MUSC
DEPARTMENT of PATHOLOGY & LABORATORY MEDICINE

PATHOLOGY & LABORATORY MEDICINE NEWSLETTER

Volume 2, Issue 2 2011

Department of Pathology & Laboratory Medicine Faculty - June, 2011

Inside this issue:

FROM THE CHAIR

This has been an exciting spring. We just completed the final lectures of the restructured curriculum for the second year medical students. We graduated one PhD student, one masters student, six Anatomic and Clinical Pathology residents and seven Fellows. Our residents did very well on the **Resident In-Service Examination** (RISE). Our cumulative pass rate for the **American Board of Pathology** far exceeds the national average. In order to handle the increased clinical needs of the oncologic surgeons at ART, we moved the offices of two senior pathologists over to ART. While our clinical service volume has increased by approximately 1%, the complexity of cases continues to rise.

Renovations in the Children's Hospital created three new office spaces to house our growing clinical faculty. **Dr. Ana Maria Medina**, who recently joined the faculty, moved into one of those offices. She is certified by the American Board of Pathology in Anatomic and Clinical Pathology, and subspecialty certified in Hematopathology and Cytopathology. Welcome Dr. Medina!

In order to enhance patient care, our clinical pathology colleagues are bringing on line new molecular assays for genetic alterations in **EGFR, KRAS, BRAF**, and **ALK**. This shortens the time to complete analysis of a patient's tumor and allows the patient's case to be presented at the very next subspecialty tumor board conference.

Our Research Division hired one hearing research investigator, Chandrakala Puligilla, Ph.D., from the NIDCD, NIH. Interviews are underway for additional cancer research faculty. A number of candidates have been back for second visits. **Dr. Carl Croce** from Ohio State University will be the key note speaker for our **Pathology Research Day** on Friday, September 2, 2011. His talk is entitled, "Causes and Consequences of microRNA dysregulation in Cancer." Additional speakers that day will include Melissa Scheiber, Claire Hinsch, Yazhi Xing, Ph.D., and Julie Woolworth, Ph.D.

Next **Departmental All Hands** meeting will be July 26, 2011. Results of the most recent satisfaction survey will be presented. Remember to nominate candidates for our, "**You're in the Spot Light,**" award. Upcoming **South Carolina Society of Pathologists** annual meeting in Asheville, NC, will be held on September 16-18, 2011. Faculty, residents and fellows are all welcome to attend.

Janice Lage, M.D.,
Professor and Chair

NEWS FROM DEPARTMENT ADMINISTRATION & BUSINESS OFFICE

You're in the Spotlight
Tony Eisenhart

Congratulations to Tony Eisenhart, selected and recognized as the Employee of the Quarter for taking the terror out of getting IT help.
Thanks, Tony, for never making us feel like we're computer illiterate ... even when we are.

The next ALL-HANDS Meeting is JULY 26, 2011 at 9:30 AM in 2W Hospital Amphiteater. Please mark your calendar, and plan to attend.

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.

National Laboratory Professionals Week was a great success again this year. **A Lab Employee Slide Show** was presented and tours were offered of the ***Micro/Molecular Pathology Lab*** and the ***Fast Flow Lab***.

Snack & Learn talks were presented by **Dr. Rick Nolte, Laurie Williams** and **Tiffany Walters** MT(ASCP) SBB, from the American Red Cross

National Laboratory Professionals Week, once each year, reminds us of this important team who watch over our health from behind the scene.

TRAVEL UPDATES

REIMBURSEMENT FOR TRAVEL EXPENSES:
UNIVERSITY PURCHASING AND ACCOUNTS PAYABLE UPDATE

The University Accounts Payable Department complies with what the IRS refers to as an "Accountable Plan" as outlined in IRS Publication 463. An Accountable Plan allows the University to reimburse business travel expenses without withholding income tax, and requires that all travel related expenses be substantiated within **60 calendar days** from the return date of the trip. If an employee does not substantiate a trip's expenses within the 60 day period, the total amount of prepaid expenses may be reported as income and be taxed.

When submitting Travel Reimbursement Requests, please be sure that they are submitted in a timely manner.

MOTOR POOL CARS:
UNIVERSITY PURCHASING AND ACCOUNTS PAYABLE UPDATE

With the change in reimbursement rates based on whether a motor pool car is available, a number of questions have been received about how to find out if such a vehicle is available.

MUSC Transportation Services operates the process to secure a **state vehicle** for MUSC. The Motor Pool for state vehicles is actually housed at The Citadel. MUSC personnel who need to secure a motor pool vehicle should call Wanda Connor in University Transportation Services at 727-2175. She will then arrange for a vehicle, if it is available, or respond that one is not available.

Please remember that the new state rules require that if you are requesting 50.5 cents per mile, you must attest to the fact that a **motor pool vehicle was not available**. If you do not check and want to drive your own vehicle, the rate will automatically be reimbursed at 46.5 cents per mile.

As you fill out your travel reimbursement forms, please keep this in mind and claim ONLY 46.5 cents per mile unless you can affirm on the form that you have checked and no motor pool vehicle was available. Then, and only then, can you claim the 50.5 cents per mile reimbursement.

IT update by Tony Eisenhart

Remotely Accessing MUSC Resources

Have you ever been off campus and needed to access your office computer? Maybe the I drive or K drive? There are several ways of accessing on campus resources, including your office desktop, while off site. In this installment, I'll go over two ways of remotely accessing MUSC resources while off campus.

Webapps: https://webapps.musc.edu/vpn/index.html

Most of you are probably most familiar with this method. Webapps can be used to access Cerner, E-Care Net Viewer (formally Oacis), financial applications such as UMS & Smart Stream, Adobe Acrobat, the Microsoft Office suite, and a bevy of other useful software tools. Focusing on our topic, Webapps can also allow you to remotely connect to your office computer using the Windows Remote Desktop utility. Your office computer needs to be **preconfigured** to accept the remote connection and you will need to request the Remote Desktop utility be added to your Webapps account. Please contact Tony Eisenhart (eisenhaj@musc.edu 792-2032) if you would be interested in having this configuration implemented or if you are interested in having one of the above mentioned applications added to your Webapps account.

