selectin adhesion molecules and their fucosylated ligands in the development and progression of atherosclerosis. These mouse strains will be used to continue their studies that define the selectin-dependent contribution of several leukocyte lineages to the atherosclerotic disease process. The second goal is to determine the mechanisms whereby the FUTs regulate hemostasis and thrombosis. These studies are determining the mechanisms whereby fucosylation of selectin ligands and/or other blood molecules alters coagulation and thrombosis. These studies also utilize the mouse strains described above to modulate generalized and leukocyte lineage-specific FUT expression.

### PEIQI HU, M.D.

Dr. Hu's current research, in collaboration with Dr. Jennette, is focused on 1) investigating involvement of genetic factors in pathogenesis of ANCA induced glomerulonephritis. They recently found that anti-MPO IgG caused different severity of ANCA disease in different strains of mice, which mimics disease variation in ANCA patients. Next, they will test the ANCA-mediated disease induction in eight different founder strains and try to explore genetic basis responsible for variations in severity of disease, and hopefully to find out candidate genes and their protein products that involved in pathogenesis of the disease. 2) trying to identify specific epitopes that are targeted by pathogenic anti-MPO IgG. They have already created recombinant mouse/human MPO chimeric molecules and will use them to detect the portion of mouse MPO that is responsible for the disease induction. 3) generating PR3-ANCA disease mouse model. Success with this model would advance their understanding of mechanism of PR3-ANCA disease.

## J. CHARLES JENNETTE, M.D.

A major portion of Dr. Jennette's recent basic research has utilized an animal model of ANCA disease discovered in his laboratory that is induced by i.v. injection of mouse antimyeloperoxidase (anti-MPO) IgG antibodies or anti-MPO lymphocytes into mice that is mediated primarily by activation of neutrophils. Activation of the alternative complement pathway is critically involved in the pathogenesis of disease in this model. ANCA-activated neutrophils release factors that activate complement, which in turn primes neutrophils for further activation by ANCA. These effects and other ANCA-mediated pathogenic events depend on generation of C5a by alternative pathway activation and on engagement of C5a receptors on neutrophils. Blockade of this critical pathogenic step abrogates disease induction, which suggests a possible novel therapeutic strategy in humans. Recent observations show that another receptor for C5a in addition to C5aR, i.e. C5L2, is an inhibitory rather than an activating receptor for inflammation. Knock out of this receptor worsened anti-MPO induced disease. Ongoing studies using this mouse model as well as patient samples indicate that Fc gamma receptors are involved in pathogenesis and in the modulation of disease phenotype. Genetic variations among mouse strains have a dramatic influence on disease severity. Genomic studies are underway to identify the genes responsible for these differences in disease severity. Candidate genes or genetic polymorphisms are being studied in parallel in patients with ANCA disease. Bone marrow transplant studies of anti-MPO disease have demonstrated that these genetic influences act primarily on and through bone marrow derived cells. Experiments are underway to assess the induction of disease by antibodies against specific MPO sense and anti-sense peptides. Pathogenic epitopes are being mapped using human-mouse chimeric molecules. In the mouse model, antibodies against recombinant mouse MPO are pathogenic but antibodies against recombinant human MPO are not. The Lab is preparing chimeric molecules from clones that have various segments of the murine MPO gene mixed with segments of the human MPO gene. These studies are demonstrating that some but not all of these chimeric molecules will induce antibodies that cause disease, thus identifying the portion of the MPO molecule that is the target of pathogenic antibodies.

## HARVEY MICHAEL JONES, M.D.

His research activities are primarily within the area of the history of medicine. He published one book chapter in last year titled Pellagra, Progress, and Public Polemics: Joseph Goldberger, E.J. Wood, and the Osler Connection, appearing in The Persisting Osler IV. He functions as a research support pathologist with the Translational Pathology Laboratory, assisting in the selection and quality assurance for pathologic materials that form the basis of molecular and genetic studies for other principal investigators across the campus. These services are provided on demand. He wrote, produced, and narrated a 23 minute video documentary about the life of William MacNider, MD, for whom the first building on the medical campus was named. He will be implementing a link to this video posted on university servers as a part of the ongoing orientation of incoming medical classes. It will be used as well in the 60<sup>th</sup> anniversary celebrations of the hospital and four year medical school in September 2012.

## KATHLEEN A. KAISER-ROGERS, Ph.D.

Research in the clinical cytogenetics laboratory involves the use of both traditional and molecular cytogenetic techniques including both fluorescence *in situ* hybridization (FISH) and single nucleotide polymorphism (SNP) microarray analysis to identify and characterize rearrangements in their patient population. In addition to identifying copy number gains and losses in the human genome, the SNP array technology also enables them to identify long continuous stretches of homozygosity associated with uniparental disomy (the inheritance of both copies of a chromosome, or chromosome part, from a single parent) and consanguinity (matings between closely related individuals), both of which can result in genetic disease. While the microarray technology is currently being used to detect constitutional chromosome abnormalities, during the next year they hope to validate the SNP microarray technology for the detection of acquired chromosome changes in some of their oncology specimens. The laboratory also continues to serve as a resource for researchers on campus who are interested in applying cytogenetic techniques to their research projects

## MASAO KAKOKI, M.D., Ph.D.

In collaboration with Dr. Maeda and Dr. Smithies, Dr. Kakoki's current research aims at finding ways to mitigate/decelerate complications of diabetes and aging. Recently I found that the senescence-associated phenotype in diabetic mice is enhanced by lack of bradykinin receptors. I have also generated mice with different genetical levels of transforming growth factor beta1 or endothelin-1. In the coming year(s), I will see if they have altered susceptibilities to diabetic complications and aging and study the mechanisms.

### DAVID G. KAUFMAN, M.D., Ph.D.

He is studying the temporal order of replication during the S phase using high throughput DNA sequencing. Initial studies are aimed at validating the methodology by verifying the location of the DNA replicated in the first hour of the S phase as found in his earlier studies involving the cloning of the early replicating DNA. He is also attempting to use this methodology to identify the sites of the origins of DNA replication from throughout the genome. He is also using studies of extended single DNA fibers to discover the locations of origins of DNA replication in early replicating regions. The single DNA fiber technique has also been applied to the quantification and location of sites of DNA damage in DNA and the alterations of DNA replication resulting from DNA damage. Efforts are ongoing to develop automated techniques for analysis of fluorescently-labeled newly-replicated DNA fibers and his collaborators and he are patenting this process and seeking commercial partners of other funding for its further development. There are studies planned to evaluate the translational application of this process to assess "cell stress" in cells obtained from patients. In parallel studies, techniques have been developed to assess extended chromatin fibers and demonstrate sites of DNA replication or DNA damage together with the ability to localize multiple proteins simultaneously at these sites of replication or repair. These studies have been shown to provide the temporal pattern of association of these proteins in addition to their localization

His other studies of reconstructed human endometrial tissue in co-culture have a more clinical/translational focus. Co-cultures of endometrial cells structured to resemble normal endometrium and endometrial intraepithelial neoplasia (EIN) have been used to assess differences in gene expression in the two states using cDNA microarrays. Immunohistochemical studies using antibodies selected based on the findings from microarray analysis are being assessed on tissue microarrays of normal, hyperplastic, EIN and invasive neoplastic endometrium. The goal of these studies is to develop an immunohistochemical test that can aid in the distinction between benign endometrial hyperplasias and EIN, which can be a difficult diagnosis to make based only on H&E stained slides. He has plans for preclinical studies to assess methods to modulate the chemotherapeutic effectiveness of arsenic trioxide (As<sub>2</sub>O<sub>3</sub>) in advanced endometrial cancer. These studies will use co-cultures to assess the status of a pathway providing protection against the effects of  $As_2O_3$  and determine whether this pathway can be inhibited to enhance the effects of  $As_2O_3$ . He also has plans to determine whether the process of implantation of the human embryo in the endometrium can be simulated by adjusting the hormonal status of the endometrial co-cultures and determining whether they provide an appropriate surface for the attachment of embryonic human trophoblastic cells. If this model can be validated it may prove useful for studies of certain forms of female sterility and aid in development of strategies for their correction.

## WILLIAM K. KAUFMANN, Ph.D.

Dr. Kaufmann's research is focused on the mechanisms of chromosomal instability in melanoma. Studies are monitoring components of the DNA damage response in normal human melanocytes and melanoma cell lines to identify protective elements of DNA metabolism that function in normal melanocytes but are degraded in melanomas. The p53-dependent G1 checkpoint response to DNA damage was found to be degraded in 64% of melanoma cell lines, the p53-independent G2 checkpoint response was degraded in 33% of melanoma lines, and the intra-S checkpoint response to UV-induced DNA damage was found to be fully functional in all melanoma lines tested. This result may speak to the fact that the intra-S checkpoint is indispensible and performs an essential function during DNA replication to stabilize DNA replication forks that are stalled at natural replication barriers. Future studies will focus on targeting this checkpoint for selective killing of cancer cells. Goals in the upcoming year are to renew funding for their work.

## APRIL KEMPER, M.H.S.

Ms. Kemper's one-on-one training of the 1<sup>st</sup> year pathology residents and overseeing the grossing of the 2<sup>nd</sup>, 3<sup>rd</sup>, and 4<sup>th</sup> year residents and the Duke PA students continues. One of her main goals for the upcoming year is to continue working to improve upon her teaching skills and to maintain a fun exciting learning environment. Monthly gross conferences were initiated last year. Ms. Kemper along with her co-workers led the organ based conferences. These conferences were a big success and will be continued next year. Cerner CoPath Advance Barcoding and Tracking module was initiated last fall and Ms. Kemper work with others to get the system implemented. This year, Ms. Kemper will take part in giving the orientation for this system to the new residents. This new system has increased efficiency, work flow, and reduced errors in the laboratory.

## HYUNG-SUK KIM, Ph.D.

Dr. Kim studies complex genetic diseases, various animal models for cardiovascular diseases had been generated by gene targeting techniques. Resulting animals had shown the genetic factors to be key role. Then to understand homeostatic response to the genetic changes, Dr. Kim developed a molecular phenotyping procedures by gene expression study using high-throughput real time RT-PCR method. His publications showed its power for recognizing subtle phenotypic changes in animals even with minimal genetic differences. Using this powerful technique, currently he as a core director of gene expression study, have been collaborating with many researchers in many fields, mainly cardiovascular disease with Drs. Smithies and Maeda group, kidney problems with Drs. Arendshorst, Coffman (Duke Univ.), Williams (Temple Univ.), Luther (Vanderbilt Univ.) and Sharma (UCSD). Heart failure with Dr. Meissner, neurogical disease with Hand (UNC) and Dr. O'Connor (UCSD). He seeks more development in procedures of molecular and physiological phenotype for characterization of animal models.

## RUTH A. LININGER, M.D.

Dr. Lininger is a surgical pathologist who is a specialist in gynecologic and breast pathology. She enjoys teaching residents, fellows, medical students, and graduate students and sharing what she has learned. She works with medical colleagues in multidisciplinary conferences to help to identify the best treatment and care for patients. Her research interests have become more clinical during her career. She participates in collaborative studies, primarily in gynecologic research on molecular markers in endometrial cancer and infertility states. She also has entrepreneurial interests and has a growing private outside consult service focusing in gynecologic and breast pathology and is a consultant for difficult gynecologic and breast pathology cases for two regional reference laboratories. She enjoys helping to bring new diagnostic tests to the special procedures laboratory, and also enjoys the business and fiscal aspects inherent of running a surgical pathology laboratory where she provides input on billing, charging, and other fiscal issues.

### CHRISTOPHER P. MACK, Ph.D.

The overall goal of the Dr. Mack's lab is to identify the signaling pathways and transcription mechanisms that regulate smooth muscle cell (SMC) differentiation. They have recently shown that nuclear localization of the myocardin family SRF co-factors by RhoA signaling is an important mechanism by which extrinsic factors regulate SMC-specific transcription. Their current studies are focused on identifying the signaling pathways upstream and downstream of RhoA that regulate SMC transcription with a particular focus on the role of this pathway in the nucleus. The Mack lab recently identified the histone demethylase, jmjd1a, as an MRTF-A interacting protein, and a relatively new and exciting research focus is on the epigenetic control of SMC-specific transcription. The identification of the chromatin modifications that regulate SMC-specific transcription is a major goal as is the identification of the chromatin modifying factors that mediate these effects. They hope that their *in vitro* and *in vivo* studies will lead to therapeutic targets for several cardiovascular pathologies that involve altered SMC phenotype.

## NOBUYO MAEDA, Ph.D.

Apolipoprotein E plays a central role in lipoprotein metabolism and is required for the efficient receptor-mediated clearance from plasma of chylomicron remnants and VLDL-remnants by the liver. ApoE deficient mice as well as mice expressing human apoE isoforms instead of mouse apoE have provided them tools to develop a deep understanding of the genetic factors underlying atherosclerosis for some years. The apoE-/- mice in two inbred strains (C57BL and 129) develop atherosclerotic plaques at different rates at different locations of their aorta. There are also differences in geometric parameters of aorta between these strains. To test a hypothesis that genetic factors determining aortic geometry determines susceptibility to plaque development, they have been conducting Quantitative Trait Loci analyses of F2 mice between 129apoE-/- and B6apoE-/- mice and between 129apoE-/- and DBAapoE-/- mice. The second project is to determine the mechanism by which different apoE isoforms in humans influence lipid metabolism, metabolic syndrome and cardiovascular incidents. They have recently found that the mice with human apoE4 isoform are resistant to high fat-induced obesity compared to mice with apoE3. However, adipose tissues in mice with apoE4 show reduced functionality, and mice develop diet-induced insulin resistance earlier than apoE3 mice. Moreover effect of rosiglitazone, an insulin sensitizer, on adipocyte differentiation is blunted in mice with apoE4 compared to mice with apoE3. They are currently investigating the isoforms-specific interaction of apoE with PPARy during adjpocyte differentiation and how it impacts to the susceptibility to atherosclerosis.

## TRACIE MASSEY, B.S., P.A.

Ms. Massey is primarily responsible for triaging and banking specimens for the Tissue Procurement Facility. She has increased the amount of specimens banked from about 20% to 60-80%. Her goal is to have 95-98% of the cases consented banked. She has also implemented the banking of prostate cancer from prostatectomy specimens, which before she came, were not getting banked at all. She has become the clinical instructor of the Frozen Section Room. She has standardized the work flow and implemented the lean concept. She is now the sole instructor responsible for training all first year residents as well as assisting/training 2<sup>nd</sup>-4<sup>th</sup> year residents and fellows in the frozen section room. She is also responsible for the upkeep and training /troubleshooting for the Zeiss microscope. She covers the frozen section bench to allow the resident on service to be trained for renal biopsies. She has also become the primary person for freezing all the muscle biopsy specimens since the muscle biopsy service has shup down and specimens are now sent to the Mayo Clinic.

### **STEPHANIE MATHEWS, M.D.**

Dr. Mathews has worked part-time over the last two years which has allowed her to maintain and sharpen clinical diagnostic skills and build necessary confidence as a hematopathologist. As she transitions to full-time employment, she would like to expand her role in both teaching and scholarship, while maintaining a focus on the clinical efforts. Their interesting and varied case load provides opportunities to publish on clinically relevant findings, and she has already identified several projects of particular interest.. Additionally, many of her clinical

hematology/oncology colleagues have large on-going studies and she would like the opportunity to gain experience with her translational research efforts.

# SUSAN J. MAYGARDEN, M.D.

Susan Maygarden, M.D., continues to be involved in clinical and translational research in cytopathology and prostate pathology. She works with scientists and clinicians at Roswell Park Cancer Institute, Buffalo, NY in submitting a prostate SPORE grant that will be collaborative with UNC, Roswell Park, and Louisiana State University. Her role is working with tissue procurement at UNC in collecting prostate samples, and assisting in grading and scoring tumors. In clinical research, she is interested in the role of cytopathology in classifying tumors and adding to diagnostic yield of operative cases. She has completed studies with Dr. Scanga on classifying renal tumors by cytology, with Dr. Greene on classifying lung tumors by cytology, and with Dr. Pierce and Dr. Veermachaneni on immediate cytologic interpretation of needle biopsies and bronchial brushings during endobronchial ultrasound guided procedures.

# GAYLE C. McGHEE

Gayle McGhee's responsibilities for this year will include provision of gross organs for all of the organ blocks in the 2<sup>nd</sup> year Medical School sequence, Graduate Courses, First Year Dental Pathology and various other 'one-time'' requests such as the provision of lungs and heart for anti-smoking lectures in local High Schools. The work is being made more complicated this year by the necessity to rearrange our library of gross organs in the recently renovated Autopsy Suite. Unfortunately, the available space has been rearranged and compressed making this into a difficult project.

Provision of gross specimens is a multistep process as follows;

- Selection of appropriate organ specimens with the assistance of Drs. Hadler, Reisner and other faculty
- Careful examination of specimens and washing for overnight
- Draining specimens and arraying on appropriate display trays with supplies of towels, gloves, etc.
- Moving specimens to the various teaching rooms and placing them out on desks/tables
- After use specimens are returned, inspected and replaced in new formalin
- Collection maintenance is an ongoing process which involves discarding old, damaged specimens and consultation with Mr. Moylan and others to replace organ sets and enhance our collection

Another major component of her work is the scanning of microscope slides for use in Virtual Microscopy. To some extent this is a "hands-on" process which requires knowledge and experience in the use of the Aperio system and includes the ability to trouble shoot common problems. Scanning is done for teaching and in house research needs at no cost. In addition she scans for non-departmental faculty as a fee for service. The proceeds are used to support the yearly contract for service and upgrades for the Aperio slide-scanner. Additionally, Ms. McGhee helps in the organization of various teaching blocks by acquisition of teaching material and more importantly-by helping to organize and enter material for the Medical School on-line examination system. In the absence of Dr. Reisner Ms. McGhee serve as a delegate to the CC2 Course Directors meeting and help to prepare surveys as needed by Dr. Reisner for his role on

that committee. For the coming year Ms. McGhee plans on helping implement changes that are required to make Pathology teaching a excellent experience for the students we teach. She wants to provide more help toward lectures and lab preparation.

## C. RYAN MILLER, M.D., Ph.D.

Dr. Miller's current activities are focused on translational research involving comparative genomics analysis of glioblastomas (GBM) from both humans and genetically-engineered mice (GEM). The main goals of this work are to 1) develop a protein-level molecular classification of human GBM with distinct response to the current standard-of-care therapy (temozolomide + radiation (TMZ-XRT)); 2) define the impact of engineered genetic alterations and secondary genetic events on astrocytoma subtype-specification in GEM; and 3) determine molecular signatures of GEM GBM after TMZ-XRT.

# MELISSA B. MILLER, Ph.D.

Dr. Melissa Miller's major interests reside in the use of molecular technology to improve clinical infectious disease testing and to utilize these technologies to explore the epidemiology of viral infections and antimicrobial resistance in bacterial infections. During the past year, Dr. Miller and colleagues completed and published a multi-year study of the prevalence and risk factors of MRSA carriage in child care centers in North Carolina and Virginia. In addition to the continued study of the molecular epidemiology of community-associated MRSA, she has begun researching the prevalence of heteroresistant vancomycin-intermediate *S. aureus* (hVISA) using clinical isolates. In collaboration with colleagues in the School of Pharmacy, she has initiated risk factor analyses and outcome studies for patients identified as having an infection due to hVISA. Dr. Miller's laboratory serves as the core laboratory for the molecular characterization of MRSA isolated from cystic fibrosis patients in two collaborative multi-center studies with Dr. Muhlebach in the Department of Pediatrics. In addition, she is also is employing and comparing a variety of molecular technologies, including microarrays and sequencing technologies, in the clinical diagnosis and epidemiology of respiratory viral infections, the molecular diagnosis of sepsis, and the detection of drug resistant *Mycobacterium tuberculosis*.

# VINCENT J. MOYLAN, M.S., P.A. (ASCP)

Mr. Moylan is currently involved in three research activities. He is a co-investigator in a recently funded NCTracs research grant entitled *Characterization of Brain White Matter Development using High Resolution Diffusion Tensor Imaging with Histologic Confirmation*. He will be assisting Drs. Joe Kornegay, Hongyu An, and Diane Armao. The second project is the *LCCC Tumor Donation Program*. This is a rapid autopsy program headed up by Drs. Lisa Carey and Leigh Thorne. This research program involves breast cancer patients that have previously consented to autopsy upon their death. The third and final project is the *CIMA (Comprehensive Individual Molecular Atlas) project* that is being coordinated through the Carolina Center for Genomic Sciences. This project involves harvesting and dissection of all human body organs from a previously consented donor. Additionally, he is working with Dr. Howard Reisner on developing a searchable autopsy digital image database for use by appropriate departmental staff. Also, he continues to work closely with Dr. Nickeleit and the Nephropathology department

handling all of the medical kidney specimens, and assisting the surgical PA's by processing and photographing select explant cases (cardiac, hepatic, lungs). He looks forward to continuing work with Drs. Hadler and Aylsworth and other medical student related teaching projects as they become available.

## VOLKER R. NICKELEIT, M.D.

The research activities of Dr. Nickeleit focus on different aspects of renal allograft pathology. 1) Adjunct markers (in particular tubular MHC-class II expression and capillary C4d deposition) for the diagnosis of cellular and humoral graft rejection episodes in kidney and liver grafts are under investigation. 2) A major research effort addresses polyomavirus infections in kidney allograft recipients. A new and exciting line of investigation focuses on non-invasive diagnostic strategies to establish a diagnosis of "polyomavirus nephropathy" without an (invasive) biopsy (in close cooperation with H. K. Singh, MD). Negative staining electron microscopy on voided urine samples and the search for three-dimensional polyomavirus clusters, termed "Haufen", have proven in pilot analyses to be highly robust diagnostic methods with negative and positive predictive values of greater than 90%. Extended prospective studies are currently conducted in order to validate the initial findings further. These efforts are in part funded by extra-mural support from Astellas Pharmaceuticals. In additional, efforts are under way to establish a mouse animal model of "polymavirus nephropathy"; preliminary observations are encouraging.

# JUDITH N. NIELSEN, D.V.M.

Dr. Judith Nielsen's collaboration with Dr. Nancy Raab-Traub from the Lineberger Cancer Center in her studies of Epstein Barr Virus LMP influence on tumor formation in mice has resulted in a second paper demonstrating that the Epstein-Barr virus LMMP1 and LMP2A function cooperatively to promote carcinoma development in her mouse carcinogenesis model. We plan to begin analyzing the data gained from observations of ocular lesions suggestive of squameous cell carcinoma on the cornea of mice carrying these viral genes. Dr. Nielsen has also continued my collaboration with Dr. Kirsten Nielsen, a faculty member in the Department of Microbiology, School of Medicine at the University of Minnesota, who is studying pathogenesis of Cryptococcus neoformans in a mouse model. This collaboration has resulted in the funding of an R01 grant in which she will serve as a collaborator. In addition, a three-way collaboration with Dr. Beverly Koller at UNC has begun, using Dr. Koller's knock-out mice to identify key steps in the establishment and progression of cryptococcal infection. It is hoped that preliminary studies will result in preparation and submission of further R01 grants. Further collaborations investigating the immune responses to Titan cell cryptococcal infection of mice are planned. She collaborated with Dr. Sha Chang in preparation of an R01 grant to validate development of new imaging and treatment modalities for cancer, using the pig model to test and validate new stateof-the-art CT imaging equipment, submitted in 2011. While the initial grant was not funded, Dr. Chang plans to re-submit.

## SIOBHAN O'CONNOR, M.D.

Dr. Siobhan O'Connor is currently reviewing cases for project LCCC 9830, for which over 800 new breast cancer cases have been collected. Tumor is being cored from paraffin-embedded

tissue to be used for molecular studies and tissue microarrays. As part of this study, genetic variability in breast cancer is being investigated in relation to how it affects response to various chemotherapy regimens. This tissue will also be available for Dr. O'Connor to develop her own projects. Also, she is expecting to receive 20% salary support from the breast SPORE and will work on additional projects in collaboration with the oncologists and Dr. Charles Perou. Dr. O'Connor is working with Dr. John Woosley on educational videos for the AAMC, which will result in publications, the first of which is on acute chorioamnionitis.

# YARA A. PARK, M.D.

Dr. Park's research focuses on thrombotic thrombocytopenic purpura (TTP), specifically the causes and exacerbating factors. Currently, she is investigating the role of infection in both the initial presentation of TTP as well as exacerbations during treatment. Recently, Dr. Park also studied the levels of thrombopoirtin in TTP patients undergoing treatment. Additionally, Dr. Park is the co-PI for the UNC site of the Transfusion Medicine and Hemostasos Clinical Trials Network grant. Future projects are focused on other otential markers of TTP.

## KATHLEEN W. RAO, Ph.D.

In April 2011, Dr. Kathleen Rao was elected Chair of the Children's Oncology Group Cytogenetics Committee – term to begin July 1, 2011. Over 100 Cytogenetics laboratories in the US and foreign countries participate in COG Cytogenetics studies. Non-US labs include laboratories in Canada, Australia, New Zealand, Ireland, and Switzerland. The Children's Oncology Group (COG) is the world's largest, cooperative children's cancer research group.

### HOWARD M. REISNER, Ph.D.

Dr. Reisner enjoys teaching and the preparation of course related material. The ability to design and execute a course on one's own (such as the Dental General Pathology and the Undergraduate Mechanisms of Disease Class) allows for creativity, some degree of authority along with the responsibility. One is likely to deserve the student comments one receives (and his continue to be been quite good). His work with the Aperio Image Analysis platform has led to collaboration in a project with Dr. Nancy Thomas, Drs. Singh and Nickeleit, and others. He will continue to undertake projects involving new educational materials in collaboration with Dr. Woosley. The most recent involves adapting an Ajax/Seadragon browser for use with pathology images and use of such in 2<sup>nd</sup> year pathology blocks. Dr. Reisner plans to complete two pathology textbooks during the 2012-2013 year.

### ASHLEY G. RIVENBARK, Ph.D.

The focus of Dr. Rivenbark's lab is breast cancer epigenetics. Her long-term research goal is to elucidate epigenetic mechanisms in breast cancer (and other cancers) that can be exploited for development of new diagnostics and therapeutic treatments. Dr. Rivenbark's lab employs novel technology using artificial transcription factors (ATFs) to epigenetically target genes in cancer cells. We have shown that site-specific DNA methylation and long-term stable repression of the tumor suppressor *Maspin* and the oncogene *SOX2* can be achieved in breast cancer cells via zinc

finger ATFs targeting DNA methyltransferase 3a (DNMT3a) to the promoters of these genes. Using this approach, we show *Maspin* and *SOX2* downregulation is more significant compared to transient knockdown, which is also accompanied by stable phenotypic reprogramming of the cancer cell. These findings indicate that multimodular zinc finger proteins linked to epigenetic editing domains can be used as novel cell resources to selectively and heritably alter gene expression patterns to stably reprogram cell fate. Another ongoing project in the Rivenbark lab is to explore the DNA methylation-dependent epigenetic mechanism of gene silencing that may account for loss of ER expression in most ER- breast cancers (triple-negative breast cancers). The hope is that re-expression of ER could be accomplished through application of demethylating drug treatments. Dr. Rivenbark's research program as a basic science cancer biology faculty member in the Department of Pathology and Laboratory Medicine is greatly facilitated by her ongoing collaborations with several investigators at UNC and elsewhere.

