

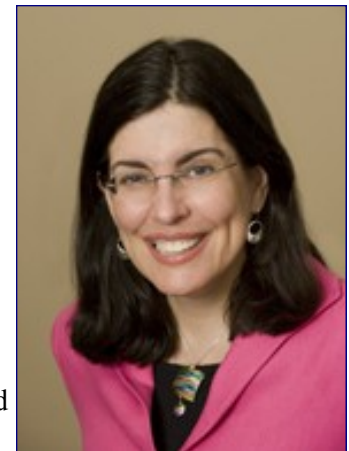
## *Pathology and Laboratory Medicine Newsletter*

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### *Letter from the Chair*

We are very lucky to have Dr. Etta Driscoll Pisano as our new Dean, College of Medicine. Dr. Pisano graduated from Dartmouth College and Duke University School of Medicine. She trained in Radiology at the Beth Israel Hospital, one of the Harvard-affiliated hospitals, and joined the faculty at the University of North Carolina in 1989. She has served as UNC's Vice Dean for Academic Affairs since 2006.



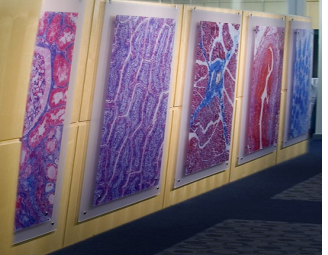
Dr. Pisano is recognized as one of the top twenty most influential radiologists in the US. She is a world-leader in mammography and was the principal investigator of a huge, multi-institutional study on digital mammography which demonstrated its advantages in detecting malignancies, especially in younger women. Since 2008, she has lead UNC's Translational and Clinical Science Institute. That organization has a tripartite mission: promoting translational research, engaging the community in research activities, and supporting the training of developing clinical research investigators. Also, it has led to the development of new biotechnical companies and increased grant funding. Dr. Pisano is clearly very interested in translational research and looks to advance MUSC into the top quartile of American Medical Schools in NIH funding. She has established a research strategic planning committee at MUSC to guide these endeavors. Dr. Brad Schulte, Director, Division of Research, was invited to serve on this committee.

Dr. Pisano is very interested in medical student education, priding herself on her mentorship relations with students. We expect that she will also be very active in Women's health and professional advancement initiatives. Please join me in welcoming Dr. Pisano to MUSC.

(Source: MUSC COM)



# DEPARTMENT OF PATHOLOGY AND LABORATORY MEDICINE



## News from Department Administration and Business Office...

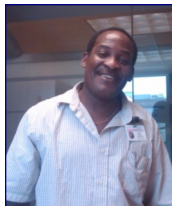
### *Department "All Hands" Meetings*

The first "All Hands" meeting was held on June 11, 2010. Thank you for your participation.

**Save the Date:** The next "All Hands" meeting will be September 8 at 9:00 a.m. in 2West Amphitheater, Main Hospital Room, 282. Please mark your calendar and plan to attend.

### *You're in the Spotlight!*

**Congratulations to Jarvis Jenkins,** selected and recognized as the Employee of the Quarter! A number of nominations were received for our first "All Hands" meeting.



Nomination cards can be found at each of the Department's MUSC Excellence Communication Board locations: 2nd floor Walton Research Building and 3rd Floor Children's Hospital.



### *Conflict of Interest*

The Conflict of Interest Disclosure Statement does not involve CATTS this year. This year, the COI Disclosure Statement is a MUSC developed web-based application that is linked on the MUSC Conflict of Interest Web Page. The deadline to complete this year's Disclosure Statement is August 31, 2010. Not sure if you completed one for this year or need to update it? Follow the link below, log on and find out. It keeps track of when you completed the last disclosure and allows you to view and copy your completed disclosure. Link: <http://coi.musc.edu>

### *New On-Line Performance Evaluation System "Success Factors"*

#### Update on FY2010

Planning Stage — complete  
Evaluation Stage—In progress or complete  
Signature Stage — In progress or complete

#### Upcoming Key Dates:

September 15, 2010—Annual Review Cycle ends  
September 16, 2010 — Planning Stage Cycle for FY2011 begins  
November 1, 2010 — Planning Stage Cycle for FY2011 complete

### *Research Tracking*

A worksheet will be distributed to each investigator on a monthly basis for review. The worksheet will include:

1. Percent effort being charged to grants, sponsored projects, and other support projects. This will provide a complete listing of time and effort.
2. Proposals submitted, which will include: title of the project, PI, budget period, project period and the percent effort requested on each proposal.

# Anatomic Pathology goes to USCAP

By: *M. Timothy Smith, M.D., Professor and  
Director, Anatomic Pathology Division*



