MUSC
MEDICAL UNIVERSITY of SOUTH CAROLINA

THE PATHWAY

September & December 2018 Volume 9 Issue 3 & 4

MUSC docs rock!

Three pathology residents and musicians -- Iris Martin, Ryan Jones and Peter Houston -- delivered a dose of joy to patients and care team members in the Transitional Care Unit recently, bringing live musical performance to the bedside! If you would like to share your talents with the MUSC community, please contact the Arts in Healing Program at artsinhealing@musc.edu.

*Story in MUSC Update, September 2018, Emailed to all employees at MUSC on behalf of Office of Communications and Marketing

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

UPDATE
Inside this issue:

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 Linda McCarson (mccarsli@musc.edu) or Lori Roten (roten@musc.edu).

WELCOME!

New Hires:

Faculty

- **Dr. Bailey Glen 7-1-18 - Clinical Assistant Professor**
- **Dr. Adviye Ergul – 10/1/18 - Professor**
- **Dr. Weiguo Li—10/1/18 - Research Assistant Professor**
- **Dr. Moussa – 11/1/18 - Associate Professor**

Residents – arrived 7/1/18

- **Jay Alden, DO - PGY1**
- **Luke Cypher, MD, PhD - PGY1**
- **Yana Ding, MD, PhD - PGY1**
- **Hao Liu, MD, PhD - PGY1**
- **Daniel Ogden, MD- PGY1**

Fellows– arrived 7/1/18

- **Ashley Cross, MD - Cytopath Fellow**
- **Alex Elliott, MD - Cytopath Fellow**
- **Charles Newman, MD - Cytopath Fellow**
- **David Perry, MD, PhD - Derm**
- **Daniel Skipper, DO - Derm**
- **Aitemad Lander, DO - Hematopath**
- **Cynthia Schandl, MD, PhD – Molecular Pathology**
- **David LeBel, MD - Surgpath**

Staff

- **Ahmad Elmansi - CGS - Dr. Hill 's lab 8/2018**
- **Dmitry Kondrikov - Dr. Hill's lab – 7/23/18**
- **Galina Kondrikov - Dr. Hill's lab - 7/30/18**
- **Sara Jamil—Research Specialist I - Dr. Ergul's lab - 10/1/18**
- **Lianying He – Research Specialist II – Dr. Ergul's lab - 10/1/18**
- **Yasir Abdul – Staff Scientist I – Dr. Ergul's - 10/1/18**
- **Shan Xu – Postdoc – Dr. Sha's lab - 11/19/18**
- **Sunita Kolwalker – RSI – Dr. Mehrotra's lab – 8/20/18**
- **Kelley Nevill – Technical Medical Associate – Dr. Presnell - 7/23/18**
- **Ludivine Renaud – Postdoc - Dr. Ethier's lab – 9/1/18**
- **Fan Wu – Student – Dr. Sha's lab - 10/10/18**

Departures:

- **Bart Smits, PhD - Assistant Professor - last day - 11/28/18**
- **Sally Donegan - Grants Administrator - last day - 12/31/18**
- **William da Silveira - Postdoc - Dr. Hardiman's lab - last day 12/13/18**
- **Yanzhong Wang - Visiting Student - Dr. Gavin Wang's lab - last day 12/24/18**
- **Sheng Qin - Postdoc - Dr. Gavin Wang's lab - last day 12/26/18**

CONGRATULATIONS!!

PROGRESSNOTES
MUSC'S MEDICAL MAGAZINE / / FALL 2018

Christopher Metts, MD, is featured in the "Enabling citizen science" part of the "Machine Learning in Medicine Article". The entire article is available to read at the link below:

https://muschealth.org/health-professionals/progressnotes/2018/fall/features/machine-learning

Ellen C. Riemer, M.D., J.D. and our former chief resident, **Emily Curl, M.D.** had a paper accepted for publication in the European Heart Journal, entitled "Caseous necrosis of mitral anulus: case report and brief review". They are the only two authors on the paper.

