



DEPARTMENT OF SURGERY  
THE OHIO STATE UNIVERSITY WEXNER MEDICAL CENTER



# 24th Annual Department of Surgery Research Conference



Thursday, May 30, 2019  
115 Biomedical Research Tower



**THE OHIO STATE UNIVERSITY**  
WEXNER MEDICAL CENTER



Welcome to the 24th annual Ohio State University Department of Surgery Research Conference! This conference is designed to bring students, residents, fellows, faculty and guests together to share and discuss results of research relevant to surgery. It is also an opportunity for a variety of students training with faculty in the Department of Surgery (DOS) (including medical students, residents, graduate students and postdoctoral research trainees) to develop their scientific communication skills. Each year, the Department of Surgery invites a leader in surgery to visit The Ohio State University and get to know the students and faculty in the department through a variety of activities, including participation as a faculty judge at the annual DOS Research Conference. This year, we are delighted to welcome Henri Ford, MD, MHA, FACS, dean and chief academic officer with the Leonard M. Miller School of Medicine, University of Miami, as our guest.

We received a number of exceptional abstract submissions this year, reflecting a broad collection of basic/translational, clinical, health services and surgical education research topics. The abstracts were reviewed and scored by members of the Department of Surgery Research Council and selected for oral and poster presentation based on the quality of the science, novelty and diversity of the topic. DOS faculty were invited to serve as faculty discussants, who will provide comments to frame the context and importance of the research and to stimulate discussion. To enhance our residents' experience with public comment and discussion, each oral presentation also has an invited resident discussant. Several of the conference presenters are either currently enrolled in or graduates of the College of Medicine Master of Medical Science Program or other Ohio State advanced degree programs. Some of the presenters are current or prior National Institutes of Health T32-supported research trainees.

Again, welcome, and we hope these conference interactions will stimulate new ideas, projects and collaborations.

A handwritten signature in black ink that reads "Ginny Bumgardner".

Ginny Bumgardner, MD, PhD  
 Associate Dean for Research Education  
 Professor of Surgery  
 Director, DOS Research Training Program  
 Director, Master of Medical Science Program  
 Program Director/PI, NIH T32 AI106704-01A1 "Advanced Research Training in Immunology for Surgical Trainees"  
 Comprehensive Transplant Center  
 The Ohio State University



### **Henri Ford, MD, MHA, FACS**

Henri Ford, MD, MHA, FACS is dean and chief academic officer of the University of Miami Leonard M. Miller School of Medicine. Dr. Ford is a Haitian-born pediatric surgeon who returns regularly to Haiti to provide medical care to its residents. In May 2015, he performed the first successful separation of conjoined twins in Haiti, alongside surgeons he helped train.

Motivated by a desire to have a positive impact on the world and drive change, Dr. Ford has conducted groundbreaking research on the pathogenesis of necrotizing enterocolitis and has been funded by the NIH and the RWJ Foundation, among others. He is the author of multiple publications, book chapters, invited manuscripts, abstracts and presentations.

Dr. Ford is a fellow of the American College of Surgeons, the Royal College of Surgeons (England) and the American Academy of Pediatrics. He serves on the editorial board of numerous scientific journals, the Harvard Medical School Visiting Committee and the Executive Committee of the Board of Trustees of Princeton University. He received his bachelor's degree in public and international affairs from Princeton University and his medical degree from Harvard Medical School. He is the recipient of numerous honors, including the Gold Humanism in Medicine Award from the AAMC.

Thursday, May 30, 2019

### Welcome and Introduction of Visiting Professor

8 a.m.

Timothy Pawlik, MD, PhD, MPH

Professor and Chair, Department of Surgery

The Urban F. Meyer III and Shelley M. Meyer Chair for Cancer Research  
Surgeon in Chief

### Introduction to the Conference

Ginny Bumgardner, MD, PhD

Professor of Surgery, Division of Transplantation

Associate Dean for Research Education, Ohio State College of Medicine

Director, Master of Medical Science Program

Director, Department of Surgery Research Training Program

### Judges

Henri Ford, MD, MHA, FACS Dean and Chief Academic Officer, University of Miami

Christopher Breuer, MD, Nationwide Endowed Chair in Surgical Research, Nationwide Children's Hospital

Jianjie Ma, PhD, Professor and Karl P. Klassen Chair of Thoracic Surgery, Ohio State

Raphael Pollock, MD, PhD, Professor and Director, OSU Comprehensive Cancer Center

**Moderator:** Session 1 and 2 moderated by Ginny Bumgardner, MD, PhD

Biographies of the conference presenters begin on page 46.

### Session I: Oral Presentations

8:15 – 9:30 a.m.

***Correlating Presence of Tumor Associated Macrophages and Neutrophils with Recurrence in***

***Differentiated Thyroid Cancers. Amblessed Onuma, MD*** – Faculty Advisor: Lawrence Shirley, MD, MS –

Faculty Discussant: William Carson III, MD – Resident Discussant: Kara Rossfeld, MD, MS

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***Laparoscopic Sleeve Gastrectomy is an Independent Predictor for Poor Follow-Up and Weight Loss after***

***Bariatric Surgery. Anahita Jalilvand, MD*** – Faculty Advisor: Sabrena Noria, MD, PhD – Faculty Discussant:

David Renton, MD – Resident Discussant: Michael Villarreal, MD

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***Novel Probiotic Therapeutic in a Murine Model of Clostridium difficile Colitis. Rita Shelby, MD, MS*** –

Faculty Advisor: Gail Besner, MD – Faculty Discussant: Alan Harman, MD – Resident Discussant:

Shayna Brathwaite, MD, MS

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***Hepatitis C Positive Deceased Donor Kidney Transplantation into Hepatitis C Negative Recipients:***

***a Pilot Study. Taehwan Yoo, MD, MS*** – Faculty Advisor: Ashraf El-Hinnawi, MBBS – Faculty Discussant:

Lisa Cunningham, MD – Resident Discussant: Daniel Lodwick, MD, MS

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***Nanotechnology-Based Approaches Towards Elucidating and Modulating the Immunology of the Tumor***

***Niche. Silvia Duarte-Sanmiguel, BS*** – Faculty Advisor: Daniel Gallego-Perez, PhD – Faculty Discussant:

Alan Tsung, MD – Resident Discussant: Clifford Akateh, MD, MS

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***The Development and Characterization of a Murine Model of Volumetric Muscle Loss.* Dathe Benissan-Messan, MD** – Faculty Advisor: Peter Lee, MD, PhD, MPH – Faculty Discussant: John Phay, MD – Resident Discussant: Joseph Drews, MD, MS  
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### Break

9:30 – 9:45 a.m.

### Poster Session

9:45 – 10:45 a.m.

### Judged Posters

***Decreasing Surgical Site Infections in Pediatric Stoma Closures.* Hira Ahmad, MD** – Faculty Advisor: Marc Levitt, MD  
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***Comparison of Lymph Node Evaluation and Yield Among Patients Undergoing Open and Minimally Invasive Surgery for Gallbladder Adenocarcinoma.* Ahmad Hamad, MD** – Faculty Advisors: Aslam Ejaz, MD, MPH, and Timothy Pawlik, MD, PhD, MPH  
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***Comparative Changes in Subcutaneous and Visceral Adipose Tissue Depots following Medical and Surgical Weight Loss.* Anahita Jalilvand, MD** – Faculty Advisors: Sabrena Noria, MD, PhD, and Willa Hsueh, MD  
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***Increasing Patient Engagement and Access to Providers During the Transition of Care Period to Improve Outcomes.* Shan Lansing, MS** – Faculty Advisor: Syed Husain, MBBS  
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***Improvement of Novel Electrospun Small Diameter Tissue Engineered Arterial Graft Performance With Heparin Modification.* Yuichi Matsuzaki, MD, PhD** – Faculty Advisor: Toshiharu Shinoka, MD, PhD  
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***Discharge Disposition to Skilled Nursing Facility After Emergent General Surgery Predicts a Poor Prognosis.* Anghela Paredes, MD, MS** – Faculty Advisor: Daniel Vazquez, MD  
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***Hospital Transfer Center Involvement Improves Clinical Trial Enrollment Performance.* Michael Villarreal, MD** – Faculty Advisor: David Evans, MD  
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***The Crosstalk Between Innate and Adaptive Immunity Through Formation of Neutrophil Extracellular Traps in Nonalcoholic Steatohepatitis-Associated Hepatocellular Carcinoma.* Han Wang, PhD** – Faculty Advisors: Allan Tsung, MD, and Hai Huang, MD  
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***Late-Term Performance of Tissue Engineered Vascular Grafts.* Jason Zakko, MD, MS** – Faculty Advisor: Christopher Breuer, MD  
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***TRIC-A Channel Maintains Store Calcium Handling by Interacting With Type 2 Ryanodine Receptor in Cardiac Muscle.* Xinyu Zhou, PhD** – Faculty Advisor: Jianjie Ma, PhD  
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## General Posters

***MG53 Protein Protects Aortic Valve Interstitial Cells From Membrane Injury and Fibrocalcific Remodeling.*** T.M. Ayodele Adesanya, PhD – Faculty Advisor: Jianjie Ma, PhD

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***Variability Between the Lateral and Anterior-Posterior (AP) Sacral Ratios in Anorectal Malformations.***

Hira Ahmad, MD – Faculty Advisor: Richard Wood, MD

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***Dedifferentiated Liposarcoma Extracellular Vesicular MDM2 Induces Preadipocyte MMP2 Production.***

Lucia Casadei, PhD – Faculty Advisor: Raphael Pollock, MD, PhD

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***The Relative Effects of Obesity, Diabetes and Elevated Hemoglobin A1c on Post-Operative Wound Infections after Colorectal Surgery.*** Lisa Cunningham, MD – Faculty Advisor: Syed Husain, MBBS

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***Determination of the microRNA Expression Profile Associated with Tumor Ulceration in Melanoma.***

Mallory DiVincenzo, DVM – Faculty Advisor: William Carson III, MD

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***NRAS mRNA is Differentially Spliced to Give Five Distinct Isoforms: Implications for Melanoma Therapy and Clinical Outcome.*** Megan Duggan, PhD – Faculty Advisor: William Carson III, MD

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***Recurrence of Pilonidal Disease; Our Best is Not Good Enough.*** Devin Halleran, MD – Faculty Advisors:

Jennifer Cooper, PhD; Katherine Deans, MD, MHSc; and Peter Minneci, MD, MHSc

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***Predicted Risk of Right Ventricular Failure After Minimally Invasive Left Ventricular Assist Device Implantation.*** Madonna Lee, MD – Faculty Advisor: Bryan Whitson, MD, PhD

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***Radiology Resources in the Modern Management of Appendicitis: Do They Really Matter?*** Kevin Ricci, MD, MS – Faculty Advisor: Heena Santry, MD, MPH

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***Does Decreased Length of Stay After Colorectal Surgery Translate into Increased Readmission Rate?***

Taehwan Yoo, MD, MS – Faculty Advisor: Syed Husain, MBBS

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**Session II: Oral Presentations**

10:45 a.m. – Noon

***Racial Disparities in Hepatocellular Carcinoma Outcomes Are Driven by Access to Care.*** Clifford Akateh, MD, MS – Faculty Advisor: Sylvester Black, MD, PhD – Faculty Discussant: Peter Minneci, MD, MHSc – Resident Discussant: Anghela Paredes, MD, MS

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***Preoperative Exercise Therapy Protects the Liver From Ischemia-Reperfusion Injury.*** Hongii Zhang, MD – Faculty Advisors: Allan Tsung, MD, and Hai Huang, MD – Faculty Discussant: Sylvester Black, MD, PhD – Resident Discussant: Clifford Akateh, MD

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***SPECT/CT Imaging Detects Perfusion Responses to Lower Extremity Revascularization and Is Significantly Correlated With Toe-Brachial Index in Patients With Peripheral Arterial Disease.*** Ting-Heng Chou, PhD – Faculty Advisor: Mitchel Stacy, PhD – Faculty Discussant: Peter Lee, MD, PhD, MPH – Resident Discussant: Taehwan Yoo, MD, MS

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***A Genome-wide CRISPR Screen Identifies Galectin2 that Contributes to Exacerbation of Intestinal Inflammation.*** Haiwen Li, PhD – Faculty Advisor: Renzhi Han, PhD – Faculty Discussant: Gail Besner, MD – Resident Discussant: Rita Shelby, MD, MS

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***Exogenous MG53 Protects Adult Mouse Cardiomyocytes by Preventing Mitochondria Damage in Response to Oxidative Stress.*** Kristyn Gumper, MS – Faculty Advisor: Jianjie Ma, PhD – Faculty Discussant: Bryan Whitson, MD, PhD – Resident Discussant: Joseph Drews, MD, MS

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***NIH Funding for Pediatric Surgeon-Scientists.*** Kejal Shah, MD – Faculty Advisors: Gail Besner, MD, and Christopher Breuer, MD – Faculty Discussant: Ginny Bumgardner, MD, PhD – Resident Discussant – Ekene Onwuka, MD, MS

**Page 45****Research Conference Conclusion**

Noon



**Abstracts**  
Oral Session I

## Correlating Presence of Tumor Associated Macrophages and Neutrophils with Recurrence in Differentiated Thyroid Cancers

*Amblessed Onuma, MD\*, Lynn Schoenfield, MD, Charity Edwards, Pamela Brock, John Phay MD, Lawrence Andrew Shirley, MD MS*

**Introduction:** The tumor microenvironment (TME) is a complex milieu of “normal” cell types, including immune cells, that assist in the growth and spread of cancer. Previous studies have correlated the presence of tumor associated macrophages (TAMs) with worse outcomes in differentiated thyroid cancer (DTC). However, there is little information on the prognostic factor of tumor-associated neutrophils (TANs) in DTCs.