The United States and Canadian Academy of Pathology is the largest academic pathology society. At the recent meeting, 20-27 March, in Washington D.C., the Department of Pathology and Laboratory Medicine was well represented and contributed significantly to the academic content of the meeting. Requested/invited participation in the meeting's many courses, poster sessions, platform sessions, and evening specialty sessions are indicators of national peer recognition. **Mary Richardson, M.D., D.D.S.** collaborated with colleagues from Vanderbilt, Massachusetts General Hospital, Clariant Inc., Children's Hospital of Pittsburgh, UHS Hospitals of Binghamton, NY, and Carolinas Medical Center in Charlotte presented "Coexistence of Langerhans Cell Histiocytosis and Rosai-Dorfman Disease: Related Disorders?" One of the chief residents, **Angie Duong, M.D.**, was first author. Dr. Richardson who is also a member of the elected USCAP council also was the organizer and moderator for an evening session on Head and Neck/Endocrine Pathology in which the participants were nationally and internationally recognized pathologists. **David Lewin, M.D.** co-presented a short course entitled "Pancreatic Tumors, an Integrated Cyto/histopathologic Approach." While at the meeting, Dr. Lewin also presided as president over the prestigious Roger C. Hagitt Gastrointestinal Pathology Society. He also presented a case at the Head and Neck/Endocrine Pathology evening session. **Cynthia Welsh, M.D.** co-presented, with Dr. Smith, a neuropathology short course. The popular course was entitled "Intraoperative Neuropathology for the Non-Neuropathologist." **Mokhtar Desouki, M.D.** and **Sally Self, M.D.** presented "Histopathological Comparison of Idiopathic and Secondary IgA Nephropathy Associated with Liver Cirrhosis." **Tim Smith, M.D.**, as secretary/treasurer of the Association of Directors of Anatomic and Surgical Pathology, again organized the ADASP council meeting and main meeting. The topics of this year's program were "Peer Review and Best Practices/Individual Pathologist Evaluation" and "Telepathology and Other Future Technologies." He also collaborated with colleagues at Massachusetts General Hospital and presented "Joint Commission Standards for Ongoing and Focused Performance Evaluation in Anatomic Pathology: Current Trends in Practice." He also co-presented a short course on frozen section neuropathology.

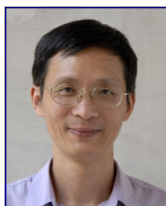
## Arrivals

We are delighted to welcome the following people to the Department:



**Erica Nelson** joined Dr. Dennis Watson's laboratory in June as a Research Specialist I.

**Suhua Sha, M.D.**, Assistant Professor, joined the Research Division on July 1.



**Yuan Shao, Ph.D.**, joined Dr. Moussa's laboratory as a Research Specialist II.

## Departures

**Hideki Furuya, Ph.D.** moved to The University of Hawaii with Dr. Kawamori (see page 10). **Masayuki Wada, Ph.D.**, who also worked in Dr. Kawamori's lab transferred to the Department of Biochemistry and Molecular Biology. **Jason Barnes, M.D.**, and **LaQuita King, M.D.** completed the Surgical Pathology Fellowship. **Brent McCarragher**, who worked in Dr. Watson's laboratory and **Christopher Williams**, who worked in Dr. Ogawa's laboratory, both left for medical school.

We wish everyone all the best in their future endeavors!

# *MOLECULAR TESTING FOR GASTROINTESTINAL DISEASES*



*By: David Lewin, M.D., Professor and  
Director of Gastrointestinal and Hepatic Pathology*

Molecular testing has reached the world of gastrointestinal malignancies similar to other organ systems. A number of molecular tests are now used to help guide therapeutic and prognostic decisions in gastrointestinal malignancies. The four major areas of molecular testing are HER2/neu testing in gastrointestinal adenocarcinoma, KIT mutation analysis for Gastrointestinal Stromal Tumors (GIST), DNA mismatch repair gene testing in colon cancer and KRAS mutational testing in metastatic colon cancer. Each will be discussed briefly.

## ***HER2 (HER2/neu, ErbB-2) targeted therapies in gastric adenocarcinoma***

Overexpression and amplification of HER2 growth factor receptor has been described in 6%-35% of gastric and GEJ adenocarcinomas. Trastuzumab (Herceptin) is a monoclonal antibody which specifically targets HER2 protein by directly binding the extracellular domain of the receptor. The efficacy of trastuzumab in breast cancer patients has led to investigate its antitumor activity in patients with HER2-positive cancers, including gastric adenocarcinomas. HER2/neu positivity rates have been reported to be more frequent in intestinal type gastric cancer (21.5%) than in diffuse gastric cancer (2%) or mixed types (5%). In addition, HER-2/neu amplification in gastric carcinoma is associated with poor outcome and has been shown to be an independent prognostic factor. Results from the largest study to date (ToGA trial) evaluating the addition of trastuzumab (Herceptin) to chemotherapy in HER2-positive advanced gastric cancer were reported at the 2009 ASCO meeting. The trial enrolled 3,883 patients from 24 countries. A HER2-scoring system modified from the protocol in breast cancer was used: a score of IHC 3+ and/or FISH positive was defined as HER2 positive. In the ToGA trial, patients with HER2-positive gastroesophageal and gastric adenocarcinoma (locally advanced, recurrent, or metastatic) were randomized to receive Trastuzumab (H; Herceptin) H+CT (5-fluorouracil or capecitabine and cisplatin) every 3<sup>rd</sup> week for 6 cycles or CT alone. Median overall survival was significantly improved with H+CT compared to CT alone: 13.5 vs. 11.1 months, respectively (p=0.0048; HR 0.74; 95% CI 0.60, 0.91). Overall response rate was 47.3% in the H+CT arm and 34.5% in the CT arm (p=0.0017). This first randomized trial showed the efficacy of the addition of herceptin in HER2/neu positive gastric adenocarcinomas. Your medical oncologists will be asking for HER2/neu testing of all advanced gastric adenocarcinomas.