European Heart Journal is considered the second most prestigious/2nd most highly ranked journal in the field of cardiovascular medicine, after only the Journal of the American Academy of Cardiology.

S. Erin Presnell, M.D., and John W. Powell III, M.A. (MUSC, College of Medicine, Class of 2019) won second place for their poster at the SCTR Opioids Research Retreat!

Ahmed Elmansi, a PhD Student in our Department has received the 2nd place award in the MUSC Student Research Day for the Center on Aging category.

Hongkuan Fan, Ph.D. - *EurekAlert! Science News* link. The website posted an article introducing Dr. Fan's recently published paper. The link is below:

https://www.eurekalert.org/pub_releases/2018-12/muos-tst120318.php.

Jack Yang, M.D., Alexis Elliott, M.D, Anne Hoffa, M.D., Nicole Herring, M.D. and Patricia Houser had their paper, "Potential influence of p16 immunohistochemical staining on the diagnosis of squamous cell lesions in cervical biopsy specimens: Observation from cytologic□histologic correlation" published in Cancer Cytopathology.

Cancer Cytopathology is a peer-reviewed journal of the American Cancer Society. It is the elite journal in its field, offering the highest impact factor (3.866) among cytopathology journals.

Their paper has been further selected to be profiled on the December 2018 cover of the journal as a featured article.

You can read their article at the link below:

https://onlinelibrary.wiley.com/doi/epdf/10.1002/cncy.22063

CONGRATULATIONS!!

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ASCP Presents 2018 Mastership to David N.B. Lewin, MD, MASCP

Chicago/Oct. 8, 2018—The American Society for Clinical Pathology (ASCP) presented the 2018 Mastership to David N.B. Lewin, MD, MASCP, during its 2018 Annual Meeting held Oct. 3-5 in Baltimore. This award honors ASCP's members who have made a significant contribution to pathology through sustained service to the profession and to ASCP.

A past president of ASCP, David N.B. Lewin, MD, FASCP, is an experienced pathologist who specializes in gastrointestinal, liver, and pancreatic pathology at the Medical University of South Carolina, in Charleston, SC. Dr. Lewin has held numerous volunteer positions with ASCP, including serving on the Steering Committee for the ASCP-led Partners for Cancer Diagnosis and Treatment in Africa and the Diagnostics and Technology Steering Committee.

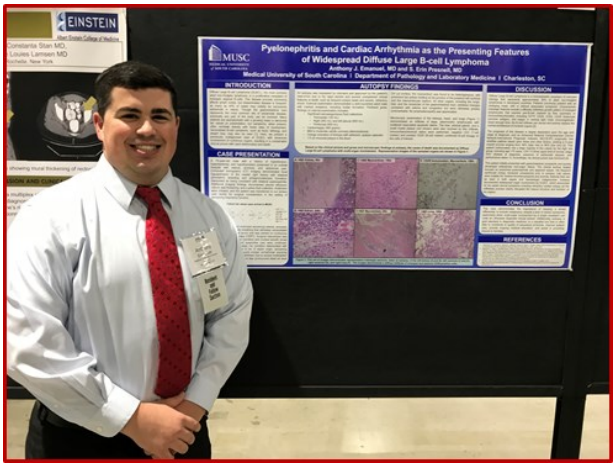
Recognition through the ASCP 2018 Mastership represents a pinnacle of his successful career. "ASCP has been my pathology home for my entire career, 25 years," he said. "I have had the honor to serve on the Board of Directors on two separate occasions and been involved in multiple aspects of ASCP."

He began his involvement with ASCP during his residency at the University of California, Los Angeles (UCLA). While on faculty in the department of pathology since 1996, Dr. Lewin has also excelled in several administrative appointments. These include serving as director of gastrointestinal and hepatic pathology, director of the pathology residency program, director of the gastrointestinal pathology fellowship, director of digital pathology, chair of the Institutional Review Board and vice chair for medical affairs.

