

# THE PATHWAY

June, 2017

Volume 8, Issue 3

## END OF YEAR AWARD & RECOGNITION CELEBRATION



Laura Spruill, M.D., Ph.D.  
House Staff Award  
for Anatomic Pathology Faculty



Angie Duong, M.D.  
House Staff Award  
for Clinical Pathology Faculty



Kirtesh Patel, M.D.  
2016-2017  
Surgical/GI Pathology Fellow



Natalie Matics, M.D.  
2016-2017  
Surgical Pathology Fellow



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

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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@muscc.edu).

# END OF YEAR AWARD & RECOGNITION CELEBRATION cont'd



Ashley Cross, M.D.  
2016-2017  
Chief Resident



Mike Stump, M.D.  
2016-2017  
Chief Resident



Christopher Wenzinger, M.D.  
2016-2017  
4<sup>th</sup> Year Resident



Kate Eichel, M.D.  
2016-2017  
4<sup>th</sup> Year Resident



Daniel Skipper, M.D.  
2016-2017  
4<sup>th</sup> Year Resident



Kari Valente, M.D.  
2016-2017  
Cytopathology Fellow



Nicole Dominiak, M.D.  
2016-2017  
Dermatopathology Fellow



Justin Bandino, M.D.  
2016-2017  
Dermatopathology Fellow



Joni Skipper, M.D.  
2016-2017  
Forensic Pathology Fellow

## Recognition & Award Winners not pictured

Anne Hoff, M.D., 2016-2017 Cytopathology Fellow

Nicole Herring, M.D., 2016 Cytopathology Fellow

Katie Echols, M.D., Dermatopathology Fellow

Amanda Prechtel, Ph.D., 1<sup>st</sup> Place Presentation in  
Postdoctoral Fellow Category

Bradley Krisanits, M.S., 1<sup>st</sup> Place Presentation in



Yun Wang, M.D., Ph.D.  
2015-2017  
Clinical Chemistry Fel-



Jamie Mills, M.D., Ph.D.  
1<sup>st</sup> Place Presentation in  
Ph.D. Category

# CONGRATULATIONS!

## College of Medicine Faculty Excellence Awards Ceremony

The College of Medicine's Faculty Excellence Awards Ceremony, sponsored by the COM Student Council, was held on May 13, 2017, to celebrate our faculty who were nominated by our student body and honored for their commitment to medical education.

### COM 1: In Top 10 Nominees

- **Debra Hazen-Martin, Ph.D.**, Professor and Associate Dean for Curriculum in the Basic Sciences, Pathology and Laboratory Medicine

### COM 2: In Top 10 Nominees

- **Jerry E. Squires, M.D., Ph.D.**, Professor, Pathology and Laboratory Medicine
- **Nicholas I. Batalis, M.D.**, Associate Professor, Pathology and Laboratory Medicine
- **Sally E. Self, M.D.**, Professor and Associate Dean for Student Progress
- **Steven Carroll, M.D., Ph.D., FASCP, FCAP**, Professor and Chair, Pathology and Laboratory Medicine
- **Susan E. Presnell, M.D.**, Professor, Pathology and Laboratory Medicine
- **Angie Duong, M.D.**, Assistant Professor, Pathology and Laboratory Medicine

**Hainan Lang, M.D., Ph.D.** has been nominated to be a standing committee member on CDRC, the Communication Disorders Review Committee of NIDCD. Her term is from July 1, 2017 till June 30, 2021.



**Demetri D. Spyropoulos, Ph.D.**, as the winner of a raffle held for turning in your Evaluation forms at the SCTR Microbiome Retreat. He won a \$500 SCTR Voucher.



# FAREWELL DROP IN May, 26, 2017



**Dr. Lee Marie Tormos**



**Dr. Jonathan Ralston**



## HLA ASHI Inspection

Congratulations to the HLA Team for a successful ASHI Inspection held on April 26, 2017.

A demonstration of the high-quality work they do every day to support our transplant patients.

