MUSC
Medical University
of South Carolina

Department of Medicine

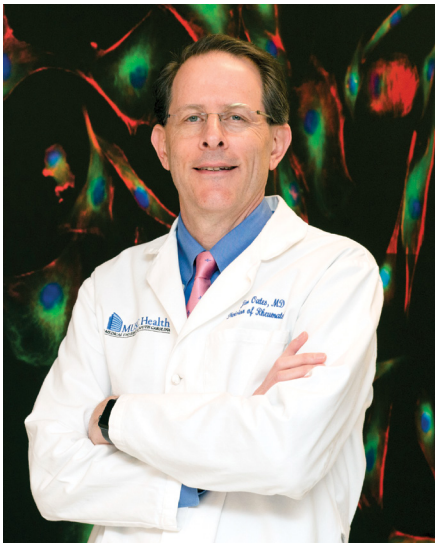
2024 RESEARCH SYMPOSIUM

Friday, April 19, 2024 | 8:00 a.m. - 2:00 p.m.

Drug Discovery Lobby, Bioengineering Lobby and
Bioengineering 112 Classroom

FOR MORE INFORMATION VISIT
musc.edu/researchsymposium

From the Vice Chair for Research



We would like to thank all of the participants for sharing their innovative research, as well as those who coordinated and attended this event. Your support for our research mission is greatly appreciated.

Many thanks to the judges who contributed their time and effort to make the 17th Annual Department of Medicine Research Symposium a successful event.

Galina Bogatkevich, M.D., Ph.D.
Melissa Cunninghamm, M.D., Ph.D.
Ahmed Daoud, M.D.
Ashley Duckett, M.D.
Gary Gilkeson, M.D.
Andrew Goodwin, M.D.
Zain Gowani, M.D.
Josh Lipschutz, M.D.
John McKinnon, M.D.
Marharyta Semenikhina, Ph.D.
Zengdun Shi, M.D.
Daniel Silverman, M.D.
Charlie Strange, M.D.
Meghan Thomas, M.D.
Justin Van Beusecum, Ph.D.
Anna Brady, M.D.
Rachana Krishna, M.D.

Sincerely,

Jim Oates, M.D.
Professor and Director
Division of Rheumatology & Immunology
Vice Chair for Research, Department of Medicine
Medical University of South Carolina

Meeting Agenda and Schedule

Friday, April 19, 2024

Welcome and Poster Sessions: Bioengineering & Drug Discovery Lobbies

8:00 am: **Registration, Poster set-up, coffee**

8:20 am: **Welcome and Introduction**
Ben Clyburn, M.D., Chair, Department of Medicine
Jim Oates, M.D., Vice Chair for Research

8:30 - 11:00 am: **Poster Presentations**

11:30 am - 12:00 pm: LUNCH - Bioengineering Lobby

Oral Presentations, Keynote, Awards: Bioengineering 112 Classroom

12:00 - 12:30 pm: **Oral Abstract Presentations**

12:30 - 1:15 pm: **Keynote: Garth Swanson, M.D.,** Professor and Director of the Division of Gastroenterology and Hepatology, MUSC
"It's About Time: Bringing Circadian Rhythms from the Bench to Bedside in Inflammatory Bowel Disease."

1:15 - 2:00 pm: **Research Day Poster Award Ceremony**
Awards recognizing the best research day presentations
Jim Oates, M.D., Vice Chair for Research
Ben Clyburn, M.D., Chair, Department of Medicine

Keynote: Garth Swanson, M.D., MS

Garth Swanson, M.D., MS
Professor of Medicine
Director, Division of Gastroenterology and Hepatology
Medical University of South Carolina

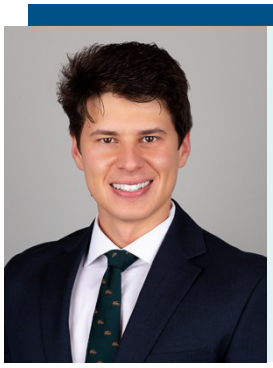
"It's About Time: Bringing Circadian Rhythms from the Bench to Bedside in Inflammatory Bowel Disease"

Garth R. Swanson, MD, MS, AGAF, is a Professor of Medicine and currently serves as the Division Director of Gastroenterology and Hepatology at the Medical University of South Carolina. He is a practicing gastroenterologist and physician-scientist with a specialty in managing complex patients with inflammatory bowel disease.

Dr. Swanson's overall translational research program is primarily focused on the impact of environmental factors, like alcohol or circadian misalignment, on the gastrointestinal barrier homeostasis, gut-derived inflammation, and the microbiome. Dr. Swanson currently has two R01s examining the impact of circadian misalignment and chronotherapy in Inflammatory bowel disease.

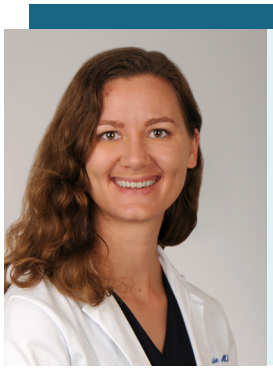
Dr. Swanson is an active mentor to residents, fellows, masters, and Ph.D. students who rotate in his lab. Dr. Swanson was instrumental in establishing the Rush Crohn's and Colitis Center at RUMC in 2018, which includes the Inflammatory Bowel Disease Multidisciplinary (IBD) Clinic, which he used to Co-Direct with Surgery and multidisciplinary (combined medical and surgical) inpatient consults in IBD service. The establishment of this multidisciplinary clinic in Inflammatory Bowel Disease has helped advance state-of-the-art and cutting-edge treatments in a coordinated care center for patients facing a complex medical and surgical disease. He completed a Master's in Clinical Research at Rush University, was formally the Director of the Rush Crohn's & Colitis Center, the Director of the Clinical Chronobiology Unit and the Associate Director of the Rush Center for Integrated Microbiome and Chronobiology Research at Rush University Medical Center, Chicago, IL.

Oral Abstract Presenters



Hayden Braun

Medical Student, MUSC College of Medicine
Category: Medical Student
Mentor: Valerian Fernandes, M.D.
Title: "Outcomes for Different ST-Elevation Myocardial Infarction Activation Criteria in the Pre-COVID vs Post-COVID Era"



Helen (Jensie) Burton, M.D.

Infectious Diseases Fellow, Co-Chief Fellow
Category: Resident/Fellow
Mentor: Krutika Hornback, PharmD
Title: "Limited Impact of Streptococcus pneumoniae Urinary Antigen Testing"

Laura Novotny, Ph.D.

Staff Scientist, Division of Infectious Diseases
Category: Staff Scientist, Research Specialist, Program Coordinator
Mentor: Eric Meissner, M.D., Ph.D.
Title: "Expression of interferon lambda receptor-1 isoforms shapes the hepatocellular response to interferon lambda"

Michelle Spiegel, M.D.

Assistant Professor, Division of Pulmonary, Critical Care, Allergy and Sleep Medicine
Category: Junior Faculty
Mentor: Andrew Goodwin, MD, MSCR
Title: "Development and Implementation of Electronic Health Record-embedded Clinical Decision Support to Reduce Central Line-associated Bloodstream Infections"

Poster Participants | Bioengineering Lobby

Poster No.	Presenter	Title
BE1	Leonidas Walthall	Patient Ambulation as a Predictor of Hospital Outcomes
BE2	Susan Evenhouse	Targeted Obesity Treatment in Primary Care
BE3	Ahmed Ibrahim	Octreotide therapy for patients with LVAD and angiodysplasia
BE4	Jad Allam	Causes of markedly elevated aminotransferases in patients with cirrhosis
BE5	Rachael Werner	Evaluating Selective Estrogen Receptor Modulators in Systemic Lupus Erythematosus: A Potential Therapeutic Approach
BE6	Brennan Winkler	Cilia Deficient Renal Tubule Cells are Primed for Injury via Mitochondrial Defects
BE7	Marice McCrorey	Dysregulation of the Endothelin System in a Pre-Clinical Lupus Prone Mouse Model
BE8	Shailza Sharma	YAP1: A key mediator in Enolase-1 driven pulmonary fibrosis
BE9	Soroush Moradi	Targeting of Endothelial Dysfunction in Lupus Nephritis: Effect on Human Renal Endothelial Cell Gene Expression and Outcomes in Murine Lupus Nephritis
BE10	Tim Adewale	IGF-II Regulates Lysyl Oxidase Propeptide and Mediates its Effects in part via Basic Helix-Loop-Helix e40
BE11	Kennedy Hawkins	Piezo1 Sex Differences in the Cardio-Renal Axis of Accelerated Systemic Lupus
BE12	Kane Banner	Human Cardiac Fibroblast Responsiveness to in vitro Unloading With or Without Omnidirectional Stretch
BE13	Jena Wirth	Membrane-localized estrogen receptor alpha (ERα) is required for normal development of multiple myeloid cell subsets
BE14	Jessalyn Rodgers	From lungs to blood – An “omics” approach to Pulmonary Sarcoidosis biomarker identification
BE15	Kristy Waldrep	Predicting mechanisms of IGF2-mediated fibrosis in primary human lung fibroblasts.
BE16	Laura Novotny	Expression of interferon lambda receptor-1 isoforms shapes the hepatocellular response to interferon lambda
BE17	Lauren Bracken	Elucidating the Role of Estrogen Receptor Alpha in Systemic Lupus Erythematosus

Poster Participants | Drug Discovery Lobby

Poster No.	Presenter	Title
DD18	Alissa Mingo	Rising into Relevance: A Rare Case of Saccharomyces Pyelonephritis in an Immunosuppressed Patient with Exposure to Sourdough Starter
DD19	Elizabeth Blalock	Delirium in Acute Stroke Patients: A Retrospective Cohort Study
DD20	Joie Zabec	Exploring the Ethical Implications of Augmented Intelligence (AI): A Survey of Residents on Perspectives and Education on the Ethics of AI in Healthcare
DD21	Kelly Sokevitz	Esophageal Dilation in Bronchiectasis
DD22	Elizabeth Hogue & Danielle Weinberg	Nightmare of Fatal Familial Insomnia
DD23	Abhinav Rao	The utility of Cologuard in a real-world community setting
DD24	Nicholas Smith	The Association of Statins with Chronic Liver Disease Progression: A Cohort Study
DD25	Adrienne Lorek	Candida auris cluster in a center with no previous infections associated with a single organ donor
DD26	Eily Hayes	A Successful Resuscitation: Training Nephrology Fellows to Perform Native Kidney Biopsies
DD27	Taylor Chaney	Off The Cuff
DD28	Ubaid Naeem	A a case of peritoneal dialysis-associated peritonitis caused by Bacillus Priestia
DD29	Sarah Smith	Risk Factors for Herpes Zoster in Patients with Lupus Compared to Controls
DD30	Victoria Delk	Impact of Systemic Lupus Erythematosus and Social Determinants of Health on Health-Related Quality of Life
DD31	Duaa Alkhader	Coping with Systemic Lupus Erythematosus: Associations with Neighborhood-Level Measures of Social Vulnerability
DD32	Jessica English	Pregnancy Outcome Disparities Among Women with Systemic Lupus Erythematosus
DD33	Alec Biscopink	Amiodarone Association with PGD After Heart Transplant
DD34	Yadis Arroyo	The reality of health care disparities: Lack of knowledge driving decreased rates of colon cancer screening in the underserved population

Poster Participants | Drug Discovery Lobby

Poster No.	Presenter	Title
DD35	Ariel Faber	Improving Care of Patients Prescribed Controlled Substances in Med-Peds Clinic
DD36	Jered Schenk	Use of bedside ultrasound in the diagnosis of cardiac tamponade: A Case Report
DD37	Kush Patel	Missed and Delayed Diagnoses of Chronic Liver Disease in Primary Care Patients with Cirrhosis
DD38	Ty Higginbotham	Quality Improvement of Intake and Output Data on General Medicine Wards
DD39	Jerome Deas	Length-of-Stay Index Outliers Discharged by Hospital Medicine Teams at MUSC Charleston
DD40	Nancy Hagood	Understanding the Impact of Hospital Acquisitions on Quality of Care
DD41	Alison Travers	A Clinical Decision Support Tool to Improve the Performance of Spontaneous Breathing Trials and Extubations among Eligible Patients in the Intensive Care Unit
DD42	Vidhya Aroumougame	Clinical Evaluation of Standard Convex Probe Endobronchial Ultrasound versus a Novel Thin Convex Probe Endobronchial Ultrasound Bronchoscopy System

View the abstracts listed above beginning on page 9 below.

Poster: BE1

Title: Patient Ambulation as a Predictor of Hospital Outcomes

Author: Leon Walthall, MD, Assistant Professor, Division of Hospital Medicine, Dept of Medicine

Introduction: Lack of mobility amongst inpatients is prevalent and deleterious. Hospitalized patients have been shown to spend an average of 83% of their stay in bed[1], leading to complications including loss of independence in activities of daily living, lower rates of discharge to home, worsening length of stay, and increased mortality[2].

We are instituting a culture of mobility at the Medical University of South Carolina. We standardized interdisciplinary assessment and communication of mobility using the Activity Measure for Post-Acute Care (AM-PAC) with all inpatients. Given limited resources, we aim to identify patients that would be most likely to benefit from a low effort, high impact intervention.

Methods: We identified patients with an AM-PAC score of 18 or above which indicates a patient able to ambulate. Taking this subset of patients, we assessed whether ambulation during admission would be associated with a change in mobility (as measured by delta AM-PAC during hospitalization), discharge disposition (home vs facility), or length of stay.

Results: Discharges from September - December 2023 showed significant uptake of new documentation goals: 96.6% of patients (9783/10132) had at least 2 AM-PAC scores recorded during their hospitalization. Nurses also documented ambulation during admission in binary terms (yes/no). Controlling for demographics, Charlson Comorbidity Index, and primary diagnosis group, patients who ambulated were 1.3x more likely to have an improvement in AM-PAC compared to those who did not ambulate. Also, patients who ambulated were 75% less likely to discharge to a facility and had a 20% shorter length of stay compared to those who did not ambulate.

Conclusions: We demonstrated strong uptake of new documentation goals amongst nursing staff. Additionally, ambulation was positively associated with all primary outcomes, including improved mobility assessment (AM-PAC), decreased need for discharge to facility, and reduced length of stay.

Our next steps include creating an interprofessional course to educate students on benefits and mechanics of mobility. These students are currently mobilizing patients in the hospital. We plan to analyze the effect of their mobilization efforts on the primary outcomes.

Type of project: Clinical

Mentor: Maggie Thomas, M.D.

References:

1) Brown CJ, Redden DT, Flood KL, Allman RM. The underrecognized epidemic of low mobility during hospitalization of older adults. J Am Geriatr Soc. 2009 Sep;57(9):1660-5.
2) Brown CJ, Friedkin RJ, Inouye SK. Prevalence and outcomes of low mobility in hospitalized older patients. J Am Geriatr Soc. 2004 Aug;52(8):1263-70.