**Methods:** Paraffin-embedded samples (n=41) of resected DTCs were collected via our Endocrine Neoplasia Repository. Immunohistochemical staining for TAM marker CD 163 and TAN marker CD 66b were performed. Expression levels were scored with the assistance of a clinical pathologist, L.S. Clinical data were obtained through review of electronic medical records.

**Results:** In this cohort, neither CD163 nor CD66b scores correlated with tumor size, presence of lymph node metastases, multifocal tumors, lymphovascular invasion, capsular invasion, or presence of BRAFV600E mutation (all  $p > 0.05$ ). CD 66b positive tumors trended towards a higher recurrence-free survival (RFS) compared to CD 66b negative tumors (mean RFS 169.1 months vs 148.1 months,  $p = 0.23$ ). Tumors with high CD 163 density trended towards a lower RFS compared to low CD 163 density although not statistically significant (mean RFS 121.3 months vs 205.2 months,  $p = 0.54$ ). Interestingly, when scoring from both markers were combined, patients with high CD163 scores and CD66 positive scores had a statistically significant higher RFS (mean RFS 187.3 months vs 50.7 months,  $p = 0.04$ ).

**Conclusion:** In our cohort of DTCs, a high density of TAMs in the presence of TANs confers better outcome than tumors with high TAMs only. This suggests a potential protective role for TANs. Furthermore, assessment of multiple immune cell types could more accurately predict outcomes in differentiated thyroid cancer. Further work should focus on understanding mechanisms of this phenomenon.

*\*Supported by the National Institute of Allergy and Infectious Diseases of the National Institutes of Health under Award Number 1T32AI106704-01A1 (Advanced Research Training in Immunology for Surgery Trainees).*

## Laparoscopic Sleeve Gastrectomy is an Independent Predictor for Poor Follow-Up and Weight Loss after Bariatric Surgery

Anahita Jalilvand MD\*, Alecia Blaszczyk PhD, Jane Dewire BS, Andrew Detty BA, Bradley Needleman MD, Sabrena Noria MD PhD.

**Introduction:** There is conflicting data regarding comparative weight loss outcomes following sleeve gastrectomy and gastric bypass. Currently, while most studies cite comparable weight loss outcomes between both procedures, some have reported poorer short and long-term weight loss outcomes following sleeve gastrectomy. Institutional data has similarly shown that sleeve gastrectomy patients lose significantly less weight compared to gastric bypass cohorts. This prompted us to evaluate if suboptimal patterns associated with known predictors of poor weight loss, such as baseline comorbidities, socioeconomic status, and poor follow-up, accounted for this finding. As such, the primary objective of this study was to characterize differences in patients undergoing sleeve gastrectomy and gastric bypass, while secondary objectives included determining if these characteristics were implicated in reduced post-operative weight loss outcomes.

**Methods:** We retrospectively reviewed all patients undergoing primary laparoscopic sleeve gastrectomy (LSG) and Roux-en-Y gastric bypass (LRYGB) between 2014-2016 at a single institution (n=571). Exclusion criteria included patients with post-operative pregnancies or baseline chronic heart failure. Baseline demographic, psychosocial, and medical data were obtained on all patients. Patients who did not present to the bariatric clinic at scheduled post-operative visits were categorized as “no-shows” and were recorded at 6, 12, 24, and 36 months post-operatively. The first part of the study characterized differences in demographic, medical, socioeconomic data, as well as post-operative no-show rates between LSG (n=322) and LRYGB (n=249) patients. Next, the same cohort (n=571) was stratified by whether patients were in the lowest quartile ( $\leq 25^{\text{th}}$ ) of % excess body weight loss (%EBWL-25<sup>th</sup>) compared to the highest quartile (%EBWL-75<sup>th</sup>) at 12, 24, and 36 months after surgery and compared in terms of demographic, medical, socioeconomic, and follow-up data. All univariate associations ( $p < 0.1$ ) were included in multivariate logistic regressions (MLR) to model independent predictors of %EBWL-25<sup>th</sup> at each time point. Lastly, LSG patients were categorized by whether they had attained “successful weight loss” (%EBWL-Success, defined as  $> 60\%$  EBWL) or demonstrated “poor” weight loss (%EBWL-poor, defined as  $< 37.5\%$  EBWL), and predictive models of %EBWL-poor after LSG were created using univariate associations ( $p < 0.1$ ). All final models were achieved using backwards selection. A p value  $< 0.05$  was considered statistically significant.

**Results:** In comparison to patients undergoing LRYGB, LSG patients presented with significantly lower baseline BMI ( $47.9 \pm 8.2$  vs  $51.5 \pm 10.1$ ,  $p < 0.0005$ ), lower incidences of diabetes (24.1% vs 36.6%,  $p = 0.001$ ), obstructive sleep apnea (49.5% vs 66.7%,  $p < 0.005$ ), hyperlipidemia (30.0% vs 38.6%,  $p = 0.03$ ), bipolar disease (2.8% vs 6.8%,  $p = 0.02$ ) and were more likely to have a college or greater education (35.3% vs 23.7%,  $p = 0.02$ ). LSG was associated with significantly higher no-show rates at 6, 12, and 24 months ( $p < 0.05$ ) compared to LRYGB and remained an independent predictor of no-shows up to 2 years post-operatively (OR= 1.4-1.6,  $p < 0.05$ ). Independent predictors of overall %EBWL-25<sup>th</sup> at 12 months include LSG (OR=5.2,  $p < 0.005$ ), increasing intake BMI (OR=1.1,  $p = 0.001$ ), and having less than a high school education (OR=11.9,  $p = 0.04$ ). At 24 months, %EBWL-25<sup>th</sup> was independently predicted by LSG (OR=5.3,  $p < 0.005$ ), African American race (OR=7.1,  $p = 0.002$ ), and major depression (OR=4.6,  $p = 0.001$ ), while LSG and no-shows at 6 and 12 months were predictive of %EBWL-25<sup>th</sup> at 3 years. Independent risk factors associated with %EBWL-poor after LSG at 12 months include baseline hypertension (OR=2.5,  $p = 0.02$ ), African American race (OR=2.6,  $p = 0.05$ ), major depression (OR=2.2,  $p = 0.05$ ), and less than high school education; at 24 months major depression (OR=2.8,  $p = 0.02$ ) and no-shows at 6 month were predictive of %EBWL-poor; and high binge eating score and no-shows at 6 & 12 months were independent predictors of %EBWL-poor after LSG. Next, to compare the impact of these high-risk features by procedure type, the cohort was stratified

by predictors of %EBWL-poor after LSG. Within these high-risk patients, the proportion of %EBWL-poor was significantly higher following LSG compared to LRYGB at 12 (60% vs 25.0%,  $p<0.05$ ), 24 (43% vs 18%,  $p<0.05$ ), and 36 months (70% vs 21%,  $p<0.05$ ), resulting in a 2.5-3.5x increase in the relative risk of poor weight loss after bariatric surgery.

**Conclusions:** In this study, LSG was associated with significantly reduced %EBWL compared to LRYGB at each post-operative time point, and this relationship was not accounted for by typical predictors of poor weight loss, such as higher comorbidities, lower socioeconomic status, and poor follow-up. Furthermore, within patients with high-risk features, LSG was associated with a marked increase in the relative risk of having poor post-operative weight loss compared to LRYGB, suggesting that the impact of such predictors is magnified after LSG and mitigated by gastric bypass. Finally, given the precipitous rise in sleeve gastrectomy procedures, identification of predictors associated with poor weight loss may be imperative in improving decision-making and helping patients choose the appropriate procedure to optimize weight loss outcomes.

*\*Supported by the National Institute of Allergy and Infectious Diseases of the National Institutes of Health under Award Number 1T32AI106704- 1A1 (Advanced Research Training in Immunology for Surgery Trainees).*

## Novel Probiotic Therapeutic in a Murine Model of *Clostridium difficile* Colitis.

Rita D. Shelby, MD, Grace Janzow, BA, Lauren Mashburn-Warren, PhD, Natalie Tengberg, BS, Miriam Conces, MD, Michael T. Bailey, PhD, Steven D. Goodman, PhD, Gail E. Besner, MD

**Introduction:** *Clostridium difficile* infection (CDI) is the most common cause of antimicrobial-associated diarrhea, impacting all patient populations across healthcare centers worldwide. Affecting over 450,000 patients with 29,000 deaths a year, CDI is associated with annual excess medical costs of \$4.8 billion. We previously demonstrated the beneficial effect of a novel probiotic delivery system in the *prevention* of experimental CDI, in which efficacy is increased by delivering the probiotic bacteria in a biofilm state. In the current study we sought to investigate the effects of our novel therapeutic in the *treatment* of established experimental CDI.

**Methods:** A verified murine model of *C. difficile* colitis was used. Mice were exposed to an oral antibiotic cocktail (kanamycin, gentamicin, colistin, metronidazole, and vancomycin) for 96h followed by an intraperitoneal injection of clindamycin, and 24 hours later received an oral gavage of *C. difficile* ( $1.0 \times 10^8$  CFU). Signs of sickness were monitored for the initial 24h post administration of *C. difficile*. Twenty-four hours after *C. difficile* administration, mice were randomized to receive a single dose of: (1) no treatment (vehicle control) (2) planktonic *Lactobacillus reuteri* (*Lr*), (3) *Lr* pre-adhered to unloaded dextranomer microspheres (*Lr* + DM-water) in which some biofilm is formed, or (4) *Lr* pre-adhered to maltose-loaded dextranomer microspheres (*Lr*+DM-maltose) in which increased biofilm is formed. Signs of sickness were monitored for the subsequent 6 days, and scored using an established clinical sickness scoring system (CSS) (range 0-12; scores  $\geq 6$  consistent with moderate to severe *C. difficile* colitis). Mice were sacrificed when they exhibited severe illness or 6 days post *C. difficile* inoculation. Intestinal tissue was collected upon sacrifice and histologically graded in a blinded fashion utilizing an established histologic injury scoring system (HIS) (range 0-9; scores  $\geq 4$  consistent with moderate to severe *C. difficile* colitis).

**Results:** CSS: control mice that were not exposed to *C. difficile* showed no signs of sickness, whereas 75% of untreated mice exposed to antibiotics + *C. difficile* demonstrated signs of moderate to severe sickness ( $p \leq 0.05$ ). Moderate to severe sickness was seen in 65% of mice given antibiotics + *C. difficile* and treated with *Lr* alone, in 50% of mice treated with *Lr*+DM-water, and in only 25% of mice treated with *Lr*+DM-maltose. HIS: control mice did not demonstrate any histologic injury, whereas 76% of untreated mice exposed to antibiotics + *C. difficile* had moderate to severe histologic injury ( $p \leq 0.05$ ). Moderate to severe histologic injury was present in 75% of mice given antibiotics + *C. difficile* and treated with *Lr* alone, in 50% of mice treated with *Lr*+DM-water, and in no mice treated with *Lr*+DM-maltose.

**Conclusions:** We have developed a novel probiotic delivery system in which *Lr* is adhered to microspheres leading to biofilm formation. We previously showed that when delivered in the biofilm state, *Lr* significantly reduces the incidence and severity of experimental CDI when delivered prophylactically. We now show that *Lr* in its biofilm state additionally acts as a therapeutic for established CDI. This novel probiotic delivery system may be beneficial in preventing and treating clinical *C. difficile* infections in the future.

## Hepatitis C positive deceased donor kidney transplantation into Hepatitis C negative recipients: a pilot study

Taehwan Yoo, MD, MS, Ashraf El-Hinnawi, MBBS

**Introduction:** Kidneys procured from Hepatitis C Virus positive (HCV+) donors are not routinely used due to risk of transmission into recipients. Given the increasing organ shortage, the unclear transmission rate of HCV in patients without active viremia by nucleic acid testing (NAT-), and novel medications that can clear HCV infection, we hypothesize that kidney transplantation from HCV+/NAT- donors to HCV- recipients is safe without significant risk of HCV transmission or graft loss.