## Magnolia Award

**Dr. Ryan Boerner**, Resident (Otolaryngology) and **Dr. Phong Le**, Resident (Otolaryngology), rotating in Dr. Hainan Lang's Lab, has won the Magnolia Award for their miRNA studies in Dr. Lang's lab at the 17th Annual Charleston Magnolia Conference on June 3, 2017.

Dr. Boerner received first place and Dr. Le received second place.

## GRADUATE STUDIES UPDATE

February 15, 2017

### GRADUATE STUDIES UPDATE

#### Student Update

- Two second year MS students successfully defended their thesis: Laurel Black (Carroll's Lab) and Bradley Krisanits (Turner's Lab)
- Bradley Krisanits won the College wide Distinguished Graduate Award for MS students
- Jamie Mills, MSTP student (Ethier's Lab) successfully defended
- Two students; Kenyaria Noble (Lang's Lab) and Jaime Randise (Turner's Lab) were accepted into the microscope workshop this summer with partial scholarships
- Three students took the qualifying exam, responses are being graded

#### Council News

- Stipend is increasing this Fall to \$28,000
- Tuition is increasing this Fall by \$500/student/year
- The qualifying exam format is currently under revision



# RESEARCH DIVISION UPDATE

Statistics for the Division of Research from **April** through **June**. **Nine** grant proposals were submitted requesting \$2,245,553 in total first year costs. Also, during this period six grants was awarded totaling \$224,485.

Congratulations and many thanks to everyone involved in obtaining these awards.

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

## GRANT APPLICATIONS SUBMITTED - 4/1/2017-6/30/2017

Principal Investigator	Proposed Start Date	Title	Total 1st YR Dollars
Mehrotra, Meenal	6/1/2017	Regulation of Osteosarcoma Progression by Osteoblasts through Sphk 1/S1P Signaling	\$30,000
Spyropoulos, Demetri	9/1/2017	Area C: Lung Cancer Cryopreservation Method to Maintain Cell Viability and Tissue Architecture	\$506,431
Lazarchick, John	4/26/2017	A Global Epidemiologic Study to Determine the Prevalence of Neutralizing Antibodies and Related Adaptive Immune Responses to Adeno-Associated Virus (AAV in Adults with Hemophilia	\$63,300
Lazarchick, John	6/14/2017	An Open-Label Multicenter, Phase 1/2 Study of the Safety and Dose Escalation of BAX888, an Adeno-associated Virus Serotype 8 (AAV8) Vector Expressing B-domain Deleted Factor VII (BDD-FVIII) in Severity	\$15,450
Mehrotra, Meenal	4/1/2018	Characterizing Hematopoietic-Derived Cells from PDL & their Role in Regeneration	\$370,038
Spyropoulos, Demetri	4/1/2018	Investigation of Maternal Exposures and Childhood Obesity	\$495,184
Turner, David	1/1/2018	AGE Levels During Pubertal Mammary Development Imprint Mitometabolic Memory to Increase Breast Cancer Risk	\$354,025
Turner, David	1/1/2018	Subcellular Characterization of Pubertal Pathognomonic Mammary Structures Induced by Dietary-AGEs	\$186,875
Findlay, Victoria	34/1/2018	miR-204 as a Driver of Neuroendocrine Differentiation in Prostate Cancer	\$224,250
<b>Total Proposals</b>	<b>9</b>		<b>\$2,245,553</b>

## GRANTS AWARDED - 4/1/2017-6/23/2017

Mehrotra, Meenal	6/1/2017	Regulation of Osteosarcoma Progression by Osteoblasts through Sphk 1/S1P Signaling	\$30,000
Lazarchick, John	4/26/2017	A Global Epidemiologic Study to Determine the Prevalence of Neutralizing Antibodies and Related Adaptive Immunt Responses to Adeno-Associated Virus (AAV) in Adults with Hemophilia	\$63,300
Lazarchick, John	6/14/2017	An Open-Label Multicenter, Phase 1/2 Study of the Safety and Dose Escalation of BAX888, An Adeno-associated Virus Serotype 8 (AAV8) Vector Expressing B-Domain Deleted Factor VII (BDD-FVIII) in Severity	\$15,450
Nolte, Frederick	1/6/2017	Clinical Trial of GenMark ePlex Blood Culture Identification Panels	\$83,735
Hardiman, Gerald	6/22/2017	A Novel Mltiscale Data Inegration Framework for Omics Big Data Modeling (in Genomes to Phenoms framework)	\$7,000
Wang, Gavin	6/1/2017	Development of Novel c-Myc Small Molecule Inhibitors	\$25,000
<b>Totals Awarded</b>	<b>6</b>		<b>\$224,485</b>



