UC DAVIS HEALTH
Department of Surgery

35th Annual

JAMES E. GOODNIGHT, JR. LECTURESHIP &

RESEARCH DAY SYMPOSIUM

APRIL 16, 2024

TRIALS AND TRIBULATIONS: FINDING YOUR ACADEMIC NICHE AS A SURGEON

FEATURING KEYNOTE SPEAKER, **DR. CAROL SWALLOW**

MEDICAL EDUCATION BUILDING
LECTURE HALL 2222

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PROGRAM NOTES

WELCOME FROM THE CHAIRS

Research is fundamental to advancement of medicine, surgery, and disease prevention strategies. Pursuit of knowledge and the discovery of breakthroughs translate into better outcomes for our patients. Every year, the Research Day Symposium gives us an opportunity to celebrate science and technical advancements made possible with the hard work and dedication of students, residents, fellows, staff, and faculty.

Our department continues to grow its research footprint and we can proudly point to many successes and new collaborations within the department and campus-wide. The breadth of studies is remarkable, spanning cell and molecular systems, data innovation, human research, and clinical trials of new treatments and devices. This environment creates a wealth of opportunities for training, supporting a core value of the Department of Surgery: to enable growth and scholarly activity among our early career investigators and surgeons.

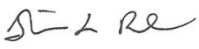
This year's Research Day Symposium spotlights this core value through oral and poster presentations covering an array of topics. The event allows us all to celebrate our innate curiosity, connect with peers, and form new collaborations.

At the end of the day, we will award prizes for the best clinical and translational science oral presentation, best basic science oral presentation, as well as awards for the best clinical and translational science and basic science posters.

We thank you for joining us today to celebrate science and research that will ultimately improve the lives of the patients we serve!

Sincerely,

Diana L. Farmer, MD, FACS, FRCS
Distinguished Professor and Pearl Stamps Stewart Endowed Chair
Chair, Department of Surgery, UC Davis School of Medicine
Surgeon-in-Chief Emeritus, UC Davis Children's Hospital
Chief of Pediatric Surgery, Shriners Hospitals – Northern California
Founder and Co-Director, Center for Surgical Bioengineering



Tina Palmieri, MD, FACS, FABA, MCCM
Research Day Co-Chair
Vice Chair for Clinical Trials Research
Professor and Helen Marian Bart Endowed Professor
Burn Division Chief, UC Davis
Chief of Burns, Shriners Children's Northern California

Sean H. Adams, MS, PhD, FTOS
Research Day Co-Chair
Vice Chair for Basic Research
Scientific Director, Center for Alimentary and Metabolic Science

RESEARCH DAY CO-CHAIRS

Dr. Tina Palmieri is Professor of Surgery, Burn Division Chief, and Vice Chair for Clinical Trials Research at the University of California Davis as well as Chief of Burns at Shriners Children's Northern California. Dr. Palmieri employs a team-based approach to both patient care and research. Clinically, she leads the UC Davis/Shriners burn center, providing state-of-the-art burn care to adults and children. She has also spearheaded translational burn injury research via team science and multicenter randomized prospective trials in blood transfusion, patient-centered outcomes, and critical care nationally and internationally. Her research focuses on uniting diverse teams of stakeholders to translate science into optimal clinical care.

Dr. Sean Adams serves as the Scientific Director for the UC Davis Center for Alimentary and Metabolic Science (CAMS). The mission of the CAMS is to conduct research that spans from the molecule to the bedside and to expand fundamental knowledge that has relevance to improve health and thwart disease.

Dr. Adams and his team work closely with clinical colleagues in Surgery and other departments to study the origins of metabolic disease and to identify factors that promote metabolic health. He has special expertise in nutrition, metabolic physiology, and "omics" applications.

CAMS investigators are at the forefront of understanding mechanisms that drive robust and rapid health improvements following metabolic surgery, the biology of pancreatic and gut hormones, factors that underlie cardiometabolic health profiles in obesity, and the role of gut microbe metabolism in shaping our physiology.

AGENDA | APRIL 16, 2024

TIME	SESSION	LOCATION
6:30 – 7:15 a.m.	Breakfast and Registration	ED 2222 & North Foyer
7:15 – 7:30 a.m.	Welcome and Introduction	ED 2222
7:30 – 8:45 a.m.	Oral Presentations Session 1	ED 2222
8:45 – 9:00 a.m.	*Break*	
9:00 – 10:15 a.m.	Oral Presentations Session 2	ED 2222
10:15 – 10:30 a.m.	*Break*	
10:30 – 11:30 a.m.	Goodnight Lecture/Keynote Presentation	ED 2222
11:45 a.m.– 1:15 p.m.	Lunch and Poster Sessions	BIMH 1000 & Lobby
1:30 – 2:45 p.m.	Oral Presentations Session 3	ED 2222
2:45 – 3:00 p.m.	*Break*	
3:00 – 4:15 p.m.	Oral Presentations Session 4	ED 2222
4:15 – 4:30 p.m.	Closing Remarks	ED 2222
5:00 – 7:00 p.m.	Awards Reception, Poster Viewing, and Social Hour	BIMH 1000 & Courtyard

ORAL PRESENTATIONS | SESSION 1 | ED2222 | 7:30–8:45 A.M.

TIME	PRESENTER AND TITLE
7:30–7:45 a.m.	***Annie Wang*** — Roux-en-y gastric bypass surgery decreases intestinal aryl hydrocarbon receptor signaling in male mice
7:45–8:00 a.m.	***Kathleen Doyle*** — A comparison of in vivo tumor-homing abilities of placental-derived and bone marrow-derived mesenchymal stromal cells in high-risk neuroblastoma
8:00–8:15 a.m.	***Melanie Reuter*** — Dietary resistant starch supplementation increases gut luminal deoxycholic acid abundance in mice
8:15–8:30 a.m.	***Marshall Lammers*** — Inhibitory receptor TIGIT has differential effects on circulating versus intratumoral natural killer and CD8+ T cells in human and mouse sarcoma models
8:30–8:45 a.m.	***Jean Debédat*** — Not all saturated lipids are equal: the case of Cyclopropane Fatty Acids (CpFAs) as anti-inflammatory mediators

Moderators: Drs. Miquell Miller, Ara A. Salibian

ORAL PRESENTATIONS | SESSION 2 | ED2222 | 9:00–10:15 A.M.

TIME	PRESENTER AND TITLE
9:00–9:15 a.m.	***Ashli Barnes*** — Elevated cell-free hemoglobin: a novel early biomarker following traumatic injury
9:15–9:30 a.m.	***Alyssa Bellini*** — Does community health impact individual patient inflammatory response to critical injury?
9:30–9:45 a.m.	***Emily Byrd*** — Treatment of pediatric intestinal ischemia reperfusion injury with engineered extracellular vesicles
9:45–10:00 a.m.	***Dattesh Dave*** — Defining the zone of acute peripheral nerve injury using Fluorescence Lifetime Imaging in a crush injury sheep model
10:00–10:15 a.m.	***Gregory Brittenham*** — Short Term Results of Cyclic Peptide LXW7 Coating on Prosthetic Graft Arteriovenous Fistula Creation in a Porcine (Sus scrofa) Model

Moderators: Dr. Hira Abidi, Lin-Chiang Philip Chou

LUNCH AND POSTER SESSIONS | BIMH1000 | 11:45 – 1:15 P.M.

SESSION 1 POSTERS	TITLE
Session 1, Poster 1	***Rahaf Shishani*** — Vertical Sleeve Gastrectomy Reduces Gut Luminal Deoxycholic Acid Concentrations in Mice
Session1 , Poster 2	***Rosalinda Moreno*** — Bile Acid Composition Changes Within Specific Brain Regions in Mice and with Dietary Resistant Starch
Session 1, Poster 3	***Kathleen Doyle*** — Novel Bioengineered MicroRNA Therapy for High-Risk Neuroblastoma
Session 1, Poster 4	***Louise Lanoue*** — In vivo functional risk assessment of patient-specific genetic variants for COVID-19 using novel genetically humanized polygenic mice.
Session 1, Poster 5	***Emily Byrd*** — Revisiting an ovine model for in utero repair of gastroschisis
Session 1, Poster 6	***Aryana Razmara*** — Canine NK cell atlas: Genomic profiling of blood and tissue-resident NK cells including genomic biomarkers from first-in-dog immunotherapy trials
Session 1, Poster 7	***David Wang*** — Hybridization of Extracellular Vesicles for the Targeted Treatment of Alzheimer's Disease
Session 1, Poster 8	***Kewa Gao*** — Densely PEGylated lipid nanoparticles globally transfect the brain in utero with mRNA for gene editing enzymes

SESSION 2 POSTERS	TITLE
Session 2, Poster 1	***Omar Ortuno*** — Pause the Repeat: Evaluating the Efficacy of Repeat Imaging In Transferred Pediatric Patients With Suspected Appendicitis
Session 2, Poster 2	***Daniel Castro*** — Incidental DVT Diagnosed on Lower Extremity CT Is a Rare but Clinically Impactful Finding.
Session 2, Poster 3	***Tyra Furtado*** — Biodegradable Temporizing Matrix Does Not Change Metabolic Rates After First Burn Excision Compared to Autografting
Session 2, Poster 4	***Cyrus Sholevar*** — Higher body mass index is associated with decreased circulating and intratumoral natural killer cells in soft tissue sarcoma.
Session 2, Poster 5	***Samuel Emerson*** — Size tunable Lipid Raft Nanovesicles (LRNVs) derived from placental mesenchymal stem cells as an EV-mimetic drug delivery platform

LUNCH AND POSTER SESSIONS | BIMH1000 | 11:45 – 1:15 P.M.

Session 2, Poster 6	***Leora Goldbloom-Helzner*** — Optimization of Aptamer Surface Conjugation onto Extracellular Vesicles (EVs) for Improved Function in the Context of Spinal Cord Injury (SCI)
Session 2, Poster 7	***Jordan Pitman*** — Preoperative Metabolic Health Status Alters Microbiota Response to Roux-en-Y Gastric Bypass
Session 2, Poster 8	***Kaitlin Clark*** — Biodistribution and Neuroprotective Effects of Placental Mesenchymal Stem Cell derived Extracellular Vesicles in Neonatal Hypoxic-Ischemic Encephalopathy: A Near-Term Ovine Model Study

SESSION 3 POSTERS	TITLE
Group 3, Poster 1	***Alexis Woods*** — Incidence, Characteristics and Costs of Patients Readmitted for Hypoparathyroidism after Thyroidectomy for Thyroid Cancer in California
Group 3, Poster 2	***John Lew*** — Sex Differences After Roux-en-Y Gastric Bypass (RYGB): Increased Preoperative Hypertension Severity in Men Portends Worse Hypertension Outcomes Postoperatively
Group 3, Poster 3	***Jessica Guzman*** — Upregulation of Inflammatory Marker Cytokine Profiles Immediately Following Traumatic Injury Predict 28-Day Mortality
Group 3, Poster 4	***Annie Wang*** — Metabolic Disease Remission Rates after Gastric Bypass are Dependent on Pre-Operative Disease Severity: Use of a New Objective Metabolic Scoring System
Group 3, Poster 5	***Ryan Cohen*** — Hyperkinetic Biliary Dyskinesia: An Underrecognized Problem with Good Surgical Outcomes After Cholecystectomy
Group 3, Poster 6	***Julia Riccardi*** — Predictors of Opioid Prescriptions Refill After Lung Cancer Resection
Group 3, Poster 7	***Matthew Farajzadeh*** — Use of ultra-high frequency ultrasound for lymphovenous bypass planning: initial experience
Group 3, Poster 8	***Diego Anaya*** — Single retrograde thoracic branch endoprosthesis versus traditional endovascular repair with subclavian coverage for treatment of blunt thoracic aortic injuries
Group 3, Poster 9	***Rachel Chan*** — Creation of a Surgical Outcomes Dashboard Incorporating Social Determinants of Health: A Novel Quality Improvement Tool to Address Health Equity

ORAL PRESENTATIONS | SESSION 3 | ED2222 | 1:30–2:45 P.M.

TIME	PRESENTER AND TITLE
1:30–1:45 p.m.	***Matileen Cranick*** — Rapidly Degrading Lipid Nanoparticles with an Acid-Degradable Cationic Lipid Serve as Lung-Targeting Therapeutic Delivery Vehicles to Rescue Lung Inflammation
1:45–2:00 p.m.	***Zoe Saenz*** — Bioengineered hydrogel with placental mesenchymal stem cell derived extracellular vesicles rescue ambulation in an ovine myelomeningocele model.
2:00–2:15 p.m.	***Sylvia Cruz*** — Inhaled IL-15 combined with amputation and chemotherapy for dogs with localized osteosarcoma
2:15–2:30 p.m.	***Julia Riccardi*** — Uncovering the Role of Platelet-driven Thrombo-inflammation in Post-traumatic ARDS-
2:30–2:45 p.m.	***Yofiel Wyle*** — Rescue Potential of Placenta- and Amniotic Fluid-Derived Mesenchymal Stem Cell Extracellular Vesicles (EVs) in Human Lung Models of Oxidative Stress and Apoptosis

Moderators: Drs. Jinhwan Kim, Melissa Keller

ORAL PRESENTATIONS | SESSION 4 | ED2222 | 3:00–4:15 P.M.

TIME	PRESENTER AND TITLE
3:00–3:15 p.m.	***Karima Alghannam*** — Immune Responses After Vaccination Against SARS-CoV-2 in Kidney Transplant Candidates and Recipients
3:15–3:30 p.m.	***Alexandra Coward*** — Burn Block Party: Fascia Iliaca Catheters for Donor Site Pain after Split-Thickness Skin Grafting for Acute Burn Injury
3:30–3:45 p.m.	***Aliyah Parker*** — Comprehensive Interpretation Services Use for Patients who are Non-English Primary Language Speakers undergoing Surgery for NSCLC
3:45–4:00 p.m.	***Matthew Vuoncino*** — Prophylactic Caval Stenting in Patients Undergoing Retroperitoneal Lymph Node Dissection
4:00–4:15 p.m.	***Alexis Woods*** — Definitive Treatment Coordination in Rectal Cancer Patients

Moderators: Drs. Jason Heard, Jamie E. Anderson

PROGRAM NOTES

JAMES E. GOODNIGHT JR. LECTURESHIP & KEYNOTE SPEAKER – DR. CAROL SWALLOW, M.D., Ph.D.

We are delighted to announce the distinguished **Dr. Carol Swallow** as this year's James E. Goodnight Jr. Lectureship and Research Symposium Keynote Speaker.

Dr. Swallow is a surgical oncologist and the RS McLaughlin Professor and Chair of the Department of Surgery at the University of Toronto. She is a Professor in the Department of Surgery and Institute of Medical Science at the University of Toronto as well as a surgeon at Princess Margaret Hospital and a member of the Division of General Surgery at Mount Sinai Hospital in Toronto. Dr. Swallow graduated from the University of Toronto Medical School and trained in the General Surgery residency program at the University of Toronto as a member of the Surgical Scientist Training Program, completing a PhD in cell biology and surgical sepsis in 1993. She completed a clinical fellowship training in Surgical Oncology at Memorial Sloan Kettering Cancer Center.

Her areas of clinical expertise include retroperitoneal sarcoma, gastrointestinal stromal tumor, gastric cancer, and advanced/recurrent rectal cancer. Her laboratory research is focused on predictors of tumor progression and resistance to therapy, including molecular/cellular mechanisms of tumor invasion and metastasis. She is the author of more than 175 peer-reviewed articles.

Dr. Swallow was the Director of the University of Toronto General Surgical Oncology Fellowship Program from 1997-2009, Head of the Division of General Surgery at Mount Sinai Hospital from 2008 to 2020, Chair of the Division of General Surgery at the University of Toronto since 2014, and Chair of the Department of Surgery at University of Toronto since July 1, 2022.

Currently, Dr. Swallow is the Governor of the Ontario Chapter of the American College of Surgeons. She has served as the President of the Canadian Society of Surgical Oncology and is the immediate Past-President of the Connective Tissue Oncology Society, and the Sarcoma Section Editor for the Annals of Surgical Oncology.

ORAL PRESENTATIONS

SESSION 1

ED 2222 | 7:30–8:45 A.M.

Annie Wang
Roux-en-y gastric bypass surgery decreases intestinal aryl hydrocarbon receptor signaling in male mice

Kathleen Doyle
A Comparison of in vivo Tumor-Homing Abilities of Placental-Derived and Bone Marrow-Derived Mesenchymal Stromal Cells in High-Risk Neuroblastoma

Melanie Reuter
Dietary resistant starch supplementation increases gut luminal deoxycholic acid abundance in mice

Marshall Lammers
Inhibitory receptor TIGIT has differential effects on circulating versus intratumoral natural killer and CD8+ T cells in human and mouse sarcoma models

Jean Debédat
Not all saturated lipids are equal: the case of Cyclopropane Fatty Acids (CpFAs) as anti-inflammatory mediators

Roux-en-y gastric bypass surgery decreases intestinal aryl hydrocarbon receptor signaling in male mice

Dr. Annie Wang MD[1], Ms. Madelynn Tucker BS[2], Dr. Michael Goodson PhD[3], Dr. Bethany Cummings DVM, PhD[4], Dr. Allison Ehrlich PhD[5]

[1]Department of Surgery, Center for Alimentary and Metabolic Sciences, School of Medicine, University of California -- Davis, Sacramento, CA, USA. [2]Department of Surgery, Center for Alimentary and Metabolic Sciences, School of Medicine, University of California - Davis, Sacramento, CA, USA. [3]Department of Anatomy, Physology, and Cell Biology, School of Veterinary Medicine, University of California, Davis, CA, USA. [4]Department of Surgery, Center for Alimentary and Metabolic Sciences, School of Medicine, University of California -- Davis, Sacramento, Sacramento, CA, USA. [5]Department of Environmental Toxicology, University of California – Davis, Davis, CA, USA

ABSTRACT

Introduction

Bariatric surgery has been associated with gut inflammation, though the pathophysiology remains elusive. The gut microbiota influence host health through several mechanisms, including the generation of indole metabolites. While bariatric surgery alters microbial indole metabolism, interpretation of these data are confounded by the fact that both weight loss and surgery may differentially impact microbial indoles. Therefore, we assessed weight-loss-dependent versus surgery-dependent effects on indole metabolites in a murine model.