Poster: BE2

Title: Targeted Obesity Treatment in Primary Care

Authors: Susan Evenhouse, M.D., Assistant Professor, General Internal Medicine**;** Justin Marsden, M.B.A., General Internal Medicine**;** Jingwen Zhang, M.S., General Internal Medicine

Introduction: Despite obesity's high prevalence and large economic burden, there are only 8,263 physicians board certified in obesity medicine, placing a tremendous onus upon primary care providers to treat the condition. We aimed to study the impact of a primary care-based weight management clinic (WMC) on weight loss and blood pressure management in patients with obesity.

Methods: We performed a prospective cohort study of patients referred to a primary care WMC from January 2023 through February 2024. Patients with a body mass index (BMI) $\geq$30 kg/m^2 and a referral to the WMC were included. The clinic offered weight loss medications, lifestyle interventions, and frequent follow-up as therapeutic options. The primary exposure of interest was patient attendance of at least one WMC visit. Primary outcomes included changes in weight (% change from baseline) and systolic blood pressure (SBP) at 3- and 6-months following referral. Cohort characteristics were described using means and proportions. Continuous variables were compared using two sample t-tests. All statistical analyses were performed in SAS 9.4. The MUSC IRB deemed this study quality improvement.

Results: The cohort included 77 patients, with 47 and 43 having outcomes at 3 and 6 months, respectively. Patients who attended the WMC had greater mean percent body weight loss at 3 months (-5.5% vs. -1.6%, p =0.003) and 6 months (-7.3% vs. -1.7%, p <0.001) than referred patients without a completed visit. Patients attending the WMC had a lower mean SBP at 3 months (-4.7 mmHg vs. +0.1 mmHg, p=0.339) and 6 months (-4.9 mmHg vs. +1.1 mmHg, p=0.393), compared to patients unexposed to the clinic intervention, but these differences were not statistically significant.

Conclusion: Our project shows that attendance at a WMC in primary care is feasible and effective at reducing weight and may also contribute to reducing blood pressure.

Project: Prospective cohort study

Mentor: Andrew Schreiner M.D., General Internal Medicine

Poster: BE3

Title: Octreotide therapy for patients with LVAD and angiodysplasia

Authors: Ahmed Ibrahim, Jad Allam, Don C. Rockey

Background: Angiodysplasias are vascular malformations that commonly develop in patients with left ventricular assist devices (LVADs) and often bleed recurrently. Standard treatment for angiodysplasias is endoscopic, typically with argon plasma coagulation. For patients that do not respond to standard endoscopic treatment, long-acting octreotide has been proposed to reduce recurrent gastrointestinal bleeding. Therefore, we aimed to investigate the effectiveness of octreotide for treatment of AVMs in LVAD patients.

Methods: Between May 2012 and December 2023, 65 patients with LVAD and angiodysplasia were identified using MUSC's Clinical Data Warehouse search engine. Of those, 33 patients received octreotide therapy. Complete clinical data were abstracted from the medical record, and outcomes were studied pre and post octreotide therapy.

Results: We identified 33 patients (61 ± 8 years old and 9 women) who received long-acting octreotide for recurrent angiodysplasia bleeding that failed to respond to endoscopic therapy (**Table**). The small intestine was the most common location for angiodysplasia (42% of patients had one or more small bowel lesions). Over a period of 2 years before octreotide therapy, GI bleeding events and the number of endoscopic therapies per year decreased from 4 ± 6 to 2 ± 2 and from 6 ± 9 to 2 ± 2, respectively. Prior to octreotide, patients received an average of 16 ± 27 (SD) units of PRBCs per year, which decreased to 6 ± 9 units per year on therapy. In the 32 patients who did not receive octreotide treatment, who were followed for 4 years, the average number of GI bleeding events, number of endoscopic therapies, and number of PRBCs transfused remained the same at 3 ± 5, 4 ± 6, and 5 ± 10, respectively.

Conclusion: Patients with LVADs have a propensity to bleed from small bowel angiodysplasia. Octreotide appeared to be effective in reducing GI bleeding events, the need for GI endoscopic therapies, and the frequency of PRBC transfusions.

Table 1. Patient characteristics

Characteristic	Patients on Octreotide N=33, (% or SD)	Patients not on Octreotide N=32, (% or SD)
Age (yrs)	61 ± 8	61 ± 10
Sex		
Men	24 (73%)	24 (75%)
Race		
White	12 (36%)	16 (50%)
Black	21 (64%)	16 (50%)
Location of angiodysplasia		
Stomach	8 (12%)	Stomach
Small Intestine	27 (42%)	Small Intestine
Colon	3 (5%)	Colon
Multiple	27 (42%)	Multiple

Table 2. Outcomes

	Pre-Octreotide (N=33, SD)	Post-Octreotide (N=33, SD)	No- Octreotide (N=32, SD)
Average number of GI bleeding events/ yr	4 ± 6	2 ± 2	5 ± 10
Average number of PRBCs (units/yr)	16 ± 27	6 ± 9	3 ± 5
Average Number of GI procedures/ yr	6 ± 9	2 ± 2	4± 6
Hematocrit	29 ± 6	33 ± 7	26 ± 6
INR	3.1 ± 3.9	2.0 ± 1.5	2.4 ± 1.0

Poster: BE4

Title: Causes of Markedly Elevated Aminotransferases in Patients with Cirrhosis

Author: Jad Allam, Post Doctoral Research Scholar, Division of Gastroenterology and Hepatology, Department of Medicine

Introduction: Marked elevations in aminotransferases (≥1000 IU/L) typically indicates acute injury to the liver. Here, we hypothesized that the cause of elevation in aminotransferases ≥1000 in patients with cirrhosis is likely due to a limited number of disorders and may also be associated with poor clinical outcomes.

Methods: From May 2012 to December 2022 all patients with cirrhosis and an AST or ALT ≥1000 IU/L were identified through MUSC's Clinical Data Warehouse search engine. Complete clinical data were abstracted for each patient, and outcomes were examined.

Results: The cohort was made up of 152 patients, who were 57±12 years old, with 51 (34%) women. Underlying liver disease included mainly hepatitis C cirrhosis, alcohol related cirrhosis, metabolic dysfunction-associated steatohepatitis (MASH) cirrhosis, autoimmune cirrhosis, primary sclerosing cholangitis (PSC) cirrhosis, and cryptogenic cirrhosis. The most common cause of marked elevation in aminotransferases in cirrhotic patients was ischemic hepatitis (73%), followed by chemoembolization (7%), autoimmune hepatitis (6%), drug induced liver injury (DILI) (3%), post-transjugular intrahepatic portosystemic shunt (TIPS) placement (3%), and hepatitis C (2%). During hospitalization and over a one-month period follow-up, the mortality rate in patients with ischemic hepatitis was 73% (79/108), while that for other causes of liver injury was 25% (9/40).

Conclusion: Ischemic hepatitis is the leading cause of marked elevation of aminotransferases in patients with cirrhosis; with distinctive clinical characteristics than other etiologies, and significantly poorer outcomes.

Type of project: Clinical science

Mentor's name: Don Rockey

Poster: BE5

Title: Evaluating Selective Estrogen Receptor Modulators in Systemic Lupus Erythematosus: A Potential Therapeutic Approach

Author: Rachael J. Werner, MD/PhD, Rheumatology Fellow, PGY-4, Division of Rheumatology

Introduction: Systemic lupus erythematosus (SLE) is a devastating autoimmune disease that can affect multiple organs and systems, leading to chronic inflammation, tissue damage, and a range of debilitating symptoms. Nine out of ten SLE patients are female, highlighting the significance of sex hormones in SLE susceptibility. Estrogen, acting through estrogen receptor alpha (ERα), has been linked to SLE onset and severity, particularly during reproductive years when estrogen levels are highest. Nonetheless, the potential therapeutic use of estrogen receptor modulators (SERMs) in SLE is not well-defined.

Methods: Murine and human immune cell lines will be used to assess the anti-inflammatory effects of SERMs. Initial testing will be performed with Pathway Preferential Estrogen (PaPE), a low-affinity estrogen-based ligand that activates non-nuclear kinase cascades and propyl pyrazole triol (PPT), a potent estrogenic compound that is selective to ERα. Following baseline testing, TLR7-agonism will be used to assess the ability of both SERMs to minimize TLR7-induced inflammatory responses.

Results: Preliminary studies have shown that PAPE is effective in blunting TLR7-induced inflammatory cytokines IL-6 and MCP1. Further investigations employing PPT in a murine dendritic cell line have demonstrated a dose-dependent decrease in TGFβ and IFNβ levels, implying that PPT might operate through the classical genomic pathway of estrogen receptor signaling, leading to a decrease in anti-inflammatory cytokines. Once the mechanism is verified in vitro, we plan to expand our testing to include patient-derived B-cells and lupus-prone mouse models.

Conclusion: This research indicates that targeting ERα with PaPE and PPT could lead to the development of personalized treatment strategies for SLE patients. Conducting further studies with these compounds in relevant models will enhance our understanding of their efficacy and potential for clinical translation.

Type of project: Basic Research

Mentor: Melissa Cunningham, MD/PhD

Poster: BE6

Title: Cilia Deficient Renal Tubule Cells are Primed for Injury via Mitochondrial Defects

Author: Brennan Winkler, PhD Candidate, Nephrology Division, Department of Medicine

Introduction: Acute kidney injury (AKI) is a significant and increasing problem, occurring in 1-7% of hospitalizations and up to 25% of intensive care unit (ICU) admissions with mortality rates, especially in ICUs, as high as 50-70%. Medical management of consists of supportive care, with dialysis implemented for the most severe cases. Among the many critical pathways that have been identified in AKI are alterations of renal tubular mitochondrial metabolism. Mitochondria are known to be involved in ciliopathies, such as polycystic kidney disease (PKD). AKI is also known to enhance cystogenesis in PKD. The goal of this study was to determine if and how primary cilia are involved in AKI. We previously showed that the highly-conserved eight-protein exocyst trafficking complex is necessary for ciliogenesis, that knockdown (KD) of Exoc5 (aka Sec10), a central exocyst component, resulted in very short or absent cilia, that overexpression (OE) of human EXOC5 resulted in cilia with increased length, and that kidney tubule-specific knockout (KO) of Exoc5 in mice led to polycystic kidney disease (PKD). Mutations in an exocyst gene in humans results in Joubert syndrome, a form of PKD. Intraflagellar transport protein 88 (Ift88) is also necessary for ciliogenesis. Overexpression of EXOC5 protected cultured renal tubule cells against hydrogen peroxide-induced injury, whereas knockdown of Exoc5 worsened injury.

Methods: To investigate mitochondrial structure and function following perturbations in primary cilia length we performed Seahorse assays, staining for reactive oxygen species (ROS), and transmission electron microscopy (TEM) in EXOC5 OE, Exoc5 KD, Exoc5 ciliary targeting sequence point mutant (cts-mut), and control Madin-Darby canine kidney tubule (MDCK) cells, as well as in murine Ift88 KO and rescue cells. To gain mechanistic insight, a non-biased metabolomics screen in EXOC5 OE, Exoc5 KD, Exoc5 cts-mut, and control MDCK cells, as well as in Ift88 KO and rescue cells was performed. In AKI, proximal tubules are the most susceptible to injury. To determine the effect of ciliary loss on AKI *in vivo*, we crossed Exoc5$^{fl/fl}$ and Ift88$^{fl/fl}$ mice with mice expressing CreERT2 driven by the sodium-dependent inorganic phosphate transporter in the proximal tubule (SLC34a-CreERT2). Proximal tubule-specific heterozygous (CreERT2-SLC34a1;Exoc5$^{fl/+}$ & CreERT2-SLC34a1;Ift88$^{fl/+}$) and homozygous (CreERT2-SLC34a1;Exoc5$^{fl/fl}$ & CreERT2-SLC34a1;Ift88$^{fl/fl}$) Exoc5 and Ift88 knockout (KO) mice and littermate controls were subjected to bilateral ischemia reperfusion (I/R) injury by clamping the renal arteries for 18 minutes. The mice were followed for eight days, and blood and tissue collections were performed.

Results: Seahorse assays revealed diminished basal respiration and mitochondrial maximal and spare respiratory capacity in Exoc5 KD, Exoc5 cts-mut cells, and in Ift88 KO cells compared to control MDCK and Ift88 rescue cells. Mitochondrial respiration was increased in EXOC5 OE cells. Next, we used CellROX staining in live cells to visualize levels of ROS. Exoc5 KD, Exoc5 cts-mut cells, and Ift88 KO cells had significantly higher levels of ROS than EXOC5 OE, control MDCK, and Ift88 rescue cells; moreover, using MitoRed staining, colocalization of mitochondria and ROS was observed. TEM imaging revealed abnormal mitochondria in Exoc5 KD, Exoc5 cts-mut, and Ift88 KO cells compared to EXOC5 OE, MDCK control, and Ift88 rescue cells. In our metabolomics screen, principal component (PCA) and hierarchical clustering analysis (HCA) of Exoc5 canine cells revealed readily apparent separation of the four groups

(control MDCK, Exoc5 KD, Exoc5 cts-mut, and EXOC5 OE) as well as between murine Ift88 KO and Ift88 rescue samples. The most significant finding was an extremely high elevation of tryptophan levels in both Exoc5 cts-mut and Exoc5 KD samples compared to control samples (113-fold and 58-fold increase, respectively). Concomitantly, kynurenine which is directly downstream of tryptophan was decreased in these cells (20% in the Exoc5 cts-mut and 83% in the Exoc5 KD). Similar results were seen in the Ift88 KO cells compared to the rescue cells (21% increase in tryptophan and a 49% decrease in kynurenine. In EXOC5 OE compared to control cells tryptophan was decreased (59%) and kynurenine was increased (25%). Importantly, tryptophan metabolism has recently been implicated in both AKI and PKD. Metabolism of tryptophan to kynurenine in kidney cells occurs via indoleamine 2, 3-dioxygenases (IDO1 and IDO2); changes in mRNA levels of IDO1 and IDO2 by RT-qPCR were consistent with the metabolomics data. Proximal tubule-specific Exoc5 and Ift88 KO mice had decreased levels of mitochondrial ATP synthase and increased tryptophan. There was also aggravated renal injury by histology and higher serum creatinine levels at day one following I/R injury compared to WT control mice ($p=0.005$ for Exoc5, $p=0.04$ for Ift88).

Conclusion: For the first time we show data suggesting that presence or absence of primary cilia lead to separate distinct intracellular metabolic phenotypes. We also show that primary cilia are centrally involved in AKI and the effect is mediated through mitochondria and correlates with changes in tryptophan metabolism.