## FACULTY FOCUS

by **Olga Chajewski, M.D.**



When my dad moved to Charleston in 1993, all I knew about it was that it was far away from where we lived - Nuremberg, Germany. My parents had just divorced, my dad moved to 'America', and my mom, step-dad, brother and I moved to Warsaw, Poland. After finishing middle school 1 ½ years later, I joined my dad in Charleston, starting my own love-affair with this city.



When I moved to Charleston in the summer of 1995, all I knew was that the English phrases I learned in school were not useful ('the dog is in the house' and 'the ball is on the table'), Dr. Pepper was the best thing I had ever tasted, and everything from neighborhoods to grocery stores was "just like the movies". Most immigrants will tell you that they learned English from watching TV. This is true. I watched a lot of TV that first summer. I learned both language and culture from re-runs of The Facts of Life, Wings and Saved by the Bell. By the time I started 9<sup>th</sup> grade at James Island High School, I could communicate much more than locations of random objects.

In 11<sup>th</sup> grade, I became a volunteer at MUSC. My duties spanned a wide array of tasks from changing flyers in the elevators, distributing magazines to waiting rooms and hand-writing thank you notes in the Alumni Affairs office. However, my favorite assignment was delivering mail and flowers to patients. Walking the halls of the hospital, I always felt that good things happen here and how great it would be to work in a place like this someday.

I enrolled at the College of Charleston but didn't really know what I wanted to study. Medical school had long been in the back of my mind, but after graduating high school with twice the number of required science courses, I did not want to major in Biology. A guidance counselor explained that I did not have to major in Biology, so I chose to study other things that interested me. In the end, I graduated with a degree in Political Science and a minor in German Literature.

In the spring of my senior year I was accepted to medical school at MUSC. When I finally started my clinical rotations, I only had eyes for Surgery. My rotation was everything I had hoped for. In my excitement, I would wake up before my alarm, round on my patients and everyone else's, spend 10 hours retracting in surgery with a smile on my face and go on 7 organ procurement runs with the transplant team. I could tell that the job was hard, but it felt very rewarding to me. I spent the rest of the year preparing my applications for Surgery residency.

## Continuation - Faculty Focus by Dr. Olga Chajewski

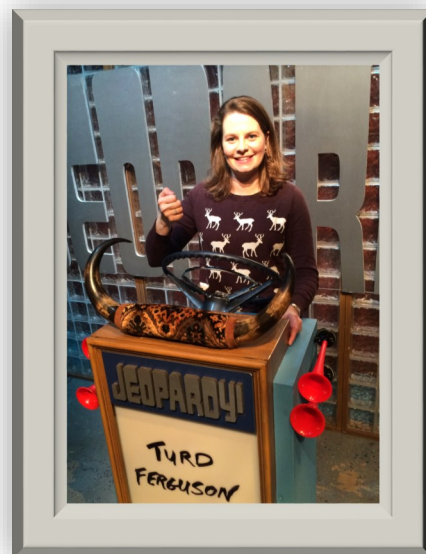
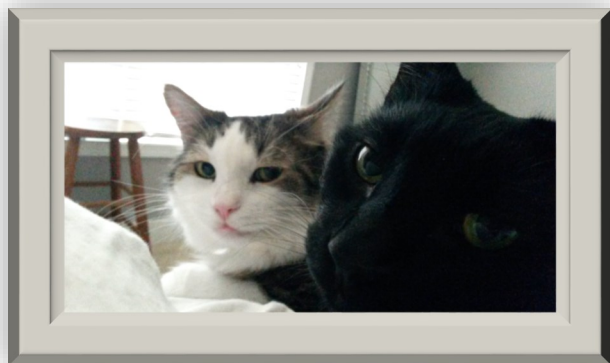
Then, the unthinkable happened. I changed my mind. It was September of my 4<sup>th</sup> year and my applications were about to be sent. I was studying for Step 2 and had heard that Pathology electives only took up half the day. This was great news to me. I had enjoyed Pathology lectures and was excited to see cool things for half the day and study for the rest.

