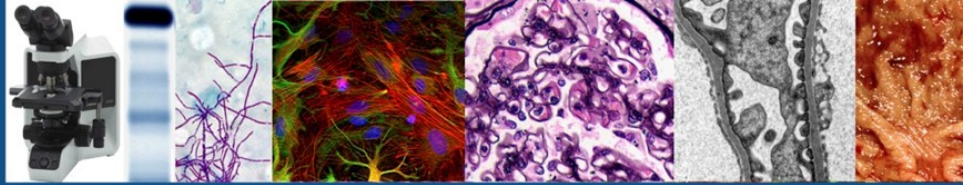


# THE PATH WAY

June & September 2016

Volume 7, Issue 2 & 3



DEPARTMENT of PATHOLOGY & LABORATORY MEDICINE



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

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## Pathology and Laboratory Medicine Resident Highlights - 2015-2016

- ◆ House Staff Award for Anatomic Pathology Faculty—**Laura Spruill, M.D, PhD.**
- ◆ House Staff Award for Clinical Pathology Faculty—**Angie Duong, M.D.**  
*As an aside, both of these faculty members have won this award two years in a row.*
- ◆ Chief Resident 2015-2016 – **Jessica Forcucci, MD**
- ◆ Chief Resident 2015-2016 – **Tripp Tracy, M.D.**

### Committees:

- ◆ 2015-2016 Undergraduate Curriculum Committee – **Kendall Brewer, M.D.**
- ◆ 2015-2016 Infection Control Committee – **Jon Gullett, M.D.**
- ◆ 2015-2016 Resident House Staff Council Representative – **Kendall Brewer, M.D.**
- ◆ 2015-2016 – Peer Review Committee - **Michael Stump, M.D.**
- ◆ 2015-2016 – Peer Review Committee – **Natalie Matics, M.D.**
- ◆ 2015-2016 – Peer Review Committee – **Tripp Tracy, M.D.**
- ◆ CAP Resident's Forum – **Michael Stump, M.D.**
- ◆ College of American Pathologists (CAP) 15189 Committee (Jr. Member) - **Jon Gullett, M.D.**
- ◆ MUSC Hospital Infection Control Committee (Resident Representative) - **Jon Gullett, M.D.**

### Best Grand Rounds Presentation:

- ◆ **1<sup>st</sup> place: Kate Eichel, M.D. "MYH-9 Related Disorders"**
- ◆ **Runner-up: Alisa Caudell, M.D. – "Chagas Disease (American Trypanosomiasis)"**

### Poster Presentation:

- ◆ **1<sup>st</sup> place: Nicole Dominiak, M.D. - "Peritoneal Deciduoid Mesothelioma: An Unusual Presentation Complicating an Already Challenging Diagnosis"**
- ◆ **Runner-up: David LeBel, M.D. - "Transfusion Transmitted Babesiosis: A Diagnostic Dilemma"**

### Best Resident Publication:

- ◆ **1<sup>st</sup> place: Kate Eichel, M.D. – "Preoperative use of platelets in a 6-year old with acute appendicitis and a myosin chain 9-related disorder: a case report and review of the literature"**
- ◆ **Runner-up: Jessica Forcucci, M.D. – "Benign soft tissue lesions that may mimic malignancy"**

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@muscedu).

# END OF YEAR RESIDENT AWARDS





## NEWS FROM DEPARTMENT ADMINISTRATION & BUSINESS OFFICE

# CONGRATULATIONS!

**Dr. Jerry Squires  
Promoted to Professor  
Effective 7/1/16**

**Dr. Amanda LaRue  
Promoted to Professor  
Effective 7/1/16**

### **Dr. Amanda LaRue Named Associate Chief of Staff for Research at VAMC**

Dr. Amanda LaRue was appointed the permanent Associate Chief of Staff (ACOS) for Research at the VAMC in May. She had served as Acting ACOS for Research for several months prior, working to expand the VAMC's research program. Dr. LaRue is an Professor in the Department of Pathology and Laboratory Medicine, a member of the Hollings Cancer Center, and the Scientific Director of the Hollings Cancer Center's Flow Cytometry & Cell Sorting Shared Resource.