Type of Project: Basic Science

Mentor's Name: Josh Lipschutz, MD

Poster: BE7

Title: Dysregulation of the Endothelin System in a Pre-Clinical Lupus Prone Mouse Model

Author: Marice K. McCrorey, Ph.D Student, Division of Nephrology

Introduction: Systemic Lupus Erythematosus (SLE) is the most common form of lupus autoimmunity. One characteristic of SLE is the overactivation of Toll-like receptor 7 (TLR7) and immune complex deposition in end organs. Interestingly, SLE disproportionately affects women to men (4:1), with a high prevalence in minority women. Clinically, SLE patients can present with multiple pathologies affecting the heart, kidneys, and brain resulting in chronic hypertension (HTN) and systemic vasculature dysfunction. Chronic HTN is the leading risk factor for the development of cardiovascular disease (CVD). Importantly, women with SLE are at a significantly higher risk of CVD and HTN than their healthy counterparts. However, the causative link between increased CVD prevalence in SLE remains to be elucidated. Interestingly, HTN, CVD, and SLE share a common factor where multiple studies find Endothelin-1 (ET-1), the most potent vasoconstricting peptide, elevated in patients' samples. However, few studies have explored the potential pathological role of ET-1 in the development of SLE-associated CVD.

Methods: To investigate this, we recruited both Non-SLE (n=17) and SLE (n=13) female patients and analyzed plasma samples for ET-1, endothelial activation, and characteristic lupus markers. In addition, utilizing female Resquimod-induced (100ug/ 30ul; topically; twice a week for 4 weeks) B6.Nba2 SLE prone murine model we performed a longitudinal study measuring cardiac dysfunction with echocardiography and analysis of the ET system at the terminal timepoint at both the protein and mRNA levels.

Results: No significant differences in patient demographic measurements were found between SLE and Non-SLE groups. Plasma ET-1 levels were significantly elevated in the SLE group compared to Non-SLE ($p=0.01254$). Plasma sVCAM-1, a marker of endothelial activation, was also found significantly elevated in the SLE group compared to Non-SLE ($p=0.0015$). The common clinical inflammation marker C-Reactive Protein (CRP) was found to not be different between the SLE and Non-SLE groups. However, a strong correlation was found between ET-1 and office pulse pressure ($r = 0.6236$; $p = 0.0009$). Using the B6.Nba2 mouse model, Resiquimod treatment led to significantly increased plasma sVCAM-1 ($p = 0.0451$) and cardiac ET-1 levels ($p = 0.0048$). In addition, a significant reduction in ejection fraction ($p = 0.0113$) and cardiac ET_B, a cognate receptor of ET-1, was observed ($p=0.0025$).

Conclusions: The current findings of this study warrants further exploration into the pathological role of the ET system in SLE-associated CVD. Moreover, we demonstrate that the B6.Nba2 model does develop cardiovascular dysfunction similar to what is found in patients with SLE. Furthermore, this study may have broad impacts on the development of ET system targeting medications in the treatment of cardiovascular disease in SLE patients.

Type of Project: Clinical and Basic

Mentor's Name: Dr. Justin Van Beusecum, Ph.D., Assistant Professor COM DOM Nephrology

Poster: BE8

Title: YAP1: A key mediator in Enolase-1 driven pulmonary fibrosis

Author: Shailza Sharma, Postdoctoral fellow, Division of Rheumatology & Immunology, Department of Medicine, Medical University of South Carolina, Charleston, SC, 29425, USA.

Introduction: Fibrosis is characterized by excessive extracellular matrix (ECM) component production and deposition. Systemic sclerosis (SSc) is a connective tissue disease of unknown etiology. Lung involvement is the leading cause of death of patients with SSc. Two drugs, tocilizumab and nintedanib, were approved by the FDA for the treatment of SSc. However, these drugs slow disease progression but do not stop or reverse the fibrosis. We recently demonstrated that the glycolytic enzyme Enolase-1 (ENO) promotes a fibrotic phenotype. independently of the commonly used pro-fibrotic factor TGF-β1. Yes-associated protein (YAP1), a downstream nuclear effector of Hippo signaling whose function is primarily regulated by its subcellular localization, translocates to the nucleus, and increases the expression of ECM proteins in TGF-β1-treated fibroblasts via the transcription factor TWIST-1. Here, we aim to elucidate the the role of YAP-1/TWIST-1 signaling as a potential mechanism mediating the profibrotic activity of ENO.

Methods: Human lung fibroblasts from normal donors were transfected with siRNA targeting ENO and YAP1 or control siRNA followed by treatment with TGF-β1 or vehicle control (VC). Plasmid-encoded ENO was overexpressed in human lung fibroblasts. Human lung fibroblasts were also treated with recombinant ENO (rENO) protein. The effect of ENO on YAP1 and TWIST-1 expression and the effect of YAP1 on ENO-mediated fibrosis was assessed by subcellular protein fractionation and western blotting.

Results: Plasmid-encoded ENO upregulated the expression of YAP-1 and TWIST-1 in primary human lung fibroblasts. Comparable results were obtained with rENO protein. Silencing ENO not only reduced the TGF-β1 mediated translocation of YAP-1 into the nucleus of primary lung fibroblasts but also downregulated the expression of TWIST-1 in the nucleus. Additionally, a significant downregulation of the ECM proteins Fibronectin (FN), Collagen Type I, alpha chain 1 (COL1α1), and α-smooth muscle actin (α -SMA), Plasminogen Activator Inhibitor-1 (PAI-1) and Connective tissue growth factor (CTGF) was observed in TGF-b1 treated primary lung fibroblasts in which YAP-1 was silenced. Similarly, the profibrotic activity of ENO was significantly reduced upon YAP-1 silencing in primary lung fibroblasts.

Conclusions: Our study demonstrates that ENO mediates its profibrotic activity via YAP-1. Silencing ENO ameliorates fibrosis by inhibiting YAP1 nuclear localization and blocking its downstream signaling mediated by transcription factor TWIST-1 in fibroblasts derived from normal lungs. Our findings identify novel pathways that can be targeted therapeutically in SSc-associated lung fibrosis.

Type of Project: Basic research

Mentor's name: Carol Feghali-Bostwick, Professor

Funding: NIH R01 HL121262, R01 HL133751, T32 HL144470, K24AR060297

Poster: BE9

Title: Targeting of Endothelial Dysfunction in Lupus Nephritis: Effect on Human Renal Endothelial Cell Gene Expression and Outcomes in Murine Lupus Nephritis

Authors: Dayvia L Russell[1], Sandra Mungaray[2], **Soroush Moradi [2]**, Jim C. Oates[1,2]. 1. Rheumatology Section, Ralph H. Johnson VAMC 2. Division of Rheumatology and Immunology, Department of Medicine.

Introduction: Lupus nephritis (LN), a severe manifestation of Systemic Lupus Erythematosus (SLE), involves chronic endothelial cell dysfunction (ECD), partly due to endothelial nitric oxide synthase (eNOS) uncoupling. This study evaluates whether sepiapterin (L-Sep) can improve LN outcomes in a murine model by restoring eNOS coupling and explores L-Sep's impact on inflammatory redox pathways in human LN.

Methods: We investigated L-Sep as a treatment for LN in NZM2410/J mice, comparing vehicle, low-dose (20 mg/kg/day), and high-dose (60 mg/kg/day) treatments after proteinuria onset. Urine protein and kidney dysfunction were monitored weekly. Survival was analyzed using Kaplan-Meier curves and log-rank tests, with proteinuria differences evaluated by one-way ANOVA.

Human renal glomerular endothelial cells (HRGECs) were treated with LN serum ± L-Sep. RNA sequencing identified changes in gene expression to determine pathways targeted by L-Sep in LN.

Results: NZM2410 LN-prone mice receiving L-Sep showed improved renal function as measured by urine albumin/creatinine compared to vehicle ($p=0.001$ for 20 mg/kg; $p=0.017$ for 60 mg/kg), and enhanced survival. L-Sep treatment resulted in lower renal activity, chronicity scores, and reduced C3 and IgG levels.

RNA sequencing revealed that genes involved in oxidative-stress and hypertension were differentially upregulated in HRGECs cultured with LN serum compared to Healthy Control (HC) serum (STK24, padj= 0.001; STK39, padj= 0.005). PIM3, which increases eNOS expression, was the most significantly downregulated gene in LN compared to HC (padj=0.0006). HRGECs treated with L-Sep had increased expression of SDC4 (padj=2.49E-11), a component of the glycocalyx that functions to protect ECs.

Conclusion: This study suggests L-Sep, a drug that activates eNOS, may be beneficial in the treatment of LN, in part by ameliorating renal endothelial cell dysfunction. RNA sequencing further implicates the eNOS pathway is impaired in ECs in LN and may be a useful therapeutic target.

Type of Project: Basic Science Research

Mentor: Jim Oates, M.D.

Poster: BE10

Title: IGF-II Regulates Lysyl Oxidase Propeptide and Mediates its Effects in part via Basic Helix-Loop-Helix e40

Author: Adegboyega Tim Adewale (Rheumatology Division, DOM)

Introduction: The dominant complication of Systemic Sclerosis (SSc) is clinically severe and commonly fatal pulmonary fibrosis (PF). We sought to determine the downstream regulatory role of the Basic Helix-Loop-Helix protein 40 (BHLHe40), in response to Insulin-like Growth Factor II (IGF-II) on Pro-Lysyl Oxidase cleavage products.

Methods: We examined the response of primary pulmonary fibroblasts cultured from the lungs of control donors and SSc lung explants to IGF-II as well as human recombinant Lysyl Oxidase Propeptide (LOX-PP). In addition, we utilized an experimentally-induced model of lung fibrosis with intratracheal bleomycin administration. We used qPCR and immunoblotting to quantify mRNA and protein levels, respectively. We used sequence-specific small-interfering RNA to silence targeted genes. Immunoblots were quantified in ImageJ (NIH) and statistical analyses were performed in GraphPad Prism.

Results: IGF-II regulates levels of Pro-LOX, LOX, LOX-PP, Bone Morphogenetic Protein 1 (BMP1) and Tolloid-like 1 (TLL1) isoforms. Transcription factor BHLHe40 localizes to the nucleus in response to IGF-II. BHLHe40 silencing downregulates TLL1, and decreases LOX-PP levels but upregulates Matrix Metalloproteases 1 and 3 as well as Cathepsin K. SSc lungs have higher baseline levels of the total (N-glycosylated/unglycosylated) LOX-PP than normal lung tissues, and baseline levels of LOX-PP correlate with TLL1 Isoform 2 in SSc lungs. LOX-PP contributes to SSc-PF by mediating changes consistent with the extracellular matrix deregulation implicated in SSc-PF: elevated RNA and protein levels of Collagen type III α1, Fibronectin-1, and Plasminogen Activator Inhibitor-1.

Conclusion: Our findings indicate that IGF-II, BHLHe40, and LOX-PP may serve as targets of therapeutic intervention to stop the progression of SSc-PF. Activation of common fibrotic pathways are involved in different diseases characterized by lung fibrosis such as IPF, so our findings may have wider implications for lung fibrosis associated with other diseases.

Type of Project: Basic Science Research

Mentor: Carol Feghali-Bostwick

Poster: BE11

Title: Piezo1 Sex Differences in the Cardio-Renal Axis of Accelerated Systemic Lupus

Author: Kennedy Hawkins, Research Specialist, Division of Nephrology

Introduction: Lupus is a chronic autoimmune disease disproportionally affecting women (9:1), particularly women of color, but men with this disease often have more pronounced symptoms than their female counterparts. Individuals with lupus are anywhere from two to fifty times as likely to experience a cardiovascular (CV) event than the general population. Though such complications are widely known, the mechanisms driving these disease processes are unknown. One well established pathogenesis of many CV diseases stems from an alteration of mechanical forces. The cation channel Piezo1 is a mechanosensitive channel receptive to such forces, and is known to play a critical role in CV diseases like heart failure and hypertension. Therefore, we hypothesized that inducing lupus-associated cardiovascular pathology in a lupus-prone mouse model would lead to increased expression of Piezo1 in a tissue-specific manner.

Methods: To investigate this, lupus-prone male and female B6.Nba2 mice aged 10-14 weeks were subjected to Resiquimod (R848; a TLR7/8 agonist; 100µg/30µL) treatment or acetone vehicle twice a week for four weeks. Echocardiograms were performed every four weeks. Mice were sacrificed and their tissues harvested at 4- and 16-weeks after the start of R848 treatment. Piezo1 levels were subsequently analyzed in the heart and kidney by real time quantitative polymerase chain reaction (RTqPCR), immunoblot, and immunofluorescent staining.

Results: In the kidney we found glomerular damage via blinded injury scoring to be significantly higher in R848-treated mice of both sexes compared to their acetone controls (phi=.522, p<.001 in females and phi=.510, p<.001 in males) at the 16-week timepoint. Interestingly, female R848-treated mice were found to have more significant glomerular injury than their male counterparts (phi=.239, p<.001). Additionally, *Piezo1* gene expression by RTqPCR in the 16-week female kidneys showed a downward trend (p=.0578) compared to the male kidney's no change. By echocardiography, hearts of female mice treated with R848 showed an increase in left ventricle (LV) wall thickness at 4 weeks, followed by an increase in internal diameters over the following 12 weeks, culminating in cardiac dysfunction by 16 weeks via significantly decreased ejection fraction (EF; p=0.0012). Males showed no significant cardiac dysfunction at any timepoint. By RTqPCR, female cardiac *Piezo1* levels were higher overall than their male counterparts. Cardiac *Piezo1* gene expression at 4 weeks was decreased in the R848-treated group of both sexes. At 16 weeks this trend was reversed in both male and female mice, showing R848 treatment induced an upregulation of *Piezo1* compared to each sex's respective vehicle controls. Interestingly, while Piezo1 protein expression followed the same 4-week trend of downregulation in R848-treated mice regardless of sex, protein expression at 16 weeks in the female R848-treated heart continued in a trending increase, while the male R848 heart showed no change. We found that this increase in cardiac Piezo1 in female, R848-treated is significantly correlated with higher left ventricular internal diameters (both LV-EDV (p=0.0122) and -ESV (p=0.0042)).

Conclusion: This data demonstrates a sex difference phenotype in lupus-associated murine cardiovascular dysfunction, potentially through a Piezo1-mediated pathway. Further investigation is warranted to elucidate Piezo1-dependent mechanisms behind lupus-associated cardiovascular disease.

Type of Project: Basic Science

Mentor's name: Justin Van Beusecum

Poster: BE12

Title: Human Cardiac Fibroblast Responsiveness to in vitro Unloading With or Without Omnidirectional Stretch

Participant's Name: Kane J. Banner, MS. 3rd Year medical Student at MUSC

Authors: Kane J. Banner, MS, Lauren Wakefield, MHA, Jane Fortunado, MS, Rachel Biggs, BS, Yuhua Zhang, MD, Daniel N. Silverman, MD, Lucas Witer, MD, Arman Kilich, MD, Michael R. Zile, MD, Amy D. Bradshaw, PhD

Introduction: Excessive myocardial interstitial fibrosis is a common link amongst cardiomyopathies, independent of etiology. Increased hemodynamic load promotes fibroblast activation and increased collagen deposition, while relief of that load does not reliably attenuate/reverse fibroblast collagen production in human heart failure or an in vitro model previously examined by our group. These data suggest a persistently altered fibroblast phenotype in heart failure. We sought to examine whether a combination of in vitro unloading along with pulsatile, omnidirectional stretch could alter human cardiac fibroblast (HCF) activation state.