One day during Surgical Pathology signout, Dr. Smith asked me what I was going to be when I grew up. I proudly stated that I was going to be a surgeon. Dr. Smith looked me up and down and, with that knowing smile and twinkle in his eyes, said “no, you’re not”. I was offended. I thought he meant that I couldn’t make it, but of course, that is not what he meant. I’d like to think that he saw a skill set and character that would thrive in Pathology. After all, I have always been a visual learner and a puzzle solver. And so with that small comment, the seed for a new pursuit was planted.

I followed through on applying to Surgery residency. I only applied to preliminary (1-year) positions, allowing me to truly experience Surgery residency for myself before considering another specialty. I matched to a small community hospital in Waterbury, CT where I completed a full year of training. Just like my third year rotation, I enjoyed everything about the year. However, in the back of my head I kept thinking about Pathology.

When my 1-year contract was up, I applied for Pathology residency and matched to Baystate Medical Center in Springfield, MA. I completed my AP/CP residency and Cytopathology fellowship there, before moving to Baltimore, MD for a Transfusion Medicine fellowship at the Johns Hopkins Hospital. When I started to look for my first job out of training, the stars aligned and a path for my return to Charleston appeared.

I joined the faculty at MUSC in the summer of 2014. I spend three weeks out of the month on Cytology and one week on Transfusion Medicine. It has been incredibly stimulating to alternate between anatomic and clinical pathology on a regular basis. I am also involved with the Cytology Fellowship program. Teaching has been an unexpected treat. I greatly enjoy working with our outstanding students, residents and fellows. The past three years have been full of ups and downs, many of which I could not have weathered without the support of my friends and colleagues in our department. I am so grateful to be home; and by that I mean both Charleston and MUSC.







## Increased Microsatellite Instability Testing As A Result of New FDA Approved Cancer Treat-

by Evelyn T. Bruner, M.D.

At the time of writing this, I have received six requests for microsatellite instability testing in the few weeks since the US Food and Drug Administration granted accelerated approval of the use of pembrolizumab (Keytruda) for treatment of a wide variety of cancer types. This new approval includes the treatment of either adult or pediatric patients with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors. Criterion for use include tumors that are unresectable or metastatic and have progressed following prior treatment and have no satisfactory alternative treatment options.

Keytruda is a humanized monoclonal antibody targeting the PD-1 receptor (programmed death receptor-1). This blocks interaction between PD-1 and its ligands, PD-L1 and PD-L2, allowing the immune system to recognize and target cancer cells which otherwise would go unrecognized and continue to proliferate. The approval of Keytruda is based on data across five clinical trials showing that of 149 patients with MSI-H or dMMR cancers, 39.6% of patients either had a complete or partial response with 78% of these patients having responses of six months or longer.

Microsatellites are short tandem repeats (STRs) in DNA sequences. Simply put, these are short segments of DNA where a 2 nucleotide or more segment repeats up to hundreds of times. The National Cancer Institute defines microsatellite instability as “a change that occurs in the DNA of certain cells (such as tumor cells) in which the number of repeats of microsatellites (short, repeated sequences of DNA) is different than the number of repeats that was in the DNA when it was inherited. The cause of microsatellite instability may be a defect in the ability to repair mistakes made when DNA is copied in the cell.” The inability to repair these errors in the DNA sequence stems from defective mismatch repair proteins also termed mismatch repair deficiency (dMMR). This occurs by one of two mechanisms: either promoter hypermethylation silences gene expression or, secondly, there is a germline mutation, as you would see in hereditary cases such as Lynch Syndrome (hereditary nonpolyposis colorectal cancer).