## ***KIT and PDGFR mutation molecular analysis in GIST***

Gastrointestinal stromal tumors (GIST) are tumors that are thought to arise from interstitial cell of Cajal precursor cells. The majority of tumors (95%) are positive for KIT (CD 117) by immunohistochemical staining. On a molecular basis these lesions have activating mutations in either KIT (85%-90%) or platelet derived growth factor receptor A (PDGFRA, 3%-4%) genes. These mutations are mutually exclusive and result in ligand independent kinase activation. Primary treatment for these lesions is surgical resection; however chemotherapy by a small molecule inhibitor (imatinib mesylate [Gleevec]) that is directed against the kinase domain of both KIT and PDGFRA is very effective. Response is dependent on the location of the mutation. Primary resistance is seen predominately in KIT and PDGFRA wild-type (non-mutated) GISTs as well as the most common PDGFRA mutant. KIT Exon 9 mutant GISTs are less responsive to imatinib, requiring increased dosage for efficacy. A few other molecular correlations have been observed: KIT exon 9 duplications of A-502 and Y-503 are found almost exclusively in small bowel GISTs and tend to be clinically aggressive. They are also less sensitive to imatinib and may be more susceptible to sunitinib (another kinase inhibitor typically used as a second-line treatment). GISTs with PDGFRA mutations tend to arise in the stomach, have an epithelioid morphology and a less aggressive phenotype. Deletions of the proximal portion of exon 11 (W-577 and K-558) are associated with aggressive behavior while duplications of the distal portion of exon 11 are associated with better prognosis. Due to the clinical implications of molecular mutation analysis of GISTs, many oncologists are asking for this to be performed on these lesions.

*(Continued on page 5)*

# MOLECULAR TESTING FOR GASTROINTESTINAL DISEASES (cont.)

## DNA Mismatch Repair Gene Testing in Colonic Adenocarcinoma

Evaluation of DNA mismatch repair gene testing, microsatellite instability testing, or both has become important in colorectal cancer for a couple reasons. First is to identify inherited syndromic colon cancer (Lynch syndrome or Hereditary non-polyposis colon cancer [HNPCC]). This represents approximately 2%-3% of all colorectal carcinomas and individuals have germline mutations in the genes belonging to the DNA mismatch repair gene family (MLH1, MSH2, MSH6, and PMS2). These individuals usually get colon cancer at an earlier age than sporadic carcinomas (age 45 compared to greater than 60) and are at risk for extracolonic carcinomas including endometrial, ovarian, gastric, urinary tract, and bile ducts. The second reason to do the testing is that there is evidence that tumors with mutations in the DNA mismatch repair genes (microsatellite instability [MSI] pathway) have a better prognosis and they may not respond as well to 5-FU based chemotherapy. There are two testing approaches to identify these individuals: 1. Do molecular microsatellite instability testing or 2. Immunohistochemistry for DNA mismatch repair gene family proteins. Immunohistochemistry can be performed by most immunohistochemistry laboratories, however there is some concern that this represents genetic molecular testing (as mutations in MSH2, MSH6, and PMS2 almost always correlate to HNPCC and a germline mutation). The molecular test avoids this ethical complication, however does not identify the mutated gene product. If looking for inherited cancer syndromes there are a couple of approaches different institutions have used. One is to test all colorectal carcinomas. A second is to use Bethesda Guidelines for testing: Age less than 50; or Synchronous or metachronous colorectal cancer or HNPCC-associated tumors regardless of age; or MSI-H histology and age less than 60 {histologic features are intratumoral lymphocytes, mucinous or signet ring histology, poorly differentiated, and medullary carcinoma}; Colon cancer with family history of HNPCC associated cancer at age less than 50; or Colon cancer with family history of 2 family members with HNPCC associated cancer at any age.

## KRAS Mutations in metastatic colorectal carcinoma

KRAS protein is GTPase protein that works as a signal transduction pathway, transmitting a signal from the cell membrane to the nucleus. Most mutations are activating mutations that constitutively turn on the KRAS protein, meaning there is signal independent activation. A number of epithelial growth factor receptor (EGFR) inhibiting drugs (panitumumab and cetuximab [Erbix or Vectibix]) are potential chemotherapeutic drugs in the therapy of metastatic colorectal carcinoma. These drugs will not work if there is an activating mutation in the KRAS gene (found in approximately 40% of colorectal carcinomas). For this reason most metastatic colorectal carcinomas are analyzed for KRAS mutation prior to starting these expensive therapies. These represent the beginning of what is certain to be an explosion of molecular testing to be seen in all malignancies. As we move more toward an era of personalized medicine, more therapeutic decisions will be based on molecular characteristics of neoplasms.

## HER2 expression and amplification in gastric cancers

Authors	Number	Region	Over-expression (%)	IHC method	Amplification (%)	Method
Yano et al.	200	Japan	23	HercepTest	27	FISH
Gravalos et al.	166	Europe	13	HercepTest	if IHC 2+	FISH
Allgayer et al.	203	Europe	91	Elite kit	-	-
Park et al.	Gast: 182	Korea	16	HercepTest	7 patients	FISH/CISH
Lordick et al.	1527	Europe; Asia; Latin America	22*	HercepTest	-	FISH
Tanner et al.	Gast: 131 GEJ: 100	Europe	-	-	12.2 24	CISH
Bang et al.	Gast; GEJ	14 countries	Gast: 20.9 GEJ: 32.2	HercepTest		FISH**

**HER2 expression and amplification in gastric and GEJ cancers** (modified from Gravalos et al. 16) \* HER2 overexpression by IHC or FISH\*\* (PharmDx). IHC (immunohistochemistry); CISH (chromogenic in situ hybridization).