Methods

Male C57BL/6J mice were placed on chow-based high fat diet for 2 months prior to undergoing sham or RYGB surgery. Sham-operated mice were either fed *ad libitum* (S-AL) or food restricted to match body weight to the RYGB-operated mice (S-WM). We compared glucose metabolism, gut luminal and plasma indole metabolite concentrations.

Results

RYGB-operated mice exhibited improved glucose tolerance, increased insulin secretion and increased glucagon-like peptide-1 (GLP-1) secretion compared with both S-WM and S-AL (P<0.05). Among immunoregulatory indoles, plasma levels of indole-3-propionic aid (I3PA) and kynurenic acid (KA) were reduced in RYGB mice compared to S-WM mice. Notably, these changes were in opposition to the effect of food restriction: S-WM increased plasma I3PA and KA concentrations compared to S-AL. A similar trend was observed in gut luminal I3PA levels. RYGB reduced *Cyp1a1* expression by 93% compared to S-WM mice (P<0.01). RYGB also resulted in a significant increase in *Lcn2*, a marker of intestinal inflammation, compared to S-WM mice (P<0.01)

Conclusion

Several indole metabolites are increased in S-WM compared to S-AL groups. However, RYGB resulted in body weight loss-independent reductions in I3PA and KA which was associated with a reduction in gut AhR signaling. Impaired AhR ligand production may be a previously undescribed mechanism through which bariatric surgery increases intestinal inflammation.

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A Comparison of in vivo Tumor-Homing Abilities of Placental-Derived and Bone Marrow-Derived Mesenchymal Stromal Cells in High-Risk Neuroblastoma

Dr. Kathleen Doyle MD[1], Ms. Maria Sutter BS[2], Ms. Monica Rodriguez BS[2], Dr. Abd-Elrahman Hassan MD[1], Dr. Priyadarsini Kumar PhD[2], Dr. Erin Brown MD[1]

[1]University of California Davis Department of Surgery, Sacramento, CA, USA. [2]Surgical Bioengineering Laboratory, Department of Surgery, Sacramento, CA, USA

ABSTRACT

Background

Neuroblastoma is the most common extracranial malignancy in young children. Survival remains poor in high-risk disease. Mesenchymal stromal cells (MSCs) may represent a novel cellular delivery vehicle due to their innate tumor-homing properties. We compared *in vivo* homing abilities of placental-derived MSCs (PMSCs) and bone marrow-derived MSCs (BM-MSCs) in a cell-derived orthotopic xenograft model of neuroblastoma.

Methods

Using an orthotopic xenograft model, 26 mice underwent direct injection of neuroblastoma cells (cell line NB1643) into the adrenal gland. Tumor growth was monitored with ultrasound, and once tumors were 0.5-1x the size of the ipsilateral kidney, mice underwent intraperitoneal injection of $5x10^6$ MSCs (PMSC n=13, BM-MSC n = 13). MSCs were labeled with GFP and luciferin gene. MSC migration was monitored with in vivo imaging system (IVIS) at 0, 6, 24, 48, and 72 hours post injection. 10 mice were euthanized at 72 hours (n=5 for each group), and 16 mice were survived to 7 days (n=8 for each group). Ex vivo IVIS was performed on adrenal masses and select organ tissues. Immunohistochemistry (IHC) confirmed presence of MSCs in tumor tissue.

Results

IVIS demonstrated initial diffuse MSC signal that migrated to the left abdomen. The signal decreased over time but persisted at day 7 in all animals. Ex vivo IVIS demonstrated signal in the adrenal tumor but not within other organs. There was no significant difference in average adrenal mass ex vivo radiance between PMSC mice and BM-MSC mice (p=0.74). IHC confirmed presence of both PMSCs and BM-MSCs in the tumor after necropsy.

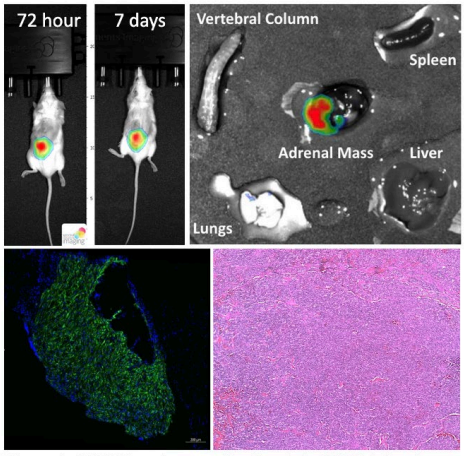

Figure 1: MSC homing results. Top left: IVIS bioluminescence signals *in vivo* at 72 hour and 7 day timepoints. Top right: IVIS ex vivo bioluminescence signals of organ tissues. Bottom left: GFP immunohistochemistry staining of adrenal mass for MSCs demonstrating signal within the tumor. Bottom right: H&E staining of adrenal mass confirming neuroblastoma.

Conclusion

Both PMSCs and BM-MSCs successfully migrated to neuroblastoma tumor tissues *in vivo* without evidence of migration to other organs. MSCs migrated within 72 hours and persisted in the tumor for up to 7 days. There was no significant difference in homing of PMSCs compared to BM-MSCs. Thus, either cell type has the potential to act as a drug delivery vehicle.

MELANIE REUTER, B.S.

Dietary resistant starch supplementation increases gut luminal deoxycholic acid abundance in mice

Ms. Melanie Reuter BS[1,2], Ms. Madelynn Tucker BS[1,2], Ms. Zara Marfori BS[1], Ms. Rahaf Shishani BS[1,2], Ms. Jessica Miranda Bustamante MS[1,2], Ms. Rosalinda Moreno BS[1,2], Dr. Michael L Goodson PhD[3], Dr. Allison Ehrlich PhD[3], Dr. Ameer Y. Taha PhD[4], Dr. Pamela J. Lein PhD[2], Mr. Nikhil Joshi MS[5], Dr. Ilana Brito PhD[6], Dr. Blythe Durbin-Johnson PhD[5], Dr. Renu Nandakumar PhD[7], Dr. Bethany P. Cummings DVM PhD[1,2]

[1]University of California - Davis, Center for Alimentary and Metabolic Sciences, Sacramento, CA, USA. [2]University of California - Davis, Department of Molecular Biosciences, Davis, CA, USA. [3]University of California - Davis, Department of Environmental Toxicology, Davis, CA, USA. [4]University of California - Davis, Department of Food Science and Technology, Davis, CA, USA. [5]University of California - Davis, UC Davis Genome Center, Davis, CA, USA. [6]Cornell University, Meinig School of Biomedical Engineering, Ithaca, NY, USA. [7]Columbia University, Irving Institute for Clinical and Translational Research, New York, NY, USA

ABSTRACT

Introduction

Bile acids (BA) are among the most abundant metabolites produced by the gut microbiome. Primary BAs produced in the liver are converted by gut bacterial 7-α-dehydroxylation into secondary BAs, which can differentially regulate host health via signaling based on their varying affinity for BA receptors. Despite the importance of secondary BAs in host health, the regulation of 7-α-dehydroxylation and the role of diet in modulating this process is incompletely defined. Understanding this process could lead to dietary guidelines that beneficially shift BA metabolism. Dietary fiber regulates gut microbial composition and metabolite production.

Methods

We tested the hypothesis that feeding mice a diet rich in a fermentable dietary fiber, resistant starch (RS), would alter gut bacterial BA metabolism. Male and female wild-type mice were fed a diet supplemented with RS or an isocaloric control diet (IC).

Results

Metabolic parameters were similar between groups. RS supplementation increased gut luminal deoxycholic acid (DCA) abundance. However, gut luminal cholic acid (CA) abundance, the substrate for 7-α-dehydroxylation in DCA production, was unaltered by RS. Further, RS supplementation did not change the mRNA expression of hepatic BA producing enzymes or ileal BA transporters. Metagenomic assessment of gut bacterial composition revealed no change in the relative abundance of bacteria known to perform 7-α-dehydroxylation. *P. ginsenosidimutans* and *P. multiformis* were positively correlated with gut luminal DCA abundance and increased in response to RS supplementation.

Conclusion

These data demonstrate that RS supplementation enriches gut luminal DCA abundance without increasing the relative abundance of bacteria known to perform 7-α-dehydroxylation. This supports a role for bacteria not directly involved in 7-α-dehydroxylation in the regulation of the pathway and shows how much there is to learn about complex gut microbial regulation and its impact on host health.

MARSHALL LAMMERS, B.S.

Inhibitory receptor TIGIT has differential effects on circulating versus intratumoral natural killer and CD8+ T cells in human and mouse sarcoma models

Mr. Marshall Lammers B.S[1], Dr. Sean Judge MD[2], Dr. Cyrus Sholevar MD[3], Dr. Alicia Gingrich MD[4], Ms. Khurshid Iranpur B.S[5], Ms. Lauren Farley B.S[6], Mr. Ryan Nielsen M.S[7], Dr. Arta Monjazeb MD, PhD[8], Dr. Steven Thorpe MD[9], Dr. William Murphy PhD[7], Dr. Robert Canter MD[1]

[1]UC Davis, Surgical Oncology, Sacramento, CA, USA. [2]MSK, Surgical Oncology, New York, NY, USA. [3]UC Davis, Surgery, Sacramento, CA, USA. [4]MD Anderson, General Surgery Oncology, Houston, TX, USA. [5]UC Santa Cruz, Toxicology, Santa Cruz, CA, USA. [6]Neogene Therapeutics, Santa Monica, CA, USA. [7]UC Davis, Dermatology, Sacramento, CA, USA. [8]UC Davis, Radiation Oncology, Sacramento, CA, USA. [9]UC Davis, Orthopaedic Surgery, Sacramento, CA, USA

ABSTRACT

Introduction

TIGIT has been identified as a key inhibitory receptor on natural killer (NK) and CD8+ T cells, but clinical trials of anti-TIGIT antibodies have shown mixed results. We hypothesized that a subset of TIGIT+ NK and CD8+ T cells are associated with increased anti-tumor function given the interplay of stimulation and inhibition in regulating immune responses.

Method

NK and CD8+ T cells were analyzed from the circulation and tumor microenvironment (TME) of human and murine sarcomas for phenotype and function. Immune readouts, including TIGIT expression, were also analyzed for their association with outcomes.

Results

In contrast to NK cells from the TME, TIGIT+ NK cells from the blood of sarcoma patients were more activated (CD69, NKp46, Granzyme B) than TIGIT- NK cells ($p<0.05$). Compared to TIGIT- NK cells, TIGIT+ NK cells from the blood of sarcoma patients also showed greater expansion in vitro ($p=0.005$) with less apoptosis. We observed significantly more TIGIT+ NK cells in the TME compared to the blood of sarcoma patients ($p<0.05$), but the hyper functionality of TIGIT+ NK cells was not observed. Overall NK function was decreased consistent with immune exhaustion. In a mouse osteosarcoma model TIGIT+ NK cells from the spleen were significantly more activated than TIGIT- NK cells ($p< 0.05$), whereas TIGIT+ NK cells from the TME were more inhibited . TIGIT+ CD8+ T cells from human and mouse TME showed significantly higher expression of additional inhibitory markers (PD-1, TIM-3). There was no difference in clinical outcomes between sarcoma patients with high and low TIGIT expression, but higher expression of CD155, the TIGIT ligand, was associated with worse survival.

Conclusion

Our data suggest that circulating TIGIT+ NK and CD8 T cells display increased activation and decreased apoptosis which appears to be lost when they enter the TME, suggesting tissue-specific effects of TIGIT with implications for how TIGIT block may be applied clinically.

DR. JEAN DEBÉDAT, Pharm.D, Ph.D.

Not all saturated lipids are equal: the case of Cyclopropane Fatty Acids (CpFAs) as anti-inflammatory mediators

Dr Jean Debédat PharmD/PhD, Ms Lorena Pastor BS, Dr Trina Knotts PhD, Dr Sean Adams PhD
University of California Davis, Department of Surgery, Sacramento, CA, USA

ABSTRACT

Introduction
The human gut is home to at least a trillion microbes that produce a myriad of xenometabolites derived from food, host, and environmental precursors linking the host and the gut microbiome. Cyclopropane fatty acids (CpFAs), unique saturated lipids harboring a cyclopropane ring, are synthesized by bacteria and found in certain foods. Our preliminary results and the literature suggest that CpFAs are part of the human plasma and tissue lipidome; yet, their functions are mostly unexplored. CpFAs are structurally bent, and thus resemble unsaturated FAs. We hypothesize that CpFAs, like unsaturated FAs, could reduce inflammation in cultured macrophages.

Method
Five CpFAs, including 2 novel odd-chain CpFAs, were studied: C15:Δ11-12, C16:Δ9-10, C17:Δ13-14, C18:Δ9-10 and C18:Δ11-12. RAW 264.7 macrophages were serum starved (0.25%) for 4 hours before being exposed to 37.5 to 150 µM of FAs conjugated to BSA (2%) for 24 hours. For LPS stimulation, 5 ng/mL of LPS was added 5 hours before the end of the FA treatment. The differences in expression of different inflammatory cytokines (IL6, NOS2, TNFa, IL1b, CCL2, CCL5) were studied by qPCR.

Results
Treatment with CpFAs led to a significant reduction in the expression of pro-inflammatory cytokines in both basal and LPS-induced inflammatory conditions in a dose-dependent manner. Most CpFAs were as effective, if not more so, than related MUFAs, but not as good as DHA, a potent anti-inflammatory PUFA. CpFA pools (30 µM each; total: 150 µM) induced a greater reduction of inflammatory signals than MUFA pools at the same concentrations.

Conclusion
Cyclopropane fatty acids effectively attenuate inflammation in RAW 264.7 macrophages. These novel results provide support for the concept that raising levels of CpFAs through supplementation or strategic probiotics could have utility in the treatment of inflammatory bowel diseases. Studies are planned to test this idea in rodent models of colitis.

ORAL PRESENTATIONS

SESSION 2

ED 2222 | 9:00–10:15 A.M.

Ashli Barnes
Elevated Cell-free Hemoglobin: A Novel Early Biomarker Following Traumatic Injury

Alyssa Bellini
Does community health impact individual patient inflammatory response to critical injury?

Emily Byrd
Treatment of pediatric intestinal ischemia reperfusion injury with engineered extracellular vesicles

Dattesh Dave
Defining the zone of acute peripheral nerve injury using Fluorescence Lifetime Imaging in a crush injury sheep model

Gregory Brittenham
Short Term Results of Cyclic Peptide LXW7 Coating on Prosthetic Graft Arteriovenous Fistula Creation in a Porcine (Sus scrofa) Model

ASHLI BARNES, B.S.

Elevated Cell-free Hemoglobin: A Novel Early Biomarker Following Traumatic Injury

Dr. James Ross MD[1], Dr. Anamaria Robles MD[1], **Ms. Ashli Barnes BS[1]**, Dr. Alyssa Bellini MD[1], Dr. Alexandre Mansour MD[2], Dr. Nicholas Nesseler MD, Ph.D.[2], Dr. Kenneth Remy MD, MHSc, MSCI[3], Dr. Rachael Callcut MD, MSPH[1]

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ABSTRACT

Introduction

Cell-free hemoglobin (CFH) is a potent mediator of endotheliopathy and organ injury in sepsis but its role in trauma is unknown. In sepsis, injured erythrocytes release CFH and ultimately heme, which are cleared by haptoglobin and hemopexin respectively. This study investigates the presence of circulating CFH immediately after injury.

Methods

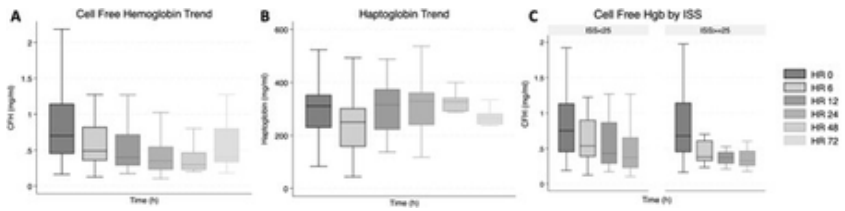
Adult traumas presenting as highest-level activations were enrolled (2021-2023) prospectively at a level-1 trauma center. Venous blood was collected at ED arrival (pre-transfusion), 6, 12, 24, 48 and 72 hours. Plasma CFH, haptoglobin and hemopexin were measured (Drabkin's and ELISA).