# ARLIN B. ROGERS, D.V.M., Ph.D.

The Rogers Lab studies sex-dependent liver carcinogenesis. Using a combination of mouse and cell culture models, the Lab is pursuing parallel mechanisms to account for female resistance and male susceptibility to hepatocellular carcinoma (HCC). On the female side, the group is testing the hypothesis that prolactin represses HCC by constraining innate immunity. Many of the pathways under investigation are amenable to intervention, and present immediate therapeutic opportunities. On the male side, the Lab is exploring the role of physiologic chromatin remodeling in generating hypersensitivity to tumor-promoting inflammation. This model accounts for the absence of direct tumor promotion by androgens, and introduces a new way of thinking about the role of sex in chronic inflammatory disease. Combined discoveries will help us understand why men are >3X as likely as women to develop HCC, and suggest new translational targets. Goals for the Rogers Lab in the coming year include securing a major grant and publishing at least one high-impact publication.

## LORI R. SCANGA, M.D., Ph.D.

Dr. Scanga's current clinical service activities include anatomic pathology signout in the areas of both surgical and cytopathology. She has signed out over three thousand anatomic pathology cases since she began clinical service as faculty including surgical pathology, outside surgical pathology consults, gynecologic cytology, fine needle aspirations, exfoliative cytology, and outside cytology consults. Also, she has covered frozen sections and surgical pathology call. She started clinical service in the areas of cytology and gynecological surgical pathology, and has since added service on the ENT surgical pathology bench. Her clinical service on the ENT bench will surpass her clinical service weeks on gynecologic pathology in the next six months. In the first half of the 2011-2012 academic year, she will be on ENT service for six weeks, gynecologic pathology for five weeks (both benign and oncologic gynecology services), and cytology for six weeks. The surgical pathology areas of both ENT and gynecologic pathology are complementary to her cytology service, and plan to continue with signing out all four of these service benches. Her research goals include publishing her work studying kidney fine needle aspirations which she recently published as an abstract in Cancer Cytopathology entitled "Utility of Fine Needle Aspiration and Core Biopsy with Touch Prep in the Diagnosis of Renal Lesions" and presented as a poster at a national meeting of the American Society of

Cytopathology 58<sup>th</sup> Annual Scientific Meeting in Boston, November 12-16, 2010. She received IRB approval of this project and she is writing a manuscript to publish this work in an anatomical pathology journal. She enjoyed teaching medical students in the MS2 Reproductive Medicine Block and will continue to teach in this block. She enjoys teaching around the scope sessions to residents and will continue to teach residents in formal teaching lectures and at the microscope during sign out.

### JOHN L. SCHMITZ, Ph.D.

Dr. Schmitz's current and upcoming research activities are focused in the areas of HIV Immunology and Transplant Immunology. With the successful re-competition of the UNC CFAR Dr. Schmitz' CFAR Immunology Core will be funded for 5 years as part of this effort (2011 – 2016). In addition to the support provided to HIV researchers at UNC and Duke University, Dr. Schmitz has been awarded 3 contracts with the National Marrow Donor Program to provide laboratory infrastructure and testing services for clinical trials of bone marrow transplant in HIV patients. In addition, Dr. Schmitz is conducting 2 vendor sponsored clinical evaluations of HIV testing method including a rapid diagnostic test and a point of care CD4 test. In the upcoming year, Dr. Schmitz will have 3 additional contracts with Becton Dickenson to support HIV related clinical studies of a CD4 testing method and to conduct a pediatric CD4 normal range study in collaboration with Dr. Steiner from Pediatrics. In the context of transplant immunology Dr. Schmitz continues to collaborate with clinical transplant colleagues on defining the role of HLA antibody in liver transplant recipients. In addition, Dr. Schmitz's laboratory is participating in a multicenter study describing the natural history of alloantibody production post-transplant in solid organ recipients. This work is being performed as a study for the 2012 International Histocompatibility Workshop. Dr. Schmitz is also planning to collect peripheral blood lymphocytes from these same patients to assess B cell phenotypes and function with the goal of applying for TRACS funding to study the regulation of B cell responses in allotransplant recipients. This work will be done in collaboration with UNC investigators studying the role of B cell responses in graft versus host disease.

### **DENNIS A. SIMPSON, Ph.D.**

Dr. Simpson's research, in collaboration with Dr. Kaufmann, the primary research activity is centered on understanding the interaction of ultraviolet light (UV) with human melanocytes and how this interaction leads to melanoma. This research has lead to the development of two novel methods for human melanocytes. The first was the construction of melanocytes that allow regulated expression of common melanoma oncogenes. The second allows measurements of UV induced cytotoxicity in normal human melanocytes and human melanocytes with defined genetic changes. During the next year these experiments will be extended using the Exon Capture Sequencing technology targeted to the 50 most commonly altered genes in melanoma. This information is expected to yield mutation frequencies of each of these genes which should then allow a better understanding of the early changes in the transition of melanocytes to melanoma.

## HARSHARAN K. SINGH, M. D.

Dr. Singh will continue to work further in the characterization and development of a novel, noninvasive, diagnostic test to diagnose a major infectious complication post kidney transplantation known as polyomavirus nephropathy. This new diagnostic technique developed by Dr. Singh and her colleagues at UNC avoids invasive biopsy procedures, and could potentially have profound implications for the care of kidney allograft recipients worldwide. Currently, this test requires the use of electron microsocopy. New methods including ELISA assays and flow imaging techniques are being evaluated to eliminate the necessity of using electron microscopy for test performance. The clinical impact of this novel discovery will continue to be confirmed in a multi-center prospective study with unrestricted funding from Astellas Pharma, US Inc. for which UNC Nephropathology is the lead investigative center. The Division of Nephropathology is also the lead investigator with centers participating from the US, Canada, and Europe in developing an International Consensus Classification of Polyomavirus nephropathy. Initial results from this work will be presented at the International Banff Meeting, Paris, France, in June 2011.

## SCOTT V. SMITH, M.D.

Dr. Smith's current clinical activities are focused in surgical pathology with broad emphasis in pediatric, ENT, thoracic, genitourinary, prostate, cardiovascular, pancreaticobiliary, endocrine, bone, and soft tissue pathology. Dr. Smith was appointed as Associate Director of Surgical Pathology for UNC Hospitals in January 2012. Dr. Smith's teaching activities are substantial within the medical center including lecture series within the School of Medicine, Dentistry, and Public Health, as well as ongoing clinical teaching on the Surgical Pathology service. Dr. Smith has ongoing research collaborations with Dr. Julie Blatt and Dr. Ian Davis in the Division of Pediatric Hematology Oncology in the Department of Pediatrics. Dr. Smith is working with Dr. Ian Davis in Pediatric Oncology on genome-wide identification of active regulatory elements in fresh and archival human cancers.

### **OLIVER SMITHIES, D. PHIL.**

Over the past 20 years much of my research has been focused on identifying genetic factors that control blood pressure. Recently, I have shifted its emphasis towards understanding factors that cause some pregnant women to develop pre-eclampsia, which is characterized by hypertension and proteinuria. I am encouraged in this transition by learning that my main research grant, which is now focused on this problem, will be funded. Indeed it was rated in the top 1% of proposals reviewed by the study section. A second new research area that is occupying my attention concerns the way that the kidney glomerulus discriminates between large proteins, which do not cross the glomerular barrier, from small proteins, which do. This work has also been recognized by our being awarded a grant from a UNC fund (TraCS) that encourages new basic research likely to have a translational impact on clinical practice.

## JOAN M. TAYLOR, Ph.D.

The long-term goal of Dr. Taylor's research is to identify signaling mechanisms that contribute to normal and pathophysiological cell growth in muscle (smooth, cardiac, and skeletal). She is interested in studying cardiac and vascular development as well as mechanisms involved in heart failure, atherosclerosis, and muscle degenerative diseases. The current directions of the Taylor lab are to characterize components of the integrin signaling cascade in these specialized cell types and to target disruption of these regulatory molecules in vivo in an effort to determine their precise role in cardiovascular growth and development. Plans for 2011/2012 are focused on cardiac muscle, skeletal muscle, and smooth muscle. Cardiac: One of their lines exhibits sudden death after pressure overload that is associated with the redistribution of FAK to cell-cell junctions. They are using a proteomics approach coupled with telemetry to uncover the mechanisms by which alterations in integrin signaling may promote arrhythmia. Skeletal: They have uncovered a novel pathway that is regulated by beta dystroglycan and likely plays a critical role in the pathogenesis of muscular dystrophy. They are exploring new concepts with respect to how muscle cells differentiate and fuse in the hopes of creating new compounds that will be effective in blocking muscle wasting that occurs in a multitude of diseases. Smooth: They are particularly interested in defining the mechanisms that regulate the induction and recruitment of smooth muscle cells from the epicardium to the coronary vasculature. They have data that implicate LIM domain containing proteins in this process and will continue to develop animal models to precisely define their role(s) in this important developmental process.

## LEIGH B. THORNE, M.D.

Dr. Thorne will continue to work with the LCCC Tissue Procurement Facility to bank tissue for research as well as to facilitate the collaboration with the NCI/Cancer Gemone Atlas. She is also involved in the Carolina Breast Cancer Study Phase 3 and is working with a surgeon collaborator on a mucoepidermoid project. She has taken the lead for the Tissue Core section for the resubmission of the GI SPORE grant for the cancer center. She is also working with the Cancer Survivorship group on text mining pathology data. She is working with Lisa Carey on her tumor donation protocol (rapid autopsy). She is on a SOM task force to implement the recently approved Strategic Plan. Clinically she also continues to rotate on the Molecular and Autopsy services,

## RICHARD R. TIDWELL, Ph.D.

Dr. Tidwell will continue the collaboration with the Genomics Institute of Novartis Research Foundation (GNF). This collaboration has allowed the Tidwell led Consortium for Parasitic Drug Development (CPDD) to access to a library of over 300,000 small molecules to screen and optimize for development as treatments for late stage human African trypanosomiasis (HAT). This developmental program is being funded under the current Gates Foundation Grant and supplemented by GNF scientist and facilities. In addition, work continues on another Gates funded grant to determine mechanism of toxicity for new drug candidates to treat HAT. This grant is a collaborative study with the Hamner Institute for Drug Safely. This grant's ultimate goal is to uncover specific markers to predict renal and liver toxicity of new classes of molecules. An R01 grant proposal entitled "Novel Approaches to Ensure Safety of Promising New Drugs for Sleeping Sickness" was submitted to NIH during the past year. Although the grant received mixed reviews ranging from all ones by one review to twos and threes by another review it was not funded. This proposal is being rewritten in response to reviewers' comments and will be resubmitted in 2012. At the invitation of the NIH, Dr. Tidwell submitted a P01 proposal entitled "Development of New Molecular Scaffolds to Treat Stage 2 Sleeping Sickness" in the spring of 2011. This proposal is in collaboration with the University of Washington with a requested direct cost budget of \$3,657,354 spanning a five year period. A joint venture is current being negotiated between the University of North Carolina (for the CPDD) and Developing World Health (DWH). Once this JV is completed with this Scottish based non-profit, DWH will assume the role of raising money for the CPDD. Finally, they continue their collaboration with Bayer Animal Health to jointly research new drugs to treat animal diseases.

## MICHAEL D. TOPAL, Ph.D.

Michael Topal's current research involves 1) helping The Cancer Genome Atlas project in its goal to characterize gene expression in many types of tumor samples, and 2) bioinformatics analysis of gene organization in human viruses. The rest of his time is spent on administrative initiatives associated with basic and translational science core facilities at UNC, as described in Section E, and as Faculty Director of the Genomics and Mammalian Genotyping core facilities. The coming year will see discussions to build a regional genomics institute concentrating on high throughput sequencing, to reform HR policies concerning core directors and staff, to centralize core facilities on campus and to provide centralized management of the facilities, and to build a web portal that will be transformative in its ability to educate clinical researchers about research infrastructure applicable to clinical samples.

## DIMITRI G. TREMBATH, M.D., Ph.D.

Dr. Trembath is currently investigating novel markers for the diagnosis and prognosis of brain tumors, in collaboration with Dr. Ryan Miller. Dr. Trembath also wants to develop collaborations with researchers in the neurosciences investigating animal models of developmental neurologic disorders such as autism.

### CYRUS VAZIRI, Ph.D.

Dr. Vaziri's major goal is to publish results of ongoing research projects in high quality journals in order to maintain existing grants and to provide additional funding opportunities. Another goal is to identify novel areas for future research and to initiate new projects that will provide vehicles for extramural funding. To this end, he has initiated trans-disciplinary studies with several colleagues at UNC including Dr. Bill Janzen (School of Pharmacy), Dr. Jim Swenberg (CEHS), and Dr. Monte Willis (Pathology). The collaborative drug discovery project with Dr. Janzen has resulted in an award from the UCRF (\$187K) and a graduate student working on this project (Alicia Greenwalt) has procured support from the Program in Translational Medicine. Two grant applications to support the collaborative projects with the Swenberg lab have been submitted to the NIEHS and a collaborative proposal with Dr. Willis for submission to the NIH is in preparation.

### KAREN E. WECK, M.D.

Dr. Weck's recent research efforts are focused on developing pharmacogenetic testing to predict response to drug therapy. Her laboratory is collaborating in several clinical trials at UNC to study the clinical utility of pharmacogenomic guided therapy. One ongoing clinical trial is a prospective randomized study to determine the utility of pharmacogenomic guided dosing of warfarin, incorporating genotyping for variants in the VKORC1 and CYP2C9 genes associated with altered warfarin response. Dr. Weck is a member of the International Warfarin Pharmacogenomics Consortium, whose goals are to study the effect of clinical and genetic factors on warfarin response and to devise a pharmacogenomic dosing algorithm for warfarin. This work has resulted in two recent publications. Plans are underway to further analyze genomic and clinical factors associated with warfarin response in different ethnic populations including African Americans. In addition, Dr. Weck has collaborated with a group in Brazil to identify VKORC1 mutations associated with warfarin resistance. Dr. Weck is also a coinvestigator in a multicenter collaborative clinical trial to study the efficacy of CYP2D6 genotype-guided dosing for tamoxifen in breast cancer that includes UNC and several other sites across North Carolina. The preliminary results of this trial indicated that CYP2D6 genotypeguided dosing of tamoxifen resulted in normalization of plasma concentration of endoxifen, the active metabolite of tamoxifen, in women who are CYP2D6 intermediate metabolizers. The tamoxifen trial has been expanded to include 500 women across North Carolina, with escalated recruitment of African American and Hispanic women. Dr. Weck is also collaborating with investigators in the Departments of Cardiology to conduct a clinical trial on the efficacy of CYP2C19 genotype-guided dosing for clopidogrel.

Another major effort is translation of new knowledge of the genetic causes of disease into diagnostic testing. Dr. Weck's laboratory has developed mutation testing for genes associated with primary ciliary dyskinesia, X-linked Alport syndrome, and focal segmental glomerulosclerosis (FSGS). The goal is to better characterize the spectrum, incidence and genotype-phenotype correlation of mutations associated with disease and to develop clinical testing in those genes with clinical utility. The UNC Molecular Genetics Laboratory is now one of the only laboratories in the country that offers clinical genetic testing for mutations associated with these diseases. Finally, efforts are underway to incorporate whole exome sequencing technology for clinical diagnosis. Dr. Weck collaborated on a study to evaluate the accuracy of massively parallel sequencing for detection of genetic variants associated with primary ciliary dyskinesia, published recently in the journal Genetics in Medicine. She is co-investigator on two new NIH grant submissions to continue this work.

## BERNARD E. WEISSMAN, Ph.D.

Dr. Weissman's current research focuses upon the role of aberrant chromatin remodeling in cancer development. Specifically, his laboratory concentrates upon loss of activity of the SWI/SNF chromatin remodeling complex in the development of non-small lung carcinoma, a cancer strongly associated with environment pollution, small particle exposure and smoking and malignant rhabdoid tumor, a rare pediatric cancer. Previous studies from Dr. Weissman's laboratory have shown that inactivation of individual components of the complex alter gene expression through changes in chromatin organization. Furthermore, the loss of SWI/SNF

complex may induce epigenetic instability in cancer cells leading to gene silencing via a mechanism independent of DNA methylation. Current studies focus upon understanding how loss of SWI/SNF complex remodeling activity alters signaling of major signaling pathways associated with cancer development including the WNT, NFkB, and KEAP/NRF2 pathways. The laboratory employs cell culture and genetically engineered mouse models combined with the latest molecular genetic techniques including ChIP-seq and MNase-seq to address these questions.

## HERBERT C. WHINNA, M.D., Ph.D.

Dr. Whinna's research interest is in how the normal process of hemostasis occurs in time and space to plug an injury site without causing pathologic thrombosis in the entire vasculature. First, this involved basic protein chemistry studies on the structure-function aspects of thrombin inhibition by the serine protease inhibitors antithrombin III and heparin cofactor II (PhD thesis work). Next, he began engineering and testing of chimeric antithrombin molecules that combine favorable properties of sometimes diverse naturally occurring molecules that can act when and where it is most desirable (postdoctoral and early faculty work). As part of the testing of these engineered antithrombins he established and refined thrombosis models in mice and has been using these models to study the effects of not only the molecules he has engineered, but also (through collaborations) other naturally occurring and synthetic molecules. He has shown previously unreported pathophysiologic differences in two of the most widely used models of thrombosis in mice, which have important implications for studies utilizing these models and the conclusions drawn from them. Most recently, he has developed improved murine hemostasis models that can be correlated with know phenotype in human disease. These models are being used to test the effects of both pro- and anti-coagulant compounds in order to delineate both normal and pathologic hemostasis. Additionally, these models are being applied in mouse models of human disease to investigate both pathophysiologic mechanism and possible treatments.

## JULIA W. WHITAKER, M.S., D.V.M.

Dr. Whitaker will continue to provide veterinary clinical care for the research animals on campus as her primary function. With the new animal facilities opened on campus, the mouse census will more than double, which will significantly increase the case load. She will also continue to pursue research on the effect of caging environment on mouse reproduction and behavior, in collaboration with Dr. Sheryl Moy in the Department of Psychiatry, for which Dr. Whitaker has submitted grant applications this year. Her interest and specialty training in aquatic animal medicine will continue to be used to support the aquatic research species on campus. She will also continue to be involved in teaching and training of laboratory animal residents in the Research Triangle area through the new Research Triangle Laboratory Animal Training Program seminar, Pathology graduate students on animal models, and investigators and laboratory staff on the use of animals in research. She will continue to co-chair the Southeastern location of the International Mock Board Exam Coalition for the ACLAM board exam and to serve as Interim Associate Director of Veterinary Services.

## MONTE S. WILLIS, M.D., Ph.D.

The Willis laboratory investigates the role of the ubiquitin proteasome system in the pathophysiology of cardiac hypertrophy and heart failure. Cardiac hypertrophy develops in response to biomechanical stress most commonly from extrinsic pressures such as hypertension, valvular heart disease, or myocardial infarction. The development of cardiac hypertrophy results in metabolic and structural changes in cardiomyocytes. One metabolic change prominent during adaptive cardiac hypertrophy involves a switch from utilization of fatty acids as an energy source; while fatty acid oxidation is not detrimental to the healthy heart, during prolonged periods of stress fatty acid intermediates contribute to free radical stress. Instead, the stressed heart relies on glucose utilization, allowing reduced oxidative stress, a metabolic switch widely believed to preserve cardiac function in cardiac hypertrophy and heart failure. Recently, the peroxisome proliferator-activated receptor (PPAR) family of nuclear receptor transcription factors has been shown to regulate the cardiac switch from fatty acid to glucose energy at the level of gene transcription. As such, decreasing PPAR- $\alpha$  levels in the setting of cardiac hypertrophy reduces expression of "bad" or "lipotoxic" fatty acid oxidative enzymes while simultaneously enhancing those responsible for "good" glucose oxidation. Identification of the factors that regulate PPAR mediated metabolic adaptation during the development of cardiac hypertrophy and heart failure would open up new therapeutic options for preserving heart function. The Willis laboratory has recently identified that the cardiac ubiquitin ligase Muscle Ring Finger-1 (MuRF1) is an essential regulator of the adaptive changes in metabolism that accompany cardiac hypertrophy and heart failure. They have further identified that MuRF1 specifically interacts with and inhibits PPAR- $\alpha$  activity, by changing its nuclear localization via mono-ubiquitination and nuclear export, which is consistent with PPAR inhibition accompanying adaptive cardiac hypertrophy. In the next year, the focus of the laboratory will be on determining the how MuRF1 regulates nuclear export of nuclear receptors as well as how its own expression is regulated transcriptionally through external forces. These studies will establish the molecular mechanisms by which characteristic shifts in metabolism occur in response to cardiac stress and lead to heart failure.

# **RUTH E. WINECKER, Ph.D.**

The laboratory is currently researching the implications of post mortem redistribution of SSRI's in death investigations. There is one planned publication and one planned abstract from this research for 2011-2012. The laboratory recently submitted an abstract on metaxalone involved deaths for presentation at AAFS in Feb 2012. A manuscript of this research is currently being prepared. Also, manuscripts for research already conducted and presented at scientific meetings in 2010-2011 are currently in preparation. Topics include levetiracetem and buprenorphine.

## ALISA S. WOLBERG, Ph.D.

The major goals of Alisa Wolberg, PhD, are to: 1) examine cellular, biochemical, and biophysical features that modulate thrombin generation, and 2) determine how the pattern of thrombin generation dictates clot formation, structure, and stability. Dr. Wolberg's group has made substantial progress towards both goals during this year. They have used *in vitro* assays and developed novel *in vivo* models of thrombosis and thrombolysis to examine how plasma

hypercoagulability and vessel injury promotes thrombus formation. Their studies suggest pathogenic roles for cell-derived microvesicles in clot formation, and correlate thrombus formation and stability with extent of vessel injury. Their techniques for measuring fibrin formation and stability may provide important information on the therapeutic dosing window of novel thrombolytic and hemostatic agents.

# JOHN T. WOOSLEY, M.D., Ph.D.

Dr. Woosley has continued and expanded his research in GI and Liver pathology. He is the study pathologist in a large (~800 cases) population-based study of colon cancer in 33-counties of North Carolina examining traditional dietary and lifestyle risk factors, access and utilization of health services; and polymorphisms of carcinogen metabolizing enzymes. As a companion study, they have enrolled some of these subjects in a national colorectal cancer family registry that will have the potential to identify genetic markers for colon cancer risk. A major objective of this study is to determine why African-Americans with colon cancer fare more poorly than Caucasian Americans. A follow-up proposal dealing with the same issues for rectal cancer has also been funded. In addition, Dr. Woosley continues his scholarly activity on the technology of pathology education.

## HONG XIAO, M.D.

Dr. Xiao's major research goal, in collaboration with Dr. Jennette, is by using their innovative mouse models of antineutrophil cytoplasmic autoantibody (ANCA) induced glomerulonephritis (ANCA disease), to advance the understanding of mechanism of the ANCA mediated autoimmune disease. Her current focus on studies: (1) testing involvement of Fcγ receptors and alternative complement pathway in pathogenesis and therapeutic interventions in ANCA disease mouse model, such as by blockage of Fcγ receptors or C5a receptors with specific antibodies or small molecule inhibitors, which may have important implications for therapies of human diseases; (2) inducing experimental ANCA disease models by neutrophil antigens in addition to MPO protein, such as Proteinase-3 (PR-3) and lysosomal membrane protein-2( LAMP-2), or different portions of MPO for identifying specific epitopes that are targeted by pathogenic anti-MPO antibodies; (3) investigating genetic basis for variations in ANCA disease among different strains of mice, which mimics disease variations in ANCA patients and trying to identify candidate genes and their protein products responsible for the differences in disease severity, which might be new markers for disease activity and potential targets for novel therapeutic strategy in humans.

# XIANWEN YI, M.D., Ph.D.

The research in my group has made a fine progress. We have developed and applied several useful techniques including isolation of mitochondria, protocols for mitochondrial enzyme activity analysis, and measurement of mitochondrial functions such as membrane potential, energy production and oxygen consumption rate. They are continuously testing more mitochondrial analytic approaches. Last academic year, Dr. Yi published two articles and delivered 2 invited talk for national and international diabetes conferences, and received four grants including two extramural grants. My goals for the coming year are to expand my

collaborations (I have been benefitting from successful and sustained collaborations with senior researchers at UNC and other universities), publish more papers, and get grants.

## MAIMOONA B. ZARIWALA, Ph.D.

Dr. Zariwala's research is focused in several areas: (1) Test for new candidate genes for primary ciliary dyskinesia, (2) To test new patients for known gene mutations, (3) Continue to expand the CLIA approved clinical genetic test panel for Primary Ciliary Dyskinesia, (4) Provide consultation and ongoing support to the Molecular Pathology Lab for clinical genetics test panel for Primary Ciliary Dyskinesia, and (5) Decipher possible genetic causes of idiopathic bronchiectasis that is not related to the CF or environmental causes. Dr. Zariwala's laboratory has made significant progress towards each of these goals in the last year. The work on DNAH11 mutation profiling is complete and manuscript is under revision. Collaboration is ongoing with Dr. Omran in Germany on the newly identified PCD-causing genes CCDC39, CDC40 and previously known DNAH5 mutation profiling. The replication work on DNAH5 and CCDC40 is near complete and additional mutations have been identified from our patient cohort. Ongoing collaboration with the national and international laboratories through the Primary Ciliary Dyskinesia consortia, additional patient material is acquired and tested for known genes and mutations, as well as for defining novel mutations. Additionally, Dr. Zariwala is involved with Drs. Evans, Weck and Berg to test the possible usage of the next generation sequencing technology in the clinical setting and manuscript is already published. Through the collaboration formed with Drs. Shendure, Nickerson and Bamshad at Seattle Genomic Sequencing Center, work on Whole-Exome sequencing of 24 unrelated PCD patients is continued. Of these 24 samples, they identified a novel founder mutation in 3 families with Ashkenazi Jewish ethnicity in the previously known DNAI2 gene. Additionally, they found mutations in the known DNAH5 gene in two families and RSPH9 in one family. Furthermore, Dr. Zariwala identified TWO NOVEL PCD causing genes from this cohort. Mutation Profiling of novel genes identified additional patients harboring mutations, thus these are indeed PCD-causing genes. Functional analysis of splice mutations in the genes revealed that mutations were affecting splicing machinery. Further work on novel genes is underway. Additionally, with the group in Seattle, Dr. Zariwala carried out Whole-exome sequencing in 24 samples from 17 families with non-CF bronchiectasis. Many of these patients have some overlap with PCD phenotype and/or idiopathic bronchiectasis. The initial analysis revealed TWO NOVEL cilia related genes in two families that had non-classic PCD phenotype. Large scale mutation profiling and further characterization work is underway. Additionally, the data analysis and validation studies of whole-exome sequencing for PCD as well as non-CF bronchiectasis group is ongoing in patients where genetic causes are not yet identified. Moreover, Dr. Zariwala has formed collaboration with Dr. Hildebrandt (University of Michigan) and Dr. Cecilia Lo (University of Pittsburg) to carry out whole-exome sequencing in additional ~50 PCD families, and that work is underway. In a nutshell, 4 novel cilia related genes have been identified in the past year and additional work is ongoing to find new targets for PCD and non-CF bronchiectasis. The success of this test will open the door for expanded clinical tests as early diagnosis will allow early intervention and will improve clinical outcome of classic and non-classic PCD as well as idiopathic bronchiectasis. This study will also represent a significant step forward in the application of new approaches to genetically heterogeneous disorders in humans.