Dr. Lewin received his bachelor's degree from the University of California, Berkeley, and his MD from UCLA. He also completed his pathology internship, residency and gastrointestinal pathology fellowship (under the tutelage of his father Dr. Klaus Lewin) at UCLA, and a surgical pathology fellowship at University of Southern California. He is a past president of the Rodger Haggitt Gastrointestinal Pathology Society and current secretary/treasurer of the Pancreatobiliary Pathology Society.

About ASCP
Founded in 1922 in Chicago, ASCP is the world's largest professional membership organization for pathologists and laboratory professionals. ASCP provides excellence in education, certification, and advocacy on behalf of patients, anatomic and clinical pathologists, and medical laboratory professionals. To learn more, visit http://www.ascp.org. Follow us on Twitter at http://www.twitter.com/ascp_chicago and connect with us on Facebook at http://www.facebook.com/ASCP.Chicago.

Jake Emanuel, MD, presenting 'Pyelonephritis and Cardiac Arrhythmia as the Presenting Features of Widespread Diffuse Large B-cell Lymphoma' at the 16th Annual AMA Research Symposium on November 9, 2018.



RESEARCH DIVISION UPDATE

Statistics for the Division of Research from **October** through **December**.
Eight grant proposals were submitted requesting **$1,815,995** in total first year costs.
Also, during this period **eleven grants were awarded** totaling **$1,926,903**.
Congratulations and many thanks to everyone involved in obtaining these awards!

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

GRANT APPLICATIONS SUBMITTED - 10/1/2018 - 12/31/2018			
Principal Investigator	**Proposed Start Date**	**Title**	**Total 1st YR Dollars**
Nikolina Babic	10/8/2018	Alinity I Stat	$331,724
Nikolina Babic	1/1/2019	VERAVAS Samples Study	$14,929
Meenal Mehrotra	1/1/2019	SCTR - T- Regulatory (Treg) Cell Transplantation in Osteogenesis Imperfecta	$25,000
Demetric Spyropoulos	1/31/2019	GEAR Program	$30,000
William Hill	7/1/2019	Age-Related Lynurenine Accumulation Impairs miRNA and Hdac Epigenetic Regulation of the SDF-1 axis resulting in Bone Loss	$745,295
Demetric Spyropoulos	7/1/2019	Preservation of debrided or excised traumatic limb injury vasculature for later reconstructive surgery	$186,875
Gavin Wang	7/1/2019	Targeting GSK3 as a novel therapeutic approach to tackle cancer stem cells	$224,250
Stephen Ethier	7/1/2019	Using functional genomics to reverse engineer metastatic human breast cancer cells	$257,922
Total Proposals	**8**		**$1,815,995**
GRANTS AWARDED - 10/1/2018 - 12/31/2018			
Hongkuan Fan	9/1/2018	The Role of Pericytes in the Vascular Dysfunction of Sepsis	$284,050
Hongkuan Fan	9/1/2018	Admin: Supplement The Beneficial effects of Endothelial progenitor cells in the Vascular Dysfunction of Sepsis	$58,511
Victoria Findlay	9/1/2018	U54 Rsearch Education Core	$296,513
Hainan Lang	9/1/2018	Auditory Nerve Degeneration & Repair	$299,000
Nikolina Babic	10/8/2018	Alinity I Stat	$331,724
Lazarchick, John	11/1/2018	A prospective, multi-national, non-interventional study in haepmophillia A and B patients with or without inhibitors treated according to routine clinical treatment practice (Explorer 6)	$21,943
David Turner	11/1/2018	Center for Enhanced Biological Resilience through Phytochemical AGE Inhibitors	$10,000
Adviye Ergul	12/1/2018	Progressive post stroke cognitive impairment: Mechanisms & Intervention	$476,236
William Hill	12/1/2018	Age Induced Impairment of Nutrient Signaling Results in Bone Lonss.	$133,997
Nikolina Babic	1/1/2019	VERAVAS Samples Study	$14,929
Totals Awarded	**10**		**$1,926,903**

FACULTY FOCUS

by William Bailey Glen, Jr., Ph.D.