Results

The cohort (n=115) had a median age 48 years [31-65], 85% male, with a median ISS 21 [11-29], 11% 28-day mortality, and 61% transfused in first 24h. Median plasma CFH was elevated at 0h and was significantly lower at 12 and 24h (0.7 mg/ml [0.5-1.1] 0h vs. 0.4 mg/ml [0.3-0.7] 12h, p=0.005, **Fig A**). Plasma haptoglobin decreased significantly from 0 to 6h, suggesting CFH binding, returning to presentation levels by 24h (311 mg/ml [229-353] 0h vs. 250 mg/ml [158-302] 6h, p=0.0096, **Fig B**). There was no change in hemopexin. For ISS≥25, there was a dramatic decrease in CFH within 6h (0-6h p=0.005), with a trend towards lower 6h CFH in ISS≥25 compared to ISS<25 (p=0.08, **Fig C**). The haptoglobin nadir remained at 6h in the ISS≥25 subset and recovered significantly by 24h (p=0.03).

Conclusions

This is the first study to our knowledge to demonstrate that endogenous hemolysis very early after injury generates excess plasma CFH, which is present at ED arrival prior to transfusion, and sufficient to deplete haptoglobin. Notably, more severely injured patients tended towards a lower CFH at 6 hours, possibly due to haptoglobin induction.



DR. ALYSSA BELLINI, M.D.

Does community health impact individual patient inflammatory response to critical injury?

Dr. Alyssa Bellini MD[1], Dr. Tyler Carcamo MD[1], Dr. Jessica Guzman MD[1], Dr. Julia Riccardi MD[1], Ms. Ashli Barnes BS[1], Dr. James Ross MD[2], Dr. Anamaria Robles MD[1], Dr. Rachael Callcut MD[1]

[1]Department of Surgery, Sacramento, CA, USA. [2]Case Western University, Cleveland, OH, USA

ABSTRACT

Introduction

Upregulation of inflammation has been implicated as a potential driver of differential outcome after traumatic injury. Non-trauma data has shown community health impacts chronic stress levels measured by inflammatory marker upregulation. The California Healthy Places Index (HPI) measures community health based on factors such as educational level, air/water pollution, and economic status. This study aims to investigate the impact of community health on the inflammatory response to critical injury.

Methods

Highest level trauma activation patients enrolled in a prospective cohort study from 2021-2023 were included. Those with an initial blood sample obtained within 30 minutes of arrival were enrolled. Baseline patient and injury factors were collected. HPI was used to group patients into high and low groups (low=lower community health). A 26-plex cytokine Luminex panel was performed. Groups were compared using Kruskal Wallis, Wilcoxon, and regression modeling as appropriate.

Results

385 patients were enrolled, with median age 43 y (IQR 30-59), 71% bluntly injured, 35% with injury severity score (ISS) >15, and 37% in the low HPI group. There were no demographic differences across groups ($p>0.05$). Overall mortality was 7% and did not vary between HPI groups ($p=0.2$). When comparing baseline inflammatory markers across HPI groups, pro-inflammatory markers IL4 ($p=0.003$), IL5 ($p=0.004$), IL7 ($p=0.03$), and TNF-alpha ($p=0.02$) were different between groups (Table) with IL5 and IL7 ($p=0.002$, 0.039) remaining significant when controlling for increasing age (a known pro-inflammatory state). Multivariate regression controlled for age, ISS, and HPI found markers IL1 alpha ($p=0.02$), IL5 ($p=0.004$), IL7 ($p=0.002$), and IL8 ($p=0.01$) were independent predictors of 28-day mortality.

Conclusions

Community health measured by HPI is associated with differential cytokine profiles immediately following injury and these cytokine biomarkers were associated with poor outcomes.

Treatment of pediatric intestinal ischemia reperfusion injury with engineered extracellular vesicles

Dr. Emily Byrd MD, PhD[1], Dr. Zoe Saenz MD[1], Mr. Chris Pivetti MS[1], Mrs. Leora Goldbloom-Helzner MS[2], Dr. Shinjiro Hirose MD[1], Dr. Diana Farmer MD[1], Dr. Aijun Wang PhD[2]
[1]University of California Davis, Division of Pediatric General, Thoracic, and Fetal Surgery, Sacramento, CA, USA.
[2]University of California Davis, Department of Surgery, Sacramento, CA, USA

ABSTRACT

Introduction
Intestinal ischemia reperfusion injury (IRI) is one of the primary mechanisms of intestinal injury in multiple pediatric diseases. Extracellular vesicles (EVs) derived from placental mesenchymal stem cells (PMSCs) may represent a potent therapy for the treatment of IRI via known pro-angiogenic, anti-inflammatory, and neuroprotective mechanisms. PMSC-EVs labeled with a collagen binding peptide (SILY) may demonstrate increased therapeutic efficacy due to local tissue retention of SILY- EVs.

Methods
EVs were cultured from PMSCs and analyzed with Nanoparticle Tracking Analysis (NTA) and western blot. TAMRA-labeled SILY peptide was conjugated to PMSC-EVs via click chemistry with conjugation efficiency determined by Exoview co-labeling of EV particles with CD9 and CD63 (n = 2). IRI was induced in postnatal day 14 rats by clamping of the superior mesenteric artery for 30 minutes, followed by intraperitoneal administration of DiD-labeled PBS or SILY-EVs, with *in vivo* fluorescent imaging every 48-72 hours.

Results
PMSC-EVs were isolated and successfully validated by NTA for size (~100 nm) and by western blot with expression of EV-specific membrane proteins (ALIX, TS101, CD9, CD63, CD81). Exoview analysis demonstrated a SILY conjugation efficiency of 77% (n = 2). A pilot study with 2 rats that underwent IRI with administration of PBS or SILY-EVs demonstrated SILY-EVs successfully localized to the abdomen, with SILY-EV retention up to 7 days after treatment (Fig. 1).

Conclusion
We demonstrate successful PMSC-EV collection with high SILY-EV conjugation efficiency. In addition, SILY-EV conjugation resulted in increased local retention up to 7 days post-treatment in a pilot study. Ongoing investigations will continue to compare SILY-EV retention to un-conjugated PMSC-EVs and will assess the therapeutic effects of PMSC-EVs and SILY-EVs in the treatment of intestinal IRI.

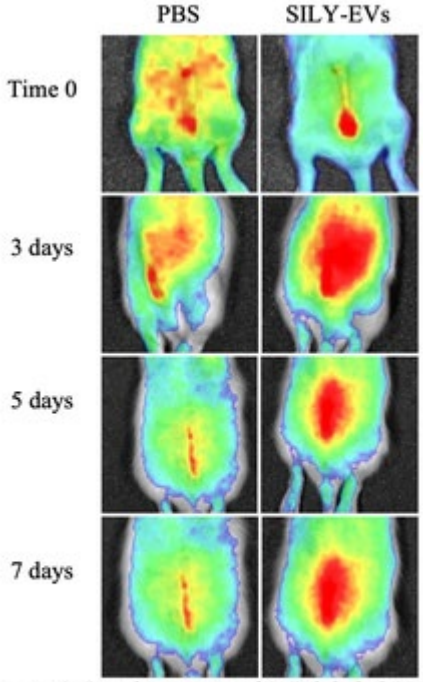


Figure 1: Local retention of DiD labeled PBS vs. SILY-EVs after intraperitoneal administration in a rat IRI model by fluorescent in vivo imaging at post-treatment days 0, 3, 5, and 7 (n = 1).

DR. DATTESH DAVE, M.D.

Defining the zone of acute peripheral nerve injury using Fluorescence Lifetime Imaging in a crush injury sheep model

Dr. Dattesh Dave MD[1], Dr. Alba Alfonso-Garcia PhD[2], Ms. Lisanne Kraft M.S.[3], Dr. Laura Marcu PhD[3], Dr. Clifford Pereira MD[1]

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ABSTRACT

Hypothesis

Current technologies to define the zone of acute peripheral nerve injury intraoperatively are limited by surgical experience, time, cumbersome electrodiagnostic equipment and interpreter reliability. In this pilot study, we evaluate a novel, real-time label-free optical technique for intraoperative nerve injury imaging. We hypothesize that fluorescence lifetime imaging (FLIm) will detect a difference between the time-resolved fluorescence signatures for acute crush injuries versus uninjured segments of sheep peripheral nerves.

Methods

Label-free FLIm uses ultraviolet laser pulses to excite endogenous tissue fluorophores and detect their fluorescent decay over time – generating real time tissue-specific signatures. A crush injury was produced in 8 peripheral nerves of 2 sheep. A handheld FLIm instrument captured the time-resolved fluorescence signatures of injured and uninjured nerve segments across 3 spectral emission channels (390/40 nm, 470/28 nm, and 540/50 nm). Two-sample T-test evaluated average FLIm parameters (i.e., lifetime and intensity ratios) for injured and uninjured nerve segments. We harnessed linear discriminant analysis (LDA) to differentiate between crushed and uninjured nerve segments.

Results

Sampling produced a total of 23,692 point- measurements from 8 peripheral nerves of two sheep. Histology confirmed the zone of injury. Average lifetime at 470 nm and 540 nm were statistically different between crushed and uninjured sheep nerve segments ($p<.01$, 95% CI 1.9-4.4). The LDA analysis differentiated between crushed and uninjured areas of 8 nerve segments with 92% sensitivity, 85% specificity, and 88% accuracy.

Summary

• In this pilot study, FLIm significantly detected differing average lifetime values for crushed versus uninjured sheep peripheral nerves with high sensitivity, specificity, and accuracy.

• Future studies will evaluate FLIm's ability to detect more subtle acute and chronic nerve injuries.

Short Term Results of Cyclic Peptide LXW7 Coating on Prosthetic Graft Arteriovenous Fistula Creation in a Porcine (Sus scrofa) Model

Dr. Gregory Brittenham DO, Dr. Mimmie Kwong MD, Mr. Christopher Pivetti MS, Dr. Aijun Wang PhD
UC Davis Medical Center, Sacramento, CA, USA

ABSTRACT

Introduction
Previous in vitro and in vivo studies using LXW7-coated grafts have demonstrated successful capture of endothelial progenitor cells and endothelial cells, which then promotes re-endothelialization of these materials. This study aims to assess the function of LXW7 coating on arteriovenous fistula expanded polytetrafluoroethylene (ePTFE) graft thrombus formation and patency in a large animal model.

Method:
Eight female and two male Yorkshire pigs underwent implantation of bilateral common carotid artery to internal jugular vein fistulas using plain and LXW7-coated ePTFE grafts. Angiography intra-op immediately after graft implantation was used to confirm patency. Ultrasound was performed at 3- and 6-weeks post implantation to assess for graft patency, after which, animals were sacrificed and grafts were harvested for histological evaluation.

Progress:
Anesthetic complications necessitated euthanasia of the two male pigs at the beginning of the study, after which, only female pigs were used. 2 of the female pigs during the post-op period experienced complications leading to death. Ultrasound performed at 3 weeks for the remainder of the pigs showed likely evidence of occlusion in all the grafts except for 2. 6-week ultrasound and subsequent graft harvesting after animal sacrifice showed complete occlusion of the bilateral grafts in all the remaining pigs.

Conclusion/Next Steps
This is the first study using an arteriovenous fistula model to assess the effectiveness of LXW7 on prosthetic graft patency in a clinically relevant large animal model. Previous studies using an interposition model showed improved patency in the grafts treated with LXW7 were not able to be reproduced in this most recent study, most likely due to turbulent flow created in the grafts. In light of these findings, we plan to begin another arm of the study with the use of an ovine model to address issues encountered with the porcine model.

ORAL PRESENTATIONS

SESSION 3

ED 2222 | 1:30–2:45 P.M.

Matileen Cranick
In utero delivery of mRNA to the heart, diaphragm and muscle with lipid nanoparticles to treat Duchenne muscular dystrophy

Zoe Saenz
Bioengineered hydrogel with placental mesenchymal stem cell derived extracellular vesicles rescue ambulation in an ovine myelomeningocele model.

Sylvia Cruz
Inhaled IL-15 combined with amputation and chemotherapy for dogs with localized osteosarcoma

Julia Riccardi
Uncovering the Role of Platelet-driven Thrombo-inflammation in Post-traumatic ARDS

Yofiel Wyle
Rescue Potential of Placenta- and Amniotic Fluid-Derived Mesenchymal Stem Cell Extracellular Vesicles (EVs) in Human Lung Models of Oxidative Stress and Apoptosis

MATILEEN CRANICK, B.S.

Rapidly Degrading Lipid Nanoparticles with an Acid-Degradable Cationic Lipid Serve as Lung-Targeting Therapeutic Delivery Vehicles to Rescue Lung Inflammation

Matileen Cranick B.S.[1], Sheng Zhao PhD[2], Kewa Gao MD, PhD[1], Hesong Han PhD[2], Yofiel Wyle B.S., M.S.[1], Boyan Yin B.S.[1,2], Hengyue Song MD, PhD[1], Aijun Wang PhD[1], Niren Murthy PhD[2], Diana Farmer MD, FACS, FRCS[1]

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ABSTRACT

Introduction

Acute lung injury (ALI) is characterized by inflammatory tissue damage. IL-22, an anti-inflammatory cytokine, is a promising therapeutic due to its ability to enhance tissue repair. In this study, we developed a treatment strategy of administering IL-22 mRNA in lung-targeting acid-degradable cationic lipid nanoparticles (ADC-LNPs) to LPS-induced ALI mouse model, effectively inhibiting the inflammatory response.

Methods

Ai9 mice were intravenously injected with ADC-LNPs loaded with CRE mRNA and after 2 weeks, the biodistribution and transfection efficiency of ADC-LNPs were assessed by flow cytometry and histological analysis. The ALI murine model was induced by non-invasive intratracheal LPS administration and treated by intravenous injection of IL-22 mRNA in Std-LNPs and ADC-LNPs. Bronchoalveolar lavage fluid (BALF) was collected 4 days later and the amount of protein in the BALF was measured using BCA to evaluate the immuno-regulatory function of the treatment.

Results

After a single intravenous injection of CRE mRNA in ADC-LNPs, approximately 70% of cells in the alveolus (Fig1A) and 50% of total lung cells (Fig1B) in Ai9 mice were transfected after 2 weeks, with minimal transfection in other internal organs (Fig 1B). IL-22 mRNA in either ADC-LNPs or Std-LNPs was injected intravenously into C57BL/6 mice 4 hours before intratracheal LPS administration. At 4 days post-injection, IL-22 in ADC-LNPs notably alleviated lung edema and inflammation. The BCA analysis of the BALF demonstrated that the ADC-LNPs significantly decreased protein quantity in the lung fluid compared to the LPS only group, whereas the Std-LNPs did not ($p<0.01$).

Conclusion

These results demonstrate that ADC-LNPs can effectively deliver mRNA to the lung tissue after systemic administration. The IL-22 delivered by ADC-LNPs can significantly alleviate the inflammatory response in the LPS-induced ALI mouse, and offers a lung-targeting therapeutic strategy for various lung disorders.

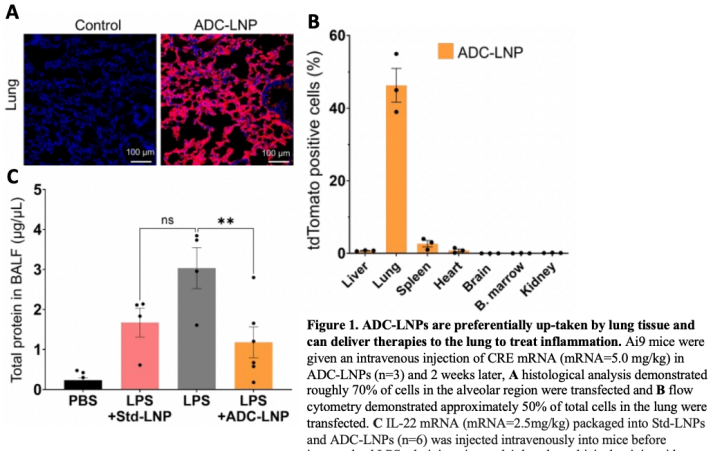


Figure 1. ADC-LNPs are preferentially up-taken by lung tissue and can deliver therapies to the lung to treat inflammation. Ai9 mice were given an intravenous injection of CRE mRNA (mRNA=5.0 mg/kg) in ADC-LNPs (n=3) and 2 weeks later, **A** histological analysis demonstrated roughly 70% of cells in the alveolar region were transfected and **B** flow cytometry demonstrated approximately 50% of total cells in the lung were transfected. **C** IL-22 mRNA (mRNA=2.5mg/kg) packaged into Std-LNPs and ADC-LNPs (n=6) was injected intravenously into mice before intratracheal LPS administration and 4 days later, bicinchoninic acid (BCA) analysis of the BALF demonstrated that the ADC-LNPs significantly decreased protein quantity in the lung fluid compared to the LPS only group, whereas the Std-LNPs did not ($p<0.01$).

DR. ZOE SAENZ, M.D.