# *Life and Death in the Inner Ear*

By: Lisa Cunningham, Ph.D., Assistant Professor



## Research on Sensory Hair Cells

Our research is focused on the mechanosensory hair cells that are the receptor cells of hearing and balance. Specifically we are interested in the molecular signals that regulate the survival, homeostasis, and death of these cells. Mammalian hair cells are terminally differentiated and are not regenerated when they are lost. Therefore human hair cells must survive and function for up to a century (or longer) in order to transduce sound and head movement into the neural signals of hearing and balance throughout a normal lifespan. During this lengthy period of time, the hair cell may encounter multiple potentially-toxic stimuli, including exposure to excessive sound and/or exposure to therapeutic drugs with ototoxic side effects. Hair cells must be able to respond rapidly and effectively to these and other potentially-toxic stimuli if they are to survive and continue to function.

We are currently studying the role of stress-induced proteins called heat shock proteins (HSPs) in protecting against hair cell death. Induction of HSPs in response to cellular stress is a highly-conserved response that can inhibit apoptosis in many systems. Initial studies in our lab carried out by research specialist

**Carlene Brandon** showed that HSP induction protects against hair cell death caused by both of the major classes of ototoxic drugs, namely the aminoglycoside antibiotics and the anti-cancer drug cisplatin. **Dr. Mona Taleb** (an MSTP student in the lab who graduated in May) showed that HSP70 in particular is required for this protective effect, and HSP70 alone inhibits ototoxic hair cell death. Mona also showed that HSP70 is protective against aminoglycoside-induced hearing loss and cochlear hair cell death *in vivo*. Taken together, these data indicate that HSP70 induction is a critical stress response that can promote survival of hair cells exposed to major stressors.



Pictured (L to R): Shimon Francis, Helen Gosnell, Tiffany Baker, Carlene Brandon, Lisa Cunningham, and Inga Kramarenko

## Current Projects

Currently our studies are broadly divided into two groups: 1) those aimed at understanding the molecular mechanisms underlying the protective effects of HSPs and 2) those aimed at translating our findings into clinical therapies to prevent hearing loss caused by exposure to ototoxic drugs. **Tiffany Baker**, an MSTP student in the lab, is currently examining the interactions between HSPs and pro-apoptotic signaling in hair cells exposed to cisplatin. Post-doctoral fellow **Dr. Inga Kramarenko** is working with research specialist **Helen Gosnell** to develop reagents that will allow us to examine the role of the chaperone activities of HSPs in mediating their protective effects against ototoxic hair cell death. In collaboration with Dr. Christina Voelkel-Johnson in the MUSC Department of Microbiology and Immunology, Carlene Brandon has recently shown that the glia-like “supporting cells” in the inner ear mediate the protective effect of HSP70 against hair cell death. These data suggest that supporting cells can directly mediate hair cell survival. We recently obtained a grant from RNID to begin a collaborative project with Dr. Jonathan Gale’s lab aimed at understanding the intercellular signals by which hair cells send stress signals and supporting cells sense and respond to these signals.

Our clinical/translational projects include studies of a pharmacological heat shock protein inducer, celastrol. Celastrol is a plant extract that has been used in Chinese medicine to treat inflammation. **Shimon Francis**, a Ph.D. candidate in the lab, has shown that that celastrol induces both HSP70 and HSP32 in hair cells, and it inhibits both aminoglycoside- and cisplatin-induced hair cell death. Moreover, Shimon’s recent data indicate that celastrol inhibits aminoglycoside-induced hair cell death and hearing loss in mice receiving systemic kanamycin injections.

(Continued on page 7)

*“Every honest researcher I know admits he's just a professional amateur. He's doing whatever he's doing for the first time. That makes him an amateur. He has sense enough to know that he's going to have a lot of trouble, so that makes him a professional” - Charles Franklin Kettering (1876-1958).*

## *Life and Death in the Inner Ear (cont.)*

*By: Lisa Cunningham, Ph.D., Assistant Professor*

### Why study hair cell death and survival?

From a clinical perspective, our research program is significant because ototoxic drug exposure results in permanent hearing loss for over half a million Americans each year. HSPs are protective against both aminoglycosides and cisplatin, and thus represent a potential therapeutic target for both classes of ototoxic drugs. From a basic science perspective, our research addresses the basic cell biology of interactions between pro-survival and pro-apoptotic signaling in hair cells under stress. In addition, we are examining the fundamental nature of the interactions between hair cells and supporting cells. The roles of supporting cells as mediators of hair cell survival and death are only beginning to be explored, and the mechanisms underlying these cell-cell interactions are largely unknown.

I am very proud of the students, post-docs, technicians, and collaborators who are essential to the success of this research program! It is an honor to work with them every day.

### Collaborators

MUSC: Dr. Christina Voelkel-Johnson (Microbiology and Immunology), Dr. Craig Beeson (Pharmaceutical Sciences), Dr. John Lemasters (Pharmaceutical Sciences), Dr. Judy Dubno (Otolaryngology).  
Other institutions: Dr. Jonathan Gale (University College London), Dr. Mark Warchol (Washington University in St. Louis), Dr. Edwin Rubel and Dr. David Raible (University of Washington, Seattle).

