

2021

THE 32<sup>ND</sup> ANNUAL  
**RESEARCH  
DAY SYMPOSIUM**

**APRIL 20, 2021**

Lecture Hall 2222  
Medical Education Bldg



**ASKING THE RIGHT QUESTIONS:  
HOW RESEARCH AND RESIDENTS CAN IMPACT PRACTICE**

Keynote Speaker | **Julie Ann Sosa, MD, MA, FACS, MAMSE, FSSO**  
Leon Goldman, MD Distinguished Professor of Surgery and  
Chair, Department of Surgery  
Professor, Department of Medicine  
Affiliated Faculty, Philip R. Lee Institute for Health Policy Studies  
University of California San Francisco - UCSF

# PROGRAM NOTES

# AGENDA | APRIL 20<sup>TH</sup>, 2021

TIME	SESSION	LOCATION
6:30 AM - 7:00 AM	BREAKFAST AND REGISTRATION	NORTH FOYER/ LH 2222
7:15 AM - 7:30 AM	WELCOME AND INTRODUCTION	LH 2222
7:30 AM - 9:00 AM	ORAL PRESENTATIONS SESSION 1	LH 2222
9:00 AM - 9:15 AM	BREAK	
9:15 AM - 10:15 AM	QUICK SHOT SESSION 1A	LH 2222
9:15 AM - 10:15 AM	QUICK SHOT SESSION 1B	LH 1222
10:15 AM - 10:30 AM	BREAK	
10:30 AM - 12:00 PM	ORAL PRESENTATIONS SESSION 2	LH 2222
12:00 PM - 12:30 PM	LUNCH	NORTH FOYER
12:30 PM - 1:30 PM	KEYNOTE SPEAKER PRESENTATION DR. JULIE ANN SOSA	LH 2222
1:30 PM - 3:00 PM	ORAL PRESENTATION SESSION 3	LH 2222
3:00 PM - 3:15 PM	BREAK	
3:15 PM - 4:25 PM	QUICK SHOT SESSION 2A	LH 2222
3:15 PM - 4:25 PM	QUICK SHOT SESSION 2B	LH 1222
4:30 PM - 4:45 PM	FINAL REMARKS	LH 2222
5:00 PM - 6:00 PM	AWARDS ANNOUNCEMENT	LH 2222

# PROGRAM SCHEDULE | SESSIONS IN LH 2222

6:30 AM - 7:00 AM  
7:15 AM - 7:30 AM

**BREAKFAST AND REGISTRATION**  
**WELCOME AND INTRODUCTION**

## ORAL PRESENTATIONS SESSION 1 LH 2222 | 7:30 AM - 9:00 AM

**MODERATORS - DR. KATHLEEN ROMANOWSKI & DR. BETHANY CUMMINGS**

- 7:30 AM - 7:45 AM** **CHRISTINA THEODOROU** - Efficacy of Clinical-Grade Human Placental Mesenchymal Stromal Cells in Fetal Ovine Myelomeningocele Repair
- 7:45 AM - 8:00 AM** **JOHN ANDRE** - Major Psychiatric Illness and Substance Use Disorder influence mortality in major burn injury: a secondary analysis of the Transfusion Requirement in Burn Care Evaluation (TRIBE) study
- 8:00 AM - 8:15 AM** **SYLVIA CRUZ** - Natural Killer and Cytotoxic T Cell Immune Infiltrates are Associated with Superior Outcomes in Soft Tissue Sarcomas
- 8:15 AM - 8:30 AM** **MARLENA HOLTER (VIRTUAL)** - Beta-cell glucagon-like peptide-1 receptor signaling activates alpha-cell glucagon-like peptide-1 expression through a paracrine protein factor
- 8:30 AM - 8:45 AM** **SEAN JUDGE** - Gene expression analysis of sarcoma-infiltrating NK cells identifies signatures correlating with favorable prognosis and potential new targets for augmenting NK function
- 8:45 AM - 9:00 AM** **ASHLY RUF** - Incidental Findings found on Abdominal Imaging performed for Acute Care Surgery Patients
- 9:00 AM - 9:15 AM** **BREAK**

## QUICK SHOT SESSION 1 A LH 2222 | 9:15 AM - 10:15 AM

**MODERATORS - DR. ROBERT CANTER & DR. MINNA WIECK**

- 9:15 AM - 9:25 AM** **CHRISTINA THEODOROU** - Fetal Myelomeningocele Repair with Placental Mesenchymal Stromal Cells Results in Normal Bowel and Bladder Function in Lambs
- 9:25 AM - 9:35 AM** **DAKE HAO** - Developing a novel vascular device coating technology to improve rapid endothelialization, inhibit platelet binding and suppress thrombosis
- 9:35 AM - 9:45 AM** **SARAH STOKES** - Central Venous Catheter Placement in Pediatric Oncology Patients: What is the impact of thrombocytopenia?
- 9:45 AM - 9:55 AM** **JOHN ANDRE** - Modified Frailty Index is an independent predictor of death in the burn population: a secondary analysis of the Transfusion Requirement in Burn Care Evaluation (TRIBE) study
- 9:55 AM - 10:05 AM** **ALICIA GINGRICH (VIRTUAL)** - Missing a "Missing Self" Mechanism: Modeling and Detection of Ly49 Expression in Canine Natural Killer Cells
- 10:05 AM - 10:15 AM** **PRIYADARSINI KUMAR (VIRTUAL)** - Manufacturing Clinical Grade Placenta-derived Mesenchymal Stem Cells for In Utero Fetal Repair of Myelomeningocele: Path to a Successful FDA Investigational New Drug (IND) Application
- 10:15 AM - 10:30 AM** **BREAK**

# SESSIONS IN LH 2222

## ORAL PRESENTATIONS SESSION 2 LH 2222 | 10:30 AM - 12:00 PM

**MODERATORS - DR. DAVID COOKE & DR. MICHAEL CAMPBELL**

- 10:30 AM - 10:45 AM** **CHRISTOPHER HOLLAND** - The Analysis of Intravenous Dexmedetomidine Use in Total Hip Arthroplasty
- 10:45 AM - 11:00 AM** **NIKIA MCFADDEN** - Patient and provider perceptions of the trauma and emergency general surgery discharge process
- 11:00 AM - 11:15 AM** **YUFENG XUE** - Biomechanical Study of Biodegradable Screw Fixation in Maxillofacial Distraction Osteogenesis
- 11:15 AM - 11:30 AM** **TAJIA GREEN (VIRTUAL)** - Cytokine responses to bacterial byproducts is individual specific and may be influenced by glucocorticoid receptor
- 11:30 AM - 11:45 AM** **DAKE HAO** - Engineering the developmental milieu to repair spina bifida bony defect in utero
- 11:45 AM - 12:00 PM** **LALITHASRI RAMASUBRAMANIAN** - Characterization of Lipid Raft Nanovesicles as Neuroprotective and Angiogenic Exosome-Mimics
- 12:00 PM - 12:30 PM** **LUNCH**
- 12:30 PM - 1:30 PM** **KEYNOTE SPEAKER PRESENTATION BY DR. JULIE ANN SOSA**  
*"Asking the Right Questions: How Research and Residents can Impact Practice"*

## ORAL PRESENTATION SESSION 3 LH 2222 | 1:30 PM - 3:00 PM

**MODERATORS - DR. LUIS GODOY & DR. DEBORAH KELLER**

- 1:30 PM - 1:45 PM** **SARAH STOKES** - Impact of Gestational Age on Neuroprotective Function of Placental Mesenchymal Stromal Cells
- 1:45 PM - 2:00 PM** **JEREMY BOLIN** - Barriers and Opportunities for Improving Abdominal Aortic Aneurysm Screening in an Open Healthcare System
- 2:00 PM - 2:15 PM** **ANNA XUE** - Structured Team Training Improves Efficiency of Robot-assisted Mitral Valve Surgery
- 2:15 PM - 2:30 PM** **KAITLIN CLARK** - Comparison of Canine Adipose and Placenta-derived Mesenchymal Stromal Cells: Applications to Inflammatory Brain Disease
- 2:30 PM - 2:45 PM** **DATTESH DAVE** - Modified Frailty Index Identifies Increased Risk of Post-Operative Complications Following ORIF for Distal Radius and Ulna Fractures: Analysis of 5,654 geriatric patients, From the 2005-2017 NSQIP database
- 2:45 PM - 3:00 PM** **KATHRYN DILOSA** - Intern Perceptions and Participation in the Operating Room
- 3:00 PM - 3:15 PM** **BREAK**

# SESSIONS IN LH 2222

QUICK SHOT SESSION 2A - LH 2222 | 3:15 PM - 4:25 PM

MODERATORS - DR. VICTORIA LYO & DR. TANYA RINDERKNECHT

- 3:15 PM - 3:25 PM** *ANNA XUE* - The role of TachoSil® fibrin sealant patch in reducing postoperative air leak in patients undergoing minimally invasive lung resection
- 3:25 PM - 3:35 PM** *MATTHEW ZEIDERMAN* - Trends in Adult and Pediatric Upper Extremity Peripheral Nerve Injury—Why Are Costs Increasing?
- 3:35 PM - 3:45 PM** *KEWA GAO* - In utero transplantation of placenta-derived endothelial progenitor cells for Hemophilia A treatment in an operable mouse model
- 3:45 PM - 3:55 PM** *LEORA GOLDBLOOM-HELZNER (VIRTUAL)* - Optimizing the yield of placental mesenchymal stromal cell-derived extracellular vesicles in 3D culture systems
- 3:55 PM - 4:05 PM** *LAUREN PERRY (VIRTUAL)* - Is the Improved Survival in Early-Stage Pancreatic Cancer Worth the Extra Cost at High-Volume Centers?
- 4:05 PM - 4:15 PM** *JOSEPH FIRRIOLO* - Craniopagus Separation Using A Novel Tissue Expander Design
- 4:15 PM - 4:25 PM** *TATYANA POLYAK* - Opioid Utilization and Prescribing Patterns in the University of California Davis Medical Center Department of Surgery: An Overview of the Current State
- 4:30 PM - 4:45 PM** **FINAL REMARKS**
- 5:00 PM - 6:00 PM** **AWARDS ANNOUNCEMENT**

# SESSIONS IN LH 1222

## 7:30 AM - 9:00 AM LH2222 ORAL PRESENTATION SESSION 1 VIEWING

### QUICK SHOT SESSION 1B - LH 1222 | 9:15 AM - 10:15 PM

#### MODERATORS - DR. ANDREW LI & DR. CLAIRE GRAVES

- 9:15 AM - 9:25 AM** **ASHLY RUF** - Dedicated Acute Care Surgery Operating Room: The Halo Effect of COVID
- 9:25 AM - 9:35 AM** **SIOBHAN LUCE** - Outcomes of Renal Transplantation in Undocumented Immigrants
- 9:35 AM - 9:45 AM** **CHAOXING ZHANG** - 3D bioprinting of Multifunctional bioengineered scaffolds for spina bifida repair
- 9:45 AM - 9:55 AM** **SIRJAN MOR** - Efficient Maintenance and Manipulation of Chicken Embryonic Stem Cells Acting as a Potential Bioreactor for the Mass Production of Human Therapeutic Proteins
- 9:55 AM - 10:05 AM** **TATYANA POLYAK** - The impact of dedicated social media strategy on increasing traffic to Surgical Research
- 10:05 AM - 10:15 AM** **KAITLIN CLARK** - Postnatal treatment of Canine Spina Bifida using Placenta-derived Mesenchymal Stem/Stromal Cells: Clinical Trial Update
- 10:15 AM - 10:30 AM** **BREAK**

## 10:30 AM - 12:00 PM LH 2222 ORAL PRESENTATION SESSION 2 VIEWING

## 1:30 PM - 3:00 PM LH 2222 ORAL PRESENTATION SESSION 3 VIEWING

### QUICK SHOT SESSION 2B - LH 1222 | 3:15 PM - 4:25 PM

#### MODERATORS - DR. FADWA ALI & DR. JONATHAN KOHLER

- 3:15 PM - 3:25 PM** **JENNIFER GEIGER** - A Needs Assessment for Palliative Care Curriculum Development in Surgical Residents
- 3:25 PM - 3:35 PM** **CHRISTOPHER HOLLAND** - Opioid Use in Revision Total Knee Arthroplasty
- 3:35 PM - 3:45 PM** **ANAMARIA ROBLES** - Relationship of Post-Resuscitation Hemoglobin to Future Blood Transfusion Needs
- 3:45 PM - 3:55 PM** **CHRISTINA BROWN (VIRTUAL)** - Changes in Early Post-Operative Toe-Brachial Indices May Reflect Positive or Negative Remodeling
- 3:55 PM - 4:05 PM** **GILLIAN HOSHAL** - Surgical Trainee Perspectives During COVID - 19
- 4:05 PM - 4:15 PM** **MATTHEW KIM (VIRTUAL)** - Hyaluronidase (HYAL) Availability in Emergency Rooms: A Californian Census
- 4:15 PM - 4:25 PM** **TREVOR PLESCIA** - The impact of bariatric surgery on the development of small intestinal bacterial overgrowth (SIBO)

# Welcome from the Chairs

Welcome to the 32<sup>nd</sup> Annual Department of Surgery Research Symposium at the University of California, Davis. The current pandemic has provided us the opportunity to develop new research initiatives, technologies, and collaborations.

This year we are hosting Julie Ann Sosa, MD MA FACS, Leon Goldman MD Distinguished Professor of Surgery and Chair of the Department of Surgery at the University of California San Francisco (UCSF), where she is also a Professor in the Department of Medicine and affiliated faculty for the Philip R. Lee Institute for Health Policy Studies. Her clinical interest is in endocrine surgery, with a focus in thyroid cancer. We are looking forward to her lecture presentation on *Asking the Right Questions: How Research and Residents can Impact Practice*.

This Symposium celebrates our research successes and provides an opportunity for trainees to hone their research presentations as they share their work. Research is a core value of the Department of Surgery and is made possible by the hard work of the faculty, staff, and trainees. Our program includes oral presentations and quick-shot oral poster presentations that highlight the diverse research in the Department of Surgery. We will award prizes for the top clinical and basic science oral presentations as well as the best quick-shot oral presentation.

Thank you for joining us today to celebrate research in the Department of Surgery!

Sincerely,

Diana L. Farmer, MD, FACS, FRCS

Distinguished Professor and Pearl Stamps Endowed Chair, Department of Surgery UC Davis Health, Surgeon-in-Chief, UC Davis Children's Hospital

Tina L. Palmieri, MD, FACS, FCCM

Burn Division Chief, Professor and Director, Firefighters Burn Institute Burn Center at the University of California Davis, Assistant Chief of Burns, Shriners Hospital for Children Northern California

Sean H. Adams, MS, PhD

Professor and Vice Chair for Basic Research, Department of Surgery





# RESEARCH VICE CHAIRS



**Tina Palmieri, MD, FACS, FCCM**  
Vice Chair, Clinical Research



**Sean H. Adams, MS, PhD**  
Vice Chair, Basic Research



**Rachael Callcut, MD, MSPH**  
Vice Chair, Clinical Sciences



**Aijun Wang, PhD**  
Vice Chair, Translational  
Research, Innovation, and  
Entrepreneurship

# RESEARCH COMMITTEE



**Shushmita Ahmed, MD**  
Foregut, Metabolic,  
and General Surgery



**Erin Brown, M.D.**  
Pediatric General Surgery



**Ian Elliott Brown, MD, PhD**  
Trauma, ACS



**Lisa M Brown, MD, MAS**  
General Thoracic Surgery



**Robert J. Canter, MD**  
Surgical Oncology



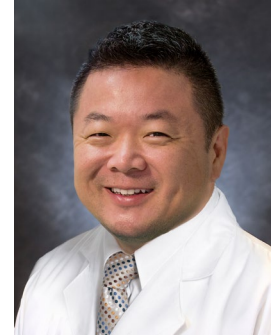
**Kiho Cho, DVM, PhD**  
Research, Burns



**Bethany Cummings, DVM, PhD**  
Metabolism and Obesity  
Researcher



**David Greenhalgh, MD**  
Burn Surgery &  
Reconstruction



**Shinjiro Hirose, MD**  
Pediatric General Surgery

# RESEARCH COMMITTEE



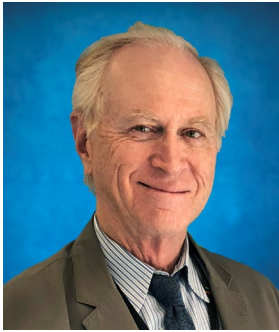
**Misty Humphries, MD,  
MAS, RPVI**  
Vascular Surgery



**Deborah Keller, MD**  
Colorectal Surgery



**Bob Kiaii, MD**  
Cardiac Surgery



**Kent Lloyd, DVM, PhD**  
Research, Surgery



**Victoria Lyo, MD, MTM**  
Foregut, Metabolic,  
and General Surgery



**Clifford Pereira, MD**  
Plastic Surgery &  
Reconstruction



**Lee LQ Pu, MD, PhD**  
Plastic Surgery &  
Reconstruction



**Junichiro Sageshima, MD**  
Transplant Surgery

# Keynote Speaker – Julie Ann Sosa, MD, MA, FACS



Dr. Sosa is the Leon Goldman MD Distinguished Professor of Surgery and Chair of the Department of Surgery at the University of California San Francisco (UCSF), where she is also a Professor in the Department of Medicine and affiliated faculty for the Philip R. Lee Institute for Health Policy Studies. Dr. Sosa came to UCSF in 2018 from Duke. Her clinical interest is in endocrine surgery, with a focus in thyroid cancer. She is an NIH- and FDA-funded investigator and author of more than 340 peer-reviewed publications and 80 book chapters and reviews, all largely focused on outcomes research, health care delivery, hyperparathyroidism, and thyroid cancer, with a focus on clinical trials. She has authored or edited 7 books. Dr. Sosa is Treasurer of the American Thyroid Association (ATA) and serves on the Board of Directors/Executive Council of the ATA and International Thyroid Oncology Group, as well as practice guidelines committees for the ATA, NCCN, and the American Association of Endocrine Surgeons; for the ATA, she is chairing the committee responsible for writing the next iteration of differentiated thyroid cancer guidelines. She is the Editor-in-Chief of the *World Journal of Surgery* and is an editor of *Greenfield's Surgery: Scientific Principles and Practice*. She has mentored more than 90 students, residents, and fellows, for which she was recognized with induction as a full member to the American College of Surgeons Academy of Master Educators in 2020, and with the Lewis E. Braverman Distinguished Lectureship Award from the ATA in 2017. Dr. Sosa was born in Montreal and raised in upstate New York. She received her AB at Princeton, MA at Oxford, and MD at Johns Hopkins, where she completed the Halsted residency and a fellowship.