VPN: https://vpn.musc.edu

The MUSC Virtual Private Network (VPN) is a system that enables secure access to the MUSC local network from a remote location. The VPN server provides secured access through a SSL Web Portal or SSL client tunnel. This utility and website are only available when you are off-campus. You must register your Net ID before using VPN at MUSC but please be patient; the registration can take up to an hour to fully process. Go here to register:

https://www.musc.edu/infoservices/vpnreg/cgi-bin/index.cgi

Are you an iPhone/iPad/iPod user? If so, there's a VPN client available for your device! Sorry Droid users, Motorola and Google are working on a VPN solution for their products, but it isn't available at this time.

For more information on MUSC'a VPN client, the Apple product VPN client, and other supporting documentation please visit:

http://nstwiki.musc.edu/index.php/Remote_Access

News from the UMA Compliance Office

The UMA Compliance Department is currently working with various areas to get the word out, coordinate efforts and provide education about the Health Information Technology for Economic and Clinical Health Act (HITECH).

Some of the highlights of the new HITECH act include **Breach Notification**. If a breach involves more than 500 individuals, the entity has 60 days to notify the individuals. It also must notify DHHS and the local news media. For other breaches, such as misdirected faxes, items sent to the wrong address, lost thumb drives, etc, a log must be kept and annually submitted to DHHS. To avoid breaches, encrypt email that goes outside the MUSC network. Do not store PHI on your C:/drive, and make sure that your laptops, PDAs, flash drives and other portable devices are data encrypted, password protected and inventoried. We suggest placing a sticker with your contact information on your flash drives to ensure safe return to you in the event they are lost. If you find a flash drive, do not put it in your computer to find out who it belongs to. Instead turn it in to your nearest Compliance Office.

Jennifer Simmons CPC

The MUHA Health Information Services Department is the overseer of all health information. All requests for copies of health information must come to the HIS department for processing (except Carolina Family Care). All requests received from any legal entity should go to the HIS department for disclosure. If you send information to an attorney, and if so required, you will have to attest to the authenticity of the record which leaves you accountable.

The UMA Compliance Department will continue to monitor the requirements regarding the HITECH Act. We are currently working with the MUHA Health Information Management Department on several projects including HIPPA/HITECH/ Release of Information training classes for staff on the front line. For more information, please contact Suzanne Collins, RHIA, CPC, CEMC in the UMA Compliance Department, collinsu@musc.edu, 876-1323.

MUSC
DEPARTMENT *of* PATHOLOGY & LABORATORY MEDICINE

Mission Statement:
To serve patients, health care providers, research scientists, scholars, and society by providing excellence and innovation in diagnostic services and educational resources in a respectful, professional and culturally diverse atmosphere.

Vision:
To become a preeminent leader in academic anatomic and clinical pathology while translating basic science discovery to improved clinical care.

2011 YES Campaign

www.musc.edu and click on the **YES** link

Gifts are used...

To heal

Your gifts help us maintain an environment for optimal patient care, with the best facilities, scientists and technologies available. Private gifts have helped us build many of our clinical centers of excellence, including the Children's Hospital, the Storm Eye Institute and Hollings Cancer Center, to name a few.

To discover

Your support helps us find new ways of treating cancer, heart disease, blindness, kidney problems, birth defects and hundreds of other health care problems.

To help train the next generation of health care providers

Private gifts provide scholarships, equipment and teaching materials, classroom and laboratory renovations, expanded educational opportunities for students and alumni, emergency loans, student travel and student research.

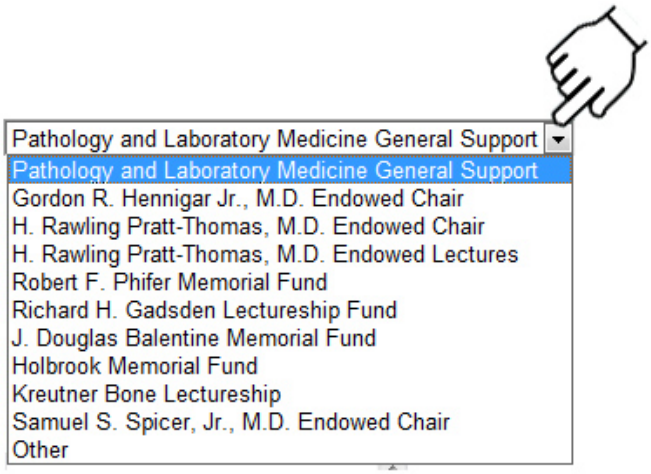
To Target Your Support to the Department of Pathology & Laboratory Medicine

You can choose to offer support to the Department or any of its endowed chairs, memorial funds and lectureship funds by using this link:

http://academicdepartments.musc.edu/development/online_donation/index.html

and selecting

Department of Pathology and Laboratory Medicine



Pathology Spring Symposia

The annual pathology meeting gained an extra day, and a new name as the Gadsden-Holbrook Symposium in Clinical Pathology joined the Pratt-Thomas Symposium in Surgical Pathology and the McKee Cytology Seminar to make the Pathology Spring Symposium. Thanks to Dr. Cynthia Schandl, SAMs were offered for the first time. The meeting was held this year on April 12 -16, 2011 at the Francis Marion Hotel.