**Methods:** We performed a retrospective case series on our single-center experience transplanting HCV+/NAT- deceased donor kidneys into HCV- recipients from the implementation of our multi-disciplinary pilot program in 2017. Donor and recipient characteristics were collected. Recipients were followed post operatively every 3 months with serial HCV antibody and NAT testing as well as graft function testing with serial serum creatinine. Our primary outcome was conversion to HCV+ or NAT+ status. Our secondary outcomes were graft function.

**Results:** We performed a total of 15 deceased donor kidney transplants. Our mean follow-up was  $5.4 \pm 3.1$  months. Donor characteristics were as follows: 53.3% (N=8) male, mean age  $41.6 \pm 8.6$  years. Recipient characteristics were as follows: 53.3% (N=8) male, mean wait-list time  $54.7 \pm 48.7$  months. 6.7% of our population (N=1) converted to HCV+ status, without viremia. There were no cases of delayed graft function with all grafts functioning within the follow up time-period.

**Conclusions:** Our results demonstrate that HCV can transmit from non-viremic donor grafts to recipients, however the transmission rate within our follow up period remained low. Given the rise of NS5A/B inhibitors that can clear patients from HCV, we propose that HCV+ donor kidney transplantation into HCV- recipients is relatively safe as long as recipients adhere to ongoing follow-up and protocols for rescue HCV clearance therapy should they convert to HCV+ status. Further study is needed to determine HCV risk, and graft function over a longer follow-up period.

## Nanotechnology-based approaches towards elucidating and modulating the immunology of the tumor niche

*Silvia Duarte-Sanmiguel, BS., Vasudha Shukla, PhD., Carlie Francis., Brooke Brenner, BS., Natalia Higuiter-Castro, PhD., William Carson, MD., Daniel Gallego-Perez, PhD.*

**Introduction:** The tumor niche is highly heterogeneous, with cancer cells co-habiting with stromal and immune cells that include tumor associated macrophages (TAMs) and Myeloid Derived suppressor cells (MDSCs), among others. Such cellular interaction plays a role in the modulation of tumor progression, metastasis and therapy resistance. MDSCs are immature innate immune cells that exert immunosuppressive activity, protecting cancer cells from the host's immune system and exogenous immunotherapies. Once MDSCs infiltrate the tumor, they can either remain as immature, or transition to TAMs, exhibiting a "tumor-protecting" M2-like phenotype that inhibits the anti-tumoral activity of T cells. While current research has been mostly focused in countering MDSC immunosuppression within tumors, our knowledge of the mechanisms by which MDSCs disseminate and infiltrate cancerous tissue in the first place to exert immunosuppression is rudimentary. Moreover, efforts to counter MDSC/TAM-mediated immunosuppression within the tumor have been hampered by the lack of approaches that selectively target the immune cell compartment of the tumor, and/or that effectively reverse the M2-like fate towards an "anti-tumor" M1-like phenotype. We developed two different nanotechnology-enabled strategies to better understand the dissemination and tumor-infiltration mechanisms of MDSCs, and to selectively target and convert tumor-associated MDSCs into anti-tumor immune cells.

**Methods:** Nanotextured biomimetic cell migration surfaces were fabricated from polydimethylsiloxane (PDMS) using a combination of photolithography and replica molding. MDSCs (cell line and patient-derived) were seeded on the PDMS surfaces, and single-clone migration was monitored for 24h. MDSC-targeting exosomes were engineered via nanochannel-based non-viral transfection of donor cells. Such exosomes were decorated with MDSC/TAMs targeting ligands, and loaded with pro-inflammatory molecular cargo. These exosomes were then injected into tumor-bearing mice (i.e., PyMT breast cancer model), and the effects on the immune cell compartment of the tumor were evaluated via flow cytometry.

**Results:** We were able to use nanotextured surfaces to study MDSC migration with single-clone resolution. MDSCs exhibited significant intra- and inter-population differences in motility capabilities, with velocities ranging from  $<5 \mu\text{m/h}$  to  $>40 \mu\text{m/h}$ , indicating the presence of multiple sub-populations with different degrees of myelosuppressor and tumor-infiltrating abilities, as confirmed by qRT-PCR and in vivo assays in tumor-bearing mice (i.e., orthotopic breast tumor xenografts). Studies with MDSC-targeting nano-engineered exosomes indicate that weekly intra-tumoral injections led to hampered tumor progression compared to injections with sham exosomes, with volumetric increases of approximately 24% compared with controls. Flow cytometry analyses of the tumors also indicated a shift in the phenotype of the immune cell population towards a more pro-inflammatory state, suggesting that the nanoengineered exosomes were able to target and modulate the phenotype of tumor-associated immune cells.

**Conclusions:** Our study demonstrated that nanotexture surfaces successfully allow the identification of different populations of MDSCs with stratified myelosuppressive and tumor-infiltrative activity. Moreover, we also developed a new platform nanotechnology for selective delivery of reprogramming cargo into the immune cell compartment of tumors, which was shown to effectively hinder tumor progression, presumably by converting tumor-associated immune cells into pro-inflammatory macrophages.

## The development and characterization of a murine model of volumetric muscle loss

*Dathe Benissan-Messan, MD, MS; Weina Zhong, MD; Jianjie Ma, PhD; Peter H. Lee, MD, PhD, MPH*

**Introduction:** Volumetric muscle loss (VML) refers to muscle injuries involving a loss of at least 20% of a given muscle's mass and leads to significant morbidity and impacts on quality of life. It is often the result of severe trauma or intentional muscle excision for cancer treatment. VML has a considerable impact on the health care system with billions of dollars in medical expenses. Unfortunately, treatment options are limited to autologous muscle transfers and muscle transpositions. In an effort to develop and evaluate a novel tissue-engineering and gene therapy based treatment for VML, we have established and characterized a murine model of VML.

**Methods:** Three-month-old C57BL/6 mice were divided into VML (n=5) and Sham (n=5) groups. Under anesthesia, the right tibialis anterior (TA) muscles of the mice were isolated and a full thickness core (40% of the total TA muscle mass) was excised. The mice were allowed to recover over 4 weeks. Baseline, 1-, 2-, and 4-week measurements were made of right leg forces as well as overall gait. At 4 weeks, the mice were sacrificed, and ex vivo TA muscle force measurements were made, as well as morphometric analyses with H&E and trichrome staining.

**Results:** VML injury resulted in a significant decrease in forces in the affected leg compared to sham controls, with some recovery over 4 weeks. VML also resulted in a noticeable impact on the animals' gait. After 4 weeks of recovery, VML TA muscles had a 72.6% decrease in force compared to sham controls. Morphological analyses demonstrated decreased muscle size and fibers, as well as increased fibrosis in VML TA muscles.

**Conclusion:** VML injury involving the removal of 40% of the TA muscle resulted in a significant loss of force, impairment in gait, a decrease in muscle size, and an increase in fibrosis, consistent with clinical findings. Although further characterization of the model is needed, this suggests that the proposed murine VML model is appropriate for future studies on the treatment of VML.



**Abstracts**  
Judged Posters

## Decreasing surgical site infections in pediatric stoma closures

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**Introduction:** Gastrointestinal (GI) surgeries represent a significant proportion of the surgical site infection (SSI) burden in pediatric patients, resulting in significant morbidity. We have previously demonstrated that a GI bundle (including bowel prep, preoperative warming, preoperative cleansing, skin prep, and a closing protocol) decreases SSI rates, length of stay (LOS), and hospital charges. Following this success, we hypothesized that by targeting the preoperative antibiotics for stoma closures based on organisms found in infected wounds we could further decrease SSI rates.

**Methods:** As part of a broad quality improvement effort to reduce SSI rates for GI surgery we noted high infection rates for stoma closure patients. We reviewed the responsible pathogens and their sensitivities as well as the preoperative antibiotic used, and found that 15% of wound infections were caused by enterococcus. Based on this information, starting in May 2017, we changed the prior preoperative antibiotic, cefoxitin, to ampicillin-sulbactam which more accurately targeted the prevalent pathogens. This changed the bundle by only one variable. We then reanalyzed our SSI rates.

**Results:** The baseline SSI data for all stoma takedown patients was 21.4% (25 of 119). After bundle implementation, this decreased to 7.9% (17 of 221;  $p=0.03$ ) resulting in a 63% decrease in SSI. Then, after changing the preoperative antibiotics in May 2017 from cefoxitin to ampicillin-sulbactam, our rate of SSI decreased further to 2.2% (1 of 44;  $p=0.039$ ), resulting in a further decrease in SSI by another 72%. From baseline to present, our SSI rates have percent decreased by 90%.

**Conclusions:** Significant reduction of SSI in GI surgery (stoma closures in this case) can be accomplished with several prevention strategies (our GI bundle). Then, a change of the preoperative antibiotic choice, chosen based on causative wound infection organisms, may further decrease SSI rates. We recommend an institution specific analysis of wound infections, and modification of preoperative antibiotics if the responsible organisms are resistant to the original antibiotic choice.

## Comparison of Lymph Node Evaluation and Yield Among Patients Undergoing Open and Minimally-Invasive Surgery for Gallbladder Adenocarcinoma

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**Introduction:** Assessment of regional lymph nodes (LN) is essential for determining prognosis among patients with gallbladder cancer (GBC). The impact of surgical technique on LN yield has not been well explored. We investigated the impact of minimally-invasive surgery (MIS; robotic or laparoscopic) on the evaluation and retrieval of regional LN for patients with GBC.

**Methods:** We queried the National Cancer Database (NCDB) to identify patients with GBC who underwent curative-intent surgery between 2004-2015. Patients with metastatic disease or those with missing data on surgical resection or LN evaluation were excluded.

**Results:** We identified 10,488 patients who underwent an open (n=7,585, 72.3%) or MIS approach (n=2,903, 27.7%) for GBC and met the inclusion criteria. Patients who underwent MIS were older (median age MIS: 73 years, IQR: 64, 82 vs. Open: 72 years, IQR: 63, 80; P=0.002) and had smaller median tumor size (MIS: 3.0cm, IQR: 2.3, 9.9 vs. Open: 5.0cm, IQR: 1.8, 9.9; P<0.001) as compared to patients who underwent an open operation. Less than half of patients (n=4,872, 46.5%) underwent an evaluation of regional LN, with nearly half of these patients (n=2,152, 43.8%) having LN metastasis. The percentage of patients who received a regional lymphadenectomy increased over time among all patients (P<0.001). Patients undergoing MIS less commonly underwent a regional lymphadenectomy as compared to patients undergoing an open operation (MIS: n=1,291, 44.5% vs. Open: n=3,581, 47.2%; P=0.012). Among patients who underwent a regional lymphadenectomy, overall LN yield was lower for patients undergoing MIS (1 LN, IQR: 1, 4) versus an open (2 LN, IQR: 1, 4) operation (P=0.013).

**Conclusions:** As compared to patients undergoing an open operation for GBC, patients undergoing MIS had lower rates of LN evaluation and a lower LN yield. Further studies are needed to identify barriers to complete LN evaluation among patients undergoing MIS for GBC.

## Comparative Changes in Subcutaneous and Visceral Adipose Tissue Depots following Medical and Surgical Weight Loss

Anahita Jalilvand MD\*, Alecia Blaszczyk PhD, Bradley Needleman MD, Sabrena Noria MD PhD, Willa Hsueh MD

**Introduction:** Adipose tissue (AT) immunology is a key player in diet-induced obesity and has been linked to the development of insulin resistance and type 2 diabetes. In fact, reduced adipose tissue regulatory T cells (Tregs) abundance and pro-inflammatory shifts in adipose tissue macrophages (ATMs) and adipocytes are key contributors to the pathophysiology of obesity in both murine models and human subjects. However, the impact of weight loss on AT inflammation remains unclear, and emerging literature in murine models has not only demonstrated persistence but also increased levels of inflammation following significant weight reduction. **As such, the objective of this study was to characterize changes in AT inflammation in visceral and subcutaneous AT (VAT/SAT) depots in bariatric patients after 1) preoperative medical weight loss and 2) following bariatric surgery.**

**Methods:** VAT/SAT were obtained from patients undergoing bariatric surgery (n=161). SAT samples were obtained from twenty-eight patients who had baseline VAT/SAT samples 12-18 months following bariatric surgery by liposuction. The first part of this analysis evaluated the association between preoperative excess body weight loss (EBWL) on the livershrink diet (EBWL-LS) and adipocyte gene expression and T cell characterization from VAT/SAT obtained at the time of surgery. The second part of the study evaluated gene expression changes in SAT adipocytes, macrophages, and resident T-cells following bariatric surgery. Briefly, VAT/SAT was collagenase digested followed by density centrifugation allowing for the separation of adipocytes and the cellular stromal vascular fraction (SVF). The SVF was further processed by sequential bead isolation of adipose tissue macrophages (ATM) and adipose resident T cells (ARTs). Real-time PCR was utilized to characterize gene expression in adipocytes, ATMs, and ARTs and flow cytometry was conducted on the SVF to characterize T cell populations. **Statistical Analysis:** For analysis of gene expression changes pre and post-operatively, Mann-Whitney U, Spearman's correlations, and paired Mann-Whitney tests were utilized. A p value <0.05 was considered statistically significant.