# ORAL PRESENTATIONS

## ORAL PRESENTATIONS SESSION 1 LH 2222 | 7:30 AM - 9:00 AM

### MODERATORS

## DR. KATHLEEN ROMANOWSKI & DR. BETHANY CUMMINGS

1. **CHRISTINA THEODOROU** - Efficacy of Clinical-Grade Human Placental Mesenchymal Stromal Cells in Fetal Ovine Myelomeningocele Repair
2. **JOHN ANDRE** - Major Psychiatric Illness and Substance Use Disorder influence mortality in major burn injury: a secondary analysis of the Transfusion Requirement in Burn Care Evaluation (TRIBE) study
3. **SYLVIA CRUZ** - Natural Killer and Cytotoxic T Cell Immune Infiltrates are Associated with Superior Outcomes in Soft Tissue Sarcomas
4. **MARLENA HOLTER (VIRTUAL)** - Beta-cell glucagon-like peptide-1 receptor signaling activates alpha-cell glucagon-like peptide-1 expression through a paracrine protein factor
5. **SEAN JUDGE** - Gene expression analysis of sarcoma-infiltrating NK cells identifies signatures correlating with favorable prognosis and potential new targets for augmenting NK function
6. **ASHLY RUF** - Incidental Findings found on Abdominal Imaging performed for Acute Care Surgery Patients

## Efficacy of Clinical-Grade Human Placental Mesenchymal Stromal Cells in Fetal Ovine Myelomeningocele Repair

Christina Theodorou MD, Sarah Stokes MD, Jordan Jackson MD, Christopher Pivetti MS, Priyadarsini Kumar PhD, Kaeli Yamashiro DO, Zachary Paxton BS, Lizette Reynaga BS, Alicia Hyllen MA, Aijun Wang PhD, Diana Farmer MD

UC Davis Medical Center Department of Pediatric Surgery

**Background:** While fetal repair of myelomeningocele improved outcomes, many children are still unable to walk. Preclinical studies demonstrated that research-grade placental mesenchymal stromal cells (PMSCs) rescue spinal cord neurons and prevent paralysis in fetal ovine myelomeningocele, but this has not been replicated with clinical-grade cells that could be used in an upcoming human clinical trial. We produced clinical-grade PMSCs seeded on an extracellular matrix (PMSC-ECM) in a Good Manufacturing Practice setting to evaluate the effect on motor function in fetal ovine myelomeningocele repair.

**Methods:** Myelomeningocele defects were surgically created in 20 ovine fetuses (median 74.5 days gestational age, GA). At a median of 101 days GA, defect repair was performed with either application of a clinical-grade PMSC-ECM ( $n = 12$  lambs, density of  $3 \times 10^5$  cells/cm<sup>2</sup>) directly to the exposed spinal cord or application of an ECM without PMSCs ( $n = 8$  lambs) directly to the exposed spinal cord. Three normal lambs underwent no surgical interventions. The primary outcome was motor function measured by the Sheep Locomotor Rating scale (SLR, range 0: complete paralysis to 15: normal ambulation) at birth. The secondary outcome was correlation of lumbar spine large neuron density with SLR.

**Results:** Clinical-grade PMSC-ECM lambs had significantly better motor function than ECM-only lambs (SLR score 14.5 vs. 6.5,  $p=0.04$ ) and were similar to normal lambs (14.5 vs. 15,  $p=0.2$ ). Lumbar spine large neuron density was strongly correlated with motor function ( $r = 0.753$ ,  $p < 0.001$ ).

**Conclusions:** Clinical-grade placental mesenchymal stromal cells seeded on an extracellular matrix rescued ambulation in a fetal ovine myelomeningocele model. Lumbar spine large neuron density correlated with motor function, suggesting a neuroprotective effect of the PMSC-ECM in prevention of hindlimb paralysis. A first-in-human clinical trial of PMSCs in human fetal myelomeningocele repair is underway.

# John Andre

Major Psychiatric Illness and Substance Use Disorder influence mortality in major burn injury: a secondary analysis of the Transfusion Requirement in Burn Care Evaluation (TRIBE) study

Dr. John Andre MD, Dr. Soman Sen MD, FACS, Dr. David Greenhalgh MD, FACS, Dr. Tina Palmieri MD, FACS, FCCM, Dr. Kathleen Romanowski MD, FACS

UC Davis Medical Center, Burn Surgery, Sacramento, CA, USA

**Introduction:** Prior studies of burn patients with <20% total body surface area (TBSA) burns have found that 15.4% of patients have major psychiatric illness (MPI) and 27.6% have Substance Use Disorder (SUD). In patients with small burns, SUD is associated with larger burn size and with longer length of stay, while MPI is associated longer lengths of stay. The purpose of this study was to determine whether MPI or SUD dependence affects outcomes such as mortality in patients with major burn injuries ( $\geq 20\%$  TBSA).

**Methods:** A secondary analysis from the prospective, randomized, multicenter TRIBE study was conducted. Patients with MPI and SUD were compared with patients without these disorders. Statistical analysis with chi-square for categorical variables and student's t-test for continuous variables was conducted. Mortality between those with and without MPI and SUD were analyzed with a multivariable regression analysis.

**Results:** A total of 347 patients were analyzed. In this study population 29.1% had SUD, 7.5% had MPI, and 2.3% had both. There was no difference with respect to age, gender, TBSA, or frailty based on the presence of MPI, SUD or both. Inhalation injury was more common in patients with MPI (27%) or SUD (35%) when compared with patients without these comorbidities (18%) or those who have both (11%) ( $p=0.006$ ). Patients with MPI were more likely to die of their burn injuries (27%) when compared with those with SUD (17%), both (11%), or neither (8%) ( $p=0.014$ ). On multivariate analysis for mortality controlling for TBSA and inhalation injury, MPI was found to be an independent predictor of death with an odds ratio of 5 (95% confidence interval 1.7-15,  $p=0.003$ ).

**Conclusions:** In burns  $>20\%$  TBSA, both MPI and SUD influence patient's likelihood of sustaining inhalation injury. MPI is also independently associated with mortality in the study. Further work must be done to mitigate the effects of mental illness on burn outcomes.

## Natural Killer and Cytotoxic T Cell Immune Infiltrates are Associated with Superior Outcomes in Soft Tissue Sarcomas

Sylvia M Cruz<sup>1</sup>, Sean J Judge<sup>2</sup>, Morgan A Darrow<sup>3</sup>, Cordelia Dunai<sup>4</sup>, Shuai Chen<sup>5</sup>, Steven W Thorpe<sup>6</sup>, Robert J Canter<sup>2</sup>

<sup>1</sup>University of California Davis School of Medicine, Sacramento, CA, USA. <sup>2</sup>Surgery, University of California Davis School of Medicine, Sacramento, CA, USA. <sup>3</sup>Pathology and Laboratory Medicine, University of California Davis School of Medicine, Sacramento, CA, USA. <sup>4</sup>Dermatology, University of California Davis School of Medicine, Sacramento, CA, USA. <sup>5</sup>Public Health Sciences, University of California Davis School of Medicine, Sacramento, CA, USA. <sup>6</sup>Orthopedic Surgery, University of California Davis School of Medicine, Sacramento, CA, USA

**Background:** Tumor infiltrating lymphocytes (TILs) have been shown to predict survival in soft tissue sarcomas (STS); however, the contribution of specific lymphocyte subsets such as natural killer (NK) and memory T cells to STS outcomes is undefined. We sought to characterize the extent of NK and memory T cell infiltration in STS to determine the correlation of these cytotoxic immune cells to outcomes.

**Methods:** Archived tumor tissue from 29 STS patients collected from 2008-2014 was evaluated. Tissue microarrays (TMAs) were constructed, and immunohistochemical analyses were performed by an STS pathologist for CD3, CD8, CD45RO, NKp46, TIGIT, and MHC-I. TIL scores of H&E slides were calculated. Metastasis-free survival (MFS) and overall survival (OS) were analyzed by Kaplan-Meier method.

**Results:** Among our cohort (mean age 56, 59% female), mean tumor size was 15.3 cm, consistent with a high-risk population. Majority of tumors (65%) were located on the extremity, 28% were retroperitoneal, and 7% trunk. The most common histologies were liposarcoma (34%), myxofibrosarcoma (21%), and pleomorphic sarcoma (21%) with 79% high grade. With a median follow up of 50 months, MFS and OS were 22 and 87 months, respectively. We confirmed a positive correlation between CD8<sup>+</sup> T cell infiltration and significantly improved MFS ( $P<0.05$ ), but not OS. Overall, NK cell infiltrates were low (median H score 0, range 0-66.5). However, we observed a trend for improved OS among patients with higher NKp46 scores (OS 68 months for NKp46 scores below median versus not reached for scores above median,  $P=0.08$ ). The expression of NK inhibitory markers TIGIT and MHC-I correlated with T cell infiltration ( $P<0.05$ ), but not NK cell infiltration.

**Conclusion:** Infiltration of cytotoxic lymphocyte subsets, including NK cells, is associated with superior OS in STS patients undergoing surgery. Further characterization of the immune infiltrate in STS may yield better biomarkers of prognosis and immune targeting.



# Marlena Holter

Beta-cell glucagon-like peptide-1 receptor signaling activates alpha-cell glucagon-like peptide-1 expression through a paracrine protein factor

Marlena M. Holter BA<sup>1</sup>, Daryl J. Phuong BS<sup>1</sup>, Dr. Mridusmita Saikia PhD<sup>1,2</sup>, Isaac Lee BS<sup>1</sup>, Lisa Weikert BS<sup>1</sup>, Dr. Bethany P. Cummings DVM, PhD<sup>1,3</sup>

<sup>1</sup>Cornell University College of Veterinary Medicine, Department of Biomedical Sciences, Ithaca, NY, USA.

<sup>2</sup>Cornell University, Nancy E. and Peter C. Meinig School of Biomedical Engineering, Ithaca, NY, USA. <sup>3</sup>UC Davis School of Medicine, Department of Surgery, Center for Metabolic and Ailmentary Disease, Sacramento, CA, USA

Glucagon-like peptide 1 (GLP1) is a hormone secreted by the gut that lowers blood glucose levels by enhancing glucose-stimulated insulin secretion from pancreatic  $\beta$ -cells. Under certain conditions, islet  $\alpha$ -cells can express prohormone convertase 1/3 (gene: *Pcsk1*) and produce GLP1 at the expense of glucagon. Identification of the precise intra-islet signaling through which  $\alpha$ -cell *Pcsk1* expression is regulated will enable targeting of the  $\alpha$ -cell for T2D treatment. We previously found that the  $\beta$ -cell GLP1 receptor (GLP1R) contributes to improved islet function after vertical sleeve gastrectomy (VSG); and further that VSG increases  $\alpha$ -cell GLP1 expression by activating *Pcsk1* expression in a  $\beta$ -cell GLP1R-dependent manner in mice. To determine if VSG-induced increases in  $\beta$ -cell GLP1R signaling increases  $\alpha$ -cell GLP1 expression through a secreted factor, we studied the impact of conditioned media (CM) generated from  $\beta$ -cell GLP1R WT and KO islets from sham or VSG-operated mice on  $\alpha$ -cell gene expression. CM from islets isolated from VSG mice increased  $\alpha$ -cell *Pcsk1* expression 4-fold in a  $\beta$ -cell GLP1R-dependent manner ( $P < 0.05$ ). We then tested if this effect could be induced by the GLP1R agonist, liraglutide. Similar to VSG, CM from islets of liraglutide-treated mice increased  $\alpha$ -cell *Pcsk1* 13-fold in a  $\beta$ -cell GLP1R-dependent manner ( $P < 0.05$ ). To assess if the factor mediating this effect was a protein, we treated CM derived from islets of liraglutide and saline-treated mice with proteinase K or a freeze-thaw. Both treatments ablated the ability of CM from islets of liraglutide-treated mice to increase  $\alpha$ -cell *Pcsk1*. We then performed a series of molecular weight fractionations on CM from islets of liraglutide and saline-treated mice. Only CM containing proteins greater than 50kD from islets of liraglutide-treated mice increased  $\alpha$ -cell *Pcsk1* ( $P < 0.05$ ). Our data demonstrate that the effect of  $\beta$ -cell GLP1R signaling to increase  $\alpha$ -cell GLP1 expression is mediated by a secreted protein greater than 50kD.

# Sean Judge

Gene expression analysis of sarcoma-infiltrating NK cells identifies signatures correlating with favorable prognosis and potential new targets for augmenting NK function

Sean Judge M.D., M.S.<sup>1</sup>, Cordelia Dunai Ph.D.<sup>2</sup>, Aryana Razmara B.S.<sup>3</sup>, Sylvia Cruz B.S.<sup>1</sup>, Robert Canter M.D.<sup>1</sup>

<sup>1</sup>University of California - Davis, Division of Surgical Oncology, Sacramento, CA, USA. <sup>2</sup>University of California - Davis, Department of Dermatology, Sacramento, CA, USA. <sup>3</sup>University of California - Davis, School of Veterinary Medicine, Davis, CA, USA

**Introduction:** The success of current immunotherapies in soft tissue sarcomas (STS) has been limited, while pre-clinical studies have shown evidence of natural killer (NK) cell activity in STS. We set out to evaluate the gene expression profile of tumor-infiltrating NK cells with the goal of identifying potential novel therapeutic targets.

**Methods:** Matched peripheral blood and freshly excised STS tissue was collected and processed for FACS isolation of purified peripheral and tumor-infiltrating NK and T cells from patients. Isolated immune populations were then evaluated by RNA sequencing analysis. To allow for analysis of survival differences and differential gene expression based on NK activity, we also queried the publicly available TCGA database to compare NK signatures associated with “NK Activating TME” and “NK Suppressing TME”.

**Results:** Comparing Differential Gene Expression (DGE) of intra-tumoral NK cells to circulating NK cells revealed upregulation of genes involved in mitogen signaling inhibition (DUSP4) and metabolic function (SMPD3, SLC7A5), but not of genes associated with cytotoxic function (e.g. IFNG, GZMB). In contrast, intra-tumoral T cells showed significant upregulation of established activating (CD137) and inhibitory genes (TIM-3) compared to circulating T cells. For the TCGA analysis, patients with an NK Activating TME had significantly improved survival compared to an NK Suppressive TME (log-rank  $p = 0.03$ ). DGE of the TCGA dataset identified unique tumor-associated gene ontology segregating these NK subsets with upregulation of the retinoic acid pathway in particular.

**Conclusion:** Unlike T cells, which demonstrate significant DGE in activating and inhibiting receptors between circulating and tumor-infiltrating subsets, NK cells appear to have more similar gene expression pattern between blood and tumor, with alterations in metabolic pathways. Although intra-tumoral NK cells appear to be prognostic in STS, their anti-tumor functions may be dictated by systemic rather than local factors.