## TEACHING HOWARD M. REISNER, Ph.D.

#### **MEDICAL:**

Second Year Medical School Involvement: Pathology content provided by our department is incorporated into 10 of the 11 blocks which comprise the second year curriculum. The blocks are predominantly organ system based. However, two blocks, an introductory "Tools" block and a Clinical Medicine Cases Block, serve special functions to be discussed. The only organ system in which the department does not play a strong role is the Musculoskeletal/Dermatology block which supplies its own expertise in Dermatology. However, we support the block in providing virtual scanned images for use. Each organ system block is represented by a member of this department serving on a "block committee". Several committees are chaired by departmental faculty members including the Tools Block and Integrated Clinical Case blocks. Each block attempts to integrate pathology and abnormal physiology/medicine into a single course with a single syllabus (all presented on-line). Different blocks have taken somewhat different approaches but, in general, independent pathology lectures remain relatively intact and are usually broken into small units. The tendency for "independent" pathology laboratory sessions to be used in several of the blocks (including respiratory, GI, endocrine, female reproductive and renal/gu) has continued and receives excellent student comments. These "mini-pathology" lab sessions are most successful when presented before the more medical sections of the laboratory (when such exist) and are designed so as to complement other material presented. The availability of laboratory staff that participate in multiple blocks (particularly Dr. Hadler) allows students to get to know our faculty members across several organ system blocks and student attendance in laboratories continues to be excellent. In addition, an introduction to Pathology as a medical career has been added to the initial block and several of our more junior faculty has been used this as an opportunity to meet students. Twelve video podcasts presenting overviews of introductory laboratory material have been added to the first block and were noted as helpful by students. The availability of gross organ specimens in the facilities of Bondurant Hall proved to be an extremely positive development in laboratory/small group sessions and the department is pleased that such specimens were available for and heavily used this academic year. Although not perfect in it's implementation AIMS based quizzes have been used in the tool block and will be expanded next year.

The Tools Block (Block 1) now includes the entire Introduction to Pathology (General Pathology) sequence and has been accompanied by a substantial increase in hours available to this department. The Clinical Case Block was founded by Dr. Clark of this department and provides a series of integrated cases in which pathology and clinical laboratory medicine play an important role.

Dr. Reisner has attempted to aid in preparation of teaching material with the assistance of Ms. McGhee and they have concentrated on making virtual microscopy slides easily available as part of the syllabi. All blocks used computer based virtual microscopy rather than glass slides and microscopes to present histopathological material and the availability of a new Aperio scanner with 40X capabilities has allowed the extension of VM technology to the area of hematopathology. Images are provided online via a specialized image server which also serves as the repository for image files. Student acceptance continues to be excellent and a far greater

interest in histopathology was noted to be present during laboratory sessions. The Aperio viewer (Imagescope) continues to be preferred by students to a virtual slide viewer used in histology.

General Pathology Sequence (in Block 1): The course was initially designed by Dr. Scott Smith and consisted of eight lecture sessions covering general pathology and five laboratory sessions using virtual microscopy and gross organ demonstrations\*. Laboratories were staffed by both Ph.D. and M.D. faculty so as to afford students the opportunity to meet both research and clinical faculty. Virtual microscopy images were presented using the image server. It is believed that these changes provided a more coherent introduction to aspects of pathology necessary for an understanding of subsequent material. The examination format (revised last year to have a "practical component") was somewhat modified to fit the integrated second year examination paradigm. Each laboratory session included a short quiz done in lab to help reinforce major points in the lecture and laboratory.

## **DENTAL:**

First Year Dental School Teaching: Pathology 127: Dr. Reisner (Course Director) provided a series of nine one hour lectures which cover all essential aspects of general pathology. Because much of this material is not reviewed in subsequent courses in systemic medical and dental pathology, a good deal of attention to details and use of the textbook (Rubin's Essentials of Pathology 5th Edition) was encouraged. All lecture material was presented as Powerpoints which are made available to students before the lecture. There are seven laboratories covering general aspects of histopathology which are supervised by Drs. Hadler (who comments on gross organ pathology) and Reisner and the expanded use of introductory laboratory "podcasts" has proven both useful and popular. Two multiple choice exams were used as evaluation tools along with short "extra credit" exercises added this year to a surprising degree of enthusiasm. In general, course comments and ratings have continued to be excellent.

Second Year Dental School Teaching (Pathology 214): The course is currently a series of eleven lectures designed to cover most areas of systemic pathology by invited Pathology Clinical Faculty with Dr. Reisner filling in where necessary. Because of this format we continue to reduce the variability between sessions. The lack of a laboratory de-emphasizes histopathology and the use of fixed organ material. Lectures are now much more standardized and *apropos* the needs of the Dental students. Given the availability of virtual microscopy short self-directed laboratory modules may also be included in the future. One sample podcast (in pulmonary pathology) has been produced for testing purposes.

\*Several of our newer faculty including Drs. Fedoriw, Homeister, Ryan Miller took an active role which will continue next year.

#### **MOLECULAR AND CELLULAR PATHOLOGY GRADUATE PROGRAM** William B. Coleman, Ph.D., Director of Graduate Studies Jonathan W. Homeister, M.D., Ph.D., Associate Director of Graduate Studies

The graduate student body of the Molecular and Cellular Pathology Graduate Program individually and collectively accumulated a number of significant accomplishments during the

past year. Seven students successfully completed the Ph.D. program (Jessica Cardenas, David Detwiler, Lance Johnson, Kellie Machlus, Jessica Rodriguez, Aleeza Roth, and Rupan Sandhu). With these graduates, the Molecular and Cellular Pathology Graduate Program has produced 173 total graduates and 126 Ph.D. graduates since 1954. For the most part, the recent Ph.D. graduates have immediate plans to continue their professional development through postdoctoral research. The Biological and Biomedical Sciences Program (BBSP) continues to admit excellent graduate students, many of whom are interested in the Molecular and Cellular Pathology Graduate Program. During Summer 2011, Fall 2011, and Spring 2012, faculty members associated with the Molecular and Cellular Pathology Ph.D. Program hosted 6 laboratory rotation experiences for 4 individual students (among 3 faculty laboratories). This was fewer laboratory rotations compared to recent years. During the 2010-2011 academic year, our faculty hosted 18 laboratory rotation experiences for 11 individual students, during 2009-2010 our faculty hosted 17 laboratory rotations for 12 individual students, and during 2008-2009 our faculty hosted 18 laboratory rotation experiences for 15 individual students. The decrease in numbers of rotations primarily reflects a diminished number of opportunities among our faculty during the most recent year (related to space and/orfunding). In June 2012, Robbie McNeil officially joined the Molecular and Cellular Pathology Ph.D. program to work with Dr. Ryan Miller. In addition, Kevin Mangum joined the laboratory of Dr. Chris Mack from the M.D.-Ph.D. Program. As of July 1, 2012, the Molecular and Cellular Pathology graduate program has a total of 16 students (14 from the BBSP and 2 from the M.D.-Ph.D. Program).

In the period spanning 2011-2012, graduate students contributed to numerous publications in peer-reviewed journals and published abstracts, many with a graduate student as first author, and several with multiple graduate students as co-authors. In addition, several graduate students were recognized for their research excellence with awards. At the 2011 Molecular and Cellular Pathology Annual Research Symposium (September 2011), Meghan Free and Kaitlin Lenhart received awards for best presentations by a graduate student. Bethany Walton was recognized for the Best Poster presentation at the UNC Program in Translational Medicine Annual Research Symposium. Patricia Casbas Hernandez received the 2012 Graduate Education Advancement Board IMPACT Award for her research project entitles "Understanding How Obwssity and Breastfeeding alter Breast Inflammatory Environments." Lantz Mackey and Kristine Wadosky received Student Travel Awards from the American Society for Investigative Pathology (to attend Experimental Biology 2012). Patricia Casbas Hernandez and Bethany Walton received travel awards from the UNC Program in Translatinal Medicine to attend the Vanderbilt Program in Translational Medicine Symposium. Research support for students in Molecular and Cellular Pathology was provided by several sources. Maria Aleman, Adam Pfefferle, Amanda Rinkenbaugh, and Alleza Roth were supported by the Environmental Pathology Training Program. Dinuka De Silva was supported by the Cancer Bioogy Training Program. Kaitlin Lenhart, Jessica Cardenas, Lantz Mackey, Jessica Rodriguez, and Laura Weise Cross were supported by the Integrative Vascular Biology Training Program. In addition, several students applied for extramural predoctoral fellowships from the American Heart Association, the Department of Defense, the NIH, or other funding agencies. Maria Aleman was awarded predoctoral fellowships from the American Heart Association and the NIH/NHLB1, and Jessica Cardenas was supported by a predoctoral fellowship from the American Heart Association. Michael Durando was supported by a predoctoral fellowship from the NIEHS. Kristine Wasosky was awarded a predoctoral fellowship from the American Heart Association. In

addition, several students were supported by the funds from the Department of Pathology and Laboratory Medicine or other units of the UNC Graduate School or School of Medicine, Jessica Rodriguez was partially supported by the William R. Kenan Jr. Fellowship. During 2011-2012, Amanda Rinkenbaugh was recognized as Robert H. Wagner Scholars in Molecular and Cellular Pathology. For 2012-2013, Amanda Rinkenbaugh will continue and Robbie NcNeill has been named as a new Robert H. Wagner Scholar in Molecular and Cellular Pathology. Four Molecular and Cellular Pathology Ph.D. students (Patricia Casbas-Hernandez, Meghan Free, Amanda Rinkenbaugh, anmd Bethany Walton) are HHMI Fellows participating in the Program in Translational Medicine. Robbie McNeill was selected as an HHMI Fellow beginning in 2012-2013. Jessica Rodriguez, Aleeza Roth, and Rupan Sandhu were awarded the Certificate in Translational Medicine concurrent with their graduatin from the Molecular and Cellular Pathology Ph.D. Program in recognition of their completion of the Program in Tranlational Medicine.

During the last year, the Graduate Student Seminar Series (that began in fall of 2001) continued to showcase the excellent research of the graduate trainees. During spring 2007, the seminar series was moved to Tuesday at noon and became a luncheon seminar to enhance attendance. This modification of seminar schedule has been very successful. The spring 2012 Seminar Series featured presentations by seven Molecular and Cellular Pathology Ph.D. students, one Masters student, and one postdoctoral fellow from the Department. Beyond our Tuesday seminar series, graduate students from our program participated in numerous other research symposia on campus. Graduate students were also featured in a Pathology Grand Rounds session in Spring 2012. Dinuka De Silva (from Dr. Young Whang's laboratory) gave a presentation entitled "Ack1 Regulation og SLIRP Mediated Repression of Androgen Receptor Signaling," Kaitlin Lenhart (from Dr. Joan Taylor's laboratory) gave a presentation entitled "The Rho GTPase Activating Protein GRAF1 Regulates Skeletal Myoblast Differentiation and Fusion," and Amanda Rinkenbaugh (from Dr. Al BAldwin's laboratory) gave a presentation entitled "The Role of the IKK/NK-kappaB Pathway in Glioblastoma Cancer Stem Cells." This series provides a valuable opportunity for students, faculty, and staff to learn more about graduate student research that is ongoing in the department. The Marc J. Mass, Ph.D., Memorial Distinguished Lecture continued to plan new speaker events. The next Lecture will occur in Fall. In the summer of 2011, the graduate students selected Dr. J. Charles Jennette as the 2011 recipient of the Joe W. Grisham Award for Excellence in Graduate Student Teaching. The award was presented in September 2011 at the home of Dr. J. Charles Jennette. In other activities, the graduate students have continued to have regular outings to local restaurants for informal discussions related to the graduate program and their research, as well as fun social events.

## **<u>RESIDENCY TRAINING PROGRAM IN PATHOLOGY</u>** THOMAS W. BOULDIN, M.D., DIRECTOR

The Department of Pathology and Laboratory Medicine currently sponsors a residency training program in anatomic and clinical pathology. The Program is fully accredited by the American Council on Graduate Medical Education (ACGME). A full description of the Program, including the curriculum and current trainees, is on the departmental web site (http://www.med.unc.edu/pathology/residency-program-in-pathology/).

The educational goals and philosophy of the residency program are to (1) Provide a flexible, broad-based training program for physicians that includes training in anatomic, clinical, and experimental pathology; (2) Encourage trainees to participate in research; and (3) Provide an educational experience sufficient to ensure that all residents develop skill levels expected of a new practitioner in the six ACGME-defined competencies (patient care, medical knowledge, practice-based learning and improvement, interpersonal and communication skills, professionalism, and systems-based practice).

The Program offers a four-year, combined anatomic and clinical pathology residency, with ample opportunities for research and post-residency fellowship training in a wide range of subspecialty areas in pathology. The Program was reviewed by the Residency Review Committee of the American Council for Graduate Medical Education and was awarded "Continued Full Accreditation" in October, 2009. The Program sucesfully completed a comprehensive internal review in 2011.

The Program requires that all residents take combined training in anatomic pathology and clinical pathology. The first three years of the Program are focused on core training in anatomic pathology (AP) and clinical pathology (CP). The curriculum is organized to intermingle AP and CP core rotations within each of the first three years of training The fourth year of the Program permits the trainee great flexibility. The fourth year of the training program includes six months of elective rotations in AP, CP or pathology research, so that the resident can concentrate on his or her particular interests. Overall, there are eight months of elective rotations interspersed within the four-year training program.

The Department of Pathology and Laboratory Medicine has a strong commitment to providing funding and faculty support for resident research. Funding for resident research projects comes from a variety of sources, including NIH research or training grants, NIH Individual Research Service Awards, and other fellowships. To encourage basic research, the Department offers a one-year research fellowship, available on a competitive basis, to post-residency trainees in the Department of Pathology and Laboratory Medicine. The fellowship pays a stipend to the resident commensurate with the fellow's level of training; and will also provide a \$5,000 bench fee to the laboratory of the trainee's research advisor. The research must be focused on discovering or elucidating basic mechanisms of disease. More applied/correlative/clinical research experiences can be obtained in the various clinical fellowships available to pathology residents. Dr. William Funkhouser is the director of this research fellowship.

The Department provides all residents in the training program with an individual study carrel, a light microscope, and a computer. The computer is fully loaded with appropriate software, connected to the internet, and fully supported by the UNC Hospitals' computer-support staff.

The residency program currently accepts four new residents per year into the four-year general residency training program. There were 16 residents in the residency program in 2011–12, and there will be 15 residents in the Program in 2012–13. Additionally, there were two trainees in our post-residency surgical pathology fellowship program, six trainees in ACGME-accredited clinical subspecialty residencies (fellowships), and three postdoctoral trainees in clinical

laboratory medicine fellowships (accredited by other agencies) in 2011–12. UNC Hospitals funded 15 of the training positions in the general residency program in 2011–12, with the remaining residency and fellowship funding coming from the Department. As of July 1, 2011, UNC Hospitals will fund 15 of the residency positions.

In 2011–12, 393 applicants applied through the Electronic Residency Application Service (ERAS®) for the four PGY1 training positions offered. The Department invited 50 of these 324 applicants for an interview, and 39 came to Chapel Hill for an interview. Thirty-five of these interviewees were listed in the 2012 National Resident Match, which is conducted by the National Resident Matching Program. The Department filled all four PGY1 positions in the 2011 Match from within the group of top-listed applicants on the Program's Match list.

Dr. Thomas Bouldin, who has directed the residency program since 1991, will step down from the directorship on June 30, 2012. Dr. Megan DiFurio, the current associate program director, will assume the directorship on July 1, 2012. Dr. Herbert Whinna will become the new associate program director on July 1, 2012.

## SUBSPECIALTY FELLOWSHIP TRAINING PROGRAM

## CLINICAL CHEMISTRY FELLOWSHIP CATHERINE A. HAMMETT-STABLER, PH.D., DIRECTOR LAURA M. BENDER, PH.D., FELLOW, 2010-2012 STEVEN W. COTTEN, PH.D., FELLOW, 2010-2012 DENISE M. MILHORN, PH.D., FELLOW, 2012-2014

#### (http:www.pathology.unc.edu/fellowship/clinchem.htm)

The Clinical Chemistry program proudly celebrates its 40<sup>th</sup> year here at UNC in 2012. The year began with notification of a 5-year re-accreditation by the Commission on Accreditation in Clinical Chemistry (ComACC). The two fellows, Drs. Laura Bender and Steven Cotten, who will complete their training on June 30<sup>th</sup>, have been extremely productive contributing to 5 abstracts/posters, 3 chapters, and 11 manuscripts. Both received travel awards to attend the annual Mass Spectrometry Applications in the Clinical Laboratory meeting in San Diego. Additionally, Dr. Bender is the recipient of the 2012 SYCL Travel Award to the AACC Annual Meeting. There she will participate in the student competition with a poster of her work with pharmacy that established whole-blood point-of-care creatinine measurements should not be used in calculating the dosing of several chemotherapeutic agents. This small study identified a significant patient safety issue and has resulted in change of practice within several of the infusion centers in the institution. Dr. Bender has accepted a position at Lab Corp, Burlington, NC. Also attending AACC, Dr. Cotten will also present one of his projects in the student competition: Differences in insulin resistance stratification using HbA1c and the metabolic *markers alpha-hydroxybutyrate, linoleoyl-GPC, and oleate.* In this he collaborated with investigators from Metabolon, Inc to assess the robustness of a potential a metabolomic profile to identify insulin resistance. He was also involved in the investigation with pediatrics and the newborn nurseries into the finding that common baby soaps can cause positive urine drug testing results for marijuana. Dr. Cotten has accepted a position at The Ohio State University,

Columbus, OH. Looking to the future, we eagerly anticipate the arrival of a new fellow, Dr. Denise Milhorn, from deployment with the US Army to Afghanistan. The Clinical Chemistry Fellowship is directed by Catherine Hammett-Stabler, Ph.D., DABCC.

## CLINICAL MICROBIOLOGY FELLOWSHIP PETER H. GILLIGAN, Ph.D., DIRECTOR KEVIN ALBY , Ph.D., FELLOW, 2011-12

The Department of Pathology and Laboratory Medicine and UNC Hospitals sponsors the Clinical Microbiology Training Fellowship, which is a two-year training program accredited by the committee on Post-doctoral Education Programs of the American College of Microbiology. The major objective of this program is to train individuals to direct clinical and public-health-microbiology laboratories. The fellows' training includes five areas: (1) Technical training to become proficient at performing and interpreting the laboratory procedures offered in the clinical microbiology laboratory; (2) Administrative training in the various aspects of laboratory management and administration, including budgeting, personnel, quality control, protocol preparation, safety regulations, and CLIA and OSHA requirements; (3) Clinical training enabling the trainee to interface effectively with infectious-disease clinicians; (4) Research in clinical microbiology; and (5) A three week external rotation at the State Laboratory of Public Health. Since beginning the program our current fellow Dr Alby, a certified medical technologist holding a doctorate from Brown University has presented 4 posters at national scientific meetings and has had one book chapter accepted for publication. The Clinical Microbiology Fellowship is directed by Peter H. Gilligan, Ph.D.

# <u>CLINICAL MOLECULAR GENETICS FELLOWSHIP</u> JESSICA K. BOOKER, Ph.D., DIRECTOR KRISTY RAE-COLLINS CROOKS, Ph.D., FELLOW, 2011-2013

The Department of Pathology and Laboratory Medicine and UNC Hospitals sponsors a Clinical Molecular Genetics fellowship, which is a one- or two-year training program in laboratory aspects of clinical molecular genetics. The program is accredited by the American Board of Medical Genetics. The Molecular Diagnostic Laboratory at UNC Hospitals provides experience with tests including cystic fibrosis, fragile X mental retardation, hemochromatosis, factor V Leiden and prothrombin,  $\alpha$ 1-antitrypsin deficiency, MCAD deficiency, connexin 26 and 30 mutations, Prader-Willi and Angelman syndromes, primary ciliary dyskinesia, EBV, CMV, and BK viral loads, hereditary cancers, acquired mutations in cancer, chromosomal breakpoints in leukemias, pharmacogenetics, and monitoring of bone marrow transplants with polymorphic microsatellite markers. State-of-the-art technologies and instrumentation are used in all of these tests. The clinical aspects of the training program are complemented by a strong research foundation. The Clinical Molecular Genetics Fellowship is directed by Jessica Booker, Ph.D. There was one fellow in the training program in 2011-2012.

## CLINICAL MOLECULAR PATHOLOGY FELLOWSHIP MARGARET L. GULLEY, M.D., DIRECTOR CHARLES SAILEY, M.D., FELLOW 2010-2011 (http://www.pathology.unc.edu/fellowsp/molecular\_path.htm)

The Department of Pathology and Laboratory Medicine and University of North Carolina Hospitals sponsors a one-year fellowship in Molecular Genetic Pathology. Trainees gain a working knowledge of molecular procedures including Southern blot, in situ hybridization/FISH, DNA sequencing (including next generation sequencing), protein truncation test, DNA amplification, tissue macrodissection and other cell enrichment procedures, and array technologies including gene expression profiling and single nucleotide polymorphism (SNP) chips that typically measure gene copy number. These modern molecular technologies are applied in a wide spectrum of clinical settings including cancer, heritable disease, infectious disease, HLA-typing, identification, and pharmacogenetics. The fellow analyzes and interprets molecular data from clinical cases and composes reports that are relied on for patient management. The fellow learns to design and carry out research aimed at understanding the molecular basis of disease and translating fundamental discoveries into laboratory assays that improve patient care. Ethical issues, quality assurance, and lab administration are discussed as they relate to clinical practice. The training program is accredited by the ACGME to to train one fellow annually. UNC has the longest track record of board certifications among all ACGMEaccredited molecular genetic pathology training programs in the nation. The program is directed by Margaret L. Gulley, MD with support from many faculty and staff. More information can be found at.

http://www.med.unc.edu/pathology/clinical-fellowships/molecular-genetic-pathology-fellowship

## <u>CYTOGENETICS FELLOWSHIP</u> KATHLEEN W. RAO, Ph.D., DIRECTOR MELISSA HAYDEN, Ph.D., FELLOW

The McLendon Clinical Laboratories of UNC Hospitals and the Department of Pathology and Laboratory Medicine sponsor a fully accredited training program in Clinical Cytogenetics, which leads to eligibility for certification by the American Board of Medical Genetics (ABMG). The usual training period is two years. Upon successful completion of the program and ABMG Certification, the fellow will be qualified to direct a clinical Cytogenetics laboratory. The Cytogenetics Fellowship Program is part of a comprehensive ABMG training program that includes Medical Genetics Residents, Clinical Molecular Fellows, Clinical Biochemical Fellows, and Molecular Genetic Pathology Fellows. All trainees and faculty involved in these programs participate regularly in multiple clinical and educational conferences, and Fellows have opportunities to teach in Medical Student and Resident courses. The UNC Cytogenetics laboratory is a full service laboratory, processing over 4000 specimens on which more than 6000 tests are performed annually for both constitutional and oncology diagnostics. Sample types include CVS, amniocentesis, products of conception, peripheral blood, bone marrow, lymph nodes, solid tumors, tissue biopsies, and paraffin sections. Fellows are trained in result interpretation and in a variety of techniques, including tissue culture, chromosome banding and analysis, FISH, and high resolution SNP microarray. The UNC Cytogenetics Laboratory is an approved Children's Oncology Group Laboratory and Cancer and Leukemia Group B

Laboratory and actively participates in both of these national cancer cooperative groups. The Clinical Cytogenetics Fellowship is directed by Kathleen W. Rao, Ph.D.

## <u>CYTOPATHOLOGY FELLOWSHIP</u> SUSAN J. MAYGARDEN, M.D., DIRECTOR DIRK STANLEY, M.D., FELLOW, 2011-2012 REBECCA VARLEY, M.D., FELLOW 2011-2012

Drs. Dirk Stanley and Rebecca Varley completed the cytopathology fellowship on June 30, 2012. After a period of supervised participation in the fine needle aspiration service, the fellows independently performed adequacy assessments for deep radiologic procedures after September, 2011. Both Drs. Stanley and Varley were exemplary fellows, and both have positions in private practice beginning August, 2012. The cytopathology fellowship had a scheduled site visit by the RRC in pathology on January 25, 2012. The site visit went smoothly and we received a 5 year accreditation cycle (the longest interval granted by the ACGME).

## **FORENSIC PATHOLOGY FELLOWSHIP** DEBORAH L. RADISCH, M.D., MPH, DIRECTOR DAVID ZIMMERMAN, M.D., FELLOW, 2011-2012 CHRISTOPHER GORDON, M.D., FELLOW, 2011-2012

The Office of the Chief Medical Examiner (OCME) in conjunction with the Department of Pathology and Laboratory Medicine and UNC Hospitals, offers a one-year fellowship in forensic pathology. The program is fully accredited by the Accreditation Council for Graduate Medical Education (ACGME) and is under the direction of the Chief Medical Examiner of the State of North Carolina. The trainee in forensic pathology performs approximately 250 forensic autopsies during the course of the one-year fellowship. Consultations in subspecialty areas, including neuropathology, pediatric pathology, forensic odontology, and forensic radiology, are available within the Department of Pathology and Laboratory Medicine and the School of Medicine and Dentistry. Ancillary laboratory studies, including clinical chemistry, microbiology, and special histology, are provided by the Department of Laboratory Medicine. Forensic anthropology, crime lab technology, and other training experiences are also provided at designated sites. The Forensic Pathology Fellowship is directed by Deborah L. Radisch, M.D., MPH. There were two fellows (one supported by the U.S. Air Force) in the training program in 2011-2012.