**Results:** The average EBWL was  $2.6\% \pm 4.9$  after the livershrink diet and  $54.3\% \pm 17.6$  fourteen months after bariatric surgery. Preoperatively, %EBWL-LS was positively correlated to Treg abundance in VAT (R=0.22, p=0.05), after adjusting for age, gender, baseline BMI, and race. In contrast, pro-inflammatory Th1 cells in SAT exhibited a strong correlation with increasing EBWL-LS (R=0.43, p=0.0002), while anti-inflammatory SAT Th2 cells were inversely correlated with %EBWL-LS (-0.32, p=0.03). Similarly, adipocyte TNF- $\alpha$  was positively correlated with EBWL-LS (R=0.37, p=0.03) in SAT but not in VAT (R=0.03, p=0.76). High **preoperative** subcutaneous adipocyte TNF- $\alpha$  and IL1- $\beta$  expression (defined as >50th percentile) was significantly associated with higher EBWL-LS (p=0.04, p=0.01). When evaluating post-surgical changes in AT, post-operative subcutaneous adipocytes trended towards a reduction in pro-inflammatory markers (IL6, TNF, NLRP3) and demonstrated globally increased expression of metabolic and mitochondrial genes. However, subcutaneous ATMs exhibited significantly increased pro-inflammatory gene expression (IL6, IL1B, NLRP3, CD11C, p<0.05). Additionally, SAT Treg abundance was significantly reduced post-operatively but remained positively correlated to %EBWL at 1 year (R=0.67, p=0.02). High **preoperative** subcutaneous adipocyte TNF- $\alpha$  gene expression was associated with significantly higher weight loss at 6 months but not at 12 months, while both preoperative subcutaneous adipocyte and post-operative subcutaneous ATM CD80 gene expression were significantly associated with increasing weight loss at one year.

**Conclusions:** This study demonstrates that medical and surgical weight loss are associated with pro-inflammatory changes in subcutaneous adipocytes, ATMs, and ARTs but not in VAT, which may be indicative of differing inflammatory set points in these depots. Secondly, CD80 gene expression, an

essential co-stimulatory signal for Treg differentiation, and preoperative VAT Treg and post-operative SAT Treg abundances were correlated with increasing medical and surgical weight loss, suggesting a synergistic role between Treg maintenance and weight status. These findings highlight the complexity of the AT inflammatory microenvironment and the differences between VAT and SAT, specifically as they relate to weight loss in patients with obesity. Future studies are needed to compare the changes in VAT and SAT depots following bariatric surgery, along with their corresponding impact on long-term weight loss outcomes and comorbidity resolution.

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## Increasing patient engagement and access to providers during the transition of care period to improve outcomes

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**Introduction:** High readmission rates following colorectal surgery increase the risk of adverse health outcomes for patients and financial penalties for hospitals. At The Ohio State Wexner Medical Center, the readmission rate following colorectal surgery is 19.7%, with national readmission rates ranging from 0-41.2%. Many of these readmissions are due to nonemergent symptoms that could be addressed at an outpatient visit. We present preliminary results of a randomized prospective trial aiming to determine if hospital readmission rates could be reduced and patient satisfaction can be improved by increasing patient access and engagement in the postoperative period.

**Methods:** This is a prospective trial where patients were randomized to an intervention arm or a conventional treatment arm. The primary outcome of interest was 30-day hospital readmission. Secondary outcomes of interest were 30-day Emergency Department visit and patient satisfaction. Patients in the intervention group were contacted via phone approximately 3 days after discharge and queried about complications that could be addressed at an out-patient visit: temperature, wound appearance, diet, stoma & urine output (when applicable), nausea/vomiting, and pain. An algorithm-based approach was used to direct patients to either proceed to the ED immediately, schedule an out-patient visit within 48 hours, or maintain their follow up appointment as scheduled at the time of discharge. All patients were contacted via phone 30-days after discharge to capture ED visits, hospital readmissions, and patient satisfaction.

**Results:** At this time, 68 patients have been enrolled in the study and 34 patients have completed the study. Of these, 20 were randomized to the control group and 14 were randomized to the intervention group. The 30-day readmission rate is 25.0% for the control group and 7.1% for the intervention group. Of the 14 patients in the intervention group, 7 have been identified during the intervention phone call with symptoms that warranted an early out-patient appointment. There appears to be no significant impact on patient satisfaction at this time.

**Conclusions:** Early results indicate that hospital readmission rates may be reduced by increasing patient access and engagement via a phone call 3-days after discharge. More data is needed before definitive conclusions can be made.

## Improvement of novel electrospun small diameter tissue engineered arterial graft performance with heparin modification

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**Introduction:** To date, small diameter (<6mm) bioabsorbable arterial tissue engineered vascular grafts (TEVG) have not been successful, with thromboembolism continuing to be a common complication in large animal models. The objective of this study is to test whether Heparin-Eluting (HE) TEVGs prevent early thrombosis.

**Methods:** TEVGs were composed of an outer poly-caprolactone (PCL) electrospun nanofiber layer with a 15  $\mu\text{m}$  average pore size and an inner layer composed of a 50:50 poly (l-lactide-co- $\epsilon$ -caprolactone) copolymer. Adult female sheep (n=6) underwent bilateral carotid artery interposition grafting, with control TEVG in one carotid and HE-TEVG in the contralateral position. Animals were recovered and followed for 8 weeks. Carotid duplex ultrasonography was performed weekly to monitor TEVG performance. To compare platelet adhesion between groups, TEVGs were incubated with ovine platelet-rich plasma, and analyzed with a colorimetric Lactate Dehydrogenase (LDH) assay as well as with scanning electron microscopy evaluation.

**Results:** All sheep survived to the designated endpoint. At 8 weeks, all six HE-TEVGs were patent. Three out of six control TEVGs had early thrombus occlusion (<1week) and the remaining three had partial thrombus at 8 weeks (p=0.002). All patent grafts gradually expanded but with no evidence of rupture. In a 14-day in vitro heparin elution study, >97% of heparin release occurred within the first 24 hours. In the LDH assay, significantly fewer platelets adhered to the HE-TEVG than the control TEVG (HE:  $1.67 \pm 1.6 \times 10^5$  vs control:  $54.5 \pm 5.6 \times 10^5$ ; p<0.001).

**Conclusions:** This pilot study suggests HE-TEVG prevents acute thrombosis of grafts. We hypothesize that the heparin-eluting properties of the HE-TEVG during vascular endothelialization is useful for maintaining TEVG patency. This technique may aid in the translation of small arterial TEVGs to the clinic, but further studies are needed to investigate drug-eluting TEVGs.

## Discharge Disposition to Skilled Nursing Facility After Emergent General Surgery Predicts a Poor Prognosis

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**Background:** Emergency general surgery (EGS) can have a profound impact on the functional status of even previously independent patients. However, the role and influence of discharging a patient to a skilled nursing facility (SNF) remains largely unknown.

**Methods:** The American College of Surgeons National Surgical Quality Improvement Program was queried for community-dwelling adults who underwent one of seven EGS procedures and were discharged home or to a SNF from 2012-2016. Propensity score matching and multivariable regression analyses were performed to determine the relationship between discharge disposition and outcomes.

**Results:** Overall, 140,922 patients met inclusion criteria. The majority were discharged home (95.9%). After applying 1:1 propensity score matching, in comparison to patients discharged home, individuals discharged to a SNF had higher odds of respiratory (OR 2.32, 95% CI 1.59-3.38) and septic complications (OR 1.63, 95% CI 1.12-2.36) after discharge. Furthermore, individuals discharged to a SNF had higher odds of 30-day readmission (OR 1.14, 95% CI 1.01-1.29), and death within 30 days of the procedure (OR 2.07, 95% CI 1.65-2.61).

**Conclusions:** After accounting for patient severity and perioperative course, discharge to a SNF is an independent risk factor for death, readmission and post-discharge complications.

## Hospital Transfer Center Involvement Improves Clinical Trial Enrollment Performance

*Michael E. Villarreal, MD, Zoe Krebs, BS*

**Introduction:** Patient recruitment is recognized as the key to successful clinical trials; unfortunately recruitment and enrollment is challenging. Inadequate patient enrollment and poor recruitment rates result in premature termination of clinical trials. Hospital transfer centers facilitate inter-hospital transfers and manage patient flow. While common at academic medical centers, they have not previously been engaged in research and are rarely aware of ongoing clinical trials. We sought to evaluate the efficacy of patient enrollment in clinical trials utilizing a nurse-staffed transfer center to notify the research team when a patient was deemed eligible for studies being conducted.

**Methods:** A retrospective analysis of institutional data for patients enrolled in our clinical trials was performed. The cohort (n=38) was divided into two groups: those the transfer center notified the research team about prior to arrival and those without transfer center notification. Included in the non-notification group were patients missed by the transfer center in pre-screening, those who presented through the emergency department, and inpatient consults. The transfer patients were all reviewed by trained transfer center nurses prior to their acceptance to our facility. If a possible research study candidate was identified, a team member from the trial team was notified and began screening for potential enrollment of the patient. The time from patient arrival to study enrollment was evaluated. Statistical significance was determined using a p-value of  $< 0.05$  and assessed using a paired t-test.

**Results:** The transfer center successfully identified 14 patients who went on to trial enrollment. 24 patients were enrolled without transfer center notification. Early research team notification by transfer center staff reduced the patient arrival to enrollment time by 5.6 hours (454 minutes vs 115 minutes,  $p=.005$ ).

**Conclusion:** This study demonstrates that including transfer centers in clinical trial pre-screening and having them provide the research team with early notification facilitates enrollment of patients into emergent general surgery clinical trials. The early notification expedites coordinator response, study screening, and preparation for enrollment prior to the patient's arrival. Overall, the additional notification time allows for improved clinical trial operational performance. Further investigation needs to be performed to determine if the transfer centers are also assisting with increasing overall enrollment rates in each of the trials.

## The crosstalk between innate and adaptive immunity through formation of Neutrophil extracellular traps in nonalcoholic steatohepatitis-associated hepatocellular carcinoma

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**Introduction:** Hepatocellular carcinoma (HCC) is the second leading cause of cancer related mortality. Nonalcoholic fatty liver disease (NAFLD) affects a large proportion of the US population and is regarded as a metabolic predisposition to HCC. Nonalcoholic steatohepatitis (NASH) is a progressive form of NAFLD, featured by exacerbated intrahepatic inflammation, more intense steatosis, and hepatocellular injury. Neutrophils aggregation and infiltration have long been shown in liver fibrosis and ductular reaction in human NAFLD and animal models of NASH. Our most recent findings provide the strong evidence for the pro-tumorigenic role of neutrophil forming neutrophil extracellular traps (NETs) in the NASH-related HCC micro-environment<sup>1</sup>. Increasing evidence show that both innate and adaptive immunity play important roles in HCC pathogenesis. However, the effect of NETs on the crosstalk between the innate and adaptive immune systems in the setting of NASH and NASH-HCC has not been elucidated. Here we aim to explore the mechanisms by which NASH induced-NETs inhibit the development of adaptive anti-tumor immunity by promoting an immune-suppressive micro-environment through programmed death-ligand 1(PD-L1) signaling for HCC survival.

**Methods:** C57Bl/6 mice were exposed to streptozotocin (STZ, 200ug I.P. <5d from birth) and high fat diet (HFD) to induce our well-established NASH model. The development of NASH and NASH-HCC was evaluated over time by serum and tissue levels of inflammatory cytokines, flow cytometry of liver non-parenchymal cells, and histology. DNase (100U I.P. 3x/week) to inhibit NETs or peptidylarginine deiminase 4 knockout (PAD4 KO) mice (genetically unable to form NETs) were utilized *in vivo* experiments.