## Incidental Findings found on Abdominal Imaging performed for Acute Care Surgery Patients

Dr Ashly Ruf MD<sup>1</sup>, Amanda Aquilio<sup>2</sup>, Rafael Rafael Ricon<sup>2</sup>, Dr. Michael Michael Corwin MD<sup>3</sup>, Dr. Tom Loefelm MD PHD<sup>3</sup>, Dr Michael Campbell MD<sup>4</sup>

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**Introduction:** Over the last several decades the rising use of computed tomography (CT) has led to increased detection of incidental findings (IF). The incidence and nature of IFs found on patients admitted to an acute care surgery (ACS) service has not been well evaluated.

**Methods:** ACS patients at a high-volume tertiary referral center admitted from January 2014 to December 2019 were reviewed. The incidence, rate of follow-up and ultimate diagnoses of IFs on an admission CT in patients with a primary care physician (PCP) within the hospital system were evaluated.

**Results:** 433 ACS patients had an IF on admission CT with an in-network PCP. 108 (24.9%) received follow-up for their IF. The most common incidental finding were kidney lesions (n=53), followed by hepatic lesions (n=31) and adrenal lesions (n=21). On univariate analysis factors associated with appropriate follow-up were having the IF highlighted in the discharge summary (p=0.0001), in the impression of the CT report (p=0.0001) and recommendations made by the radiologist within the CT report (p= 0.0005). On multivariable analysis all three of these variables remained independently associated with follow-up. Of the 108 patients with an IF that received follow-up, 12 patients had IF that was considered to be clinically significant including renal cell carcinoma, adenocarcinoma of the colon and B cell lymphoma.

**Conclusion:** IFs are frequently found on the evaluation of ACS patients. The majority of patients with an IF do not receive appropriate follow-up. IFs found on the workup for ACS patient represents an opportunity for general surgeons to improve patient care.

# QUICK SHOT PRESENTATIONS

## QUICK SHOT SESSION 1A LH 2222 | 9:15 AM - 10:15 AM

### MODERATORS DR. ROBERT CANTER & DR. MINNA WIECK

1. **CHRISTINA THEODOROU** - Fetal Myelomeningocele Repair with Placental Mesenchymal Stromal Cells Results in Normal Bowel and Bladder Function in Lambs
2. **DAKE HAO** - Developing a novel vascular device coating technology to improve rapid endothelialization, inhibit platelet binding and suppress thrombosis
3. **SARAH STOKES** - Central Venous Catheter Placement in Pediatric Oncology Patients: What is the impact of thrombocytopenia?
4. **JOHN ANDRE** - Modified Frailty Index is an independent predictor of death in the burn population: a secondary analysis of the Transfusion Requirement in Burn Care Evaluation (TRIBE) study
5. **ALICIA GINGRICH (VIRTUAL)** - Missing a “Missing Self” Mechanism: Modeling and Detection of Ly49 Expression in Canine Natural Killer Cells
6. **PRIYADARSINI KUMAR (VIRTUAL)** - Manufacturing Clinical Grade Placenta-derived Mesenchymal Stem Cells for In Utero Fetal Repair of Myelomeningocele: Path to a Successful FDA Investigational New Drug (IND) Application

# Christina Theodorou

Fetal Myelomeningocele Repair with Placental Mesenchymal Stromal Cells Results in Normal Bowel and Bladder Function in Lambs

Christina Theodorou MD, Jordan Jackson MD, Sarah Stokes MD, Christopher Pivetti MS, Priyadarsini Kumar PhD, Kaeli Yamashiro DO, Zachary Paxton BS, Alicia Hyllen MA, Lizette Reynaga BS, Arthur de Lorimier MD, Aijun Wang PhD, Diana Farmer MD

UC Davis Medical Center Department of Pediatric Surgery, Sacramento, CA

**Background:** Fetal myelomeningocele (MMC) repair improves ambulation, but patients continue to suffer from neurogenic bowel and bladder. We found that augmentation of fetal ovine MMC repair with placental mesenchymal stromal cells (PMSCs) further rescues ambulation. We hypothesized that the addition of PMSCs would improve bowel and bladder function in lambs.

**Methods:** Twelve ovine fetuses underwent MMC defect creation at median gestational age (GA) 73 days, MMC repair at GA101 with PMSCs applied directly to the spinal cord, and delivery at GA141. Primary bowel outcome was stool morphology (Bristol Stool Scale, range 1-7). Primary bladder outcome was urine void volumes, as animals with neurogenic bladder are unable to void normally. Secondary outcomes were presence of a rectoanal inhibitory reflex (RAIR) on manometry and normal voiding posture. MMC lambs were compared to normal lambs (n=3). Significance was set at  $p < 0.05$  (categorical outcomes: Fisher's exact test; continuous outcomes: Mann Whitney U test).

**Results:** Stool morphology was similar between groups (Bristol 4.5 in normal lambs vs. 5.5 in PMSC group,  $p = 0.8$ ). All normal lambs and three of five tested PMSC lambs had a RAIR. Urine void volumes were similar between groups (8.8 ml/kg in normal animals vs. 6.1 ml/kg in PMSC group,  $p = 0.3$ ). All normal lambs postured to void compared to 80% of PMSC lambs ( $p = 1.0$ ).

**Conclusion:** Repair of fetal myelomeningocele with PMSCs resulted in bowel and bladder function similar to normal lambs. A clinical trial is underway to evaluate outcomes of PMSCs in human fetal MMC repair.

# Dake Hao

Developing a novel vascular device coating technology to improve rapid endothelialization, inhibit platelet binding and suppress thrombosis

Dake Hao PhD<sup>1</sup>, Resident Jonathan Lin MD<sup>2</sup>, Laboratory Manager Christopher Pivetti MS<sup>1</sup>, Research Professor Ruiwu Liu PhD<sup>3</sup>, Resident Kaeli Yamashiro MD<sup>1</sup>, Resident Linda Schutzman MD<sup>4</sup>, Professor and Chair Diana Farmer MD<sup>1</sup>, Associate Professor Misty Humphries MD, MAS<sup>5</sup>, Executive Associate Dean Alyssa Panitch PhD<sup>6</sup>, Professor and Chair Kit Lam PhD, MD<sup>3</sup>, Associate Professor Aijun Wang PhD<sup>1</sup>

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**Introduction:** Vascular devices are widely used by the rising number of patients with different types of vascular diseases. However, currently available vascular devices are generally lack of regenerative potential and have extremely high failure rates due to thrombosis and restenosis. Establishment of a healthy endothelium on the blood contact surface of vascular devices is crucial in preventing thrombosis and restenosis. Thus, in this study, we propose to develop technology that enables generation of self-renewable “living” endothelium on the surface of vascular devices.

**Methods:** We identified LXW7, an integrin  $\alpha v \beta 3$  ligand by One-Bead One-Compound (OBOC) technology. Binding specificity and functions of LXW7 on endothelial cells (ECs) were examined. Effect of LXW7 on rapid endothelialization and patency of vascular grafts was evaluated in a rat carotid interposition graft model. We then established a parylene-based coating technology to immobilize LXW7 onto the surface of different types of vascular devices. Using clinical grade ePTFE vascular grafts as an example, we evaluated the functions of the parylene-LXW7 coating technology in two disease models in the pig: carotid artery interposition model and the carotid artery jugular vein arteriovenous graft model.

**Results:** LXW7 showed strong binding affinity to ECs, but not to platelets, monocytes, or other blood cells, promoted EC proliferation and enhanced the phosphorylation of VEGFR2 and ERK1/2 in ECs. In the rat model, LXW7 coating significantly improved endothelialization and patency of vascular grafts. In the pig models, LXW7 coating significantly improved endothelialization, suppressed platelet aggregation, thrombosis and restenosis.

**Conclusion:** Our results showed this novel LXW7 coating technology holds promising potential to generate self-renewable “living” endothelium and prevents thrombosis and restenosis on vascular devices with broad clinical applications.

# Sarah Stokes

Central Venous Catheter Placement in Pediatric Oncology Patients: What is the impact of thrombocytopenia?

Sarah Stokes<sup>1</sup>, Kaeli Yamashiro<sup>1</sup>, Erin Brown<sup>2</sup>

<sup>1</sup>University of California, Davis. <sup>2</sup>University of California, Davis, Division of Pediatric General, Thoracic and Fetal Surgery

**Background:** Concerns for bleeding complications in pediatric oncology patients with thrombocytopenia can lead to increased platelet transfusions and delays in CVC placement. We aimed to determine a platelet threshold for central venous catheter (CVC) placement in pediatric oncology patients.

**Methods:** Retrospective review of pediatric oncology undergoing CVC placement at a tertiary pediatric hospital from 2014-2019. Patients with platelet counts above and below  $50 \times 10^9/L$  were compared. The primary outcome was perioperative bleeding. Bleeding was categorized as mild if no intervention was required, moderate if the patient required a red blood cell transfusion and severe if the patient required a massive transfusion or surgical intervention.

**Results:** A total of 292 CVC placements in 242 patients were reviewed. Patients with a platelet count of  $<50 \times 10^9/L$  ( $n=22$ ) at the time of CVC placement were at increased risk of perioperative bleeding (13.6% vs. 2.2%,  $p=0.018$ ). This remained significant on multivariable regression controlling for age, weight, type of malignancy and pre-operative hemoglobin (OR 7.29, 95% CI 1.50-35.59). When evaluated by severity of bleeding patients with a platelet count of  $<50 \times 10^9/L$  remained more likely to have mild bleeding (13.6% vs. 1.1%,  $p=0.007$ ). However, there was no difference in the rate of moderate bleeding (0% vs. 1.1%,  $p>0.999$ ), and no patients experienced severe bleeding.

**Conclusion:** A platelet count of  $<50 \times 10^9/L$  at the time of CVC insertion is associated with increased risk of perioperative bleeding. However, the majority of this bleeding was mild, and there was no association between a platelet count of  $<50 \times 10^9/L$  and bleeding requiring intervention.

# John Andre

Modified Frailty Index is an independent predictor of death in the burn population: a secondary analysis of the Transfusion Requirement in Burn Care Evaluation (TRIBE) study

Dr. John Andre MD, Dr. Kathleen Romanowski MD, FACS, Dr. David Greenhalgh MD, FACS, Dr. Tina Palmieri MD, FACS, FCCM, Dr. Soman Sen MD, FACS

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**Introduction:** Previous studies in the burn population have noted frailty as an independent predictor of inpatient and outpatient mortality. The Modified Frailty Index (MFI) uses comorbidities tracked by the American College of Surgeons National Surgical Quality Improvement Program to help to predict morbidity and mortality in patients. The purpose of this study was to determine whether or not the MFI-5 and MFI-11 would predict mortality in the burn population.

**Methods:** A secondary analysis of the prospective, randomized, multicenter TRIBE study was conducted. Statistical analysis with chi-square for categorical variables and student's t-test for continuous variables were conducted. Frailty was determined using the MFI-5 and MFI-11 scales from comorbidities included in the Burn Registry. Patients were considered frail if they had an MFI > 1 on either scale. Multivariate regression was used to compare mortality between those who were and those were not considered frail based on this index.

**Results:** A total of 347 patients with a mean age of 43±17 years, 73 women and 274 men, were analyzed. Mean total body surface area burn (TBSA) was 38±18%, and 23% had inhalation injury. Having a MFI-11 > 1 was considered an independent predictor of mortality (OR 2.91; 95% CI 1.1-7.7; p-value 0.03); whereas, having a MFI-5 > 1 was not considered an independent predictor of mortality (OR 2.6; 95% CI 0.95-7; p-value 0.06).

**Conclusions:** An MFI-11 > 1 in the burn population was an independent predictor of mortality. Given these findings, further study on the predictive value of MFI-11 in major burn injury is warranted.

**Applicability to Practice:** As the age of the general population continues to increase, so do the comorbidities that are faced in the burn population. The use of the MFI-11 can be used as an adjunct to the initial assessment of a burn patient, to help identify those who are at higher risk of mortality and to help guide appropriate treatment for this population.



# Alicia Gingrich

Missing a “Missing Self” Mechanism: Modeling and Detection of Ly49 Expression in Canine Natural Killer Cells

Dr. Alicia Gingrich MD, MS<sup>1</sup>, Phillip Gingrich MS<sup>2</sup>, Dr. Justin Siegel PhD<sup>2</sup>, Dr. Robert Canter MD<sup>1</sup>

<sup>1</sup>UCDMC, Sacramento, CA, USA. <sup>2</sup>UCD, Davis, CA, USA

**Background:** Natural killer (NK) cells are a key focus of immuno-oncology research based on their ability to recognize and eliminate malignant cells. Companion canines are valuable species to explore NK species differences between mice and humans which hinder clinical translation. Central to NK biology are KIR or Ly49 receptors which bind MHC-I to inhibit NK cell function. Absence of MHC-I on cell surface allows for NK targeting and has been termed the “missing self” hypothesis. The mechanism for identification of “self” by canine NK cells is unknown, and prior studies have failed to identify how dog NK cells recognize MHC-I.

**Methods:** Our focus was to interrogate gene expression and protein function of canine Ly49. We used protein homology modeling to generate a 3-dimensional structure of canine Ly49 based on a known structure of murine Ly49 as a template. Protein-protein docking simulations between canine MHC-I and our model were performed and compared to the known murine complex. RNA sequencing was performed to detect gene expression of Ly49 in resting and cytotoxic NK cells. Lastly, we performed proteomics by mass spectrometry to identify expressed Ly49 protein in canine peripheral blood samples.

**Results:** Despite the loss of a broadly conserved disulfide bond, canine Ly49 predicted protein structure did not differ substantially as compared to known mouse structure. Molecular docking of modeled canine Ly49 with MHC-I was favorable, converging to a single binding mode highly comparable to the known murine complex. Gene expression of Ly49 was increased in the resting compared to the cytotoxic state, consistent with an inhibitory protein. Mass spectrometry detected structures consistent with C-type lectin peptides, warranting further targeted studies of protein translation.

**Conclusion:** On the basis of computational structure, differential gene expression and function studies, our data suggest that canine Ly49 is functional and allows dog NK cells to recognize self.

# Priyadarsini Kumar

Manufacturing Clinical Grade Placenta-derived Mesenchymal Stem Cells for *In Utero* Fetal Repair of Myelomeningocele: Path to a Successful FDA Investigational New Drug (IND) Application

Priyadarsini Kumar<sup>1</sup>, Lizette Reynaga<sup>1</sup>, Alicia Hyllen<sup>1</sup>, Chelsey Lee<sup>1</sup>, Christopher Pivetti<sup>1</sup>, William Gruenloh<sup>2</sup>, Christina Theodorou<sup>1</sup>, Sarah Stokes<sup>1</sup>, Jordon Jackson<sup>1</sup>, Laura Galganski<sup>1</sup>, Kaeli Yamashiro<sup>1</sup>, Zachary Paxton<sup>1</sup>, Gerhard Baeur<sup>2</sup>, Jan Nolta<sup>2</sup>, Aijun Wang<sup>1</sup>, Diana Farmer<sup>1</sup>

<sup>1</sup>UCDHS, Surgery, Sacramento, CA, USA. <sup>2</sup>UCDHS, Stem Cell Program, Sacramento, CA, USA

**Introduction:** Myelomeningocele (MMC) is a congenital defect which leads to paralysis. The standard of care is *in utero* repair. To augment *in utero* repair and improve clinical outcomes, we designed a novel product consisting of placenta-derived mesenchymal stem cells (PMSCs) procured from donor placental chorionic villus seeded on Cook Biodesign® Dural Graft Extracellular Matrix (PMSC-ECM).

**Method:** Cell manufacturing was conducted at the UC Davis Current Good Manufacturing Practice (CGMP) Facility. Release tests, including infectious disease screening, were performed by the UC Davis Quality Control Laboratory and WuXiApptec Labs. Functional characterization tests were conducted at the Surgical Bioengineering Laboratory. U.S. Food and Drug Administration (FDA) guidelines were followed, and an Investigational New Drug (IND) application was submitted.

**Results:** Eight of seventeen placenta donors passed infectious disease screening. PMSCs generated from these eight placentas were expanded and cryopreserved as seed banks. Cell lines from five of eight donors passed set screening criteria for viability and growth rate and were expanded and cryopreserved as product banks. Cell lines underwent screening for sterility (endotoxin, mycoplasma, sterility culture, human infectious viruses, bovine viruses, adventitious viruses), identity (phenotype, pluripotency, karyotype, trilineage differentiation) and functional characterization (growth factor secretion, neuroprotection). Results were used to select a single optimal line for clinical use. The PMSC-ECM product was tested in the gold-standard ovine model for safety and efficacy. All data were submitted to FDA. After several revisions, the IND was accepted by FDA.