I was born in 1981 in the upstate and have been slowing moving south east through South Carolina until stopping at the coast. I met my wife-to-be at Dorman High School. After graduation in 2000, I moved to Columbia to attend the University of South Carolina, while my wife went to study at Winthrop. In 2004, we both moved Charleston. where I began my graduate studies at the Medical University of South Carolina and have continued to study and work until today. We currently live in Goose Creek and have two beautiful daughters.

My two academic passions in life have been biology and computer science. My formal education has been entirely focused on biology. I received a B.S. in Biology from the University of South Carolina. My freshman year I unknowingly signed up for the University of South Carolina School of Medicine Neuroscience class for incoming graduate students. While I barely passed the course, I learned that the study of the brain and behavior were very appealing to me. Also, during my undergraduate studies, I began my self-training in basic programming and computer technology, building gaming PC's to sell to my friends and working on small programming projects.

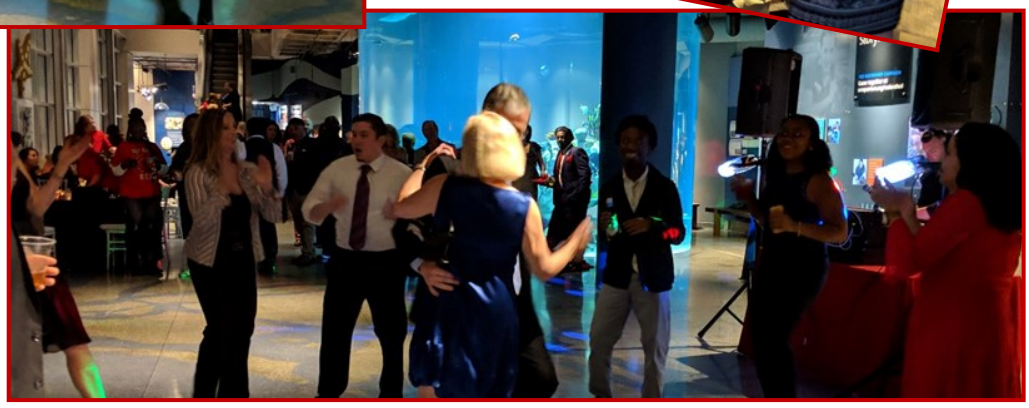
I was accepted at the University of South Carolina's graduate program in 2004 with plans to study Neuroscience. After lab rotations, I selected Dr. Antonieta Lavin Ph.D as my mentor and began to study electrophysiology. In her lab, I studied basic properties of synaptic transmission and synaptic plasticity in in-vitro animal models of neuropsychiatric disorders. I found the techniques of in-vitro field and patch-clamp recordings to be very difficult to master. While I was able to produce a few publications and thoroughly enjoyed my time with Dr. Lavin, I never truly felt like I had mastered either the technique, or the experimental design of basic electrophysiological experiments. During my undergraduate work, I found many opportunities to apply my computer expertise, building and troubleshooting computers around the department, and developing simple software tools and analysis packages for varied electrophysiological projects.

After graduation, I was determined to begin in-vivo electrophysiological studies in awake and behaving animals. I felt this would fit my interests while providing opportunities to expand on my computational and software development skills. To this end, I began a postdoc with Dr. Judson Chandler Ph.D, also here at MUSC, in 2009. While my training got off to a bit of a rocky start, with the current postdoc responsible for my training disappearing shortly after I started, over my time in the lab I was able to participate in several exciting studies exploring alcohol addiction, habits, and sleep. While working with Dr. Chandler, I learned a wide variety of skills including basic electrical engineering and computation to build our own automated T-maze for the rodents, developing an automated sleep-scoring GUI in MATLAB, and writing a set of software tools for integrated analysis of multielectrode recordings and behavioral events.