Bioengineered hydrogel with placental mesenchymal stem cell derived extracellular vesicles rescue ambulation in an ovine myelomeningocele model

Ms. Zoe Saenz MD, Mr. Dake Hao PhD, Ms. Kate Doyle MD, Ms. Monalisa Hassan MD, Mr. Juan Lopez BS, Ms. Emma Loll BS, Mr. Christopher Pivetti MS, Mrs. Priyadarsini Kumar PhD, Mrs. Diana Farmer MD, Mr. Aijun Wang PhD
UC Davis Medical Center, Department of Surgery, Research, Sacramento, CA, USA

ABSTRACT

Purpose
Myelomeningocele (MMC), is the incomplete closure of the neural tube, and the most common congenital cause of lifelong paralysis in the US. Placental derived mesenchymal stem cells seeded on extracellular matrix (PMSC-ECM) is a viable therapy for MMC in utero surgical repair using the well-established ovine model, rescuing ambulation, and improving neurologic function. Investigating an alternative cell-free therapy that mimic the paracrine effects of PMSCs to protect neurons is hence worthwhile. Extracellular vesicles (EVs) play an important role in cell-to-cell communication making them an excellent candidate for a potential cell-free therapy. Our objective is to develop a bioengineered hydrogel with PMSC-EVs and assess its neuroprotective functions in vivo using the ovine MMC model.

Methods
PMSC-EV's were mixed with 1mL solution of 2mg/mL rat tail collagen at a density of 5 X 1010 EVs/mL per and gelled for 1 hour at 37°C. Fetal lambs were treated with the PMSC-EV-ECM product at ~100 days gestation after surgical defect creation. The lambs were delivered at term via C-section and assessed at 24 hours for motor function and ambulation using the Sheep Locomotor Score (SLR).

Results
Four lambs underwent SLR scoring. Three lambs scored a 15, indicating normal motor function and one lamb scored a 13. All lambs treated with PMSC-EV-ECM were able to ambulate. These lambs were compared to historical controls that received ECM only which scored a median SLR score of 4 (n=6) and were unable to ambulate. Lambs treated with PMSC-EV-ECM had improved locomotor outcomes.

Conclusion
We present PMSC derived EVs as a novel potential cell-free therapy to augment in utero ovine repair of MMC. We have demonstrated that bioengineering an EV-based hydrogel is feasible and can rescue ambulation as previously observed with use of a PMSC-ECM cell-based product.

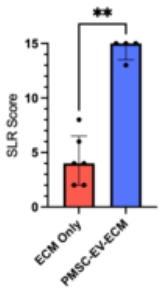


Figure 1. All lambs were scored with SLR. Lambs treated with PMSC-EV-ECM had significantly higher SLR scores in comparison to ECM only lambs (p=0.0095).

Inhaled IL-15 combined with amputation and chemotherapy for dogs with localized osteosarcoma

Ms. Sylvia M. Cruz BS[1], Dr. Robert Rebhun PhD[2], Dr. Daniel York PhD[2], Ms. Aryana Razmara MS[1], Ms. Lauren Farley BS[1], Ms. Khurshid Iranpur BS[1], Dr. Rachel Brady DVM[3], Dr. Eric Johnson DVM[2], Dr. Jenna Burton DVM[4], Dr. Jennifer Willcox DVM[2], Dr. Luke Wittenburg DMV, PhD[2], Dr. Kevin Woolard DVM, PhD[5], Dr. Cordelia Dunai PhD[6], Dr. Susan Stewart PhD[7], Dr. Ellen Sparger DVM, PhD[8], Ms. Sita Withers BVSc[9], Dr. Katherine Skorupski DVM[2], Dr. Sami Al-Nadaf DVM[2], Dr. Amandine LeJeune DVM[2], Dr. William Culp DVM[2], Dr. William Murphy PhD[6], Dr. Michael Kent DVM[2], Dr. Robert Canter MD[1]

[1]Division of Surgical Oncology, Department of Surgery, University of California, Davis, Sacramento, CA, USA. [2]Department of Surgical and Radiological Sciences, School of Veterinary Medicine, University of California, Davis, Davis, CA, USA. [3]Flint Animal Cancer Center, Colorado State University College of Veterinary Medicine, Fort Collins, CO, USA. [4]Department of Clinical Sciences, Colorado State University College of Veterinary Medicine, Fort Collins, CO, USA. [5]Pathology, Microbiology and Immunology, School of Veterinary Medicine, University of California, Davis, Davis, CA, USA. [6]Department of Dermatology, University of California, Davis, Sacramento, CA, USA. [7]Division of Biostatistics, Department of Public Health Sciences, University of California, Davis, Davis, CA, USA. [8]Medicine and Epidemiology, School of Veterinary Medicine, University of California, Davis, Davis, CA, USA. [9]Department of Veterinary Clinical Sciences, School of Veterinary Medicine, Louisiana State University, Baton Rouge, LA, USA

ABSTRACT

We have previously shown that inhaled IL-15 is associated with anti-tumor responses in dogs with metastatic osteosarcoma (OSA) and melanoma. Here, we evaluated inhaled IL-15 combined with amputation and chemotherapy for dogs with localized OSA eligible for treatment with curative intent. In a multicenter phase II trial, we hypothesized that 2 weeks of inhaled IL-15 after amputation and prior to chemotherapy could reduce the risk of metastatic failure at the completion of chemotherapy from a historical rate of 40% to 20% for dogs with limb OSA. With a 2-sided alpha of 0.05, we planned an accrual of 40 dogs to demonstrate this difference with 80% power. Immune correlative assays and sequencing of blood immune cells (PBMCs) were performed. Analysis after 36 dogs revealed a metastatic failure rate of 56% so the trial was halted for futility with oncologic outcomes statistically inferior to a well-validated historical control cohort ($P<0.01$). Cytotoxicity assays of PBMCs showed significant decreases after both surgery and chemotherapy with an overall decrease from the start to the end of therapy (-18.2±16.1%, $P<0.001$). Fold change in cytotoxicity correlated significantly with dog survival ($P=0.02$, $r=0.49$). Although plasma concentrations of key cytokines varied markedly with no significant differences between disease-free and metastatic-failure patients, inflammatory cytokines such as IL-6 showed absolute increases post-amputation and post-chemotherapy consistent with the decreases in cytotoxicity. Preliminary sequencing data are consistent with upregulation of IL-15RA on myeloid derived suppressor cells. Inhaled IL-15 as part of multimodality approach with amputation and chemotherapy appears to be associated with worse outcomes in dogs with localized OSA. Correlative assays suggest significant effects of amputation and chemotherapy on immune responses. These data have important implications for the sequencing for immunotherapy in the context of other cancer modalities.

DR. JULIA RICCARDI, M.D.

Uncovering the Role of Platelet-driven Thrombo-inflammation in Post-traumatic ARDS-

Dr. Julia Riccardi MD, Dr. Anamaria Robles MD, Dr. James Ross MD, Dr. Ian Brown MD, PhD, Ms. Carrie Lewis MPH, Dr. Matthew Mell MD, Dr. John Holcomb MD, Dr. Rachael Callcut MD, MSPH
University of California Davis, Division of Trauma, Acute Care Surgery, & Surgical Critical Care, Sacramento, California, USA

ABSTRACT

Introduction
Hemorrhagic shock has been identified as the major risk factor for the development of Acute Respiratory Distress Syndrome (ARDS). The key mechanism is hypothesized to be disordered pathophysiologic crosstalk between inflammatory and coagulation pathways. This study investigates the role of coagulation and inflammatory markers in the development of ARDS.

Methods
A secondary analysis of the biomarker profiles from patients enrolled in the Pragmatic Randomized Optimal Platelet and Plasma Ratio (PROPPR) study was performed. PROPPR was a multicenter randomized trial examining the impact of a balanced resuscitation strategy (1:1:1 vs 1:1:2 plasma:platelet:red blood cells) on mortality. Coagulation and inflammatory candidate biomarkers (n=48) were investigated. Those patients with complete data were included in a principal components analysis. This dimensionality-reduction machine learning method was used to identify initial biomarker phenotypes (principal components) associated with ARDS. LASSO regression was performed on the phenotypes to identify independent predictors of ARDS controlling for age, mechanism, injury severity score (ISS), and significant hemorrhage (>=5 units red blood cells in the first 12 hours).

Results
286 patients were included. The 24-hour mortality was 14%. For those that survived >24 hours, 18% developed ARDS by Berlin criteria. There was no difference in ARDS incidence by treatment group. Among the 14 phenotypes identified, one remained statistically significant for predicting ARDS controlling for age, ISS, blunt injury, and hemorrhage. The phenotype (p=0.039) was predominantly driven by platelet activation integrins CD41 (glycoprotein IIb), CD61 (glycoprotein IIIa), and CD42b (platelet glycoprotein Ib alpha chain).

Conclusions
This study demonstrates the predominant early predictor of ARDS is associated with platelet activated integrins which are known to induce release of immunomodulatory mediators both anti and pro-inflammatory.

YOFIEL WYLE, M.S.

Rescue Potential of Placenta- and Amniotic Fluid-Derived Mesenchymal Stem Cell Extracellular Vesicles (EVs) in Human Lung Models of Oxidative Stress and Apoptosis

Mr. Yofiel Wyle, MS[1,2], Professor Angela Haczku PhD, MD[3], Professor Aijun Wang PhD[4]
[1]Center for Surgical Bioengineering, Sacramento, California, USA. [2]Molecular Cellular Integrative Physiology, Davis, California, USA. [3]Pulmonary, Critical Care and Sleep Medicine, Davis, California, USA. [4]Center for Surgical Bioengineering, Sacramento, California, USA

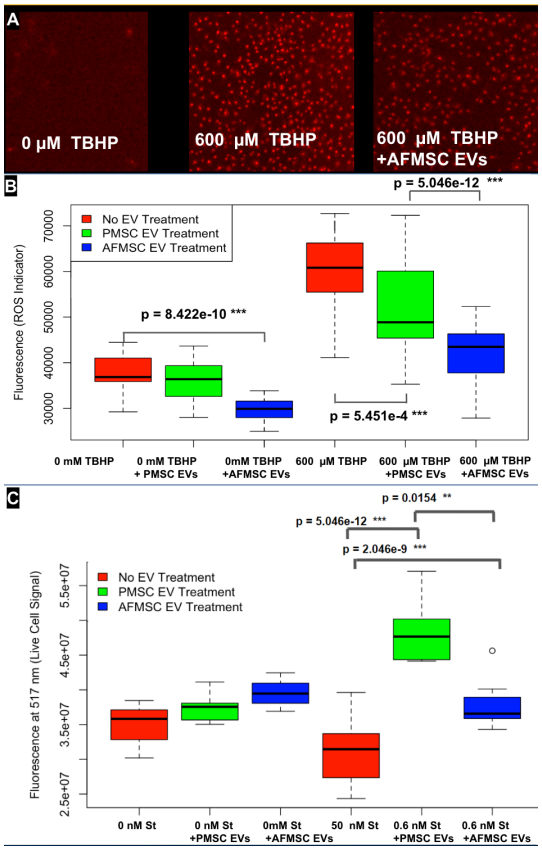
ABSTRACT

Introduction: Congenital Diaphragmatic Hernia (CDH), a deadly fetal disease marked by cell death and lung underdevelopment, has no effective treatments. Mesenchymal stromal/stem cells (MSCs), such as placental MSCs (PMSCs) and amniotic fluid-derived MSCs (AFMSCs), have shown promise in preclinical models of CDH; however, variability in MSC therapeutic potential and secretome profiles has complicated the understanding of mechanisms.

Methods: To mitigate donor variability, donor-matched PMSCs and AFMSCs were harvested from UC Davis Medical Center. A549 alveolar epithelial cells subjected to oxidative stress by Tert-Butyl hydrogen peroxide or apoptosis via staurosporine were treated with conditioned media or EVs from each MSC type. ROS were measured using Mitosox Red, and cell survival was assessed by CalceinAM. miRNA and protein sequencing were conducted on EV and conditioned media samples.

Results: Both AFMSC and PMSC EVs significantly reduced ROS and improved cell survival compared to controls. AFMSC EVs were more effective in reducing ROS at all concentrations tested, while PMSC EVs increased cell survival more at higher staurosporine doses. miR200a family miRNAs were abundant in AFMSC-EVs, and miR199a/b in PMSC-EVs. Both EVs and conditioned media contained therapeutic proteins, including HGF, BDNF, and VEGF.

Conclusion: Our findings suggest that EVs from PMSC and AFMSC conditioned media are critical for rescuing alveolar cells from TBHP-induced ROS and staurosporine-induced apoptosis. AFMSC EVs are superior in managing ROS, whereas PMSC EVs are more effective at higher staurosporine concentrations. The rescue potential is likely mediated by miRNAs, with miR199 and miR200b notably enriched in PMSC and AFMSC EVs, respectively.



A Mitosox red was used to visualize ROS after TBHP/EV exposure. **B** Graphical representation of Mitosox Assay. **C** Calcein AM was used to determine cell survival after staurosporine/EV treatment. PMSC EVs more effectively reduced apoptosis.

ORAL PRESENTATIONS

SESSION 4

ED 2222 | 3:00–4:15 P.M.

Karima Alghannam
Immune Responses After Vaccination Against SARS-CoV-2 in Kidney Transplant Candidates and Recipients

Alexandra Coward
Burn Block Party: Fascia Iliaca Catheters for Donor Site Pain after Split-Thickness Skin Grafting for Acute Burn Injury

Aliyah Parker
Comprehensive Interpretation Services Use for Patients who are Non-English Primary Language Speakers undergoing Surgery for NSCLC

Matthew Vuoncino
Prophylactic Caval Stenting in Patients Undergoing Retroperitoneal Lymph Node Dissection

Alexis Woods
Definitive Treatment Coordination in Rectal Cancer Patients

KARIMA ALGHANNAM, B.S.

Immune Responses After Vaccination Against SARS-CoV-2 in Kidney Transplant Candidates and Recipients

Ms. Hadia Lala Gul BS[1], Ms. Fransia De Leon BA[2], **Ms. Karima Alghannam B.S.[2]**, Dr. Ling-Xin Chen MD MS[1], Dr. Dennis Hartigan O'Connor MD PhD[3], Dr. Nam Tran PhD[4], Dr. Yihung Huang MD[1], Dr. Junichiro Sageshima MD FACS[2]

[1]Department of Medicine, Division of Transplant Nephrology, Sacramento, CA, USA. [2]Department of Surgery, Division of Transplant Surgery, Sacramento, CA, USA. [3]Department of Medical Microbiology and Immunology, Davis, CA, USA. [4]Department of Pathology and Laboratory Medicine, Sacramento, CA, USA

ABSTRACT

Purpose: SARS-CoV-2 has infected millions of individuals and has caused many deaths. Immunocompromised individuals, such as transplant recipients, are at an increased risk. Transplant recipients may experience a reduced immune response after COVID-19 infection. Safety and efficacy of the COVID-19 vaccine is unknown in transplant recipients. We aim to observe the immune response after the SARS-CoV-2 vaccination in kidney transplant candidates and recipients.

Methods: In this single center, prospective, observational trial, 19 kidney transplant candidates and recipients were followed for one year after the SARS-CoV-2 vaccination. The primary outcome was assessed through neutralizing antibody activity. Secondary outcomes were assessed through antibody responses to SARS-CoV-2 target protein and incidence of COVID-19. Safety questionnaires were administered to assess local and systemic side effects of the vaccination.

Results: 10 transplant candidates and 9 transplant recipients were enrolled in the trial. 9 subjects received the Moderna vaccine and 10 received the Pfizer/BioNtech. Table 1 shows the demographics of the population enrolled. There was a significant difference between BMI between the groups. Figure 1 depicts the spike antibodies over time for the control and study group. The control group displayed higher spike amounts across all time points. There was a significant difference between the control and study group for pain at the injection site (Table 2).

Conclusion: In this cohort, transplant recipients had a lower immune response to vaccination as compared to the control group as assessed by the ACOVS2 assay. Some study patients developed natural infections throughout the duration of the study and developed antibodies.

Table 1	Control (N= 10)	Study Group (N= 9)	*p-value*
Age, years	58.5 ±9	48.3 ±13	0.15
Female	2 (20)	3 (33)	0.51
BMI	30.9 [27-34]	26.0 [25-27]	**0.02**
Primary Language (English)	10 (100)	7 (78)	0.21
Race			
Asian	2 (20)	1 (11)	0.45
Black	3 (30)	2 (22)	
Hispanic	2 (20)	3 (33)	
White	2 (20)	0	
Other	1 (10)	3 (33)	
Candidate on Dialysis	10 (100)	8 (89)	0.47
Dialysis vintage, years	2.7 [2.1-3.7]	2.6 [1.8-5.2]	0.78
Dialysis Modality			
Hemodialysis	4 (40)	5 (56)	0.36
Peritoneal	4 (40)	0	
Both	2 (20)	3 (33)	
Primary Kidney Disease			
DM	3 (30)	0	0.44
FSGS	1 (10)	2 (22)	
HTN	2 (20)	1 (11)	
IgA Nephropathy	1 (10)	1 (11)	
Systemic Lupus	0	1 (11)	
Unknown Etiology	3 (30)	4 (44)	
Blood Type			
A	2 (20)	4 (44)	0.62
AB	1 (10)	1 (11)	
B	3 (30)	1 (11)	
O	4 (40)	3 (33)	

Table 1: Significance is defined as p <0.05

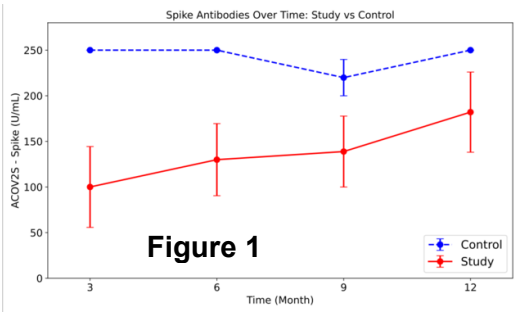


Figure 1

Table 2	Moderna (n=10)	Pfizer/BioNTech (n=9)	P-value
Pain at site (Yes, %)	6 (60%)	2 (22%)	0.096
Control (N= 10)	6 (60)	4 (40)	0.37
Study Group (N= 9)	3 (33)	6 (67)	

DR. ALEXANDRA COWARD, M.D.