**Conclusion:** We have successfully banked clinical grade PMSCs. With IND approval from the FDA, a first-in-human clinical trial evaluating the application of our PMSC-ECM product to augment *in utero* repair of MMC is underway.

# QUICK SHOT PRESENTATIONS

## QUICK SHOT SESSION 1B LH 1222 | 9:15 AM - 10:15 PM

### MODERATORS DR. ANDREW LI & DR. CLAIRE GRAVES

1. **ASHLY RUF** - Dedicated Acute Care Surgery Operating Room: The Halo Effect of COVID
2. **SIOBHAN LUCE** - Outcomes of Renal Transplantation in Undocumented Immigrants
3. **CHAOXING ZHANG** - 3D bioprinting of Multifunctional bioengineered scaffolds for spina bifida repair
4. **SIRJAN MOR** - Efficient Maintenance and Manipulation of Chicken Embryonic Stem Cells Acting as a Potential Bioreactor for the Mass Production of Human Therapeutic Proteins
5. **TATYANA POLYAK** - The impact of dedicated social media strategy on increasing traffic to Surgical Research
6. **KAITLIN CLARK** - Postnatal treatment of Canine Spina Bifida using Placenta-derived Mesenchymal Stem/Stromal Cells: Clinical Trial Update

## Dedicated Acute Care Surgery Operating Room: The Halo Effect of COVID

Dr. Ashly Ruf MD<sup>1</sup>, Dr. Lauren Coleman MD<sup>1</sup>, Dr Rachael Callcut MD, MSPH, FACS<sup>2</sup>, Dr. Scott Zakaluzny MD, FACS<sup>2</sup>

<sup>1</sup>University of California-Davis (Department of General Surgery), Sacramento, CA, USA. <sup>2</sup>University of California-Davis (Department of Trauma and Acute Care Surgery), Sacramento, CA, USA

**Introduction:** Timing of Acute Care Surgery (ACS) cases is critical to reduce morbidity and optimize patient flow. Lengthy wait times for the operating room are common in centers lacking a daily dedicated room for urgent cases. The COVID pandemic resulted in a decreased volume of scheduled procedures, creating an opportunity to simulate the impact of a dedicated operating room (DOR) for urgent laparoscopic cholecystectomy (LC). We hypothesized there would be more availability for these add-on cases thus decreasing time to operation.

**Methods:** Patients requiring urgent LC admitted between January 2016-November 2020 were reviewed. Patients were excluded if they had factors prohibiting them from being immediately available to undergo operation (choledocholithiasis and gallstone pancreatitis). A decrease in scheduled procedures occurred between March-April 2020 at our center. This 'COVID' intense time period was compared to other periods to determine if a dedicated ACS room would improve timing of urgent operations in our system.

**Results:** 1043 patients underwent urgent LC, including 632 who met inclusion criteria. During the COVID period, there was a notable decrease median time from admission to OR from 31.6 hours to 16.97 hours ( $p < 0.05$ ) and time from surgical case request to operation from 19.3 to 8.2 hours ( $p < 0.5$ ). The attributable difference was found to be secondary to increased availability of OR time. Length of stay decreased from 2.91 to 2.11 ( $p = 0.09$ ).

**Conclusion:** Increased access to the OR due to COVID scheduling restrictions created an opportunity to simulate the impact of a DOR. This study demonstrates the major barrier to patient throughput and LOS for urgent ACS cases is OR access. Having a DOR is an important factor to address quality metrics like LOS.

# Siobhan Luce

## Outcomes of Renal Transplantation in Undocumented Immigrants

M. Siobhan Luce MD<sup>1</sup>, Kara T. Kleber MD<sup>1</sup>, Alexa C. Abdallah BS<sup>2</sup>, Ugur N. Basmaci BS<sup>2</sup>, Richard V. Perez MD<sup>1</sup>, Christoph Troppmann MD<sup>1</sup>

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**Introduction:** Undocumented immigrants' access to kidney transplant remains controversial. We performed a granular analysis of our large experience with undocumented immigrants to provide much needed data for public debate and policymaking.

**Methods:** We identified 73 undocumented persons successfully transplanted at UC Davis from 2003-2019 (68 adult, 5 adolescent) after standard medical and psychosocial selection. We assessed long-term outcomes and compared observed graft survival to the risk-adjusted expected graft survival (available for the 1-year mark) from the Scientific Registry for Transplant Recipients (SRTR).

**Results:** Median age was 38 yrs (range, 13-69); 65 (90%) had a deceased donor (DD) graft; and 70 (96%) recipients were from Mexico. With 5.5 yrs median follow-up, we observed 7 (10%) graft losses; 7 (10%) recipients were lost to follow-up. For DD and live donor grafts, 1-yr observed graft survival (98.5% and 100% respectively) was higher than the expected risk-adjusted 1-year SRTR graft survival (95.7% and 97.2%, respectively). Graft survival at 8 years was 85.9% for DD and 100% for live donor recipients.

**Discussion:** Access to life-prolonging kidney transplantation remains extremely limited for nondocumented immigrants in the U.S. In our series (the largest published to date), no graft losses were due to lost insurance; only one (14%) was from medication noncompliance. For adult DD recipients, at 3 yrs we observed 95.1% graft survival (vs. 88.2% for our center's overall DD recipient cohort) with subsequent excellent long-term outcomes<sup>6</sup>. Study limitations include its retrospective nature, the homogeneous geographic origin of the study population, and the lack of adequate controls for this unique group of immigrant recipients.

We conclude that undocumented status did not confer increased graft loss risk and should therefore not preclude referral for kidney transplantation per se. Yet, the fact that 10% of recipients were lost to follow-up warrants future exploration.

# Chaoxing Zhang

3D bioprinting of multifunctional bioengineered scaffolds for spina bifida repair

Dr Chaoxing Zhang, Dr Dake Hao, Dr Diana Farmer, Dr Aijun Wang

UC Davis, Sacramento, CA, USA

**Introduction:** Myelomeningocele (MMC), the most severe form of spina bifida is the most common cause of lifelong paralysis in the US. *In utero* MMC repair with placental mesenchymal stem cells (PMSCs) prevents hind limb paralysis in the fetal ovine MMC model. However, in some animals, severe kyphosis occurs primarily due to the lack of supportive bone and paraspinal muscle tissues. Therefore, developing a regenerative scaffold that protects and supports the spinal cord is desirable for long-term durability of motor function recovery. Moreover, since the severity of MMC varies from patient to patient, engineering personalized scaffold to match the patient's individual anatomical defect is desirable. In this study, using three-dimensional (3D) bioprinting, we developed a novel multifunctional scaffold loaded with PMSCs as a "living patch" to simultaneously protect neurons and regenerate the bony defect as a patient-specific fetal treatment of MMC.

**Methods:** The 3D-printed system contains a collagen scaffold loaded with PMSCs, an anti-tethering layer made with amnion matrix, and a bony scaffold consisted of hybrid polycaprolactone (PCL)/hydroxyapatite (HA) that supports bone regeneration. LLP2A, an integrin  $\alpha 4\beta 1$  ligand that has strong binding affinity to PMSCs, was conjugated to the scaffold. The scaffolds were optimized and characterized to identify the optimal composition. PMSC viability, morphology, growth factor secretion and differentiation potential were evaluated *in vitro*.

**Results:** LLP2A modification significantly increased PMSC attachment and survival on collagen *in vitro*. The composition of PCL/HA scaffold was optimized to have proper mechanical properties and degradation mode *in vitro*. The 3D-printed scaffold possessed good cytocompatibility and maintained PMSC's growth factor secretion and osteogenic potential *in vitro*.

**Conclusion:** 3D-printed multifunctional scaffold is promising to provide sustained neuroprotection and support bone regeneration to treat MMC defect.

# Sirjan Mor

Efficient Maintenance and Manipulation of Chicken Embryonic Stem Cells Acting as a Potential Bioreactor for the Mass Production of Human Therapeutic Proteins

Graduate Student Xi Chen PhD<sup>1</sup>, Graduate Student Zheng Guo PhD<sup>1</sup>, Graduate Student Xinyi Tong PhD<sup>1</sup>, Master's Student Xugeng Liu MS<sup>1</sup>, Master's Student Sirjan Mor MS<sup>1,2</sup>, Master's Student Nima Adhami MS<sup>1</sup>, Principal Investigator Qilong Ying PhD<sup>1</sup>

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**Introduction:** Transgenic chicken eggs have immense potential to reduce the costs of producing therapeutic human proteins, yet the generation of transgenic chickens using *in vitro* cultures of chicken embryonic stem cells (ESCs) has not been achieved. In comparison to generation of transgenic chicken using viral delivery, the development using chicken embryonic stem cells allows for precise genetic manipulation - and our lab is the first to culture chicken embryonic stem cells while demonstrating their potential for germline transmission.

**Methods:** We first developed chicken ESC culture conditions *in vitro* to maintain pluripotency, which is unprecedented in this avian species. With viral delivery of the green fluorescent protein (GFP) transgene, these chicken embryonic stem cells constitutively expressed GFP and were injected into a chicken embryo at EGK.X stage (freshly laid embryo). Germline transmission was assessed by imaging the presence of GFP<sup>+</sup> cells in the gonads that also expressed germ cell proteins like DAZL and SSEA1.

**Results:** We were the first to culture and maintain the pluripotency of chicken embryonic stem cells *in vitro*. We also injected chicken embryonic stem cells into live embryos and formed chicken chimeras. These chimeras have potential for germline transmission as our GFP<sup>+</sup> donor cells express DAZL and SSEA1 inside the gonads.

**Conclusion:** We were able to culture chicken embryonic stem cells and show that our donor cells have the potential to pass genetic information onto the next generation. This system provides a platform for precise gene targeting which allows us to make transgenic eggs that produce human proteins in a cheap and efficient way, especially for therapeutic purposes.

# Tatyana Polyak

The impact of dedicated social media strategy on increasing traffic to Surgical Research

Tatyana Polyak MD<sup>1</sup>, Carly Nichola Bisset MBChB, MRCS<sup>2</sup>, Dr. Frank McDermott FRCS<sup>3</sup>, Dr. Deborah Keller MS, MD<sup>1</sup>

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**Introduction:** Social media (SoMe) is a powerful tool for networking, communication, and education amongst surgeons. Surgical journals developed a SoMe presence out of necessity, to capture readers that transitioned away from traditional media. With the increasing utilization of SoMe for surgical research, the relationship between online engagement and interaction with a journal's content warrants investigation. We sought to evaluate the impact of a dedicated SoMe strategy on engagement metrics with surgical research.

**Methods:** A retrospective review of user engagement metrics was performed from the SoMe microblog platform (Twitter®) for Colorectal Disease Journal (@Colorectaldis, the #2-rated colorectal journal internationally) from 6/2015-9/2020. The analysis was stratified into pre (6/2015-9/2018) and post (9/2018-9/2020) implementation of a targeted SoMe strategy. The outcome measures were the changes in user engagement with the journal before and after implementing a SoMe strategy.

**Results:** There was a significant increase in the total and mean monthly tweets posted before (215, 5.51) and after the SoMe strategy (835, 28.79,  $P < 0.01$ ). The mean new monthly followers increased significantly Post-SoMe (213 vs 38;  $p < 0.01$ ). Total interactions with posted articles was also significantly higher Post-SoMe than Pre-SoMe (4,096,167 vs. 269,152,  $P < 0.01$  respectively)- 92.97% were retweeted and 28.01% favorited. Article downloads increased nearly twenty-fold (210, 449 Post-SoMe vs. 10,934 Pre-SoMe;  $p < 0.01$ ). The engagement rate with the journal from tweets rose to 15.14 % from 4.06%.

**Conclusions:** A dedicated SoMe strategy increased access, user engagement, articles downloaded, and traffic to the journal's site. The readership increased, and was associated with increased journal interactions. This provides evidence that SoMe activity advances surgical research.

**Key Words:** Social media (SoMe); Twitter; colorectal surgery; surgical research; Altmetrics



# Kaitlin Clark

## Postnatal treatment of Canine Spina Bifida using Placenta-derived Mesenchymal Stem/Stromal Cells: Clinical Trial Update

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**Introduction:** The canine is increasingly recognized as a valuable pre-clinical large animal model for many human diseases. Canine spina bifida (SB) clinically presents very similarly to human SB, and English bulldogs in particular have a high incidence of naturally occurring SB. Placental mesenchymal stem cells (PMSCs) are being investigated as an adjunct to prenatal repair of SB; however, similar treatments have not been explored for postnatal repair. English bulldogs could serve as the first postnatal animal model of SB. The goal of this study is to evaluate canine PMSCs (cPMSCs) to test their efficacy as a postnatal therapy in a naturally occurring large animal disease model.

**Methods:** To date, we have enrolled 1 normal control and twelve 10-week-old English bulldogs with SB defects confirmed by neurological evaluation and magnetic resonance imaging (MRI). Each SB dog underwent a multi-segment laminectomy and 7/12 dog's treatment was coupled with transplant of allogeneic cPMSCs embedded in hydrogel and extracellular matrix scaffold.

**Results:** The first 2 dogs enrolled were initially ambulatory with notable abnormal gaits and incontinence. MRI revealed L7-S1 defects of varying severity. Electrophysiologic testing revealed low-normal conduction velocity for both motor and sensory hindlimb nerves. Both dogs recovered from posterior laminectomy and cPMSC implantation uneventfully. At 8 weeks post-treatment both dogs showed improved ambulatory gaits. No significant adverse events occurred in any dog by 12 months. The remaining animals' evaluations are currently being collected and/or analyzed.

**Conclusion:** Postnatal treatment of a naturally occurring canine model of SB with allogeneic cPMSCs is clinically feasible and appears safe. Further studies are currently being performed to evaluate efficacy. The findings from this study suggest that naturally occurring canine SB is a valuable translational model to evaluate PMSC postnatal therapy and will provide critical insights for human clinical studies.

# ***ORAL PRESENTATIONS***

## **ORAL PRESENTATIONS SESSION 2 LH 2222 | 10:30 AM - 12:00 PM**

### **MODERATORS**

**DR. DAVID COOKE & DR. MICHAEL CAMPBELL**

- 1. CHRISTOPHER HOLLAND** - The Analysis of Intravenous Dexmedetomidine Use in Total Hip Arthroplasty
- 2. NIKIA MCFADDEN** - Patient and provider perceptions of the trauma and emergency general surgery discharge process
- 3. YUFENG XUE** - Biomechanical Study of Biodegradable Screw Fixation in Maxillofacial Distraction Osteogenesis
- 4. TAJIA GREEN (VIRTUAL)** - Cytokine responses to bacterial byproducts is individual specific and may be influenced by glucocorticoid receptor
- 5. DAKE HAO** - Engineering the developmental milieu to repair spina bifida bony defect in utero
- 6. LALITHASRI RAMASUBRAMANIAN** - Characterization of Lipid Raft Nanovesicles as Neuroprotective and Angiogenic Exosome-Mimics

# Christopher Holland

## The Analysis of Intravenous Dexmedetomidine Use in Total Hip Arthroplasty

Dr. Christopher Holland M.D., Dr. Andrew Meyers M.D., Dr. Zachary Lum D.O., Dr. Mauro Giordani M.D., Dr. John Meehan M.D.

UC Davis, Orthopedic Surgery, Sacramento, CA, USA

**Background:** Enhanced recovery protocols for total hip arthroplasty (THA) have become standard of care across many institutions. Reports of novel additions to multimodal pain control regimens have been published, however a paucity of literature exists on the use of intravenous dexmedetomidine, a commonly used sedative and anti-emetic agent. The purpose of this study was to analyze our experience with intravenous dexmedetomidine; with the hypothesis that it would reduce post-operative opioid use. Secondary outcomes were also examined, including post-operative hypotension, hemoglobin, length of stay and discharge disposition.

**Methods:** All patients who underwent primary THA at a single center between January 1, 2016 and September 1, 2019, regardless of diagnosis, surgical approach, anesthetic type, body mass index (BMI), or American Society of Anesthesiologists (ASA) score, were included. Anesthetic type was determined by the anesthesia provider, as was the administration of peripheral nerve blockade. Postoperative clinical measures were analyzed, adjusting for patient and surgical characteristics.

**Results:** Out of 599 patients, 218 patients received IV dexmedetomidine, at a mean dose of 44.9mg. Using a multivariate linear mixed effects model, patients in the IV dexmedetomidine group were estimated to have a postoperative day zero morphine milligram equivalent 24% higher than those in the control group ( $p = 0.05$ ). In addition, patients in the IV dexmedetomidine group who underwent spinal anesthesia had significantly more hypotensive episodes on postoperative day zero, compared to controls, with odds of hypotension 247% higher than those in the control group ( $p=0.006$ ).