#### HEMATOPATHOLOGY FELLOWSHIP YURI FEDORIW, M.D., DIRECTOR ANDREW LARAMORE, M.D., FELLOW, 2011-2012

The Department of Pathology and Laboratory Medicine (McLendon Clinical Laboratories) and UNC Hospitals sponsor a broadly based, one-year training program in hematopathology. The program is directed by full-time hematopathologists and is fully accredited by the ACGME. The program has been highly successful in attracting high-quality applicants with a broad range of backgrounds, interests, and career goals. Our Fellowship program is organized in such a way as to provide appropriate training in all of these areas, while providing flexibility to address

personal needs, interests, and objectives of the individual fellows. Trainees gain experience in the management and medical supervision of a high volume hematology laboratory, the evaluation of peripheral blood smears, bone marrow, and lymph node biopsies. The Hematopathology fellows have been very active in presenting at national meetings and in scholarly activities with resultant journal publications. The fellowship was able to retain Dr. Andrew Laramore from our AP/CP pathology residency. Andrew worked seamlessly within our division and as an active member of the clinical team, providing excellent comprehensive care to our patients.

# NEPHROPATHOLOGY FELLOWSHIP VOLKER R. NICKELEIT, M.D., DIRECTOR DANIEL KENAN, M.D., FELLOW RACHEL CIANCIOLO, D.V.M., FELLOW

The Department of Pathology and Laboratory Medicine sponsors a one-year fellowship in renal pathology. One or two fellows are accepted into the program. The fellows are directly involved in the diagnostic evaluation of over 1800 renal biopsies/nephrectomies (both native and transplant cases) examined annually. All fellows are integrative members of the nephropathology team and receive intensive training. They prepare cases for sign out by the faculty using all standard techniques (light microscopy, immunofluorescence microscopy, immunohistochemistry and electron microscopy). Part of the fellows' responsibility is to organize clinico-pathologic and biopsy review conferences for medical faculty and housestaff, and to teach renal pathology to medical students, residents and fellows. Teaching conferences and continuous education series offered by the nephrology and transplant divisions at UNC provide additional ample learning opportunities. Although emphasis is placed on the development of diagnostic skills, fellows are expected to carry out clinico-pathological and/or basic research projects and to present their data at national meetings, such as the ASN or USCAP. Research projects focus on the pathogenesis of glomerulonephritides, allograft rejection and polyomavirus infections. All state-of-the-art facilities (including laser microdissection) are available in the department. Appropriate research studies are funded by intramural support. Clinico-pathological studies are facilitated by the Glomerular Disease Collaborative Network, which is a well established network of over 200 nephrologists participating in clinical data collection. The division of nephropathology and the fellowship training program is directed by V. Nickeleit, M.D.

#### <u>NEUROPATHOLOGY FELLOWSHIP</u> THOMAS W. BOULDIN, M.D., DIRECTOR through December 31, 2010 (http://www.pathology.unc.edu/fellowsp/neuropath.htm)

The Department of Pathology and Laboratory Medicine and UNC Hospitals has sponsored a broadly based, two-year fellowship in diagnostic and experimental neuropathology since 1980. The training program has been under the direction of Dr. Bouldin and was fully accredited by the Accreditation Council for Graduate Medical Education (ACGME). Due to a waning interest in subspecialty training in Neuropathology by Pathology residents in recent years, the Department voluntarily closed the fellowship program on December 31, 2010.

## SURGICAL PATHOLOGY FELLOWSHIP WILLIAM K. FUNKHOUSER, M.D., Ph.D., DIRECTOR DEBORAH V. SPENCER, M.D., FELLOW, 2011-2012 ELIZABETH L. BOSWELL, M.D., FELLOW, 2011-2012

The Department of Pathology and Laboratory Medicine sponsors a one-year fellowship in diagnostic Surgical Pathology. The training program focuses on surgical pathology, with correlative exposure to cytopathology, cytogenetics, electron microscopy, immunohistochemistry, and molecular genetic pathology. During the first 6 months, the fellow reviews and dictates inside cases on all service benches for 4 months, reviews /dictates outside cases and gives associated conferences for 1 month, and has 1 month of elective time. The fellow is credentialed by the hospital during the fall, and repeats the 6 month cycle above as a faculty instructor, now with independent sign-out responsibilities. We have received uniformly good feedback on this training format from our Fellows/Instructors as they have competed for and been hired as independent Pathologists in the academic or private practice workforce.

# TRANSFUSION MEDICINE FELLOWSHIP YARA A. PARK, M.D., DIRECTOR

The Department of Pathology and Laboratory Medicine and McLendon Clinical Laboratories of UNC Hospitals sponsor a comprehensive one-year fellowship program in Blood Banking/Transfusion Medicine that is fully accredited by the Accreditation Council of Graduate Medical Education (ACGME). The training program provides didactic and practical training in advanced immunohematology, therapeutic and donor apheresis, blood component donation, testing, preparation and storage, clinical coagulation, histocompatibility, hematopoietic progenitor cell collections and processing, and clinical support for an academic tertiary care hospital. Supported clinical programs include transplant programs in marrow/stem cells, liver, heart, lung and kidney; a Level I trauma program; and a neonatal intensive care unit. Ongoing projects include epidemiology and pathogenesis of thrombotic thrombocytopenic purpura (TTP) and multiple studies within the NIH funded Transfusion Medicine/Hemostasis Clinical Trials Network, of which UNC is one of 17 participating sites. Dr. Yara Park became the director of the Transfusion Medicine fellowship in October 2011. There was not a Transfusion Medicine Fellow for 2011-2012.

# GRAND ROUNDS SEMINARS 2011-12

Grand Rounds Organizing Committee: Thomas W. Bouldin, M.D. (Chair), Members: Joe N. Kornegay, D.V.M., Ph.D., Monte S. Willis, M.D., Ph.D., David G. Kaufman, M.D., Ph.D.

As has been the case in years past, the Department of Pathology and Laboratory Medicine Grand Rounds seminar series was well attended during the academic year 2011-12. The primary goals of this series is twofold: 1) to provide a venue for the dissemination of current basic science and clinical research information relevant to departmental academic activities and 2) to promote interaction and the opportunity for collaboration between Pathology faculty, residents, postdoctoral fellows, graduate students, and clinical fellows, and other members of the UNC community. Additionally, we use Grand Rounds as a venue for faculty presentations needed as part of promotion and post-tenure reviews and as a forum for announcements and discussion of items of interest and importance to faculty and trainees.

To accommodate speaker and audience needs, Grand Rounds follows a flexible format. The presenters may choose a traditional format in which there is a single presenter; or when appropriate, as when integrating basic and clinical research or two or more disciplines, some choose to share the time with a collaborator or trainee. Presentations are usually 45 minutes, followed by a question-and-answer session. The committee strives to assure a range of experimental, clinical and surgical pathology subjects are appropriated and evenly covered. The topics are dependent upon speaker availability and while many presentations are usually related to the presenter's research interests, some include scientific reviews of pertinent areas in clinical medicine, translational research, and/or basic science. The following list of 2011-12 presenters, their affiliations and topics demonstrate that both internal and external speakers are sought. Category 1 CME credit is offered for seminar participation. We provide an opportunity for the speakers to have their presentation formally evaluated, as required of all CME activities. Written comments and questions concerning the quality of the presentations are requested. Prior to each Grand Rounds seminar, refreshments are provided. This encourages a collegial atmosphere, and it also provides an opportunity for the attendees to visit and discuss science, medicine, and research.

## FALL 2011

DATE	SPEAKER/AFFILIATION	TITLE
08/25/2011	Daniel Zedek, MD	"Use of Molecular Techniques for the Diagnosis of Melanoma"
	Assistant Professor of Dermatology	
	UNC-CH	
09/08/2011	Masao Kakoki, MD, PhD Assistant Professor, Dept. of Pathology and Laboratory Medicine, UNC-CH	"Cardiovascular pathogenesis in mice underexpressing transforming growth factor beta1"
09/15/2011	Melissa A. Troester, PhD, MPH Assistant Professor of Epidemiology School of Public Health & Health Sciences, UNC-CH	"Genomics of Normal and Cancer- Adjacent Breast Tissue: Implications for Breast Cancer Etiology and Progression"
09/29/2011	Julia E. Brittain, PhD Assistant Professor of Biochemistry & Biophysics, Member, Comprehensive Sickle Cell Center, UNC-CH	"The Role of Stress Erythropoiesis in Coagulation Activation, Erythrocyte Adhesion, and Inflammation in Sickle Cell Disease"

FALL 2011 DATE	SPEAKER/AFFILIATION	TITLE
10/13/2011	Bernard E. Weissman, PhD Professor of Pathology and Laboratory Medicine, Member, Lineberger Comprehensive Cancer Center, UNC-CH	"Remodeling the Cancer Genome: The Role of the SWI/SNF Complex in Human Tumor Development"
10/20/2011	Charles M. Perou, PhD Professor of Genetics and of Pathology and Laboratory Medicine Member, Lineberger Comprehensive Cancer Center, UNC-CH	"Therapeutic Implications of the Molecular Portraits of Breast Cancer"
10/27/2011	Martin Styner, PhD Assistant Professor of Psychiatry and of Computer Science, UNC-CH	"Towards Automated MRI-based Biomarkers for Duchenne Muscular Dystrophy"
11/10/2011	Edward B. Breitscherdt, DVM Professor of Medicine, North Carolina State University College of Veterinary Medicine and Adjunct Professor of Medicine, Duke University	"Bartonellosis: Of Cats, Dogs, Mice and Men"
11/17/2011	William R. Oliver, MD Professor of Pathology and Laboratory Medicine, and Director of Forensic Pathology, East Carolina University	"Excited Delirium and TASER-related Death"
12/08/2011	Christopher Mack, PhD Associate Professor of Pathology and Laboratory Medicine, UNC-CH	"Epigenetic Regulation of Smooth Muscle Cell Phenotype"
12/15/2011	Frank C. Church, PhD, FAHA Professor, Depts. of Pathology and Laboratory Medicine, of Pharmacology, and of Medicine; Member, Lineberger Comprehensive Cancer Center, UNC-CH	"Role of Senescence in the Age- Associated Risk of Venous Thrombosis"

#### SPRING 2012

<b>SF KING 2012</b>		
DATE	SPEAKER/AFFILIATION	TITLE
01/12/2012	Peter H. Gilligan, PhD Professor of Pathology and Laboratory Medicine, UNC-CH; Director, Clinical Microbiology-Immunology Laboratories, UNC Hospitals	"Therapeutic Biologics: Promise and Pitfalls"
	John L. Schmitz, PhD	
	Professor of Pathology and Laboratory Medicine, UNC-CH; Director, Histocompatibility, Flow Cytometry and Clinical Immunology Laboratories, UNC Hospitals	
02/16/2012	Yara A. Park, MD Assistant Professor of Pathology and Laboratory Medicine, UNC-CH; Director, Transfusion Medicine Services, McLendon Clinical Laboratories, UNC Hospitals	"Thrombotic Thrombocytopenic Purpura: Searching for the Missing Pieces"
02/23/2012	Dimitri G. Trembath, MD, PhD Assistant Professor of Pathology and Laboratory Medicine; Division of Neuropathology, UNC-CH & Stergios Moschos, MD Associate professor of Medicine, Division of Hematology/Oncology, UNC-CH	"Understanding the Pathology and Biology of Melanoma Brain Metastasis"
03/08/2012	Thomas M. O'Connell, PhD Senior Director of R&D, LipoScience and Adjunct Associate Professor of Pathology and Laboratory Medicine, UNC-CH	"Applications of the NMR Clinical Analyzer for Cardiovascular Disease and Diabetes" (non-CME accredited talk)
03/15/2012	Ryan Sanford, MD Fellow, Division of Nephrology Department of Medicine, UNC-CH	"Renal Albumin Handling and Salicylate Induced Proteinuria"

# SPRING 2012DATESPEAKER/AFFILIATION

03/29/2012

Jonathan McDunn, PhD

# TITLE

"Concurrent metabolomics and

	Associate Director of Oncology R&D, Metabolon, Inc. and Adjunct Assistant Professor, Joint Dept in Biomedical Engineering, UNC-CH & NCSU	histopathologic analyses of core biopsies" (non-CME accredited talk)
04/12/12	Graduate Student Research Day:	"Ack1 regulation of SLIRP mediated
	Dinuka M. De Silva, BA Young Whang, Advisor	repression of Androgen Receptor Signaling"
	Kaitlin C. Lenhart, BS Joan M. Taylor, Advisor	"The Rho GTPase activating protein GRAF1 regulates skeletal myoblast differentiation and fusion"
	Amanda L. Rinkenbaugh, BS Al Baldwin, Advisor	"The Role of the IKK/NF-kappaB Pathway in Blioblastoma Cancer Stem Cells"
04/19/2012	Residents and Fellows Research Day – Part 1:	
	Daniel J. Kenan, MD, PhD Nephropathology Fellow	"IgG4-related renal disease: Case presentation and review of the UNC experience"
05/10/2012	Residents and Fellows Research Day – Part 2:	
	Jayson R. Miedema, MD AP/CP Pathology Resident, PGY3	"IgA pemphigus versus pyodermatitis- pyostomatitis vegetans"
	Olga Speck, MD, PhD AP/CP Pathology Resident, PGY3	"Lymphocyte-Rich Gastric Cancer: Histologic Featurs and Association with Epstein-Barr Virus"
05/17/2012	Joan M. Taylor, PhD Associate Professor of Pathology and Laboratory Medicine, UNC-CH	"Regulation of Cardiac Growth, Survival, and Repair by Adhesion- Dependent Signals"

SPRING 2012 DATE	SPEAKER/AFFILIATION	TITLE
05/24/2012	Oliver Smithies, D.Phil. Witherspoon Eminent Distinguished Professor, Dept. of Pathology and Laboratory Medicine, UNC-CH	"Challenging the Kidney with Gold Nanoparticles"
05/31/2012	Nigel Mackman, PhD, FAHA John C. Parker Distinguished Professor of Medicine; Director, UNC McAllister Heart Institute; Co-Director, Thrombosis and Hemostasis Program, Division of Hematology/Oncology, Department of Medicine, UNC-CH	"Tissue factor, coagulation proteases and PARs in thrombosis and viral infection"
06/07/2012	Paul N. Valenstein, MD, FCAP Secretary-Treasurer, College of American Pathologists CAP Presentation	"Health Care Reform and the Transformation of Pathology"
06/14/2012	C. Ryan Miller, MD, PhD Assistant Professor of Pathology and Laboratory Medicine, Division of Neuropathology; Director, Translational Pathology Laboratory, UNC-CH	"Dissecting the cellular and molecular requirements for astrocytoma initiation and progression using genetically- engineered mouse models"

#### ENVIRONMENTAL PATHOLOGY TRAINING PROGRAM DAVID G. KAUFMAN, M.D., Ph.D., DIRECTOR

The Environmental Pathology Training Program seeks to develop scientists who discover mechanisms by which environmental substances affect cellular processes to cause disease. The program trains scientists to combine an understanding of the pathogenesis of human diseases and expertise in appropriate research methods to study these diseases. The research focus of the program is on the mechanisms of pathogenesis of diseases for which environmental exposures are critical factors. Traditional program strengths included the role of environmental factors in the pathogenesis of cancer and their role in DNA damage and repair, reflecting the expertise of the faculty mentors. This program, which is currently in year 35 of support from the National Institute of Environmental Health Sciences, has 6 slots for postdoctoral fellows and 6 slots for

predoctoral trainees. During this past year all training slots on the Environmental Pathology Training Program were filled.

Some postdoctoral candidates learn about our training program by viewing our website, by reading our advertisements in national journals, or through interviews at job placement services of national societies. Others candidates have been referred to the program by prominent investigators in environmental pathology. The program gained a national recognition as one of the premier postdoctoral training programs in this field. Trainees accepted by the program typically come from fine graduate programs in related fields from around the country. Unique features of this Program were that a number of our trainees have had M.D. or D.V.M. degrees or were members of underrepresented minority groups. Several trainees supported by this institutional grant have subsequently obtained individual postdoctoral research training grants. In recent years three postdoctoral trainees have received individual training grants from the NIH and the DOD, and another has received a K08 Award from the NIH. Trainees typically have found appropriate transitional positions and permanent jobs. One of the trainees recently completing support from the program went directly to a faculty position in environmental sciences. Predoctoral trainees are chosen from among the applicants accepted into the IBMS/BBSP graduate program who select a Program faculty member as their mentor. Most of them have chosen to seek their Ph.D. in Molecular and Cellular Pathology. Predoctoral trainees are selected from among those expressing an interest in environmental research projects of the training program mentors. Typically, one or two predoctoral students are chosen per year, usually the best among the candidates interested in the work of training grant preceptors.

In May 2009, a competitive renewal application was submitted for the Environmental Pathology Training Grant. That application did not receive a good enough priority score to be funded, but an additional year of trainee support was provided to continue the Program while a revised application was prepared. An extensively revised application attempting to address the reviewers' criticism was prepared for submission in May 2010. Because of the prior criticism that there was too much emphasis on environmental carcinogenesis the membership of the Training Program was broadened to include virtually all NIEHS awardees on campus whose work on environmental studies focused on pathogenesis. In the 2010 application many new NIEHS-funded investigators were added so that only 25% of the faculty members in the 2010 application had been participants in the 2005 application. Several new areas of environmental research had been incorporated (pulmonary, renal, and cardiovascular diseases influenced by environmental factors) to dilute the focus on environmental carcinogenesis. Despite vast changes in the revised grant application the review did not get a good enough priority score to be funded. We believe that the reviewers thought that the research being pursued by the selected postdoctoral, and more importantly, predoctoral trainees was not sufficiently focused on the role of environmental factors in the pathogenesis of diseases. Consequently, the Training Grant will be terminated.

The NIEHS appears to be inclined to support trainees with further eligibility for NRSA training for at least one year beyond their previous appointment date if it falls before June 30, 2011. We will not, however, be able to appoint new trainees to fill slots that become open. It remains unclear whether it will be possible to renew support for trainees after June 30, 2011. A budget to

support the eligible trainees has been submitted to the NIEHS and we are awaiting the official approval of the plan.

# **CLINICAL SERVICES**

## **BACKGROUND McLENDON CLINCAL LABORATORIES** HERBERT C. WHINNA, M.D., Ph.D., DIRECTOR

McLendon Clinical Laboratories provides laboratory and pathology services to physicians in support of excellent patient care at UNC Hospital. Each laboratory section maintains fiscal accountability for revenue generated and expense required to produce clinical test results. The revenue contribution from the laboratory has continued to grow, despite the difficult financial climate facing health care as a whole. The directors of each laboratory, working closely with the assistant administrative directors, develop short and long range plans to assure that the laboratories are supporting the testing needs of the hospital, while continuing to provide the medical staff with cutting edge technologies. For FY 11-12, the laboratory is projected to contribute 61 million dollars to UNC Hospital's operating margin.

The Core Laboratory has been one of the early adopters of the SharePoint software. They have been using in for all of their internal communications with staff. They also piloted the use of SharePoint for procedures. All of McLendon Clinical Laboratories will be moving to SharePoint as the primary location for policies and procedures as well as procedure archiving during the next year. The Histology Laboratory successfully implemented bar code technology that begins in the gross room and carries through to block and slide labeling. This process has effectively eliminated mislabeled specimens in this area. Several areas within McLendon Clinical Laboratories have undergone renovations to either add space or make their available space function in a more productive way. The areas renovated include the back areas in Microbiology, additional workspace in Cytogenetics, reconfigured workspace in Histology and new workspace for Electron Microscopy. Laboratory volumes exceeded budget expectations by 186,000 procedures (2.8%).

## <u>SURGICAL PATHOLOGY (Histology/Special Procedures Labs)</u> WILLIAM K. FUNKHOUSER, Jr., M.D., Ph.D., DIRECTOR

UNC Surgical Pathology generates diagnoses on UNCH specimens, on specimens to be reviewed because of patient referral to UNC hospitals, and on outside expert consultations specimens. In 2010, 28,438 cases were diagnosed, including 2819 outside cases, representing an unchanged year-over-year faculty caseload. Increasing case complexities make it challenging to sign out all cases with residents each day, so we expanded 5 non-Derm SP benches to 7 non-Derm SP benches in Fall 2010, as follows: The Breast/Benign GYN bench was split into separate Breast and Benign GYN benches. The GI/Liver bench was split into separate GI/Liver small biopsies and GI/Liver resections. The separate Dermpath bench (the 6<sup>th</sup> SP bench), mostly melanoma re-excisions, was folded into the Dept. of Dermatology.

New faculty members joined us in 2010, including sign-out faculty (Drs. Greene, Scanga, O'Connor, and DiFurio) and PA faculty (Ms. Kemper, Mr. Holmes). Dr. Greene signs out GI pathology and Cytopathology. Dr. Scanga signs out GYN, ENT, and Cytopathology. Drs. O'Connor and DiFurio sign out Breast, GYN, and Cytopathology. We said farewell to Ms. Boland in May 2010, when she changed to a PA job at Duke, and hired experienced gross room PAs from Rex (Ms. Kemper) and Duke (Mr. Holmes). We continue our system for credentialing of Surgical Pathology Fellows in the fall, with transition to final signout responsibility as Instructors in the spring. This gives us flexibility in the spring to cover faculty extended leave or departure.

Goals for 2011 include validation of a remote-controlled microscope for doing off-site frozen section diagnosis, installation of an X-ray machine for selective sampling of breast specimens, and evolution to seamless barcoding of cases from accessioning to case signout.

The histology laboratory is commensurately busy. We are fortunate that the Laboratory is wellled by Ms. Maglione, and that it is well-managed by Ms. Deloney. This laboratory and its upstream accessioning personnel are critical to an efficient, error-free service. Block volume increases have been met with increased productivity, Lean analysis, improved instrumentation, and budget approval for seamless barcoding of specimens from accessioning to case signout. Lean analysis of immunohistochemistry workflow has reduced turnaround time for receipt of immunohistochemical stains. Challenges for 2011 are to automatically measure block volumes, case TATs, and error rates, and to correlate these data with staffing type and levels, in order to define optimal technical staffing.

Overall, continuing increases in workload have been met by continuing increases in effort, ingenuity, and efficiency. The management and leadership skills of Dr. Whinna, the Director of the McLendon Clinical Laboratories, and of Dr. Jennette, Chair of the Department of Pathology and Laboratory Medicine, are perceived as critical to the improvements and successes described above.

## <u>CYTOPATHOLOGY</u> SUSAN J. MAYGARDEN, M.D., DIRECTOR

The cytopathology laboratory service volume remained stable in 2011-12. The laboratory continues to provide fine needle aspiration procedures for superficial lesions and assistance with immediate adequacy assessments along with diagnostic services for aspirations, fluid specimens and gynecologic pap smears. The principle users of the fine needle aspiration service are diagnostic and interventional radiology, GI procedures, pulmonology and CT surgery, GI procedures and otolaryngology. The fine needle aspiration service has increased the numbers of lung brushing specimens immediately interpreted for adequacy performed by CT surgery when performing navigational bronchoscopy, which is a service provided at only a handful of centers in the United States.

The laboratory continues to have 5 cytotechnologist employees, and there are now two temporary employees that assist in gynecologic and non-gynecologic specimen preparation. Two fellows completed the one year cytopathology fellowship, Drs. Dirk Stanley and Rebecca

Varley, and both have secured full time employment. There are 6 cytology attendings who also have responsibilities in surgical pathology. Two additional faculty members have been hired to begin working in July and September, 2012.

During the past fiscal year, one of the most significant changes in the Cytogenetics Lab has been the in-house validation of the Affymetrix CytoScan HD SNP microarray platform. This platform, which contains 2.7 million markers, has replaced the 1.8 million marker Affymetrix 6.0 SNP microarray platform. This platform, like its predecessor, is capable of detecting copy number changes that are below the level of resolution obtained by karyotyping, as well as regions of homozygosity that are associated with consanguinity and uniparental disomy. The laboratory currently processes approximately 500 constitutional microarray cases annually. In the future, we hope to also apply this technology to our products of conception, and cancer samples.

Several of our more interesting chromosome microarray findings were reported at the 2012 American College of Medical Genetics Meeting and include a novel interstitial fibrillin-2 gene (*FBN2*) deletion in a patient with congenital contractural arachnodacty; a unique partial 19p13.3 trisomy associated with dysmorphic features and developmental delay; and a novel duplication of 2q32.1q34 associated with loss of heterozygosity of the adjacent 2q34qter region. A review of the chromosome microarray findings observed in our patients with seizures was also reported.

The caseload continued to increase in the Cancer Cytogenetics section of the laboratory through 2011 during which over 2000 oncology samples were received and 3200 tests performed, with increases seen in requests for both conventional karyotyping and FISH assays. At the current time, the laboratory offers over 30 different interphase FISH assays, most of which are designed to diagnose or monitor specific genetic abnormalities associated with various cancers. The laboratory currently offers two FISH assays that are considered "companion diagnostics" for drugs that target specific molecular features in tumors. A positive result on the HER2 assay (amplification of the ERBB2 locus) is required for a breast cancer patient to qualify for the drug herceptin, and a positive result for rearrangement of the ALK locus is required for non-small cell lung cancer patients to qualify for the drug crozotinib. Both assays use FISH technology on paraffin embedded tumor tissue. Overall the laboratory has seen a 70% increase in paraffin FISH testing in the past 2 years.

The Cytogenetics Laboratory continues to participate in the cancer cooperative groups (CALGB and COG). In collaboration with researchers at St. Jude's, the Cytogenetics Fellow, Dr. Melissa Hayden, presented a proof of principle paper at the American Cytogenetic Conference on a newly recognized rearrangement between PDGFRB and EBF1 in a child with Ph-like high risk ALL who had a dramatic and positive response to treatment with imatinib. Dr. Hayden studied the rearrangement with a high resolution SNP array which demonstrated that the gene fusion was likely to produce a tyrosine kinase of the type that would respond to the drug.