### Current Funding

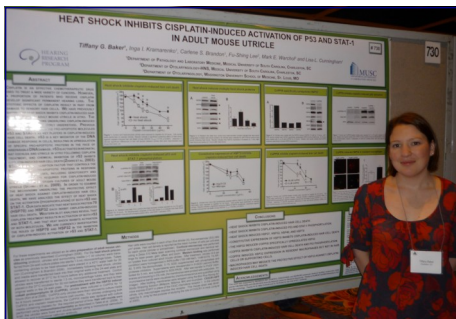
PI Cunningham: NIH/NIDCD R01 DC007613 “Mechanisms of Sensory Hair Cell Death and Survival”; NIH/NIDCD R01 007613-S2 (ARRA); RNID Flexigrant

PI Francis (sponsor Cunningham; co-sponsor Lemasters): NIH/NIDCD F31 DC010559

PI Baker (sponsor Cunningham; co-sponsor Schnellmann): NIH/NIDCD F30 DC010522

### Pending Funding

PI Cunningham: NIH/NIDCD R21 DC 011320 “Sound-Induced Heat Shock Protein Expression to Prevent Ototoxic Hearing Loss” SCTR Pilot Project



Tiffany Baker presenting her poster at the 2010 Association for Research in Otolaryngology Meeting in Anaheim, CA.



Dylan Sheridan (in sound booth) and Shimon Francis prepare a mouse for hearing testing via auditory brainstem response (ABR) measurement.



Lisa Cunningham, Ph.D. with Mona Taleb, Ph.D. at her May graduation. Mona was a MSTP student in Dr. Cunningham's laboratory.



# *HLA Testing and the Histocompatibility Laboratory: At the Corner Where Laboratory Science meets Medical Practice*

*Omar Moussa, Ph.D., Assistant Professor and  
HLA Director in Training*

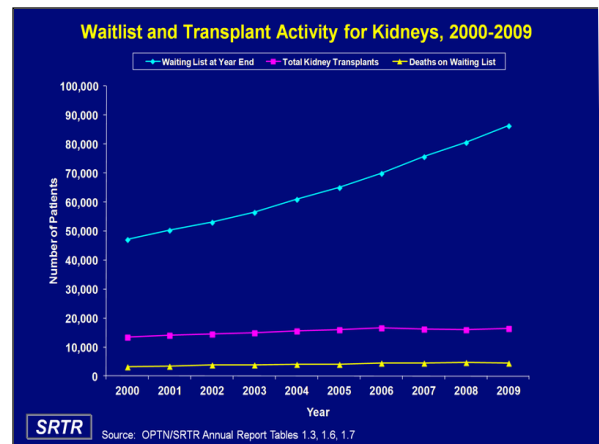
Although the number of patients transplanted yearly has slowly increased in the last decade, the number of individuals with end-stage renal diseases awaiting kidney transplantation has greatly increased. For example, between June 2008 and July 2009, 16,821 patients received a renal transplant, yet, in spite of the number of kidneys transplanted, the waitlist increased by about 9.5% (see UNOS graph). The net result is that the rate of transplantation has remained the same in the period of 2000 to 2009. Thus, overall, access to the available kidneys for transplantation continues to decline.

Access to transplantation for individuals on the waitlist is also greatly impacted by their blood group type as well as their status with regard to pre-sensitization to human leukocyte (HLA) antigens. Antibodies to HLA antigens develop as a result of pregnancy, blood transfusion(s) or previous organ transplantation. The deleterious role played by HLA antibodies in post-transplantation outcomes was first demonstrated over four decades ago by the seminal study performed by Patel and Terasaki in 1969. This study established the role of positive crossmatch (due to HLA antibodies) as a major risk factor for successful kidney transplantation.

For candidates awaiting renal transplantation, the HLA laboratory performs three important tests: 1) human leukocyte antigen (HLA) typing by molecular-based methodologies to determine the individual's unique HLA type; 2) sera of patients awaiting transplantation are tested for the degree of allo-immunization by determining the percentage of panel reactive antibodies (PRAs). If the patient is allo-immunized, additional testing is done to identify the specificity and the titer of the allo-antibodies using Single Antigens Beads (SAB). SAB assays utilize a suspension array of beads coated with recombinant HLA antigens. After incubating the beads with a serum sample from a patient, the titer of antibodies can be determined using a fluorescent dye; 3) lastly, and just prior to transplantation, a crossmatch is performed wherein the patient's serum is tested directly against lymphocytes from the potential donor. Crossmatching is now performed by flow cytometry. If all testing supports compatibility between donor and recipient, the transplant is performed.

For patients awaiting a deceased donor organ, donation can occur at any time, day or night. For that reason, the HLA lab staff must be available 24/7/365. It takes 3-4 hours for the HLA technologist to complete initial work-up which includes processing the donor blood and determining the donor HLA type. After HLA typing, the donor HLA antigens are entered into UNOS database which contains all the potential recipients. Via a matching algorithm, the UNOS computer will identify a list of potential recipients. This algorithm excludes patients with antibodies directed against the donor HLA antigens. This list is then sent to the transplant program for identifying potential candidates that are clinically ready for transplantation. The transplant coordinator will make the initial contact with the recipient patient.