While I found the behavioral component of my postdoc to be a better fit for my scientific interests than in-vitro electrophysiology and gave me plenty of opportunities to develop my computational skills, I began to develop allergies to the rodents which made my work very uncomfortable. So, in 2016, I decided to make a large change to my career path and focus on the computational side of biology rather than the behavioral. I was fortunate enough to find a Staff Scientist position working with Dr. Gary Hardiman Ph.D. in the Center of Genomics Bioinformatics core and Dr. Daynna Wolff in the Cytogenetics and Genomics Laboratory. This has given me the opportunity to work with many different types of genetic data in both clinical and research settings. Primarily I have focused on small variant analysis from high-throughput sequencing. However, I have worked with many other data types including crisper off-target identification, copy number variants from sequencing and microarray. From RNA I have worked with gene and transcript expression analysis, miRNA, and variant analysis. On the software development side, I have worked on many tasks including developing pipelines to automate clinical process, contributing to opensource bioinformatics tools, and developing a website for exploring expression analysis against a custom graph database of protein-protein interactions.

In July 2018 I accepted a position as Clinical Assistant Professor in Pathology. I am continuing and expanding my duties in the clinical laboratory. I will be expanding my contributions beyond next-generation sequencing efforts to contribute to a variety of other Pathology lab tests. Particularly exciting are initiatives from the recently formed Pathology Informatics Innovation Group (PIIG – pig@musc.edu) where we are developing clinical-decision support tools integrated with electronic medical records systems such as EPIC through FHIR interfaces. I am also continuing to contribute to research projects and continue to play an active role in the Center for Genomic Medicine Bioinformatics Core. I am very excited to be in my current position and look forward to contributing to MUSC for many years to come.

HOLIDAY PARTY



UNIVERSITY SERVICE AWARD RECIPIENTS - 2018

DISPLAY NAME	HOME UNIT NAME	YRS HIRED	TITLE
NICHOLAS BATALIS, M.D.	FORENSICS	10	PROFESSOR
AMANDA LARUE, PHD	RESEARCH	10	ASSOCIATE PROFESSOR
LAURA SPRUILL, M.D., PH.D.	CLINICAL	10	ASSISTANT PROFESSOR
JACK YANG, M.D.	CLINICAL	10	PROFESSOR
JERRY SQUIRES, M.D., PH.D.	CLINICAL	30	ASSOCIATE PROFESSOR

HOSPITAL SERVICE AWARD RECIPIENTS - 2018

DISPLAY NAME	YRS HIRED	TITLE
CARLETTE GEDDIS	10	HISTOLOGY TECHNOLOGIST
JOAN DOLAN	10	MEDICAL TECHNOLOGIST COORDINATOR
SHNEK GAILLIARD	10	PHLEBOTOMY TECHNICIAN IV/TEAM LEAD
DANIELLE RIBEIRO-NESBITT	10	MEDICAL TECHNOLOGIST SPECIALIST
CHANTAY GATHERS	10	CLINICAL/MEDICAL LABORATORY ASSISTANT
NAKEYSHIA LEGETTE	10	CLINICAL/MEDICAL LABORATORY ASSISTANT
MICHELLE GAGE	10	MEDICAL TECHNOLOGIST
KAREN CELLARS	10	MEDICAL TECHNOLOGIST ADVANCED
RENEE JENKINS	10	MEDICAL TECHNOLOGIST
GEORGE ISGITT	20	MATERIALS MANAGEMENT COORDINATOR
KENNETH BACHEWICZ	30	MEDICAL TECHNOLOGIST
CASAUNDRA PORTER	30	HISTOLOGY TECHNOLOGIST
CELESTINE ROUSE	31	MEDICAL TECHNOLOGIST

UPCOMING MEETINGS

Southeast Association for Pathology Chairs (SEAPC)
Amelia Island, Florida
January 31 - February 4, 2019

Pathology Spring Symposium
East Beach Conference Center
Kiawah Island
April 1-8, 2019

Targeting Microvascular Dysfunction to Treat Sepsis

by Hongkuan Fan, Ph.D.

Our studies focus on severe sepsis, which is defined as a life-threatening organ dysfunction caused by a dysregulated host response to an infection (1). There are over 1,000,000 cases of severe sepsis each year in the US, and the number of cases is steadily increasing over the years. Sepsis remains to be a leading cause of death in the United States, with a mortality rate at around 20%. In older populations, the mortality rate is an alarming 40-50% with long lasting debilitating sequelae in survivors. The estimated cost to treat this disease is around 24.3 billion per year (2).