Apparently, the meeting was a great success according to the feedback and comments of the 154 participants. 100% of participants that filled out an evaluation form stated that the meeting fully met their expectations. They cited:

- Excellence of presentations
- Usefulness of information presented
- Clinical relevance of lectures
- Selection of well-known faculty
- Choice of topics
- Charleston as a venue

As always, a big vote of thanks goes to Patty Houser, Teresa Kennedy, Jim Nicholson and Tony Eisenhart for the countless hours of work they perform for the meeting each year. Thanks also to the folks behind the scene, including: Beth Hansell, Lawrence Moser, Sonya Jordan, Clint Infinger, Howard Vaughan and Jarvis Jenkins

For the faculty, recognition is due to: Janice Lage, Frederick Nolte, Mary Richardson, Timothy Smith and Jack Yang for their role in obtaining guest speakers and serving as session moderators. Also thanks to: Lisa Steed, Frederick Nolte, Daynna Wolff, Jack Yang, Haytham Dimashkieh and Maria Gallego Attis for their excellent presentations.

Next year's meeting will be held at the Kiawah Island Golf Resort on April 23-28, 2012. The focus will be updates in surgical pathology, clinical pathology and cytopathology with emphasis on the role of pathologists in molecular testing. Details, as they become available, will be posted on the meeting website:

http://mckee-seminar.musc.edu/

Pathology Museum Project: Preserving and Digitizing Specimens

The Waring Historical Library has inaugurated a collaborative project with the Department of Pathology and Laboratory Medicine to preserve and digitize its pathology specimen museum.

Former WLS president Dr. Sally Self, a professor in the Department of Pathology and Laboratory Medicine, has arranged with colleague Dr. S. Erin Presnell for former faculty member Dr. Christine Papadea to work as a volunteer in the museum. In December 2010 Dr. Papadea began her project to inventory the specimens, perform preservation work required (including replacing fluids and repairing containers), and describe in both medical and laymen's terms what each of the nearly 500 specimens represent. When her work is complete, Waring Curator Susan Hoffius and Digital Archivist Jennifer Welch will schedule digital photography of the specimens to prepare them for MEDICA, the Waring's digital library.

"This project combines archival preservation, digitization, and curriculum support aimed at preserving and sharing the Pathology Museum collections with students and researchers," said Susan Hoffius of the project. "We are thrilled that the Department of Pathology and Laboratory Medicine has so enthusiastically embraced this collaborative enterprise."

Dr. Christine Papadea volunteers 15 hours per week to help the WHL and Dept. of Pathology and Laboratory Medicine.

Dr. Papadea expects the work on the specimens to continue for several more months. She is approximately one-third of the way through with the specimens on her list. ❖

The Waring Library Society Newsletter
From the Summer 2011 Issue, published by the Waring Library Society. The Waring Library, located next to St. Luke's Chapel on the MUSC Campus, is dedicated to preserving the history of the Medical University and medicine in South Carolina.

DEPARTMENT OF PATHOLOGY AND LABORATORY MEDICINE PRESS GANEY EMPLOYEE SURVEY RESULTS

Overall Partnership Score

Period	N	Mean Score	% Favorable
March 2011	35	74.0	89.2%
March 2010	36	72.9	87.3%

Overall Satisfaction Score

Period	N	Mean Score	% Favorable
March 2011	35	71.4	85.4%
March 2010	36	70.0	83.9%

Overall Engagement Score

Period	N	Mean Score	% Favorable
March 2011	35	77.3	93.1%
March 2010	36	76.7	90.7%

The Press Ganey survey helps establish how satisfied employees are, and how they perceive the sense of partnership between themselves and the Department of Pathology and Laoratory Medicine. The results are compared to national and regional peer groups.

The results showed a 93% favorable rating for a sense of engagement by the employees and an overall satisfaction score that was over 85% favorable. The overall partnership score showed an improvement when compared to one year ago.

These scores are used to improve the strength of the partnership between the department and its employees, resulting in a higher satisfaction and improved efficiency in the workplace.

ARRIVALS - We welcome:

Dr. Ying Xiong , Post Doctoral Scholar who will be working in the laboratory of Dr. LaRue.

Dr. Hongmei Luo and ***Dr. Xia Xiao***, both Visiting Scholars who will be in the laboratory of Dr Yong Wang.

Dr. Mauhamad Baarine, Post Doctoral Scholar and ***Dr. Balasubramaniam Annamalia***, staff scientist, will be working with Dr. Avtar Singh.

Dr. Yazhi Xing, Post Doctoral Scholar who will be joining Dr. Hainan Lang's lab.

Thomas O'Brien, retiree who returned to the department in equipment and facilities support.

New First Year Residents:
Shannon Butler-Williams, MD, Lily Marsden, M.D., Sherry Okun, M.D., Tiffany O'Neill, D.O., Kirtesh Patel, M.D., Tom Soike, M.D.

Post-Sophomore JKU (Jane K. Upshur) Fellows:
Joanna Dalland and Mia Taylor

New Fellows:
Cytopathology: Johann Hertel, M.D., Jason Hope, M.D., Shayna Tomchin, M.D.
Dermatopathology: Ford Rogers, M.D.
Forensic Pathology: Ashton Ennis, M.D.
Hematopathology: Todd Bruker, M.D.
Surgical Pathology: Anne Bartlett, M.D., Daniel Teague, M.D.
Surgical Pathology ENT: Dave Holloman, M.D.
Clinical Chemistry: Alina Sofronescu, Ph.D. (2nd yr), Zengliu Su, Ph.D. (1st yr).

DEPARTURES - We say farewell to:

Barbara Coleman, Administrative Coordinator to Dr. Lage, leaves MUSC after nine years of service.

Dr. Gallego-Attis, Assistant Professor in Anatomic Pathology joining LabCorp in Durham, NC.

Lawrence Moser, Department Administrator retired after more than 30 years in Pathology & Laboratory Medicine.

Dr. Makio Ogawa, Professor, who is retiring after many years of distinguished service and mentoring.