Methods: HCFs were isolated from cardiac apical myocardium obtained at time of LVAD implant in patients ("pre-LVAD") with end-stage heart failure with reduced ejection fraction (HFrEF), at time of LVAD explant and transplant ("post-LVAD"), or from structurally and functionally normal unused donor hearts ("controls"). HCFs were then isolated, passaged, and grown to confluence before being plated on Flexcell CellSoft culture plates of pre-determined 1kPa (~normal human myocardial stiffness) or 10kPa (~heart failure myocardial stiffness) substrate stiffness. HCFs on each plate stiffness were then exposed to either 48 hours of omnidirectional stretch or not, with media and cell layers collected after 48 hours for analysis by Western Blot. Protein targets of interest were COL1α1 and TIMP1 in the media along with β-actin in the cell layers.

Results: With unloading (1kPa) + omnidirectional stretch, heart failure HCFs pre- or post-LVAD unloading had relative reduction in COL1α1 production at 48 hours compared with unloaded, unstretched human cardiac fibroblasts. There was no appreciable difference in COL1α1 production between pre-LVAD and post-LVAD derived HCFs stretched or not stretched on 10kPa substrate, and no difference between either circumstance on 10kPa when compared with no stretch on 1 kPa. Control HCFs on 1kPa substrate produced more COL1α1 with stretch and produced less COL1α1 on 10 kPa with stretch, exhibiting responsiveness on either substrate stiffness.

Conclusion: While hemodynamic unloading alone does not appear to alter heart failure-derived human cardiac fibroblast phenotype, in vitro hemodynamic unloading plus cyclic omnidirectional strain can attenuate COL1α1 production, marking a change in phenotype. This data informs future studies of mechanical, antifibrotic therapies in heart failure which may rely on reinstituting pulsatility and/or targeting activated downstream pathways.

Type of Project: Basic/Translational Research

Mentor: Daniel Silverman, MD

Poster: BE13

Title: Membrane-localized estrogen receptor alpha (ERα) is required for normal development of multiple myeloid cell subsets

Author: Jena Wirth, M.Sc., Research Specialist III, Division of Rheumatology and Immunology

Introduction: Estrogen plays a crucial role in modulating the immune system, although the molecular mechanisms of estrogen action via its receptors are not well defined in immune cells. ERα is one receptor that is found throughout most tissue types. It localizes to cytoplasmic, nuclear, and membrane regions, allowing estrogen to variably enact pro-inflammatory and anti-inflammatory effects in immune cells. We hypothesize that ERα variants and ERα cellular location impact the development of lupus by modulating TLR7-induced innate immune cell functions.

Methods: Membrane Estrogen Receptor Only (MOER) and Nuclear Estrogen Receptor Only (NOER) mice were used to investigate the effects of ERα localization on immune cell development. One cohort was ovary-intact and was utilized for baseline phenotyping of *ex vivo* splenocytes and bone marrow (BM) cells via flow cytometry as well as serum hormone ELISAs. A second cohort utilized ovariectomized mice and repletion of physiological estradiol. This cohort also underwent *in vivo* TLR7 stimulation via R848 (vs. vehicle) to simulate lupus-like disease. In addition to flow cytometry and hormone serum ELISAs, whole blood was analyzed for complete blood counts and metabolic panels and serum auto-antibodies were quantified.

Results: Studies in ovary-intact mice indicated that membrane ERα was required for normal bone marrow development. Ovary intact MOER mice demonstrated a robust response to TL7 agonism, but produced significantly lower IL-6 after ovariectomy, suggesting that membrane ERα is ligand dependent. In ovariectomized mice, significant leukocytosis and blood urea nitrogen reflected a change in renal function in MOER mice. Surprisingly, the expression of membrane ERα significantly increased the development of multiple myeloid immune cell subsets, regardless of TLR7 stimulation, and increased others only after TLR7 stimulation. Membrane ERα also differentially impacted peripheral immune cells in spleen after TLR7 stimulation.

Conclusion: MOER and NOER mice appear to differentially impact the development of immune cell subsets, and possibly function, with the largest impacts seen in the myeloid compartment. They also impact TLR7-stimulated endpoints, via an as yet undefined mechanism.

Type of Project: Basic Science

Mentor: Dr. Melissa Cunningham, MD/PhD

Poster: BE14

Title: From lungs to blood – An “omics” approach to Pulmonary Sarcoidosis biomarker identification

Author: Jessalyn I. Rodgers**,** Research Specialist II, Division of Rheumatology & Immunology, Department of Medicine, Medical University of South Carolina, Charleston, SC 29425, USA.

Introduction: Sarcoidosis, a multi-organ disease, is distinctly characterized by the formation of fibrotic granulomas. Lung involvement is present in >90% of sarcoidosis patients which can lead to severe end stage pulmonary fibrosis. Biomarkers of pulmonary sarcoidosis are urgently needed for treatment assessment, patient stratification, disease severity prognosis and therapy development.

Methods: RNA from lung tissue of patients with sarcoidosis who underwent lung transplantation, normal donors whose lungs were not used for transplantation, and primary fibroblasts derived from these tissues were analyzed via microarray. Gene/protein expression signatures were validated via qRT-PCR, Western blot, and Immunostaining. Levels of two were also measured in bronchoalveolar lavage fluid (BALF) and plasma of sarcoidosis patients from the Genomic Research in Alpha-1 Anti-trypsin Deficiency and Sarcoidosis (GRADS) study using ELISA.

Results: 1032 differentially expressed genes (DEGs) were identified in sarcoidosis lungs and 346 DEGs in sarcoidosis fibroblasts compared to their normal lung (NL) counterparts. Moreover, 44 DEGs were commonly deregulated in sarcoidosis lung and fibroblasts. Of those *CTSK*, *MXRA5*, *PTGDS*, *THBS2* upregulation and *HOPX* downregulation were validated by qPCR. 861 and 279 DEGs are unique to lung and fibroblasts, respectively. Preliminary data indicate elevated BALF and plasma levels of CTSK and S100A8 associated with disease severity in sarcoidosis patients.

Conclusion: Utilizing lung tissue of patients with pulmonary sarcoidosis compared to normal donors and primary fibroblasts derived from them, our “omics” approach has identified novel potential biomarkers of pulmonary sarcoidosis. Furthermore, the overlap of commonly deregulated DEG genes in sarcoidosis lungs and fibroblasts suggests the deregulation of these genes is driven by the fibroblast population while the other DEG genes may be representative of other cell types. Using this approach, we have identified potential biomarkers that associate with sarcoidosis disease severity.

Type of Project: Basic Science

Mentor: Dr. Carol Feghali-Bostwick, Professor

Poster: BE15

Title: Predicting mechanisms of IGF2-mediated fibrosis in primary human lung fibroblasts.

Author: Kristy M. Waldrep, Research Specialist II, Division of Rheumatology, Department of Medicine, College of Medicine, MUSC

Introduction: Pulmonary fibrosis (PF) is defined by excessive extracellular matrix (ECM) production. It causes significant morbidity and mortality in patients with systemic sclerosis (SSc) and idiopathic pulmonary fibrosis (IPF). We previously reported that lung tissues and fibroblasts from SSc-PF patients overexpressed insulin-like growth factor 2 (IGF2), and IGF2 upregulated the transcription factor SOX9 in primary human lung fibroblasts. Our goal was to identify SOX9-dependent and -independent pathways downstream of IGF2 using an unbiased approach.

Methods: We transfected normal lung (NL) fibroblasts from different donors with non-targeting control (siCtrl) or SOX9-targeting siRNA (siSOX9) and stimulated with vehicle (PBS) or recombinant human IGF2 for 24h. We identified differentially expressed genes (DEG) using RNA sequencing and bioinformatic analysis. We compared “IGF2+siCtrl vs. PBS+siCtrl” to “IGF2+siSOX9 vs. PBS+siSOX9” to find common and unique genes and pathways regulated by IGF2 and SOX9.

Results: RNA sequencing identified 752 DEGs in “IGF2+siCtrl vs. PBS+siCtrl” fibroblasts and 918 DEGs in “IGF2+siSOX9 vs. PBS+siSOX9” fibroblasts with 302 DEGs (20%) commonly dysregulated. Thirty-five pathways were enriched in both comparisons, while 32 pathways were unique to “IGF2+siCtrl vs. PBS+siCtrl” and 24 were unique to “IGF2+siSOX9 vs. PBS+siSOX9.”

Conclusion: We identified SOX9-dependent and -independent genes and pathways involved in the IGF2 fibrotic response in NL fibroblasts. Our data identify novel targets downstream of IGF2 that may mediate fibrosis.

Type of Project: Basic Science

Mentor: Dr. Carol Feghali-Bostwick, Professor

Poster: BE16

Title: Expression of interferon lambda receptor-1 isoforms shapes the hepatocellular response to interferon lambda

Author: Laura A. Novotny, Ph.D., Staff Scientist, Division of Infectious Diseases, Department of Medicine

Introduction: Lambda interferons(IFNLs) are secreted by hepatocytes in response viral infection. They bind the interferon lambda receptor-1(IFNLR1) and IL10RB heterodimer to activate antiviral genes. IFNL-IFNLR1 regulation is likely influenced by *IFNLR1* transcriptional variants. IFNLR1 isoform1 is signaling-capable, isoform2 is truncated and isoform3 is secreted, the latter two predicted signaling-deficient. We've shown that isoform1 markedly increases antiviral and de novo proinflammatory gene expression while isoform2 and 3 partially support antiviral genes in the presence of endogenous IFNLR1. To test whether isoform2 and 3 can independently support IFNL signaling, we evaluated function in iHeps that lacked endogenous IFNLR1.

Methods: *IFNLR1* knock-out(KO) iPSCs generated by CRISPR-Cas9 were engineered to stably express doxycycline-inducible, FLAG-tagged IFNLR1 isoform1,2,3 or empty vector. After differentiation to iHeps, clones were treated +/-dox, then stimulated with IFNL3. Antiviral and proinflammatory gene expression and impact on HBV replication were assessed. IFNL-IFNLR1 signaling pathway activation was examined by treatment of clones with pan-JAK&TYK2 inhibitor prior to IFNL3 stimulation.

Results IFNL treatment of KO+Isoform1 iHeps induced antiviral and proinflammatory gene expression, and significant decline in HBV. KO+isoform2 iHeps were capable of antiviral gene expression without endogenous IFNLR1, although reduced relative to KO+Isoform1, promoting a nominal decline in HBV. To initially examine signaling pathways activated after IFNL engagement, cells were treated with a pan-JAK&TYK2 inhibitor, and while KO+Isoform1 iHeps had substantial reduction in antiviral and proinflammatory gene expression, the response of KO+Isoform2 iHeps remained unchanged. Therefore, IFNLR1 isoforms1 and 2 may utilize different signaling pathways, influencing the genes ultimately expressed. KO+Isoform3 iHeps were functionally impaired without endogenous IFNLR1, suggesting it may modulate signaling through the native receptor.

Conclusions: IFNLR1 isoforms varied in ability to support antiviral and proinflammatory gene expression, which directly impacted the capacity to control HBV replication. Understanding differential IFNLR1 expression and signaling may guide development of new treatment strategies.

Acknowledgements: NIGMS (P20 GM130457), NIDDK (P30 DK123704)

Type of Project: Basic Research

Mentor: Eric G. Meissner, MD, Ph.D.

Poster: BE17

Title: Elucidating the Role of Estrogen Receptor Alpha in Systemic Lupus Erythematosus

Authors: Lauren Bracken[1], Cameron Leyers[2], Jena Wirth[1], and Melissa Cunningham[1]

[1]Department of Medicine, Division of Rheumatology and Immunology, Medical University of South Carolina, Charleston SC 29407

[2]Darby Children's Research Institute, Medical University of South Carolina, Charleston SC 29407

Introduction: Systemic Lupus Erythematosus is an autoimmune disease causative of whole-body issues such as rashes, arthritis, and nephritis. Epidemiologic research has shown an increased incidence of lupus in women of reproductive age as compared to men, leading to an investigation into the role of estrogen and estrogen receptors (ERs) and how they modulate the function of immune cells. Our previous research has shown that mice expressing a functional knockout of ER alpha (ERα short) were protected from lupus disease expression, suggesting key downstream effects of ERα in disease development. We investigated two ERα variants, the classic ERα66 and a short variant, ERα46, whose structure is similar to ERα short and whose function is proposed to modulate inflammatory pathways. Herein, our current data reveal differences in gene expression in dendritic cells and B cells that overexpress ERα46, ERα66, or the combination of ERα46/ERα66. Based on our accumulating data, we hypothesize that ERα46 protects against the development of lupus by down regulating TLR7-induced effects thus modulating specific innate immune cell functions.

Methods: *In vitro* transfection studies were conducted using a murine dendritic cell line (DC2.4) and human SLE EBV-transformed B cells, using Neon Electroporation. Cells were transfected with a plasmid containing ERα46, ERα66, or ERα46/66 +/- a TLR7 agonist (loxoribine) for 1.5 hours. RNA was then isolated from the transfected cells after 48h for NanoString analysis utilizing an inflammation panel (248 genes). NanoString N solver mapped differential gene expression using an error model with a 95% confidence interval.

Results: *In vitro* transfection studies in DCs showed changes in expression between cells transfected with ERα46 vs. both ERα46/66- and ERα66-transfected cells with or without TLR7 stimulation. Unstimulated DCs expressing ERα46 versus ERα66 downregulated *il1α, il1β, il6, ccl7,* and *ccl2* while genes *oas2* and *ifi44* were upregulated. Stimulated ERα46 DCs downregulated *nfkb1, myd88, il1α* and *il1β* compared to ERα66. In transfected B cells, fewer significant changes were noted, however co-expression of ERα46/66 vs. ERα66 alone resulted in a >200 fold change in *hifa1*, a major regular of survival and proliferation among other functions. These results will be confirmed and further investigated.

Conclusion: NanoString analysis of transfected DCs and B-cells demonstrated that ERα46 and ERα66 have different effects on immune cells based on preliminary gene expression data. This exploratory NanoString data supports our earlier findings on BMDCs from mice expressing ERα short (structurally similar to ERα46) in that expression of multiple genes/pathways were similarly regulated (eg. *ccl2* and *il6)*, suggesting a correlation between ERα short and endogenous ERα46, which may be a future therapeutic target.

Type of Project: Basic Science

Mentor: Melissa Cunningham, MD, PhD

Poster: DD18

Title: Rising into Relevance: A Rare Case of *Saccharomyces Cerevisiae* Pyelonephritis in an Immunosuppressed Patient with Exposure to Sourdough Starter

Authors:

Alissa Mingo, College of Medicine Class of 2025
Drew Stone, M.D., Resident Physician, Department of Internal Medicine

Introduction: *Saccharomyces cerevisiae,* commonly known as Baker's Yeast or Brewer's yeast, has been used in breadmaking, winemaking, and beer brewing for centuries. Additionally, it is a commensal pathogen of the skin and mucosa, occasionally included in probiotic supplements to treat diarrhea. Though not known to be pathogenic, rare cases of invasive infections have occurred in patients predisposed by critical illness, immunosuppression, or prolonged antibiotic use.