**Conclusions:** We found no opioid sparing effects with use of IV dexmedetomidine. IV dexmedetomidine should be used cautiously as an anesthesia adjunct with spinal anesthesia in the setting of primary THA, as the experience at our institution illustrates increased odds of postoperative hypotension.

# Nikia McFadden

Patient and Provider Perceptions Of The Trauma And Emergency General Surgery Discharge Process

Nikia McFadden MD<sup>1</sup>, Melissa Gosdin PhD<sup>2</sup>, Gregory Jurkovich MD<sup>1</sup>, Garth Utter MD MSc<sup>1</sup>

<sup>1</sup>UC Davis Department of Surgery. <sup>2</sup>UC Davis Center for Healthcare Policy and Research

**Introduction:** Trauma and Emergency General Surgery (TEGS) patients face barriers that hinder successful recovery after discharge. Improved understanding of the challenges in the discharge process experienced by key stakeholders is necessary to develop interventions applicable to this poorly standardized care transition.

**Methods:** We performed a qualitative study of patient and provider perceptions about the discharge process. We performed semi-structured interviews that we recorded, transcribed, and analyzed thematically.

**Results:** We interviewed 20 patients and providers. Providers included attendings, residents, NPs, RNs, and case managers. Three themes emerged. (1) Communication (patient-provider and provider-provider): Providers understood that discharges do not go smoothly when communication with patients is not clear. Many patients discussed confusion about their discharge plan. All lamented that poorly written discharge summaries are an inadequate means of communication between inpatient and outpatient providers. (2) Discharge teaching and written instructions: Patients recalled discharge teaching positively but found written discharge instructions to be unhelpful. Providers want to spend more time teaching patients and understood that written instructions contain too much jargon. (3) Outpatient care coordination: Patients and providers commented on difficulties with coordinating outpatient care. Both groups endorsed that a patient's PCP and insurance coverage are central components of the outpatient experience.

**Conclusion:** TEGS patients face several challenges at discharge. Providers struggle to help their patients with this transition. Future interventions should focus on improving communication with patients using closed-loop techniques, standardizing the discharge summary to serve as a means of care coordination, insisting that written discharge instructions be patient-centered, and assisting the patient with navigating the transition.

## Biomechanical Study of Biodegradable Screw Fixation in Maxillofacial Distraction Osteogenesis

Yunfeng Xue MD<sup>1</sup>, Joseph Firriolo MD<sup>1</sup>, Jonathan Weyerbacher MD<sup>1</sup>, Tanya Garcia-Nolen MS<sup>2</sup>, Boaz Arzi DVM<sup>2</sup>, Granger Wong MD, DMD<sup>1</sup>

<sup>1</sup>UC Davis Plastic Surgery Division, Sacramento, CA, USA. <sup>2</sup>UC Davis School of Veterinary Medicine, Davis, CA, USA

**Introduction:** Internal distraction devices are commonly used to lengthen the mandible in congenital micrognathia. The eventual need for device/screw removal can be challenging and may necessitate transbuccal incision with trocar. Bioabsorbable poly-L-lactide (PLLA) screws have been used for pediatric maxillofacial osteosynthesis; unlike classical titanium screws, these materials do not need to be removed.

Previous *in vivo* studies have found that the maximal force produced by mandibular distraction is 69.4N.<sup>[1]</sup> We hypothesized that PLLA screws can support the compressive forces encountered during mandibular distraction.

**Methods:** Ten mandibles were obtained from five canine cadavers. Paired mandibles from the same cadaver were each fixated to a mandibular distractor with eight screws (either titanium or PLLA) (Fig. 1). Devices were each set to 15mm and 30mm of distraction distance. 80N of compression force was then generated parallel to the axis of the distraction device. Distractor displacement was measured to detect any mechanical failure during this pre-set load. Finally, if no failure was observed at 80N, a load-to-failure compression test was done in the PLLA group to determine the mechanical failure point.

**Results:** All distractors in both the titanium and PLLA screw groups withstood 80N of compression without failure. When load-to-failure test was performed in PLLA group, the average device failure point was 172.8N (range 148-196N) (Fig. 2). Review of high frame rate video demonstrated that all failures occurred due to the PLLA screws breaking or falling out.

**Conclusion:** Bioabsorbable PLLA screws can withstand compressive forces more than double that of the maximal *in vivo* forces needed during mandibular distraction. These screws may be used as an acceptable alternative for fixation of internal mandibular distractors.



Figure 1. Set up of mandible with distractor in place during a compression test

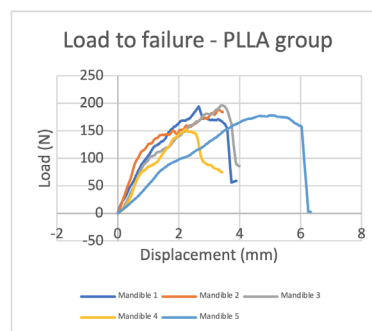


Figure 2. The load and displacement graph for each mandible in the poly-L-lactide (PLLA) screw group during the load-to-failure compression test

[1] Robinson RC et al. Mandibular distraction force: laboratory data and clinical correlation. J Oral Maxillofac Surg 59:539-544, 2001

# Tajia Green

Cytokine responses to bacterial byproducts is individual specific and may be influenced by glucocorticoid receptor

Tajia Green<sup>1,2</sup>, Debora Lim<sup>1,2</sup>, Dr. Kiho Cho DVM, PhD<sup>1,2</sup>, Dr. David Greenhalgh MD<sup>1,2</sup>

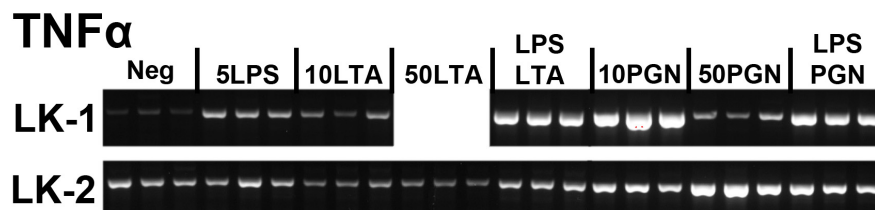
<sup>1</sup>Burn Division, Department of Surgery, UC Davis, Sacramento, CA, USA. <sup>2</sup>Shriners Hospitals for Children, Sacramento, CA, USA

**Introduction:** Pathogen associated inflammation is concomitant with injury, infection, and sepsis. Exposure to bacterial components such as lipopolysaccharide (LPS), lipoteichoic acid (LTA), and peptidoglycan (PGN) leads to the production of pro-inflammatory cytokines and other inflammatory mediators. Glucocorticoids are used to treat pathogen induced inflammation; however, patient response to treatment is variable. Pathogens may influence human glucocorticoid receptor (hGR) expression and, consequently, the effectiveness of the corticosteroids used to combat the inflammatory response.

**Methods:** Peripheral blood mononuclear cells (PBMCs) were isolated from two fresh Leukopaks and treated with LPS, LTA, or PGN for 1, 3, or 13 hours. RNA was extracted from the cells and RT-PCR was used to identify the resulting changes in hGR splice variant, cytokine and inflammatory mediator expression. Protein extracts from the treated cells were subjected to Western blot analysis of hGR expression.

**Results:** Although LPS, LTA, and PGN had similar effects on cytokine and inflammatory mediator production there were Leukopak (or individual) specific variations in intensity. The regulation of hGR transcript and protein as a result of the bacterial byproducts also displayed Leukopak specific expression.

**Conclusion:** Generalized pathogen responses are modified by patient specific characteristics. Our future studies will seek to identify how pathogens induce variant hGR expression and to link the variant expression to the different patterns of cytokine expression seen between individuals. Understanding the nuances in these different responses will be an important step towards personalized patient care.



PBMCs isolated from Leukopaks (LK) were treated with 5 µg/ml LPS, 10 or 50 µg/ml LTA, 5 µg/ml LPS + 10 µg/ml LTA, 10 or 50 µg/ml PGN, or 5 µg/ml LPS + 10 µg/ml PGN. Treatment with the bacterial byproducts elicited individual specific responses of tumor necrosis factor-α (TNFα).

# Dake Hao

Engineering the developmental milieu to repair spina bifida bony defect in utero

Postdoctoral Fellow Dake Hao PhD<sup>1</sup>, Laboratory Manager Christopher Pivetti MS<sup>1</sup>, Postdoctoral Fellow Tomas Fernandez PhD<sup>2</sup>, Research Resident Edwin Kulubya MD<sup>1</sup>, Research Resident Jordan Jackson MD<sup>1</sup>, Research Professor Ruiwu Liu PhD<sup>3</sup>, Professor and Chair Kit Lam PhD, MD<sup>3</sup>, Professor Kent Leach PhD<sup>2</sup>, Professor and Chair Diana Farmer MD<sup>1</sup>, Associate Professor Aijun Wang PhD<sup>1</sup>

<sup>1</sup>Surgical Bioengineering Laboratory, Department of Surgery, UC Davis, Sacramento, CA, USA. <sup>2</sup>Department of Biomedical Engineering, UC Davis, Davis, CA, USA. <sup>3</sup>Department of Biochemistry and Molecular Biology, UC Davis, Sacramento, CA, USA

**Introduction:** Previously, we demonstrated that *in utero* treatment with placenta-mesenchymal stem cells (PMSCs) prevented hind limb paralysis in the fetal ovine spina bifida (SB) model. However, we found that they developed severe kyphosis, causing spinal cord compression due to the lack of bone. Bone development in fetal milieu is facilitated by endogenous stem cells, such as MSCs, and is dependent on a number of factors, including growth and morphogenetic factors and integrins. However, safety concerns exist if using growth or morphogenetic factors in the gestational environment. Thus, we aimed to develop a bony scaffold, modified with integrin-based ligands to guide endogenous cells, to protect and regenerate the SB bony defect.

**Methods:** We identified two ligands, named LLP2A and LXW7, targeting integrin  $\alpha4\beta1$  and  $\alpha v\beta3$  respectively by One-Bead One-Compound (OBOC) technology. Binding specificity and functions of LLP2A and LXW7 on MSCs and ECs were examined. Bone formation and vascularization of LLP2A/LXW7 modified scaffolds were evaluated in the rat calvarial defect model and fetal ovine spinal bone defect model.

**Results:** *In vitro* results showed LLP2A had strong binding affinity to different types of MSCs. LXW7 showed high binding specificity to ECs, promoted EC proliferation and enhanced the phosphorylation of VEGFR2 and ERK1/2 in ECs. In the rat calvarial defect model and fetal ovine spinal bone defect model, the Micro-CT, Laser Doppler Perfusion Imaging (LDPI) and histological analysis results showed LLP2A/LXW7 modified scaffolds significantly improved bone formation and vascularization.

**Conclusion:** We have developed a cell-free, growth and morphogenetic factor-free, off-the-shelf product to regenerate the SB bony defect for use *in utero*. This product has the potential to not only improve the quality of life for SB patients, but also to provide insight in understanding bone development and regeneration in the adult and fetal environment.

# Lalithasri Ramasubramanian

Characterization of Lipid Raft Nanovesicles as Neuroprotective and Angiogenic Exosome-Mimics

Lalithasri Ramasubramanian B.S, Harsha Jyothi M.A, Dr. Priyadarsini Kumar PhD, Dr. Diana Farmer M.D, Dr. Aijun Wang PhD

UC Davis, Surgical Bioengineering Laboratory, Sacramento, CA, USA

**Introduction:** We have shown that exosomes derived from human placental mesenchymal stromal cells (PMSCs) possess significant neurogenic and angiogenic properties. However, clinical translation of exosomes has been challenged by their low yield and functional heterogeneity. To address these problems, we sought to synthesize PMSC-exosome mimicking nanovesicles (EMN) by engineering nanoparticles from isolated PMSC lipid rafts, which are regions of the cell membrane from which exosomes are secreted. We hypothesize that the engineered EMNs are physically and functionally similar to native exosomes while having a higher yield and greater homogeneity.

**Methods:** Lipid rafts from PMSCs were isolated and mechanically extruded to create the EMNs. Nanoparticle Tracking Analysis (NTA) was used to measure EMN size and yield while Western blotting was used to assess protein markers. Fluorescence microscopy was used to confirm EMN uptake into SH-SY5Y, a neuroblastoma cell line, and human umbilical vein endothelial cells (HUVEC). Neurogenic functions were tested with SH-SY5Y proliferation and neuroprotection assays while angiogenic functions were evaluated with HUVEC proliferation, migration, and tube formation assays. Western blotting was used to assess the effect of EMNs on Akt and VEGFR-2 expression, two angiogenic proteins, in HUVECs.

**Results:** NTA revealed a higher yield of EMNs with a size comparable to native PMSC exosomes. EMNs expressed common exosome surface markers. EMNs accumulated in both SH-SY5Y and HUVECs within 4 hours and were retained for at least 24 hours. EMNs promoted SH-SY5Y proliferation and improved recovery after induced damage. EMNs also improved HUVEC tube formation and Akt and VEGFR-2 expressions while slightly increasing HUVEC proliferation and migration.

**Conclusion:** We have shown that EMNs can be synthesized from PMSC lipid rafts at a high yield. The EMNs are physically comparable to native PMSC exosomes and possess similar biological properties.



# ***ORAL PRESENTATIONS***

## **ORAL PRESENTATION SESSION 3 LH 2222 | 1:30 PM - 3:00 PM**

### **MODERATORS DR. LUIS GODOY & DR. DEBORAH KELLER**

- 1. SARAH STOKES** - Impact of Gestational Age on Neuroprotective Function of Placental Mesenchymal Stromal Cells
- 2. JEREMY BOLIN** - Barriers and Opportunities for Improving Abdominal Aortic Aneurysm Screening in an Open Healthcare System
- 3. ANNA XUE** - Structured Team Training Improves Efficiency of Robot-assisted Mitral Valve Surgery
- 4. KAITLIN CLARK** - Comparison of Canine Adipose and Placenta-derived Mesenchymal Stromal Cells: Applications to Inflammatory Brain Disease
- 5. DATTESH DAVE** - Modified Frailty Index Identifies Increased Risk of Post-Operative Complications Following ORIF for Distal Radius and Ulna Fractures: Analysis of 5,654 geriatric patients, From the 2005-2017 NSQIP database
- 6. KATHRYN DILOSA** - Intern Perceptions and Participation in the Operating Room

# Sarah Stokes

## Impact of Gestational Age on Neuroprotective Function of Placental Mesenchymal Stomal Cells

Sarah Stokes<sup>1</sup>, Priyadarsini Kumar<sup>1</sup>, Sandra Kabagambe<sup>1</sup>, Chelsey Lee<sup>1</sup>, Aijun Wang<sup>1</sup>, Diana Farmer<sup>2</sup>

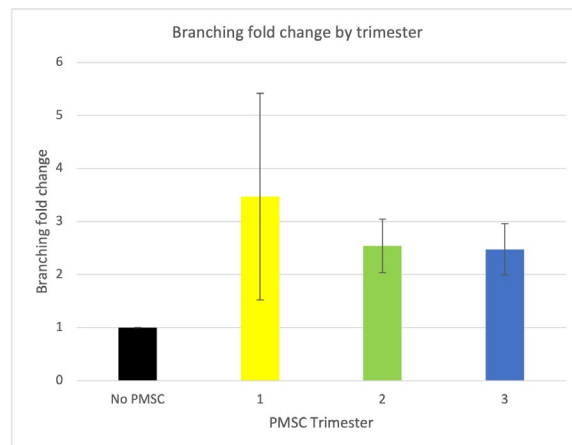
<sup>1</sup>University of California, Davis. <sup>2</sup>University of California, Davis, Division of Pediatric General, Thoracic and Fetal Surgery

**Background:** Early gestation placental mesenchymal stromal cells (PMSCs) seeded on extracellular matrix improve motor function of lambs with myelomeningocele (MMC) when used for *in utero* repair. We aimed to determine if gestational age of the placenta from which cells are derived has an impact on neuroprotective function and paracrine secretion.

**Methods:** PMSCs were isolated from donated placentas from each trimester. To evaluate neuroprotective function, human neuroblastoma cells (SH-SY5Y) were treated with staurosporine to induce apoptosis then co-cultured with PMSCs for 96 hours. Live cells were stained, and branching points of neurite outgrowths calculated. Fold increase in branching points was calculated relative to a control with no PMSCs. 24 hour conditioned media from each cell line was used to perform an enzyme-linked immunosorbent assay (ELISA) to evaluate secretion of brain derived neurotrophic factor (BDNF) and hepatocyte growth factor (HGF).