Dr. Darren Preece, Post Doctoral Scholar in Dr. Watson's lab

Virginia Roberts from the Histopathology Lab retired after 30 years, 8 mos, 17 days in Pathology and Lab Medicine.

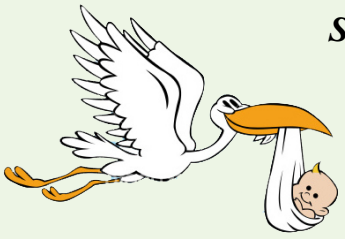
Congratulations to our:

Graduating Residents, July 2011

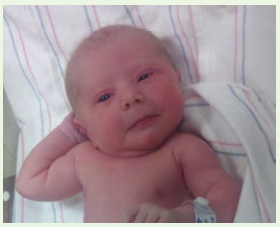
Resident:	Fellowship Training Program:
Anne Bartlett, MD	MUSC (Surgical Pathology)
Angie Duong, MD	Yale University (Hematopathology)
Jason Hope, MD	MUSC (Cytopathology)
Raford Rogers, MD	MUSC (Dermatopathology)
Mokhtar Desouki, MD	University of Pittsburgh School of Medicine (Breast and GYN pathology)
Linsheng Zhang, MD, PhD	Emory University (Hematopathology)

And Graduate Students:
Shimon P. Francis, PhD and Ashley M. Smith, MS

SPECIAL ARRIVALS



Bab Coleman's son William at 1 day old.



Jim & Becky Madory welcomed Rachel Katherine Madory, born 5/16/2011 weighing 6lbs. 10 oz.
Rachel is rumored to have arrived by train.

Kate and Chip Lindsey are the proud parents of Ella Grace Lindsey, born 4/19/2011 weighing 5 lbs. 5 oz.

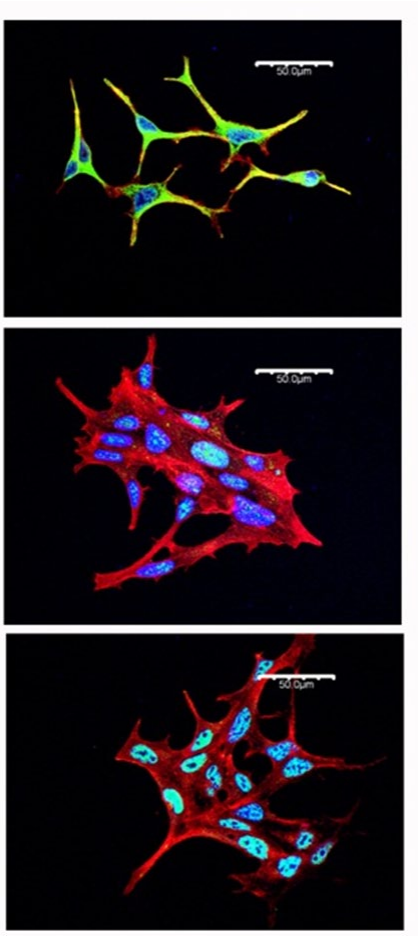
Zora Katarina Rumboldt (6 lbs. 14 oz.) has provided a new tax deduction for Tihana and Zoran Rumboldt.

Ashley Smith Defends Her Thesis

After little over a year in the laboratory of Dr David Turner in the Department of Pathology & Laboratory Medicine, Ashley M Smith recently successfully defended her Master's thesis. We asked Ashley to provide us some feedback on her thoughts and experiences during her time here at MUSC.

"I discovered my love for research while I was pursuing my BS in Biological Sciences at NC State University. After graduating in 2008, I looked to graduate school to expand my knowledge of molecular biology. I fell in love with Charleston when I visited for a friend's wedding and was thrilled when I realized that there was a great graduate program at MUSC, with an amazing and large array of research that I didn't think possible outside of a large university such as NC State or GA Tech. Having decided that I wanted to move into cancer research, I chose to apply for my Master's within the Pathology and Lab Medicine Department because of the prominent cancer research being done there within.

Adjusting to MUSC took some time. With a class of only 28 students in the core curriculum, I found there to be a significantly different atmosphere from NC State, where even the smallest lectures had at least 50 people, if not 300. However, I found that I was able to thrive in this close knit teaching environment, grasping the finite details of theories I had glazed over in my undergraduate experience. Our department is one of the few on campus that requires its Master's students to take the core curriculum the first year of the program. It was a challenge to successfully complete the core while doing rotations and fulfilling a 20- hour a week work study position on campus. However, I have found of late that the class-based training has given me an edge in my job hunting, as many employers expect a Master's degree to be entirely technical with very little class theory.



After going through my rotations, I chose to stay in the lab of Dr. David Turner to explore the progression of Prostate cancer at the transcription level. I feel that this was the best decision I have made in my educational career. Dr. Turner has been an amazing mentor, teaching me and allowing me a freedom in the lab that I feel led to a better understanding of the process of scientific discovery. My project did not always go as expected, we all know this to be the nature of research, but Dr. Turner was always patient, guiding me while also teaching me to think through each problem to achieve a solution. I am thrilled to be able to say that my Master's project has helped to provide strong data (see inset left illustrating phospho-Ets1nuclear localization in castrate resistant prostate cancer cells) for both a publication and Dr Turner's R01 submission. I feel strongly that Dr Turner will have a very successful research career and be a strong mentor for future graduate students.

I consider myself to be extremely lucky to have found so many great mentors at MUSC, especially within our department; I have found that help is always available to those who have need. I would not have been as successful in my project without the help of other professors, such as Dr. Victoria Findlay, Dr. Dennis Watson and Dr. Demetri Spyropoulos. I am currently searching for a job in molecular research. I hope to find an exciting research opportunity in which I will be able to contribute to the direction of the project and teach others techniques at the bench."