During the initial selection process, the patient's HLA type and antibody profile is examined by the HLA lab directors (Dr. Howard Gebel, Dr. Robert Bray, or the assistant director, Dr. Omar Moussa) and compared to the donor HLA type. This process is called, Virtual Crossmatch (vXM). The vXM can predict the results of the lymphocyte crossmatch test with >90% accuracy. Through the application of the vXM, when a positive crossmatch is predicted incompatible offers of deceased donor kidneys (and hearts and lungs) can be avoided. The vXM permits importation of organs over greater distances without the fear of a positive crossmatch and provides a benefit to those disadvantaged by sensitization.



*(Continued on page 9)*



## *HLA Testing and the Histocompatibility Laboratory:*

### *At the Corner Where Laboratory Science meets Medical Practice (Cont.)*

While the vXM has been quite successful, in certain instances, an unexpected positive crossmatch may occur. There are several reasons for this. Most importantly, some HLA loci are not yet part of the “standard” HLA typing for deceased donors. HLA DP and DQA are two such loci. Due to the implementation of SAB testing, we now know that patients make antibodies to these antigens. Studies are beginning to show that such antibodies are indeed harmful to the graft and should be avoided. Presently, the HLA laboratory at MUSC is typing for such antigens. Unfortunately, this is not a nation-wide standard and most organs imported from outside the state of South Carolina have not been tested for these antigens. Hence, crossmatch prediction cannot be 100%.

Another reason for a positive crossmatch is that some patients have very low antibody titer. For many years, the crossmatch was the only way to define an incompatible transplant. However, data from our lab has recently demonstrated that the titer of the antibody may not always correlate with the crossmatch. For some patients, both unanticipated positive and negative crossmatch results have been observed. Thus, measuring antibody reactivity by SAB alone is not a sufficient metric to assess the potential risk of certain HLA antibodies.

In some instances, weak antibodies directed against “Public” epitopes can result in a positive crossmatch, and, in other instances, weak donor-specific antibodies may result in a negative result. New data recently published suggests that even with a negative crossmatch, a donor-specific antibody does impart some level of risk for antibody-mediated rejection. More studies will be needed to completely understand the role of low titer HLA antibodies.

In summary, new advances in HLA technology have provided new challenges for the laboratory. More importantly, these advances are directly impacting the practice of medicine surrounding organ transplantation. More efficient organ allocation via the vXM and a new appreciation of how low level antibodies may impact outcomes have thrust the HLA laboratory into the forefront of transplant medicine.



HLA laboratory Team: Seated: Tom Thompson, Dana Gates; Standing: Dr. Omar Moussa, Anthony Pinckney, Amber O'shields, Jessica Francia, Cindi Marchman, Karen Cellars, Sheree Waslaske (Technical Coordinator), Cheryl Nasse, Deonne Francewar. Not pictured, Elise McPherson, Carissa Hagy, and Haywood Titchener

#### *Resident Highlight:*



**Mokhtar Desouki, M.D.**, 4th year resident, is having a busy year. He has recently had four articles published in peer reviewed journals as well as presentations at national and international meetings. Dr. Desouki had 2 articles presented at the March USCAP meeting in Washington: one on “Sporadic cutaneous angiosarcomas generally lack HIF-1 alpha; A histologic and immunohistochemical study of 45 cases,” and the other entitled: “Histopathological comparison of idiopathic and secondary IgA nephropathy associated with liver cirrhosis.” One poster presentation has been accepted for the CAP meeting in Chicago, IL in September, 2010. Also in September, he has a poster presentation accepted at the XV Meeting of the European Association of Hematopathology in Uppsala, Sweden. Way to go Mokhtar!!

Next year Mokhtar will continue his training at the University of Pittsburgh Medical Center at Pittsburgh as a Breast and Gynecologic Pathology Fellow.

# Research Division Update



By: *Bradley Schulte, Ph.D.*  
Vice Chair for Research

The 5<sup>th</sup> Annual Pathology Research Day is Friday, August 27, at 2:00 p.m. in BSB 302. Our keynote speaker is **Amanda LaRue, Ph.D.** Dr. LaRue's talk is entitled "Hematopoietic Stem Cell Plasticity." Dr. LaRue's talk will be followed by short talks from Pathology post-docs, graduate students, and residents. Posters, conversation, cocktails and hors d'oeuvres will be in the Education Center/Library Building at 4:00. We hope to see you there.

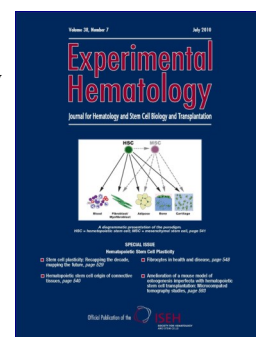


**Meenal Mehrotra, M.D., Ph.D.** received a K01 grant entitled "Hematopoietic Stem Cell Transplantation in Osteogenesis Imperfecta." This grant, mentored by Drs. Ogawa and LaRue, is to test the potential of hematopoietic stem cell (HSC) transplantation as a possible therapy in a mouse model of Osteogenesis Imperfecta or "brittle bone disease." This is the most common bone genetic disorder resulting from the abnormal amount and/or structure of Type I collagen produced by the defective osteoblasts. Dr. Mehrotra has been appointed as a Research Assistant Professor in the Department beginning April 1<sup>st</sup>.