# GRADUATE STUDIES UPDATE

**May 18<sup>th</sup> 2016**

### **Student Update**

- ◆ Ryan Kelly (Dr LaRue) 1<sup>st</sup> place PhD student in Path seminar series
- ◆ Amanda Prechtel (Dr Carroll) 1<sup>st</sup> place Post-Doc in Path seminar series
- ◆ 3 MS students recruited for admission in the Fall (Recruitment process is still ongoing)

### **Council News**

- ◆ From 151 applicants we successfully recruited 30 students from 46 offers (65%)
- ◆ New this year is Graduate of the year in MS program  
Katie Walter (Dr Turner) was named as 1 of 2 distinguished graduates
- ◆ The library is accepting ideas/wish list for ebooks for the library to obtain (for classes or departmental needs)  
Deadline for submission is June 2016 (please submit requests through me)
- ◆ Ideas for best approaches to program/faculty exposure (next meeting)  
CGS wide poster session  
Luncheons with faculty talks throughout the fall/spring
- ◆ First year mentoring committee
- ◆ Mentoring postdocs/students (training mentors in mentoring)  
Training grants (NIH) but eventually a reality of all mentors

## *ARRIVALS / DEPARTURES*

### *ARRIVALS:*

- ◆ Hongkuan Fan, Ph.D., Assistant Professor, transferred from Department of Neurosciences on 5/1/16
- ◆ Angelina Phillips, M.D., Clinical Assistant Professor, arrived on 7/1/16
- ◆ Natalie Matics, M.D., Clinical Instructor/Surgical Pathology Fellow, arrived on 7/1/16
- ◆ Kirtesh Patel, M.D., Clinical Instructor/Surgical/Gastrointestinal Pathology Fellow, arrived on 7/1/16
- ◆ Nathaniel Jensen, Graduate Assistant, arrived on 7/5/16 in Dr. Cheung's lab
- ◆ Xiaoyuan He, Visiting Scholar, arrived on 7/11/16 in Dr. Gavin Wang's lab
- ◆ John Kurtz, Research Specialist I, arrived on 7/18/16 in Dr. Cheung's lab
- ◆ Christopher Metts, M.D., Assistant Professor, arrived 8/1/16
- ◆ Lauren McLean, Graduate Assistant, arrived on 9/1/16 in Dr. Smits' lab
- ◆ Adrianna Olar, M.D., Assistant Professor, arrive on 9/15/16
- ◆ Cody Ashy, Student, arrived on 9/19/16 in Dr. Smits' lab

### *DEPARTURES:*

- ◆ James Nicholson, Media Resource Specialist II, left on 6/30/16
- ◆ Sean Courtney, Staff Scientist left on 7/15/16 from Dr. Hardiman's lab
- ◆ Benjamin Van Peel, Research Specialist II– 7/15/16 – Dr. Smits' lab
- ◆ Deanna Dong, Research Specialist, left on 7/26/16 from Dr. Sha's lab
- ◆ Mary Bridges, Research Specialist, left on 8/17/16 from Dr. Lang's lab
- ◆ Robert Bowers, Staff Scientist, left on 8/31/16 from Dr. Spyropoulos's lab
- ◆ Yazhi Xing, Staff Scientist, left on 9/29/16 from Dr. Lang's lab
- ◆ Khujista Haque transferred on 8/31/16 from Dr. Puligilla's lab to Pharmacology



SONYA JORDAN

June 2016

**Nomination:** Thank you for all that you do!

**Other Nominees:** Ashley Wooldridge,  
Lisa Reeves, Wanda Shotsberger,

*Fiscal Technician II*



September 2016

**Nomination:** Her wonderful attitude, gift with teaching and willingness to stop whatever she is doing to help in any way needed are an inspiration. I can only hope that in 30 years I am as knowledgeable, patient and as much of a joy as she is.

*Nancy Drayton  
Medical Technologist*

**Other Nominees:** Raymond Edwards and Jason Flamm

# CONGRATULATIONS!

TO: *Ashley Cross and her husband!*

IT'S  
A  
BOY!



*Landon Taylor Cross*  
*Born on April 25, 2016*  
*7 lbs. & 20 inches*

TO: *Daniel Skipper and his wife!*

IT'S A  
GIRL!



*McKenzie Elizabeth Skipper*  
*8 lbs. & 15 oz.*  
*Born 5/31/16*

# INCOMING RESIDENTS

2016-2017



*Rachel Jester*



*Iris Martin*



*Gong Feng*



*Peng Cheng "Phil" Han*



*Paige Cribb*



*Jessica Snider*

# INCOMING FELLOWS

2016-2017

## Cytopathology



Nicole Riebe



Anne Hoffa



Kari Valente

## Dermatopathology



Justin Bandino

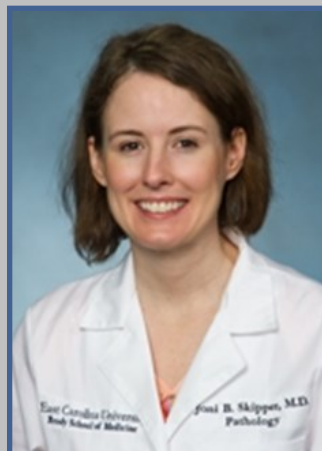


Nicole Dominiak



Kathryn Echols

## Forensic Pathology



Joni Skipper





## RESEARCH DIVISION UPDATE

Statistics for the Division of Research from **April** through **June**.