## <u>AUTOPSY PATHOLOGY</u> LEIGH B. THORNE, M.D., DIRECTOR

The UNCH Autopsy Service continues to provide valuable information to clinicians and families of patients. In 2011, a total of 121 autopsies were performed and 132 in the 2011-12 fiscal year (as of 6/25/12). We currently have eight faculty participating in the autopsy service in addition to the full time autopsy Pathologist's Assistant and two part-time autopsy technicians. A multidisciplinary committee was formed in 2009-2010 to address issues with decedent care in general. The Decedent Care program was officially begun January 2012. The mission is to improve not only the autopsy services provided to families of deceased patients but to improve the process from the time the patient passes to release of the body to the funeral home. The program is under the oversight of Cathy Holleman, Administrative Director of McLendon Labs. Pam Thorner, who has been on the Autopsy service for 9 years moved into the Decedent Care program and acts as the Decedent Care Coordinator. Heidi Dodson has also joined the team and covers the service on weekends. In addition to our clinical mission, the service continues to serve as an important resource for researchers at UNC. In this fiscal year, the breast cancer rapid autopsy program was revived, with support provided through grants from Dr. Lisa Carey. Dr. Leigh Thorne and Vincent Moylan, our autopsy PA, have been the primary collaborators, however recently the PAs from Surgical Pathology have volunteered their services (Claudia Brady, Tracie Wagner, Steve Holmes). We have also assisted several other research projects in need of postmortem tissue. We continue to assist the Office of the Chief Medical Examiner with postmortem examinations as needed. We have also maintained contracts with 2 other small hospitals in the area.

The morgue has also undergone a much needed renovation in the last year, primarily to improve ventilation. The conference room is now equipped with a downdraft table for presentation of formalin fixed organs. There is a new Mopec grossing station in one of the two autopsy rooms. A brand new customized hood was also installed in the back of the morgue for proper disposal and rinsing of formalin fixed organs. Also purchased this year was a new multiheaded (3) microscope and computer for projection of images.

## <u>MOLECULAR PATHOLOGY</u> MARGARET L. GULLEY, M.D., DIRECTOR

The Molecular Genetics Laboratory performs assays on DNA and RNA to help in diagnosis, monitoring, and treatment of infectious disease, cancer, and heritable conditions. A test menu with description of each clinical service is found on our website: http://labs.unchealthcare.org/directory/molecular\_pathology/index\_html

Research and development is an important component of our clinical and academic mission to advance healthcare using modern molecular technologies. Our training programs educate physicians, medical students, post-doctoral fellows, genetic counseling students, and clinical laboratory science students. Our fellowship training program in Molecular Genetic Pathology was the first in the nation to educate a board-certified physician in this subspecialty. We offer a month-long course in Molecular Diagnostics and Cytogenetics targeted at pathology residents and open to other interested medical professionals. Further information on our clinical, educational and research work is found at:

http://www.med.unc.edu/pathology/faculty/biosketch-of-dr-margaret-gulley

Molecular pathology is growing rapidly as clinicians increasingly use molecular tools for diagnosis and management. Increasingly we are validating panels of tests that simultaneously measure multiple RNAs to identify a profile that predicts disease outcome, or we sequence multiple genes to identify a mutation relevant to diagnosis or response to therapy. We thank UNC Hospitals, the TraCS Institute, the University Cancer Research Fund, and the Department of Pathology and Laboratory Medicine for making available the resources to implement modern molecular technologies and to validate multiple novel and informative assays. Learn more in a document entitled "Validating assays for use in clinical trials" at http://labs.unchealthcare.org/directory/molecular\_pathology/index\_html

Major Equipment in the clinical molecular genetics lab: Roche LightCycler 2.0 and 480 realtime PCR instruments, Illumina MiSeq next gen sequencer, Roche MagnaPure extractor and MagnaLyser, Perkin Elmer Janus Robotic Pipettor; Qiagen EZ1, Qiacube, and QiaSymphony extractors; Applied Biosystems 9700, 9800, 7500, and 7900 PCR instruments; two ABI Veriti thermocyclers, Idaho Technologies LightScanner, three ABI 3130xl capillary gel electrophoresis instruments, Biotage Pyromark MD pyrosequencer, Agilent array scanner, Affymetrix array scanner, RoboSep cell separator, and UVP gel documentation system.

Faculty are Margaret L. Gulley, M.D., Karen Weck, M.D., Bill Funkhouser, M.D., Ph.D., Leigh Thorne, M.D., Jessica Booker, Ph.D., and Rosann Farber, Ph.D. Fellows include Nirali Patel, M.D., and Kristy Crooks, Ph.D. Our excellent staff includes six medical technologists, three research scientists, a supervisor, and an office support assistant.

## **TRANSFUSION MEDICINE, APHERESIS, TRANSPLANT SERVICES TRANSFUSION MEDICINE (Blood Bank, Platelet Donor Program, Apheresis)** YARA A. PARK, M.D., DIRECTOR

The Transfusion Medicine Service (TMS) saw an increase in tests performed as well as products transfused in the past year. Over 39,000 of products were transfused to patients. In an effort to inform clinical teams about transfusion reaction interpretations, all of these reports are now in the electronic medical record to allow easier access to the information. TMS is in the midst of a Green Belt Project to reduce blood product wastage throughout the institution. All areas of TMS have sent multiple staff members to Yellow Belt Training to improve efficiency. The staff also underwent training about Team STEPPS skills to improve communication both within the lab and with the clinical teams. Apheresis also experienced an increase in number of procedures performed in the year. Collections of hematopoietic progenitor cells for bone marrow

transplantation for the National Marrow Donor Program began this year and have gone well. Apheresis is working towards having their forms in the electronic medical record. The Blood Donation Center (BDC) has increased collections by 10% in the year. Multiple donor drives were done including hospital volunteers and intramural sports clubs. The BDC is almost complete with an extensive computer upgrade.

The Transfusion Medicine Service (TMS) was inspected and reaccredited by CAP, AABB, FDA, and FACT within the past year. Dr. Yara Park assumed the role of Medical Director of TMS. Using data from our performance improvement process, TMS added myomectomies as a type and screen procedure to the Standard Surgical Blood Ordering Schedule. TMS recently completed a comprehensive computer upgrade which included an operating platform change. The Apheresis unit saw increased procedure volumes, particularly in hematopoietic progenitor cell (HPC) collection which were increased ~30%. Additionally, Apheresis, in conjunction with the Bone Marrow Transplant program, has been approved to be a National Marrow Donor Program apheresis collection site to collect HPC products from volunteer donors. All physician apheresis procedure notes are now being done in WebCIS to allow easier access to the information. The Blood Donation Program began to incorporate patients in the recognition of the donation program by having the t-shirt design be one that was created by a patient or family member and plan on this being an annual event. Currently, the Blood Donation Program is preparing for a major computer upgrade.

## <u>CLINICAL MICROBIOLOGY, IMMUNOLOGY LABORATORIES</u> PETER H. GILLIGAN, Ph.D., DIRECTOR

The Clinical Microbiology/Immunology Laboratory has continued to expand its test menu and test volumes through the addition of new assays and new instrumentation. We have been able to enhance service to our clinicians and patients while maintaining our training mission. One of the major accomplishments of Dr. John Schmitz, in the Immunology section, was the modification of our HIV testing algorithm with the implementation of the new HIV Ag/Ab Combo test. This test detects both HIV antibody and p24 antigen simultaneously allowing the laboratory to better detect acute HIV infection while maintaining excellent detection of chronic infection. This new algorithm eliminated the tedious task of "pooling" HIV negative sera for HIV quantitative PCR testing to detect acute infection significantly improving turnaround times. This same technology has also replaced the standard rapid HIV test for blood/body fluid exposures to provide the benefit of detecting acutely infected source patients.

The Immunology section also expanded our allergy testing menu by establishing a new childhood allergy panel. This panel is marketed to General Practitioners to improve diagnosis and treatment of patients that present to primary care clinicians with allergy-like symptoms. Before the implementation of this new panel, we have seen a 24% increase in test volume from this time last year.

The Immunology section added new instrumentation, the Diasorin Liaison. This system, our third random access platform enables us to run 12 assays that were previously performed on an outdated, batch mode instrument, or were done manually. This system also allowed us to bring some testing in-house that was previously sent to a Reference Laboratory.

Under the guidance of Dr. Melissa Miller in the Molecular Microbiology section, another major accomplishment was the implementation of a molecular test for qualitative detection of *Mycobacterium tuberculosis* complex DNA by PCR. Rapid identification of *Mycobacterium tuberculosis* complex DNA in smear positive samples is useful in both beginning appropriate therapy for an individual patient and for instituting appropriate infection control measures on a hospital and community basis.

They were also able to offer a new, rapid PCR test for the laboratory diagnosis that detects both Influenza A and B viruses. Results are available 7 days/week, 24 hrs/day with a targeted turnaround time of 90 minutes upon receipt of the specimen in the laboratory. We were also able to offer a "traditional" Influenza PCR test for inpatients and those locations that did not require a rapid turnaround time. During the 2010-11 "flu season" (Dec-April), the laboratory staff performed 1,025 Rapid Flu tests, 1,385 traditional flu tests and 2,262 Respiratory Viral Panel molecular tests.

The Molecular Microbiology section brought in new instrumentation, the Abbott M2000 system. This improved platform replaced the Roche Ampliprep system. This system fully automates HIV, HCV, HBV improving workflow and turnaround times.

The PNA FISH Yeast Traffic Light test was implemented in our Specimen Processing/Rapid Procedures area for rapid identification of *Candida* species from positive blood culture bottles. The test is performed on slides using specimens taken directly from positive blood culture bottles. The ability to rapidly report *Candida albicans* by PNA FISH allows clinicians to safely treat patients with fluconazole instead of with one of the more expensive anti-fungals. The estimated institutional cost savings is \$1,800 per candidemia patient. When comparing results of positive patients before and after implementation of PNA-FISH, *Candida* species were identified 4 days sooner with PNA-FISH and antimicrobials changes, if needed, could be made approximately 2 days sooner.

They worked very closely with the Emergency Department physicians to review data from patients that had a urine sample submitted for both urinalysis and urine culture. Their goal was to see if we could reliably use urinalysis results to limit unnecessary urine cultures (i.e. screen out the "negatives"). As a result of these efforts, Urinalysis with Culture Reflex testing began in the Emergency Department on April 11, 2011. In patients meeting certain criteria, a clinician in the ED may order a "urinalysis with culture reflex" test. The urinalysis is performed first and only set up for culture if defined parameters are positive. This has been met with great enthusiasm by the clinicians in that setting.

Finally, they continue their extensive training and educational mission within the laboratory. They taught a full complement of Clinical Laboratory Science students at both the BS and MS levels. They continue to train our clinical pathology residents and fellows in both Medical Microbiology and Medical Laboratory Immunology. They had the largest number of students ever in the Clinical Pathology elective, PATY 417. Their daily infectious disease teaching rounds are a popular component of the training of fellows in that discipline. Finally they continue our clinical microbiology training of the pediatric residents twice weekly.

## <u>PHLEBOTOMY SERVICES</u> PETER H. GILLIGAN, Ph.D., DIRECTOR

Phlebotomy Services completed the previous fiscal year under budget. Currently, we average 67.6% of test results from the 4AM draw available by 6AM, 93.0% by 7AM, and 98.8% available by 8AM. Blood Culture contamination rates continue to be a source of pride for Phlebotomy Services. Currently, we average a total BC contamination rate for Phlebotomy Services of 0.9%. Total contamination rate hospital wide is currently averaging 1.2%. The quality of specimens collected by Phlebotomy Services staff continues to be excellent: clotted only 0.04%, hemolyzed only 0.21%, and QNS only 0.05% of specimens. Since December 2010, Phlebotomy Services has participated on a Carolina Care team focused on improving patient responses for the question "courtesy of the person who took blood" on the Press-Ganey patient survey. The current ranking for this score between April 2012 and June 2012 is up from the 38<sup>th</sup> percentile to the 75<sup>th</sup> percentile. On May 14, 2012, we restructured our early AM collection model after discussion with nursing and medical staff leadership. We now have three phlebotomy teams focused on the collection of blood from patients based on the rounding times of the various medical teams. Larger teams are sent to each location making it possible to sweep an area faster and to complete all recollections attempts before the team leaves each unit. The teams are coordinated according to hospital location to avoid excess walking. This has decreased the amount of time it takes to complete the early AM collections. In consultation with nursing staff, this new approach is thought to contribute to increasing patient satisfaction. With ample staffing, we anticipate this time saving measure will make it possible to push the early AM collection start time from 3 to 4AM. This will be a patient pleaser and should improve the patient satisfaction scores even more. Additionally we have redeployed staff so that blood can be drawn on recently admitted patients on demand between 10 PM and 4 AM. This service, requested by both nursing and house staff, is currently being implemented.

#### **<u>CORE LABORATORY (Chem/UA/Coag/Hem/Tox/Endo)</u>** CATHERINE A. HAMMETT-STABLER, Ph.D., DIRECTOR

The Core Laboratory services include coagulation, clinical chemistry, hematology, urinalysis, and referral testing. The Laboratory receives 4000-5000 samples daily and performs >5 million tests annually. During 2011-12 we sought improvements in all areas of the laboratories to improve patient care and safety for staff and patients. Newly introduced services and tests include thromboelastography, a chemiluminescence-based platelet aggregation test, dabigatran testing, free T3, beta 2-microglobulin, lambda and kappa free light chains, antifungal measurements (voriconazole, posaconazole, and fluconazole), and an extended opiate confirmation (morphine, codeine, hydrocodone, oxycodone, hydromorphone, oxymorphone, 6acetylmorphine, buprenorphine, and norbuprenorphine). Five technologists earned their Green Belts (Six Sigma-Lean) through a quality improvement initiative within the processing area of the laboratory. The team worked with all staff assigned to the area to identify specific steps and processes delaying samples reaching the analytical systems within the laboratories. The changes initiated by the team produced significant reductions in processing time across all three shifts so that 98% of samples enter the analytical phase of testing in <30 min from time of receipt inlaboratory. As a result of this project and the EnGen automation, the average turnaround time, i.e., receipt to resulting, for routine testing for those samples analyzed within the Core work-cell

is 60 min, or less. In special chemistry, the addition of the Tecan pipetting station has improved consistency in this highly manual area while reducing the potential for repetitive stress injuries for the staff. During this time, referral resting staff handled ~40,000 samples (representing >85,000 individual test orders). This is a significant decrease in the number of referred testing requests, down from a high of >65,000 samples (>100,000 tests). The decrease reflects major efforts across all of the McLendon Clinical Laboratories to bring in testing where appropriate based upon volumes and clinical need. The tests currently referred to outside laboratories are typically lower volume, costly procedures; and thus each request undergoes review by staff, faculty, or trainees, a process that often leads to efforts to direct the ordering clinician to more appropriate tests. These efforts have resulted in the cancellation of ~30 orders each month. Education of house-officers regarding appropriate ordering practices of esoteric referred tests is a key role of referral testing. A highlight of the year was the investigation of the false-positive drug screening results with the faculty and staff of the Newborn Nursery. This work was published in Clinical Biochemistry 2012;45:605-9 and has received considerable attention nationwide by professional and lay media. Most importantly, it demonstrates the benefits of a multidisciplinary approach to a patient care problem.

Ten Medical Technologist 1's were accepted into the mentoring program to work on selected areas with senior technologists. The MT1 Advisory Board developed and introduced SharePoint as a key means of communication within the laboratory. Chrysa McDuffy, MT(ASCP) received the 2012 Care Award for her dedication to patient care and leadership. Faculty and staff continue to provide departmental and laboratory representation to a number of major hospital and university committees, such as the Clinical Documentation Committee (MIM), IRB, UNCH Benefits Committee, and ED COG. Many also serve on a number of smaller ad hoc committees, examples of which include the Workgroup for Handling Sensitive Conditions and Results and several pertaining to the newly initiated Chest Pain Accreditation process.

Lastly, in addition to the highlights mentioned above, a number of the staff demonstrated exceptional scholarship, among them: J. Eric Stanford MLS(ASCP) published Behind the Test Result, a paper describing the Ambassador Program, in Advance for Laboratory Professionals. Phillip Bates, MT(ASCP), received a Young Investigator Travel Award to present his work, Simultaneous Detection of Nine Opiates, including Buprenorphine and Norbuprenorphine, in Urine using UPLC/MS/MS, at the 2012 MSACL meeting in San Diego. Connie A. Bishop, MT(ASCP)SH gave a workshop at CLMA entitled Patient Safety Strategies that Enhance the Visibility and Value of the Laboratory Improve Staff Morale. She will participate in a session at the upcoming ASCLS meeting, Expanding the Role of Laboratory Professionals in Patient Safety Through Evidence-based Methods – a program developed in collaboration with the CDC.

## HEMATOPATHOLOGY GEORGETTE A. DENT, M.D., INTERIM DIRECTOR

The volume and complexity of cases has continued to increase in this Division since moving into the North Carolina Cancer Hospital. The annual in-house bone marrow volume is > 2,000 and the lymphoma-evaluation case volume is approximately 750. Outside review of Hematopathology diagnostic cases has also continued to increase as these reviews are necessary

for patients being referred to UNC for therapy. Additional immunohistochemical and flow cytometric markers are continuously being added to the diagnostic repertoire for this Division, which remains on the cutting-edge of diagnostic hematopathology. The Division looks forward to incorporating 8-color flow cytometry into clinical practice, which will allow for better definitions of hematolymphoid neoplasms on conceivably smaller numbers of neoplastic cells. Dr. Marian Rollins-Raval will be joining the Hematopathology attending faculty in August of 2012.

#### <u>SPECIAL COAGULATION LABORATORY</u> HERBERT C. WHINNA, M.D., Ph.D., DIRECTOR

Again this fiscal year, the Special Coagulation Laboratory saw a downtrend in volumes over the past fiscal year, but were able to maintain revenue levels. The laboratory also performed special studies testing for equipment companies generating additional revenue. In order to assist our clinician colleagues in providing the best care possible to UNCH patients, we have added new testing to measure levels of the direct thrombin inhibitor Dabigatran as well as whole blood platelet aggregation and secretion. Faculty and staff continue to regularly participate in the Friday Hematology Conference sponsored by the Division of Hematology & Oncology; Department of Medicine where hematology and coagulation issues on patients seen by the Hem/Onc Consult Service are discussed. We continue to optimize patient care and safety as well as plan for the development and implementation of necessary new testing in the future.

## <u>CYTOGENETICS</u> KATHLEEN W. RAO, Ph.D., DIRECTOR KATHLEEN A. KAISER-ROGERS, Ph.D., CO-DIRECTOR

During the past fiscal year, one of the most significant changes in the Cytogenetics Lab has been the in-house validation of the Affymetrix CytoScan HD SNP microarray platform. This platform, which contains 2.7 million markers, has replaced the 1.8 million marker Affymetrix 6.0 SNP microarray platform. This platform, like its predecessor, is capable of detecting copy number changes that are below the level of resolution obtained by karyotyping, as well as regions of homozygosity that are associated with consanguinity and uniparental disomy. The laboratory currently processes approximately 500 constitutional microarray cases annually. In the future, we hope to also apply this technology to our products of conception, and cancer samples.

Several of our more interesting chromosome microarray findings were reported at the 2012 American College of Medical Genetics Meeting and include a novel interstitial fibrillin-2 gene (*FBN2*) deletion in a patient with congenital contractural arachnodacty; a unique partial 19p13.3 trisomy associated with dysmorphic features and developmental delay; and a novel duplication of 2q32.1q34 associated with loss of heterozygosity of the adjacent 2q34qter region. A review of the chromosome microarray findings observed in our patients with seizures was also reported.

The caseload continued to increase in the Cancer Cytogenetics section of the laboratory through 2011 during which over 2000 oncology samples were received and 3200 tests performed, with increases seen in requests for both conventional karyotyping and FISH assays. At the current

time, the laboratory offers over 30 different interphase FISH assays, most of which are designed to diagnose or monitor specific genetic abnormalities associated with various cancers. The laboratory currently offers two FISH assays that are considered "companion diagnostics" for drugs that target specific molecular features in tumors. A positive result on the HER2 assay (amplification of the ERBB2 locus) is required for a breast cancer patient to qualify for the drug herceptin, and a positive result for rearrangement of the ALK locus is required for non-small cell lung cancer patients to qualify for the drug crozotinib. Both assays use FISH technology on paraffin embedded tumor tissue. Overall the laboratory has seen a 70% increase in paraffin FISH testing in the past 2 years.

The Cytogenetics Laboratory continues to participate in the cancer cooperative groups (CALGB and COG). In collaboration with researchers at St. Jude's, the Cytogenetics Fellow, Dr. Melissa Hayden, presented a proof of principle paper at the American Cytogenetic Conference on a newly recognized rearrangement between PDGFRB and EBF1 in a child with Ph-like high risk ALL who had a dramatic and positive response to treatment with imatinib. Dr. Hayden studied the rearrangement with a high resolution SNP array which demonstrated that the gene fusion was likely to produce a tyrosine kinase of the type that would respond to the drug.

#### **LABORATORY INFORMATION SERVICES** HERBERT C. WHINNA, M.D., Ph.D., DIRECTOR

Major projects from the past fiscal year in AP for Lab Information Services included upgrading the CoPath Anatomic Pathology system to version 3.2, which was a prerequisite for the implementation of CoPath Advanced Barcoding and Tracking module. The AB&T module, also implemented this year, allows for positive patient ID at the grossing stations and throughout the lab as well as slide level tracking and advanced statistical reports.

On the Clinical side, the SCC LIS underwent a major hardware upgrade during which all servers were replaced with the latest model IBM servers. The databases for the system were then migrated from an outdated platform to Oracle DB, allowing for the next phase of new software implementation. Currently underway is the RCM project, which will offer improved billing processes for the lab Outreach business, as well as provide a host of new SCC modules to better serve the Outreach clients. This will include electronic order entry and result delivery, remote courier management, medical compliance checking and greatly enhanced ability to determine the financial standing of the Outreach program.

LOINC coding was also enabled in the SCC LIS this year in order to help the institution meet its meaningful use eligibility requirements. In the coming fiscal year there will be a new HLA computer system implemented as well as an electronic reporting interface for reporting of significant results to the State Lab.

## <u>NEPHROPATHOLOGY LABORATORY</u> VOLKER R. NICKELEIT, M.D., DIRECTOR

The Division of Nephropathology in the Department of Pathology and Laboratory Medicine is one of few highly specialized centers in the U.S. that provides expert diagnostic evaluation of

medical renal diseases and transplant related disorders. More than 1,700 renal specimens (native & transplant biopsies and nephrectomies) from over 200 nephrologists throughout the state, region and the world are analyzed annually. During the 2010 calendar year, the Division evaluated close to 500 cases from UNC Hospitals, and the remainder from outside institutions. Over 90% of specimens are routinely evaluated not only by light microscopy at multiple levels of section with different stains, but also by immunofluorescence microscopy utilizing a panel of antibodies, electron microscopy, and occasionally additionally by immunohistochemistry. Thus, the actual number of procedures that are performed on renal specimens by far exceeds 5000 per year. The Division of Nephropathology is involved in clinical, translational and basic research on renal diseases, especially glomerulonephritides and diseases seen in renal allografts. The research activities are supported by extramural grants and are facilitated by an extensive database and archival system that currently includes data from approximately 30,000 renal specimens, 15,000 serum samples, and 1000 urine samples. Currently, one US pathologist and one pathology post doctoral research associate from Sudan are being trained on how to manage and organize a nephropathology laboratory. The UNC nephropathology faculty is also heavily engaged in continuous education series enhancing the diagnostic skills of pathologists and nephrologists, such as short courses at the annual USCAP meetings, the Columbia Presbyterian post graduate course on nephropathology in New York, or the 'Nephropathologiekurs Volhard-Fahr' in Mannheim, Germany. The Division of Nephropathology co-sponsored and coorganized the 15<sup>th</sup> International Vasculitis & ANCA Workshop in Chapel Hill. It is closely allied with the UNC Kidney Center and the Glomerular Disease Collaborative Network (GDCN). The GDCN has been in operation for over two decades and is a consortium of academic and community nephrologists; it has the goal to enhance knowledge of renal diseases and treatment strategies.

#### <u>QUALITY MANAGEMENT GROUP</u> HERBERT C. WHINNA, M.D., Ph.D., DIRECTOR

The Quality Management Group has been very active this year in participating in projects using LEAN and Six Sigma techniques. We now have all of the QM employees pursuing their green belt or having attained their green belt. We also have one employee, Cyndy Levtzow, who has obtained her black belt. This allows her to mentor other employees in their training as well as to organize Green Belt and Purple Belt (LEAN) projects. There are currently two projects underway, one to look at product wastage in the Transfusion Service and a second to work on lost revenues due to write offs. All of the QI projects are available for viewing on the McLendon Laboratories Home Page. In addition to Quality improvement efforts, the group is actively working with their laboratories to prepare for the CAP inspection that will occur between July 15-Oct 15 time period.

#### <u>NEUROPATHOLOGY SERVICE AT UNC HOSPITALS</u> THOMAS W. BOULDIN, M.D., DIRECTOR

Diagnostic services in neuropathology are provided at UNC Hospitals by C. Ryan Miller, M.D., Ph.D.; Dimitri G. Trembath, M.D., Ph.D.; and Thomas W. Bouldin, M.D. Dr. Bouldin is the director of the Division of Neuropathology. Neuropathology services include diagnostic surgical neuropathology, autopsy neuropathology, forensic neuropathology, nerve biopsy interpretation,

and ophthalmic pathology. The case load from the surgical service and autopsy service is sufficient to allow the Department of Pathology and Laboratory Medicine to provide a rich training experience in diagnostic neuropathology for the Department's residents in anatomical and clinical pathology.

The volume of surgical neuropathology cases has increased and become more complex over the last five years, due in part to the growth of the clinical neurosurgical service, the expansion of the Neuro-Oncology programs at UNC Hospitals, and the opening of the North Carolina Cancer Hospital.

The Neuropathology faculty members attend and are active participants in a variety of conferences at UNC Hospitals. A complete listing of the clinical conferences conducted by the neuropathology faculty is as follows:

Brain Cutting Conference (Autopsy Service)	Weekly
Clinical Neurosciences Conference	Monthly
Ophthalmic Pathology Didactic Conference	Monthly
Opthalmic Pathology Signout Conference	Weekly

#### <u>OUTREACH LABORATORY SERVICES</u> HERBERT C. WHINNA, M.D., Ph.D., DIRECTOR

McLendon Laboratory's Outreach Service operates as the primary interface between the diagnostic testing services of the hospital laboratory and the community. The service has grown to serve 70 clients in the research triangle area including hospital and community based clinics, skilled nursing facilities, private physician practices and home health agencies. Support is provided primarily in the areas of diagnostics, assistance with regulatory compliance and maintenance of point of care testing/competency. Twenty-four of the serviced providers perform some level of point of care testing (from waived to moderately complex) and two of the clinics are CAP accredited. Last year Outreach served over 101,000 patients ordering and processed over one-half million tests.

In addition, Outreach manages and staffs two stand-alone off-campus laboratories; one at the Ambulatory Care Center and the second at Carolina Point 2. The ACC laboratory supports the operating room expansion as well as some the clinics within the building. The laboratory at CP2 provides testing support for the many clinics within the building, the Urgent Care center and also has begun accepting walk-in patients from other clinics.

