THE PATH WAY

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DEPARTMENT of PATHOLOGY & LABORATORY MEDICINE



Steven L. Carroll, M.D., Ph.D., FASCP, FCAP

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2016 Pathology Spring Symposium

The annual trilogy of Gadsden-Holbrook/Pratt-Thomas/ McKee Pathology Spring Symposium recurred the week of 23-27 February. There were 121 attendees for the combination of educational courses in clinical pathology, surgical pathology, dermatopathology and cytopathology. Speakers were all leaders in pathology diagnostics. The venue was again Belmond Charleston Place on King street in downtown Charleston using the Riviera Theater's conference facilities.

The facilities were excellent but the cold weather dates again compromised attendance. The first portion of the conference was the Gadsden-Holbrook symposium in clinical pathology held on Tuesday. New tools for diagnos-



ing latent tuberculosis was presented by Dr. Litwin. Dr. Zhu spoke on the uses of mass spectrometry in the clinical laboratory. In addition, Dr. Linder from the University of Louisville spoke ontranslating pharmacogenomics into clinical practice. Dr. Schandl spoke on cancer surveillance by identifying circulating tumor DNA. Dr. Schmotzer from Case Western Reserve spoke on critical values and impact on patient care. The last talk of the day was provided by Dr. Procop from Cleveland Clinic who spoke on improving test utilization.

This newsletter is made possible from the generous contributions of MUSC's Pathology and Laboratory Medicine Faculty and Staff. The success of this publication is dependent upon this support. Thank you for your interest, time and information. For inquiries, suggestions or submission information please contact Lori Roten (roten@musc.edu).

Continued - 2016 Pathology Spring Symposium

On Wednesday the Pratt-Thomas symposium in surgical pathology began. Joel Greenson, MD from the University of Michigan spoke on GI tract polyposis syndromes and the colorful topic, "Colitis is a Pain in the Butt." Dr. McKenney from Cleveland Clinic spoke on mimics of urothelial carcinoma and diagnostic variants of urothelial carcinoma. Jean Simpson, MD spoke on controversial issues in breast pathology and pitfalls in diagnosis. Continuing on womens issues, Dr. Longacre from Stanford gave lectures on mesenchymal tumors of the uterus. Dr. Bruner from MUSC gave and enlightening presentation of non-neoplastic renal disease. Dr. Richardson also from MUSC provided a timely update of new sinonasal malignancies and their unique characteristics. On friday Andrew Folpe from Mayo Clinic provided updates on the spectrum of liposarcomas and angiosarcomas. Dr. Elston from MUSC spoke on cutaneous infections and unusual and borderline melanocytic neoplasms.

The 49th McKee Cytology Seminar began on Friday after a scrumptious lunch. Dr. Yang from MUSC was the moderator. Dr. Eva Wojcik, chair of pathology at Loyola spoke on the new Paris System for Reporting Urinary Cytology and on the Paris System in Practice. The world agrees that her presentations



on urine cytology are legendary. On Saturday Dr. Faquin from Massachusetts General Hospital spoke on advances in thyroid cytology and HPV-related head and neck cancer. Dr. Gong from MD Anderson spoke on EUS-FNA of the pancreas and pitfalls in diagnosis of metastatic lesions. Rounding out the day Dr. Chajewski and Dr. Lindsey both from MUSC provided a potpourri of cytology unknowns and a review of a new and improved technique for cell blocks. The speakers for the dermatopathology portion of the conference were Dr. Soike and Dr. Hamstra who presented a selection of very interesting unknowns.



Overall the conference was an educational success and included a number of significant updates and recommended practice changes. The attendees were wishing for warmer spring weather. 2017 will be the 50th McKee Cytology symposium.

Written by: M. Timothy Smith, M.D., Professor, Director, Anatomic Pathology



Leadership Council and the Apple Tree Society. Based on your "spot on" insights and recommendations, it is easy to see why you are the recipient of the 2015 Peggy Schachte Research Mentor Award. For example, you suggested that it might be helpful for a person to have a "mentoring team" to address different needs and provide different viewpoints, rather than relying on a single mentor. For mentors, you said it was important to step back and make sure your goals were separated from the goal of the mentee, focusing on making your mentee "better" rather than doing anything for yourself. For junior mentors, you recommended finding a senior co-mentor to help guide their path up the career ladder and to provide support when seeking extramural funding.

The suggestions you shared in an hour have the potential to make all the difference in the world in a person's career. You are a tremendous role model for any faculty member no matter where they are in their career. Your past, present, and future mentees are extremely fortunate to have the opportunity to learn with and from you.