Burn Block Party: Fascia Iliaca Catheters for Donor Site Pain after Split-Thickness Skin Grafting for Acute Burn Injury

Dr Alexandra Coward MD, Dr Soman Sen MD
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ABSTRACT

Regional anesthesia techniques have become increasingly popular in burn pain management. The fascia iliaca (FI) compartment block provides blockade of both the lateral femoral cutaneous nerve (LFCN) and the femoral nerve and is a useful modality for burn donor site pain. This study assesses the impact of this modality on post-operative pain scores and opioid requirements compared to matched control patients without a continuous FI catheter.

We performed a retrospective review of adult burn patients undergoing tangential excision and split-thickness skin grafting who received a fascia iliaca block from 2019 to 2022 at our institution compared to a matched control group (CON) of adult patients who did not receive FI block to the donor site. We matched the control group to the FI group by age and burn injury size and depth and compared opioid pain requirements (oral morphine equivalent (OME) between both groups in the post operative period. All mean values are mean ± standard deviation and all median values are median ± interquartile range.

214 patients met the inclusion criteria (FI- 128, CON- 86). Daily OME administration was significantly lower from postoperative day (POD) 0 to 5 in the FI group (604 (354-947) mg) compared to the CON group (1060 (557-115) mg, p=0.001). Multivariate regression analysis which controlled for age, gender, and total %TBSA of burn injury, indicates that FI catheters were independently associated with lower daily OME administration for every post-operative day (POD 0,1,2,3,4, and 5) and were independently associated with total postoperative (POD 0 to 5) OME administration.

The fascia iliaca block can be utilized to reduce pain when skin grafts are taken from the anterolateral thigh due to local anesthetic spread that covers both the femoral and lateral femoral cutaneous nerves. This retrospective review demonstrated a statistically significant decrease in opioid pain medication requirements following split thickness skin grafting.

ALIYAH PARKER, B.S.

Comprehensive Interpretation Services Use for Patients who are Non-English Primary Language Speakers undergoing Surgery for NSCLCr to Assess Transfusion Requirements in Trauma Patients

Ms. Aliyah Parker BS[1], Ms. Journne Herrera BS[2], Dr. Lisa M. Brown MD, MAS[2], Dr. Luis Godoy MD[2], Dr. David T. Cooke MD[2]

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ABSTRACT

Introduction

Language barriers make it difficult for surgical teams to engage in the discussion of important aspects of pre- and post-operative patient care with patients who are non-English speakers. We assessed the usage of comprehensive interpretation resources for non-English speaking patients undergoing surgery for NSCLC, and whether there were language interpreting resource utilization differences in the ambulatory setting compared to the inpatient setting, and whether non-English as primary language was a risk factor for prolonged length of stay.

Methods

This is a single institution retrospective cohort analysis comparing non-English primary language (non-EPL) patients to all English primary language (EPL) patients undergoing resection for primary lung cancer from January 2021 to September 2023. Primary outcomes were at least a one-time use of Martti and other comprehensive (institutional, non-family or friend) interpreter services in ambulatory and inpatient settings and postoperative length of stay (LOS).

Results

242 patients, 227 EPL (94%) and 15 non-EPL (6%) were identified. Primary languages spoken include Spanish, Mandarin, Cantonese, Punjabi, Romanian, Korean, and Vietnamese (See figure 1). The incidence of comprehensive interpreter use was documented 66.7% and 73.3% of the time in inpatient settings and outpatient settings, respectively. The average LOS among EPL patients was 3.16 days compared to the non-EPL group who had an average LOS of 2.73 days.

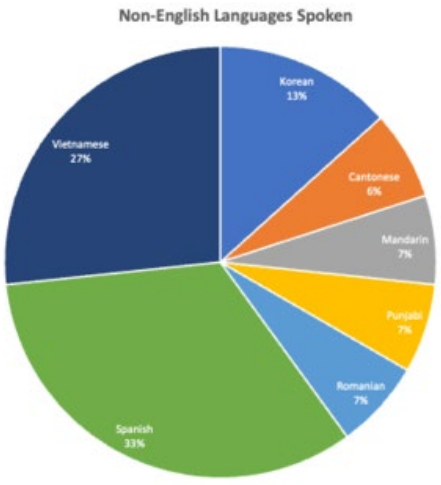

Figure 1. Non-English languages spoken

Conclusion

Over 30% of inpatient episodes and 25% of outpatient episodes for non-EPL went without documented interpreter services during their surgical lung cancer care journey. This identified a distinct area for patient-centered care improvement. A matched-cohort analysis will be conducted to further assess the influence of language barriers on patient outcomes, though non-EPL was not a risk factor for prolonged LOS.

DR. MATTHEW VUONCINO, M.D.

Prophylactic Caval Stenting in Patients Undergoing Retroperitoneal Lymph Node Dissection

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ABSTRACT

Intraoperative hemorrhage during retroperitoneal lymph node dissection (RPLND) for post-chemotherapy germ cell tumor resection is a serious concern. This project aims to describe our experience with prophylactic aorto/caval stenting to reduce intra-operative hemorrhage in patients undergoing RPLND.

Methods
All men who had RPLND post-chemotherapy for germ cell tumors between January 2014 - April 2022 were identified. Demographic information, operative variables, and outcomes were compared to patients with standard RPLND without prophylactic stent placement.

Results
39 patients underwent RPLND, and 15 had high-risk tumor anatomy defined as >50% encasement of the IVC, aorta, or iliac vessels. The average age was 37.13±10.5 years. Nine patients underwent angiography before RPLND. Of these 9, 1(11%) had no device placed due to IVC occlusion, 2 (22%) had endovascular coverage of the abdominal aorta, and 8 (88%) had endovascular coverage of the IVC and/or iliac veins. The average operative time for the endovascular intervention was 95.4±30.3 minutes. The average operative time for oncologic resection was 300.8±71.8 for those with endovascular stents versus 417.2±211 minutes for those without (p=0.17). While overall blood loss was not decreased, in patients with high-risk tumor anatomy, stented patients had lower mean EBL than non-stented patients (1072.2±737 vs. 2767±1483 ml, p=0.017). This did not translate to a significant difference in transfusion requirement after oncologic resection (55% vs. 83%, p=0.58). Of the eight patients who had undergone venous stenting, the average follow-up was 33.8±27 months. In that time, one patient (12.5%) had a stent-related complication that required lysis.

Conclusion
This case series represents the largest series of endovascular stenting to reduce hemorrhage during malignant RPLND for germ cell tumors. Our experience suggests that prophylactic endovascular intervention in high-risk surgical candidates may reduce blood loss.

Definitive Treatment Coordination in Rectal Cancer Patients

Dr Alexis Woods MD[1], Ms Rebeka Dejenie BS[2], Mx Axenya Kachen MPH[3], Dr Ankit Sarin MD MHA[4], Dr Sean Flynn MD[4], Dr Robert Kucejko MD[4], Dr Erik Noren MD[4], Dr Miquell Miller MD MSc[4]
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ABSTRACT

Background
For rectal cancer patients, timely coordination of definitive treatment is essential, and the standard of care is within 60 days. Identifying patients with delays in care and characterizing the socioeconomic or geographic barriers to care are imperative for targeted interventions.

Methods
A retrospective review of rectal cancer patients from 2013-2023 at our academic, tertiary cancer center was performed. Patients were analyzed by time from biopsy date to initiation of definitive treatment (neoadjuvant chemoradiation or surgery) as within 60 days and >60 days. Descriptive demographic statistics, chi-square analysis, and multivariable logistic regression were done comparing the time to definitive treatment and age, sex, race, ethnicity, insurance status, distance from our institution, and their social deprivation index score

Results
There were 355 rectal cancer patients meeting our inclusion criteria. From time of diagnosis, 50.4% (179/355) had initiation of definitive treatment within 60 days. On univariate analysis, factors significantly associated with delays of definitive treatment >60 days were sex (p=0.049), age (p=0.004), insurance (p=0.001), and distance from hospital (p=0.016). On multivariable analysis, factors more likely to have a delay in treatment >60 days were female sex (OR 1.53, [95% CI 1.02-2.60], p=0.036) and living >100 miles from the hospital (OR 2.53, [95% CI 1.07-6.12], p=0.04). Race, ethnicity, and social deprivation index were not significantly associated with delays to definitive treatment.

Conclusion
In this retrospective study, 50% of rectal cancer patients referred to our tertiary cancer center are initiating multidisciplinary definitive treatment within 60 days. Female sex and greater distance lived from the hospital are significantly associated with delays in definitive treatment. Further research and targeted interventions are needed to improve timely coordination of care.

POSTERS

Poster Group Sessions will run concurrently

RAHAF SHISHANI, M.S.

Vertical Sleeve Gastrectomy Reduces Gut Luminal Deoxycholic Acid Concentrations in Mice

Ms. Rahaf Shishani M.S[1,2], Dr. Annie Wang M.D.[1], Dr. Victoria Lyo M.D., M.T.M., F.A.C.S.[1], Dr. Renu Nandakumar Ph.D.[3], Dr. Bethany Cummings D.V.M., Ph.D.[1,2]

[1]Department of Surgery, Division of Foregut, Metabolic, and General Surgery, Center for Alimentary and Metabolic Sciences, School of Medicine, University of California - Davis, Sacramento, CA, USA. [2]Department of Molecular Biosciences, School of Veterinary Medicine, University of California – Davis, Davis, CA, USA. [3]Biomarkers Core Laboratory, Irving Institute for Clinical and Translational Research, Columbia University Irving Medical Center, Columbia University, New York, NY, USA

ABSTRACT

Introduction

Bariatric surgery's effect on improving metabolic health can be attributed to multiple factors, including its influence on bile acid dynamics. Bile acids play pivotal roles in regulating glycemia by binding to receptors like the farnesoid X receptor (FXR) and the G protein-coupled bile acid receptor, TGR5. The metabolism and composition of bile acids are closely intertwined with gut bacterial metabolism. Post-surgery, gastrointestinal tract alterations lead to changes in bile acid metabolism. Additionally, bariatric surgery induces changes in the composition of the gut microbiome in both rodents and humans. Despite these observations, research into the impact of bariatric surgery on gut luminal bile acid profiles is scarce. Therefore, we sought to define the changes in gut luminal bile acid composition after vertical sleeve gastrectomy (VSG).

Methods

Male C57BL/6J mice were placed on a high-fat diet (HFD) to induce obesity and were maintained on HFD throughout the study. After 2 months of diet, mice underwent sham or VSG surgery. Sham-operated mice were divided into two groups: one was fed *ad libitum*, while the other was food-restricted to match their body weight with that of the VSG-operated mice. Bile acid profiles were determined by UPLC-MS/MS in serum and gut luminal samples collected 2.5 months after surgery.

Results

VSG decreased gut luminal secondary bile acids, which was driven by a decrease in gut luminal deoxycholic acid (DCA) concentrations and abundance. However, the concentration and abundance of gut luminal cholic acid (precursor for DCA) did not differ between groups. VSG also increased circulating taurine-conjugated bile acid concentrations, which was not reflected in the gut luminal profile.

Conclusion

VSG decreased gut luminal DCA abundance independently of body weight. This suggests that the reduction in DCA abundance is not due to a decrease in substrate and, instead, may be due to a decrease in gut bacterial DCA production.

ROSALINDA MORENO, B.S.

Bile Acid Composition Changes Within Specific Brain Regions in Mice and with Dietary Resistant Starch

Ms. Rosalinda Moreno B.S.[1,2], Ms. Melanie A. Reuter B.S.[1,2], Ms. Madelynn Tucker B.S.[1,2], Ms. Jessica M. Bustamante M.S.[1,2], Ms. Rahaf Shishani M.S.[1,2], Dr. Renu Nandakumar Ph.D.[3], Dr. Bethany P. Cummings D.V.M., Ph.D.[1,2]

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ABSTRACT

Introduction

Bile acids are classically metabolized in the liver and the gut microbiome. However, low, but biologically relevant levels of bile acids are found in the brain. Recent studies report that gut microbially produced bile acid concentrations are elevated in brain tissue from individuals who had Alzheimer's disease (AD) compared to neurocognitively normal. However, our understanding of the regulation of brain bile acid dynamics is limited. Our lab has found that resistant starch (RS) supplementation upregulates gut bacterial bile acid metabolism. Therefore, we tested the hypothesis that RS supplementation with alter brain bile acid profile in mice.

Method

Male and female mice received either a RS supplemented diet or an isocaloric (IC) diet for 2 months and were then euthanized for collection of hippocampus and cortex. Bile acid profiles in hippocampus and cortex were measured by UPLC-MS/MS.

Results

RS did not alter body weight, food intake, or glucose tolerance compared to IC-fed mice. However, RS increased chenodeoxycholic acid (CDCA) compared to IC-fed mice. We also used this data set to better understand brain region-specific bile acid profiles and found that the bile acid profile of the hippocampus and cortex differ substantially. When expressed as a proportion of the total brain bile acid pool, cholic acid (CA), taurocholic acid (TCA) were higher in the cortex compared to the hippocampus in both IC and RS-fed mice. Conversely, tauromuricholic acid (TMCA) was decreased in the cortex compared to the hippocampus in both IC and RS-fed mice.

Conclusion

Increasing fermentable dietary resistant starch in mice results in changes of brain bile acid profiles. However, regardless of diet, the hippocampus and cortex differ substantially in their bile acid composition. These data provide valuable new foundational insight into the regulation of brain bile acid dynamics which may eventually help improve our understanding of AD pathogenesis.

Novel Bioengineered MicroRNA Therapy for High-Risk Neuroblastoma

Dr. Kathleen Doyle MD[1], Ms. Maria Sutter BS[2], Ms. Monica Rodriguez BS[2], Dr. Meijuan Tu PhD[3], Dr. Neelu Batra PhD[3], Dr. Aiming Yu PhD[3], Dr. Erin Brown MD[1]

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ABSTRACT

Introduction

Neuroblastoma is a common pediatric cancer with poor outcomes for patients with high-risk disease. MicroRNAs (miRs) are small RNAs that control post-transcriptional gene regulation. Dysregulation of miRs is linked to tumorigenesis and treatment resistance in neuroblastoma. Restoration of miR levels has demonstrated potent anti-tumor effects in oncologic models. miR-34a-5p and miR-124-5p are under-expressed in neuroblastoma and are potential targets for therapeutics. We investigated the *in vitro* effects of bioengineered miR-34a-5p and miR-124-5p on neuroblastoma cell viability.

Methods

Three high-risk neuroblastoma (NB) cell lines Be(2)-c, SK-N-SH, and SH-SY5Y were seeded at 12,000 cells/well and transfected with bioengineered miR-34a-5p and miR-124-3p using lipofectamine 3000 (LP) transfection agent. NB cells were treated with 25nM dose of either miR-34a-5p or miR-124-3p. Wells containing NB cells with LP only served as controls. Cells were monitored for up to 7 days. Cell viability was measured using an MTT assay.

ResultS

miR-124-3p significantly reduced cell viability in all cell lines compared to controls ($p<0.0001$ for Be(2)-c and SKNSH, $p=0.02$ for SH-SY5Y). miR-34a-5p significantly reduced cell viability in cell lines SK-N-SH ($p<0.0001$) but not in Be(2)-C ($p=0.07$) or SH-SY5Y ($p=0.10$). miR-124-3p showed greater reduction when compared to controls in cell viability all cell lines than miR-34a-5p (mean reduction: 48% for 124 and 25% for 34a, $p=0.0004$) Transfection efficacy with LP for each cell line was estimated to be 20%, 40% and 65% for SH-SY5Y, SK-N-SH, and Be(2)-C, respectively.

Conclusions

Both bioengineered miR-34a-5p and miR-124-5p demonstrated reduced neuroblastoma cell viability *in vitro*, supporting the potential of these miRs as therapeutic agents for neuroblastoma treatment. Future directions include testing of miR efficacy on neuroblastoma tumors *in vivo* and combining miRs with systemic therapies for enhanced synergistic effects.

DR. LOUISE LANOUE, Ph.D.