Methods: Using data collected from the electronic medical record and personal interactions with the patient in the inpatient setting, we present a case of complicated *Saccharomyces cerevisiae* urinary tract infection and a comprehensive review of the literature. We searched terms (and permutations of terms) including *Saccharomyces cerevisiae,* Baker's or Brewer's yeast, and urinary tract infection using libraries including PubMed and UpToDate to identify previously published evidence of this condition.

Results: A female, age 30, with a history of rheumatoid arthritis on immunosuppression, and previous admission for *Candida glabrata* UTI requiring intravenous antifungal therapies, presented to her gynecologist with complaints of vaginitis and flank pain. Vaginal and urine cultures grew *Saccharomyces cerevisiae*, and the patient was diagnosed with pyelonephritis and admitted for IV amphotericin deoxycholate. Repeat urine culture grew *S. cerevisiae* and *Klebsiella*. A further review of the patient's history revealed daily exposure to *S. cerevisiae* through baking sourdough bread.

She was treated with seven days of IV amphotericin deoxycholate (and Ertapenem for the *Klebsiella)*, and discharged on a six month course of antifungals with close follow up with infectious disease.

Conclusion: *Saccharomyces cerevisiae* is an exceedingly rare cause of invasive fungal UTI, with our literature review identifying only a few case reports of associated UTI and fungemia, all related to probiotic use. Our case emphasizes the importance of careful history taking and early diagnostic cultures in those at risk for invasive fungal infections.

Type of Project: Case Report and Review

Mentor: Andrew D Schreiner, M.D., Associate Professor, Department of Internal Medicine

Poster: DD19

Title: Delirium in Acute Stroke Patients: A Retrospective Cohort Study

Author: Elizabeth Adele Blalock, Medical Student, Hospital Medicine

Introduction: Delirium is a neuropsychiatric syndrome characterized by altered mental status, confusion, and inattention. Delirium patients are at increased risk of risk of falls, likelihood of not being discharged home, length of stay and mortality. Delirium is common in stroke patients and occurs in 10-75% of patients admitted with acute stroke. This is an evaluation of admitted stroke patients who experienced delirium, compared to those who did not.

Methods: This a retrospective cohort study of all patients admitted to a neurologic step-down unit with acute stroke from July 2022 to June 2023 at a comprehensive stroke center of a large tertiary care academic hospital. Data on stroke patients is routinely collected on all stroke patients and all patients are screened twice daily for delirium using the brief Confusion Assessment Method (bCAM). The chart of each patient admitted to this unit was manually reviewed to collect hospitalization specific data, demographics, CAM result and stroke specific data.

Results: Of the 289 patients included, 28% (n=81) screened positive for delirium during their admission. The mean age of the delirium group was 70.4 years compared to 64.7 in the group without delirium. The mean LOS in the delirium group was 9.1 days compared to 4.3 days in non-delirious group. The discharge modified Rankin Scale (mRS) was 3.8 in the delirious group and 1.6 in those without. The admission and discharge NIH Stroke Scale (NIHSS) were 14.4 and 11.9 in the delirious group, respectively and 4.6 and 2.4 in the group without delirium.

Conclusion: When evaluating patients with acute stroke, those who suffered from delirium were in the hospital over twice as long and more disabled at discharge. Although this group was older, their risk of delirium was likely influenced by the severity of their stroke given the large difference between admission NIHSS between the two groups. Although delirium is well documented to increase LOS, it is hard to ignore the impact of the difference in discharge mRS in these patients and the role their physical disability would have contributed to their ability to be ready to leave the hospital.

Type of Project: Clinical

Mentor: Dr. Benjamin Chapman Kalivas

Poster: DD20

Title: Exploring the Ethical Implications of Augmented Intelligence (AI): A Survey of Residents on Perspectives and Education on the Ethics of AI in Healthcare

Authors: Joie Zabec, Nhi Phuong Le, Hannah Neimy, Priscilla Li; Medical Students; College of Medicine

Introduction: Over the last decade, augmented intelligence (AI) has become increasingly integrated into medical practice with several potential benefits, including streamlined diagnoses, improved healthcare access, and decreased medical error. However, using AI in medicine raises ethical challenges, including patient rights, transparency, resource allocation, and trainee education. Inpatient care can benefit from AI's ability to analyze vast amounts of data, but it can also perpetuate existing disparities if trained using biased data. This study examines the medical resident's experience with AI in the clinical setting. We aim to explore their perspectives regarding its impact on healthcare and potential ethical concerns.

Methods: We will distribute a survey to residents at MUSC. The survey will assess residents' exposure to AI, understanding of ethics in AI, and their future incorporation of AI in their practice. There will be a free-form section for additional comments.

Results: After sending out the survey and collecting the data, we will analyze their responses to identify common themes among medical residents and determine their interest in health AI ethics education.

Conclusion: Early-career physicians must learn about the ethical implications of AI in medicine. Resident education should cover gaining consent for AI use, data used for clinical algorithms, and ethical and fairness analysis of models. This survey will examine medical residents' perspectives on the impact of AI on clinical practice and assess their interest in incorporating AI ethics into their curriculum. From radiology to psychiatry to surgery, AI will be used in some manner to diagnose, treat, and manage patient care. AI will be a transformative tool in healthcare, and trainees should be wary of blindly relying on it and must understand its ethical implications for equity, patient safety, and privacy.

Type of project: Qualitative

Mentor: Dr. Grant Goodrich, Director of MUSC Ethics Program

Poster: DD21

Title: Esophageal Dilation in Bronchiectasis

Authors: **Kelly Sokevitz (Medical Student),** Nhi Phuong Le (Medical Student), Spenser Staub (Fellow, Pulmonary and Critical Care) College of Medicine, Department of Internal Medicine.

Introduction: Esophageal dilation seen on computed tomography (CT) chest scans has been described in the scleroderma population, where the disease's impact on peristalsis and lower esophageal sphincter function can lead to dramatic dilations on CT, and have been associated with markers of morbidity[3]. We have frequently observed esophageal dilation in patients evaluated in a bronchiectasis clinic. We sought to systematically evaluate the prevalence of esophageal dilation in a cohort of patients with bronchiectasis as well as evaluate its association with markers of disease severity.

Methods: We evaluated a convenience sample of consecutive patients seen in our bronchiectasis clinics. Subjects must have a CT chest available for review. Esophageal dilation was defined as any segment with an air pocket >1cm in width, as measured with an independent thoracic radiologist. We also abstracted clinical data from the electronic health record and correlated esophageal measures with clinical markers of disease burden.

Results: 143 subjects were evaluated, including 25 men and 118 women. The mean age was 37 (SD) years. Esophageal dilation was present in 62% of our patient population, and associated with a higher rate of hospitalization in the 2 years preceding their clinic visit when compared to the patients without esophageal dilation on imaging (26.4% v 5.3%, p value <0.05)

Conclusion: We found a high prevalence of esophageal dilation on CT chest scans in a bronchiectasis population. This was also associated with increased rates of hospitalization. Our study is limited by sample size and an inability to prove causality. However, prior studies have reported an association between esophageal dilation and endoscopically-proven gastroesophageal reflux disease (GERD[4] [5], which could be hypothesized to be part of the pathophysiology of bronchiectasis and its sequelae

Type of Project: Clinical

Mentors: Patrick Flume, MD (Professor, Division of Pulmonary, Critical Care, Allergy & Sleep Medicine), Christina Mingora, MD (Assistant Professor, Pulmonary and Critical Care), Dhiraj Baruah, MD (Professor, Division of Radiology and Radiological Science)

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[3] Chatzinikolaou SL, Quirk B, Murray C, Planche K. Radiological findings in gastrointestinal scleroderma. J Scleroderma Relat Disord. 2020 Feb;5(1):21-32. doi: 10.1177/2397198319848550. Epub 2019 May 20. PMID: 35382407; PMCID: PMC8922595

[4] Hashemi SJ, Javad Moosavi SA, Idani E, Javaherforoushzadeh A, Raji H. Association of esophageal dilatation in chest CT scan with gastroesophageal reflux disease: A case control study. Monaldi Arch Chest Dis. 2018 Jul 2;88(2):914. doi: 10.4081/monaldi.2018.914. PMID: 29962193.

[5] Salaffi F, Di Carlo M, Carotti M, Fraticelli P, Gabrielli A, Giovagnoni A. Relationship between interstitial lung disease and oesophageal dilatation on chest high-resolution computed tomography in patients with systemic sclerosis: a cross-sectional study. Radiol Med. 2018 Sep;123(9):655-663. doi: 10.1007/s11547-018-0894-3. Epub 2018 Apr 23. PMID: 29687210.

Poster: DD22

Abstract Title: Nightmare of Fatal Familial Insomnia

Authors: Elizabeth Hogue, College of Medicine Class of 2025; Danielle Weinberg, PGY-1, Department of Internal Medicine (co-presenting)

Introduction: Creutzfeldt-Jakob disease (CJD) is a rare, incurable, and rapidly progressive disease in which prions, pathogenic misfolded proteins, accumulate in the CNS causing fatal neurodegeneration. The majority of CJD cases are sporadic or infectious with 10-15% being hereditary. Fatal familial insomnia (FFI) is a subtype of inherited familial prion disease caused by a mutation in codon 178 of the PRNP gene. FFI classically presents in middle age with symptoms of sleep disturbance, though variable symptoms are seen including weight loss, fatigue, behavior change, depression, or dizziness. Invariably, the condition advances rapidly with the onset of dementia, myoclonus, ataxia, and typical life expectancy of 1 year from diagnosis.

Methods: We present a case of genetic CJD identified on the inpatient general medicine service using data collected from the electronic medical record and personal interactions with the patient. A literature search was performed of libraries including PubMed and UpToDate to compare our case with the typical presentation and progression of CJD.

Results: The patient was a 51-year-old male with a history of recently diagnosed sleep related movement disorder who presented with new onset blood-tinged sputum and worsening mental status with significant family history of prion disease. His presentation was notable for dysautonomia, fluctuating cognitive impairment, decreased appetite, weight loss, voice changes, constipation, and dysphagia. Chest CT revealed a cavitary lung lesion suspicious for bacterial pneumonia that improved with antibiotics. Further inpatient evaluation for neurodegenerative disease including CT and MRI brain were unremarkable, EEG results were nonspecific and CSF studies including the CJD14-3-3 protein and RT-QuIC were negative. The patient was discharged with outpatient neurology and palliative care follow-up. Subsequent genetic testing revealed a heterozygous change in PRNP c.532G>A (p.Asp178Asn).

A probable diagnosis of genetic CJD requires history within a first-degree relative, symptom criteria and in vivo markers. Only genetic testing showing PRNP pathogenic variant or postmortem neuropathology confirms genetic CJD. Sleep disturbance is often the earliest sign of FFI. However, in early stages of disease, nonspecific symptoms necessitate a broad differential including autoimmune, neurologic, malignant, and infectious processes. With no disease altering treatment available, management is palliative, focusing on symptom control and genetic counseling for the family.

Conclusion: Inherited familial prion disease presents with nonspecific symptoms, progresses rapidly, and is fatal. Our case emphasizes the importance of a broad differential, comprehensive diagnostic assessment, and careful management of an emotionally distressing diagnosis.

Type of Project: Case Report

Mentor: Eric Palecek, MD, Associate Professor, Department of Internal Medicine

Poster: DD23

Title: The utility of Cologuard in a real-world community setting

Author: Abhinav Rao (PGY2 resident at Trident Medical Center)

Background: Multitarget stool DNA tests (i.e., Cologuard), serve as screening tests for colon cancer and are recommended by the USPSTF every 1-3 years. Here, in a large primary care practice setting, our aim was to evaluate the efficacy of Cologuard in a real-world setting.

Methods: This was a retrospective cohort study that included an analysis of EHR data for 5,809 Palmetto Primary Care (Summerville, SC) patients from January 1, 2019 to April 1, 2023 for which a Cologuard test was ordered. Patients who were high risk, had a prior colonoscopy or prior negative Cologuard test result were excluded. Of the remaining 5,034 patients, 3,139 patients completed the Cologuard test. Patients were followed for 36 months to determine whether a follow-up colonoscopy was performed. Statistics were performed using Microsoft Excel.

Results: Of the 3,139 patients that completed the Cologuard test, 490 had a positive Cologuard test, the majority were women, had an average age of 68, and were predominantly White. The most common reason for ordering Cologuard was as an initial screening test for colon cancer in an average risk patient. 282/490 (58%) had a follow-up screening colonoscopy. The average time from the initial Cologuard ordering to the diagnostic colonoscopy was 226 days (SD, 271). Among these 282 patients who had colonoscopy after a positive Cologuard test, 258 patients had complete colonoscopy data. Among these 258 patients, 188 patients did not have colon cancer or advanced adenomas (73% false positives), 10 patients had colon cancer (3.9% of the patients having colonoscopy; and 0.3% of the overall population), and 62 patients had advanced adenomas (24%). 2 of the 10 patients with colon cancer also had advanced adenomas. The sigmoid colon was the most common site for colon cancer, and 8 out of 10 patients had stage 1 or greater stage disease.

Conclusions: Nearly 16% of patients who had a Cologuard test had a positive result. Overall, Cologuard detected colon cancer in 10 out of 5,827 (0.2%) patients for whom it was ordered and in 10 out of 3,139 (0.3%) who completed and qualified for the test—significantly lower than the 0.7-1.0% colon cancer detection rate with colonoscopy (Shaukat et. al, Clinical Gastroenterology and Hepatology 2022).

Type of Project: Clinical research

Mentor: Don Rockey, M.D.

Poster: DD24

Title: The Association of Statins with Chronic Liver Disease Progression: A Cohort Study

Author: Nicholas P. Smith, MD, Department of Medicine Resident

Introduction: Statin medications are associated with a reduced risk of portal hypertension complications and mortality in patients with cirrhosis; however, their impact in chronic liver disease (CLD) patients prior to developing advanced fibrosis is unclear.

Methods: We performed a retrospective cohort study of primary care electronic health record (EHR) data between 2012-2021 and included patients with a diagnosis of CLD, lab inputs for a Fibrosis-4 Index (FIB-4) calculation, and no diagnoses of cirrhosis or hepatocellular carcinoma (HCC) preceding the index FIB-4. We performed two analyses: (1) patients with an index FIB-4<3.25 were followed until the occurrence of a FIB-4>3.25 (high-risk for advanced fibrosis) or end of the study period; (2) all cohort patients were followed from the index FIB-4 until the occurrence of a severe liver disease (composite of cirrhosis, a cirrhosis complication, or HCC), or the end of the study period. A statin prescription was the primary exposure. Unadjusted and adjusted Cox regression models were developed for each outcome.