Ten grant proposals were submitted requesting \$2,139,384  
in total first year costs.

Also, during this period eight grants were awarded totaling \$1,373,633.

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

### SUBMITTED 4/1/2016—6/30/2016:

**Victoria Findlay, Ph.D.**

Title: BC160692: Identification of a MicroRNA Mediated Mechanism of Stromal Cav1 Loss in Breast Cancer  
\$179,150 – Proposed Start Date 5/05/2016

**Victoria Findlay, Ph.D.**

Title: BC160692: miR-204 Regulation of Cav-1 as a Mechanism Driving Breast Cancer Disparity  
\$224,250– Proposed Start Date 4/01/2017

**Meenal Mehrotra, Ph.D.**

Title: Regulation of Osteosarcoma Progression by Sphingosine Kinase 1/Sphingosine 1-Phosphate/CD36 Signaling Axis \$30,000 – Proposed Start Date 6/01/2016

**Chandrakala Puligilla, Ph.D.**

Title: Role of Classical Cadherins in Boundary Formation within Developing Inner Ear \$224,250 – Proposed Start Date 8/01/2016

**Avtar Singh, M.D. / Je-seong Won, Ph.D.**

Title: Pathology and Mechanism of GABAergic neuronal degeneration in Alzheimer's Disease \$373,750 – Proposed Start Date 4/01/2017

**David Turner, Ph.D.**

Title: The Generation of Clinically and Molecularly Characterized PDX Animal Nodes from Racially and Ethnically Diverse Prostate Cancer Tissue \$138,869 – Proposed Start Date 7/01/2016

**Gavin Wang, M.D., Ph.D.**

Title: Targeting Cancer Stem Cells in Breast Cancer  
\$147,500 – Proposed Start Date 12/01/2016

**Gavin Wang, M.D., Ph.D.**

Title: Therapy-Induced Cancer Stem Cell Enrichment  
\$373,750 – Proposed Start Date 12/01/2016

**Dennis Watson, Ph.D.**

Title: American Cancer Society Institutional Research Grant  
\$210,000 – Proposed Start Date 1/01/2017

### AWARDED 4/1/2016—6/30/2016:

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

Title: Stereologic of the Cellular Composition of Neurofibromas \$96,507 - Awarded Date 6/01/2016

**Hongkuan Fan, Ph.D.**

Title: The Beneficial Effects of Endothelial Progenitor Cells in the Vascular Dysfunction of Sepsis \$373,750- Awarded Date 5/01/2016

**Gong Feng, M.D., Ph.D.**

Title: Liver Cell-Targeting Delivery System for Decitabine and Tetradouridine in the Treatment of Hepatocellular Carcinoma \$187,474 - Awarded Date 8/22/2016

**Amanda LaRue, Ph.D.**

Title: Enhancement of Fracture Repair by Hematopoietic Stem Cells \$285,700 - Awarded Date 4/01/2016

**John Lazarchick, M.D.**

Title: A Phase 1/2 Open-Label, Single Ascending Dose Trial of a Self-Complementing Optimized Adeno-associated Virus Serotype 8 Factor IX Gene Therapy (AskBio009) in Adults with Hemophilia B \$152,632 - Awarded Date 5/13/2016

**Meenal Mehrotra, Ph.D.**

Title: Role of Hematopoietic Stem Cells in Periodontal Ligament Homeostasis \$112,125 - Awarded Date 4/01/2016

**Demetri Spyropoulos, Ph.D.**

Title: Pilot Study examining DOSS obesogen exposure levels in pregnant women \$25,000 - Awarded Date 6/06/2016

**David Turner, Ph.D.**

Title: PQ3: AGEs and Race Specific Tumor Immune Response in Prostate Cancer \$140,445 - Awarded Date 5/01/2016



## *FACULTY FOCUS*

Stephen Guest, Ph.D.

Before there was reality T.V. and shows like '19 Kids and Counting', there was a small town church organist in Michigan named John Callaghan who, along with his wife Mary raised eighteen children. The oldest of these eighteen, Margaret, went on herself to marry a young marine and have seven children of her own. I am the youngest of those seven so saying that I come from a big family is a bit of an understatement. Growing up in such an environment, there was rarely a dull moment and my six older siblings made sure to provide me with many 'character building' experiences along the way.