**Results:** Nine cell lines were isolated, three from each trimester. Neuroprotection, as determined by fold change in branching points, varied by cell line with a range of 1.9-5.7. PMSCs isolated from the first trimester had a branching point fold change of 3.47 (SD±1.95), which was increased relative to PMSCs isolated from second trimester (2.54 SD±0.51) and third trimester (2.5 SD±0.48) placentas, though this was not statistically significant (p=0.555). First trimester PMSCs also had slightly increased BDNF secretion (69.5pg/ml SD±11.02) and HGF secretion (1049 pg/ml SD±698) relative to second trimester (BDNF 51.7 pg/ml SD±17.9; HGF 593pg/ml SD±157) and third trimester cells (BDF 38.11pg/ml SD±10.68; HGF 347 pg/ml SD±113), though this was also not statistically significant.

**Conclusion:** There is variability between individual donor PMSCs lines. First trimester cell lines may have a greater neuroprotective effect relative to cell lines from later trimesters.



# Jeremy Bolin

## Barriers and Opportunities for Improving Abdominal Aortic Aneurysm Screening in an Open Healthcare System

Dr. Jeremy Bolin MD, Ms. Janet Wells MS, RN, Ms. Angela Aguirre BS, Dr. Matthew Mell MD, MS  
University of California Davis, Sacramento, CA, USA

**Objectives:** U.S. screening for abdominal aortic aneurysm (AAA) remains wholly under-utilized. We sought to detect barriers for screening at-risk patients for AAA in an open healthcare system.

**Methods:** At-risk patients at a tertiary medical center with no record of AAA imaging were identified with an automated EMR algorithm. Data included demographics, insurance type, PCP, and in- or out-of-network status. Qualified individuals based on CMS guidelines were sent educational material and instructions for obtaining a screening ultrasound. Follow-up by telephone was done to offer the screening test. Primary outcome was acceptance of screening. If declined, reasons for refusal were documented.

**Results:** Of 1263 potentially eligible patients (age  $73 \pm 2$  years), secondary review of medical records determined 568 were ineligible (130 deceased, 63 known AAA diagnosis/repair, 375 prior imaging). For 322 in-network patients, an automatic AAA screening alert failed to trigger for 26%. Successful contact was possible for only 34.3% of the cohort due to inaccurate address/telephone but was more likely for patients with a PCP (41.9% vs. 21.1%,  $p < .001$ ) and with insurance (53.9% vs. 18.5%,  $p < .001$ ). Of successful contacts, 105 were excluded after obtaining additional information (45 deaths, 30 already screened, 4 known AAA, 24 ended call). The final cohort comprised 119 screening invites, which 31.9% accepted screening. Those with a PCP were more likely to accept screening (36% vs. 6%,  $p = .01$ ); conversely, the most common declined reason was deference to the PCP (58%). Having a PCP remained the strongest predictor of screening (OR 10.0, 95% CI 1.26-29.83,  $p = .029$ ). Those completing screening, either ectatic (13%) or aneurysmal disease (4%) requiring surveillance was identified.

**Conclusions:** Ample opportunity exists to optimize AAA screening in an open healthcare system including improving automated algorithms, updating contact information, and partnering with PCPs to get patient buy-in.

## Structured Team Training Improves Efficiency of Robot-assisted Mitral Valve Surgery

Anna Xue MD<sup>1</sup>, Ala Jamal PA-C<sup>1</sup>, Alison Ranade PA-C<sup>1</sup>, Kimberly Smith PA-C<sup>1</sup>, Peter Carnegie BS<sup>2</sup>, Bob Kiaii MD<sup>1</sup>

<sup>1</sup>University of California, Davis Health, Sacramento, California, USA. <sup>2</sup>Minimally Invasive Solutions, LLC, Ocoee, Florida, USA

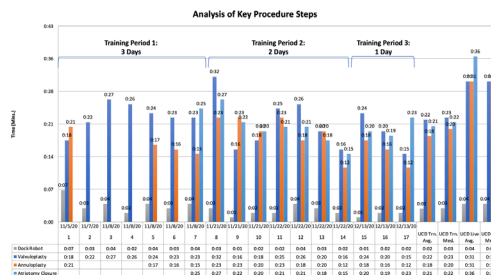
**Background:** Minimally invasive (robot-assisted) mitral valve surgery has evolved as a method to intervene on mitral valve disease without a median sternotomy and provides the advantages of excellent visualization while allowing for precise technical movements in a small space. Establishing a structured simulation platform to train surgical team members to improve the efficiency and ensure successful outcomes of complex robot-assisted cardiac surgery is critical and has not been studied previously. We aim to investigate the role of such a structured simulation platform in establishing a robot-assisted mitral valve surgery program.

**Methods:** A total of 17 simulation cases of mitral valve repair with neochords and annuloplasty were performed. A surgical robot, thoracic cage and mitral valve model were used in all simulation cases. The durations of critical procedural steps were documented and compared for each simulation case.

**Results:** Results are shown in Figure 1. Docking duration decreased from 7 minutes to a low of 1 minute. Atriotomy decreased from 8 minutes to a low of 2 minutes during the 11th simulation case and achieved an average of 4 minutes. Valvuloplasty decreased from 32 minutes to a low of 15 minutes. Annuloplasty decreased to a low of 12 minutes on simulation case 17. Atriotomy closure also decreased from a high of 27 minutes to a low of 15 minutes. Overall, the structured simulation platform steadily improved case efficiency and enhanced team dynamics, leading to a successful first live case with further improvement during the second live case.

**Conclusions:** A structured team simulation platform does improve the efficiency and flow of critical steps of robot-assisted mitral valve surgery while enhancing team dynamics. Overall, such a platform enables the surgical team to perform more complex robotic procedures at the onset of program establishment. It is a valuable and essential method to incorporate in establishing a robotic mitral valve surgery program.

Figure 1: Analysis of key procedure steps. Training was clustered as Period 1, 2, and 3. UCD Trn Avg. – Average Training Times. UCD Trn Med. – Median Training Times. UCD Live Avg. - Average times of Live cases. UCD Live Med. – Median Times of Live cases



# Kaitlin Clark

## Comparison of Canine Adipose and Placenta-derived Mesenchymal Stromal Cells: Applications to Inflammatory Brain Disease

Kaitlin Clark BS, MA<sup>1</sup>, Dr. Rogério Martins Amorim DVM<sup>2</sup>, Naomi Walker BS<sup>2</sup>, Dr. Priyadarsini Kumar PhD<sup>1</sup>, Dr. Kyle Herout MD<sup>1</sup>, Dr. Dori Borjesson PhD, DVM<sup>2</sup>, Dr. Aijun Wang PhD<sup>1</sup>

<sup>1</sup>UC Davis, Surgical Bioengineering Laboratory, Sacramento, CA, USA. <sup>2</sup>UC Davis, Veterinary Institute for Regenerative Cures, Davis, CA, USA

**Introduction:** Canine inflammatory brain disease (IBD) is a severe inflammatory disorder characterized by infiltration of activated immune cell subsets into the brain and spinal cord. Mesenchymal stromal cells (MSCs) are a promising therapy for IBD, based on their potent pro-angiogenic, neuroprotective and immunomodulatory properties. The aim of this study was to compare the immunomodulatory attributes of canine adipose-derived MSCs (ASCs) and placenta-derived MSCs (PMSCs) *in vitro*. These data will serve as potency information to help inform the optimal MSC cell source to treat canine IBD.

**Methods:** MSCs were directly stimulated with interferon gamma (IFN $\gamma$ ) and/or tumor necrosis factor alpha (TNF $\alpha$ ). Mixed-leukocyte reactions (MLRs) were performed to compare the ability of MSCs to inhibit activated peripheral blood mononuclear cell (PBMC) proliferation.

Activated canine MSCs from both tissue sources secreted high concentrations of IDO and PGE<sub>2</sub>, after direct stimulation with IFN $\gamma$  and TNF $\alpha$ , or in-direct stimulation by activated PBMCs. Both ASCs and PMSCs inhibited activated PBMC proliferation in MLR assays however, PMSCs inhibited PBMC proliferation significantly more than ASCs. Blocking PGE<sub>2</sub> and IDO in MLR assays showed that PGE<sub>2</sub> is important only for ASC immunosuppression. Activated ASCs increased IL-6 and VEGF secretion and decreased TNF $\alpha$  secretion, while activated PMSCs increased IL-6, IL-8 and VEGF secretion. ASCs inhibited lymphocyte proliferation via cell cycle arrest in the G0/G1 and PMSCs inhibited lymphocyte proliferation via induction of apoptosis.

**Results:** Our results demonstrate that ASCs and PMSCs have substantial *in vitro* potential as a cell-based therapy for IBD, however, PMSCs more potently inhibited lymphocyte proliferation by inducing apoptosis of activated lymphocytes. These data suggest that the mechanism by which ASCs and PMSCs downregulate PBMC proliferation differs. Additional studies may elucidate further mechanisms by which canine MSCs modulate neuroinflammatory responses.

# Dattesh Dave

Modified Frailty Index Identifies Increased Risk of Post-Operative Complications Following ORIF for Distal Radius and Ulna Fractures: Analysis of 5,654 geriatric patients, From the 2005-2017 NSQIP database

Dattesh Dave M.D., Clifford Pereira M.D., Andrew Li M.D.

University of California, Davis, Plastic Surgery, Sacramento, Ca, USA

**Hypothesis:** Open reduction internal fixation of distal radius and ulnar fractures is one of the most common fracture surgeries for Hand surgeons. Few studies have evaluated how frailty contributes to outcomes in hand surgery patients [1-3]. This study hypothesizes that patients scoring higher on the modified frailty index (MFI-5) are at greater risk of post-operative complications, particularly geriatric patients, following distal radius and ulnar fracture fixation.

**Methods:** The American College of Surgeons National Surgical Quality Improvement Project (NSQIP) database was reviewed for open reduction internal fixation (ORIF) for distal radius and/or ulnar fractures (DRUFs) from 2005 – 2017. Hypothesis testing for demographics, co-morbidities, MFI-5, and post-operative complications between geriatric and non-geriatric patients was performed. Statistically significant differences were then evaluated with multi-variate logistic regression analysis.

**Results:** A total of 17,097 ORIF for DRUFs were collected by NSQIP 2005-2017, with 5,654 patients older than 64 years (33.2%). Average age for geriatric patients undergoing ORIF for DRUFs was 73.7 years versus 46.7 years for non-geriatric patients. Within geriatric patients, a higher MFI-5 score confers 2.1-times increased risk for returning to the OR following ORIF for distal radius and/or ulnar fracture (OR<sup>a</sup> 2.1 p= .04). While an increase in MFI-5 score from baseline confers a 2.9-time increased risk for post-operative bleed across all ages (OR<sup>a</sup> 2.9 p<.01).

## Conclusion:

- Frailty, irrespective of age confers an adjusted increased risk of 30-day post-operative complication.
- Geriatric patients with higher frailty scores carry a significant increased risk for returning to the operative room within 30 days.
- Frailty across all ages confers increased risk for post-operative bleeding.
- Hand surgeons can use the MFI-5 to screen patients with distal radius and ulnar fractures to guide peri-operative decision making.

# Kathryn DiLosa

## Intern Perceptions and Participation in the Operating Room

Dr. Kathryn DiLosa MD, Dr. Misty Humphries MD, Dr. Matthew Mell MD

UC Davis, Vascular Surgery, Sacramento, CA, USA

**Introduction:** Improving intern operative experience is an important component of surgical education, providing a foundation for further learning. Our study examined factors impacting intern operative experience for preliminary, integrated, and categorical interns at a large academic training institution.

**Method:** Data was collected from hospital operative case logs, self-reported ACGME intern case logs, and an anonymous intern survey from the 2019-2020 academic year for three surgical services (Vascular Surgery, Burn Surgery, Trauma/Acute Care Surgery). The primary endpoint was intern presence in operative cases and perceived experience.

**Results:** From hospital logs, interns were present in 945 (46%) of 2054 operative cases. Multivariable analysis indicates the presence of an advanced practice provider (OR 1.68, 95% C.I. 1.34-2.10,  $P=0.00$ ) and a female attending (OR 1.30, 95% C.I. 1.07-1.58,  $P=0.01$ ) increased the likelihood of intern participation, while presence of an upper level resident decreased the likelihood (OR 0.35, 95% C.I. 0.22-0.57,  $P=0.00$ ). Interns were more likely to participate in cases later in the year compared to earlier (43% vs 59%,  $Z=4.72$ ,  $P<0.001$ ). Surveys demonstrate participation was associated with encouragement by faculty/senior residents and a positive learning environment. Competing floor and clinic responsibilities negatively impacted participation ( $p<0.001$ ). Comparison of average intern survey score versus self-reported ACGME case volume demonstrated a positive and exponential trend ( $P=0.00$ ), suggesting a decreased impact from non-surgical responsibilities resulted in a higher number of total cases scrubbed.

**Conclusion:** Intern operative experience can be robust in the setting of ACGME work hour guidelines. Identified factors represent areas for improvement in service organization to enhance resident education. Further study may determine if increasing intern operative experience will positively impact overall residency education.

# QUICK SHOT PRESENTATIONS

## QUICK SHOT SESSION 2A LH 2222 | 3:15 PM - 4:25 PM

### MODERATORS

### DR. VICTORIA LYO & DR. TANYA RINDERKNECHT

1. **ANNA XUE** - The role of TachoSil® fibrin sealant patch in reducing postoperative air leak in patients undergoing minimally invasive lung resection
2. **MATTHEW ZEIDERMAN** - Trends in Adult and Pediatric Upper Extremity Peripheral Nerve Injury—Why Are Costs Increasing?
3. **KEWA GAO** - In utero transplantation of placenta-derived endothelial progenitor cells for Hemophilia A treatment in an operable mouse model
4. **LEORA GOLDBLOOM-HELZNER (VIRTUAL)** - Optimizing the yield of placental mesenchymal stromal cell-derived extracellular vesicles in 3D culture systems
5. **LAUREN PERRY (VIRTUAL)** - Is the Improved Survival in Early-Stage Pancreatic Cancer Worth the Extra Cost at High-Volume Centers?
6. **JOSEPH FIRRIOLO** - Craniopagus Separation Using A Novel Tissue Expander Design
7. **TATYANA POLYAK** - Opioid Utilization and Prescribing Patterns in the University of California Davis Medical Center Department of Surgery: An Overview of the Current State



The role of TachoSil® fibrin sealant patch in reducing postoperative air leak in patients undergoing minimally invasive lung resection

Anna Xue MD<sup>1</sup>, Timothy Huynh BA<sup>2</sup>, Ganesh Rajasekar MPH<sup>2</sup>, Miriam Nuño Ph.D<sup>2</sup>, Lisa Brown MD, MAS<sup>1</sup>, Luis Godoy MD<sup>1</sup>, David Cooke MD<sup>1</sup>

<sup>1</sup>University of California-Davis, Section of General Thoracic Surgery, Sacramento, California, USA. <sup>2</sup>University of California-Davis Health, Sacramento, California, USA

**Objective:** Minimally invasive lobar and sublobar resection are frequently performed to treat lung cancer. During resection, lung dissection increases the risk of prolonged air leak (PAL). PAL, defined as  $\geq 5$  days, is associated with increased hospital length of stay (LOS), higher costs, and risk of postoperative complications. A recent meta-analysis reported applying TachoSil® fibrin sealant patch to the staple line reduces PAL and has led our institution to incorporate routine use of TachoSil® during lung resections. This study assesses the effectiveness of TachoSil® fibrin sealant patch during minimally invasive lung resection to reduce PAL.

**Methods:** We performed a single institution retrospective study of patients undergoing minimally invasive lobectomy/sublobar resection from July 2014 - September 2019. 418 patients were included. Propensity score matching (4:1) was used. Primary outcome was the incidence of PAL. Secondary outcomes included major postoperative complications, readmission, and hospital LOS.

**Results:** 185(44.3%) patients were > 70 years of age, 164(39.2%) male, 312(74.6%) underwent lobectomy, and 326(78%) smokers. 41(9.8%) patients received TachoSil®. 36(8.6%) patients developed PAL. After propensity matching, patients were comparable in age, sex, extent of resection, pulmonary function tests, and smoking status between the groups. Among patients treated with TachoSil®, two (4.9%) developed PAL, while 34(9.0%) patients who did not receive TachoSil® developed PAL (p=0.56). In the matched analysis, utilizing TachoSil® did not significantly decrease the incidence of PAL and was not associated with reducing complications overall, 30-day readmission, or LOS.