Thank you for taking the time and interest to share your knowledge, experience, and expertise.

Kind regards,

CC:

Man J. Quroud

Marc I. Chimowitz, MBChB Professor of Neurology Associate Dean of Faculty Development Director, Mentoring Leadership Council

Dr. Ray DuBois Dr. Steven Carroll

nau May

Mary Mauldin, EdD Chair, Apple Tree Society

CONGRATULATIONS!

Dr. Jim Madory received his

"Physician Builder—Analytics Certification", Version: EPIC 2015 on 2/25/16.

He is now one of three at MUSC one of 10 Pathologists in the country that has received this certification.

CONGRATULATIONS!

To our past 2014-2015 Cytopathology Fellows,

Dr. Heidi Hamilton, Dr. Jalidsa Pellicier and Dr. Matt Berstein!

They successfully passed their Cytopathology Boards on their first attempts!

The Medical Center is proud to recognize their Employees of the Month.

Our very own Wanda Shotsberger was selected as one of the

Medical Center's January 2016 Employees of the Month

http://mcintranet.musc.edu/muscexcellence/awards/EOM/employeeofthemonth.htm

Below is the nomination that won her this award:

Wanda Shotsberger is a histopathology technician in the Department of Pathology and Laboratory Medicine at MUSC. Not only does she perform her duties at the highest level on a daily basis, but I am frequently impressed by the extra efforts she makes on a consistent basis to improve care for our patients. Just this morning, a lung biopsy arrived in our department which was designated by the submitting physician for rush processing due to the severity of the patient's illness. Wanda noticed the unusual clinical information submitted along with the biopsy tissue, and called me immediately to inquire what if any special studies might benefit the patient and if so, if



I wished to request they be initiated from the get-go. This step is so unusual and so unexpected, and yet so characteristic of Wanda to anticipate the possible needs of the patient in order to make sure that the patient has the opportunity get an accurate diagnosis as soon as possible so that appropriate treatment not be unnecessarily delayed. We know that even a few minutes or hours can make an enormous difference for patient outcome, and Wanda recognizes this reality and consistently goes out of her way to make sure not only that the biopsy tissue is processed in a rush manner as required, but also that the pathologist is alerted promptly to the clinical information so that appropriate studies be performed promptly. MUSC is fortunate to have such an outstanding professional who consistently exceeds the expected standards of excellence in performance of her duties, which efforts help deliver the highest level care for our patients. Thank you, Wanda!!

Nominated by: Ellen Riemer





"MUSC Forensic Autopsy Services Not exactly like CSI" article link below:

http://academicdepartments.musc.edu/catalyst/ archives/2016/2-12Autopsy.html

ARRIVALS:

ARRIVALS

- Kyla Baron, Post Doctoral Scholar, arrived on 1/11/16 in Dr. Gavin Wang's Lab
- Deonna Dong, Lab Specialist I, arrived on 2/8/16 in Dr. Suhua Sha's Lab
- Melinda Goforth, Research Specialist I, arrived on 2/29/16 in Dr. Qi Wang's Lab
- Dr. Hao Xiong, Visiting Scholar, arrived on 3/2/16 in Dr. Suhua Sha's Lab



TO: Beth Hansell (Grandson)





Colton Ruger Hansell 7 lbs. & 4 oz. Born 4/13/16



GRADUATE STUDIES UPDATE

- Kayla Hill (Dr. Sha) Successfully defended her PhD thesis November 2nd
- Brooke King (Dr. Findlay) Successfully defended her MS thesis December 10th
- Alex Rutkovsky (Dr. Ethier) Successfully proposed her PhD thesis January 18th

Student Research Day

November 13th 2015

- I MSTP presentation (Poster)
 - Jamie Mills (Ethier Lab) won 1st place Kinard-Gadsen Award
- 9 PhD presentations (6 poster, 3 oral)
- I MS presentations (Oral)
 - Brooke King (Findlay Lab) won 2nd place oral
- 3 Post Doc presentations (2 poster, 1 oral)
- 5 Research Specialist presentations (poster)
 - Lourdes Nogueira (Findlay Lab) won 1st place

PhD Program Update

- Clarisse Panganiban (Lang Lab) passed the written qualifying exam
- 3 PhD students to take the QE this summer

Council News

- Student Stipend increase to \$27,500 starting September 2016
- New exposure format during PhD Interview weekends January 21st, February 18th, March 17th
- Dr. Traktman is reinstating the 3-way split between the CGS:mentor:dept for SURP students
 Will distribute current departmental interests for SURP candidate screening
- Formal formatting guidelines for proposals in the CGS
- Annual Evaluation of student progress (3rd year rubric assessment)
- Credentials committee
 - Lapsed membership
 - BOX
 - Revision of criteria for full membership
- Core curriculum updated to start fall 2016
- Unclaimed funds (ORSP announced)
 - List is available through the finance office
- NIH Requirements for scientific rigour and transparency



RESEARCH DIVISION UPDATE

Statistics for the Division of Research from July through September. Thirteen grant proposals were submitted requesting \$1,764,975 in total first year costs. Also, during this period eleven grants were awarded totaling \$1,533,323.