Racial Disparities in Prostate & Breast Cancer in South Carolina

David P Turner

Racial populations across the United States and around the world suffer disproportionately from cancer and its after-effects. Overcoming cancer health disparities is one of the best opportunities we have for lessening the burden of cancer. Here in South Carolina (SC) mortality rates for African American breast and prostate cancer sufferers are the highest in the US. Age-adjusted prostate cancer incidence rates are 78% higher among South Carolinian African American men than European American men and mortality rates are three times higher. In SC, breast cancer is the most commonly diagnosed cancer among women and although African-American women have a lower incidence rate than white women, black women are twice as likely to die of breast cancer due to the development of highly aggressive disease. In a Carolina Breast Cancer study of 657 breast cancers patients, the aggressive triple negative phenotype was significantly higher in African American than non-African American women (33.9% versus 21.2%, P=0.0003).

While quality of care issues, demographics and socioeconomic status clearly contribute to cancer health disparities, it is becoming increasing clear that molecular and genetic differences in tumor biology also play a critical role. The importance of biological factors in racial disparity is highlighted in a recent study investigating survival rates in almost 20,000 cancer patients treated on 35 Southwest Oncology Group (SWOG) randomized phase III clinical trials. The study confirmed that African-American breast and prostate cancer sufferers have higher mortality rates than Caucasians (Table 1) but this study was significant from previous studies because associations between race and overall survival were assessed after controlling for prognostic, treatment and socioeconomic factors. The results provide the first detailed study that shows that racial disparity in breast and prostate cancer mortality figures are due, at least in part, to the inherent genetic, biological and molecular characteristics of racial specific tumors.

Cancer Type	Patient number	Hazard Ratio	% 10 yr survival (AA vs all other)	Median survival (AA vs all other)
Pre-menopausal breast	2360	1.43 p =.006	68 vs 77	not reached
Post-menopausal breast	4316	1.48 p =.001	52 vs 62	10.2 vs 13.5 yrs
Advanced Prostate	1429	1.19 p =.002	6 vs 9	2.2 vs 2.7 yrs

Table 1. African-American (AA) breast and prostate cancer sufferers have higher mortality rates than Caucasians

Sparse information exists about the genetic and biological factors that contribute to differential cancer survival rates observed in race specific backgrounds. A greater understanding of these biological factors is critical for addressing the increased cancer mortality observed in racial groups: cancer incidence in minorities is predicted to double in the next 20 years compared to a little over 30% among European Americans.

A possible molecular mechanism which this laboratory believes may promote cancer disparity is the increased presence of advanced glycated end-products (AGE's). The dietary carbohydrates fructose and glucose are metabolized by specific biochemical pathways to produce essential metabolites that are required for metabolism. These essential metabolites produce carbohydrate intermediates which are prone to generate reactive carbonyl species (RCS's). RCS's react with macromolecules such as proteins, lipids and DNA to produce AGE's in a process known as glycation. The expression of a protein-AGE was first linked to a disease phenotype through the identification of a hemoglobin adduct found in diabetes patients and has now been developed as a clinical biomarker for diabetes diagnosis and treatment. While AGE's are best studied for their role in diabetes, they are also proposed to play a critical role in aging and neurodegenerative disease but their role in promoting cancer is unclear. Elevated glucose up-take, increased glycolysis, oxidative stress and intracellular free radical activity are cancer-associated processes that are known to increase glycation and circulating AGE levels. Glycation adducts in cell lines have been demonstrated to produce multi-base deletions, base pair substitutions, tandem mutations and base-pair additions/deletions which impair genetic fidelity to promote tumorigenesis.

Dr. David P. Turner

Racial Disparities in Prostate & Breast Cancer (cont.)

Racial specific differences in AGE levels are hypothesized because there is a direct correlation between ingested and circulating AGE levels, oxidative stress and glycation induced DNA mutations which provide a mechanistic link between dietary carbohydrates and cancer. Obese men are twice as likely to die of prostate cancer over lean men and due to low income eating habits, AGE content in the Western Diet has consistently increased over the last 50 years. This is racially significant as a larger proportion of South Carolinian African Americans (76%) are overweight when compared to European Americans (63%) (Behavior Risk Factor Surveillance System, 2007) and poverty rates in South Carolinian AA's are lower than the national average (14% compared to 12%). This provides a compelling rationale for examining glycation and AGE levels as a mechanism promoting racial disparity in prostate cancer in this state.

The above rationale forms the basis for a pilot research project to be included in an NIH P20 grant application led by Dr Marvella Ford (MUSC) and Dr Judith Salley (SC State University). The application to be re-submitted later this month aims to develop a SC Disparities Research Center in Prostate and Breast Cancer. This four-year proposal represents a collaborative partnership between South Carolina State University and the Medical University of South Carolina (MUSC) to form the South Carolina Cancer Disparities Research Center in Prostate and Breast Cancer ("SC CaDRe"). The SC CaDRe was designed, and the pilot research project chosen, by investigators at SC State University and MUSC with strong input from a Community Advisory Committee. The goals of the SC CaDRe are to create a group of well trained and experienced researchers at SC State University and MUSC focusing on cancer disparities research, and to enhance the racial and ethnic diversity of scientists who choose cancer research careers in basic, clinical, and population science.

The central hypothesis of the pilot study is that race specific differences in DNA glycation correlate with health disparities in prostate cancer. The study proposes to identify and measure dNTP-AGE levels and to analyze the expression and functional activity of anti-glycation repair proteins in a cohort of blood and tissue samples from three racial groups in SC: 1) South Carolinian Sea Island African American, 2) non South Carolinian Sea Island African American and 3) European American prostate cancer patients. The African American population in SC is an underserved population in terms of health care. A unique feature of this population is that many belong to the "Gullah community" which populates the Sea Islands bordering SC. Due to historical geographic and cultural isolation, they represent an almost pure African population (admixture less than 3.5%) providing an ideal population for the study of genetics, biomarkers and epidemiology that may provide insight into the prevailing cancer disparity mortality statistics found not only in SC but in the U.S. The study is expected to provide novel insight into racial specific cancer associated AGE expression levels and overall AGE repair capacity during prostate cancer progression. This would provide an initial assessment of the glycation process in promoting racial disparity in prostate cancer and allow the development of future individual and collaborative grant applications targeted at the development of novel strategies for the racial specific treatment of cancer.