A supervisor position was filled and a Business Development and Account Liaison person was hired. These two positions will compliment and expand the leadership capability of the department. The supervisor position will directly manage the call center and outreach processing staff. The Business Development and Account provides a direct interface to our current customers to; educate, inform of new services and problem solve. This individual also is the primary contact for new customers. Outreach was heavily involved in the startup of the Carolina Advanced Health clinic, a new initiative between UNC and Blue Cross/Blue Shield. Town of Chapel Hill Wellness clinic. We have also consulted with Chatham Medical Specialists and Dr.

William Hall in Siler City and Sanford.

The last year Outreach successfully started a courier service with its own drivers and vehicles. After several months of operations that service was successfully merged with McLaurin parking through an Owen's and Minor consulting initiative. The number and frequency of routes has been expanded to provide more frequent pickups for our largest and closest customers. This frequency enables the testing to be performed more timely and also eliminates the larger batches of deliveries resulting in less in-lab processing time.

A customer service/call center was established to combine outreach, core laboratory and microbiology customer service areas. The call center operates from 7:30 am - 8 pm, Monday through Friday. The call center provides a standardized process for answering and directing calls. These individuals also call critical values as well as perform add-on testing.

## **TRANSPLANT LABORATORIES** (HLA and Flow Cytometry) JOHN L. SCHMITZ, Ph.D., DIRECTOR

The Histocompatibility Laboratory provides specialized testing services for the solid organ and bone marrow transplant programs. Several different technologies are utilized to derive low to high resolution HLA genotypes for organ allocation and bone marrow donor selection. The second major component of the HLA laboratories workload is HLA antibody detection and identification used in pre and post-transplant analyses. The HLA laboratory experienced an 9.7% increase in workload this fiscal year compared to the previous year. A major component of the increase was due to the implementation of routine post-transplant HLA antibody monitoring for solid organ transplant recipients. The HLA laboratory implemented a twice a week testing schedule with a 7 day turn around time for this testing. The laboratory enhanced it sequence based typing technology by installation and validation of the ABI3500 automated DNA sequencer with Invitrogen SeCore typing reagents and software. This new typing system offers the laboratory advantages in instrumentation and software that enhance high resolution HLA typing efficiency. The laboratory has also validated a real time PCR HLA typing assay that offers significantly reduced turn around time that will shorten the amount of time technologists are in the laboratory on call and the time necessary for reporting of deceased donor HLA types.

The flow cytometry laboratory performs testing in support of Infectious Disease, Hematopathology, Hematology, Transplant and Transfusion Medicine Services. The laboratory has experienced a slight increase in workload compared to the previous fiscal year. The laboratory has had to deal with the retirement of two technologists in this fiscal year (50% of staff). Two new technologists have joined the laboratory and are completing their training. The retirement of two experienced technologists adversely impacted the laboratories goal of implementation of 6-color flow cytometric leukemia/lymphoma analysis. Now that the laboratory is fully staffed this effort has been reinitiated. In addition, the laboratory has been able to obtain upgrades for two flow cytometers to convert them to 8-color instruments. This will further enhance the capabilities of the laboratory for Leukemia/Lymphoma immunophenotyping and the staff are working with the Hematopathology service to design new panels for this testing to be implemented in the upcoming year.

# HUMAN PROGENITOR CELL LABORATORY YARA A. PARK, M.D., DIRECTOR

Due to rapid growth of the Bone Marrow Transplant program, the Hematopoietic Progenitor Cell lab processed a record number of products this year. The lab was inspected and re-accredited by CAP, AABB, FDA, and FACT within the past year. Renovations are almost complete on an expanded work area which will house the liquid nitrogen freezers. In conjunction with the Bone Marrow Transplant program, the lab developed a new process and form to ensure the correct and prompt determination of allogeneic donor eligibility by both the clinical program and the laboratory.

# CORE AND SERVICE LABORATORIES

# MICROSCOPY SERVICES LABORATORY C. ROBERT BAGNELL, Jr., Ph.D., DIRECTOR

Microscopy Services Laboratory is a UNC core facility for electron and light microscopy, the Light Microscopy Core facility for Lineberger Comprehensive Cancer Center, and the TEM imaging center for UNCH clinical EM and Pathology Outside Renal Referral service. During this reporting period the laboratory supported research by 343 principal investigators from 42 departments and centers at UNC. The total number of active laboratory clients now stands at 1007. In the past 12 months the light microscope facilities logged 8,462 hours of use, electron microscope facilities logged 1,795 hours of use and the laboratory performed 593 electron microscopy specimen preparations.

Significant upgrades were funded by the Department of Pathology & Lab Medicine:

- 1. Six Vibration Isolation Tables (\$24K). These replace old and failing systems and provide isolation for additional new equipment.
- 2. Zeiss LSM 700 Confocal Laser Scanning Micorscope (\$286K). This system replaces the Zeiss Pascal LSM 5 and adds new laser lines and the best light gathering power available.

## LASER CAPTURE MICRODISSECTION CORE FACILITY C. ROBERT BAGNELL, Jr., Ph.D., DIRECTOR

This facility is part of the Microscopy Services Laboratory. LCM is a method for collecting very small regions of tissue or specific cells for use in "omic" analyses. The facility houses a Zeiss PALM LCM and an Arcturus PIX-Cell II LCM, a Leica CM 1850 cryostat, and a ventilation hood for staining and dehydration. Over the past 12 months these systems were used a total of 117.5 hours.

## TRANSLATIONAL PATHOLOGY LABORATORY (TPL) C. RYAN MILLER, M.D., Ph.D., DIRECTOR

The Translational Pathology Laboratory (TPL) continues to grow, both in terms of services offered and the volume of services provided to UNC investigators. We have acquired the Definiens Image Miner analysis software package. Our Aperio Spectrum image and data management software available at <u>https://tpl-spectrum.med.unc.edu</u> now stores over 42,000

scanned digital slides and 13 terabytes of data. In 2011, over 1000 digital slides were scanned per month. In calendar year 2011, we provided services to 96 investigators (up from 54 in 2009 and 93 in 2010). Diagnostic slides and FFPE tissue blocks were pulled from the UNCH Surgical Pathology archives on nearly 2,500 patient cases. Over 18,000 unstained tissue sections, 6,600 H&E stained slides, and 3,200 IHC/IF stained slides were prepared. Our services were featured in 14 peer-reviewed publications in 2010 and 10 in 2011 and have been included in over 40 grant applications to date.

## ANIMAL CLINICAL LABORATORY FACILITY HYUNG-SUK KIM, Ph.D., DIRECTOR

The facility performs blood chemistry tests, urinalysis and hematological tests in animal samples, to characterize physiological and clinical phenotypes in animal models. For clinical tests, 44 different chemicals including general health tests, liver function tests and kidney function tests are currently available with an automated chemical analyzer, Ortho-Clinical Diagnostics Johnson & Johnson's VT350 (purchased in 2008), which can measure one test with 5 - 10 microliter sample volume. For hematological tests, the animal blood counter (HESKA's CBC Diff, Veterinary Hematology System) can measure WBC#, Lym%, Lym#, Mon%, Mon#, Gra%, Gra#, RBC#, HGB, HCT, MCV, MCH, MCHC, RDW, PLT, MPV, and 3 distribution curves of WBC, RBC, and PLT with 201 whole blood sample. Since we have various data accumulated for long period from normal or abnormal values, discussion with us will help to interpret clinical results. More than thirty principal investigators from the UNC-CH campus use these services for their research. From June 2011, the facility will provide the new service of multiplexed biomarker immunoassays for cancer biomarkers, cell signaling phosphoprotein detection, endocrine diseases, cardiovascular diseases, cytokine/chemokine detection. Recently, the new MAGPIX instrument having development of Luminex technology with magnetic beads has been purchased.

## <u>GENE EXPRESSION FACILITY</u> HYUNG-SUK KIM, Ph.D., DIRECTOR

The facility provides services for gene expression studies using quantitative real time RT-PCR by ABI 7500 and 7300 Sequence Detection Systems and high throughput preparation of total RNA and genomic DNA by ABI Prism 6100. Currently, more than 1,000 disease-related gene assays have been developed to detect their expression levels in mice, human, and rat, including various house-keeping genes. In addition, a service for mouse genotyping analysis has been well established with a high throughput performance based on detecting differences of gene copy number, with a less than two-day turn-around time. This genotyping process can exclude many laborious procedures, such as preparation of genomic DNA, PCR, gel running, Southern blot analysis. Currently, we are genotyping more than three thousand mice monthly. We can also provide a full service which includes all the steps necessary for designing and synthesizing Taqman probes and primers, preparing RNA samples, and quantitative analysis. Through full service, we are collaborating with many PIs for gene expression research. More than thirty principal investigators from ten different departments are currently using this research core facility.

## DNA SYNTHESIZING FACILITY HYUNG-SUK KIM, Ph.D., DIRECTOR

The facility serves more than 50 investigators from a variety of campus-wide departments in its function of producing oligonucleotides for use in genetic research. Three DNA Synthesizers can produce ten oligonucleotides simultaneously. During this fiscal year, about three thousand oligonucleotides have been synthesized. The fluorescent oligonucleotide TaqMan probes with 5' fluorescein (6-FAM) and 3' quencher tetramethyl rhodamine (TAMRA) are successfully prepared for users of real time RT-PCR.

## ADME MASS SPECTROMETRY CENTER ARLENE S. BRIDGES, Ph.D., DIRECTOR RICHARD R. TIDWELL, Ph.D., CHAIR, ADVISORY BOARD

As Director of the ADME Mass Spectrometry Center, Dr. Bridges' role is to provide study design assistance, bioanalytical support, and date interpretation to preclinical and clinical studies conducted by investigators at UNC and beyond. Center capabilities include quantitation by triple quadrupole mass spectrometry, molecular weight determination by ion trap mass spectrometry, and identification of novel metabolites by both types of equipment.

With regards the equipment, the Center maintains:

- 1. an Applied Biosystems API4000 triple quadrupole mass spectrometer
- 2. an Applied Biosystems API3000 triple quadrupole mass spectrometer
- 3. a Thermo-Scientific Quantum Ultra triple quadruple mass spectrometer
- 4. an Agilent 1100 MSD ion-trap mass spectrometer
- 5. five Agilent HPLCs, each with diode array (UV) and fluorescence detectors

The Center supports the work of UNC principal investigators in the Schools of Medicine, Pharmacy, and Public Health and in the College of Arts and Sciences. Primary research activities involve analysis of antiparasitic agents (in collaboration with Dr. Richard Tidwell), antibiotic and antiviral agents (in collaboration with Dr. Angela Kashuba), and anticancer nanoparticles (in collaboration with Drs. Joseph DeSimone and William Zamboni). In addition, the Center has collaborates long-distance with researchers from Duke University, East Carolina University, North Carolina Central University, and the University of Puerto Rico. Work conducted by the Center varies from simultaneously quantifying seventeen different antiretrovirals in human plasma/semen/breast milk/cervicovaginal fluid, to determining the kinetics of enzymatic reactions, to identifying novel metabolites in complex biological matrices, to determining novel bioactive compounds in dietary and herbal mixtures. Overall, users log over 200,000 hours of instrument time annually.

Over 30 students, post-doctoral fellows and faculty from across the UNC campus have been trained in the safe and effective use of the analytical equipment in the Center. More than 50 peer-reviewed publications have been written using data generated in the Center. Dr. Bridges is waiting for the results of an NIH Shared Instrumentation Grant that, if successful, will enable the Center to purchase a much needed quantitative, high resolution mass spectrometer.

# FACULTY AND SENIOR STAFF CHANGES

**ARABA AFENYI-ANNAN, M.D.** changed to Adjunct Assistant Professor effective October 1, 2011.

JOHN F. CHAPMAN, DR.P.H. retired from State service on September 30, 2011.

<u>**CHERIE H. DUNPHY, M.D.</u>** resigned her position effective March 26, 2012, to accept a position at Laboratory Corporation of America.</u>

**SANDRA BISHOP-FREEMAN, Ph.D.** was appointed Assistant Professor effective April 1, 2012. Her primary appointment is in the Office of the Chief Medical Examiner.

**JUSTIN O. BROWER, PhD.** was appointed Assistant Professor effective April 1, 2012. Her primary appointment is in the Office of the Chief Medical Examiner

**OLEG GORKUN, Ph.D.** changed to Adjunct Assistant Professor effective March 1, 2012.

**JOHANN D. HERTEL, M.D.** was appointed Assistant Professor effective July 1, 2012. He serves as attending pathologist and focuses on diagnostic pathology, cytopathology and surgical pathology.

JONATHON W. HOMEISTER, M.D., Ph.D. was promoted to Associate Professor effective May 1, 2012.

**<u>HEIKE HUNT, M.D.</u>** resigned her position effective December 31, 2012. She plans to return to work at Baystate Medical Center in Massachusetts after a brief break in service.

JOHN P. HUNT, M.D. resigned his position effective January 9, 2012, to return to work at Baystate Medical Center in Massachusetts.

**KAORU INOUE, Ph.D.** discontinued employment at UNC on July 31, 2011.

MASAO KAKOKI, M.D., Ph.D. was promoted to Associate Professor effective May 1, 2012.

**JOE N.KORNEGAY, D.V.M., PH.D.** resigned his position effective March 31, 2012 to accept a position at Texas A&M. He will continue as Adjunct Professor of UNC Pathology and Laboratory Medicine.

SUSAN T. LORD, Ph.D. retired from State service on October 31, 2011.

**<u>ROMMEL P. LU, M.D.</u>** was appointed Assistant Professor effective July 8, 2011. He serves as attending pathologist in Transfusion Medicine.

NADIA N. MALOUF, M.D. retired from State Service on June 30, 2011.

<u>CLAY NICHOLS, M.D.</u> was appointed Professor effective July 1, 2011. His primary appointment is in the Office of the Chief Medical Examiner.

KUMAR PANDYA, Ph.D. resigned his position 12/31/11, to accept a position in industry.

**JONATHAN D. PRIVETTE, M.D.** was appointed Assistant Professor effective September 1, 2011. His primary appointment is in the Office of the Chief Medical Examiner.

JAY RAVAL, M.D. was appointed Assistant Professor effective July 1, 2012. He serves as Attending Pathologist in Transfusion Medicine.

ASHLEY RIVENBARK, Ph.D. was appointed Assistant Professor effective January 1, 2012.

**<u>RUTH F. WALTERS, M.D.</u>** was appointed Adjunct Assistant Professor effective July 1, 2011. Her primary appointment is at Laboratory Corporation of America.

MONTE S. WILLIS, M.D., Ph.D. was promoted to Associate Professor effective September 11, 2011.

ALISA S. WOLBERG, Ph.D. was promoted to Associate Professor effective July 1, 2011.

# SPECIAL HONORS AND AWARDS

## WILLIAM B. COLEMAN, Ph.D.

2011 Blue Faery Award for Excellence in Liver Cancer Research from Blue Faery – The Adrienne Wilson Liver Cancer Association, April 2011

## MARILA CORDEIRO-STONE, Ph.D.

Dr. Cordeiro-Stone was asked by two graduates, one from the Curriculum in Toxicology and another from the Department of Biochemistry and Biophysics, to participate in hooding them at the May 7<sup>th</sup> 2011 Commencement Ceremony.

## SUSAN C. HADLER, M.D., M.S.

Sophomore Basic Sciences Teaching Award, Awarded by the UNC Medical Class of 2013 2011 White Coat Ceremony UNC Medical School: Coater

# CATHERINE A. HAMMETT-STABLER, Ph.D.

American Association of Clinical Chemistry Outstanding Speaker Award, 2010

## CRAIG A. FLETCHER, D.V.M., Ph.D.

Dr. Fletcher was accepted into the Office of Human Resources, University Leadership Education and Development (ULEAD) program that provides an opportunity to develop highly skilled and motivated leaders prepared to meet the challenges of the University's changing environment. The program's goals include: (1) increasing awareness of your professional strengths and developmental needs through assessment and coaching, (2) expanding the knowledge, skills, and abilities critical to those in a changing University environment through a range of experiential and classroom sessions.

## JUDITH NIELSEN, D.V.M.

2010 Citation in Faculty of 1000 Biology: evaluations for Okagaki LH, Strain AK, Nielsen JN, Charlier C, Baltes NJ, Chretien F, Heitman J, Dromer F, Nielsen K, (2010) Cryptococcal Cell Morphology Affects Host Cell Interactions and Pathogenicity. PLoS Pathog 6 (6): e1000953. Doi:10.1371/journal.ppat.1000953: e1000953 http://f1000biology.com/article/id/3866963/evaluation

## KUMAR R. PANDYA, Ph.D.

Dr. Pandya received the 2010 Commitment to Service Award for Unique Contributions in the areas of mentoring, service, or leadership – UNC Office of Post Doctoral Affairs.

## STEVEN RAY

Steven Ray, our Laboratory Specialist, became certified by the Microscopy Society of America as an Electron Microscopy Technologist. Significantly, in the letter reporting this, it was stated that he has achieved one of, if not the, best scores on the practical exam ever given by MSA! The Department awarded Steve a "Star Heels" award for this achievement.

#### JOAN M. TAYLOR, Ph.D.

2011 Star Heel Award

#### ELECTED LEADERSHIP POSITIONS

#### WILLIAM B. COLEMAN, Ph.D.

Secretary-Treasurer, The American Society for Investigative Pathology, July 2007-Present

## CHERIE H. DUNPHY, M.D.

President, North Carolina Pathology Society (through April 9, 2011)

#### WILLIAM K. FUNKHOUSER, M.D., Ph.D.

Council Member, Association of Directors of Anatomical and Surgical Pathology (ADASP)

#### PETER H. GILLIGAN, Ph.D.

Dean, American College of Microbiology Board of Goverors, American Academy of Microbiology

#### CATHERINE A. HAMMETT-STABLER, Ph.D.

President, Americal Association of Clinical Chemistry President, National Registry of Certified Chemists

#### J. CHARLES JENNETTE, M.D.

Past-President, Association of Pathology Chairs

#### HARVEY MICHAEL JONES, M.D.

Board of Governors, American Osler Society

#### SUSAN T. LORD, Ph.D.

Board of Councilors, International Fibrinogen Research Society

#### JUDITH NIELSEN, D.V.M.

North Carolina Academy of Laboratory Animal Medicine, President-Elect 2 yrs.

#### **VOLKER R. NICKELEIT, M.D.**

Vice President and Councilor, Executive Committee, Renal Pathology Society

#### KATHLEEN W. RAO, Ph.D.

Executive Committee, International Standing Committee and Human Cytogenetic Nomenclature Executive Committee, Board of Directors, American College of Medical Genetics (ACMG)

## HOWARD M. REISNER, Ph.D.

Councilor, Undergraduate Medical Educator's Section, Association of Pathology Chairs

#### JOHN L. SCHMITZ, Ph.D.

President, Association of Medical Laboratory Immunologists

#### HARSHARAN K. SINGH, M.D.

Vice Secretary, Renal Pathology Society, January-December 2010 Secretary, Renal Pathology Society, January 2011 – June 30, 2011

#### KAREN E. WECK, M.D.

Chair, Training and Education Committee, Association for Molecular Pathology

#### JULIA W. WHITAKER, D.V.M.

Board of Directors, North Carolina Academy of Laboratory Animal Medicine

#### **RUTH E. WINECKER, Ph.D.**

Chair, AAFS, Toxicology Section Program Chair Secretary, AAFS, Toxicology Section Secretary Board of Directors, ABFT, Board of Directors

#### JOHN T. WOOSLEY, M.D., Ph.D.

Member at Large, Undergraduate Medical Educator's Section, Association of Pathology Chairs

#### **LEADERSHIP POSITIONS**

#### JOHN F. CHAPMAN, Dr.P.H.

Chair, CCT Committee, NRCC Member (Advisor), CLSI Subcommittee on Serem Indices

#### WILLIAM B. COLEMAN, Ph.D.

Council, The American Society for Investigative Pathology Finance Committee Chair, The American Society for Investigative Pathology Finance Committee, Federation of American Societies for Experimental Biology Publications Committee, The American Society for Investigative Pathology Divisional Oversight Committee, The American Society for Investigative Pathology Membership Committee, The American Society for Investigative Pathology Education Committee, The American Society for Investigative Pathology

# MARILA CORDEIRO-STONE, Ph.D.

Member, Society of Toxicology, Career Resource and Development (CRAD) Committee (May1, 2009 to April 30, 2012) Interim Director, Curriculum in Toxicology Director of Graduate Studies, Curriculum in Toxicology

## CHERIE H. DUNPHY, M.D.

Chair, College of American Pathologists Diagnostic Immunology Resource Committee Chair, College of American Pathologists Hematology/Hematopathology Competency Dictionary Page Working Group, August, 2010-present

# ROSANN A. FARBER, Ph.D.

Judge, Annual DNA Day Essays, American Society for Human Genetics

# CRAIG A. FLETCHER, D.V.M., Ph.D.

Co-Chair, International Mock Board Exam Coalition for the American College of Laboratory Animal Medicine Board Exam, 2010 Interim Associate Director, Division of Laboratory Animal Medicine: Senior Clinical Veterinarian

## MARGARET L. GULLEY, M.D.

Chair, Topics Committee, Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Stakeholder's Group Chair, Epithelial Cell Section, 14<sup>th</sup> International Symposium on Epstein-Barr virus Associated Diseases, Birmingham, UK September 2010

## TRACY HEENAN, D.V.M.

Council Member, Certification of Professional IACUC Administrators (CPIA) Chair, CCPIA Leadership Committee Chair, CCPIA Exam Item Review *Ad hoc* consultant. Association for the Assessment and Accreditation for Laboratory Animal Care International (AAALAC)

# JONATHON W. HOMEISTER, M.D., Ph.D.

Section Chair, 13<sup>th</sup> Biennial Medwest Platelet Conference. Inflammation and Cardiovascular Disease.

Session Chair, American Society for Investigative Pathology, Symposium Chair

## J. CHARLES JENNETTE, M.D.

Chair, Association of Pathology Chairs.C Nominating Committee Council Member, Association of Pathology Chairs

## HARVEY MICHAEL JONES, M.D.

Chair, American Osler Society, Program Committee Chair, American Osler Society, Publications Committee

## KATHLEEN A. KAISER-ROGERS, Ph.D.

Chair, American College of Medical Genetics Salary Survey Committee

## DAVID G. KAUFMAN, M.D., Ph.D.

Chair, Society of Toxicology, Scientific Liaison Task Force

## SUSAN T. LORD, Ph.D.

Chair, International Society of Thrombosis and Haemostasis, Scientific Program Organizing Committee for XXII Congress

#### MELISSA B. MILLER, Ph.D.

Session Chair, 50<sup>th</sup> Interscience Conference on Antimicrobial Agents and Chemotherapy, "Best Practices in the Laboratory Diagnosis of Sexually-transmitted infections," Interactive Symposium, Boston, MA, September 2010

Session Chair, American Society for Microbiology, 111<sup>th</sup> General Meeting, Core Curriculum, May 23, 2011

## C. RYAN MILLER, M.D., Ph.D.

Member, National Cancer Institute, The Cancer Genome Atlas (TCGA), Glioblastoma Disease Working Group (DWG) Member, Scientific Advisory Committee, National Functional Genomics Center

#### JUDITH NIELSEN, D.V.M.

American College of Laboratory Animal Medicine, Exam Review Committee, 3 yrs.