**Results:** Progressive steatosis, hepatocellular injury and chronic inflammation appeared as early as 8 weeks in the STZ+HFD mice. Neutrophil infiltration also increased in the livers of NASH mice liver over time and plateaued by 12 weeks. However, NET formation persisted in the NASH livers through 20 weeks with development of HCC at that time. Interestingly, there was suppressed tumor growth in both STZ+HFD fed PAD4 KO mice and STZ+HFD WT mice treated with DNase, suggesting NETs play a key role during NASH-HCC development. There was also a concomitant decline in total CD4<sup>+</sup> T cells in the NASH livers but among the proportion of regulatory T cells (Treg), there was a significant increase. **Furthermore, the expression of PD-L1, which can lead to the inhibition of effective CD4<sup>+</sup> T cells but the proliferation of Treg, is increased in CD4<sup>+</sup> T cells in the NASH-HCC livers compared to normal control livers.** Blocking NETs by *pad4* gene depletion or DNase treatment led to the increase of total CD4<sup>+</sup> T cells but reduced Tregs in NASH mice while PD-L1 expression was also down-regulated. PD-L1 expression on neutrophils increased by exposure to stimuli that induce NET formation *in vitro* and immunofluorescent staining suggests that PD-L1 is expressed in the structure of NETs.

**Conclusions:** The present results indicate that NASH induced NETs are critical to the inflammation driven carcinogenesis of NASH-HCC by promoting the tumor-suppressive micro-environment through PD-1/PD-L1 signal pathway. Inhibition of NETs may provide a novel potential therapeutic target for the prevention of NASH-related HCC.

1. van der Windt, D.J., *et al.* Neutrophil extracellular traps promote inflammation and development of hepatocellular carcinoma in non-alcoholic steatohepatitis. *Hepatology* (2018).

## Late-Term Performance of Tissue Engineered Vascular Grafts

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**Introduction:** Tissue engineered vascular grafts (TEVGs) are made from biodegradable scaffolds that grow to form functional vascular conduits with growth capacity, and this technology may have widespread use in surgery. We recently completed the first FDA-approved clinical trial evaluating the use of TEVGs in children with complex cardiac anomalies, and have previously reported results from a large-animal study in juvenile sheep demonstrating spontaneous reversible stenosis. We now have late-term results from our juvenile lamb model with novel findings regarding TEVG performance.

**Methods:** Bone marrow (5 ml/kg) was aspirated from the iliac crest of juvenile lambs, and the mononuclear cell (BM-MNC) fraction was isolated by Ficoll separation. Size-matched polyglycolic acid/polycaprolactone and polylactic acid (PGA/PCLA) scaffolds were vacuum-seeded with BM-MNC and implanted as 2 cm intrathoracic inferior vena cava interposition grafts. For a control, commercially available Gore-Tex™ PTFE grafts were implanted in an identical procedure. For both groups, anastomoses to the native inferior vena cava were marked with radiopaque vascular clips. Luminal morphometry was assessed with angiography, intravascular ultrasound (IVUS), and hemodynamic pressure monitoring at a baseline of 1 week postoperatively, followed by serial imaging at 6 weeks, 6 months, and 1 year. No endovascular interventions were performed. Histology, immunohistochemistry, scanning electron microscopy (SEM), and vasoreactivity testing were performed following graft explantation. In addition, select animals were given a 40 ml/kg bolus followed by repeat catheterization in order to assess IVC and graft capacitance & compliance.

**Results:** TEVGs (14-18 mm nominal diameter) were implanted in 24 juvenile lambs (8% perioperative mortality). Control PTFE grafts were implanted in 11 juvenile lambs (9% perioperative mortality). Invasive imaging was performed at 1 week (n = 32), 6 weeks (n = 32), 6 months (n = 30), and 1 year (n = 20). Serial imaging demonstrated significant stenosis at the 6-week time point that resolved spontaneously over time. Histology and immunohistochemistry (IHC) demonstrated a TEVG with an endothelium, collagen-rich intima, and organized smooth muscle cells, just like the surrounding native IVC. Luminal SEM imaging showed endothelium with similar morphology to native IVC. Vasoreactivity testing with KCl, endothelin-1, acetylcholine, and sodium nitroprusside demonstrated TEVG constriction and dilation that mirrored native IVC. The administration of a fluid bolus produced significant diameter and area changes for TEVG and native IVC animals compared to the PTFE controls (p<.001). In addition, compliance analysis demonstrated preservation of the pressure waveform in the TEVG group compared with the PTFE control, suggesting matched waveform impedance due to increased compliance.

**Conclusions:** The assessment of TEVG function and performance is complex. With this study, we have demonstrated that late-term TEVGs attempt to approximate native vessel function, unlike Gore-Tex. Furthermore, our histology, IHC, and vasoreactivity testing have shown that TEVGs have the ability to grow into functional neovessels, which has never before been demonstrated in the literature. While TEVGs continue to be limited by well-tolerated reversible stenosis, they benefit due to growth, increased compliance, and impedance matching over time.

## TRIC-A channel maintains store calcium handling by interacting with type 2 ryanodine receptor in cardiac muscle

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**Introduction:** Trimeric intracellular cation channels, called TRIC-A and TRIC-B, are distributed to intracellular Ca<sup>2+</sup> stores and mainly mediate the permeability of K<sup>+</sup> ions in multiple cell types. The crystal structure of TRIC has recently been determined, confirming the homo-trimeric structure of a potassium channel<sup>23-26</sup>. While the pore architectures of TRIC-A and TRIC-B appear to be conserved, the carboxyl-terminal tail domains (CTT) of TRIC-A and TRIC-B are different from each other. Aside from its recognized role as a counter-ion channel that participates in excitation-contraction coupling of striated muscles, the physiological function of TRIC-A in heart physiology and disease has remained largely unexplored.

**Methods:** In cardiomyocytes, spontaneous Ca<sup>2+</sup> waves, triggered by store overload-induced Ca<sup>2+</sup> release (SOICR) mediated by the type 2 ryanodine receptor (RyR2), develop extra-systolic contractions often associated with arrhythmic events. Here we use cell Calcium imaging and biochemistry methods to test the hypothesis that TRIC-A is a physiologic component of RyR2-mediated Ca<sup>2+</sup> release machinery that directly modulates SOICR activity via CTT.

**Results:** We show that cardiomyocytes derived from the TRIC-A<sup>-/-</sup> mice display dysregulated Ca<sup>2+</sup> movement across the sarcoplasmic reticulum (SR). Biochemical studies demonstrate direct interaction between CTT-A and RyR2. In HEK293 cells with stable expression of RyR2, transient expression of TRIC-A, but not TRIC-B, leads to apparent suppression of spontaneous Ca<sup>2+</sup> oscillations. Ca<sup>2+</sup> measurements using the cytosolic indicator Fura-2 and the ER luminal store indicator D1ER suggest that TRIC-A enhances Ca<sup>2+</sup> leak across the ER membrane by directly targeting to RyR2 to modulate SOICR. Moreover, synthetic CTT-A peptide facilitates RyR2 channel activity in lipid bilayer reconstitution system and induces intracellular Ca<sup>2+</sup> release after micro-injection into isolated cardiomyocytes, whereas such effects were not observed with the CTT-B peptide.

**Conclusions:** In addition to the ion-conducting function, TRIC-A seems to function as an accessory protein of RyR2 to modulate SR Ca<sup>2+</sup> handling in cardiac muscle.



**Abstracts**  
General Posters

## MG53 protein protects aortic valve interstitial cells from membrane injury and fibrocalcific remodeling

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**Introduction:** The aortic valve of the heart experiences constant mechanical stress under physiological conditions. Maladaptive valve injury responses contribute to the development of valvular heart disease (VHD).

**Methods:** We test the hypothesis that MG53, an essential cell membrane repair protein, can protect valvular cells from injury and fibrocalcific remodeling processes associated with VHD.

**Results:** We found that MG53 is expressed in pig and human patient aortic valves and observed aortic valve disease in aged *Mg53*<sup>-/-</sup> mice. Aortic valves of *Mg53*<sup>-/-</sup> mice showed compromised cell membrane integrity. *In vitro* studies demonstrated that recombinant human MG53 (rhMG53) protein protects primary valve interstitial cells (VICs) from mechanical injury and that, in addition to mediating membrane repair, rhMG53 can enter VICs and suppress transforming growth factor- $\beta$ -dependent activation of fibrocalcific signaling. Given the preserved contractile function of *Mg53*<sup>-/-</sup> mouse hearts under physiological conditions, the observation that aged *Mg53*<sup>-/-</sup> mice display hemodynamic and histological signs of aortic valve disease highlights a critical *in vivo* mechanism of MG53-mediated valvular protection.

**Conclusions:** Our study revealed a dual function for MG53 in maintaining the integrity of the VICs and in controlling TGF- $\beta$ -mediated fibrotic remodeling associated with VHD.

## Variability between the lateral and anterior-posterior (AP) sacral ratios in anorectal malformations

*Hira Ahmad, M.D.; Devin R. Halleran, M.D.; Raquel Quintanilla, M.D.; Benjamin Thompson, M.D.; Marc A. Levitt, M.D.; Richard J. Wood, M.D.*

**Introduction:** The sacral ratio (SR) has been used as a tool to evaluate sacral development in patients with anorectal malformations (ARM) and to help (along with the type of ARM and spinal status) to predict future bowel control. Although the ratio can be calculated using images from either the AP or lateral planes, lateral images are believed to produce more reliable ratios, given that the calculation is not influenced by the tilt of the pelvis. The congruency of the sacral ratio in the AP and lateral planes has not been previously investigated. We therefore aimed to assess the variability in the AP and lateral sacral images.

**Methods:** We reviewed all patients with ARM treated at our institution between 2014 and 2018 who had both an AP and lateral image of their sacrum. The SR was calculated using the ratio of the distance from the sacroiliac joint to the tip of the coccyx as compared to the distance from the top of the iliac crest to the sacroiliac joint. All ratios were calculated by a pediatric radiologist. The lateral SR was considered more accurate because it does not change based on the plane of the radiation beam. Variation between the SRs as determined by the AP and lateral images were compared across all patients and by ARM type using sacral ratio categories (0-0.39, 0.40-0.69, >0.70) which were developed for the purpose of counseling families. Institutional approval was obtained for this study (IRB ID: STUDY00000079) and approved waiver of the informed consent was obtained.

**Results:** 570 patients were included in the study. SRs in the AP plane varied from the lateral SR by an average of 17% (IQR 4,25, range 0-154). The AP SR overestimated the lateral SR in 22.5% (N=128) and underestimated the lateral SR in 61.9% (N=354) of patients. In total, it was variable in either direction 84.4% of the time. The variability in measurements decreased with increasing sacral development, as patients with a severe hypodevelopment (SR <0.4, N=39) demonstrated a variation of 27%, patients with moderate hypodevelopment (SR 0.4-0.69, N=193) demonstrated a variation of 18%, and patients with normal sacral development (SR >0.7, N=329) demonstrated a variation of 15%. The difference in these groups was statistically significant (p=0.03).

**Conclusions:** The SR determined by images in the AP plane varied significantly from those measured using lateral images. These results demonstrate that the AP sacral ratio can lead to a significant misinterpretation of the degree of sacral development which would impair the ability to accurately counsel families on their child's future continence potential. Based on these data, we recommend the lateral SR be used as the preferred measure.

## Dedifferentiated liposarcoma extracellular vesicular MDM2 induces preadipocyte MMP2 production

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**Introduction:** Dedifferentiated liposarcoma (DDLPS) is molecularly characterized by wt p53 and *MDM2* gene amplification causing MDM2 protein over-production, the key oncogenic process in DDLPS. Commonly located in fat-bearing areas, almost 60% of DDLPS patients undergo multifocal recurrence, typically amenable to palliative treatment only, and occasionally develop distant metastasis. These factors lead to an abysmal 10% 10 year overall survival rate. Tumor cell-derived extracellular vesicles (EVs) can facilitate loco-regional malignancy dissemination by depositing molecular factors that participate in the development of pre-metastatic niches for tumor cell lodgment and growth. To date, processes potentially contributing to DDLPS pre-metastatic niche formation have not yet been identified. Here we determined the level of MDM2 in DDLPS-derived EVs isolated from both patient serum and DDLPS cell lines and evaluate the possibility for this cargo to establish the DDLPS loco-regional pre-metastatic niche, thereby enabling multifocal failure in this disease.

**Methods:** Blood samples of DDLPS patients (n=16) who would undergo surgery as part of their LPS treatment, were collected from OSU James Cancer Medical center in Columbus. Healthy controls were purchased from PrecisionMed (California). EVs derived from serum samples were tested by RT-PCR for *MDM2* level. Preadipocytes (P-a) treated with DDLPS EVs were tested for the level of MDM2 (by RT-PCR and WB), for the ability to proliferate, migrate and release active matrix metalloproteinase 2 (MMP2) (by zymography).