Testing can either be done by immunohistochemistry looking for the *loss* of expression of the MMR proteins (dMMR) or by polymerase chain reaction (PCR) for MSI. There are five immunohistochemical patterns, as highlighted in Table 1 below, including normal expression of the proteins. Crucial to understanding the IHC patterns, is having a basic understanding of the proteins themselves. These are dimerized proteins with one dominant over the other; MLH1 and PMS2 are partners and MSH2 and MSH6 are partners with the MLH1 and MSH2 proteins being dominant, respectively. It is also important to remember that these are nuclear stains and it is normal for them to be present so a *loss* of staining is abnormal.

Genetic Defect	Immunohistochemistry			
	MLH1	PMS2	MSH2	MSH6
No defect	+	+	+	+
MLH1	-	-	+	+
PMS2	+	-	+	+
MSH2	+	+	-	-
MSH6	+	+	+	-

**Table 1. Staining patterns of the mismatch repair proteins in normal and dMMR tumors.**

The laboratory that we currently send out MSI testing requests uses a commercially available PCR kit which evaluates amplification of a panel of specific mononucleotide repeat markers (BAT25, BAT26, Mono27, NR24 and NR21). The tumor is considered MSS/MSI-L (stable or low) if instability is detected in none or up to one of the five markers and is considered MSI-H if instability is found in two or more of the five markers.

To date, MSI testing has been primarily used to screen for Lynch syndrome and in the evaluation of prognosis and chemosensitivity in sporadic colorectal carcinomas. The request I have personally received so far have been for a variety of sarcomas and others have received requests for metastatic carcinomas. Clinicians are likely to request this test for more and more other tumor types as well.

The use of pembrolizumab remains contingent upon verification of clinical benefit in regard to different tumor types, which will only come with time and further clinical trials. Even so, this is groundbreaking in cancer treatment as it is the first therapy based on a marker that can be found on any tumor, regardless of type, rather than a tumor specific marker. Moving forward, our department will have to examine the number of requests we receive and consider performing at least one of these testing options within our own laboratory.

## References

Merck. (May 25, 2017) FDA Approves Merck's KEYTRUDA® (pembrolizumab) for Adult and Pediatric Patients with Unresectable or Metastatic, Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors [Press release]. Retrieved from <http://www.mrknewsroom.com/news-release/prescription-medicine-news/fda-approves-mecks-keytruda-pembrolizumab-adult-and-pediatr>

Simon, Stacy. (2017, May 24) FDA Approves Keytruda (Pembrolizumab) for Any Tumor with Specific Genetic Change. Retrieved from <https://www.cancer.org/latest-news/fda-approves-keytruda-pembrolizumab-for-any-tumor-with-specific-genetic-change.html>

<https://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=285933> Accessed 6/12/2017.

Rekhtman N and Bishop JA. *Quick Reference Handbook for Surgical Pathologists*. Berlin: Springer, 2011. Print.

# CONGRATULATIONS!



**Averie Michelle Brown** arrived on May 5, 2017  
8lbs, 7 oz, 19.75 inches long  
Mother is LaShardia Brown, PhD Student in  
Dr. Lang's Lab



## LISA COULTER

**Fiscal Manager**

**June 21, 2017**

**Nomination:** For her helpfulness in coordinating many of the medical student rotations in our department. In particular, this year she has been essential in coordinating several rotations for students from other medical schools, which helps build the reputation of our department.

**Other Nominees:** Raymond Edwards, Jason Flamm, Karen Geroulis, Dolly Hope, Jarvis Jenkins, Teresa Kennedy, Kristin Maurer, Linda McCarson, Amanda Prechtel and Ashley Wooldridge



## **NEW ARRIVALS:**

### **VISITING SCHOLARS**

**Bowen Sun**

Start Date: 4/3/17 in Dr. Qi Wang's Lab

**Ting Liu**

Start Date: 4/3/17 in Dr. Lang's Lab

### **LABORATORY TECHNICIANS III**

Charles Keppler

Start Date: 5/1/17 in Dr. Lazarchick's Lab

Yvonne Bradley

Start Date: 5/1/17 in Dr. Lazarchick's Lab

### **PGY-1 RESIDENTS**

Chad Butler, M.D.