In vivo functional risk assessment of patient-specific genetic variants for COVID-19 using novel genetically humanized polygenic mice

Dr. Louise Lanoue Ph.D.[1], Ms Hongwei Liu M.Sc[2,3], Dr. Douglas Rowland Ph.D.[4], Dr. Mollie Heffner Ph.D.[1], Dr. Lark Coffey Ph.D.[2,5], Dr. Kent Lloyd Ph.D.[1,6]

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ABSTRACT

There is considerable variability in human susceptibility and clinical manifestations in response to SARS-Cov2 infection. The reasons for this diversity are not fully characterized, but the presence of genetic variants in the host genome may confer either relative protection or increased susceptibility to COVID-19 and influence the pathological and clinical responses. To increase our understanding of patient specific genomic variability, we introduced high risk genetic single nucleotide polymorphisms (SNPs), shown by GWAS to be associated with increased illness, in genes regulating interferon signaling (*Plscr1*) and immunological and inflammatory response (*Tyk2*), in *ACE2*/*TMPRSS2* mice using CRISPR/Cas9.

We developed the *ACE2*/*TMPRSS2* knockin (KI) mouse model to investigate the pathological manifestations of COVID-19. These mice, upon intranasal inoculation with SARS-CoV-2 omicron B.1.1.529 had detectable infectious SARS-CoV-2 in nasopharyngeal swabs 1- and 2-days post inoculation (dpi), and in lung tissues 2-6 dpi. SARS-CoV-2 caused a significant reduction in body weight and locomotion at 4 and 15 dpi in *ACE2/TMPRESS2* KI mice compared to mock-inoculated animals. Mild acute changes in cardiac activity and reduced end-expiration lung volume were also detected in inoculated *ACE2/TMPRSS2* KI.

We now propose to assess *in vivo* infection rate, viral burden, body weight, general health, and cardiac and pulmonary functions in *ACE2*/*TMPRSS2* KI mice carrying high risk genetic coding humanized SNP (*Tyk2* or *Plscr1*). Mice will be challenged with 10^5 plaque forming units (PFU) of SARS-CoV-2 Omicron-XBB1.5, or virus diluent as a mock inoculation and evaluated for acute changes in these physiological parameters. Preliminary data show increased viral load in throat swabs and trachea and lung titers in *ACE2/TMPRSS* KI mice expressing the*Tyk2* SNP compared to *ACE/TMPRSS2* KI mice without the genomic variant. Additional assessment of disease severity is forthcoming.

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DR. EMILY BYRD, M.D., Ph.D.

Revisiting an ovine model for in utero repair of gastroschisis

Dr. Emily Byrd MD, PhD[1], Dr. Su Yeon Lee MD[2], Dr. Monalisa Hassan MD[1], Mr. Chris Pivetti MS[1], Dr. Jamie Anderson MD[1], Dr. Geoanna Bautista MD[3], Dr. Shinjiro Hirose MD[1]
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ABSTRACT

Introduction: Gastroschisis is a congenital abdominal wall defect resulting in bowel herniation into the amniotic sac. Outcomes range in severity from simple gastroschisis resulting in prolonged bowel dysmotility to complex gastroschisis, resulting in intestinal atresias, volvulus, and/or necrosis causing short bowel syndrome. We aim to optimize an ovine model of simple gastroschisis and hypothesize that *in utero* repair of simple gastroschisis will decrease bowel inflammation and improve postnatal bowel motility.

Methods: Gastroschisis defect creation was completed by creation of a 2 or 3cm abdominal wall defect, with securement of a ring to maintain defect size and shape at gestational age (GA) 76-80 days. Fetuses underwent either primary or patch repair at GA 101-105, with ex-utero intrapartum treatment (EXIT) procedure at GA 139-142. Lambs were administered barium contrast by gavage and monitored with twice daily abdominal x-rays to assess transit.

Results: Seven fetuses underwent defect creation with a stiff 3cm ring; however, three fetuses died *in utero* due to ring dislodgement. Two fetuses were repaired *in utero,* with one requiring patch repair due to significant loss of abdominal domain. We then optimized the model by utilizing a 2cm defect size with a flexible ring with no incidences of ring dislodgement in the subsequent seven fetuses. Preliminary results of two lambs that underwent *in utero* repair and two lambs repaired at EXIT revealed complete passage of gavage fed barium contrast by day 3 and 4 for *in utero* lambs (Fig. 1). In contrast, one lamb repaired at EXIT failed to pass barium at study endpoint (day 7) while one passed barium on day 3 (Fig. 1).

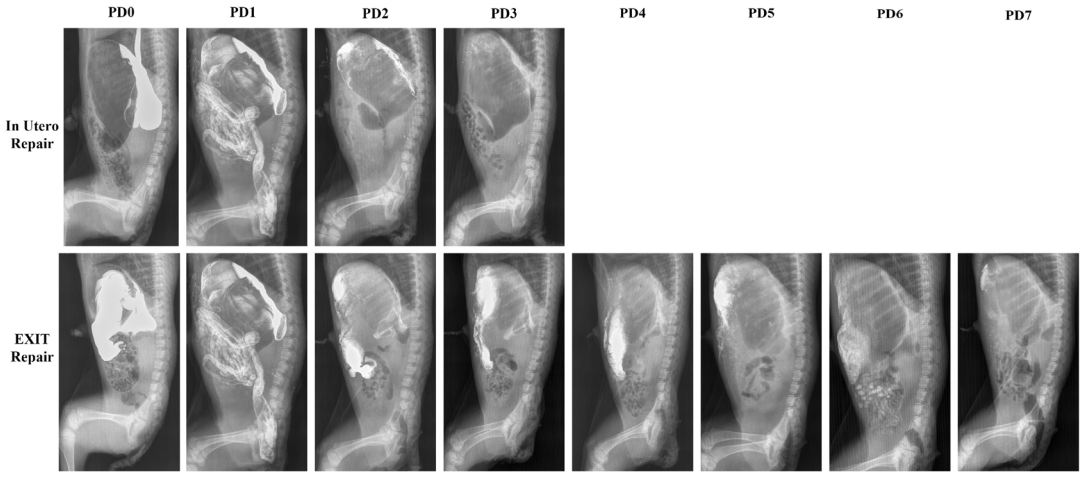

Figure 1: Barium transit of one in utero repair lamb demonstrating complete passage of contrast at postnatal day (PD) 3 and one EXIT repair lamb with residual contrast at PD7.

Conclusions: These studies successfully optimized an ovine model of simple gastroschisis with reduced obstruction and atresia rates. Preliminary data suggests *in utero* repair of gastroschisis may improve postnatal bowel motility, with additional studies ongoing.

ARYANA RAZMARA, M.S.

Canine NK cell atlas: Genomic profiling of blood and tissue-resident NK cells including genomic biomarkers from first-in-dog immunotherapy trials

Ms Aryana Razmara MS[1], Mr Marshall Lammers BS[1], Dr William Culp VMD[2], Dr Sean Judge MD[1], Dr William Murphy PhD[3], Dr Zachary Morris MD PhD[4], Dr Robert Rebhun DVM PhD[2], Dr Titus Brown PhD[5], Dr David Vail DVM MS[6], Dr Michael Kent DVM[2], Dr Robert Canter MD[1]

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ABSTRACT

Natural killer (NK) cells are key effectors in anti-tumor responses with great potential to extend the promise of immunotherapy. However, additional work is needed to understand NK immunoregulation across tissues and activation states in both dogs and people. Here, we used bulk RNA sequencing (RNAseq) with CIBERSORTx deconvolution combined with single cell (SC) RNAseq to interrogate the NK gene expression and signaling pathways across canine tissues, including spleen, liver, sarcomas, lung, placenta, ovary, and uterus. Additionally, we compared peripheral NK gene expression signatures among dogs receiving three novel NK-targeting canine immunotherapies, including autologous NK transfer, allogeneic NK transfer, and molecularly targeted radiotherapy with IL-2 immunocytokine. Overall, canine spleen had the largest absolute number of NK cells, followed by placenta, and sarcoma had the lowest. Unique signatures were observed across organs consistent with conventional, activated, and stem-like NK cells in the spleen, lung, and placenta, respectively. Importantly, integrated analysis of NK trials showed distinct signatures with greater DGEs related to activation and recruitment post treatment in responders compared to non-responders. This comprehensive genomic analysis provides insight into the canine NK profiles across tissues and in response to immunotherapy, increasing our understanding of canine NK cells and advancing mechanistic investigations into novel therapeutic approaches.

DAVID WANG, B.S.

Hybridization of Extracellular Vesicles for the Targeted Treatment of Alzheimer's Disease

Mr. David Wang BS[1,2], Dr. Lalitha Ramasubramanian PhD[1,2], Dr. Kaitlin Clark PhD[2], Mrs. Leora Goldbloom-Helzner BS, MS[1,2], Dr. Priyadarsini Kumar PhD[2], Dr. Diana Farmer MD[2], Dr. Aijun Wang PhD[1,2]

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ABSTRACT

Background & Aim

Mesenchymal stem cells (MSCs) have been investigated as a therapeutic for CNS disorders and confer their therapeutic effects via paracrine mechanisms, with MSC-derived extracellular vesicles (MSC-EVs) as a part of the MSC secretome. EVs offer advantages over other nanoparticle formulations such as liposomes including biocompatibility and intrinsic functional properties due to their biomolecular composition. However, EVs are naturally heterogeneous which limits therapeutic potency.

The goal of this study is to establish a platform to synthesize and characterize an engineered EV product through the fusion of EVs from different cellular sources. MSC-EVs and astrocyte-derived EVs were selected as a proof of concept targeting neurodegenerative diseases. We hypothesize that optimization and comprehensive characterization of the resulting hybrid EV product will allow for increased therapeutic potency and treatment response across a range of diseases.

Methods

Placenta-derived MSC-EVs (PMSC-EVs) and astrocyte EVs were isolated by sequential ultracentrifugation and combined to form hybrid EVs via either extrusion or sonication. Confirmation of EV fusion was performed through super resolution microscopy and ExoView, an fluorescent-based immunocapture microscope. Functional properties including EV uptake into brain cell types, neuroprotection, and immunomodulation were assessed and optimized by altering hybrid EV synthesis methods or formulations.

Results

PMSC-EVs and astrocyte EVs were successfully isolated following an ultracentrifuge isolation protocol. Cryo-electron microscopy showed no morphological changes of hybrid EVs following fusion and super resolution microscopy along with ExoView confirmed successful fusion. Hybrid EVs demonstrated statistically significant increase in neuroprotective function, immunomodulation, and targeting to brain cell types. Proteomics revealed changes in EV protein content during fusion.

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DR. KEWA GAO, M.D., Ph.D.

Densely PEGylated lipid nanoparticles globally transfect the brain in utero with mRNA for gene editing enzymes

Dr. Kewa Gao MD, PhD[1,2], Dr. Hesong Han PhD[3], Ms. Matileen Cranick BS[1], Dr. Sheng Zhao PhD[3], Ms. Shanxiu Xu MS[1], Ms. Boyan Yin BS[1,3], Dr. Hengyue Song MD[1], Ms. Jessica Wong Undergraduate[1,4], Mr. Zehua Zhao High School[1], Dr. Diana Farmer MD[1], Dr. Niren Murthy PhD[3], Dr. Aijun Wang PhD[1,2,4]

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ABSTRACT

Treating central nervous system (CNS) disorders *in utero* with mRNA-based therapeutics offers a groundbreaking approach to intervene before disease onset. A critical bottleneck in clinical application has been the lack of safe and efficient delivery mechanisms. This study introduces a novel densely PEGylated lipid nanoparticle (ADP-LNP) as a safe and potent delivery vehicle, capable of transfecting 30% of the fetal mouse brain with mRNA via intracerebroventricular (ICV) injection. ADP-LNPs exhibit a remarkable safety profile, evidenced by the normal brain and body weights of treated mice and no detectable adverse effects on postnatal development. The transfection efficacy extends to neural stem and progenitor cells, with over 40% of cortical neurons and 60% of hippocampal neurons showing sustained gene editing 10 weeks postnatally (Figure 1). Furthermore, targeting Angelman Syndrome, a paradigmatic neurodevelopmental disorder, we demonstrate that ADP-LNPs carrying Cas9 mRNA and gRNA induce indels in 17% of brain cells within three days postpartum, underscoring the precision and potential of this approach. The findings illuminate the promise of ADP-LNPs as a transformative tool for the *in utero* treatment of neurodevelopmental disorders, ensuring high transfection rates with an unparalleled safety profile, thereby setting the stage for a new frontier in fetal gene therapy.

OMAR ORTUNO, B.A.

Pause the Repeat: Evaluating the Efficacy of Repeat Imaging in Transferred Pediatric Patients with Suspected Appendicitis

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ABSTRACT

Current imaging practices in pediatric patients transferred with suspected appendicitis to tertiary children's hospitals may result in repeated imaging study or image overread. This results in more time in the emergency department and higher healthcare costs. This study aims to evaluate whether repeat imaging improves outcomes by comparing pre- and post-transfer imaging to surgical pathology to determine the accuracy of imaging performed at referring centers.

This is a retrospective observational study using electronic medical record data from a single tertiary children's hospital. Inclusion criteria were age < 18 years, transfer from a referring hospital with abdominal imaging, and a suspected diagnosis of appendicitis as the reason for referral. Exclusion criteria included transfers for alternate diagnoses and no imaging prior to transfer. Statistical analysis included descriptive statistics and sensitivity calculations. Fisher's Exact Test was used to determine statistical significance between each diagnostic modality.

519 patients transferred to a tertiary care center with previous imaging were analyzed. 134(26%) of patients had US and 348(67%) had CT, and 26 (0.05%) patients had US followed by CT. After transfer, 122 (23.5%) of patients had US, 8(0.02%) had repeat CT, and 331(62%) of patients received a second read of a prior CT. Outside ultrasound was 93% sensitive. Outside CT scan was 99.6% sensitive, while overread was 97.9% sensitive. Post-transfer repeat US was 98.9% sensitive. There was no statistical significance between the sensitivities of US or CT.

Pre-transfer US and CT imaging had comparable sensitivity in the diagnosis of acute appendicitis to post-transfer imaging for pediatric patients referred for suspected appendicitis. Repeat imaging or overread by in-house radiologists. Additional repeat imaging or reinterpretation following transfer may be unnecessary in the diagnosis of acute appendicitis.

DANIEL CASTRO, B.S.

Incidental DVT Diagnosed on Lower Extremity CT Is a Rare but Clinically Impactful Finding

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ABSTRACT

Introduction
In thrombotic events, computed tomography (CT) studies provide reasonable sensitivity for the diagnosis of deep venous thrombosis (DVT). However, the incidence and accuracy of a DVT diagnosis on CT studies not targeted for the detection of DVT is not well described. Additionally, the clinical impact of DVTs incidentally identified on CT is unknown.

Methods
This single institution retrospective study queried all contrasted CT studies of the lower extremities over a 10-year period. Regular expressions applied to CT study radiology reports identified positive findings for DVT. Selected reports were reviewed to confirm a DVT. Patient demographics, relevant medical, and surgical history were obtained through chart review. Follow-up information for 1 year post-incident CT included treatment, imaging, and adverse events. An incidental DVT refers to a patient where a DVT wasn't previously noted or suspected based on the study indication.

Results
Out of 16,637 lower extremity CT studies, 37 identified a DVT. However, only 13 patients had incidental DVTs (0.08% incidence). Among them, 11 had additional imaging: 9 venous duplex and 2 CT scans. In subsequent duplexes, DVT was not found in 8 and confirmed in 1, while in subsequent CT scans, DVT was not found in 1 and confirmed in 1. 3 patients received anticoagulation based on initial CT findings; 2 had no complications, 1 had major bleeding, needing further treatment.

Discussion
Incidental lower extremity DVTs are rare CT findings, present in 0.08% of studies. Most patients with incidental DVTs receive additional imaging, with negative findings in 80% of cases. Anticoagulation was started in 23% of cases due to CT findings, resulting in a 33% rate of significant complications. Despite CT venogram not being recommended as a primary diagnostic tool for DVT, there's no consensus on repeat imaging for incidentally diagnosed cases. Further research is necessary for guideline development.

TYRA FURTADO, B.S.

Biodegradable Temporizing Matrix Does Not Change Metabolic Rates After First Burn Excision Compared to Autografting

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ABSTRACT

Introduction
Burn injuries induce significant physiological stress, causing hypermetabolic changes. Research suggests burn patients' caloric needs may increase by 20% to 100%. Biodegradable Temporizing Matrix (BTM) is used as a temporary wound closure for large burns. This study compares metabolic rates in patients treated with BTM versus primary autografting post-excision.

Methods
After institutional board approval, a retrospective cohort study analyzed adult burn patients admitted from 2017-2022. Inclusion criteria were burn service admission with a resting energy expenditure (REE) order. Exclusions were lack of thermal cutaneous injuries, REE assessments, or excision/grafting. Data collected included demographics, injury details, surgical information, REEs, and outcomes. Patients were categorized based on primary treatment post-excision. Statistical analysis used R software.

Results
There were 168 patients who met inclusion criteria with 146 patients in the mostly autograft group and 22 patients in the mostly BTM group. The median % TBSA BTM rate in the mostly autograft group was 0% TBSA (IQR 0-8) and 20.5 % TBSA (IQR 2.7-29) in the mostly BTM group. The groups were relatively similar in age (44±15 vs 50±21 years), burn size (42±18 vs 46±24 % TBSA), rates of inhalation injury (32% vs 18%), initial REE (2812±760 vs 2746±877 kcal) and second REE (2812±840 vs 2807±615 kcal). On multivariate linear regression comparing difference between REE1 and REE2, there was no significant different between patients based on age, TBSA, % TBSA BTM, or inhalation injury.