Somehow I survived those early days and eventually went on to attend the University of Michigan where my love for Chemistry and Math led me to choose Chemical Engineering as my major. Things were going relatively according to plan until my junior year when I decided to take Biology 101 as an elective class. I had hoped that the class would be somewhat interesting while at the same time provide me with an opportunity to get an easy A. By the third week of class, however, I was already scheduling an appointment with my school counselor to officially change my major to Biology. Soon after that, I sent out an email (cutting edge technology at the time) to twenty different professors begging any of them to give me a lab job that would allow me to begin my career as a biomedical research scientist. Two professors actually replied to my email and one, Dr. Jessica Schwartz, agreed to bring me in for an interview. I remember the first question she asked me was, "Do you have any wet lab experience?" to which I replied, "What's wet lab experience?" Despite that inauspicious beginning, Jessica took me under her wing and I spent the next two years working in her lab soaking up everything that I could about life as a research scientist.

Those experiences in Dr. Schwartz's lab reaffirmed my decision to pursue a career in biology and after graduation, I headed to the University of Chicago where I obtained my Ph.D. in Virology under the mentorship of Dr. Raymond Roos. After six years in the windy city, I took my first post-doc position as a part of Dr. Russ Finley's lab at Wayne State University. It was in Russ' lab that I began the work that I continue to this day in the field of Functional Genomics. Working in Russ' lab prepared me perfectly for my second post-doc, which was in the laboratory of Dr. Stephen Ethier at the Karmanos Cancer Institute and later here at MUSC. Under Steve's guidance, I have developed a research program that is focused on applying Functional Genomics to the study of breast cancer and this past September, I transitioned to an independent position running my own lab.

This is truly an exciting time to be involved in cancer research. Targeted therapies and immunotherapies are starting to fulfill the promise of delivering durable responses with significantly reduced side-effects. These breakthroughs are even being realized in malignancies that have traditionally been some of the most difficult to treat such as melanoma and lung cancer. I don't think that my wife and I will be trying for eighteen children, but hopefully the two that we do have will someday live in world where cancer is no longer the threat to human health that it is today.



## The Pathophysiological Implications of Hematopoietic Stem Cells Plasticity

**Amanda LaRue, Ph.D.**

Many of our body's tissues and organs have the capacity for tissue repair and regeneration. Our bone marrow, skin, and gastrointestinal tract mucosa are characterized by life-long cell turnover. In these organs the mature cells have finite life spans and are continually replaced by more primitive progenitor cells. Others tissues such as skeletal muscle and liver are characterized by limited cell turnover in the steady state, but display significant regeneration capacity after tissue injury. One hypothesis for the observed cell turnover and replacement is that the tissues contain stem cells, cells that can self-renew and generate progenies committed to differentiation in specific pathways. While this theory accounted for the ability of a tissue to repair and regenerate, it was generally thought that stem cells possess organ/tissue specificity; for example, hematopoietic stem cells (HSCs) generate only blood cells. Against this long-held belief, a number of cell culture and preclinical transplantation studies supported the paradigm-shifting concept of the tissue-reconstituting ability of HSCs. These novel findings suggested exciting new avenues of radical HSC-based therapies for disorders of many organs and tissues outside of the blood and bone marrow. However, these reports were soon followed by others with negative results and papers offering different interpretations<sup>1,2</sup>. Thus, the field became mired in controversy.

To address this controversy, our lab reasoned that only transplantation based on a single HSC would provide definitive information about HSC plasticity. In order to generate such mice efficiently, we combined single cell deposition of bone marrow cells that are highly enriched for HSCs with short-term cell culture to generate a clonal population of cells for transplantation and bone marrow reconstitution. The short-term cell culture takes advantage of the known cell-cycle dormancy of steady state HSCs. The use of mice that are genetically engineered to ubiquitously express enhanced green fluorescent protein (EGFP) as bone marrow donors allows for lineage tracing of the resulting cells in tissues back to the single sorted EGFP<sup>+</sup> HSC. Based on this transplantation strategy, pioneered by Dr. Makio Ogawa (Professor Emeritus, Pathology and Laboratory Medicine), our laboratory has demonstrated an HSC origin for fibroblasts, myofibroblasts, adipocytes, chondrocytes, osteoblasts, and osteocytes, major cell types that make up connective tissue throughout the body.