Results: The cohort included 2,957 patients with CLD and a mean index FIB-4 of 1.2. Analysis 1: 2,587 patients with index FIB-4 <3.25 were followed for a mean of 5.4 (±2.6) years. 862 (33%) received a statin prescription and 627 (24%) progressed to a high-risk FIB-4. A statin prescription was associated with a lower risk of progressing to FIB-4 >3.25 (adjusted HR 0.37; 95% CI 0.30-0.44). Analysis 2: 2,957 patients were followed for a mean of 3.8 (±2.7) years. 892 (30%) received a statin prescription and 463 (16%) experienced a severe liver disease outcome. Statin prescription was associated with a lower risk of developing the composite severe liver disease outcome (adjusted HR 0.61; 95%CI 0.46-0.82).

Conclusion: In a primary care population, statin prescription was associated with a lower risk of progressive fibrosis or a severe liver disease outcome.

Type of Project: Retrospective Cohort

Mentors: Andrew D. Schreiner MD MSCR, David G. Koch MD MSCR, Jingwen Zhang MS

Poster: DD25

Title: *Candida auris* cluster in a center with no previous infections associated with a single organ donor

Subject categories: outbreaks

Authors: Evan Rivere, MD; Eric G. Meissner, MD, PhD; Alexandra Mills, MD; Courtney E. Harris, MD; Adrienne Lorek McGarity MPH, MLS, CIC (presenting); Scott R. Curry, MD, MS

Affiliations: Department of Medicine, Division of Infectious Diseases, Medical University of South Carolina; Infection Prevention and Control, Medical University of South Carolina

Background: *Candida auris* is an opportunistic pathogen reported in the US since 2016. *C. auris* infections (CAI) are frequently healthcare-associated, but only one case of donor-derived CAI in a lung transplant recipient has been reported (PMID 28520901). We describe a cluster of two CAIs at a single center in South Carolina occurring in 2 different recipients from the same solid organ transplant donor.

Methods: We describe two cases of invasive CAIs occurring in an academic medical center without prior CAI in Charleston, SC in October 2023. *C. auris* was identified using Bruker MALDI-TOF and confirmed by the state health department.

Results: Patient 1: 40-49 year-old male underwent heart transplantation on day 19 from admission complicated by growth of *C. auris* on post-op day #15 from a drain. He was readmitted post-op days 22-63 with positive blood cultures for *C. auris* and underwent re-operation with debridement and hardware removal. *C. auris* pericarditis required multiple returns to the OR (Figure). He was discharged on micafungin/posaconazole with plans for long-term antifungal therapy. **Patient 2**: 50-59 year-old male underwent liver and kidney transplantation on day 25 from admission from the same donor as Patient 1 in a separate hospital complex. His course was complicated by possible infected biloma not amendable to drainage and *C. auris/C. glabrata* fungemia, which was further complicated by abdominal wall collection cultures growing *C. auris* on post-operative day 35 on washout. He was managed with dual micafungin/posaconazole however, he died of unrelated causes at 93 days after transplant (Figure). **Investigation**: The donor for both recipients was a 10-19 year-old male who suffered brain death after trauma and was hospitalized for 56 days prior to procurement in Atlanta, GA without known CAI. Airway cultures at the time of organ procurement were positive for rare *Pseudomonas* and light unidentified yeast of multiple morphologies; urine cultures also grew 40,000 cfu/ml un-identified yeast. Screening of 35 and 4 inpatients in units exposed to patients 1 & 2, respectively, with axilla/groin PCR was negative (Figure). A third organ recipient for this donor (kidney) at our center was identified and had negative urine fungus cultures.

Conclusions: Despite no definitive link to a known donor infection, this cluster of CAI occurring simultaneously in 2 patients in separate hospitals/units at a single center with no known prior cases represents likely donor-derived CAI. Our experience suggests that organ procurement organizations should consider improved screening techniques for *C. auris* in donor cultures.

Type of Project: Clinical

Mentor: Scott Curry, M.D.

Poster: DD26

Title: A Successful Resuscitation: Training Nephrology Fellows to Perform Native Kidney Biopsies

Author: Eily Hayes DO, chief fellow, Division of Nephrology

Introduction: Biopsy is the gold standard for diagnosing renal pathology. The ACGME program requirements for graduate medical education in nephrology note that fellows should be provided with the opportunity to train and achieve competence in the performance of kidney biopsies. The growth of interventional radiology and COVID-19 pandemic-related department restructuring and staffing turnover significantly decreased fellows' opportunity to perform kidney biopsies at MUSC. Nephrology faculty and fellows developed a new protocol for performing low-risk ultrasound guided biopsies at bedside, resulting in a significant increase in kidney biopsies performed by nephrology. More recently, in partnership with the hospital, the nephrology program has added a biopsy clinic to improve both access to care and training opportunities for the next generation of nephrologists.

Methods: A protocol for low-risk kidney biopsies performed at bedside by nephrology was developed and implemented. The protocol included indications and contraindications for biopsy, characteristics of low-risk biopsy patients, pre-biopsy clinical management guidelines, the biopsy procedure, standardized post-biopsy orders, and templates for related documentation. The protocol was revised to address institution-specific challenges as they arose. Data regarding the number of biopsies, complications, and diagnoses were recorded and analyzed.

Results: From June of 2020 through December 2021, two bedside kidney biopsies were performed by nephrology fellows (0.11 biopsies per month, or 1.26 biopsies per year). The new protocol was implemented at the start of the 2022-2023 academic year. In the subsequent 19-month period, 26 biopsies were performed at bedside by nephrology fellows, (1.37 per year, or 16.45 per year), a 1306-percent increase. Four of the 26 biopsies (15.4%) were complicated by bleeding. Two of these bleeds were insufficient to cause hematoma, two resulted in small subcapsular hematoma (7.7%); though our sample size is small, our rate of hematoma was slightly lower than the 11% rate for post-biopsy hematoma in a systemic review and meta-analysis of over 118,000 renal biopsies as published in CJASN in 2020. Data collection is ongoing, but an additional benefit at our institution has been that patients can be biopsied, and diagnosis obtained, earlier in the clinical course.

Conclusion: At MUSC, a protocolized approach to performing kidney biopsies has significantly increased the number of biopsies performed by nephrology. Unanticipated benefits include shorter wait-times for biopsy patients, obtaining tissue diagnoses and initiating treatment earlier in the clinical course, and the recent expansion of the biopsy program to include a dedicated renal biopsy clinic.

Type of Project: Clinical

Mentor: Natalie Freidin, MD

Poster: DD27

Title: Off The Cuff

Authors: Taylor Chaney, DO; Natalie Freidin MD

Department of Medicine, Division of Nephrology, Medical University of South Carolina

Introduction: The large bore, dual-port, non-tunneled, non-cuffed Central Venous Catheter (CVC) remains in frequent use today particularly in the inpatient setting for temporary (short-term) utilization in patients requiring relatively urgent extracorporeal dialysis or pheresis. Excessive duration of use for these temporary dialysis catheters is associated with increased risk of complications, including Central Line Associated Bloodstream Infections (CLABSI). With this study, we seek to discover areas within the realm of inpatient temporary vascular access for improvement in patient safety and quality of medical care with patients followed by General Nephrology. This study is a part of the Medical University of South Carolina (MUSC) Resident Incentive Project, funded through MUSC, in efforts to improve the quality of patient care delivered.

Methods: We are conducting a retrospective observational study of patients admitted to a single academic medical center followed by the General Nephrology service. Preliminary data is presented from patients admitted from September through December 2023 who received insertion of a non-tunneled, non-cuffed, dual-port CVC for dialysis or pheresis indications. This data was collected as a conglomerate effort by the MUSC Nephrology Fellows during the Research rotation. The mean and median number of catheter days per occurrence (number of days from catheter placement to catheter removal) were calculated.

Results: A total of 73 catheters placed in 56 patients followed during the study resulted in mean numbers of catheter days per occurrence of 14.43 days and 10.54 days for catheters placed in the Internal Jugular vein and Femoral vein, respectively.

Conclusion: This preliminary data suggests that improvements could be made to limit the duration of catheter days for non-tunneled, non-cuffed dialysis catheters in hospitalized patients. This could reduce the incidence of CLABSI and improve the quality of patient care. The planned next phase of this project will tentatively compare more in depth the mean duration of catheter days per occurrence to Central Line Associated Bloodstream Infection risk and location of catheter placement.

Type of Project: Quality Improvement/Retrospective Observation

Faculty Mentor: Natalie Freidin, MD, Director, Nephrology Fellowship Program

Poster: DD28

Title. A case of peritoneal dialysis-associated peritonitis caused by *Bacillus Priestia*

Authors: Ubaid Naeem MD, Salem Vilayet MD, Michael E Ullian MD

Division of Nephrology, Medical University of South Carolina

Introduction. A major challenge to peritoneal dialysis (PD) as a renal replacement therapy is bacterial peritonitis. Usual pathogens are gram-positive species, but unusual pathogens pose a challenge for diagnosis and treatment. Here, we present our experience with PD-associated peritonitis (PDAP) caused by *Bacillus Priestia* (*B priestia*).

Case Report. A 76 year-old male with renal failure from diabetic nephropathy on chronic PD presented with altered mental status after a cerebrovascular accident. He developed fever, cloudy PD fluid, leukocytosis, and slightly elevated absolute neutrophil count in the PD fluid ($108/mm^3$), with a negative culture (even after several week), and he was started on intra-peritoneal (IP) cefepime and systemic Zosyn. Despite antibiotics, peripheral leukocytosis worsened and fever recurred. Repeat PD fluid culture grew *B Priestia* on the 7^{th} day, sensitive only to Ciprofloxacin and Vancomycin. He was switched to IP Vancomycin for 2 weeks and recovered completely.

Discussion. The natural habitat of *B Priestia* is soil, feces, sea sediment, and cotton plants. PDAP from other Bacillus subspecies has been reported but not from *B Priestia*. *B Priestia* rarely causes soft tissue infections in immunocompromized hosts. Our patient responded well to IP Vancomycin. It is unclear why this patient was susceptible to an environmental pathogen.

Conclusion. PDAP is the most feared complication in PD patients, often leading to modality loss. To our knowledge, this is the first case of PDAP from *B Priestia,* and society guidelines for treatment are not available. This organism is slow growing, and thus clinicians must be patient in waiting for a positive culture.

Type of Project: Clinical

Mentor: Michael E Ullian, MD

Poster: DD29

Title: Risk Factors for Herpes Zoster in Patients with Lupus Compared to Controls

Author: Sarah Smith, MD, Department of Internal Medicine

Introduction: This study was conducted to determine the burden of herpes zoster (HZ) in patients with systemic lupus erythematosus (SLE) compared to controls, and to elucidate underlying risk factors associated with HZ in SLE.

Methods: Data was obtained from an IRB-approved longitudinal registry of patients with SLE and non-SLE controls at MUSC. Information on demographics, social and medical histories was obtained through in-person interviews and chart review. Participants missing HZ history were excluded. Validated measures of disease-related damage (SLICC Damage Index) were used. Pearson's chi-squared testing was performed for categorical variables and two-sample t-tests were performed for continuous variables. Variables associated with HZ were assessed for inclusion in a multivariable model.

Results: A history of HZ was noted in 202 of the 822 (24.6%) SLE cases and 14 of the 564 (2.5%) controls. The adjusted odds ratio (OR) for HZ in SLE cases was 8.93 (95% CI=4.75-16.79). The risk of HZ in SLE cases increased significantly with increasing age. The OR for SLE cases compared to controls at age 30 was 9.32 (95% CI= 4.73-18.4). ORs (95% CI) for age 40, 50, 60 and 70 were 10.12 (4.45-23.00), 10.54 (4.23-26.26), and 10.98 (3.98-30.26), respectively.

In a multivariate regression model, a higher risk of HZ in SLE cases was significantly associated with age (OR=1.14; 95% CI=1.06-1.22), mycophenolate use (OR= 1.65; 95% CI=1.12-2.46), cyclophosphamide use (OR=2.86; 1.75-4.67), having any SLE disease damage (SLICC-DI > 0) (OR 1.98, 95% CI: 1.38-2.83), low complement levels (OR=2.17; 95% CI:1.43-3.31), history of myocardial infarction (OR=3.08; 95% CI=1.74-5.46), stroke (OR=2.54; 95% CI=1.57-4.09), depression (OR=1.78; 95% CI=1.21-2.61)) and malignancy (OR=2.57; 95% CI=1.46-4.51).

Conclusions: Our study finds patients with SLE to have a 9-fold higher risk of shingles by age 30 compared to non-SLE controls. Within the SLE population, we found significant relationships between history of HZ and SLE disease damage, immunosuppressive medication exposure, and medical comorbidities that are consistent with previous literature. This data supports a critical need for earlier and more widespread use of vaccination against HZ and emphasizes the importance of preventive measures to mitigate the high burden of shingles among patients with SLE.

Type of Project: Clinical Research

Mentor: Diane Kamen, MD, MSCR

Poster: DD30

Title: Impact of Systemic Lupus Erythematosus and Social Determinants of Health on Health-Related Quality of Life

Author: Victoria Davis Delk, Internal Medicine PGY-1

Introduction: Systemic lupus erythematosus (SLE) is a systemic autoimmune disease with the potential to severely diminish patients' quality of life (QoL). SLE disproportionately affects young Black females in both prevalence and disease severity. One goal of this study was to measure the impact of race and other demographic features on mental and physical QoL domains in patients with SLE compared to controls.

Methods: This study was nested in a longitudinal IRB-approved observational registry of patients with SLE and population-matched unaffected controls. We included adults ≥18 years with and without diagnosed SLE who completed at least one 36-Item Short Form version 2 (SF- 36) questionnaire. The SF-36 includes 4 physical component score (PCS) domains and 4 mental component score (MCS) domains. Disease damage was measured using the SLICC/ACR Damage Index (SDI) at the most recent visit. Comparisons were made between demographic factors, disease factors, and SF-36 scores using t-tests for continuous variables, Chi-squared tests for categorical variables, and multivariable logistic regression.

Results: Included were 514 patients with SLE (71.4% identified as Black, 93.2% female) and 215 controls (81.4% Black, 82.3% female). There were no statistically significant differences between patients and controls in high school graduation or insurance status (comparing insured to uninsured), however a greater proportion of controls had private insurance (76.1% vs. 57.3%, $p<0.01$). When comparing QoL scores, patients with SLE had significantly worse scores in all domains compared to controls (all $p<0.01$), with the exception of mental health ($p=0.84$). Compared to non-Black patients with SLE, Black patients had significantly worse SF-36 scores in 3 of the 4 PSC domains (physical function, role-physical, bodily pain) and 1 of the 4 MSC domains (role-emotional). Although the total PCS was worse in Black patients (38.2±11.2 vs 40.9±12.9, $p=0.02$), the total MCS was similar between Black and non-Black patients ($p=$NS). Black patients with SLE compared to non-Black had higher rates of discoid rash (21.0 vs 13.1, $p<0.01$), alopecia (50.3% vs. 27,7%, $p<0.01$), arthritis (80.1% vs. 67.2%, $p<0.01$), renal disease (56.4% vs. 27.0, $p<0.01$), any disease damage (SDI>0) (69.9% vs. 54.7%, $p<0.01$), and high disease damage (SDI≥2) (50.4% vs. 31.4%, $p<0.01$). MCS and PCS scores were not significantly different in patients with renal disease compared to those without a history of renal disease. Over 68.8±44.6 months of follow-up, patients with SLE had no significant change in PCS scores but did have a significant improvement in MSC scores over time (by 1.6±11.4, $p=0.02$), predominately among the Black patients (by 1.8±11.9, 0.02). In a multivariate regression model, there was no significant association between Black race and either total PCS or MCS once adjusted for age, disease duration, sex, insurance status, BMI, SDI damage score, and depression.