Conclusion
Initial hypothesis suggested lower metabolic rates with BTM versus autograft. However, findings show no significant difference. This is crucial clinically, suggesting BTM selection doesn't raise metabolic rates, averting adverse effects. Further analysis will include majority allograft patients for better understanding of metabolic rate variances.

Higher body mass index is associated with decreased circulating and intratumoral natural killer cells in soft tissue sarcoma

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ABSTRACT

We have previously observed improved survival in soft tissue sarcoma (STS) patients who harbor greater numbers of intratumoral natural killer (NK) cells. However, the impact of immune-modifying variables such as obesity on immune infiltrates in STS is not well-defined. Here we investigated the relationship between BMI and NK cell populations in the blood and tumor of STS patients.

Blood and tumor specimens were prospectively collected on 31 STS patients undergoing surgery from 2018 – 2023. Clinical data were abstracted from the medical record, and specimens were processed for immune phenotyping by flow cytometry.

86% of patients were AJCC stage 3, 52% of tumors were located on the extremity, and 33% were retroperitoneal. 81% received preoperative radiotherapy, and the median BMI was 27 (range, 18.4 - 39.4). With a median follow up of 24.4 months, median metastasis free survival was 12.6 months (2.0 - 45.7), and median overall survival was 24.4 months (5.9 - 75.6). Overall, NK cells were approximately 55-fold more frequent in the blood (mm3) than tumor (mg, $P<0.05$). The frequency of cytotoxic CD56dim NK cells was also greater in the blood than tumor (91.7% ± 5.35 vs. 82.4% ± 12.5, $P = 0.0001$). Increasing BMI was significantly associated with lower intratumoral NK cells ($r = -0.46$, $P = 0.048$) and lower intratumoral CD56dim NK cells ($r = -0.51$, $P = 0.03$). When stratifying by lean (BMI <25) versus obese (BMI≥30), lean patients had a greater proportion of peripheral CD56dim NK cells compared to obese (94.0% vs 89.4%, $P = 0.014$) as well as 9-fold greater intratumoral CD56dim NK cells compared to obese ($P = 0.02$). When stratifying by the median BMI of 27, there was a trend for improved overall survival among lower BMI patients ($P=0.08$)

Obesity is associated with differences in numbers and phenotype of NK cell infiltrates in STS patients undergoing surgery. Obesity-associated NK dysfunction may be prognostically relevant in STS.

SAMUEL EMERSON, B.S.

Size tunable Lipid Raft Nanovesicles (LRNVs) derived from placental mesenchymal stem cells as an EV-mimetic drug delivery platform

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ABSTRACT

Introduction

Extracellular vesicles (EVs) of placental mesenchymal stem/stromal cells (PMSCs) have shown therapeutic potential with robust neuroprotective, immunomodulatory, and angiogenic properties. However, their relatively low yield and heterogeneity of cargo has limited their clinical applications. Extruded lipid raft regions of PMSC membranes form lipid raft nanovesicles (LRNVs), which present a homogenous, high yield alternative while preserving the endogenous abilities of native EVs.

Methods

PMSCs cultured in EV-depleted media until confluency are collected by manual scraping and lysed. Lipid rafts are isolated by density gradient ultracentrifugation of lysate. Extrusion of lipid raft through polycarbonate membranes of different pore sizes yielded LRNVs which were then analyzed for chemical, biochemical and functional properties.

Results

Lipid rafts were isolated from 3 different PMSC sources, fraction 8 was identified as containing the most proteins associated with lipid rafts, and the least contaminating proteins. Preliminary results suggest that LRNVs exhibited immunomodulation similar to native EVs.

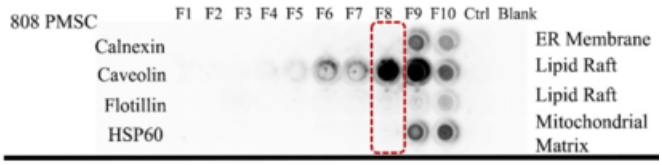

Figure 1: Lipid raft isolate can be harvested from a density gradient of cell lysate. Presence of lipid raft marker (Caveolin) and absence of other membrane protein contaminants indicate fractions of interest.

Pore size (nm)	Mean size (nm)	Concentration (p/mL)	Zeta potential (mV)
200	132.5 ± 51.2	2.00E+10	-19.63 ± 0.29
100	106.2 ± 52.3	1.20E+10	-28.76 ± 0.00
50	99.4 ± 53.3	5.30E+10	-38.34 ± 0.44

Conclusion

Preliminary results indicate promising results of functional ability and similar characteristics to native EVs. Next steps include analysis of homogeneity of LRNVs including lipidomics, proteomics, transmission electron microscopy as well as engineering drug loading and/or surface modifications to develop a novel platform technology for further therapeutic application. Further experiments will be required to validate *in-vitro* functional efficacy.

Optimization of Aptamer Surface Conjugation onto Extracellular Vesicles (EVs) for Improved Function in the Context of Spinal Cord Injury (SCI)

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ABSTRACT

Extracellular vesicles (EVs) are cell-secreted nanovesicles that play an important role in long range cell-cell communication. Though EVs pose a promising alternative to cell-based therapy, targeted delivery *in vivo* still falls short. We engineered EVs with a myelin-targeting aptamer, LJM-3064, to improve EV targeting and retention in the context of SCI. EV conjugation efficiency has not yet been measured on a single nano-vesicular level nor has it been used to assess correlation between EV conjugation and function. In this study, ExoView was used to determine conjugation efficiency of carboxyfluorescein (FAM)-labeled LJM-3064-modified EVs (Apt-EVs) and informed optimization efforts.

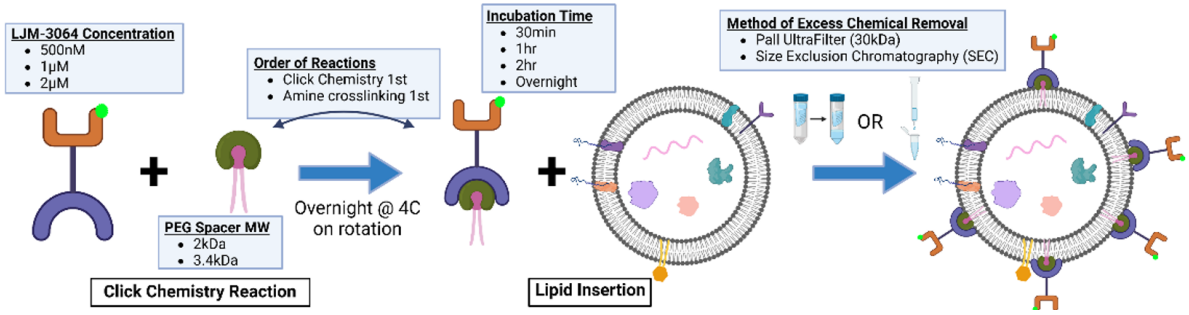

Figure 1. Conjugation Strategy for EV Surface Modification with Myelin-Targeting Aptamer

SK-OV-3 EVs were modified with 5'FAM 3'azide group LJM-3064 using lipid insertion-aided click chemistry (Figure 1). ExoView quantified total EVs through immobilization using antibodies for standard EV markers. LJM-3064 conjugation on EVs was measured by dividing 6-FAM+EVs by total EVs. Chemistry parameters (e.g. order of reactions, incubation times, etc.) were varied to inform optimization. With optimized conjugation conditions, placental-derived mesenchymal stromal cell-derived EVs (PMSCs-EVs) were modified with LJM-3064 and tested for improved oligodendrocyte (OL) protection/targeting properties *in vitro* and preserved regenerative properties native to PMSCs-EVs.

Apt-EVs were optimized to reach 50% efficiency. Physical and biomarker characterization were performed to confirm preserved EV integrity post-chemical modification. Preliminary results reveal optimized Apt-EVs exhibit OL protective properties, improved OL uptake compared to native EVs, and preserved neuroprotective and immunomodulatory properties.

In this study, we informed optimization of Apt-EVs and showed promising functional and targeting properties. With this optimized conjugation method, we will continue studies to determine the degree of conjugation required to see therapeutic effects in a demyelinating SCI model.

JORDAN PITMAN, B.S.

Preoperative Metabolic Health Status Alters Microbiota Response to Roux-en-Y Gastric Bypass

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ABSTRACT

Background
Higher preoperative severity of metabolic comorbidities can lead to sub-optimal metabolic recovery and decrease the incidence of disease remission following Roux-en-Y gastric bypass (RYGB). Gut microbiota are recognized as mediators of obesity and metabolic dysfunction and are altered by RYGB. We hypothesize that differences in microbiota reflect metabolic health severity and may impact response to RYGB.

Methods
Using a novel scoring system, we objectively scored diabetes mellitus, hypertension, and dyslipidemia in women undergoing RYGB to identify two groups as “metabolically healthy obesity” (MHO) (n=15) or “metabolically unhealthy obesity” (MUHO) (n=15). We then compared the pre- and 2-month post-RYGB comorbidity severity and fecal microbiota patterns between these groups.

Results
Mean age was 42 ± 9.1 years. There was no difference in preoperative BMI between groups (MHO 46.9 vs. MUHO 44.5 kg/m^2, p= 0.39). RYGB significantly reduced BMI in both groups (MHO –5.8; MUHO -6.2 kg/m^2), but postoperative BMI was not different between groups (p=0.67). HbA1c improved postoperatively (MHO-preop 5.8 vs MHO-2M 5.4 (p<0.001); MUHO-preop 7.8 vs MUHO-2M 6.6 (p<0.001)). Microbiota composition was not different between MHO and MUHO preoperatively. However, RYGB altered 55 species in MHO (ANCOM, p<0.05), but no significant compositional changes were detected in MUHO post-RYGB.

Conclusions
The lack of response of the gut microbiome to RYGB in the MUHO group suggests a RYGB-resistant microbiota community in these patients. Further study to understand the associations of microbial communities with metabolism could unmask unique mechanisms that drive disease phenotypes and the metabolic responses to RYGB.

DR. KAITLIN CLARK, Ph.D.

Biodistribution and Neuroprotective Effects of Placental Mesenchymal Stem Cell derived Extracellular Vesicles in Neonatal Hypoxic-Ischemic Encephalopathy: A Near-Term Ovine Model Study

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ABSTRACT

Neonatal hypoxic-ischemic encephalopathy (HIE) presents a significant risk of long-term disabilities and mortality in children. Placenta derived mesenchymal stem/stromal cells (PMSCs) and secreted extracellular vesicles (PMSC-EVs), offer promising therapeutic potential for HIE. However, understanding the biodistribution, safety, and neuroprotective effects of PMSC-EVs for HIE remains limited.

In this study, using a near-term ovine model of umbilical cord occlusion (UCO) resembling neonatal HIE, we aimed to evaluate biodistribution of fluorescently labeled PMSC-EVs. Short-term biodistribution studies of MemGlow-labeled PMSC-EVs were conducted in healthy and UCO animals. To assess route of administration, saline and PMSC-EVs were fluorescently labeled and administered peripherally via jugular intravenous (IV) injection or locally via intranasal (IN) administration. Animals were sacrificed 24h post-treatment, and organs were harvested and imaged using the LagoX imaging system.

Preliminary findings indicate PMSC-EVs were detected following IN administration at 24h. Dose-response relationships and organ uptake were observed. In healthy animals, signal was detected in kidneys across all treatments and increased uptake was noted in the thymus and lung for IN and IV administered PMSC-EVs, respectively. In UCO animals, repeated biodistribution studies showed increased PMSC-EV uptake in brain tissue, liver, and thymus, particularly with IN administration. Whole brain digests revealed enhanced PMSC-EV uptake via IN delivery using flow cytometry. These data suggest that PMSC-EVs readily cross the blood-brain barrier and home to CNS tissue, with IN administration demonstrating increased brain tissue uptake.

This study provides unique data on the fate mapping of PMSC-EVs for neonatal HIE and will help to elucidate optimal delivery routes and dosing strategies to maximally capitalize on the neuroprotective mechanisms of PMSC-EVs.

Incidence, Characteristics and Costs of Patients Readmitted for Hypoparathyroidism after Thyroidectomy for Thyroid Cancer in California

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ABSTRACT

Introduction

Post-thyroidectomy hypoparathyroidism is common, usually managed outpatient. Our aim was to identify the incidence, characteristics and costs associated with inpatient readmissions for postoperative hypoparathyroidism.

Methods

The California Cancer Registry and Health Care Access and Information (HCAI) databases were linked to identify patients with total thyroidectomy for thyroid cancer between 2005-2018, with subsequent inpatient readmission within 2 years. Cumulative incidence and multivariable Cox proportional hazards models were used to evaluate factors associated with readmission. Total charges were extracted from the HCAI database.

Results

Among 41,474 patients who underwent thyroidectomy, 572(1.38%) required readmission for hypoparathyroidism. Median time between surgery and first readmission was 5 days, and 52.9% of inpatient readmissions occurred within one month. Median number of readmissions for hypoparathyroidism 2 years after surgery was 3 and median length of stay was 2 days.

Patients with >4 lymph nodes (LN) removed had an increased two-year cumulative incidence of readmission(0.27%vs0.19%,p=0.027), while those treated at an American College of Surgeons Commission on Cancer (ACS CoC) center had a lower incidence(0.19%vs0.23%,p=0.055). In multivariable analysis, >4 LN removed at surgery(HR 1.61 [95% CI=1.13, 2.29],p= 0.008) was associated with readmission.

Charges for hypoparathyroidism readmission were higher than charges for readmission for other reasons(median charge/day of $9,493vs$7,868,p<0.001). 739/1513 hospital readmissions for hypoparathyroidism had charges recorded totaling $19,209,513 over the study period.

Conclusion

Most readmissions for post-thyroidectomy hypoparathyroidism occur soon after surgery and the costs are significant. Patient factors do not appear to be associated with readmission, but patients undergoing neck dissection or not seen at an ACS CoC center may be at increased risk of readmission.

JOHN LEW, M.S.

Sex Differences After Roux-en-Y Gastric Bypass (RYGB): Increased Preoperative Hypertension Severity in Men Portends Worse Hypertension Outcomes Postoperatively

Mr. John Lew MS[1], Dr. Annie Wang MD[2], Ms. Tiffany Wong BS[1], Dr. Shushmita Ahmed MD[2], Dr. Hazem Shamseddeen MD[2], Dr. Mohamed Ali MD[2], Dr. Victoria Lyo MD[2]
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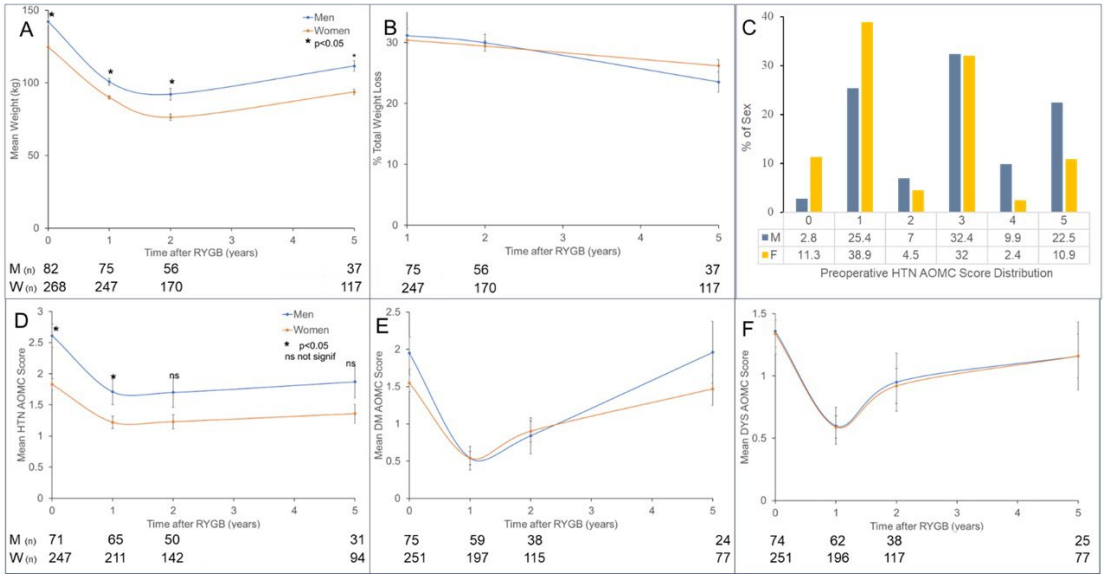
ABSTRACT

Introduction: The effect of sex as a biologic variable in the pathophysiology of obesity and on metabolic disease recovery following RYGB is incompletely understood. We used an objective scoring system, the Assessment of Obesity-related Metabolic Comorbidities (AOMC), to assess sex-specific metabolic responses including diabetes (DM), hypertension (HTN), and dyslipidemia (DYS) following RYGB.

Methods: AOMC combines medication and biochemical data to assess the severity of DM, HTN, and DYS on a 6-point scale (0: no disease, 1: pre-disease, 2: untreated, 3: controlled, 4: controlled with more meds, 5: severe uncontrolled/untreated). Weight loss data and AOMC scores were calculated pre- and post-RYGB over five years at our academic institution. AOMC trends were tested with the Wilcoxon signed-rank test (pairwise) and the Jonckheere-Terpstra test (>2 groups).