**Conclusions:** The routine use of TachoSil® intraoperatively during minimally invasive lung resection surgery did not reduce the odds of PAL, major complications, 30-day readmission, or LOS in this study and suggests that it may not be effective for the specific purpose of mitigating the incidence of PAL.

<b>Table 1. Outcomes associated with TachoSil® use.</b>		
<b>Outcome</b>	<b>Matched Cohort Odds Ratio (95% CI)</b>	<b>p value</b>
Prolonged air leak	0.48 (0.11-2.17)	0.34
Major complication	1.11 (0.29-4.19)	0.88
30-Day Readmission	0.39 (0.05-3.12)	0.37
Hospital length of stay	0.86 (0.70-1.04)	0.12

# Matthew Zeiderman

## Trends in Adult and Pediatric Upper Extremity Peripheral Nerve Injury—Why Are Costs Increasing?

Matthew Zeiderman MD<sup>1</sup>, Jacob Burns MD<sup>1</sup>, Ava Mandelbaum BS<sup>2</sup>, Peyman Benharash MD<sup>2</sup>, Clifford Pereira MD<sup>1</sup>

<sup>1</sup>UC Davis, Division of Plastic Surgery, Sacramento, CA, USA. <sup>2</sup>UCLA Division of Cardiothoracic Surgery, Los Angeles, CA, USA

**Introduction:** Upper extremity peripheral nerve injuries (UEPNI) are common but devastating, disabling injuries. Given the diversity of patients and injury mechanism, we hypothesize that there will be differences between adult versus pediatric patients.

**Methods:** The 2010-2018 Nationwide Readmissions Database (NRD) was used to identify all patients admitted for UEPNI. International Classification of Diseases 9th and 10th Revision codes and the NRD data dictionary were utilized to tabulate patient and hospital data. Multivariable regression models were developed to evaluate the differences between adult and pediatric populations with regards to injury mechanism, operative intervention, utilization of primary nerve repair versus grafting, and costs.

**Results** Adults comprised 66,146 (91.4%) of 72,411 estimated admissions for an UEPNI. Annual admissions declined significantly for both cohorts from 2010-2018 ( $p < 0.05$ ). Both cohorts demonstrated decreases in UEPNI from stabbing ( $p < 0.05$ ) but there was a significant increase in pediatric UEPNI by firearm (5.6% to 19.3%,  $p < 0.05$ ). Both groups had similar overall rates of primary nerve repair and nerve graft (NS). Frequency of primary nerve repair decreased, while nerve grafting procedures increased significantly for adult (3.6 to 10.7%,  $p < 0.05$ ) and pediatric (2.7 to 8.2%,  $p < 0.05$ ) patients. Mean overall costs were significantly higher for patients requiring nerve grafts (\$30,922 vs. \$17,004,  $p < 0.05$ ), and mean costs increased significantly for both groups over the study period, outpacing inflation ( $p < 0.05$ ). On regression analysis, adult patients are associated with increased adjusted hospitalization costs ( $\beta$  \$+2,717,  $p < 0.05$ ) among patients undergoing surgery.

**Summary** Overall UEPNI rates are trending down, with a surprising increase in pediatric gunshots. The health care burden of UEPNI is increasing, especially for patients requiring surgery. This seems to be due to a trend towards nerve grafting rather than primary repair.

In utero transplantation of placenta-derived endothelial progenitor cells for Hemophilia A treatment in an operable mouse model

Kewa Gao MD, PhD<sup>1</sup>, Hengyue Song MD<sup>1,2</sup>, Priyadarsini Kumar PhD<sup>1</sup>, Siqi He MD<sup>1,2</sup>, Diana Farmer MD<sup>1</sup>, Aijun Wang PhD<sup>1</sup>

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**Background:** Hemophilia A (HA) is an X-linked recessive disorder caused by mutations in the Factor VIII (FVIII) gene leading to deficient blood coagulation. The current standard of care for HA is FVIII infusions every 3-5 days with a possibility of FVIII inhibitor formation and patients becoming non-responsive. Hence it is an expensive therapy posing undue burden on patients. Being a monogenic hereditary disease that can be diagnosed prenatally, *in utero* stem cell-based gene therapy holds great potential for a life-long cure of the disease without FVIII inhibitor formation. Our earlier study demonstrated that endothelial progenitor cells (EPCs) possess a higher rate of engraftment compared to mesenchymal stromal cells.

**Method:** An operable HA murine model was developed to tolerate *in utero* injections without causing death of the pregnant mouse. EPCs isolated from murine placenta (PEPCs) were transduced with B domain deleted FVIII, luciferin/Td-tomato expressing lentiviral vector.  $0.25 \times 10^6$  FVIII-PEPCs were transplanted intraperitoneally at embryonic day 14.5 into fetuses of heterozygous HA pregnant mouse.

**Results:** FVIII-PEPCs secreted significantly high levels of active FVIII compared to non-transduced cells and the transduction rate was 83.5%. The plasma FVIII levels of heterozygous HA mice ( $27.7 \pm 18.73$  IU/ml) (n=3) were not significantly different from wild-type mice ( $38.17 \pm 11.37$  IU/ml) (n=3) but were significantly higher than homozygous HA mice ( $0.006 \pm 0.006$  IU/ml) (n=5). The heterozygous HA females tolerated *in utero* surgery without death due to uncontrolled bleeding and the pups were delivered by normal vaginal delivery. Persistence of transplanted cells in pups was observed by IVIS 7 days after birth.

**Conclusion:** This study demonstrated an operable mouse model for prenatal therapy HA and provided a proof-of-concept that *in utero* transplantation of FVIII gene-modified placenta-derived endothelial progenitor cells can serve as a treatment of HA patients.

# Leora Goldbloom-Helzner

Optimizing the yield of placental mesenchymal stromal cell-derived extracellular vesicles in 3D culture systems

Leora Goldbloom-Helzner M.S.E.<sup>1</sup>, James Gomez<sup>2</sup>, Dr. Priyadarsini Kumar Ph.D.<sup>2</sup>, Dr. Aijun Wang Ph.D.<sup>2</sup>

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Extracellular vesicles (EVs) are small membranous vesicles derived from the cell's plasma membrane and function in paracrine signaling to regulate cellular behavior and intercellular functions. EVs derived from placental mesenchymal stromal/stem cells (PMSC-EVs), for instance, have been shown to provide neuroprotection at sites of injury. However, a rate limiting step in EV research is 2D culture, low yield, high technical time, and high cost of current isolation procedures. To address this inefficiency, we tested long-term culture of PMSCs on commercially available decellularized porcine small intestinal submucosa (SIS) 3D matrix. PMSCs were cultured on SIS for 5 weeks. EV-conditioned media was collected every 3 days and EVs were isolated through differential centrifugation. Nanoparticle tracking analysis measured EV size and total number. Expression of EV markers (CD9, CD63, and CD81 and Calnexin(-)) was tested by Western blotting. Upcoming studies will determine if SIS-cultured PMSC-EVs demonstrate preserved neuroprotective properties when used to treat apoptotic neuroblastoma cells. EV morphological features showed consistent size profiles and negligible decreases in EV concentration over 5 weeks. Absolute EV yield from SIS-cultured PMSCs was considerably increased compared to EV yield observed from 2D-cultured PMSCs. Western blots revealed typical expression of CD9, CD63, and CD81 and negative expression of Calnexin. Lowered labor time and material cost were also observed using SIS-cultured PMSCs compared to 2D culture when normalized to EV yield. This initial study uses a clinically relevant porcine SIS matrix for culturing of a unique source of cells and has brought us closer to optimizing PMSC-EV yield and maintaining sample purity, while simultaneously lowering costs and time commitment. Future studies will assess the optimization parameters using additional 3D culture systems including hollow fiber bioreactors, microspheres, and spheroid culture.

# Lauren Perry

Is the Improved Survival in Early-Stage Pancreatic Cancer Worth the Extra Cost at High-Volume Centers?

Lauren M. Perry MD<sup>1</sup>, Sarah B. Bateni MD<sup>2</sup>, Richard J. Bold MD, MBA<sup>1</sup>, Jeffrey S. Hoch PhD<sup>3,4</sup>

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**Background:** Volume of operative cases may be an important factor associated with improved survival for early-stage pancreatic cancer. Most high-volume pancreatic centers are also academic institutions, which have been associated with additional healthcare costs. We hypothesize that at high-volume centers the value of the extra survival outweighs the extra cost.

**Methods:** This retrospective cohort study used data from the California Cancer Registry linked to the Office of Statewide Health Planning and Development database from January 1, 2004 through December 31, 2012. Stage I-II pancreatic cancer patients who underwent resection were included. Multivariable analyses estimated overall survival and 30-day costs at low- versus high-volume pancreatic surgery centers. The incremental cost-effectiveness ratio (ICER) and incremental net benefit (INB) were estimated, and statistical uncertainty was characterized using net benefit regression.

**Results:** Of 2,786 patients, 46.5% were treated at high-volume centers and 53.5% at low-volume centers. There was a 0.45-year (5.4 months) survival benefit (95% CI, 0.21-0.69) and a \$7,884 extra cost associated with receiving surgery at high-volume centers (95% CI, \$4,074-\$11,694). The ICER was \$17,529 for an additional year of survival (95% CI \$7,997-\$40,616). For decision-makers willing to pay more than \$20,000 for an additional year of life, high-volume centers appear cost-effective.

**Conclusions:** Although healthcare costs were greater at high-volume centers, patients undergoing pancreatic surgery at high-volume centers experienced a survival benefit (5.4 months). The extra cost of \$17,529 per additional year is quite modest for improved survival and economically attractive by many oncology standards.

## Craniopagus Separation Using A Novel Tissue Expander Design

Dr. Joseph Firriolo MD, Dr. Granger Wong MD, DMD

Division of Plastic and Reconstructive Surgery, University of California, Davis, Sacramento, CA, USA

**INTRODUCTION:** Craniopagus twins (conjoined twins connected at the cranium) occur at an estimated incidence of 1 in 1.6-2.5 million births. Very few of these twins bear the anatomy permissive of cranial separation and reconstruction. The authors present their successful surgical approach to cranial separation and reconstruction of craniopagus twins.

**METHODS:** Babies A and B are female twins diagnosed with angular partial craniopagus. The occipital region of Baby A was joined to the left parietal region of Baby B. They demonstrated connection of the scalp, calvaria, and dura; they also had a venous fistula connecting the two sinus systems.

Superiorly, the fused calvaria was a thick, rigid strip of bone, which was selected as a base for tissue expansion. A novel wedge-shaped tissue expander with a thin crescentic base was designed. The tissue expander was engineered such that the pressure of tissue expansion could be concentrated on this region of thick bone and spare the neighboring calvaria of deformational forces. At 6 months, the expander was placed in the subgaleal plane at the cephalad bony fusion point to gain soft tissue for reconstruction. Tissue expansion occurred over 4 months. At 10 months of age, the infants underwent cranial separation, venous fistula ligation, duraplasty, cranioplasty, and successful soft tissue closure using only native expanded scalp.

**RESULTS:** The twins underwent tissue expansion without complication; they had successful cranial separation at 10 months of age. Scalp flaps were of the exact shape and dimension required for soft tissue coverage; an aesthetically pleasing result was achieved.

**CONCLUSION:** Craniopagus twin anatomy should be closely studied to assess candidacy for separation and to determine what anatomic traits may be leveraged for reconstruction. In the presented case, the interplay between bony anatomy and tissue expansion allowed for tissue expansion at a young age, thereby expediting definitive separation.

# Tatyana Polyak

Opioid Utilization and Prescribing Patterns in the University of California Davis Medical Center Department of Surgery: An Overview of the Current State

Tatyana Polyak MD, Summer Smith MSN, RN, CNL, Dr. Deborah Keller MS, MD, Dr. Elizabeth Raskin MD  
Department of Surgery, University of California at Davis Medical Center, Sacramento, CA, USA

**Background:** There is an escalating opioid epidemic that warrants attention. The inpatient surgical episode is a common gateway to new persistent use and abuse in opioid-naïve patients. Thus, developing standards for prescribing and minimizing opioids provided is critical for providers to actively participate in opioid reduction. Knowing the local opioid prescribing patterns is essential as the foundation. Our goal was to evaluate the departmental trends in opioid prescribing. Our hypothesis was there would be widespread use of opioids and variations in prescribing.

**Methods:** A focused audit of the NSQIP participant user file was performed for patients undergoing abdominal surgery at UC Davis from 5/1/2020-12/31/2020. Patients were included if 18 years or older, admitted for Inpatient abdominal surgery, and had complete medical records for opioid data. Patients undergoing same-day procedures, with a length of stay (LOS) of zero were excluded. The main outcome measures were the rates and variation across divisions of intraoperative and discharge opioid prescriptions.

**Results:** During the study period, 540 cases were performed. The case mix was 60.6% elective, 28.7% emergent, and 10.7% trauma. The mean patient age was 53 (SD 18) and mean ASA 2.76. Eighteen patients (3%) were chronic opioid users before surgery. All patients received intraoperative opioids. The mean LOS was 8.1 days, with significant variation by division. At discharge, 99.6% were prescribed opioids. There were 20 different variations at discharge of opioid medication and dose. The median prescription number was for 30 pills (range, 10-60).

**Conclusions:** Opioid use during surgery is universal, regardless of case type. Opioid prescribing at discharge was also ubiquitous, but with wide variations in prescribing patterns. These results show opioid prescribing is a prime target for standardization. Further work can assess the impact on quality outcomes from this initiative.

# ***QUICK SHOT PRESENTATIONS***

## **QUICK SHOT SESSION 2B LH 1222 | 3:15 PM - 4:25 PM**

### **MODERATORS DR. FADWA ALI & DR. JONATHAN KOHLER**

- 1. JENNIFER GEIGER** - A Needs Assessment for Palliative Care Curriculum Development in Surgical Residents
- 2. CHRISTOPHER HOLLAND** - Opioid Use in Revision Total Knee Arthroplasty
- 3. ANAMARIA ROBLES** - Relationship of Post-Resuscitation Hemoglobin to Future Blood Transfusion Needs
- 4. CHRISTINA BROWN (VIRTUAL)** - Changes in Early Post-Operative Toe-Brachial Indices May Reflect Positive or Negative Remodeling
- 5. GILLIAN HOSHAL** - Surgical Trainee Perspectives During COVID – 19
- 6. MATTHEW KIM (VIRTUAL)** - Hyaluronidase (HYAL) Availability in Emergency Rooms: A Californian Census
- 7. TREVOR PLESCIA** - The impact of bariatric surgery on the development of small intestinal bacterial overgrowth (SIBO)



# Jennifer Geiger

## A Needs Assessment for Palliative Care Curriculum Development in Surgical Residents

Dr. Jennifer Geiger MD, MPH<sup>1</sup>, Dr. Misty Humphries MD, MAS, RPVI, FACS<sup>2</sup>, Dr. Eleanor Curtis MD, MPVM<sup>3</sup>, Dr. Miriam Nuno PhD<sup>4</sup>

<sup>1</sup>UC Davis Medical Center, Department of Surgery, Sacramento, CA, USA. <sup>2</sup>UC Davis Medical Center, Division of Vascular Surgery, Sacramento, CA, USA. <sup>3</sup>UC Davis Medical Center, Division of Trauma, Acute Care Surgery and Surgical Critical Care, Sacramento, CA, USA. <sup>4</sup>UC Davis Medical Center, Departments of Surgery and Public Health Sciences, Sacramento, CA, USA

**Introduction:** Primary palliative care skills are essential when treating patients with serious illness. Currently, there is no dedicated palliative care curriculum for surgery residents at our institution. We administered a needs assessment that defined the current environment.

**Methods:** A 51-item survey adapted from validated instruments was distributed to general surgery residents assessing their palliative care and end-of-life (EOL) training and experience, clinical competencies, and priorities for learning using 5-point Likert responses. A grid mapping of perceived skill against priority for learning was developed to facilitate curriculum design.

**Results:** Fifty-one percent (37/73) of residents completed the survey. 73% cared for >10 dying patients throughout training and 76% conducted at least one family meeting. Of those reporting faculty observation of meetings, 43% indicated never receiving formal feedback. Most (84%) rated the quality of palliative care teaching as fair/poor. 51% of residents reported not being explicitly taught when to refer patients for palliative care. 57% reported feeling comfortable overall in providing palliative and EOL care; there were no statistical differences in overall level of comfort by gender ( $P=0.89$ ) or training level ( $P=0.17$ ). Of 26 self-assessed core competencies, resident ratings of perceived knowledge/skill were lowest for management of EOL symptoms and ratings for priority for learning were highest in delivering bad news. An example of grid mapping results for competencies in the communication domain is displayed in the figure below.