Bradley Schulte, Ph.D., Vice Chair of Research

SUBMITTED 1/1/2016—3/31/2016:

Sean M. Courtney, Ph.D., MS Title: Omics Big Data Integration in Cancer Research \$178,391 – Proposed Start Date 10/1/2016

Stephen Ethier, Ph.D. Title: Oncogenic Signaling in Basal Type Breast Cancer \$371-478 – Proposed Start Date 9/1/2016

Stephen Ethier, Ph.D. Title: Oncogenic Signaling in Basal Type Breast Cancer Breast cancer oncogenes on the 8p11 amplicon \$371-478 – Proposed Start Date 9/1/2016

Hainan Lang, M.D., Ph.D. Title: Roche Consulting \$7,000 – Proposed Start Date 1/16/2016

Omar Moussa, M.Sc., Ph.D. Title: Pleiotrophin Serum Levels in Pediatric Heart Transplant Patients: Correlation with Antibody Mediated Rejection \$50,000 – Proposed Start Date 2/11/2016

Frederick Nolte, Ph.D. Title: Comparison of cobas Liat and Alere i Influenza A and B Tests for Diagnosis of Influenza Virus Infection \$48,586 – Proposed Start Date 2/01/2016

Chandrakala Puligilla, Ph.D. Title: Molecular regulation of sensory epithelial cell patterning in the mouse inner ear \$371,478 – Proposed Start Date 9/01/2016

Bradley Schulte, Ph.D. Title: Roche Consulting \$7,000 – Proposed Start Date 1/01/2016

Suhua Sha, M.D. Title: Deceleration of Age-Related Hearing Loss \$112,125 – Proposed Start Date 9/01/2016

Demetri Spyropoulos, Ph.D.

Title: The Obsesogenic Potential of DOSS: a Novel Low-Risk/High-Benefit Approach to Managing Obesity \$77,000 – Proposed Start Date 7/01/2016

David Turner, Ph.D.

Title: Pharmacological manipulation of advanced glycation end product (AGE) levels in prostate cancer patients \$94,252 – Proposed Start Date 5/01/2016

Gavin Wang, Ph.D.

Title: Sensitization of Lung Cancer to Radiotheraphy by ABT-263 \$74,750 – Proposed Start Date 12/01/2016

Yusheng Zhu, Ph.D.

Title: Evaluation of theV8 Capillary Electrophoresis Analyzer for Hemoglobin IEF \$1,437 – Proposed Start Date 2/22/2016

AWARDED 1/1/2016—3/31/2016:

Hui Cheng, Ph.D. Title: Functional Genomics Approaches to Identify Ovarian Cancer Genes \$150,000 - Awarded Date 2/1/2016

Hainan Lang, Ph.D.

Title: Experimental and Clinical Studies of Presbyacusis Project 4 \$261,836 - Awarded Date 1/1/2016

Hainan Lang, Ph.D. Title: Auditory Nerve Degeneration and Repair: Research Supplement to Promote Diversity in Health-Related Research Program \$47,572 - Awarded Date 2/1/2016

Hainan Lang, Ph.D. Title: Roche Consulting \$7,000 - Awarded Date 1/6/2016

Meenal Mehrotra, Ph.D. Title: Mechanisms Regulating HSC-derived Osteogenic Population in Osteogenesis Imperfecta in Osteogenesis Imperfecta \$296,010 - Awarded Date 1/1/2016

RESEARCH DIVISION UPDATE—continued

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Meenal Mehrotra, Ph.D. Title: Mechanisms Regulating HSC-derived Osteogenic Population in Osteogenesis Imperfecta in Osteogenesis Imperfecta \$296,010 - Awarded Date 1/1/2016

Omar Moussa, Ph.D.

Title: Pleiotrophin Serum Levels in Pediatric Heart Transplant Patients: Correlation with Antibody Mediated Rejection \$50,125 - Awarded Date 2/1/2016

Frederick Nolte, Ph.D.