## VOLKER R. NICKELEIT, M.D.

Session Chair, ASN 2010: Clinico-Pathologic Correlation Conference, November 2010 Banff- Group: Chair of Working Group / Task Force on "Polyomavirus Nephropathy Classification"

#### ARLIN B. ROGERS, D.V.M., Ph.D.

Chair, ACVP, Annual Meeting Plenary Session Co-Chair, ASIP, Liver Workshop Faculty Director, Animal Histopathology Core

#### JOHN L. SCHMITZ, Ph.D.

Chair, Credentials Committee: American Board of Medical Laboratory Immunology Co-Chair, ASHI Accreditation Review Board

#### JOAN M. TAYLOR, Ph.D.

Chair, AHA, Early Career Development Committee

#### RICHARD R. TIDWELL, Ph.D.

The Bill and Melinda Gates Foundation, Initiative on Public-Private Partnerships for Health (IPPPH)

World Health Organization, Drug Development, Preclinical and Clinical Studies; Treatment and Drug Resistance section for the World Health Organizations Scientific Working Group on African Trypanosomiasis Product Development Partnerships for Neglected Global Health Medicines for Malaria Ventures, Expert Scientific Advisory Committee

#### HERBERT C. WHINNA, M.D., Ph.D.

Chairman, Scientific Subcommittee on Plasma Coagulation Inhibitors of the International Society for Thrombosis and Hemostasis

#### JULIA W. WHITAKER, M.S., D.V.M.

Co-Chair, International Mock Board Exam Coalition for the American College of Laboratory Animal Medicine Board exam review

#### MONTE S. WILLIS, M.D., Ph.D.

Chair, Nomination Committee, National Sigma Xi Research Society Chair, Program Committee for Experimental Biology, American Society of Investigative Pathologists

## MEMBER OF BOARD OF DIRECTORS OF NATIONAL/INTERNATIONAL ACCREDITATION AGENCY

## JOHN F. CHAPMAN, Dr.P.H.

Member, National Registry of Certified Chemists

#### **GEORGETTE A. DENT, M.D.**

Member, Liaison Committee on Medical Education

#### CATHERINE A. HAMMETT-STABLER, Ph.D.

Member, BOD, National Registry of Certified Chemists

#### MELISSA B. MILLER, Ph.D.

Member, Board of Governors, American College of Microbiology

#### JOHN L. SCHMITZ, Ph.D.

Member, American Society of Histocompatibility and Immunogenetics Accreditation Review Board Member, American Board of Medical Laboratory Immunology

#### MEMBER OF FDA, CDC OR COMPARABLE COMMITTEE

#### JOHN F. CHAPMAN, Jr., Dr.P.H.

Member, (Advisor) CLSI Subcommittee on Serum Indices

#### FRANK C. CHURCH, Ph.D.

Organizer for the 6<sup>th</sup> International Meeting on Serpins, planned for October, 2011, UNC-CH

#### WILLIAM K. FUNKHOUSER, Jr., M.D., Ph.D.

Member, Medical Devices Advisory Committee

#### MELISSA B. MILLER, Ph.D.

Member, FDA Microbiology Devices Panel

## VOLKER R. NICKELEIT, M.D.

Member: OPTN/UNOS Ad Hoc Disease Transmission Advisory Committee

#### KATHLEEN W. RAO, Ph.D.

Member, Children's Oncology Group Cytogenetics Central Review Committee Member, Children's Oncology Group, Infant Leukemia Committee Member, Cancer and Leukemia Group B (CALGB) Cytogenetics Review Committee

#### JOHN L. SCHMITZ, Ph.D.

Member, United Network for Organ Sharing (UNOS) Histocompatibility Committee

#### KAREN E. WECK, M.D.

Member, Molecular and Clinical Genetics Devices Panel Consultant, FDA Medical Devices Advisory Committee

#### ALISA S. WOLBERG, Ph.D.

Member, FDA, Steering Committee, Workshop on IGIV and Thrombosis, "Risk Mitigation Stratigies to Address Potential Procoagulant Activity in Immune Globulin Products", 2011

#### MEMBER OF NIH OR COMPARABLE STUDY SECTION

#### WILLAM B. COLEMAN, Ph.D.

*ad hoc* External Grant Reviewer for the National Institutes of Health, Cancer Therapy Special Emphasis Panel, August 2011

*ad hoc* External Grant Reviewer for the Medical Research Council, United Kingdom, August 2011

*ad hoc* External Grant Reviewer for the American Institute of Biological Sciences, August 2011 *ad hoc* External Grant Reviewer for the National Institutes of Health, Cancer Diagnostics and Treatment SBIR/STTR Study Section, November 2011

*ad hoc* External Grant Reviewer for the National Institutes of Health, Special Emphasis Panel (P01 Study Section), January 2012

*ad hoc* External Grant Reviewer for the National Cancer Institute, National Institutes of Health, NCI-F Manpower and Training Study Section, February 2012

*ad hoc* External Grant Reviewer for the National Institutes of Health, Cancer Diagnostics and Treatment SBIR/STTR Study Section, March 2012

*ad hoc* External Grant Reviewer for the Medical Research Council, United Kingdom, May 2012 *ad hoc* External Grant Reviewer for the National Cancer Institute, National Institutes of Health, NCI-I Career Development Study Section, June 2012 *ad hoc* External Grant Reviewer for the National Institutes of Health, Cancer Diagnostics and Treatment SBIR/STTR Study Section, June 2012

# MARILA CORDEIRO-STONE, Ph.D.

NIH, ZRG1 FO5-R (20) L, Cell Biology and Development Training Fellowships, ad hoc March 2012

## DAVID EBERHARD, M.D., Ph.D.

Member, NCI, Clinical Assay Development Program Member, Genome Canada, Genomics and Personalized Health

## WILLIAM K. FUNKHOUSER, M.D., Ph.D.

Member, UNC TRACS Study Section (4 half-day meetings/year)

## MARGARET L. GULLEY, M.D.

NIH study section, Program in Innovative & Applied Emerging Technologies in Biospecimen Science, and Validation & Advanced Development of Emerging Technologies in Biospecimen Science, Special Emphasis Panel (2012)

#### DAVID G. KAUFMAN, M.D., Ph.D.

IMAT Program Grant Review Committee, NCI

#### WILLIAM KAUFMANN, Ph.D.

Member, Cancer Etiology, NIH

#### **VOLKER NICKELEIT, M.D.**

United Network of Organ Sharing (UNOS), Sub-committee 'Disease Tranmission Advisory Committee'

#### ARLIN B. ROGERS, D.V.M., Ph.D.

NCI, N01-CN-25002-78. Preclinical Efficacy and Intermediate Endpoint Biomarkers, Special Emphasis Panel

## RICHARD R. TIDWELL, Ph.D.

NIH, NIAID, ICTDR, Human African Trypanosomiasis: Strategic Research Direction

## DIMITRI TREMBATH, M.D., Ph.D.

Selection Committee for the American Medical Association (AMA) Foundation's 2011-12 Seed Grant Research Program

#### BERNARD E. WEISSMAN, Ph.D.

Study Section, NIH/CSR, Cancer Genetics

#### MONTE S. WILLIS, M.D., Ph.D.

Study Section Reviewer. American Heart Association. Cardiac Biology BCT5. March 20, 2012.

Molecular and Developmental Biology grant review panel, National Science Foundation Graduate Research Fellowship Program. January 2012.

## SERVICE AS EDITOR OR ON EDITORIAL BOARDS

#### FRANK C. CHURCH, PH.D.

Editorial Board, The Journal of Biological Chemistry Editorial Board, Journal of Thrombosis and Haemostasis Editorial Board, Thrombosis

#### WILLIAM B COLEMAN, Ph.D.

Member, Clinica Chimica Acta (C.-W. Lam, Editor-in-Chief), August 2000-Present
Member, The American Journal of Pathology (M.P. Lisanti, Editor-in-Chief), January 2007-Present
Member, Experimental and Molecular Pathology (J.M. Cruse, Editor-in-Chief), January 2007-Present
Member, Archives of Pathology and Laboratory Medicine (P.T. Cagle, Editor-in-Chief), April 2007-Present
Member, Laboratory Investigation (G.P. Siegel, Editor-in-Chief), July 2007-Present
Membr, BMC Cancer (M. Norton, Editor-in-Chief), February 2010-Present
Member, PLoS ONE (D. Pattinson, Executive Editor), December 2011-Present
Member, Current Pathobiology Reports (S.S. Monga, Editor-in-Chief), May 2012-Present

#### **GEORGETTE A. DENT, M.D.**

Member, Editorial Advisory Committee, UNC Medical Bulletin

## CHERIE H. DUNPHY, M.D.

Chief Editor, E-Medicine, Hematopathology Section, Pathology Member, Archives of Pathology and Laboratory Medicine Member, Haematologica Member, Case Reports in Medicine Member, International Journal of Medical and Biological Frontiers

## **GEORGE FEDORIW, M.D.**

Editorial Board, eMedicine Pathology

#### WILLIAM FUNKHOUSER, JR., M.D.

Section Editor, Molecular Pathology, Arch Path Lab Med

## PETER H. GILLIGAN, Ph.D

Editor, Journal of Clinical Microbiology Associate Editor, Clinical Microbiology Reviews Editorial Board, Mbio Editorial Board, Diagnostic Microbiology Editorial Board, Infectious Disease

#### MARGARET L. GULLEY, M.D.

Editorial Board, Diagnostic Molecular Pathology Editorial Board, American Journal of Surgical Pathology Editorial Board, PLOS Currents, Evidence for Genomic Applications

#### **CATHERINE HAMMETT-STABLER, Ph.D.**

Associate Editor, Clinical Biochemistry

#### TRACY HEENAN, D.V.M.

Associate Editor, Journal of the American Association for Laboratory Animal Science, #JAALAS-11-000107 "The Impact of Public Disclosure Laws on Biomedical Research", August 2011.

#### JONATHON HOMEISTER, M.D.

Editorial Board, Journal of Molecular and Cellular Cardiology

#### HEIKE HUNT, M.D.

# Editorial Board, Annals of Hepatology, Digestive Diseases and Science J. CHARLES JENNETTE, M.D.

Section Editor-Immunopathology, American Journal of Clinical Pathology Section Editor-Pathology, Journal of Nephrology Editorial Board, Clinical and Diagnostic Laboratory Immunology Editorial Board, Clinical Journal of the American Society of Nephrology Editorial Board, Journal of Rheumatology Editorial Board, Journal of Rheumatology Editorial Board, Kidney International Editorial Board, Laboratory Investigation Editorial Board, Clinical Nephrology Editorial Board, Pathology Case Reviews

## DAVID G KAUFMAN, M.D.

Editorial Board, Experimental and Molecular Pathology Editorial Board, Frontiers of Biosciences Editorial Board, Translational IncoGenomics Editorial Board, Clinical Medicine: Pathology Editorial Board, The Open Reproductive Science Journal

#### CHRISTOPHER MACK, Ph.D.

Editorial Board, Arteriosclerosis, Thrombosis, and Vascular Biology

#### MELISSA B. MILLER, Ph.D.

Editorial Board, Journal of Clinical Microbiology Editorial Board, Diagnostic Microbiology and Infectious Disease

#### C. RYAN MILLER, M.D.

Editorial Board, Journal of Clinical Microbiology Editorial Board, Brain Pathology Editorial Board, Brain Research Bulletin

#### **VOLKER NICHELEIT, M.D.**

Editorial Board, Kidney and Blood Pressure Research Editorial Board, World Journal of Transplantation Editorial Board, Nephrology Dialysis Transplantation Educational eTOC

## ASHLEY RIVENBARK, Ph.D.

ad hoc Reviewer, Archives of Pathology & Laboratory Medicine ad hoc Reviewer, BMC Cancer ad hoc Reviewer, Molecular and Cellular Biology ad hoc Reviewer, The EMBO Journal

## ARLIN ROGERS, M.D.

Editorial Board, Veterinary Pathology

## JOHN L. SCHMITZ, Ph.D.

Editorial Board, Clincial and Vaccine Immunology Editorial Board, Journal of Immunologic Methods

## DIMITRI TREMBATH, M.D.

Editorial Board, Journal of Neuropathology Editorial Board, Experimental Neurology

## KAREN WECK, M.D.

Editorial Board, Journal of Molecular Diagnostics Associate Editor, Molecular Genetics and Pharmacogenomics Editorial Board, Expert Review of Molecular Diagnostics Associate Editor, Genetics in Medicine

#### BERNARD E. WEISSMAN, Ph.D.

Editorial Board, Journal of Cellular Physiology Editorial Board, Genetics Research International Editorial Board, Lung Cancer Editorial Board, Targets and Therapy

## MONTE S. WILLIS, M.D., Ph.D.

Editorial Advisory Board, <u>Assistant Editor</u>, Laboratory Medicine, Fall 2008-Present Editorial Board, Skeletal Muscle, July 2010-present Editorial Board, World Journal of Hypertension, December 2010-present Editorial Board, Americal Journal of Physiology – Heart and Circulatory Physiology, January 1, 2011-December 31, 2011 Editorial Board, Journal of Molecular and Cellular Cardiology, January 1, 2011-December 31, 2013 Associate Editorial Board, Americal Journal of Cardiovascular Disease, March 2011-present Editorial Board, Americal Journal of Pathology, July 2011-present (3 year term) Editorial Board, Journal of Hypertension: Open Access. October 2011-present
Editorial Board, *Expert Opinion on Medical Diagnostics*. March 1, 2012-present (1 year term).
Editorial Board, *Cardiovascular Pathology*. January 1, 2012-present (3 year term).
Editorial Board, *American Journal of Pathology*. July 2011-present (3 year term).
Editorial Board, *Journal of Molecular and Cellular Cardiology*, January 1, 2011-December 31, 2013.
Editorial Board, *American Journal of Physiology – Heart and Circulatory Physiology*, January 1, 2011-December 31, 2012.
Editorial Board, *Journal of Microbial & Biochemical Technology*, November, 2010-present.
Editorial Board, *World Journal of Hypertension*, December 2010-present.

## ALISA WOLBERG, Ph.D.

Co-Editor, Thrombosis Research Supplemental Issue for 6<sup>th</sup> Symposium on Hemostasis with Special Focus on Tissue Factor, Factor VIIa, and Tissue Factor Pathway Inhibitor: Hemostasis and Beyond: 2012

Member, Editorial Board, Arterioscl, Thromb, Vasc Biol

Member, Advisory Board, J Thromb Haemost

#### JOHN T. WOOSLEY, M.D., Ph.D.

Editorial Board, Human Pathology

#### XIANWEN YI, Ph.D.

Ad hoc Reviewer, European Journal of Pharmacology Ad hoc Reviewer, European Journal of Nutrition Ad hoc Reviewer, The Journal of Nutrition Ad hoc Reviewer, PLoS ONE Ad hoc Reviewer, Journal of Diabetes & Metabolism

#### **INVITED LECTURES AT STATE/NATIONAL AND INTERNATIONAL MEETINGS**

#### JESSICA BOOKER, Ph.D.

"Making the Transition from Southern Blots to PCR-based Methylation Testing" in the Advancements in FMR1 Methylation PCR" workshop at the Association for Molecular Pathology annual meeting, November 18, 2011.

#### WILLIAM B COLEMAN, Ph.D.

American Society for Investigative Pathology, Annual Meeting, April 2012, San Diego, CA

Oral Presentation: "Identification of new pathways for targeted breast cancer therapy." A.G. Rivenbark, R. Sandhu, J.D. Roll, and W.B. Coleman (Presenter)

# DAVID A. EBERHARD, M.D., Ph.D.

Eberhard DA. QA of Tumor Samples for Molecular Analyses. Molecular Med Tri-Con 2012, San Francisco, CA Feb 19-23 2012.

## CRAIG A. FLETCHER, Ph.D.

International Mock Board Exam Coalition for the American College of Laboratory Animal Medicine Board exam review. The North Carolina Association of Laboratory Animal Medicine Workshop in Laboratory Animal Medicine, Thursday, May 20, 2012, Co-chair for Southeast region. 2010-unspecified

"Take 2 Tabs and Call Me in the Morning", A discussion of USDA / PHS expectations of clinical care, disease surveillance, & surgical requirements- Update to the Guide for the Care and Use of Laboratory Animals: The National Academy of Sciences' 8th Edition: A Professional Development Conference for Researchers, March 18, 2011 North Carolina Biotechnology Center, Research Triangle Park, N.C.

#### PETER H. GILLIGAN, Ph.D

The use of algorithms in the laboratory diagnosis of *Clostridium difficile* infections. Alere Webinar Two sessions. March 2012

Emerging Pathogens: How do we detect them; how do we track them. ASMCUE, Santa Rosa,CA June 2012 Clinical Microbiology Quiz General Meeting of the Ameican Society for Microbiology, San Francisco, CA June 2012

## MARGARET L. GULLEY, M.D.

"Molecular Surgical Pathology for the Practicing Pathologist", 8 lectures in a continuing medical education course, American Society for Clinical Pathology, Santa Fe, April 13-1519-21, 2012.

"New Molecular Oncology Lab Tests", Hematology/Oncology Conference, UNC Chapel Hill, April 30, 2012.

## CATHERINE HAMMETT-STABLER, Ph.D.

Turning Lies, Misconceptions, a d Myths into Truth: Using Pharmacokinetics to Unravel Urine Drug Testing. Drug Enforcement Agency HIDTA Pharmaceutical Diversion Training. Greensboro, NC. October 12, 2011 What's New in Endocrinology Testing? Department of Pathology and Laboratory Medicine Conference, Selected Topics in Endocrine Pathology for the Practicing Pathologist; Chapel Hill,NC. April 28, 2011.

What's in Your Sample? Keynote address, Innovative Sample Prep and Target Enrichment in Clinical Diagnostics. Cambridge Healthtech Institute; Newport Beach, CA. April 18-19, 2012.

## TRACY HEENAN, D.V.M.

2012 Public Responsibility in Medicine and Research (PRIM&R) IACUC Conference – Boston, MA; Facilitator Workshop A16, Closing the Loop: Semi-Annual Evaluation Follow-Up and Institutional Official (IO) Reporting (Program Oversight Track), March 20, 2012.

2012 PRIM&R IACUC Conference – Boston, MA; Didactic/Workshop C14, Guide 8th Edition: Implications of Chapters 1 & 2 for Your IACUC (IACUC Administration/Management and Process Track), March 21, 2012.

North Carolina Association for Biomedical Research (NCABR), IACUC 2012 Conference. Workshop: Safeguarding Animal Welfare: Investigating and Reporting Animal Welfare Concerns. May 3, 2012.

## J. CHARLES JENNETTE, M.D.

Invited Lectures, Columbia University Postgraduate Review Course: Renal Biopsy in Medical Diseases of the Kidney, "Rapidly Progressive Glomerulonephritis and ANCA" and "IgA Nephropathy and H-S Purpura", New York, NY, August 3, 2011,

Invited Lectures, American Society of Nephrology Renal Week Postgraduate Education Course: Basic Renal Pathology – from Bedside to Bench, "IgA Nephropathy," "Diabetic Glomerulosclerosis," "Crescentric Glomerulonephritis," and "Vasculitis," Philadelphia, PA, November 8-9, 2011.

Invited Lectures, American Society of Nephrology Renal WeekPostgraduate Education Course: Glomerulonephritis Update: "Pathology of Rapidly Progressive Glomerulonephritis" and "Pathology and Classification of Lupus Nephritis and IgA Nephopathy", Philadelphia PA, November 9, 2011.

Invited Lectures, International Society of Nephrology Pre-Conference Renal Pathology Course, "Concentric Glomerulonephritis" and "Lupus Nephritis, " Dubai, December 9, 2011.

Invited Lecture: Asia Pacific Vasculitis and ANCA Workshop Meeting, "Pathology and Pathogenesis of ANCA Vasculitis: Implications for Treatment," Shinagawa, Japan, March 30, 2012.

Invited Lecture: Asia Pacific Vasculitis and ANCA Workshop Meeting, "2012 Chapel Hill Consensus Conference Nomenclature of Vasculitides," Shinagawa, Japan, March 28, 2012. Invited Lectures (2), Nephropathology Course, Instituto Nacional de Ciencias Medicas, "The CHCC 2012 Nomenclature of Vasculitis" and "Pathogenesis of Antineutrophil Cytoplasmic Autoantibody Vasculitis", Mexico City, March 9, 2012. Visiting Professor, "Rapidly Progressive (Crescentic) Glomerulonephritis", Department of Nephrology, Union Hospital, Tongji Medical College, Wuhan, China, April 11, 2012 Visiting Professor, "Diagnosis and Classification of Vasculitides," Department of Nephrology, Xi-Jing Hospital of Fourth Military Medical University, Xi-An, China, April 5, 2012. Visiting Professor, "Pathology and Pathogenesis of ANCA Vasculitis", Department of Nephrology, First Hospital of Beijing University, Beijing, China, April 2, 2012. Visiting Professor, "Pathology and Pathogenesis of ANCA Vasculitis", Sendai, Japan, March 27, 2012.

# H. MICHAEL JONES, M.D.

American Osler Society, Annual Meeting, Chapel Hill, NC April 22-25, 2012: *The Way of a Teacher-William deBerniere MacNider*, a video documentary

# KATHLEEN KAISER-ROGERS, PH.D.

"Structural Chromosome Rearrangements" UNC-Greensboro Genetic Counseling students, 120 minutes 1/26/12

Problem solving conference, UNC-Greensboro Genetic Counseling students, 60 minutes 1/26/12 "Molecular Cytogenetics" UNC-Greensboro Genetic Counseling students, 120 minutes 2/2/12 Problem solving conference, UNC-Greensboro Genetic Counseling students, 60 minutes 2/2/12

# MASAO KAKOKI

University of Texas Health Science Center, "Cardiovascular pathogenesis in mice underexpressing transforming growth factor beta1", 10/3/12

## DAVID G KAUFMAN, M.D.

Johnson C. Smith University, Charlotte, NC, November 7, 2011.

## WILLIAM K. KAUFMANN, Ph.D.

New York University, "The DNA damage response and environmental cancer" September 27, 2011

University of Kentucky, October 31, 2011, "The human replication fork protection complex" Purdue University, November 10, 2011, "Cell cycle checkpoints and cancer"

Indiana University, December 1, 2011, "Cell cycle checkpoints and cancer"

University of South Carolina School of Medicine. January 12, 2012, "The human replication fork protection complex"

# APRIL E. KEMPER

Maglione M. and Kemper AE. Barcoding and Tracking: Improving Workflow and Reducing Errors in a Large Academic Medical Center's Anatomic Pathology Laboratory. The North

Carolina Society of Histopathology Technologists 2012 Spring Meeting. Research Triangle Park, North Carolina

## CHRISTOPHER MACK, Ph.D.

Epigenetic regulation of vascular smooth muscle phenotype, University of North Carolina, Dept. of Cellular and Molecular Physiology, 1/9/12

#### NOBUYO N. MAEDA, Ph.D.

Invited Speaker, University of Tennessee Knoxville, April 8, 2012

#### MELISSA B. MILLER, Ph.D.

Association for Molecular Pathology, 2011 Annual Meeting, "Transforming the rapid diagnosis of influenza," Grapevine, TX, November 16, 2011

Infectious Disease Society of America, 49<sup>th</sup> Annual Meeting, Interactive Session, Molecular Microbiologist Expert, "The Venn Diagram of Diagnosis: The Contribution of Histopathology, Microbiology, and Molecular Technology in the Diagnosis of Infectious Diseases," Boston, MA, October 21, 2011

American Society for Microbiology, 51<sup>st</sup> Interscience Conference on Antimicrobial Agents and Chemotherapy, Meet-the Experts Session, "Diagnostic Considerations and Challenges and Challenges for Chlamydia trachomatis and Neisseria gonnorrhoeae," Chicage, IL, September 19, 2011.

American Society for Microbiology, 112<sup>th</sup> General Meeting, "The impact of MALDI-TOF on the clinical microbiology laboratory," San Francisco, CA, June 18, 2012. American Society for Microbiology, 112<sup>th</sup> General Meeting, Workshop, "Case Studies and Statistics for the Verification and Validation of Molecular Methods in the Clinical Laboratory," San Francisco, CA, June, 16, 2012.

Children's Advocacy Centers of North Carolina, Child Abuse and Neglect Symposium, "Evaluating sexually transmitted infections in children," Fayetteville, NC, May 11, 2012. Pan American Society for Clinical Virology, 28<sup>th</sup> Annual Clinical Virology Symposium, "HCV patient management: translating molecular diagnostics into clinical care," Daytona Beach, FL, April 23, 2012.

Pan American Society for Clinical Virology, 28<sup>th</sup> Annual Clinical Virology Symposium, "Comparison of four commercial respiratory viral panels for analytical performance and workflow," Daytona Beach, FL, April 23, 2012.

First Coast Infectious Disease/Clinical Microbiology Symposium, 19<sup>th</sup> Annual Meeting, "Update on the diagnosis and treatment of hepatitis C," St. Augustine, FL, January 28, 2012.

Infectious Disease Grand rounds (co-presented with Anne Lachiewicz and Ralph Raasch), "Can  $\beta$ -lactam/ $\beta$ -lactamase inhibitor combinations be used for treatment of ESBL-producing E coli?" April 13, 2012.

## C. RYAN MILLER, M.D.

Dissecting the cellular and molecular requirements for astrocytoma initiation and progression using genetically-engineered mouse models. Preston Robert Tisch Brain Tumor Center. Duke University. Durham, NC. May 16, 2012.

Genomic classification of glioblastoma. Alliance for Clinical Trials in Oncology. Chicago, IL. March 17, 2012.

Genomic subtype-specific mouse models for glioblastoma drug development. Damon Runyon – Accelerating Cancer Cures Research Symposium. New York, NY. March 5, 2012.

## VOLKER NICKELEIT, M.D.

Update on Polyomavirus Nephropathy; Astellas Pharmaceutical Research Advisory Group Meeting, December 15, 2011.

Course on *The Practice of Nephropathology* (Nephropathologiekurs Volhard-Fahr), lecturer on 'Transplant Pathology', Mannheim Germany, March 2012

Glomerular-Disease Collaborative Network meeting (GDCN 26th annual conference): "Renal biopsy case discussion: an interactive forum". May 2012, Chapel Hill, NC, USA

## YARA PARK, M.D.

Invited Lecturer, The use of Therapeutic Plasma Exchange in ABO Incompatible Renal Transplants, North Carolina Association of Blood Bankers Spring Workshop, 2012

Invited Lecturer, Neonatal Transfusions and Transfusion Related Acute Gut Injury, University of North Carolina Hospitals, Department of Pediatrics, Division of Hematology/Oncology, 2012

Invited Lecturer, Bone Marrow and Solid Organ Transplants, University of North Carolina Hospitals, Department of Medicine, Hematology/Oncology Fellows, 2012

## ASHLEY G. RIVENBARK, Ph.D.

American Society for Investigative Pathology, Annual Meeting, San Diego, CA Oral Presentation: "Epigenetic reprogramming of cancer cells via targeted DNA methylation." A.G. Rivenbark (Presenter), April 2012

## JOHN L. SCHMITZ, Ph.D.

North Carolina Association of Blood Banks Annual Meeting, HLA testing in support of platelet transfusion: Impact of molecular typing and solid phase antibody detection methods. September 13, 2011

Overview of Laboratory Inspection Process. Inspector Training Workkshop. ASHI Annual Meeting. October 17, 2011

UNC Transplant Educational Conference Series. Feb 8, 2012 "Coming to grips with HLA antibody testing"

## HARSHARAN SINGH, M.D.

Glomerular Disease Collaborative Network Annual Meeting, Chapel Hill, NC. May 19-20, 2012: Renal Biopsy Case Presentations.

Department of Transplantation Surgery Transplant Conference, May 9, 2012: Screening Tests for Polyomavirus Nephropathy.

## SCOTT V. SMITH, M.D.

Selected Topics in Endocrine Pathology for the Practicing Pathologist, The Department of Pathology and Laboratory Medicine, UNC School of Medicine, April 28, 2012; "Tumors of the Adrenal Gland and Extra-Adrenal Paraganglia"

#### **OLIVER SMITHIES, D.Phil.**

Breadth of Research at Carolina, High-level Administrators from UNC General Administration who advocate on UNC's behalf with State Legislature and Congress, UNC-CH, September 15, 2011

Board of Visitors, "A Conversation with a Nobel Laureate" with Chancellor Holden Thorp, George Watts Hill Alumni Center, UNC-CH, October 14, 2011

University of Alberta, Edmonton, Canada, E. Garner King Memorial Lecture, "On Being a Scientist for 60 Years", October 31, 2011

2011 Nobel Laureate Lecture, Scientific Sessions, American Heart Association, Orlando, Florida, "On Being a Scientist for 60 Years", November 14, 2011

Interview with David Fisher, WUNC Studio, August 9, 2011

Meeting with Dr. Kyung-Soo Chun and his pharmacy students from Korea, January 18, 2012

NC State University, College of Veterinary Medicine, Litwack Lecture, January 20, 2012

Duke University Medical Center, 2012 Merel Harmel Lecture, Departments of Anesthesiology and Surgery, January 25, 2012

Oliver Smithies Nobel Symposium, UNC-CH, March 14, 2012

Host to Dr. Michiaki Abe, Nephrologist from Japan, March 19, 2012

Experimental Biology, APS Nobel Prize in Physiology or Medicine Lecture Series, Inaugural Lecture, "On Being a Bench Scientist for 50 Years", San Diego, California, April 25, 2012

University of California, San Diego, Department of Pharmacology, Graduate Studies, "On Being a Scientist for 60 Years", April 26, 2012

Georgia Health Sciences University, Augusta, Georgia, Department of Physiology, Ninth Annual Virendra B. Mahesh Lecture, "On Being a Scientist for 60 Years", May 10, 2012

UNC-CH, Grand Rounds, Department of Pathology and Laboratory Medicine, "Challenging the Kidney with Gold Nanoparticles" May 24, 2012

Seawell Elementary School Nobel Prize Lecture, Chapel Hill, NC, June 6, 2012

## DIMITRI TREMBATH, M.D., Ph.D.

UNC CME event April 28th, 2012, "Intra-op Dx of Pituitary Tumors"

## CYRUS VAZIRI, Ph.D.

"Integrating TLS with the Cell Cycle", NIEHS, NC, Nov 2011

"Regulation of DNA Polymerase eta by Rad18", NC State University, NC, March 2012

"Integrating TLS with DNA Replication", 244<sup>th</sup> ACS Meeting, Pennsylvania, August 2012

## KAREN WECK, M.D.

"Case Studies in Molecular Genetics: Cystic Fibrosis Mutation Analysis and BRCA1/2 Analysis," Association of Molecular Pathology Outreach Course, Dallas, TX November 16, 2011.