**Makio Ogawa, M.D., Ph.D.** was an invited speaker at a Marcus Wallenberg Symposium "Hematopoiesis in Health and Disease" in Lund, Sweden, May 15-17 and gave a lecture entitled "Hematopoietic Stem Cell Origin of Connective Tissues."

**Dr. Ogawa** is a Guest Editor of a special issue of *Experimental Hematology* entitled "Hematopoietic Stem Cell Plasticity," an official publication of ISEH - Society for Hematology (see cover at right). The aim of the issue is to revitalize the notion that HSCs generate many types of cells in tissues and organs, which has been discredited due to earlier controversial papers. This issue was published July, 2010 and contains three papers from Investigators of Department of Pathology and Laboratory Medicine, MUSC, including a review by Drs. Ogawa, LaRue, Watson and Watson entitled "Hematopoietic Stem Cell Origin of Connective Tissues," a brief report by Drs. Mehrotra, Rosol, Ogawa and LaRue entitled "Amelioration of a Mouse Model of Osteogenesis Imperfecta with Hematopoietic Stem Cell Transplantation: Micro-Computed Tomography Studies" and a method paper by Drs. Abe, Masuya and Ogawa entitled "An Efficient Method for Single Hematopoietic Stem Cell (HSC) Engraftment in Mice Based on Cell Cycle Dormancy of HSCs."



**Toshi Kawamori, M.D., Ph.D.**, Assistant Professor, moved to the University of Hawaii in March, where he accepted an appointment as an Associate Professor in the Cancer Research Center of Hawaii. Toshi was a valuable member of the Department for eight years and played a major role in the development of a shared animal carcinogenesis core research facility. A drop-in was held on April 13<sup>th</sup> to thank Toshi for his service to the University. We wish him well.

# Chief Residents' Page

By: Anne Bartlett and Angie Duong, Chief Residents



**What an exciting summer! We all had a chance to say goodbye to old fellows and a few of the 2010 Class, as well as had a chance to welcome new fellows, residents, and our first post-sophomore fellow. The year is already off to a great start! The new and exciting surgical pathology schedule is keeping everyone on their toes. We all are looking forward to a really productive year!**

**Good luck and best wishes,**

**Anne and Angie**



# FELLOWSHIPS



The Hematopathology Fellowship Program, directed by **John Lazarchick, M.D.** recently received the results of the ACGME site visit that took place in 2009. The RRC for Pathology accredited the program for another 5 years. The letter stated that "The Review Committee commended the program for its demonstrated substantial compliance with the ACGME's Requirements for Graduate Medical Education without citations." Congratulations Dr. Lazarchick!

## New Fellows

### Forensic Pathology Fellow



**Lee Marie Tormos, M.D.** joined the Forensic Pathology Section. Lee Marie, her husband, Otto G. Carretero, and children, Lyanne Marie and Otto Enrique moved from San Juan, Puerto Rico where Dr. Tormos was an anatomic pathologist at the Institute of Forensic Sciences.

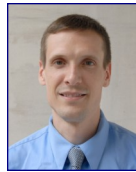
### Dermatopathology Fellow



**Kristopher Fisher, M.D.** joins us from the University of Tennessee, Memphis, where he completed his residency in Dermatology.

### Hematopathology Fellow

**Brian Davis, M.D.** joins us from the University of Kentucky AP/CP residency program. Brian, his wife Elizabeth, and son, James, welcomed a daughter, Abigail, on July 7, 2010. Congratulations!



### Cytopathology Fellows



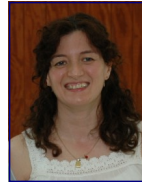
We have a regionally and educationally diverse group of cytopathology fellows this year: **Ningli Cheng, M.D.** joins us after completing Mount Sinai School of Medicine's Gynecologic Pathology Fellowship; **Kyle Perry, M.D.** joins us after completing a Surgical Pathology Fellowship at Mayo Clinic; and **Mary Wren, M.D.** completed her residency with us.

### Surgical Pathology Fellow



**Paul Eberts, M.D.** completed his residency with us and joined the Surgical Pathology Section.

### Clinical Chemistry Fellow



**Alina Sofronescu, Ph.D.** is our first Clinical Chemistry Fellow. She joins us from the University of Manitoba, Canada, where she received her doctorate in Physiology.

*Welcome to the Department!!*

# ARRIVALS



**Jonathan Ralston, M.D.** joined the faculty in the Dermatopathology Section on July 1. Dr. Ralston, a native of Louisville, Kentucky, received his undergraduate degree at Xavier University. He then completed a Master of Science in Physiology and

Biophysics at the University of Louisville, where he also attended medical school. Dr. Ralston completed his residency training in Anatomic and Clinical Pathology followed by a fellowship in Dermatopathology at New York University. In his free time, Dr. Ralston enjoys woodworking, playing guitar and golfing. Dr. Ralston's wife, Mariela Perez-Ralston is a native of Puerto Rico. She graduated from Georgetown University where she obtained an undergraduate business degree in finance and international business. Currently, she works as an online editor and project manager with clients in the entertainment industry, and is also pursuing a second degree in culinary arts. Mariela is an avid baker, tennis player and tireless traveler. Welcome Jon and Mariela!



**Ana Maria Medina, M.D.,** Hematopathology fellow for year 2009/2010, gave birth to twins, Abigail and Benjamin on July 7, 2010. They are the first children for Ana Maria and husband, **Luis Fernandez de Castro, M.D.,** 2nd year resident in Ophthalmology.