Title: Comparison of cobas Liat and Alere i Influenza A and B Tests for Diagnosis of Influenza Virus Infection \$48,586 - Awarded Date 1/21/2016

Bradley Schulte, Ph.D. Title: Experimental and Clinical Studies of Presbyacsis Project 3 \$346,069 - Awarded Date 1/01/2016

Bradley Schulte, Ph.D. Title: Roche Consulting 7,000 - Awarded Date 1/06/2016

Yusheng Zhu, Ph.D. Title: Evaluation of theV8 Capillary Electrophoresis Analyzer for Hemoglobin IEF \$1,437 - Awarded Date 2/22/2016

UPCOMING MEETINGS

APC ANNUAL MEETING (Association of Pathology Chairs) 7/12/16-7/15/16

ASCP / APF 2016 ANNUAL MEETING (American Society of Clinical Pathology / American Pathology Foundation) 9/14/16-9/16/16

CAP16-The Pathologists' Meeting (College of American Pathologists) 9/25/16-9/28/16



FACULTY FOCUS

Julie Woolworth Hirschhorn, Ph.D., TS(ABB)

During my senior year in high school, the Lakeville Outlook, my hometown newspaper, published an article on the top ten graduates from our high school class. During my interview, I told the reporter that I planned to "pursue a career in cancer research". I have displayed a passion for science from a young age and have been determined, for the majority of my life, to be involved in an area of cancer biology.

I first visited Charleston the summer of 2002 after graduating from Albion College in Michigan. Following my graduation, I reached out to John Vournakis, Ph.D., one of our Albion College trustees, who was at the time a member of the Hollings Cancer Center. I met Dr. Vournakis while I was still a student at Albion, giving tours of the Biology Department and our sequencing facility. During our conversation, Dr. Vournakis mentioned that there were several research positions available at the Hollings Cancer Center and he encouraged me to come down and meet some of the faculty. During my visit, I met Drs. Demetri Spyropoulos, Dennis Watson, and Ioanna Maroulakou. All members of the Department of Pathology and Laboratory Medicine! Dr. Maroulakou would become my first postcollege laboratory PI. I worked with Ioanna for a year before taking a position in Dr. Tien Hsu's laboratory (another member of our Pathology Department), where I would a year later enter the graduate program at MUSC. I will always remain a fan of the Hollings Cancer Center because I met my husband there during my graduate studies.

I have continued to work in the Pathology Department since starting at MUSC in 2002, over 13 years! My graduate work involved genetics and ovarian cancer research in *Drosophila melanogaster*. This work was followed by postdoctoral scholar research with Dr. Omar Moussa in bladder cancer. During my postdoctoral work, I became familiar with clinical laboratory services and met with Dr. Daynna Wolff for an informational interview. My undergraduate knowledge of sequencing and my interest in Molecular biology assisted me to a transition to the Molecular Pathology Laboratory as part of clinical services under the direction of Drs. Frederick Nolte, Daynna Wolff, and Cynthia Schandl.

Over the last 5 years, I have been encouraged and supported by those around me in the Department to develop an expertise in Molecular Pathology and Molecular Genetics. I have been involved in increasing the menu of cancer testing offered at MUSC to our patients. I have been able to bring inhouse testing that has a direct impact on patient care and management. It is the type of rewarding work that I dreamed of doing.

My daily activities include the verification of patient test results and interpretation of mutations detected in patient cancers. I am also involved in troubleshooting in the laboratory and daily quality control activities. I am still very involved in the research and development of new assays in the laboratory. As Dr. Schandl mentioned in her Faculty Focus piece in the December 2015 version of *The Path Way*, we have been busy working on developing a 5-year strategic plan to expand precision medicine in clinical services at MUSC. It is an exciting time to be involved in Molecular Pathology and I am proud to continue to be a member of this department!



"Small RNAs Have a Large Impact on Breast Cancer"

Victoria Findlay, Ph.D

Breast cancer (BC) is a worldwide health issue as it represents the leading cause of cancer in women and the second leading cause of cancer-related mortality in women, with an increasing incidence. BC is becoming increasingly recognized as a very complex disease with multiple subtypes based on both receptor expression as well as the identification of molecular subtypes. Nothing speaks more clearly to the shock-

ing breast cancer health disparities than the fact that African American (AA) women are as likely to get breast cancer as Caucasian American (CA) women, yet have a higher breast cancer death rate. In 2010, the CDC reported that the breast cancer death rate for women aged 45--64 years was **60% higher for AA women than CA women** (56.8 and 35.6 deaths per 100,000, respectively (). Cur-