Conclusion: In addition to previously reported disparities in health outcomes between Black and non-Black patients with SLE, our study finds substantial differences in self-reported QoL that are likely multifactorial in etiology. The continuation of this work will help inform future interventions to improve QoL for patients with SLE.

Type of Project: Clinical science

Mentor: Diane Kamen, M.D., M.S.C.R., Professor, Division of Rheumatology & Immunology

Poster: DD31

Title: Coping with Systemic Lupus Erythematosus: Associations with Neighborhood-Level Measures of Social Vulnerability

Author: Duaa Alkhader, MD, PGY-3 Internal Medicine Resident.

Introduction: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease associated with significant morbidity, mortality, and reduced quality of life

Methods: This study, based on a cross-sectional analysis within the larger Peer Approaches to Lupus Self-management (PALS) randomized trial, investigates the association between baseline disease coping skills among African American women with SLE and neighborhood-level social vulnerability. Utilizing the Centers for Disease Control and Prevention's Social Vulnerability Index (SVI). We hypothesized that higher neighborhood vulnerability would be associated with greater difficulty in coping with the disease.

Discussion: This study is the first to explore interactions between personal and neighborhood factors on coping skills in lupus patients, focusing on an historically vulnerable population, which mitigates the confounding effect of race. Despite its cross-sectional nature and post hoc analysis design, this study provides valuable insights for clinicians. The identified associations offer potential targets for interventions aimed at enhancing self-efficacy and supplementing services, particularly for lupus patients with limited education residing in minority or low mobile home density neighborhoods.

Results: In this study, SLE patients with less than a high school education residing in neighborhoods predominantly comprised of minorities exhibited lower coping skills. Associations between depression, anxiety, and reduced coping scores were also observed, particularly in socially vulnerable environments, highlighting the amplified impact of personal and neighborhood-level factors. Surprisingly, those with lower levels of education had lower coping skills when in neighborhoods with fewer mobile homes. This finding underscores the importance of considering contextual factors such as housing conditions in understanding coping disparities.

Conclusion: The results underscore the need for further research to disentangle the complex interplay of personal and environmental factors contributing to coping and self-management in lupus patients, with the ultimate goal of improving outcomes and tailoring interventions to the most vulnerable populations.

Type of project: Clinical

Mentor: Jim C. Oates, MD, Department of Medicine, Division of Rheumatology and Immunology

Poster: DD32

Title: Pregnancy Outcome Disparities Among Women with Systemic Lupus Erythematosus

Author: Jessica English, MD, Rheumatology Fellow, Division of Rheumatology

Introduction: Women with systemic lupus erythematosus (SLE) have increased rates of pre-term birth, small for gestational age babies, and pre-eclampsia compared to women without a diagnosis of SLE. Ongoing research has shown a dysregulated immune system, adversely affects patients even if SLE is not yet diagnosed suggesting a “pre-SLE disease state” exists. We hypothesize that a pre-SLE disease state impacts pregnancy outcomes among women with circulating SLE-associated autoantibodies prior to a diagnosis of SLE.

Methods: Case control study including women with at least one prior recorded pregnancy from an ongoing longitudinal SLE registry at a single center. Controls (related or unrelated) were included if unaffected by SLE. Associations between different pregnancy outcomes with patient-pregnancy type and demographic variables were evaluated with univariate and multivariable modeling.

Results: 630 women (SLE and controls) were included in our analysis with 1715 pregnancies. Of those, 303 women (736 pregnancies) were prior to a diagnosis of SLE. A higher proportion of related controls were ANA positive (47.7%) as compared to unrelated controls (30.5%). Overall, 80% of women self-identified at Black. Multivariable analysis revealed no differences in ANA positive versus negative controls in odds of live birth, preeclampsia, low-birthweight, premature delivery. Those with pregnancies prior to a diagnosis of SLE had lower odds of live birth, OR 0.64 (0.45-0.92) and increased odds of preeclampsia, OR 2.11 (1.04-4.28) as compared to ANA positive controls. There were no significant differences in this group for outcomes of low birth weight, premature birth, or spontaneous abortion. Pregnancy outcomes were worse in all categories for women who had pregnancies after a diagnosis of SLE, the highest being low birth weight, OR 4.71 (2.91-7.60), and premature birth, OR 4.06 (2.53, 6.51).

Conclusion: In a large SLE cohort, we note differences in pregnancy outcomes among women with SLE compared to two groups of controls. Women prior to their diagnosis of SLE had fewer live births (76.6 vs 81.3%) & higher preeclampsia risk (9.3% vs 4.9%) compared to ANA positive controls, which remained statistically significant after controlling for potential confounders. A pre-disease state, beyond ANA positivity, may exist increasing pregnancy risk before the diagnosis of SLE in some patients.

Type of project: Clinical research

Mentor: Diane L. Kamen MD, MSCR, Professor of Medicine

Poster: DD33

Title: Amiodarone Association with PGD After Heart Transplant

Authors: N. Stringer Dorsey[1], A. Biscopink[1], J. Atkins[2], S. K. O'Connor[3], A. Carnicelli[2], V. Rao[2], L. Witer[2], C. Inampudi[2], D. Silverman[2], A. Van Bakel[2], G. Jackson[2], B. Houston[2], A. Kilic[2], R. J. Tedford[2], J. M. Griffin[2].

[1]Medical University of South Carolina, Department of Medicine, Charleston, SC, [2]Medical University of South Carolina, Division of Cardiology Heart Failure and Transplant, Charleston, SC, [3]Cornell University, Ithaca, NY

Introduction: Amiodarone use prior to heart transplantation (HT) has been associated with primary graft dysfunction (PGD), although data are mixed. Our aim was to determine if amiodarone use was associated with severe PGD at MUSC.

Methods: After IRB approval, we retrospectively reviewed consecutive single organ adult HTs at MUSC between January 2018 and April 2023. Data for amiodarone use in the 6 months prior to HT was collected (duration, cumulative dose, use at time of HT). Vasoactive inotropic score (VIS) was also compared. The primary endpoint was occurrence of severe PGD.

Results: One hundred eighty-three patients underwent HT: age 54 years (IQR 18), 72.7% male, BMI 28.4 kg/m2, and 42.1% Black. At time of HT, (N=41) 22.4% had a durable left ventricular assist device, (N=57) 31.1% had prior sternotomy and (N=38) 20.8% had temporary mechanical support. Amiodarone use was common: Sixty-nine (37.7%) patients received amiodarone within 6 months pre-HT, with a median duration 87 days (IQR 158) and cumulative dose of 12.4g (IQR 7.1). Of those with amiodarone use, just over half remained on amiodarone at the time of HT (53.6%). Nine of 183 (4.9%) patients developed severe PGD post-HT. Amiodarone use (any use within 6 months or continued use at HT) was not associated with severe PGD. There was also no difference in post-transplant VIS score between those who did and did not receive amiodarone (20 [19.6] vs 16.3 [13.8], p=0.122).

Conclusion: Amiodarone use was common in our cohort, yet rates of severe PGD were relatively low. We found no association with pre-transplant amiodarone use and severe PGD or higher VIS scores. Further investigation of this complex population is warranted to determine the effects of amiodarone versus other contributing factors to severe PGD.

Type of Project: Quality Improvement (QI)

Mentor's Name: Jan Marie Griffin, MD

Poster: DD34

Title: The reality of health care disparities: Lack of knowledge driving decreased rates of colon cancer screening in the underserved population

Author: Yadis Arroyo, PGY-6 Gastroenterology Fellow, MUSC Gastroenterology and Hepatology Department

Introduction: Inadequate access to health care, most commonly amongst the uninsured population, is one of the main barriers to colon cancer screening in the United States. Screening for colorectal cancer (CRC) has been shown to reduce mortality associated with this malignancy which is the second cause of cancer related death in the US. It is also important to recognize that this population often have GI related symptoms that require evaluation and management by a specialist in the field, however due to poor access to sub specialized services, they are mostly overlooked and under managed. With this quality improvement project, we aim to justify the need for better access to subspecialty gastroenterology care and reinforce the importance of CRC education, awareness, and screening.

Methods: This project was performed in conjunction with the CARES clinic of the Medical University of South Carolina (MUSC). It is a nonprofit student run organization that provides free medical care to uninsured residents of South Carolina. A 10-item questionnaire was created in both Spanish and English languages to better understand the baseline knowledge of this population with regards to colorectal cancer screening and identify the need for specialized GI care. The data from the questionnaires was analyzed utilizing SPSS software for simple descriptive statistics and chi-square test.

Results: A total of 136 questionnaires were collected from January 2023 to December 2023. Mean age group 46.5$\pm$14.2 years, 74% female and 64% white. The data revealed that patients with knowledge about colon cancer screening (CCS) 37.5% had a colonoscopy, however those that did not know about CCS 12% had a colonoscopy. Of the total group, only 20% had a prior screening colonoscopy (Figure 1).

Conclusion: Underserved populations experience low rates of screening based on numerous barriers to test uptake and follow-up. Based on this study patients were 5.8 times more likely to get a colonoscopy if they had prior knowledge regarding screening. We need novel approaches to identifying these individuals. Creating a specialized evening GI clinic might help in mitigating these challenges.

Type of project: Quality Improvement

Mentors: Garth Swanson, M.D.; Puja Elias, M.D.

Poster: DD35

Title: Improving Care of Patients Prescribed Controlled Substances in Med-Peds Clinic

Author: Ariel Faber, MD, Medicine-Pediatrics Resident

Introduction: Following evidence-based guidelines and adhering to state law are critical skills for residents who care for patients taking chronic opioid medications. As of 2021, South Carolina practitioners must review a patient's controlled substance prescription history before prescribing. The 2022 CDC guidelines outline multimodal pain therapy, tapering medications as appropriate, discussing risks of opioid therapy with patients, toxicology testing, avoiding opioid use with other medications (benzodiazepines), among other recommendations. The aim of this quality improvement project was to align patient care for those who are prescribed chronic opioids with current evidence-based practices and South Carolina law.

Methods: Adults prescribed long term opioids through the MUSC Med-Peds clinic met the inclusion criteria for this project. Residents identified and reviewed charts for these patients. At the beginning of the project, multiple EMR dot phrases for patient visit notes and patient instructions were created. These became available in March 2023. In August 2023, residents participated in a self-directed peer education activity. In February 2024, Med-Ped clinic education included two more lectures about opioid prescriptions.

Results: From November 2022 to February of 2023, residents identified nine patients. These formed a pre-intervention baseline. Initial data showed that all had a signed contract and were not on other controlled substances. Adjunctive therapy was provided to 78% and 89% had SCRIPTS reviewed. However, very few patients had a recent documented UDS, had Narcan prescribed, or had documentation of a pain rating or that their provider had discussed Narcan, medication taper, risks of opioids, or information regarding safe storage. From March of 2023 to October 2023, residents only prescribed opioids three times for patients that met the inclusion criteria. Of this group, all were prescribed Narcan and were on adjunct therapy. In 67% SCRIPTS was reviewed, a pain contract was signed and a UDS was done. Narcan, safe storage, and risks of opioids were discussed in the same 67%. None had their pain rated or had a taper in place.

Conclusions: It is not clear why residents prescribed significantly more opioids in the four months prior to the project's interventions compared to eight months after. These small patient numbers limited involvement of residents. In the place of patient encounters, more educational activities may be required to ensure residents gain the expertise to safely prescribe chronic opioids in alignment with evidence-based care and the law.

Type of Project: Quality Improvement

Mentor: Kathleen C. Head, MD, MS, MPH, Assistant Professor of Internal Medicine and Pediatrics

Poster: DD36

Title: Use of bedside ultrasound in the diagnosis of cardiac tamponade: A Case Report

Authors: Jered Schenk, MD (MUSC, Internal Medicine Resident); Stephen Sexauer, MD (MUSC, Pulmonary & Critical Care Fellow); Maggie Thomas, MD (Department of Medicine Assistant Professor, Assoc. Clerkship Director)

Introduction: Utilization of ultrasound technology in the medical field has expanded dramatically over the past several decades. Although it was used as early as the 1940s, ultrasound was not routinely performed in the hospital until cardiologists adopted the technology in the 1960s. Soon after, emergency medicine providers pioneered the use of point-of-care ultrasound (POCUS) while triaging patients. More recently, further advancements in ultrasound technology have resulted in better image quality and provider accessibility. This has allowed POCUS to enter the inpatient setting for use in emergent situations and to improve safety of invasive bedside procedures. Skillful use of POCUS allows bedside visualization of multiple organ systems and can aid in the rapid diagnosis of pathology that might otherwise be delayed due to patient instability or limited availability of other imaging modalities. We report a case of POCUS aiding in the diagnosis of cardiac tamponade in an unstable patient on a general medicine floor.

Case: A 73 year-old male with a history of metastatic pancreatic cancer was admitted to the general medicine ward. During his hospitalization, a rapid response was called after the patient became acutely unstable with blood pressure of 78/52 mmHg and a heart rate of 138 bpm. Believed to be in afib with RVR, IV metoprolol was given without improvement. Repeat EKG was obtained, and on review, it was more consistent with sinus tachycardia. Patient was too unstable to take for CT, so a bedside ultrasound was performed which showed a large pericardial effusion with evidence of tamponade physiology **(Figures 1-2)**. With this finding, he was transferred to the ICU where a pericardiocentesis was performed. Following the procedure, the patient's vital signs normalized. Repeat echo showed significant reduction in the size of the pericardial effusion with resolution of tamponade physiology.

Discussion/Conclusion: POCUS can be a useful tool in diagnosing both cardiac and non-cardiac causes of patient decompensation. Its ability to be used quickly and non-invasively at the bedside allows for more timely diagnoses in patients who otherwise may be too unstable for advanced imaging modalities. This case demonstrates the utility of POCUS in assessing the etiology of tachycardia and undifferentiated shock in patients on a general medicine floor. Increasing provider access to ultrasound equipment and expanding ultrasound training can result in more timely diagnoses and improved patient outcomes in the inpatient setting.

Type of Project: Case Report

Mentor Name: Maggie Thomas, MD

DD37

Title: Missed and Delayed Diagnoses of Chronic Liver Disease in Primary Care Patients with Cirrhosis

Authors: Kush M. Patel MD, Jingwen Zhang MS, Andrew D. Schreiner MD MSCR

Department of Medicine, Division of General Internal Medicine

Introduction: Chronic liver disease (CLD) causes significant morbidity and mortality in the USA. Unfortunately, CLD often goes undetected in many patients that present with end-stage liver disease.