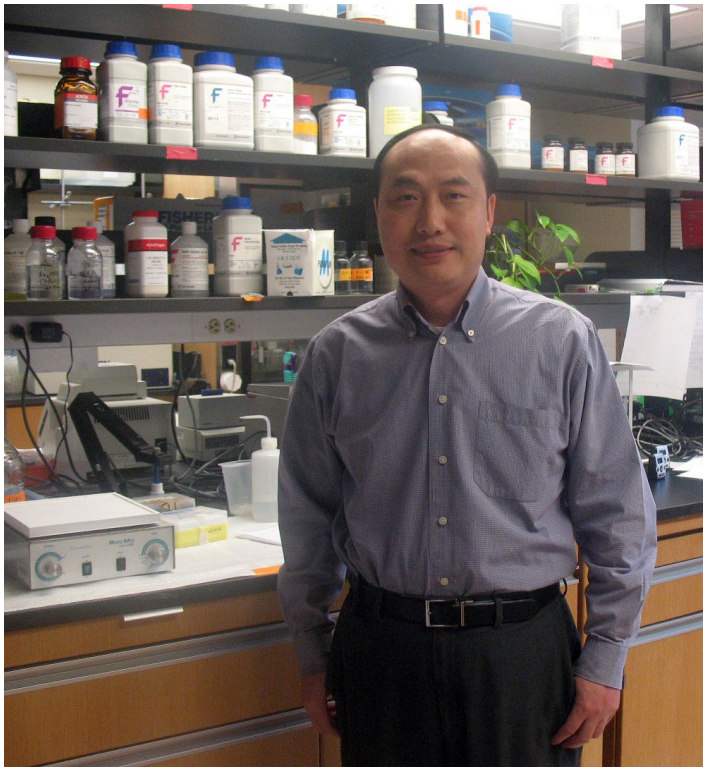
The Division of Research has had a productive time from January through March. Eight grant proposals were submitted requesting $1,393,786 in total first year costs. Also, during this period six grants were awarded totaling $699,577 over a one-year period (see table below). Congratulations and many thanks to everyone involved in obtaining these awards.

Principal Investigator	Title and Sponsor	Award Date/Amount
Singh, Avtar	AMP Kinase Activity in Stroke Injury (VA Merit Grant)	1/1/11 $125,000
Dammai, Vincent	Cellular Factors Promoting Renal Cell Carcinoma	2/1/11 $249,660
LaRue, Amanda	Hematopoietic Stem Cell-Derived Carcinoma Associated Fibroblasts in Tumors	2/1/11 $261,449
Francis, Shimon	Celestrol as a Co-Therapy for Inhibition of Aminoglycoside-Induced Ototoxicity	2/7/11 $19,184
Lang, Hainan	Proteomic Analysis of Degenerated Auditory Nerve (SCTR voucher pilot program)	2/8/11 $1,000
Spyropoulos, Demetri	Developmental Transcription Factors in Prostate Cancer (Emory Sub-Award)	3/1/11 $13,284
		TOTAL = $669,577

Hematopoietic Stem Cells Ex Vivo Expansion

By: Yong Wang, M.D., Ph.D., Assistant Professor

Hematopoietic stem cells (HSCs) possess the unique capacity to self-renew and give rise to all the mature cells within the blood and immune systems. Thus, HSCs are essential for replenishing dead and aged blood and immune cells and maintaining homeostasis of the hematolymphoid system. HSC transplantation has been widely used for the treatment of a variety of human diseases including hematopoietic and non-hematopoietic malignancies, but also has potential important applications in cell and tissue bioengineering, regenerative medicine and gene therapy research. It is well established that a minimum number of long-term repopulating HSCs is required to ensure durable engraftment after transplantation, thus both the number and quality of HSCs are critical to the success of HSC transplantation therapy. Since it is difficult to obtain large numbers of HSCs, HSC expansion is an important approach to enhancing the success of donor engraftment in clinical transplantation therapy and to facilitate basic stem cell research.

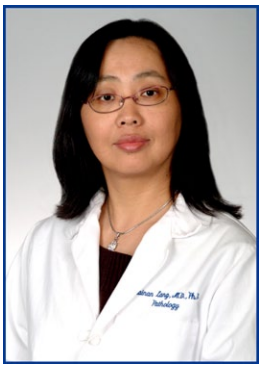


Dr. Wang in his laboratory

Numerous strategies for the expansion of HSCs have been reported using various combinations of hematopoietic growth factors such as stem cell factor (SCF, or c-kit ligand), thrombopoietin (TPO, or c-pml ligand), Flt-3 ligand, and interleukin-11 (IL-11). It has been shown that TPO as a single growth factor supports survival and modest proliferation of highly purified HSCs in vitro. However, addition of these growth factors into the culture system only leads to limited (less than 5-fold) HSC expansion. Transduction of HoxB4 or HoxA9 genes into HSCs significantly enhances self-renewal and ex vivo expansion, but genetically manipulation of HSCs raises safety concerns for clinical applications. Although several new cytokines (e.g., Notch ligands, Wnt3a, angiopoietin-like proteins, pleiotrophin, and prostaglandin E2) have been shown recently to promote HSC self-renewal and ex vivo expansion, the present ex vivo culture conditions using a combination of various hematopoietic growth factors/cytokines only modestly expand HSCs. Also, this technique often results in significant loss of long-term repopulating capacity of expanded HSCs. Therefore, new approaches to improve HSC ex vivo expansion are needed.