rently, the 5-year relative survival rate is 77 percent for AA women compared to 90 percent among CA women. Racial disparities in cancer outcomes have been observed in several malignancies. However, it remained unclear if survival differences persist after adjusting for clinical, demographic, and treatment variables. The study by the Hershman group addressed this issue and found that, after controlling for stage, demographics, socioeconomic variables, tumor characteristics, and treatment factors, disparity remained among both premenopausal and postmenopausal women who were diagnosed with early-stage breast cancer. It is becoming increasingly clear that due to molecular and genetic differences in tumor biology, racial disparity exist independent of standard of care issues and are due in part to poorly understood inherent genetic and molecular characteristics of racial specific tumors.

In South Carolina (SC), mortality differences between African American (AA) and Caucasian American (CA) breast cancer patients are amongst the highest in the country. It is becoming increasingly clear that racial disparity exists independent of socioeconomic and standard of care issues and are also due to poorly understood inherent genetic and molecular characteristics within racial specific tumors. Sparse information exists regarding the molecular mechanisms that promote cancer health disparity. A greater understanding of the risk factors and biological links associated with aggressive breast cancer, will significantly impact African American communities due to the higher deaths associated with this disease in this population.

Our group has identified a factor, a microRNA, that potentially drives the disparities observed in breast cancer. MicroRNAs are small molecules that are encoded in our DNA that were previously overlooked until quite recently (the past decade or so). They were identified as negative regulators of protein coding genes. This discovery led to an exciting new area of research in cancer biology. Our lab identified a microRNA that was elevated in breast cancer tissue and was involved in the negative regulation of tumor suppressor genes. We also observed that the circulating levels of this microRNA were higher in AA breast cancer patients when compared to CA women with breast cancer suggesting that this miRNA was disparate. Tumors are complex and are made up of many different cell types. These cells can 'talk' to each other and this can occur through the transport of microRNAs in discrete vessels called exosomes. Our group is interested in examining whether microRNAs from the tumor epithelial cells are transferred to other cell types in the tumor microenvironment (stroma) and result in a downregulation of specific tumor suppressor genes resulting in more aggressive tumor growth.

Caveolin-1 (Cav1) loss in the stroma of the tumor microenvironment is a novel biomarker for predicting poor clinical outcome in all of the most common subtypes of human breast cancer, including the more lethal triple negative subtype which is significantly more common in (AA) women. A loss of stromal Cav1 predicts early tumor recurrence, lymph node metastasis, tamoxifen-resistance, and poor survival. Studies suggest that loss of stromal Cav1 expression might be a critical initiating event leading toward a more aggressive tumor

Continued - "Small RNAs Have a Large Impact on Breast Cancer"

microenvironment. Although the loss of stromal Cav1 is well established as a marker of poor outcome in women with breast cancer, the mechanism of this loss is unknown. Our group is investigating a novel mechanism as to how Cav1 is lost in the stromal compartment and how this loss may lead to a more aggressive tumor microenvironment. A major hurdle to the identification of biological mechanisms conferring cancer health disparity is a lack of suitable experimental models with which to investigate race specific differences in tumor biology. Therefore, our lab has developed a unique inducible miRNA transgenic mouse model to examine the mechanism of stromal Caveolin-1 loss as a potential driver of breast cancer disparity. We have collected data to support our hypothesis that tumor derived exosomes deliver microRNA to cells in the tumor environment resulting in a loss of stromal Cav1 protein expression and that this may provide a biological mechanism promoting cancer health disparity in breast cancer. Tumor derived exosomes can also result in circulating miRNAs in the blood and can serve as accessible biomarkers for diagnosis and prognosis and/or may define a novel area of potential therapeutic intervention to reduce cancer disparity. Therapeutics to mimic and inhibit miRNAs are underway at several companies and the first miRNA therapeutics are currently in Phase I clinical trials. Treating cancers with microRNA therapeutics offers a promising new approach to many different cancers and therefore understanding the mechanism of a microRNA-related cancer disparity will bring us to the forefront of cutting edge research with high potential for the prevention of cancer development and a reduction in cancer disparities. Currently, stromal Cav1 loss has been validated for its prognostic value in breast cancer in ten different countries worldwide. Therefore, models deficient in Cav1 will be a valuable resource for the discovery of new predictive stromal biomarkers that could be used as companion diagnostics with Cav1. If our studies are successful, we will be able to utilize this model to explore therapeutic strategies to prevent or reverse the loss of Cav1 and reduce breast cancer disparity.



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.

www.musc.edu/pathology