**Self-Assessed Clinical Competencies in the Communication Domain**

	LOW CLINICAL COMPETENCY <sup>a</sup>	HIGH CLINICAL COMPETENCY
	Possible interpretation: "Concentrate here"	Possible interpretation: "Keep up the good work"
HIGH LEARNING PRIORITY <sup>b</sup>	Leading family meetings Educating patients/families on end-of-life Discussing withdrawal of life-sustaining therapy	Determining goals of care Delivering bad news <sup>c</sup> Discussing code status
LOW LEARNING PRIORITY	Describing suffering at end-of-life <sup>d</sup> Discussing Advance Care Planning	Describing supportive care at end-of-life Documentation of goals of care
	Possible interpretation: "Require creative strategies"	Possible interpretation: "Overkill?"

<sup>a</sup> Criteria for low competency: mean score < 3.0 and/or > 24% rating competency level below average (threshold determined by average of all competencies' mean scores/% below average)

<sup>b</sup> Criteria for high priority: mean score > 3.6 and/or > 55% rating priority level above average (threshold determined by average of all competencies' mean scores/% above average)

<sup>c</sup> Lowest scoring competency in communication

<sup>d</sup> Highest scoring priority in communication

**Conclusions:** Residents at a tertiary institution would benefit from a formal palliative care curriculum. These findings will guide the creation of meaningful program that can be scaled nationally.

# Christopher Holland

## Opioid Use in Revision Total Knee Arthroplasty

Dr. Christopher Holland M.D., Dr. Daniel O'Connor M.D., Dr. John Meehan M.D., Dr. Zachary Lum D.O.

UC Davis, Orthopaedic Surgery, Sacramento, CA, USA

**Introduction:** Opioid use after revision total knee arthroplasty (rTKA) has not been well described. The purpose of our study was to analyze opioid use during rTKA.

**Methods:** Patients undergoing revision TKA from 2010 to 2018 were identified in the electronic health record, and evaluated for opioid use 3 months prior to revision surgery and 24 months postoperatively by prescriptions reported as oral morphine milligram equivalents (MME) in 3 month intervals. Patients were categorized as naïve or tolerant depending on if they had a narcotic prescription preoperatively. Patient demographics were collected, and opioid prescriptions and average MME were compared between the two groups.

**Results:** 91 of 173 (53%) patients were in the tolerant group with average preoperative MME of 23.5mg/day. Patient age, surgery duration, BMI, diabetes, and functional status were not significantly different between naïve and tolerant groups. Postoperatively, tolerant patients received significantly higher daily MME at 3 months 21.6 vs 31.2 mg/day ( $p=0.011$ ) and 6 months 4.9 vs 11.9 mg/day ( $p<0.001$ ) and were more likely to have an opioid prescription at 6 months; 37% vs 17% ( $p=0.002$ ) and 12 months 36.3% vs 23.2% ( $p=0.043$ ). The opioid tolerant group had significantly longer postoperative length of stay, 4.82 vs 3.78 days ( $p=0.004$ ), and were more likely to be discharged to a skilled nursing facility 40.7% vs 18.3% ( $p=0.004$ ), than the naïve group.

**Discussion:** Patients with preoperative opioid prescriptions had significantly higher MME requirements 6 months after surgery and were more likely to require a prescription at 6 and 12 months, compared to naïve patients. Preoperative opioid use correlated with significantly longer hospital stay, increased postoperative MME usage and prolonged postoperative narcotic use. Implementing an opioid sparing strategy, preoperative narcotic wean and pre-habilitation may mitigate some of these factors.

# Anamaria Robles

## Relationship of Post-Resuscitation Hemoglobin to Future Blood Transfusion Needs

Anamaria Robles MD<sup>1</sup>, Zhuowei Cheng MS<sup>2</sup>, Zachary Matthey MD<sup>3</sup>, Brenda Nunez-Garcia BS<sup>3</sup>, Lucy Kornblith MD<sup>3</sup>, Linda Petzold PhD<sup>2</sup>, Rachael Callcut MD MSPH<sup>1</sup>

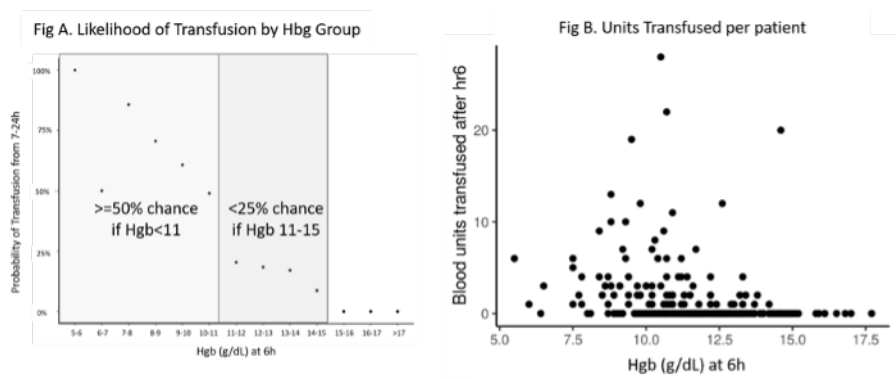
<sup>1</sup>University of California Davis Department of Surgery, Division of Trauma, Acute Care Surgery and Surgical Critical Care, Sacramento, CA, USA. <sup>2</sup>University of California Santa Barbara, Computer Science, Santa Barbara, CA, USA. <sup>3</sup>University of California San Francisco, Department of Surgery, San Francisco, CA, USA

**Introduction:** Goal post-resuscitation (PR) hemoglobin (Hgb) remains unclear in the 24 hours (h) following injury. Although guidance exists for stable all-comer critically ill patients (Hgb $\geq$ 7), no clear criteria exists in the first 24h for injured patients. With empiric balanced resuscitation protocols, concerns about 'over-transfusion' exist given initial PR Hgbs of 9-11g/dL. This study investigates the relationship between PR Hgb & subsequent likelihood of packed red blood cell (PRBC) transfusion out to 24h.

**Methods:** Adult highest-level trauma activations enrolled in a prospective cohort study who were alive at 6h & had a PR Hgb were included. PR Hgb was defined as the Hgb 6h from initial presentation. Demographics, injury characteristics, vital signs, lab data, and complications were collected. Those receiving & not receiving PRBC transfusion 6-24h were compared.

**Results:** 282 patients were alive at 6h (median ISS 26, age 38y, 70% blunt). Between 6-24h, 32% were transfused PRBCs. 28-day survival was 87%. Likelihood of PR PRBC transfusion was inversely correlated to 6h Hgb reaching at least a 50% chance if Hgb $<$ 11g/dL (Fig A). There was no trend difference by mechanism. Median PR PRBC units(u) transfused was 1u if Hgb $<$ 11g/dL vs. 0u for Hgb $>$ 11g/dL (p $<$ 0.001), with 24% receiving  $>$ 4u if Hgb $<$ 11g/dL (Fig B).

**Conclusion:** Applying transfusion criteria of Hgb $<$ 7g/dL is likely not appropriate in the 24h post-injury. Initial PR transfusion practices should be based upon physiology in combination with a higher Hgb trigger threshold.



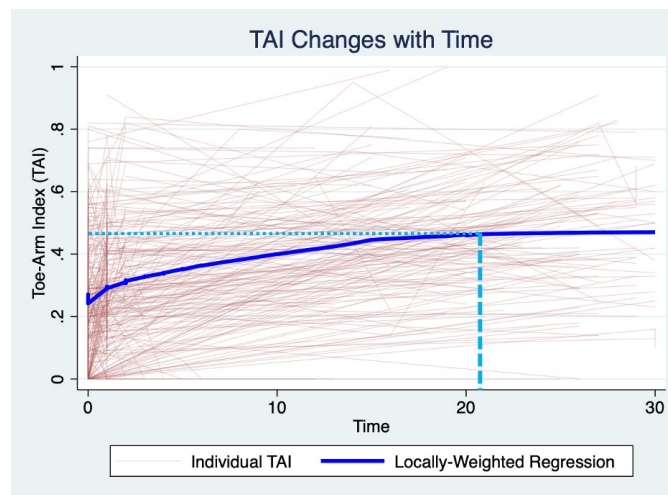
# Christina Brown

## Changes in Early Post-Operative Toe-Brachial Indices May Reflect Positive or Negative Remodeling

Christina Brown, Matthew Mell MD MS, Mimmie Kwong MD

Division of Vascular Surgery, University of California, Davis, Sacramento, CA, USA

Society for Vascular Surgery guidelines recommend utilization of ankle brachial index (ABI) for surveillance after infrainguinal revascularizations. This study investigates the optimal time course of the initial post-procedural exam. A retrospective review of all infrainguinal revascularizations completed between July 2014 and November 2019 at our academic center was performed. Patient information, procedural details, and pre- and post-operative ABI and toe-arm indices (TAI) were collected. A total of 711 patients underwent infrainguinal revascularization for peripheral arterial disease. Of these, 37.4% (266) did not obtain a post-operative ABI or TAI within 30 days, 3.1% had invalid studies due to incompressible vessels, and 2.5% were excluded for other reasons. Among the 404 patients that had a valid post-procedural ABI or TAI, locally-weighted regression of the TAI values was performed for all patients that had at least two studies. This showed early improvement with a steep rise in TAI within two days post-procedure followed by continue improvement until a plateau after 20 days [Figure]. A cohort of 36 patients had two studies performed within 30 days post-procedure. Of these, five (13.9%) had a significant decrease ( $>0.15$ ) in TAI, 19 (52.8%) had no significant change, and 12 (33.3%) had a significant increase. 40% of those with a significant drop in TAI required reintervention within 1 year compared with 30% of those whose TAI increased or remained unchanged. Our findings demonstrate that ABI and TAI are reliable tools to show baseline arterial perfusion post-procedure, with less than 5% of studies invalidated by incompressible vessels. A plateau in the post-procedural TAI occurs after 20 days, implying that early baseline studies may not correctly reflect the peak interventional benefit, possibly due to ongoing remodeling. However, when serial studies are performed, decreased TAI may identify patients requiring reintervention.



# Gillian Hoshal

## Surgical Trainee Perspectives During COVID-19

Gillian Hoshal DO<sup>1</sup>, Steven Hoshal MD<sup>2</sup>, Rodney Diaz MD<sup>3</sup>, David Leshikar MD<sup>1</sup>, Edgardo Salcedo MD<sup>1</sup>

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**Objective:** To determine the impact of the COVID-19 pandemic on surgical residency from the perspective of surgical trainees.

**Methods:** Electronic survey study comprising a 24-item questionnaire was sent to all residents in surgical training programs at the University of California, Davis May-June 2020. Descriptive statistics were used for data analysis. A Wilcoxon signed rank test was used to compare monthly operations data.

**Results:** 228 surveys were administered to study subjects, with a total of 64 responses (28.07% response rate). The median number of surgical operations performed by residents per month from October-November 2019 (baseline) was 21-40 cases per month, which declined to 5-10 cases per month during March-April 2020 (pandemic) ( $P < .0001$ ). Subjects reported no participation in telehealth visits prior to the pandemic. During the COVID-19 peak months (March-April 2020), 30 subjects (56.61%) participated in telehealth visits, with 20 (37.74%) participating in an average of 1-5 visits per week, 4 (7.55%) participating in an average of 6-10 visits per week, and 6 (11.32%) participating in greater than 20 average telehealth visits per week. With regard to the most concerning changes in their surgical education, 29 (55.77%) had moderate to considerable concern regarding their exposure to specific operations, and 32 (61.54%) had moderate to considerable concern regarding cancellation of national and regional conferences.

**Conclusion:** The COVID-19 pandemic has had an impact on surgical education at the University of California, Davis from the perspective of the surgical trainee. The most notable differences were a decline in the average surgical cases per month, as well as an increase in telehealth visits per week. In the setting of the ongoing COVID-19 pandemic, further adaptations are required to optimize surgical training.

# Matthew Kim

## Hyaluronidase (HYAL) Availability in Emergency Rooms: A Californian Census

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**Introduction:** Hyaluronic acid filler injection is generally regarded a safe procedure. However major ischemic complications do exist, notably blindness and skin necrosis. Hyaluronidase (HYAL) is an enzymatic reversal agent for immediate ischemic complications of hyaluronic acid fillers. Unfortunately, many injector sites are not equipped with HYAL due to pricing, short shelf-life, and the rare incidence of ischemic complications. As a result, emergency rooms (ERs) are expected to operate as a safety net when injector sites encounter an ischemic complication. Currently, little is known on the availability of HYAL in ERs. As such, the authors sought to determine the immediate availability of HYAL in ERs across the state of California.

**Methods:** Authors conducted a scripted telephone survey of all Californian ERs, inquiring about HYAL availability. Proportions of HYAL availability were compared among different geographical regions, various trauma center level designations, and children's hospital status, using  $\chi^2$  tests. A Mann-Whitney U test was used to compare median bed counts between hospitals that had HYAL available and those that did not.

**Results:** The present study included 330 Californian ERs and achieved an 89.7% response rate (n=296). Overall, 45.6% of ERs were found to not have HYAL immediately available. HYAL availability was positively associated with level I-III adult trauma center status, pediatric trauma center status, children's hospital status, hospitals with higher median bed counts, and regional geography (p<0.05, all).

**Conclusion:** HYAL availability in ERs is unreliable across the state of California, posing a risk to patient safety as ERs are often expected to function as a safety net for hyaluronic acid filler ischemic complications. In emergent situations for which injectors have inadequate supplies of HYAL, the authors recommend calling hospitals in advance to verify HYAL availability.

# Trevor Plescia

The impact of bariatric surgery on the development of small intestinal bacterial overgrowth (SIBO).

Victoria Lyo MD<sup>1</sup>, Trevor Plescia MD<sup>2</sup>, Alexis Chirco BS<sup>3</sup>

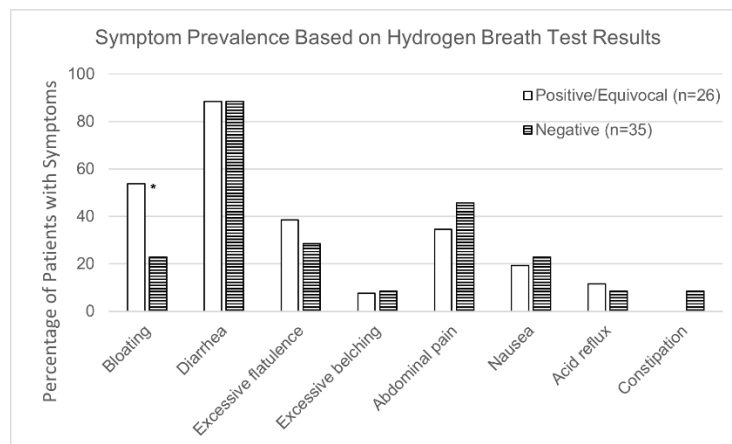
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**Introduction:** Small intestinal bacterial overgrowth (SIBO) is a common problem in obesity leading to abdominal pain, bloating, and diarrhea. However, little is known about SIBO after bariatric surgery. We sought to define the prevalence, risk factors, and outcomes of SIBO in a bariatric population through a retrospective cohort study.

**Methods:** A retrospective chart review of patients undergoing Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG) from 2002–2020 was performed. Demographics, symptoms, and outcomes were collected for patients suspected of or tested for SIBO using hydrogen breath testing (HBT). Chi-square and t-tests were performed.

**Results:** Of 3,110 bariatric patients, 86 (2.77%) were suspected of having SIBO: 71 (82.6%) underwent RYGB and 15 (17.4%) SG. Average time from surgery to first HBT was  $8.6 \pm 14.3$  years. Symptoms prompting testing for SIBO included diarrhea (86%), abdominal pain (40.7%), bloating (32.6%), excessive flatulence (25.6%), and nausea (17.4%). There was no difference in symptom prevalence after RYGB or SG. Only bloating was significantly associated with SIBO diagnosis (53.8% vs 22.9%;  $p$ -value=0.013). SIBO was diagnosed in 42.6% (26/61) of patients who completed HBT: 45.1% (23/51) after RYGB vs 30% (3/10) after SG, which was not significant ( $p$ -value=0.38). Average BMI in patients with SIBO was 37.2 kg/m<sup>2</sup> versus 34.6 kg/m<sup>2</sup> without ( $p$ -value=0.65). 43% (37/86) received therapeutic or empiric antibiotics, of whom 75.7% clinically improved. Rifaximin and Ciprofloxacin had equal rates of improvement (70% vs 76.9%, respectively;  $p$ -value=0.66). PPI use was not associated with SIBO diagnosis (42.3% vs 25.7%;  $p$ -value=0.17).

**Conclusion:** A high index of suspicion for SIBO in bariatric patients is recommended, especially following RYGB and those complaining of bloating. Further work to define optimal treatment courses and risk reduction is necessary.



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