Results: Of 351 patients, men were underrepresented (23.4% vs. 76.6%). There was no association between sex with race/ethnicity or insurance type. Preoperatively, men presented at higher weight (148.4 kg vs. 130.3 kg, p<0.05 **Fig. A**) but similar BMI (**Fig. B**) compared to women. Men presented with more severe HTN compared to women (**Fig C-D**), but DM, and DYS severity were similar (**Fig. E-F**). Post-operatively, men continued to have higher weight and HTN severity compared to women (**Fig. D**, p<0.05). However, the relative decrease in HTN severity scores was equal between sexes. Consistent and sustained improvement in total weight loss, DM and DYS severity was the same between sexes.



Conclusion: Our study reinforces that men are disproportionately underutilizing bariatric surgery despite presenting with more severe HTN resulting in worse weight and HTN response to RYGB. Therefore, there is a need for increased awareness of bariatric surgery for men and earlier referrals to address HTN.

DR. JESSICA GUZMAN, M.D.

Upregulation of Inflammatory Marker Cytokine Profiles Immediately Following Traumatic Injury Predict 28-Day Mortality

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ABSTRACT

Introduction
The complex role inflammation plays in post-trauma outcomes has many unanswered questions and it is hypothesized that differential expression of pro- and anti-inflammatory cytokines contribute to variable patient outcomes. To further elucidate the early biomarker profiles, we characterized the baseline inflammatory cytokines among a cohort of highest-level trauma activations.

Methods
A prospective cohort study was conducted from March 2021–February 2024 at a Level I trauma center and patients were enrolled if a time zero blood sample was obtained within 30 minutes of arrival to the Emergency Department and prior to transfusion of any blood products. Demographics, injury characteristics, labs, and outcomes were collected prospectively. A 26-plex Luminex panel of cytokine marker (reported as pg/mL) was compared across injury severity (ISS) groups [minor<15, moderate 15-24, severe ≥25] using Kruskall Wallis, Wilcox rank sums, and t-tests as appropriate with significance defined as p≤0.05 (STATA v1815); medians (+/-IQR) are reported.

Results
401 patients were prospectively enrolled with median age 43 years (IQR 30-59), 69% blunt trauma, and 37% with ISS≥15. Overall 28-day mortality was 7% with significantly higher mortality in more severely injured groups (p<0.05, minor 1.2%, moderate 10.6%, severe 21.74%). Pro-inflammatory markers eotaxin (p=0.0001), MCP-1 (p=0.0005), MIP-1β (p=0.0002), and anti-inflammatory or protective markers PDGF-BB (p=0.0028) and IL-10 (p≤0.0006) increased across injury severity groups. Time zero biomarkers eotaxin, IL-6, IL-7, MCP-1, IL-10, PDGF-BB, and VEGF-alpha were also higher in patients who died (p<0.05, see table).

Biomarker	Mortality		p-value
	No	Yes	
Eotaxin	16.27 (10.15-24.35)	32.83 (17.87-36.69)	**<0.0001**
IL-6	12.89 (10.55-12.89)	34.34 (12.89-137.66)	**0.0005**
MCP-1	28.42 (12.93-57.34)	100.37 (25.78-164.24)	**0.0003**
MIP-1β	8.06 (6.64-25.95)	15.18 (5.45-50.19)	0.2255
IL-1ra	40.06 (31.22-40.06)	40.06 (40.06-512.44)	**0.0447**
PDGF-BB	20.38 (8.95-53.97)	60.32 (11.52-177.45)	**0.0229**
IL-7	2.36 (1.32-3.99)	4.38 (2.06-7.44)	**0.0026**
VEGF-alpha	56.60 (32.90-90.14)	85.10 (50.49-220.02)	**0.0088**
IL-10	1.66 (0.50-2.57)	3.20 (0.52-18.44)	**0.0278**

Conclusions
Cytokine expression differences occur very early following traumatic injury. These early biomarkers appear to cluster in more severely injured patients and are associated with mortality differences at 28-days, which has implications for potential therapeutic targets for future investigation.

Metabolic Disease Remission Rates after Gastric Bypass are Dependent on Pre-Operative Disease Severity: Use of a New Objective Metabolic Scoring System

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ABSTRACT

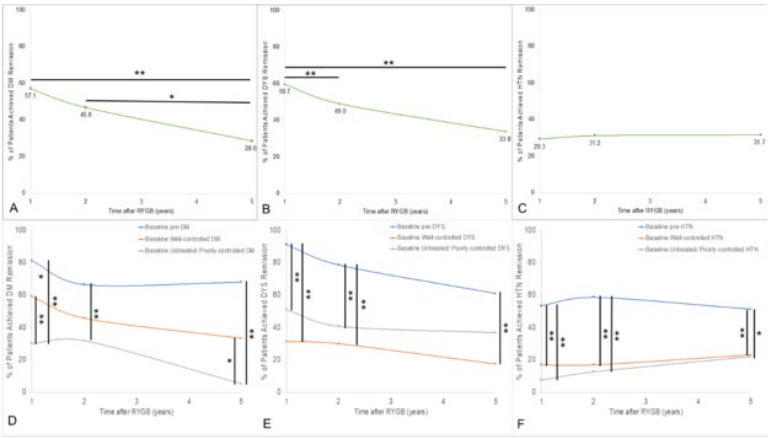
Introduction

Severity stratification and longitudinal evaluation of metabolic comorbidities in response to Roux-en-y gastric bypass (RYGB) are not standardized. We updated our previously published comorbidity severity scoring system to combine treatment and biochemical data and develop a more objective Assessment of Obesity-related Metabolic Comorbidities (AOMC) system, which assigns comorbidity severity on a 6-point scale to more precisely and reproducibly measure metabolic disease response to RYGB.

Methods

AOMC scores for diabetes (DM), dyslipidemia (DYS), and hypertension (HTN) were calculated pre- and post-operatively (1-, 2-, and 5-years) in patients who underwent RYGB over 5 years at our academic institution. AOMC trends were tested with Cochran's Q test, while differences between disease severity categories were assessed using Chi-squared analysis and post-hoc Fisher's exact tests.

Results



Of 351 patients, 214, 188, and 303, presented with any DM, DYS, or HTN respectively. Overall, one-year remission rates were: DM 57.1%, DYS 59.7%, HTN 29.3%. Over 5 years post-RYGB, remission rates declined for DM (Figure A, $p<0.05$) and DYS (Figure B, $p<0.05$), but remained steady for HTN (Figure C, $p>0.05$). Furthermore, remission was associated with preoperative disease severity: those with pre-metabolic disease had the highest remission rates (i.e. one-year: pre-DM 81.4%, pre-DYS 91.4%, pre-HTN 53.5%, Figure D-F blue, all $p<0.05$), while those with most severe scores preoperatively (untreated/poorly-controlled) and had the lowest remission rates (Figure D-F).

Conclusions

AOMC allows precise assessment of comorbidity severity and disease-specific postoperative quantification of comorbidity responses and remission rates. These findings can guide preoperative metabolic disease optimization and postoperative metabolic recovery expectations as well as standardize communication regarding comorbidity severity.

DR. RYAN COHEN, M.D.

Hyperkinetic Biliary Dyskinesia: An Underrecognized Problem with Good Surgical Outcomes After Cholecystectomy

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ABSTRACT

Introduction

Hyperkinetic biliary dyskinesia (HBD) is an underrecognized condition with no standardized management guidelines. HBD is typically defined as a gallbladder ejection fraction (EF) ≥80% on hepatobiliary iminodiacetic acid (HIDA) scan. We aimed to identify the prevalence and radiographic reporting of HBD, physician referral patterns, and clinical outcomes following cholecystectomy.

Methods

A retrospective chart review of HIDA scans completed over 21 years at UC Davis was performed. Patient demographics, symptomatology, referral patterns, and operative data were collected. HBD was defined as HIDA EF ≥80%. Patients with HBD who underwent cholecystectomy were analyzed.

Results

Of 1,999 patients who had HIDA scans with reported EF, 679 (34.0%) had an EF≥80%. Only 13.7% of HIDA scans with EF≥80% were reported as hyperkinetic. Cholecystectomy was performed in 56 patients (7.7%) with EF≥80%, most being elective (89.3%) and all minimally invasive. PCPs referred most elective cases to surgery (62.5%). When HIDA was “normal”, PCPs were more likely than specialists to refer (68.6 vs 31.4%). Chronic cholecystitis was common on pathology (94.0%), while 39.3% had cholelithiasis. Excluding four patients lost to follow-up, 47 patients (83.9%) reported symptom improvement at a median follow-up of 16.5 days (IQR 11.75). Patients without improvement had a significantly higher prevalence of chronic gastrointestinal (GI) (92.1 vs 66.7%, P=0.024) and psychiatric conditions (96.0 vs. 74.2%, P=0.029), but not significantly more cholelithiasis, cholecystitis, or elective surgery status.

Conclusions

HBD is relatively common but often underrecognized by treating physicians. Most patients with HBD benefit from cholecystectomy, regardless of cholelithiasis. Patients with persistent symptoms after cholecystectomy may have confounding GI or psychiatric diagnoses. Increased awareness about HBD and postoperative outcomes is needed to ensure HBD is adequately treated.

Predictors of Opioid Prescriptions Refill After Lung Cancer Resection

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ABSTRACT

Introduction

Patients undergoing thoracic surgery are the least likely to be on opioids before surgery but have the highest rate of new persistent opioid use after surgery compared to other surgical cohorts. Nearly 27% of opioid naïve lung cancer resection patients become new persistent opioid users.

Methods

We performed a retrospective, single center, cohort study of opioid naïve patients undergoing lung cancer resection between July 2018 and May 2021. The primary outcome was opioid refills between discharge and 180 days after surgery.

Results

The cohort included 152 patients, 100 (65.8%) women with a median (IQR) age of 71 (65-75), 115 (75.7%) of whom lived with family or friends (vs alone). Twenty-nine (19.1%) patients had an opioid refill after discharge. Of these, 11 patients (37.9%) had 1 refill, 11 (37.9%) had 2 refills, 5 (17.2%) had 3 refills, one had 4 refills (3.4%), and one had 5 refills (3.4%). There were several independent predictors of opioid refill including living with others (odds adjusted ratio [aOR] 5.31, 95% CI 1.06-26.64), undergoing thoracotomy (4.31, 1.37-13.52), increasing chest tube duration (days) (1.14, 1.02-1.27), age (1.08, 1.01-1.16), and morphine milligram equivalents (MME) on the day before discharge (1.07, 1.02-1.11) (Table 1).

Table 1: Multivariable Logistic Regression Model of Opioid Prescription Refill (N=152), *c*-statistic: 0.859

Patient Characteristics	aOR	(95% CI)	p-value
Age	**1.08**	**(1.01 - 1.16)**	**0.02**
Male	0.46	(0.14 - 1.44)	0.18
Lives with family or friend (vs alone)	**5.31**	**(1.06 - 26.64)**	**0.04**
Thoracotomy	**4.31**	**(1.37 - 13.52)**	**0.01**
Chest tube duration (by day)	**1.14**	**(1.02 – 1.27)**	**0.02**
Number of chest tubes (2 vs 1)	0.49	(0.15 – 1.67)	0.26
MME on day before discharge	**1.07**	**(1.02 – 1.11)**	**0.002**
Average inpatient daily MME	1.02	(1.00 – 1.04)	0.08

aOR: Adjusted Odds Ratio, MME: Morphine Milligram Equivalents

Conclusion

We identified several modifiable predictors of opioid refill after lung cancer resection, specifically undergoing thoracotomy, increasing chest tube duration, and MME on the day before discharge that can aid patient-centered prescribing. These findings should be validated in other thoracic surgical cohorts and future studies will focus on incorporating pain and health-related quality of life metrics into prediction models to further refine opioid prescribing.

DR. MATTHEW FARAJZADEH, M.D.

Use of ultra-high frequency ultrasound for lymphovenous bypass planning: initial experience

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ABSTRACT

Introduction
Ultra-High Frequency Ultrasound (UHFUS) allows for visualization of superficial structures with frequencies up to 70 MHz and resolution up to 30 µm. This new advanced imaging modality may aid in identification and selection of appropriate lymphatic vessels as an adjunct to indocyanine green (ICG) lymphography in preoperative planning for lymphovenous bypass (LVB).

Methods
A retrospective review of initial experience using UHFUS-assisted LVB from a single surgeon at UC Davis Medical Center was performed. Data on lymphedema etiology, clinical and ICG grading, bypass type, lymphatic vessel size and quality were collected and analyzed.

Results
Lymphovenous bypass using UHFUS preoperative mapping was performed in three patients with secondary upper extremity lymphedema. All patients had International Society of Lymphology (ISL) grade 2 and one patient had MD Anderson grade 3 ICG staging. Average lymphatic vessel size was 0.4mm (range 0.2 to 0.6mm) and 83% were Type 1 vessel quality. Anastomoses were most commonly performed at a site of linear ICG pattern though one dilated lymphatic channel was identified using UHFUS within dermal backflow. All anastomoses were successfully performed in end-to-end fashion with patency confirmed with ICG.

Conclusion
UHGUS may be a useful advanced imaging modality for preoperative planning and optimization of LVBs. Direct visualization of lymphatics allows for selection of dilated Type I vessels, when possible. The ability to visualize lymphatic channels within dermal backflow patterns may expand indications for LVB in patients that might not otherwise be candidates.

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DR. DIEGO ANAYA, M.D.

Single retrograde thoracic branch endoprosthesis versus traditional endovascular repair with subclavian coverage for treatment of blunt thoracic aortic injuries

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ABSTRACT

Introduction
The Gore thoracic branch endoprosthesis (TBE) allows zone 2 thoracic endovascular aortic repair (TEVAR) with graft placement proximal to the left subclavian artery origin while maintaining vessel patency through a retrograde side branch. We compared experience with the TBE device for zone 2 and 3 blunt thoracic aortic injuries (BTAI) to traditional TEVAR with subclavian coverage.

Methods
We retrospectively identified patients undergoing repair for BTAI. Patient characteristics, procedural details, and outcomes are reported and compared between cohorts.

Results
Between 2005-2023, 51 patients underwent TBE placement, 11 for BTAI, while 152 patients underwent TEVAR for BTAI, 47 (31%) with subclavian coverage. Mean age of the TBE cohort was 63 (±20) versus 45 years (±19) in the TEVAR cohort.

The mean treatment length (length of aorta excluded by covered endograft) was 15 cm (±0cm) in the TBE cohort versus 11 cm (±2.4cm) in the TEVAR cohort ($p<0.001$).

Technical success, defined as successful injury exclusion was 100% in both groups. In the TEVAR cohort, 8 patients (17%) underwent subclavian revascularization, 3 (38%) for extremity ischemia and 1 (12.5%) for ipsilateral vertebral territory stroke. The remaining patients (4, 50%) underwent revascularization at the discretion of the operating surgeon. With operative complications as a combined endpoint, there were no post-operative complications observed in the TBE cohort, while 11 patients in the TEVAR cohort experienced complications: wound infection, extremity ischemia, stroke, endoleak, or retrograde dissection (0% versus 23%, $p=.64$). There were no aortic related mortalities in either cohort. Side branch patency and BTAI exclusion was observed on follow up imaging at a mean of 18.5 days (range 2-69) in all TBE cohort patients.

Conclusion
Use of the Gore TBE device offers a safe alternative to traditional TEVAR with subclavian coverage in the management of BTAI requiring zone 2 coverage.

RACHEL CHAN, B.S.

Creation of a Surgical Outcomes Dashboard Incorporating Social Determinants of Health: A Novel Quality Improvement Tool to Address Health Equity

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ABSTRACT

Introduction: The World Health Organization defines social determinants of health (SDH) as "non-medical factors that influence health outcomes." Surgical specialties are increasingly recognizing the impact of SDH on surgical outcomes. Interactive clinical dashboards are a tool to visualize data trends in simplified formats and inform operational decision-making. Dashboards highlighting disparities concerning diversity, equity, and inclusion (DEI) have been described; however, SDH dashboards focused on surgical outcomes are not described in current literature. We describe the development of a novel dashboard focused on the intersection of DEI and surgical outcomes.

Methods: The Surgical DEI Dashboard was developed incorporating data from EPIC through Caboodle to a Tableau-based dashboard. Demographic and SDH data collected include age, gender, race/ethnicity, language, insurance type, and healthy places index quartile. Surgical outcomes include hospital length of stay, readmission rate, Patient Safety Indicators (PSI), discharge location, and mortality. Quality benchmarks such as risk-adjusted indexes were incorporated from the Vizient database and Agency for Healthcare Research data model. The dashboard was deployed in February 2024 and patient data is updated bimonthly.

Results: At time of inquiry, the Surgical DEI Dashboard contained data from 966 cases from July 2022 to January 2024. Relevant DEI display tabs include an Equity Snapshot (Fig 1) and an Equity Deep Dive (Fig 2). In addition to tracking usual surgical metrics such as case volume and complications, the incorporation of SDH variables and DEI tab design allow for a deeper dive and identification of potential disparities in surgical outcomes.

Conclusion: The Surgical DEI dashboard is a novel interactive tool that allows clinicians and researchers to identify, intervene on and subsequently track outcome disparities in a prospective manner, enhancing equitable patient experiences and quality of care.

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