Methods: This is a retrospective cohort study of EHR data from a primary care clinic between 2012-2021 that included patients with a diagnosis of cirrhosis, complication(s) of cirrhosis, or hepatocellular carcinoma (HCC). The outcomes of interest were missed and delayed diagnoses of CLD in patients with cirrhosis, defined as the absence of a CLD diagnosis (missed) or the first appearance of a CLD diagnosis on the same day as the cirrhosis diagnosis (delayed). ICD-9/10 codes and chart review were used for diagnosis ascertainment. Univariate and covariate analyses were performed for the cohort. We performed logistic regression models to determine the association of aminotransferase elevations with missed/delayed diagnoses. SAS 9.4 was used for statistical analyses.

Results: The cohort included 667 patients, and 376 (56%) had missed or delayed CLD diagnoses. Compared to patients with a CLD diagnosis prior to cirrhosis/HCC, a higher proportion of patients with missed/delayed diagnoses had alcohol-related liver disease (ARLD). A significantly lower proportion of patients with missed CLDs had an elevation in ALT or AST compared to patients with diagnosed CLD. After adjusting for other signals of liver disease, demographics, and comorbidities, abnormal ALT or AST values were associated with a lower odds of a missed CLD diagnosis.

Conclusion: Earlier diagnosis of CLD could lead to improvements in health outcomes. In our cohort, most patients did not have a diagnosis of CLD before their cirrhosis diagnosis. Of these, 42% had either ARLD or NAFLD. When compared to those who had a diagnosis of CLD prior to cirrhosis, patients with a missed/delayed diagnosis were more likely to have ARLD, supporting the need to better screen for alcohol use in primary care. Further, patients with elevated aminotransferases had lower odds of having a missed/delayed diagnosis of CLD, suggesting that overreliance on AST and ALT abnormalities may lead to missed or delayed diagnosis of CLD. Screening for high-prevalence CLD, regardless of aminotransferase values, should be considered.

Type of Project: Clinical (Retrospective Cohort Study)

Mentor: Andrew D. Schreiner, MD MSCR

Poster: DD38

Title: Quality Improvement of Intake and Output Measurement on General Medicine Wards

Author: Ty Higginbotham, MD, PGY-2 Internal Medicine Resident, Department of Medicine

Introduction: Fluid balance is an important determining factor of clinical decision making, especially in cases of hospital admission primarily for diuresis. Current intake and output data at our institution is perceived as unreliable or at times not recorded on patients who have strict intake and output orders. Our goal was to increase the rate of strict intake and output (I/O) data recorded in patients who have strict intake and output orders, ("I/O data recording rate") and therefore improve the accuracy and reliability of I/O data.

Methods: We obtained control data on general medicine patients admitted to med/surge status by individual chart review. We determined if the patient had a strict I/O order, and if the order is appropriate. We determined if that patient had urine output, PO intake and IV intake recorded and reported these binary values as under the categories of "PO intake recorded", "IV intake recorded", "Any Intake Recorded", and "Output Recorded". As a consensus of three internal medicine physicians, we included the following diagnoses as being proper to have strict I/O orders: Heart failure, acute kidney injury, pulmonary hypertension, sepsis, hyponatremia, peri-operative patients, and Gastrointestinal losses (vomiting, diarrhea). Interventions included developing a worksheet that allowed patients to self-record their own intake and output data, educating hospitalists and house staff on appropriate intake and output data, and educating nursing and patient care techs on the worksheet and importance of accurate I/O data. (Figure 1.)

Baseline data was collected from 117 patients admitted under general internal medicine in across 10 wards at a single hospital. Of these 117 patients, 33 were admitted to the experimental floor. The interventions were implemented and one week later, data was collected on 48 patients admitted to the experimental floor.

Results: The experimental floor showed an improvement in PO recording rate from 27% to 48% of patients having PO intake recorded. This not only represented a 21% improvement, but also took the experimental floor from below 11% below average, to 10% above the average for all general medicine wards. The experimental floor also showed improvement in the" output recorded" category improving from 51% to 69% and again moving from below average to above average when compared to baseline data for all wards. IV intake recorded showed a decrease from 27% to 23%. The "Appropriate order rate" showed an improvement from 73% to 83%.

Conclusion: The experimental floor showed improvement in both PO intake recording rate and output recording rate. While there is still room for improvement in these parameters, these results support that the I/O recordings can be improved through education and implementing innovative ideas. Our next steps will be to continue to encourage the use of the worksheet to help improve I/O recording and to roll out the worksheet as an intervention on other hospital wards. We hope that through the above data, we showed that there is a deficiency in the intake and output receding rate and that this intervention has been shown to improve data recording.

Type of Project: Quality Improvement Research

Mentors: Meghan Thomas, MD, Department of Medicine

Poster: DD39

Title: Length-of-Stay Index Outliers Discharged by Hospital Medicine Teams at MUSC Charleston

Participant: Jerome Deas, MD: Department of Medicine, Division of Hospital Medicine, Internal Medicine Resident, PGY-2

Introduction: With the transition to diagnosis related group (DRG)-based hospital reimbursement, length of stay has become a significant financial driver of every health system and hospital medicine group. To understand how one health system compares to national peers, length-of-stay index (LOSi) has become the standard method of reporting. While LOSi is a valuable metric, it can be skewed by a small number of patients that stay an incredibly long period of time, defined as “outliers.” The goal of this study is to better understand the variables that drive LOSi outliers for hospital medicine discharges and potential opportunities for both hospitalists and health system leaders to improve these metrics.

Methods: Cross-sectional analysis of FY23 LOSi outliers discharged by hospitalistsChart review was conducted of the 100 patients classified as LOSi outliers, with extraction of descriptive statistics including age, gender, and payer status. Hypothesized variables that may contribute to LOS were reviewed and included admit source, admit service, time spent in the ICU, days spent on other inpatient services prior to transfer to hospital medicine, discharge disposition, and reason for discharge delay.

Results: Of the 6202 patients discharged by hospitalists, 100 patients were classified as LOSi outliers. The mean LOS was 49.2 days (SD 58.8, range 8-471) with a median of 33 days. Of the 100 LOSi outliers, 57 patients were admitted from the emergency department, 32 from an outside hospital, 10 from a clinic, and 1 from skilled nursing facility. Regarding admit service, 77 were initially admitted to hospital medicine, 15 to an ICU, 4 to surgery, and 4 to other subspecialty services. Of the 23 LOSi outliers admitted to a non-hospital medicine service, the mean hospital day in which they were transferred to hospital medicine was 25; median 18. In reviewing discharge barriers, 42 patients were classified as having a medical reason for discharge delay, 37 patients had challenges with placement, 16 patients had both a medical and placement delay, and 5 patients died prior to discharge. Of the 34 patients that had a placement barrier, only 5 were eventually able to be discharged home.

Conclusions: Of the 32 LOSi outliers admitted from an outside hospital, only 4 were discharged back to the hospital and may represent an opportunity for improvement. Of the 34 patients that had a placement barrier, only 5 were eventually able to be discharged home, suggesting the need for increased support from health system leaders.

Type of Project: Hospital Administration

Project Mentor: Marc Heincelman, MD, MPH

Poster: DD40

Title: Understanding the Impact of Hospital Acquisitions on Quality of Care

Author: Nancy L. Hagood, MD, Department of Medicine

Introduction: Mergers and acquisitions are accelerating in the healthcare industry. While financial impacts of hospital mergers are well demonstrated, quality impacts are less clear. A systematic review conducted through January 2020 reported inconsistent findings and few statistically significant results of hospital mergers on healthcare quality measures. The purpose of our study is to understand the effect of recent Medical University of South Carolina (MUSC) Health regional hospital acquisitions on healthcare quality and to identify future opportunities to improve patient care.

Methods: A pre/post-acquisition observation study was performed assessing quality measures of five hospitals within MUSC Health's Regional Health Network (RHN) recently acquired between 2019 and 2021. Given reporting limitations in Leapfrog Hospital Safety Grades, CMS Overall Star Ratings, and CMS Patient Experience Star Ratings, we utilized Vizient® data to allow accurate, real-time data analysis. Outcome measures included change in rank of overall Vizient® hospital rank, mortality, safety, and patient centeredness. Vizient® Quality and Accountability (Q&A) data sheets were used to compare pre/post-acquisition data. Pre-acquisition data was defined as metrics obtained within 6 months immediately following acquisition. Post-acquisition data was defined as metrics obtained ≥1 year following acquisition. Raw ranks were adjusted to percentile ranks, as the number of hospitals in Vizient® cohorts varied each year, with lower percentile rank indicating improvement.

Results: MUSC Health acquired six regional hospitals between 2019 and 2021: four in 2019 and two in 2021. Given the small size and paucity of comparable data, one regional hospital (RHN #4) was excluded in the analysis. Overall Vizient® percentile rank is improving post-acquisition for all five regional hospitals (Figure 1). Individual Vizient® outcome measures show mixed results based on timing of acquisition and the specific hospital (Figure 2). RHN #3 appears to be an outlier, as it demonstrates worse percentile ranks for mortality, safety, and patient centeredness. Mortality, safety, and patient centeredness are improving post-acquisition at RHN #5 and RHN #6, which are the two newest acquisitions.

Conclusion: All five MUSC regional hospital acquisitions show currently improving overall percentile rank, with 4 of 5 hospitals currently better than average. Individual quality outcomes vary in association with acquisition. Safety is worse for earlier acquisitions, noting that the pre/post-acquisition timeline spanned the Covid-19 pandemic, during which hospital-acquired conditions worsened nationally. More recent acquisitions show improved post-acquisition quality measures, suggesting lessons learned from earlier acquisitions, as well as system-level standardization with implementation of governed management plans.

Type of Project: Clinical/Quality

Mentors: Meghan K. Thomas, MD MS MPH; Marc Heincelman, MD MPH; Danielle Scheurer, MD MSCR

Poster: DD41

Title: A Clinical Decision Support Tool to Improve the Performance of Spontaneous Breathing Trials and Extubations among Eligible Patients in the Intensive Care Unit

Authors: Alison Travers, MD, Michelle Spiegel, MD and Andrew Goodwin, MD, MSCR
Division of Pulmonary and Critical Care, Medical University of South Carolina

Introduction: Daily spontaneous breathing trials (SBT) are associated with reduced mechanical ventilation days and reintubation rates and have become a standard of care practice in the intensive care unit (ICU). The COVID-19 pandemic disrupted the performance of routine care processes through capacity strain and staffing turnover, a phenomenon that has persisted despite a reduction in COVID-19 related hospitalizations. We sought to develop a clinical decision support (CDS) tool to augment the adherence to daily SBTs among eligible patients and to measure its impact on extubation rates.

Methods: We developed and implemented a mechanical ventilation-focused tool across all adult ICUs at a quaternary academic medical center. The tool consisted of a unit-specific list of patients receiving mechanical ventilation and provides relevant information including: ventilator mode and settings, eligibility for an SBT, and documentation of an SBT that day. The tool utilized a logic structure to determine SBT eligibility by comparing current clinical features and settings to the institution's SBT policy and incorporated human factors by providing color coded flags to denote SBT eligibility, performance and result. Education and demonstration were provided to the medical directors, nurse managers and respiratory therapists of each of the adult ICUs. The performance rates of SBTs before and after checklist implementation were measured and compared via chi square analysis.

Results: In SBT eligible patients across all ICUs, the rate of daily SBTs increased after list implementation (25.8% vs. 41.8%, $p < .00001$) (Figure 1A). The rate of eligible patients who were extubated also increased after list implementation (15% vs. 18.7%, $p = .002$) (Figure 1B).

Conclusion: Implementation of a ventilation-focused CDS tool was associated with an increased rate of daily SBTs and extubations across a variety of ICUs, and may represent a viable approach to improving adherence to best practices in the setting of staffing strain.

Type of Project: Clinical

Mentors: Michelle Spiegel, MD and Andrew Goodwin, MD, MSCR, Division of Pulmonary and Critical Care, Medical University of South Carolina

Poster: DD42

Title: Clinical Evaluation of Standard Convex Probe Endobronchial Ultrasound versus a Novel Thin Convex Probe Endobronchial Ultrasound Bronchoscopy System

Authors: Vidhya Y. Aroumougame, MD, MBA[1], Christopher R. Gilbert DO, MS[1], Adam H. Fox MD, MS[1], Nichole T. Tanner, MD, MSCR[1], Travis L. Ferguson, MD[1], Nicholas J. Pastis, MD[2], Gerard A. Silvestri, MD, FCCP[1]

[1]Department of Medicine, Division of Pulmonary and Critical Care, Allergy and Sleep Medicine, Medical University of South Carolina, Charleston, South Carolina

[2]Department of Medicine, Pulmonary, Allergy, Critical Care and Sleep Medicine

The Ohio State University Wexner Medical Center, Columbus, Ohio

Introduction: Standard convex probe endobronchial ultrasound bronchoscope (CP-EBUS) allows direct visualization of centrally located lesions using real-time ultrasound, which is both safe and accurate[1,2]. The diameter of CP-EBUS (6.9mm) limits its ability to reach lesions in the outer portion of the lung as it cannot pass through smaller bronchi[3]. The Olympus BF-Y0069 thin bronchoscope (TCP-EBUS) incorporates real-time ultrasound, with a smaller outer diameter (5.9mm). We aimed to assess the safety and feasibility of TCP-EBUS to evaluate lesions not accessible with CP-EBUS.

Methods: A single center, prospective, pilot study was performed. Patients with lesions located within the inner two-thirds of the lung underwent attempted visualization and biopsy of the lesion with CP-EBUS. If unsuccessful, TCP-EBUS was attempted to visualize and biopsy the lesion. Data related to procedural safety, lesion characteristics, and pathology results was collected.

Results: 51 patients were enrolled. No adverse safety events related to TCP-EBUS occurred. In 7 (13.7%) cases, the target lesion was visualized and biopsied by CP-EBUS. To assess safety and visualization of targets, no biopsies were performed in the first 4 uses of the TCP-EBUS. In the remaining 44 cases, CP-EBUS could either not visualize (n=37) or biopsy (n=44) the lesion and TCP-EBUS was used. TCP-EBUS visualized 36/44 (81.8%) lesions and of those visualized, 27 were biopsied (23–diagnostic, 4–non-diagnostic). 8 (15.7%) lesions were unable to be visualized with either device. Mean and median lesion size biopsied with CP-EBUS was 37.71mm (SD 15.44mm) and 41mm, respectively. Mean and median lesion size visualized and biopsied with TCP-EBUS was 27.65 mm (SD 15.88mm) and 21.5 mm.

Conclusions: The use of the novel TCP- EBUS appears safe and feasible, without observed patient-associated complications. It provides real-time ultrasonographic visualization and biopsy of lesions that were not accessible with CP-EBUS.

Type of Project: Clinical Science

Mentors: Gerard Silvestri, MD, MS, Christopher Gilbert, DO, MS, Adam Fox MD, MS