The use of umbilical cord blood (CB) as a source of HSCs for transplantation therapy is rapidly expanding, particularly for the treatment of acute myeloid leukemia (AML). CB HSCs hold many advantages over BM-derive HSCs such as the use of simple procedures for cell processing and lower risk of graft-versus-host disease (GVHD). However, CB-derived HSCs are of limited use in adults because the number of HSCs available in CB is not sufficient for transplant; thus, ex vivo expansion of HSCs is needed to bridge this gap in availability. Delayed myeloid engraftment after CB transplantation (CBT) is thought to be a consequence of inadequate numbers of HSCs/HPCs in the graft and is associated with increased early transplant-related mortality. Therefore, new culture strategies to augment the expansion of CB HSCs will markedly benefit CBT and stem cell-based gene therapy. Unfortunately, previous attempts at ex vivo expansion of CB HSCs have resulted in a progressive loss of long-term repopulating cells with few significant clinical effects. To address this issue, our laboratory is investigating the signaling pathways that are involved in modulating HSC self-renewal and ex vivo expansion, with a long-term goal of developing a novel strategy for CB HSC expansion.

Activation of p38 mitogen-activated protein kinase (p38 MAPK, or p38) has been implicated in the pathogenesis of a variety of hematopoietic disorders, including Franconi anemia (FA) and myelodysplastic syndromes (MDS). Furthermore, oxidative stress, mutation of ATM, loss of FoxO3 and serial transplantation all activate p38 MAPK through up-regulation of reactive oxygen species (ROS) and lead to premature exhaustion of HSCs. These studies suggest that activation of the ROS-p38 pathway may negatively affect HSC self-renewal and expansion. Interestingly, inhibition of p38 has been shown to improve the function of HSCs and hematopoietic progenitor cells (HPCs) in FA and MDS patients and to rescue p38 activation-mediated premature exhaustion of HSCs in FoxO3 knockout mice. However, the role of the ROS-p38 MAPK pathway in the regulation of human HSC self-renewal and ex vivo expansion is unclear. We recently found that inhibition of p38 significantly promotes murine HSC expansion and increases the numbers of cobblestone area-forming cells (CAFCs) in ex vivo culture of sorted mouse Lin-Sca1+c-Kit+ (LSK) cells. Moreover, LSK cells expanded in the presence of p38 specific inhibitor (SB203580) exhibit markedly higher levels of donor-derived engraftment in recipient mice as determined by completive repopulation assay (Wang Y, et al. Stem Cell Dev 2011). These novel findings suggest that inhibition of the ROS-p38 pathway may represent a novel approach to enhance ex vivo expansion of HSCs. Ongoing work in the lab is currently focused on validating whether targeted inhibition of the ROS-p38 pathway enhances CB HSC ex vivo expansion using a stem cell serum-free culture system, immunophenotypic flow cytometry analysis and a NOD/SCID mouse repopulation cell assay.



Stem Cell Research Offers Hope for Hearing Loss

Hainan Lang, M.D., Ph.D., Assistant Professor

Research Projects on Cochlear Stem Cells:

Approximately 278 million people worldwide are affected with hearing loss, according to a recent report from the World Health Organization (http://www.who.int). In the US, an estimated 17 % of adults, or about 36 million Americans report some degree of hearing loss. For the majority of individuals, hearing deficits result from the loss or degeneration of cochlear cells, including sensory hair cells, spiral ganglion neurons and cells in the stria vascularis and spiral ligament. My training as an otolaryngologist with a background in clinical otology and 18 years of experience in auditory neuroscience research has directed my research efforts to rescue, regenerate or replace lost or degenerated cochlear cells using a variety of stem cell resources such as bone marrow (BM) stem cells, neural stem cells (NSCs), and stem cells isolated from adult inner ears. The long-term goal of my research is to seek efficient therapeutic strategies for hearing loss.

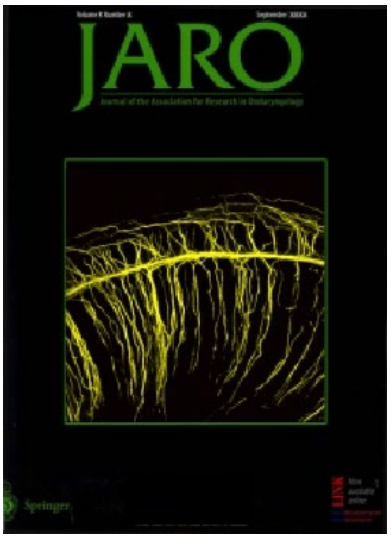
BM stem cells have the potential to differentiate into multiple non-hematopoietic cell lineages including fibroblasts/myofibroblasts in a number of tissues and organs such as kidney, heart, liver and brain. Our studies are the first to document that some non-sensory cells in the cochlea of the adult mouse are continually derived from BM stem cells. Moreover, we have found an increase in BM derived cells present in the cochlea after ototoxic drug exposure. In research studies with Drs. **Bradley Schulte**, **Judy Dubno**, **Makio Ogawa** and **Amanda LaRue**, we are investigating the potential of human BM stem cells to differentiate into specific non-sensory cells in young and aging ears using a humanized mouse model. This study will help further the understanding of how BM stem cells contribute to cellular homeostasis in the human inner ear and will provide the intellectual foundation needed to design treatments for hearing loss, especially age-related hearing loss.

Research Specialist Nancy Smythe

The transplantation of NSCs to facilitate regeneration and repair of neural tissues offers a promising therapeutic strategy for treatment of neurodegenerative disorders including auditory nerve degeneration. However, evidence from neurodegenerative disease animal models indicates that the time window for successful transplantation of NSCs after injury is narrow and that long-term survival of NSCs in the chronically injured host environment is limited. Using a well-established mouse model of auditory nerve degeneration, we are investigating the role of the host microenvironment with a focus on endogenous glial cells, in regulating the survival and differentiation of transplanted NSCs and stem cells isolated from adult inner ears. These experiments will reveal the critical role glial cells play in stem cell transplants and will impact the design of efficient therapies for hearing loss using glial cells as targets.