"Pharmacogenomic Testing to Individualize Cancer Therapy," Next Generation Diagnostics Summit, Washington, DC, August 22, 2011.

"Anedotes of Success in Personized Medicine: Pharmacogenomics," Association for Pathology Chairs Annual Meeting, Monterey, California, July 13-15, 2011.

"Pharmacogenetic testing", Duke School of Medicine, Department of Genetics, June 29,, 2011. "Application of Pharmacogenomic Technologies in the Clinical Laboratory," 2<sup>nd</sup> Latin American Pharmacogenomic and Personalized Medicine Congress, Rio deJaneiro, Brazil, June 28-29, 2012. Pharmacogenomic Testing to Direct Clinical Therapy at UNC, Gentris Corporation, RTP, Morrisville, NC, December 15, 2011 BERNARD E. WEISSMAN, Ph.D.

November 17, 2011 Invited Speaker, Laboratory of Molecular Carcinogenesis, NIEHS, RTP, NC "Remodeling the Cancer Genome: The Role of the SWI/SNF Complex in Human Tumor Development"

November 18, 2011 Keynote Speaker, 11<sup>th</sup> Annual Hollings Cancer Center Research Retreat, MUSC, Charleston, SC "Remodeling the Cancer Genome: The Role of the SWI/SNF Complex in Human Tumor Development"

February 10, 2011 Invited Speaker, University of Texas at Brownsville, Brownsville, TX "The Role of Aberrant Chromatin Remodeling in Human Tumor Development"

## MONTE S. WILLIS, M.D., Ph.D.

American Heart Association Scientific Sessions 2012. Symposium titles: "Post-translational Regulation in Cardiac Physiology and Disease". Invited by chair Dr. Heinrich Taegtmeyer. Talk entitles "The role of sbiquitin ligases in the regulation of cardiac metabolism and mitochondrial biology in cardiac disease". November 14, 2011.

12th Annual Career Development Program: Fundamental Basics for Success: How to Write Award-Winning Grants. April 22. 2012. American Society of Investigative Pathology. Experimental Biology, San Diego, CA. Talk entitled "Developing ideas into fundable research grant proposals".

International Society of Heart Research (ISHR)/North American Section, "Ubiquitin proteosome system inhibition as a therapeutic target in cardiac disease". Banff, Alberta, Canada. May 29, 2012.

Elizabeth City State University Graduate Seminar Series, Department of Biology, Elizabeth City, NC. Talk entitled "Regulating cardiomyocyte size and energy metabolism by the ubiquitin proteasome system". March 21, 2012.

Learner Research Institute, The Cleveland Clinic, "Muscle Ring Finger 1(MuRF1)'s Regulation of Cardiac Hypertrophy and Energy Metabolism". Cleveland, OH. June 6, 2012.

#### ALISA WOLBERG, Ph.D.

XXIIIth Annual Meeting for the International Society on Thrombosis and Haemostasis, Scientific Subcommittee on Vascular Biology, Kyoto, Japan, "Differntial Contributions of Monocyte-and Platelet-derived Microparticles towards Thrombin Generation and Fibren Formation and Stability", July 23, 2011 AHA Council on Arteriosclerosis, Thrombosis, and Vascular Biology Annual Meeting, Chicago, Il, "Roles of Factor VIII and fibrogen in venous thrombosis", April 18, 2012

# XIANWEN YI, M.D., Ph.D.

2012- Keystone Symposium, Complications of Diabetes: Mechanisms of Injury and Failure of Repair, (C5), Boston, MA

2012- Hohhot International Endocrine Disease Forum, Hohhot, Inner Mongolia, China

# MAIMOONA ZARIWALA, Ph.D.

PCD Foundation: Family Education Day, Durham, NC, USA, Status of current PCD Genetics., June 30, 2012.

ESP Steering Committee Meeting, Teleconference, Idiopathic Bronchiectasis., August 4, 2011.

# **DIRECTOR OF CONTINUING EDUCATION COURSES**

# WILLIAM B COLEMAN, Ph.D.

Experimental Biology 2012, April 2012, San Diego CA, Breast Cancer Workshop: Breast Cancer and Personalized Medicine. Workshop Organizers and Session Chairs: A.G. Rivenbark and W.B. Coleman.

## WILLIAM FUNKHOUSER, JR., M.D.

ASCP Educational Course, "Molecular Surgical Pathology", Santa Fe, NM, 4/19-21/12

## KEVIN E. GREENE, M.D.

Selected Topics in Endocrine Pathology for the Practicing Pathologist, The Department of Pathology and Laboratory Medicine, UNC School of Medicine, April 28, 2012; "Neuroendocrine Tumors of the GI Tract and Pancreas"

## J. CHARLES JENNETTE, M.D.

International Summer School of Renal Pathology, Lectures and Labs, Bari, Italy, May 28-31, 2012

Long Course (CME), National Kidney Foundation Spring Clinical Meeting, "A Practical Approach to Renal Pathology", Washington, DC, May 9, 2012

Short Course (CME), United States and Canadian Academy of Pathology Annual Meeting, Short Course (CME), United States and Canadian Academy of Pathology Annual Meeting, "Pathology

of Blood Vessels: Vasculitides, Vasculopathies and Coagulopathies", Vancouver, Canada, March 21, 2012

# SUSAN J. MAYGARDEN, M.D.

UNC Department of Pathology CME course: Selected topics in endocrine pathology for the practicing pathologist, Friday Center, April 28, 2012

## ASHLEY G. RIVENBARK, Ph.D.

Experimental Biology 2012, Discussion – Breast Cancer Scientific Interest Group Lunch/Networking Session, April 2012

Experimental Biology 2012 Breast Cancer Workshop: Personalized Medicine and Breast Cancer, April 2012

# SCOTT V. SMITH, M.D.

Selected Topics in Endocrine Pathology for the Practicing Pathologist, The Department of Pathology and Laboratory Medicine, UNC School of Medicine, April 28, 2012; "Tumors of the Adrenal Gland and Extra-Adrenal Paraganglia"

## KAREN WECK, M.D.

Course Director, "Current Applications of Molecular Pathology: Real time updates and **case** studies," Association of Molecular Patholigy Outreach Course, November 16, 2011, Dallas, TX.

## ALISA WOLBERG, Ph.D.

Co-Chair, 6<sup>th</sup> Symposium on Hemostasis with Special Focus on Tissue Factor, Factor Vlla, and tissue Factor Pathway Inhibitor: Hemostasis and Beyond, May 3-5, 2012

## SERVICE ON UNC AND UNCH COMMITTEE

## ROBERT C. BAGNELL, Ph.D.

Member, Microscopy Core Labs Sub-Committee

## DWIGHT A. BELLINGER, D.V.M., Ph.D.

Member, Institutional Biosafety Committee Member, Institutional Animal Care and Use Committee

## THOMAS W. BOULDIN, M.D.

Member, Graduate Medical Education Committee Member, North Carolina Cancer Hospital Executive Committee

## CLAUDIA M. BRADY, M.H.S.

I was a member of committees that created a new part type dictionary in Co-Path and helped implement and unveil Advanced Barcode and Tracking that was initiated in Surgical Pathology in September 2011. This process has been crucial in minimizing laboratory clerical errors and more effectively moves specimens through the entire laboratory process from receipt to long term storage.

## ARLENE S. BRIDGES, Ph.D.

Chair, UNC Health Sciences Labrary Advisory Committee Member, University Library System Advisory Committee Member, UNC TraCS Core Ditrytors Committee Member, Committee to Develop HR Tracks for Core Facilty Personnel

## FRANK C. CHURCH, Ph.D.

Member, Strategic Priority Group 1 Member, Morehead-Cain Foundation, Central Selection Committee Member, University Research Council Grants Review Panel Member, 2<sup>nd</sup> year Course Directors Committee (CC2) Member, Medical School Admissions Committee Member, Academy of Distinguished Teaching Scholars, UNC-CH Fellow, Academy of Educators, UNC-CH School of Medicine Member, Teaching Champions

## WILLIAM B. COLEMAN, Ph.D.

Member, Department of Pathology and Laboratory Medicine Research Advisory Committee

#### MARILA CORDEIRO-STONE, Ph.D.

Member, Executive Committee of the Curriculum in Toxicology Member, Executive Committee of the Biological and Biomedical Science Program Member, Mentoring Committee Chair, Executive Committee of the Curriculum in Toxicology

## **GEORGETTE A. DENT, M.D.**

Member, Curriculum Operations Committee Member, Education Committee Member, 1<sup>st</sup> year Course Directors Committee Member, 2<sup>nd</sup> year Course Directors Committee Member, 3<sup>rd</sup> & 4<sup>th</sup> year Course Directors Committee Member, LCME Operations Committee Member. Student Promotions Committee Chair, Hospital Infection Control Committee Chair, Hematopathology Directory Search Committee *Ex officio Member*, Student Admissions Committee

## DAVID EBERHARD, M.D., Ph.D.

Member, UNC Tissue Procurement Facility (TPF) External Advisory Committee Member, UNC Heme-Onc Tissue Procurement Committee (HOTP Member, UNC Committee for the Communication of Genetic Research Results (CCGR) Chair, UNCseq (LCCC1108) Pathology Committee

#### ROSANN A. FARBER, Ph.D.

Member, University APT Committee Member, SOM Conflict of Interest Committee Member, Department of Genetics Advisory Committee

#### **GEORGE FEDORIW, M.D.**

Member, UNC Cancer Sequencing Project: Pathology Committee (Lineberger CCC) Member, UNC Heme/onc tissue procurement committee (HOTPC: Lineberger CCC)

## CRAIG A. FLETCHER, D.V.M., Ph.D.

Member, IACUC subcommittee on Animal Concerns Member, Ad Hoc SOM/DLAM Space committee Member, DLAM Advisory Committee Member, University-wide Laboratory Animal Strategic Planning/Stakeholder's Committee Member, SOM Office of Research Member, Institutional Animal Care and Use Committee Member, Institutional Biosafety Committee

#### WILLIAM K. FUNKHOUSER, Jr., M.D.

Member, Chair's Clinical Advisory Committee

#### PETER H. GILLIGAN, Ph.D.

Chair, Admissions Committee

## VIRGINIA GODFREY, D.V.M., Ph.D.

Member, SOM Fixed Term Promotions Member, Search Committee for DLAM Director

#### KEVIN G. GREENE, M.D.

Member, MS2 GI Block Planning Committee, Course Co-Director Member, 2 CC2 (2nd year curriculum committee)

#### MARGARET L. GULLEY, M.D.

Member, UNC Clincal Translational Science Award, Section Leader Member, UNCH RAM Lab Clinical Genetics Advisory Group to UCRF Member, Executive Director's Advisory Group, Department of Pathology and Laboratory Medicine Chair, Biobanking Committee for UNC TraCS Institute

#### SUSAN HADLER, M.D.

Member, 2<sup>nd</sup> Year Curriculum Committee (Medical School) Member, 4<sup>th</sup> Year Clinical Capstone Course (Medical School) Member, Interview MS 2 Students for Ashville Program (Medical) Member, Assessment Committee (Medical School) Member, Research in the Medical Curriculum (Medical School) Member, Dental School Admissions Committee Member, Dental School 1<sup>st</sup> Year Teaching Committee Member, Assessment Revision Committee (Dental School)

#### CATHERINE A. HAMMETT-STABLER, Ph.D.

Member, Clinical Documentation Committee Member, CDC Forms Review Committee Member, 2<sup>nd</sup> year Course Director Chair, IRB Committee B

#### TRACY HEENAN, D.V.M.

Member, Faculty Council (July 2010 - May 2013) Member, DLAM Advisory Committee (appointed June 2004) Member, IACUC Animal Concern Subcommittee Member, IACUC Member, Child Care Advisory Committee Member, Vice Chancellor for Research Senior Staff Member Search Committee Chair – Training and Compliance Manager Chair, IACUC/DLAM Leadership Committee Vice Chancellor, Research (VCR) Compliance Task Force Founder and Co-Chair, Network of Laboratory Animal Coordinator [NLAC] Steering Committee

## JONATHON HOMEISTER, M.D., Ph.D.

Chairman, Education Committee, Molecular and Cellular Pathology Graduate Program Member, Executive Committee, Molecular and Cellular Pathology Graduate Program Member, ASIP Education Committee Member, ASIP Meetings and Courses Task Force

## J. CHARLES JENNETTE, M.D.

Member, UNC Health Care System Executive Council Member, Dean's Advisory Committee of the UNC School of Medicine Member, UNC Physician's & Associates Member, Medical Staff Executive Committee Member, UNC Physicians and Associates Payor Relations Committees Chair, 5 Year Review Committee, Chair of Biochenistry and Biophysics

## DAVID G. KAUFMAN, M.D., Ph.D.

UNC SOM, Bridge Funding Selection Committee Chair, Radiation Safety Committee Chair, UNC SOM, Jefferson-Pilot and Woods Award Selection Committee

## WILLIAM K. KAUFMANN, Ph.D.

Member, Research Advisory Committee Chair, Grisham Search Committee Director, Interdisciplinary Research Director, Center for Environmental Health and Susceptibility

## CHRISTOPHER P. MACK, Ph.D.

Member, UNC McAllister Heart Institute Executive Committee Member, IVB Trainng Grant Executive Committee Chair, Department Of Pathology Faculty Assessment

#### NOBUYO MAEDA, Ph.D.

Member, DLAM Space Committee Member, Pathology Research Advisory Committee Member, MHI Search Committee Member, Pathology Junior Faculty Search Committee Member, Pathology Metabolomics Search Committee Member, Pathology Grisham Professor Search Committee Chair, DLAM Advisory Committee

## SUSAN J. MAYGARDEN, M.D.

Member, Graduate Medical Education Committee

## MELISSA B. MILLER, Ph.D.

Member, Hospital Infection Control Committee, UNC Health Care Member, Anti-Infective Subcommittee of the Pharmacy and Therapeutics Committee, UNC Health Care

## C. RYAN MILLER, M.D., Ph.D.

Member, Lineberger Comprehensive Cancer Center Clinical Genomics Member, Lineberger Comprehensive Cancer Center Clinical Sequencing Pathology Committee

## JUDITH N. NIELSEN, D.V.M.

Member, Network of Laboratory Animal Coordinators Steering Committee – approx. 4 meetings/yr. Member, Institutional Animal Care and Use Committee – 14 meetings plus ~ 4 semiannual facility inspections/yr. Member, IACUC subcommittee on Pharmaceuticals for Use in Laboratory Animal Research – did not meet this year, but fielded questions from faculty regularly. Member, Ad Hoc SOM/DLAM Space committee, 5 meetings. Member, DLAM Advisory Committee, 4 meetings Member, University-wide Laboratory Animal Strategic Planning/Stakeholder's Committee 4-6 meetings Member, DLAM/IACUC Animal Enrichment Committee, newly organized; 1 meeting so far.

# YARA A. PARK , M.D.

Member, Pharmaceuticals and Therapeutics Committee Member, Graduate Medical Education Committee

## KATHLEEN W. RAO, Ph.D.

Member, Curriculum Committee Member, Block 9 Course Committee Member, Strategic Planning Task Force: Curriculum Redesign Co-Chair, UNCH Second Year Curriculum Committee

## ASHLEY G. RIVENBARK, Ph.D.

Session Chair and Organizer, Lineberger Comprehensive Cancer Center 36<sup>th</sup> Annual Postdoc-Faculty Research Day, September 2011

Co-Organizer, Department of Pathology and Laboratory Medicine Annual Research Symposium, September 2011

## ARLIN B. ROGERS, D.V.M., Ph.D.

Member, Molecular and Cellular Pathology Preliminary Exam Committee

#### JOAN M. TAYLOR, Ph.D.

Member, Core Facilities Advisory Committee Member, Animal Models Core Oversight Committee Member, Department of Pathology, Research Advisory Committee Member, School of Medicine Strategic Planning Committee (SP3) Member, McAllister Heart Institute, Executive Committee Member, School of Medicine Conflict of Interest Committee Member, Integrative Vascular Biology Training Program Admissions Committee Chair, Animal Models Cores Oversight Committee

#### LEIGH B. THORNE, M.D.

Member, SOM Core Facility Advisory Committee Member, SOM Strategic Planning Committee (Task Force 2) Member, HOTPC (Hematology Oncology Tissue Procurement Committee) Member, NC TraCS Institute Biobanking Committee

#### RICHARD R. TIDWELL, Ph.D.

Member, Biomedical IRB Board (thru Nov. 2011) Member, UNC-CH Research Advisory Council Member, UNC-CH Aids Clinical Trials Group Member, UNC-CH Advisory Board for the Centers for Infectious Disease Chair, Carolina Center for Clinical Drug Development Advisory Board

#### MICHAEL D. TOPAL, Ph.D.

Chair, UNC Core Facilities Advocacy Committee, 2008-present (monthly) Chair, UNC Office of Translational Technologies Core Facilities, 2009-present (weekly) Member, Vice Dean of Research Management Team, 2010-present (weekly) Chair, UNC Regional Genomics Facility Committee, 2011 (monthly) Chair, Committee to Establish Fixed-Term Faculty Positions for Core Directors (monthly) Chair, Strategic Plan Implementation 3, Initiative 1 Committee (weekly) Member, Biobanking Committee (monthly)

## CYRUS VAZIRI, Ph.D.

Member, Research Advisory Committee (Dept of Pathology) Member, Faculty Search Committee (Dept of Pathology) Member, UCRF Pilot Project Award Review Committee Member, Pathology Department Faculty Evaluation Committee Member, Pathology Qualifying exam Committee Member, GMB Program Qualifying committee Member, Curriculum in Toxicology Executive Committee

# KAREN E, WECK, M.D.

Member, Department of Pathology & Laboratory Medicine Research Advisory Committee

# BERNARD E. WEISSMAN, Ph.D.

Member, Graduate Education Committee, DPLM Member, Executive Committee, Toxicology Curriculum

# HERBERT C. WHINNA, M.D., Ph.D.

Member, UNCH POC Committee Member, UNCH Transfusion Committee Member, UNC Quality Council Member, UNCH MSEC

## JULIA W. WHITAKER, M.S., D.V.M.

Member, Institutional Animal Care and Use Committee

# ALISA S. WOLBERG, Ph.D

Member, UNC Thrombosis and Hemostasis Program Seminar Series Member, Biological and Biomedical Sciences Program (BBSP) Pathogenesis Admissions Committee Member, UNC School of Medicine Strategic Planning Task Force #7 Member, Liaison Committee on Medical Education (LCME) Steering Committee Member, Faculty Search Committee, McAllister Heart Institute

#### DEPARTMENTAL FACULTY HANDBOOK

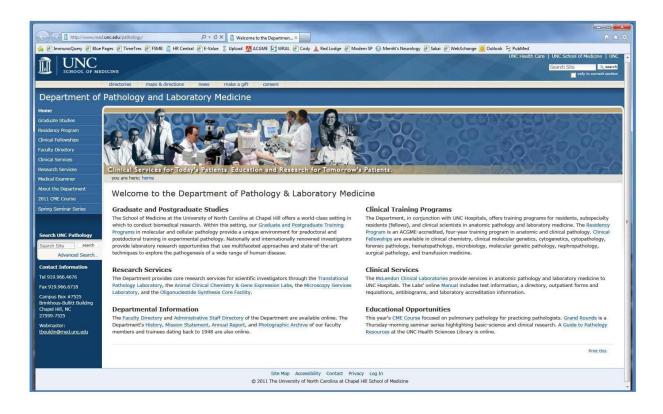
The Department of Pathology and Laboratory Medicine has established an online faculty handbook. The handbook is updated regularly as new information becomes available. The idea for this handbook came from the faculty, who wished to have a centralized, easily accessible source of information on topics of interest for new and established faculty members. The Faculty Handbook provides our faculty members with detailed and up-to-date information on such topics as faculty appointments, promotion policies, School of Medicine policies, purchasing, grant proposals, human resources, equipment available within the Department, and core research services available within the Department, School of Medicine, and University. The handbook also provides an introduction and overview of the faculty orientation process. The Department of Pathology and Laboratory Medicine's Faculty Handbook is accessible though the Departmental web site.



#### **DEPARTMENTAL WEB SITE**

The Departmental web site (<u>http://www.pathology.unc.edu</u>) was inaugurated in 1995 as a means of making potential applicants more aware of our graduate, postdoctoral, and residency training programs. Today, the web site is a comprehensive, detail-rich resource for those seeking information about the educational, research, and clinical training programs of the Department. The web site includes information on the residency training program, the thirteen fellowship and research symposia.

The web site is maintained by Dr. Thomas Bouldin. In June, 2010, the web site was moved to a server maintained by the UNC School of Medicine. Web pages for the graduate program are authored by Dr. William Coleman and Dr. Jonathon Homeister. Web pages for the residency and fellowship training programs and for the faculty are maintained by Dr. Bouldin. Individual faculty members now have the ability to construct and edit their own biographical sketches and laboratory web pages on the Departmental web site.



#### PUBLICATIONS

#### Department of Pathology and Laboratory Medicine School of Medicine University of North Carolina at Chapel Hill July 1, 2011 – June 30, 2012

#### C ROBERT BAGNELL, JR., Ph.D.

Banerjee S, Paik R, Mino RE, Blauth K, Fisher ES, Madden VJ, Fanning AS, Bhat MA. A Laminin G-EGF-Laminin G module in Neurexin IV is essential for the apico-lateral localization of Contactin and organization of septate junctions. PLoS One. 2011;6(10):e25926. Epub 2011 Oct 14. PubMed PMID: 22022470; PubMed Central PMCID: PMC3195077.

Jurgens CK, Young KR, Madden VJ, Johnson PR, Johnston RE. A novel self-replicating chimeric lentivirus-like particle. J Virol. 2012 Jan;86(1):246-61. Epub 2011 Oct 19. PubMed PMID: 22013035; PubMed Central PMCID: PMC3255904.

Monte S. Willis, Jonathon W. Homeister, Gary B. Rosson, Yunus Annayev, Darcy Holley, Stephen P. Holly, Victoria J. Madden, Virginia Godfrey, Leslie V. Parise, and Scott J. Bultman: Functional Redundancy of SWI/SNF Catalytic Subunits in Maintaining Vascular Endothelial Cells in the Adult Heart. Circulation Research. 2012;CIRCRESAHA.112.265587published online before print June 27 2012, doi:10.1161/CIRCRESAHA.112.265587

#### DWIGHT A BELLINGER, D.V.M., Ph.D.

Sabatino DE, Nichols TC, Merricks E, Bellinger DA, Herzog RW, Monahan PE. <u>Animal models of hemophilia</u>. Prog Mol Biol Transl Sci. 2012;105:151-209. Review. <u>Bellinger DA</u>, Merricks EP, Nichols TC. Minipig models of diabetes mellitus: in McAnulty PA, Dayan AD, Ganderup NC, Hastings KL (eds), The Minipig in biomedical research, CRC Press, Taylor & Francis Group, Boca Raton, FL, 2011, Chapter 30, pp 445-468.

#### ARLENE S. BRIDGES, Ph.D.

Gillingwater K, Gutierrez C, Bridges A, Wu H, Deborggraeve S, Ekangu RA, Kumar A, Ismail M, Boykin D, Brun R. Efficacy study of novel diamidine compounds in a Trypanosoma evansi goat model. PLoS One. 2011 Jun;6(6). PMID: 21698106.

Zamboni W, Combest A, DeLoia J, Edwards R, Bridges A, Zamboni B, Walko C, Yu A, Krivak T, Kelly J, Pharmacologic and phenotypic study of docetaxel in patients with ovarian or primary peritoneal cancer. Cancer Chemother Pharmacol. 2011 Nov;68(5)1255-62. PMID: 21437702.

Cohen-Wolkowiez M, White N, Bridges A, Benjamin D, Kashuba A. Development of a liquid chromatography-tandem mass spectrometry assay of 6 antimicrobials for pharmacokinetic studies in premature infants. J Chromatogr B Analyt Technol Biomed Life Sci. 2011 Nov;879(30):3497-506. PMID: 21983195.

Huang H, Allen J, Mabb A, King I, Miriyala J, Taylor-Blake B, Sciaky N, Dutton J Jr, Lee H, Chen X, Jin J, Bridges A, Zylka M, Roth B, Philpot B. Topoisomerase inhibitors unsilence the dormant allele of Ube3a in neurons. Nature. 2011 Dec;481(7380):185-9. PMID 22190039.

Xu Y, Wang Z, Liu R, Bridges A, Huang X, Liu J. Directing the biological activities of heparin sulfate oligosaccharides using a chemoenzymatic approach. Glycobiology. 2012 Jan;22(1)96-106. PMID: 21835782.

Joy M, La M, Wang J, Bridges A, Hu Y, Hogan S, Frye R, Blaisdell J, Goldstein J, Dooley M, Brouwer K, Falk R. Cyclophosphamide and 4-hydroxycyclophosphamide pharmacokinetics in patients with glomerulonephritis secondary to lupus and small vessel vasculitis. Br J Clin Pharmacol. 2012 Mar;[Epub ahead of print]. PMID 22380171.

Hertz D, Walko C, Bridges A, Hull H, Herendeen J, Rollings K, Clarke S, Watkins P, Dees E. Pilot study of rosiglitazone as an in vivo probe of paclitaxel exposure. Br J Clin Pharmacol. 2012 Jul;74(1):197-200. PMID 22680343.

Ju W, Ansede J, Stephens C, Bridges A, Voyksner R, Ismail M, Boykin D, Tidwell R, Hall J, Wang M. CYP1A1 and CYP1B1 catalyzed formation of novel metabolites of an anti-Trypanosomal prodrug through an atypical P450 reaction mechanism. J Pharm Sci [Under revision 2012].

Gonzalez-Perez V, Connolly E, Bridges A, Wienkers L, Paine M. Impact of organic solvents on cytochrome P450 probe reactions: filling the gap with (s)-warfarin and midazolam hydroxylation. Drug Metab Dispos [Re-submitted 2012].

Dufek M, Knight B, Bridges A, Thakker D. P-glycoprotein reduces first-pass intestinal metabolism and enhances portal bioavailability of loperamide in mouse. J Pharmacol Exp Ther [Submitted, 2012].

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