So far, there are no effective pharmacologic therapies for sepsis. The only drug approved by FDA to treat sepsis is Activated Protein C. However, after 10 years on the market, it has shown no significant effect and has been taken off the market. Thus, there is a critical need for a pharmacologic therapy for sepsis.

After many years studying sepsis, it is now realized that suppression of systemic inflammation alone would not cure sepsis. The major focus of our studies is understanding the pathophysiology of vascular dysfunction in sepsis from which novel treatment strategies can be designed. Recently NIH NHLBI redefined sepsis as a "severe endothelial dysfunction syndrome in response to intravascular and extravascular infections causing reversible or irreversible injury to the microcirculation responsible for multiple organ failure". The new definition highlights endothelial dysfunction in sepsis, which is a direct cause for multiple organ failure.

One of our projects focuses on endothelial progenitor cells (EPCs) and vascular repair. EPCs are bone marrow derived endothelial precursor cells that are regulated, in part, by the chemokine CXCL-12, which is critical in recruitment, function, and homing of EPCs to sites of endothelial injury. Dysfunction of circulating EPCs has been associated with sepsis and EPC proliferation is inversely related to organ dysfunction when compared to EPCs from healthy controls. Our recent data demonstrates that treatment with human cord blood derived EPCs improves survival, attenuates pulmonary vascular leak, and ameliorates organ injury in the murine cecal ligation and puncture (CLP) model of sepsis (3). A better understanding of the mechanisms by which EPCs exert their protective effects is crucial to the design of new therapeutic strategies.

EPCs release exosomes and extracellular vesicles containing micro RNAs (miRNAs) that regulate endothelial function and barrier integrity. We have shown that treatment with human EPCs alters circulating levels of EC-relevant miRNAs in murine sepsis, and that miR-126 plays a critical role in regulating EPC/EC homeostasis in sepsis (4). We hypothesize that 1) Endothelial progenitor cell exosomes regulate endothelial function and barrier integrity through specific miRNAs in sepsis and 2) EPC exosomes or EC-targeted specific miRNA nanoparticles may improve outcomes in human sepsis.

Continued . . .

The aims of another project are directed toward understanding the role of pericytes in vascular dysfunction in sepsis. Pericytes are specialized cells embedded in the capillary basement membrane that wrap around endothelial cells of the microcirculation throughout the body and are important regulators of microcirculatory homeostasis. However, the role of pericytes in the endothelial dysfunction of sepsis is largely unknown. Our preliminary data demonstrates that pericytes are depleted in the mouse lung and kidney microvasculature during CLP-induced sepsis, which results in vascular leakage (5). We observed that the transcription factor friend leukemia virus integration 1 (Fli-1), is critical to pericyte dysfunction and viability in sepsis by mediating pericyte programmed cell death through pyroptosis. We also demonstrated that MiR-145 inhibits Fli-1 expression and is abundantly expressed at baseline in pericytes. We hypothesize that pericyte viability regulated by the miR-145/Fli-1 axis is a critical determinant of sepsis outcomes through pericyte-mediated stabilization of endothelial permeability.

Based on our previous and ongoing studies, we will continue to unravel the complex etiology of vascular dysfunction of sepsis with the ultimate goal of designing novel and critically needed treatment strategies for sepsis.

References:

Singer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016; 315(8):801-10.

Kaukonen KM, et al. Mortality related to severe sepsis and septic shock among critically ill patients in Australia and New Zealand, 2000-2012. JAMA. 2014; 311(13):1308-16.

Fan H, et al. Endothelial progenitor cells and a stromal cell-derived factor-1α analogue synergistically improve survival in sepsis. Am J Respir Crit Care Med. 2014; 189(12):1509-19.

Goodwin AJ, et al. Plasma levels of microRNA are altered with the development of shock in human sepsis: an observational study. Crit Care. 2015;19:440.

Li P, et al. Fli-1 Governs Pericyte Dysfunction in a Murine Model of Sepsis. J Infect Dis. 2018 Jul 20.

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.