Fibroblasts and myofibroblasts play an important role in the steady state physiology of many tissues, providing structural integrity and support for proliferation and differentiation of other cell types. Specialized myofibroblasts such as the kidney glomerular mesangial cells, hepatic stellate cells, and pericytes are contractile and function as regulators of blood flow. Fibroblasts and myofibroblasts also have significant roles in pathological processes. In some cases, these cells participate in resolution of injury (e.g., wound healing). In others, uncontrolled proliferation and/or activation of fibroblasts and myofibroblasts may, itself, lead to pathological conditions such as tissue fibrosis. Using our unique clonal transplantation strategy, we discovered that many types of fibroblasts/myofibroblasts, including glomerular mesangial cells of the kidney, brain microglial cells, brain perivascular cells, inner ear fibrocytes, fibroblasts/myofibroblasts in adult cardiac valves, cancer-associated fibroblasts/myofibroblasts, and pulmonary fibroblasts are derived from HSCs<sup>3-5</sup>. These findings were expanded by similar transplantation studies from other laboratories that reported HSC-derived fibroblasts/myofibroblasts at the site of myocardial infarction<sup>6</sup> and hepatic stellate cells<sup>7</sup>. These findings strongly suggest that the HSC is a significant source of fibroblasts/myofibroblasts for tissue homeostasis and repair. Current work in our lab is focused on the role of these HSC-derived fibroblasts and their precursors in a variety of pathologies including cancer and pulmonary fibrosis.

## Continued: The Pathophysiological Implications of Hematopoietic Stem Cells Plasticity

Given the close association between fibroblasts and adipocytes, we also examined the potential of HSCs to give rise to adipocytes<sup>8</sup>. Studies based on clonally engrafted animals that were fed rosiglitazone, a peroxisome proliferator-activated receptor-gamma (PPAR- $\gamma$ ) agonist, demonstrated HSC-derived EGFP<sup>+</sup> adipocytes in both white and brown adipose tissues. In vitro and in vivo studies have demonstrated that HSC-derived adipocytes may participate in adipogenesis associated with disease and inflammation. Ongoing work is aimed at understanding the mechanisms regulating HSC-derived adipogenesis in the context of cancer and obesity<sup>9</sup>.

Our studies using clonally engrafted animals have also uncovered an HSC origin for bone cells (osteoblasts and osteocytes) and chondrocytes<sup>10</sup>. In steady state, the contribution of the HSC to osteo-chondrogenic cells is low, in agreement with the known slow cellular turnover in these tissues. However, during fracture repair, numerous HSC-derived hypertrophic chondrocytes were observed early after fracture and HSC-derived osteoblasts and osteocytes were identified throughout bone healing.

These studies were further supported by work in collaboration with Dr. Meenal Mehrotra demonstrating that clonal HSC transplantation ameliorated the clinical abnormalities<sup>11</sup>, corrected bony defects, and replaced mutant collagen in a murine model of osteogenesis imperfecta, or brittle bone disease. We are currently working to develop methods to manipulate the HSC-derived osteo-chondrogenic cell to therapeutically enhance healing in hard to heal fractures and osteoarthritis.

Together, our findings suggest that the HSC can give rise to cells of mesenchymal tissues. These studies have been supported by evidence from other laboratories that demonstrates even broader HSC plasticity. Several groups have shown that HSCs give rise to hepatocytes in normal mice<sup>12,13</sup>. Equally strong evidence exists for HSC origin of skeletal muscle cells<sup>14</sup>. The contribution of HSCs to other cell types, including lung epithelial cells<sup>15</sup> and cardiomyocytes is still controversial<sup>16,17</sup>.

These pre-clinical findings of an HSC origin of connective tissue cells suggest a number of pathologies and genetic disorders of these tissues will be impacted by HSC-based therapies. For example, HSC transplantation may offer potent treatment for genetic diseases such as osteogenesis imperfecta in which the HSC-derived cell replaces the defective cell. In other cases, such as difficult to heal fractures, timely mobilization of HSCs or precursors may facilitate regeneration of normal osteogenic tissues. Finally, in cases such as fibrosis and cancer where HSC-derived cells may contribute to disease, inhibition of HSC-derived cells may offer novel therapies. Thus, understanding the functions of HSC-derived cells in tissues, elucidating the mechanisms regulating their participation in physiological and pathological conditions, and discovering methods to control these cells will have far-reaching impact on human health and disease.

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# UPCOMING MEETINGS

**NEXT ALL HANDS MEETING  
WEDNESDAY, DECEMBER 21, 2016**

**DEPARTMENT HOLIDAY CELEBRATION  
AT THE SC AQUARIUM  
ON DECEMBER 9, 2016**

**PATHOLOGY SPRING SYMPOSIA  
APRIL 4 - 8, 2017  
AT KIAWAH ISLAND**

**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](http://www.musc.edu/pathology)**