**Results:** High number of *MDM2* DNA molecules was identified within EVs from DDLPS patient serum (ROC vs normal; 0.95) as well as from DDLPS cell lines. This *MDM2* DNA could be transferred to P-a, a major and ubiquitous cellular component of the DDLPS tumor microenvironment (TME), with subsequent P-a production of MMP2, a critical component in the metastatic cascade.

**Conclusions:** Since multifocal loco-regional DDLPS spreading is the main cause of the remarkably high lethality of this disease, a better understanding of the underlying oncogenic process and their regulatory mechanism is essential to improve the outcome of this devastating disease.

## The Relative Effects of Obesity, Diabetes and Elevated Hemoglobin A1c on Post-Operative Wound Infections after Colorectal Surgery

*Lisa Cunningham, MD, Taehwan Yoo, MD, Alessandra Gasior, MD, Amber Traugott, MD, Mark Arnold, MD, Alan Harzman, MD, Syed Husain, MBBS*

**Introduction:** Diabetes (DM) has been historically associated with an increased risk of superficial surgical site infection (SSI). However, DM is frequently coincident with a higher Body Mass Index (BMI), which in itself is a strong predictor of SSI. Our previous work using a large NSQIP dataset indicated that the association between superficial SSI and DM loses statistical significance when the sample was controlled for BMI. On the other hand, BMI remained significant despite controlling for DM. The NSQIP data was limited by the lack of availability of hemoglobin A1c (HbA1c) values. Therefore, we sought to evaluate our institutional data including HbA1c values, BMI and DM to determine if the same relationship existed between these variables and superficial SSI after colorectal surgery.

**Methods:** After IRB approval, a query of patients who underwent colorectal surgeries between 2011-2017 was performed. Colectomies performed by Board Certified Colon and Rectal Surgeons were included and superficial SSI were documented. Patient demographics and post-operative wound related outcomes were recorded. Emergent cases were excluded. HbA1c levels within a month immediately preceding the surgery were used for this analysis. Univariate analysis was performed using Fisher's Exact Test and two-tailed p values were calculated.

**Results:** A total of 3174 patient records were included. The average age of our patients was 62 years in the diabetic group and 55.9 years in the non-diabetic group, 17.3% were diabetic, 36.8% had a BMI >30. HbA1c levels were available for 777 patients out of which 430 (55.3%) had a HbA1c of 5.7% or higher. Our research revealed that BMI >30 had a significant association with superficial SSI ( $p=0.042$ ). The association between superficial SSI and DM or elevated HbA1c (5.7% or higher) was not statistically significant ( $p=1$  and  $0.11$  respectively).

**Conclusions:** Based on our data, it appears that BMI >30 is a stronger predictor of superficial SSI after colorectal operations compared to DM or elevated HbA1c levels. Our results also suggest that the increased superficial SSI rate observed in diabetics is primarily due to co-existent elevations in BMI in this patient population rather than poor glycemic control, concordant with the findings from the NSQIP dataset.

## Determination of the microRNA Expression Profile Associated with Tumor Ulceration in Melanoma

*Mallory J. DiVincenzo, DVM, Casey Ren, Maribelle Moufawad, Paolo Fadda, PharmD, Lianbo Yu, PhD, Alejandro Gru, MD, William E. Carson, III, MD*

**Introduction:** Melanoma is the most deadly form of skin cancer, leading to approximately 55,000 deaths annually. The presence of ulceration at the time of melanoma diagnosis is among top 3 most powerful predictors of patient survival, as the presence of ulceration consistently correlates with more aggressive tumor behavior, resulting in elevation of the tumor stage designation for the patient. However, little is understood regarding changes to the tumor microenvironment of ulcerated tumors and how they contribute to this more aggressive phenotype. microRNAs (miRs) are small, non-coding RNA sequences that regulate gene expression through modulation of protein translation. miRs are known to contribute to the progression of cancer when miR expression is dysregulated. The miR expression profile and the subsequent biologic effects of dysregulated miR expression in ulcerated melanoma tissue have not been explored. We hypothesize that there is a unique pattern of microRNA expression in the presence of tumor ulceration, and that the gene targets of these dysregulated microRNAs contribute to tumor progression.

**Methods:** RNA was isolated from formalin fixed, paraffin embedded human melanoma tissue with histologic evidence of the presence (n=4) or absence of tumor ulceration (n=4), as well as benign nevi (n=4). microRNA expression was determined using the NanoString nCounter microRNA Expression assay. After technical normalization, miRs with greater than 2-fold change in expression between groups were identified (p<0.01). Gene target and pathway analyses were performed on the identified dysregulated miRs to highlight how altered miR expression may contribute to tumor progression.

**Results:** There was significantly downregulated expression of 10 miRs, including hsa-miR-4286, hsa-miR-4488, hsa-miR-1469, hsa-miR-218-5p, hsa-miR-4284, hsa-miR-4532, hsa-miR-877-5p, hsa-miR-1285-5p, hsa-miR-320e, and hsa-miR-575, and upregulation of hsa-let-7g-5p in ulcerated relative to non-ulcerated melanoma. Pathway analysis demonstrated involvement of multiple miRs with dysregulated expression in ulcerated tumors in the following pathways: hippo signaling, ECM-receptor interactions, proteoglycans in cancer, viral carcinogenesis, Hepatitis B, fatty acid biosynthesis, and fatty acid metabolism.

**Conclusions:** A unique microRNA expression profile is present in the setting of tumor ulceration that may impact the metabolism and adhesion of melanoma tumor cells. Further investigation to define the role of these miRs in tumor progression is warranted to determine how microRNAs may impact the function of melanoma tumor cells, as well as patient outcomes and responses to therapy observed in cases of ulcerated melanoma. The resulting miR expression profile generated in this study defines a framework for future study of the effects of miR expression in ulcerated melanoma.

## NRAS mRNA is differentially spliced to give five distinct isoforms: implications for melanoma therapy and clinical outcome

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**Introduction:** NRAS is the second most commonly mutated oncogene in melanoma and efforts to therapeutically target NRAS have been difficult. Recently, our group discovered that the NRAS gene transcript is differentially spliced to give rise to 5 distinct NRAS isoforms of varying size, expression patterns and downstream effects.

**Methods:** We characterized the expression of these isoforms in melanoma by studying isoform transcript levels in tumor tissues and RNAseq datasets. We then characterized phenotypic functions by over-expressing each isoform in a melanoma cell line and analyzing for proliferative ability, invasiveness, anchorage-independent cell growth, downstream signaling and *in vivo* growth.

**Results:** All five NRAS isoform transcripts were expressed in melanoma tumor tissue, with canonical NRAS (isoform 1) expressed to the highest degree. NRAS isoform 1 mRNA expression was also significantly increased in metastases compared to primary melanoma lesions ( $p < 0.001$ ). Isoform 5 mRNA expression showed a significant correlation with survival, as high levels of isoform 5 in metastases were associated with enhanced survival in patients with stage IV disease ( $p < 0.05$ ). Forced over-expression of each the isoforms led to enhanced proliferation, but invasiveness was only increased with over-expression of isoforms 1 or 2. Over-expression of isoform 4 led to significantly decreased ability to engage in anchorage-independent cell growth ( $p < 0.05$ ). Downstream signaling analysis indicated that the isoforms varied in their ability to mediate signaling through the mitogen-activated protein kinase (MAPK) and phosphatidylinositol 3-kinase pathways. *In vivo* growth of A375 cells over-expressing each of the isoforms showed that cells over-expressing isoform 5 had significantly decreased tumor growth ( $p < 0.05$ ). Finally, A375 cells over-expressing isoforms 2 or 5 showed marked resistance to vemurafenib treatment *in vitro*.

**Conclusions:** The results from this study indicate that the five different isoforms of NRAS play varying roles in melanoma phenotype and progression and that they can potentially serve as biomarkers for therapeutic response and disease prognosis.

## Recurrence of pilonidal disease; our best is not good enough

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**Introduction:** Pilonidal disease is a common and painful disorder among adolescents and young adults, affecting males at a rate of 2 to 4 times that of females. Approximately 1% of the population will be diagnosed with pilonidal disease between the ages of 15-30 years. Patients with recurrent pilonidal disease can develop chronic wounds and draining sinuses that incur long term morbidity, disability, and decreased quality of life. Recurrence rates have been conservatively reported at 16% and as high as 30%. The aim of this study was to characterize rates of recurrence in patients with pilonidal disease treated by pediatric surgeons.

**Methods:** We conducted a retrospective review of patients at our institution diagnosed with pilonidal disease and evaluated by surgery from 2010-2015. Demographic and clinical characteristics were collected from the electronic medical record. Summary measures were used to examine patient demographics and clinical outcomes. This study was approved by our institutional review board.

**Results:** In 360 patients with pilonidal disease treated at our institution over the study period, 51% were male and the median age at presentation was 16 years (IQR 14-17) (Table). Approximately 66% of patients eventually underwent surgical excision of their pilonidal disease. Recurrent pilonidal disease was seen in 34.4% of the patients in our cohort with approximately 22% of patients have their recurrences within the first year of initial evaluation. In patients treated after their first episode of disease, recurrence rates were 21.3% after treatment with antibiotics only, 26.8% after treatment with incision and drainage, and 30.4 % after surgical excision.

**Conclusions:** Pilonidal disease has a substantial recurrence rate even after surgical excision. Future studies investigating treatments that can prevent disease recurrence are needed.

## Predicted Risk of Right Ventricular Failure After Minimally Invasive Left Ventricular Assist Device Implantation

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**Introduction:** Currently, risk scores exist that predict postoperative right ventricular failure (RVF) after left ventricular assist device (LVAD) implantation. However, a minimally invasive approach has been shown to improve survival and decrease morbidity. Thus, it is unclear whether current RVF predictive models accurately risk-stratify patients who undergo LVAD placement through a minimally invasive approach.

**Methods:** We retrospectively analyzed our patients from April 30, 2016 until December 21, 2017. We had 11 patients who had a LVAD implanted with a minimally invasive procedure. We collected demographic information and preoperative risk factors such as preoperative ventilation, central venous pressure/pulmonary capillary wedge pressure ratio > 0.63, BUN > 39 mg/dL (Kormos et al., 2010)<sup>1</sup>. We also used the Right Ventricular Failure Risk Score (RVFRS) with vasopressor requirements, aspartate aminotransferase > 80 IU/l, bilirubin > 2.0 mg/dl, and creatinine > 2.3 mg/dl (Matthews et al., 2008)<sup>2</sup>.

**Results:** The average RVFRS was 4.05; being on vasopressors was the most significant risk factor. The overall likelihood ratio of RVF was 2.8. However, postimplant, only 1 patient (9.09%) had severe/severe-acute RVF as defined by INTERMACS. 3 Yet, this patient did not have the highest RVFRS. Eight out of the 11 patients (72.7%) had elevated bilirubin levels > 2.0 and central venous pressure > 16 mmHg on the first postoperative day that resolved on postoperative day 2 with diuresis. Two out of 11 patients were on the ventilator preoperatively, but these patients did not develop postimplant RVF. No patients had preoperative elevated serum creatinine levels > 2.0 or BUN > 39 mg/dL.

**Conclusions:** Although some risk scores include nonhemodynamic parameters as predictors for RVF after LVAD placement, they do not appear to be consistent for patients who undergo a minimally invasive approach. To determine a better risk-stratification system, more analysis needs to be done, looking specifically at echocardiographic risk factors for RVF post-LVAD implant in patients who have had a minimally invasive approach.

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## Radiology resources in the modern management of appendicitis: Do they really matter?

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**Introduction:** Appendectomy remains a frequently performed emergency general surgery (EGS) operation. In the modern era imaging typically is obtained prior to surgical consultation. This study was evaluated the association of radiology resources on timing of appendectomy and outcomes.

**Methods:** 2,811 U.S. hospitals were surveyed on emergency general surgery practices, including diagnostic radiology structures and processes. Survey data from 513 hospitals was linked to 2015 Statewide Inpatient Sample data using American Hospital Association identifiers. Patients admitted with primary diagnosis of appendicitis who underwent appendectomy were included. We compared differences in radiology resources and outcomes for patients undergoing appendectomy on the date of admission (EARLY) to those at any other date (LATE) using univariate and multivariate analysis.

**Results:** 11,492 patients underwent an appendectomy; 2.8% (N=320) underwent a LATE operation. Compared to EARLY patients, patients undergoing LATE operation were older (median 53 yo vs 44 yo) and had >3 comorbidities (36% vs 15%). All p-value <0.001. Lack of advanced CT scans and overnight US technicians had lower odds of EARLY operation (aOR 0.58 [0.36,0.93] and aOR 0.78 [0.62, 0.99]). LATE operation had increased the odds of surgical complications (aOR 2.27 [1.75, 2.93]) and systemic complications (aOR 1.87 [1.38, 2.54]).