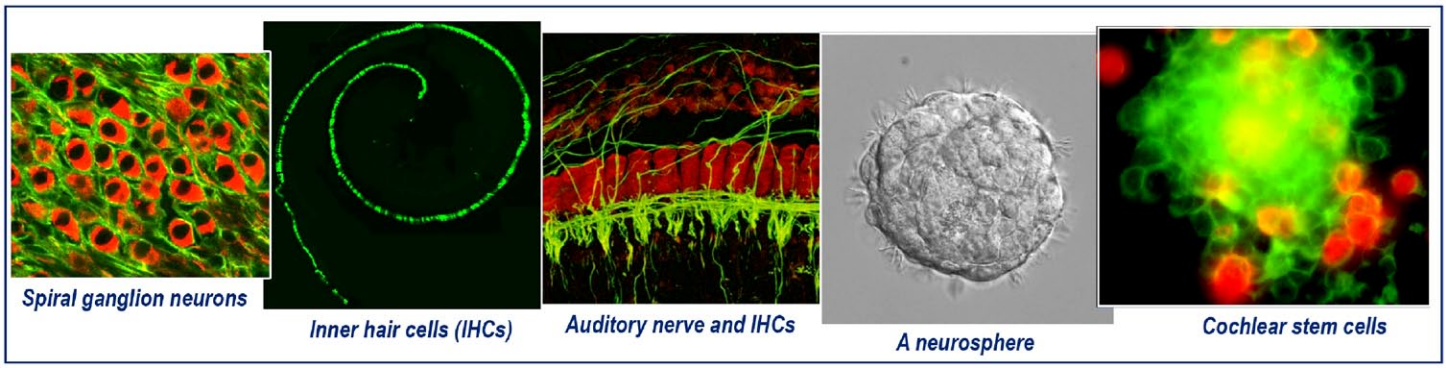
The Department of Pathology and Laboratory Medicine offers a highly collaborative research environment. The establishment and growth of our research team is indebted to the support of the Department and long-term collaborations with Dr. **Bradley Schulte**, and Drs. **Richard Schmiedt** and **Judy Dubno** from the Department of Otolaryngology. Recently, we embarked on an exciting project in collaboration with Dr. **Su-hua Sha,** an auditory neuroscientist and a new faculty member in the Department. In this project, we will study endocochlear potential changes and hair cell degeneration using a mouse model of TNFα gene mutation.

One of our recent publications, "Sox2 Up-regulation and Glial Cell Proliferation Following Degeneration of Spiral Ganglion Neurons in the Adult Mouse Inner Ear" (*Lang et al., J Assoc Res Otolaryngol, 2011 Vol:12 (2), 151-171; Cover image*), has been selected and evaluated by a Member of the Faculty of 1000 (F1000), which places our work in this library of the top 2% of published articles in biology and medicine.



"The finding of this paper that upregulation of Sox2 and S-phase label uptake after drug-induced spiral ganglia loss in an adult animal is very interesting, and opens up new questions about what these glial-like cells are and their significance…It would be interesting to study the significance of these Sox2-positive cells, since no neuron regeneration is reported, but Sox2 can also function to direct prosensory specification and induce neuronal cell fate during development ."
-- Anthony Ricci, Professor of Otolaryngology - Head and Neck Surgery, and Molecular and Cellular Physiology at Stanford University.

Stem Cell Research Offers Hope for Hearing Loss (cont.)



Collaborators on Current Projects:

MUSC: Drs. **Bradley Schulte**, **Makio Ogawa** and **Amanda LaRue** (Pathology and Laboratory Medicine); Drs. **Richard Schmiedt**, **Judy Dubno**, and **Mark Eckert** (Otolaryngology-Head and Neck Surgery); Dr. **Yiannis Koutalos** (Ophthalmology); Dr. **Edward Krug** (Regenerative Medicine & Cell Biology); Dr. **John Baatz** (Pediatrics); and Dr. **Saeid Taheri** (Radiology).

Other Institutions: **Donna Fekete** (Professor of Developmental Biology, Purdue University); **Karen Steel** (Professor of Genetics at Welcome Trust Sanger Institute, UK; Fellow of the Academy of Medical Sciences, UK); **Karen Avraham** (Chair of the Department of Human Molecular Genetics at Tel Aviv University, Israel; Past Present of the Association for Research in Otolaryngology); **Xuezhong Liu** (Associate Professor of Otolaryngology, and Human Genetics and Pediatrics at University of Miami); **Robin Davis** (Professor of Cell Biology & Neuroscience, Rutgers University); **Fred Gage** (Professor of Genetics at the Salk Institute; Past President of Society for Neuroscience and the Member of National Academy of Sciences).

Current Funded Projects:

PI Lang: NIH P50 DC00422 "Human Hematopoietic Stem Cells and the Aging Inner Ear".

PI Schulte: R01DC00713 "Inner Ear Ion Transport Mechanisms"

Pending and Planned Grant Applications:

NIH NIDCD R01 DC012058 "Auditory Nerve Degeneration and Repair" (pending).

RNID International Grant "Rescuing a Congenital Form of Progressive Hearing Loss in Mice Using Viral Gene Transfer of a microRNA" (pending).

NIH NIDCD "Exploring the Ability of Cochlear Specific microRNAs to Regenerate Hair Cells in a Mouse Model of Sensorineural Hearing Loss" (planned).

Research team members and friends spent a happy-hour at the City Marina Restaurant

Research Specialist Juhong Zhu