Congratulations Ana Maria and Luis!

# *43rd McKee Cytology Seminar & Pratt-Thomas Surgical Pathology Symposium in Gastrointestinal & Hepatic Pathology*

The 43<sup>rd</sup> McKee Cytology Seminar & Pratt-Thomas Surgical Pathology Symposium in Gastrointestinal & Hepatic Pathology was held on beautiful Kiawah Island, SC in April 21-24, 2010. Building on the success of previous conferences, the McKee Seminar this year focused on new developments in the field of cytology and provided a comprehensive review of selected problematic areas, while the Pratt-Thomas Symposium focused on Gastrointestinal & Hepatic Pathology.

One hundred and twenty-six pathologists and cytotechnologists from the United States and Canada attended the conference. The chair of the Department of Pathology and Laboratory Medicine of the Medical University of South Carolina, **Janice M. Lage, M.D.**, served as the course director. **M. Timothy Smith, M.D.**, Director of Anatomic Pathology, and **Jack Yang, M.D.**, Director of Cytopathology, moderated the McKee seminar. **David N. Lewin, M.D.**, Director of Gastrointestinal and Hepatic Pathology, moderated the Pratt-Thomas Symposium.

The speakers for the McKee Seminar included nationally and internationally recognized cytopathologists. Edmund S. Cibas, M.D., from Brigham and Women's Hospital, gave an excellent summary of the newly developed Bethesda system for reporting thyroid cytopathology; Michael R. Henry, M.D., from the Mayo Clinic, provided a comprehensive review of the role of Human Papilloma Virus in cervical pathology; Martha B. Pitman, M.D., from Massachusetts General Hospital, and Michael W. Stanley, M.D., from the United Hospital, talked about multiple approaches in diagnosis of pancreatic cystic lesions and body fluid cytology respectively, which represent difficult areas in the field of cytology. MUSC faculty, Haytham Dimashkieh, M.D. and Jack Yang, M.D., presented unknown cases in Non-Gynecologic and Gynecologic Cytology, respectively.

The speakers for the Pratt-Thomas Symposium included 11 internationally recognized Gastrointestinal Pathologists and Gastroenterologists. The 3-day symposium was packed full of information on Hepatic and Gastrointestinal Pathology. The first day focused on Hepatic pathology with presentations from Drs. John Hart (University of Chicago), Ken Batts and Larry Burgart (Abbott Northwestern Hospital). The remaining days focused on the gastrointestinal tract from esophagus to colon with presentations from Drs. Audrey Lazenby (University of Nebraska), David Lewin and Larry Comerford (MUSC), Greg Lauwers (Massachusetts General Hospital), John Goldblum and Mary Bronner (Cleveland Clinic), Joel Greenson (University of Michigan), and Elizabeth Montgomery (Johns Hopkins).

As in previous years, the McKee Cytology Seminar and the Pratt-Thomas Symposium were well received by the participants. We wish to thank everyone involved who made this a great success and we look forward to seeing old friends and meeting new ones next year; April 11-16, 2011 at the Francis Marion in downtown Charleston (mark your calendars). The Pratt-Thomas Symposium will focus on gynecologic and urologic pathology.



# Upcoming National Pathology and Pathology-related and Laboratory Medicine-related Meetings

## July 25-29, 2010

American Association of Clinical Chemistry  
Anaheim, CA

## September 26-29, 2010

CAP — College of American Pathologists  
Chicago, IL

## October 27-31, 2010

ASCP — American Society of Clinical Pathology, Annual Meeting  
San Francisco, CA

## December 8-12, 2010

San Antonio Breast Symposium  
San Antonio, TX

## Conference Schedules

*Conferences are held at 8:00 am in CH204 unless otherwise noted*

### GME Schedule

#### 2010 – 2011

Date	Residents Presenting
August 11, 2010	Bartlett and Duong
September 8, 2010	Zhang and Hope
October 6, 2010	Bernstein and Rogers
November 3, 2010	Desouki and Stone
December 1, 2010	Spruill and Bruner
January 5, 2011	Coulter and Goldin
February 2, 2011	Hendryx and Ogden
March 9, 2011	Allen and Lindsey
April 6, 2011	Robinson and Wassum
May 4, 2011	Brooks and Pellicier
June 1, 2011	Stallworth and Hendricker

### Journal Club Schedule

#### 2010 – 2011

Date	Residents/Faculty Presenting
August 25, 2010	Rogers/Zhu and Zhang/Self
September 22, 2010	Goldin/Lewin and Desouki/Lazarchick
October 20, 2010	Bartlett/Squires and Hope/Madory
November 17, 2010	Duong/Steed and Coulter/Welsh
December 15, 2010	Ogden/Wolff and Lindsey/Bilic
January 19, 2011	Hendryx/Nolte and Bruner/Metcalf
February 16, 2011	Bernstein/Gallego Attis and Spruill/Alsharif
March 23, 2011	Robinson/Riemer and Stone/Yang
April 20, 2011	Pellicier/Schandl and Hendricker/Richardson
May 18, 2011	Allen/Rumboldt and Stallworth/Batalis
June 15, 2011	Brooks/Presnell and Wassum/Smith

### **MUSC DEPARTMENT OF PATHOLOGY AND LABORATORY MEDICINE**

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