**Conclusions:** Some diagnostic radiology resources are associated with a LATE appendectomy and LATE appendectomy has increased odds of both major operative and systemic complications. These findings suggest that process changes in areas of care other than diagnostic radiology services are necessary to improve timing and outcomes for acute appendicitis.

## Does Decreased Length of Stay After Colorectal Surgery Translate into Increased Readmission Rate?

*Taehwan Yoo, MD, MS, Lisa Cunningham, MD, Syed Husain, MBBS*

**Introduction:** The advent of Enhanced Recovery after Surgery (ERAS) protocols for Colorectal Surgery has led to a marked decrease in the length of stay (LOS) after colon and rectal surgeries. However, there is concern that fast-track protocols can result in premature discharge, leading to an increased rate of readmissions. Thus, we hypothesize that post-operative Colorectal Surgery patients with shorter LOS will have a higher readmission rate.

**Methods:** We performed a single-institution retrospective cohort study of our patients undergoing laparoscopic and open operations involving small and/or large bowel resection performed by colorectal surgeons from 2011 to 2017. Patient characteristics and readmission data were collected. Patients who had an inpatient complication were excluded from analysis. Our primary outcome measure was 30-day readmission

**Results:** There was no significant difference in patient age, sex, BMI, IBD, cancer, or patient co-morbidities (Table 1). Our 30-day readmission rate was 11.5%. There was a nearly significant positive association between LOS and 30-day readmission (OR=1.06 per day admitted, P=0.06). In patients that had LOS $\leq$ 6 days or less, there was a nearly significant reduction in readmission rate (OR=0.71, 10.0% vs 13.6%, P=0.06).

**Conclusions:** Our data demonstrate that there is no significant increase in readmission rate in patients with shorter LOS. In fact, our data trended towards the opposite effect, with patients that had LOS $\leq$ 6 days or less having a nearly significant decreased risk of readmission. In summary, decreased LOS is not associated with increased 30-day readmission rate and may have an overall protective effect.



**Abstracts**  
Oral Session II

## Racial disparities in Hepatocellular Carcinoma outcomes are driven by access to care.

Clifford Akateh, MD\*; Yasaman Navari, MD; Victor Heh, PhD.; Sylvester M. Black, MD, PhD

**Introduction:** Hepatocellular carcinoma (HCC) remains a major leading cause of end-stage liver disease and cancer-related mortality in the United States. While advances in various treatment strategies have contributed to improved outcomes overall, surgical resection remains the preferred choice of therapy and in many cases the only hope of a cure. Despite improving outcomes, minority patients with HCC continue to have worse outcomes compared to non-minorities. The goal of this study is to identify underlying mechanisms for disparities in HCC outcomes.

**Methods:** The Surveillance, Epidemiology and End Results (SEER) database was used to identify White and Black patients diagnosed with hepatocellular carcinoma between 2000-2014. Age, race, marital status, stage, and receipt of surgery were evaluated as predictors of disparate outcomes and mortality in multivariate analyses.

**Results:** 43,877 patients (75.6% White, 12.8% Black and 11.6% Other Races) were identified, 73% of whom were male, and 26% were female. Black patients were significantly younger at diagnosis compared to Whites (60 vs. 64 ( $p<0.001$ )) and were slightly more likely to have the advanced/regional disease at presentation (18.8 vs. 21.2%,  $p<0.001$ ), respectively. Overall, blacks were significantly less likely to undergo cancer-directed surgery, including liver transplantation (OR 0.84, 95% CI= 0.76-0.92). This decrease in odds of surgery persisted after adjusting for patient-level factors such as age, sex, marital status, and year of diagnosis (adjusted OR 0.80, 95% CI= 0.73-0.88). However, these odds of surgery were equivalent when adjusted for disease stage (adjusted OR 0.94, 95% CI= 0.82-1.10). The unadjusted hazard of mortality was 1.11 times higher in blacks compared to whites ( $p<0.001$ ). However, these hazards disappeared when adjusted for disease stage (HR 0.99,  $p=0.908$ ).

**Conclusion:** Significant racial disparities in HCC outcomes are largely related to the advanced presentation at diagnosis and resulting underuse of cancer-directed surgery. It is therefore imperative to address barriers to care as receipt of appropriate care eliminates these disparities.

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## Preoperative exercise therapy protects the liver from ischemia-reperfusion injury

Hongji Zhang, MD

**Introduction:** Hepatic ischemia/reperfusion (IR) injury is a major cause of post-operative liver dysfunction, morbidity and mortality following liver transplantation and hepatic resectional surgery. Preoperative exercise therapy has been shown to enhance physical capacity at the moment of hospital admission and may facilitate better recovery after surgery. However, the mechanisms behind this protection remain to be elucidated. Here, we present the evidence that preoperative exercise can favorably alter numerous components of the immune system and relieve sterile inflammatory, which, in turn, protect the liver from I/R injury.

**Methods:** Eight-week-old male C57BL/6 mice were randomly divided into exercise or sedentary groups. The exercise group ran on a motorized treadmill for 60 min/day, 5 days/week at a speed of 12.5m/min for 1~4 weeks. 70% partial liver warm I/R was performed in both exercised and sedentary mice at 72 hours after the final exercise session.

**Results:** After 4 weeks of preoperative exercise therapy, 60% exercised mice showed a 3%-6% weight loss whereas the weight of all sedentary mice were increased. All the exercised mice showed significantly lower ALT than the sedentary mice after liver I/R as well as the sinusoidal dilation and pericentral hepatocellular necrosis in the ischemic liver lobe has been improved. Increased Natural Killer (NK) cells and Regulatory T cells(Treg)were seen in the ischemic liver lobe of exercised mice after 4weeks exercise by flow cytometry. As well as less neutrophil infiltration was seen in exercise mice after I/R, suggesting a mechanism for exercise to stimulate liver immune environment. Exercise mice livers exhibited less NET formation after I/R by immunofluorescence and western blot for citrullinated histone-3, a specific NET marker. Which we have previously reported that blocking NETs can reduce the organ damage and initiates inflammatory responses during liver I/R[1]. Conditional media derived from NK and Treg cells can effectively decrease the formation of NET in vitro, especially in the exercise group. RNA-seq showed more DNase I&IL3 expression in the liver of training mice which can digest the NET structure, also the secretion of DNase I&IL3 from training mice increased, especially from the Treg. After 4 weeks exercise, the lactate dehydrogenase(LDH),apoptosis, reactive oxygen species (ROS) in hepatocyte were all decreased.

**Conclusions:** These data show beneficial effects of preoperative exercise therapy in liver I/R injury, which offer a rationale for encouraging predisposed patients of HCC or other end-stage liver diseases that need liver surgery.

## SPECT/CT imaging detects perfusion responses to lower extremity revascularization and is significantly correlated with toe-brachial index in patients with peripheral arterial disease

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**Introduction:** Patients with peripheral arterial disease (PAD) often require revascularization procedures that are directed at improving downstream foot perfusion to facilitate wound healing and limb salvage. However, no standard imaging tool currently exists for assessing changes in microvascular perfusion in response to lower extremity revascularization. Ankle-brachial index (ABI) and toe-brachial index (TBI) are standard measures that are used clinically for screening and evaluating the lower extremity hemodynamic status of PAD patients, but do not directly measure foot perfusion. Radiotracer imaging with single photon emission computed tomography (SPECT)/CT imaging has been clinically utilized for decades to assess myocardial perfusion, but has not been used for evaluating perfusion responses in the lower extremities of PAD patients who are undergoing medical treatment. Therefore, in the present study we utilized SPECT/CT imaging to assess the utility of this technique for quantifying regional perfusion responses to lower extremity revascularization in patients with PAD and compared SPECT/CT-derived perfusion responses to the standard hemodynamic measurements of ABI and TBI.

**Methods:** SPECT/CT perfusion imaging of the feet was performed before and after endovascular revascularization of the lower extremity in diabetic patients with PAD and non-healing ulcers (n=17).  $^{99m}\text{Tc}$ -tetrofosmin (dose:  $14.9 \pm 0.9$  mCi) was intravenously injected 15 min before each SPECT/CT image acquisition to allow for adequate circulation time and radiotracer retention in muscle tissue. CT images were used for segmenting the revascularized foot into various angiosomes (i.e. vascular run-off territories) and average radiotracer uptake was quantified within the region of the foot that contained a non-healing wound. The relative percent change in SPECT-derived foot perfusion was calculated from the pre- to post-revascularization time point for the ulcerated region of the foot. In addition to SPECT/CT perfusion imaging, ABI (n=17 pts) and TBI (n=15 pts) measures were also acquired at each patient's baseline pre-revascularization visit. Pearson's correlation coefficient was used to assess the relationship between SPECT-derived perfusion responses and ABI / TBI measurements. Statistical significance for all analyses was set at  $P < 0.05$ .

**Results:** A wide range of perfusion responses were non-invasively detected by SPECT/CT imaging within the specific ulcerated regions of the foot that were being targeted for revascularization, with treatment-induced perfusion responses ranging from 0.3% to 22.4%. Foot perfusion responses, as quantified by SPECT/CT imaging, were significantly correlated with baseline TBI measures ( $r=0.72$ ,  $p=0.002$ ) but not baseline ABI ( $r=0.02$ ,  $p=0.94$ ).

**Conclusions:** SPECT/CT imaging provides a non-invasive quantitative approach for evaluating regional foot perfusion responses to lower extremity revascularization in PAD patients. Perfusion responses to revascularization are related to the baseline hemodynamic status of the foot (as measured by TBI), but are not related to the overall hemodynamic status of the lower extremity (as measured by ABI). Thus, baseline TBI may be an important measure for predicting which PAD patients will be "high" or "low" perfusion responders to revascularization procedures. Future analysis of the potential relationship between perfusion responses and clinical outcomes (i.e. diabetic wound healing, amputation rates) should elucidate the role that radiotracer imaging may have in the evaluation of patients with PAD.

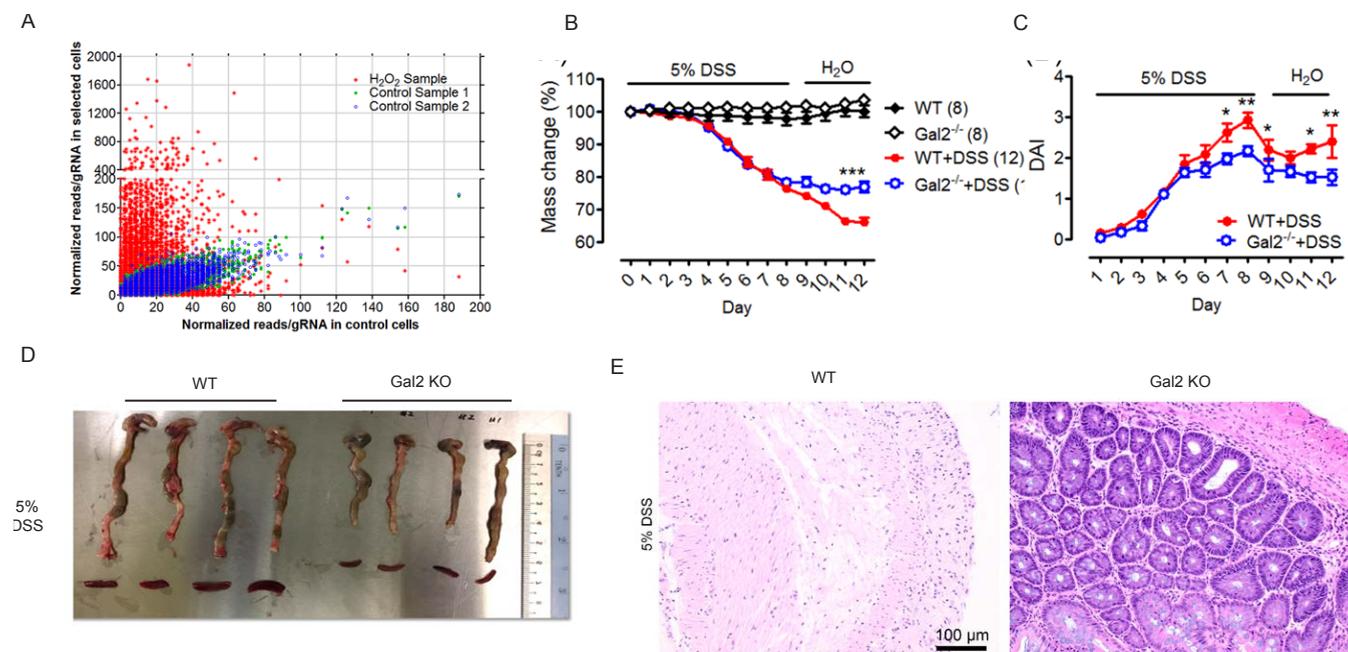
## A Genome-wide CRISPR Screen Identifies Galectin2 that Contributes to Exacerbation of Intestinal Inflammation

Haiwen Li PhD, Yeh S Lau PhD, Li Xu PhD, Yandi Gao MS, Renzhi Han PhD

**Introduction:** Inflammatory bowel disease (IBD) mainly includes ulcerative colitis and Crohn's disease and is characterized by chronic or recurring inflammation of the gastrointestinal tract. In the United States, it is currently estimated that about 1-1.3 million people suffer from IBD. However, the cause of IBD remains unclear. In our study, we demonstrated that glycan-binding protein Galectin-2 promoted the intestinal inflammation.