Start Date: 7/1/17

Jake Emanuel, M.D.

Start Date: 7/1/17

Madison Hannay, D.O.

Start Date: 7/1/17

Peter Houston, M.D.

Start Date: 7/1/17

Heather O'Connor, D.O.

Start Date: 7/1/17

### **FELLOWS:**

#### **Clinical Chemistry:**

Dan Wang, Ph.D.

Start Date: 7/5/17

#### **Cytopathology:**

Derrick Green, M.D.

Start Date: 7/1/17

Virginia Miller, M.D.

Start Date: 7/1/17

Daniel Skipper, D.O.

Start Date: 7/1/17

#### **Dermatopathology:**

Jessica Forcucci, M.D.

Start Date: 7/1/17

Brett Keeling, M.D.

Start Date: 7/1/17

#### **Hematopathology:**

Michael Stump, M.D.

Start Date: 7/1/17

### **FACULTY**

Kate Eichel, M.D. – Clinical Instructor

Start Date: 7/1/17

Ashley Cross, M.D. – Clinical Instructor

Start Date: 7/1/17

Nikolina Babic, Ph.D. – Clinical Chemistry Lab Director

Start Date: 7/5/17

## **DEPARTURES:**

### **STUDENTS**

Cody Ashy

Left Dr. Smits Lab on 5/8/17

Christopher Duckworth

Left Dr. Smits Lab on 5/19/17

### **VISITING SCHOLAR**

Hao Xiong - Visiting Scholar

Left Dr. Sha's Lab on 4/20/17

### **RESEARCH SPECIALIST I**

Zachary Kratche

Left Dr. Guest's Lab on 6/3/17

### **PATHOLOGY GRADUATE STUDENTS**

Jamie Mills - Graduate Student

Left Dr. Ethier's Lab on 6/17/17

Jon DiMaina - Graduate Student

Left Dr. Cheung's Lab on 6/30/17

### **CLINICAL CHEMISTRY FELLOW**

Yun Wang, M.D., Ph.D.

Left Dr. Nolte's Lab on 5/31/17

### **CLINICAL INSTRUCTORS**

Natalie Matics, M.D.

Left on 6/30/17

Kirtesh Patel, M.D.

Left on 6/30/17

### **RESEARCH ASSISTANT PROFESSOR**

Stephen Guest, Ph.D.

Left on 6/14/17

### **ASSISTANT PROFESSOR**

Chandrakala Puligilla, Ph.D.

Left on 6/30/17

Lee Tormos, M.D.

Left on 6/30/17

### **ASSOCIATE PROFESSOR**

Jonathan Ralston, M.D.

Left on 6/30/17

### **RESIDENTS**

Christopher Wenzinger, M.D.

Left on 6/30/17

### **FELLOWS**

Anne Hoffa, M.D.

Left on 6/30/17

Nicole Herring, M.D.

Left on 6/30/17

Kari Valente, M.D.

Left on 6/30/17

Justin Bandino, M.D.

Left on 6/30/17

Nicole Dominiak, M.D.

Left on 6/30/17

Kathryn Echols, M.D.

Left on 7/14/17

Joni Skipper, M.D.

Left on 6/30/17

## UPCOMING MEETINGS

**APC Annual Meeting**  
(Association of Pathology Chairs)  
July 25 - 28, 2017, Washington, DC

**ASCP / APF 2017 Annual Meeting**  
(American Society of Clinical Pathology /  
American Pathology Foundation)  
September 6 - 8, 2017, Chicago, Illinois

**Inner Ear Biology Meeting**  
September 13-16, 2017, Hannover, Germany

**All Hands Meeting**  
September 20, 2017

**CAP16 - The Pathologists' Meeting**  
(College of American Pathologists)  
October 8 - 11, 2017, Gaylord National, Maryland

**Holiday Celebration**  
December 8, 2017, SC Aquarium

**Pathology Spring Symposium**  
April 17-21, 2018, 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)**