**Methods and Results:** Firstly, we used a genome-wide Crispr KO library to identify Galectin-2 mediating H<sub>2</sub>O<sub>2</sub>-induced cell death. Next, We tested WT and Galectin2-deficient (Gal2<sup>-/-</sup>) mice for the development of colon inflammation 8 days after DSS administration before changing to water. Both groups started to lose weight 3 days after treatment, but Gal2<sup>-/-</sup> mice exhibited considerable protection from the loss of body weight manifesting in WT controls. Characteristic inflammatory parameters such as Disease Activity Index (DAI) and colon length revealed Gal2<sup>-/-</sup> mice were protected from inflammatory destruction. Furthermore, HE staining further confirmed that Galectin2 depletion attenuated the morphological disruption of intestine compared with WT mice under DSS treatment.

**Conclusions:** On the one hand, our study used the unbiased screen to identify Galectin2 as an important molecules for H<sub>2</sub>O<sub>2</sub>-mediated cell death. On the other hand, our study used the genetic mice model to demonstrate that Galectin2 promoted the intestinal inflammation.



## Exogenous MG53 Protects Adult Mouse Cardiomyocytes by Preventing Mitochondria Damage in Response to Oxidative Stress

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**Introduction:** Ischemic heart disease is a major cause of mortality and morbidity world-wide and its incidence is continually increasing as other health factors, such as diabetes type II and obesity, climb. Ischemic injury of any tissue causes a loss of healthy mitochondria, due to an increase in reactive oxygen species leading to oxidative stress. MG53, also known as TRIM72, is highly expressed in skeletal muscle and modestly in other tissues and is essential to repair damage to plasma membrane by acting as a myokine. We have previously shown that MG53's membrane repair function is associated with changes in oxidative state inside the cell. Moreover, we have shown that *mg53*<sup>-/-</sup> mice are more susceptible to ischemia-reperfusion injury, whereas treatment with exogenous recombinant human MG53 (rhMG53) reduces both infarct damage and fibrosis and restores cardiac function. We hypothesize that in addition to cell membrane repair, exogenous MG53 enters cardiomyocytes and can act as a myokine to protect cardiomyocytes by maintaining mitochondrial function through control of oxidative-stress induced mitophagy.

**Methods:** In this study, MG53 protection of cardiomyocyte mitochondria was assessed by subjecting HL-1 cells (an immortalized mouse atrial cardiomyocyte cell line) to oxidative stress followed by analysis for mitochondrial structure and function.

**Results:** Overall, we show that treatment with rhMG53 allowed cells to maintain a healthy mitochondrial membrane potential to protect mitochondrial function. We are currently dissecting the mechanism that facilitates the endocytic uptake of MG53 from the circulation into the cardiomyocytes as well as downstream signaling pathways that mediate the protection of the mitochondria function.

**Conclusions:** The novelty of this study is that it shows exogenous MG53 can protect mitochondria in cardiomyocytes upon oxidative stress. This provides a mechanism behind how rhMG53 treatment may be a clinically relevant strategy to reduce cardiomyocyte injury and maintain cardiac function in patients after ischemic injuries.

Research Support: R01 grants (DK106394 and AR070752) from NIH to J. M and AHA predoctoral fellowship (18PRE34030430) to K.G.

## NIH Funding for Pediatric Surgeon-Scientists

*Kejal Shah MD, Joseph Drews MD MS, Julie Breuer RN, Gail Besner MD, Christopher K Breuer MD*

**Introduction:** There were 37 National Institutes of Health (NIH)-funded pediatric surgeons in 2015. Despite overall increases, the relative funding allocated to surgeons has declined by 25% recently. Academic productivity has played an important role in the growth of pediatric surgery, but the characteristics of successfully-funded pediatric surgeons are incompletely understood. Our objective was to characterize traits of NIH-funded pediatric surgeons.

**Methods:** The American Pediatric Surgical Association (APSA) database was queried for all members and run through the NIH Research Portfolio Online Reporting tools (RePORT) system. The system was queried for 2018 NIH funding, funding institute, and grant mechanism. PubMed and department websites were used to extract surgeon-scientist and institution-specific characteristics, including academic rank, years in practice, publications, previous Career Development (K) award, number of hospital beds, size of practice, and institution. Single and multivariable linear regression were used to determine associations between surgeon or institutional characteristics and 2018 funding.

**Results:** Among 851 APSA members, 24 surgeons (2.8%) from 13 institutions received Research (R), Training (T), Program (P), or Cooperative Agreement (U) level NIH funding in fiscal year 2018. Eighteen (75.0%) are professors, with a median of 19 years in practice (IQR 16-24). Six (25%) received a previous K award. Funded pediatric surgeons have a median of 94 peer-reviewed publications (IQR 73-131.5). Median 2018 funding is \$780,123 (IQR \$442,180-\$1,220,206), with R as the most common grant mechanism (19 surgeons). On univariate analysis, professorship ( $p=0.02$ ), years in practice ( $p=0.001$ ), and P grant mechanism ( $p<0.001$ ) were significantly associated with increased funding. No characteristics were significantly associated with 2018 funding on multivariate analysis. Two additional surgeons received K awards in 2018.

**Conclusions:** NIH-funded pediatric surgeons are predominantly senior faculty. There are currently only three assistant professors and two pediatric surgeons with development awards, suggesting the pediatric surgeon-scientist pipeline is drying up.

## Presenters



**T.M. Ayodele Adesanya, PhD**

MED IV

**Hometown:** Greenville, Illinois

**Undergraduate:** BS, The University of Chicago, Chicago, Illinois

**Doctorate:** PhD, The Ohio State University, Columbus, Ohio; In progress, MD, The Ohio State University, Columbus, Ohio

**Research Interests:** Preventive cardiovascular health

**Faculty Advisor(s):** Jianjie Ma, PhD



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Pediatric Surgery Colorectal Clinical Fellow

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**Undergraduate:** BS, Biology, University of San Francisco, California

**Doctorate:** MD, Creighton University School of Medicine, Omaha, Nebraska

**Research Interests:** Pediatric colorectal surgery clinical outcomes

**Faculty Advisor(s):** Marc Levitt, MD



**Clifford Akateh, MD, MS**

Postdoctoral Fellow

**Hometown:** Fontem, Cameroon

**Undergraduate:** BS, Chemistry, Salem State University, Salem, Massachusetts

**Master's:** MS, Medical Science, The Ohio State University, Columbus, Ohio

**Doctorate:** MD, University of Michigan, Ann Arbor, Michigan

**Research Interests:** The role of CD38 in the hepatic stellate cell activation and response to ischemia reperfusion injury in the liver

**Faculty Advisor(s):** Sylvester Black, MD, PhD, and Ginny Bumgardner, MD, PhD



**Dathe Benissan-Messan, MD**

Clinical Instructor House Staff, General Surgery

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**Undergraduate:** BS, Biology, Creighton University, Omaha, Nebraska

**Master's:** MS, Clinical Anatomy, Creighton University, Omaha, Nebraska; In progress, Master of Medical Science, The Ohio State University

**Doctorate:** MD, University of Nebraska, Omaha, Nebraska

**Research Interests:** Tissue engineered muscles as a vehicle for the delivery of MG53 in the treatment of volumetric muscle loss

**Faculty Advisor(s):** Peter Lee, MD, PhD, MPH



**Lucia Casadei, PhD**

Research Specialist

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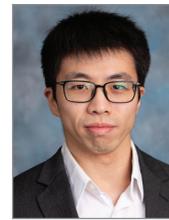
**Undergraduate:** BS, Pharmaceutical Biotechnology, University of Bologna, Italy

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**Research Interests:** miRNA, EVs, and sarcoma

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**Research Interests:** Radiotracer imaging, peripheral arterial disease, diabetes mellitus

**Faculty Advisor(s):** Mitchel Stacy, PhD



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**Research Interests:** Patient outcomes and quality improvement in colorectal surgery

**Faculty Advisor(s):** Syed Husain, MBBS



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**Undergraduate:** BA in biochemistry, New York University, New York, New York

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**Research Interests:** microRNA expression in melanoma and melanocytic lesions as diagnostic biomarkers and therapeutic targets

**Faculty Advisor(s):** William Carson III, MD



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 Graduate Research Associate  
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**Research Interests:** Novel nanotechnologies for immunomodulation and cell reprogramming in inflammation  
**Faculty Advisor(s):** Daniel Gallego-Perez, PhD, and William Carson III, MD



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 Postdoctoral Researcher  
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**Research Interests:** Targeting myeloid-derived suppressor cells in cancer, characterizing NRAS spliceforms in cancer  
**Faculty Advisor(s):** William Carson III, MD



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**Research Interests:** Cell survival, autophagy/mitophagy  
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 Research Fellow, Center for Surgical Outcomes  
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**Undergraduate:** Hamilton College, Clinton, New York  
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**Research Interests:** Pediatric general surgery, pediatric colorectal surgery, pediatric gastroenterology  
**Faculty Advisor(s):** Jennifer Cooper, PhD; Katherine Deans, MD, MHSc; and Peter Minneci, MD, MHSc



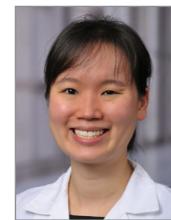
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**Research Interests:** Clinical trials and clinical outcomes in surgical oncology with a focus on pancreatic, liver and gallbladder cancer. Clinical outcomes in robotic-assisted hepatobiliary surgery  
**Faculty Advisor(s):** Aslam Ejaz, MD, MPH; Timothy Pawlik MD, PhD, MPH; and Allan Tsung, MD



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**Research Interests:** Adipocyte immunology post bariatric surgery, minimally invasive surgery, disparities in bariatric surgery  
**Faculty Advisor(s):** Willa Hsueh, MD; Sabrena Noria, MD, PhD; and Bradley Needleman, MD



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 MED III  
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**Doctoral:** In Progress, The Ohio State University, Columbus, Ohio  
**Research Interests:** Perioperative interventions to improve quality of care  
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 Cardiothoracic Surgery Clinical Fellow  
**Hometown:** East Lansing, Michigan  
**Undergraduate:** Biomedical Engineering, Johns Hopkins University, Baltimore, Maryland  
**Doctorate:** MD, Michigan State University, East Lansing, Michigan  
**Research Interests:** Mechanical circulatory support  
**Faculty Advisor(s):** Bryan Whitson, MD, PhD



**Haiwen Li, PhD**

Postdoctoral Fellow

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**Undergraduate:** Lanzhou University, Lanzhou, Gansu Province, China

**Master's:** Huazhong Agricultural University, Wuhan, Hubei Province, China

**Doctorate:** Beijing Institute of Radiation Medicine, Beijing, China

**Research Interests:** Mechanisms underlying muscular dystrophy and plasma membrane repair

**Faculty Advisor(s):** Renzhi Han, PhD



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**Hometown:** Shinjuku, Tokyo, Japan

**Undergraduate:** BA, Faculty of Science Department of Chemistry, Tokyo University of Science, Tokyo, Japan

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**Research Interests:** Regenerative Medicine, Cardiothoracic Surgery, Vascular Surgery

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Postdoctoral Fellow

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**Research Interests:** Immune mechanisms of tissue injury; outcomes research in surgical oncology; endocrine tumors

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**Research Interests:** Patient-provider communication

**Faculty Advisor(s):** Daniel Vazquez, MD; Timothy Pawlik, MD, PhD, MPH



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**Research Interests:** Assessing emergency general surgery care

**Faculty Advisor(s):** Heena Santry, MD, MS



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**Research Interests:** Tissue engineering, vascular grafts and implantation

**Faculty Advisor(s):** Christopher Breuer, MD



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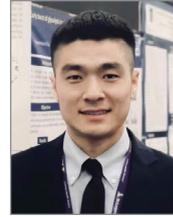
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**Faculty Advisor(s):** Christopher Breuer, MD



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**Research Interests:** Innate immune and inflammatory responses in liver sterile injury. Innate immunity in development of HCC. The role of hepatic immune responses after pre-operative exercise therapy  
**Faculty Advisor(s):** Allan Tsung, MD, and Hai Huang, MD



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**Faculty Advisor(s):** Jianjie Ma, PhD



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