RESEARCH DAY SYMPOSIUM

APRIL 12, 2022

Surviving and Thriving in Academic Medicine

Keynote Speaker:

Vice Dean for Research - KIM BARRETT, PhD

UC DAVIS HEALTH | Department of Surgery

PROGRAM NOTES

AGENDA | APRIL 12TH, 2022

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. KIM BARRETT	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
6:00 PM – 7:30 PM	DINNER AND AWARDS CEREMONY	SUTTER CLUB

PROGRAM SCHEDULE | SESSIONS IN LH 2222

6:30 AM - 7:00 AM	**BREAKFAST AND REGISTRATION**
7:15 AM - 7:30 AM	**WELCOME AND INTRODUCTION**
	ORAL PRESENTATIONS SESSION 1 LH 2222 | 7:30 AM - 9:00 AM
	MODERATORS – KENT LLOYD & SEPIDEH GHOLAMI
7:30 AM - 7:45 AM	***KEWA GAO*** - Non-viral gene editing in utero with lipid nanoparticles complexed to mRNA
7:45 AM - 8:00 AM	***SEAN JUDGE*** - Transcriptome analysis of tumor infiltrating lymphocytes identifies gene signatures associated with immune infiltration and survival in soft tissue sarcoma
8:00 AM - 8:15 AM	***SYLVIA CRUZ*** - Characterization of the Immune Tumor Microenvironment in Soft Tissue Sarcoma Patients Undergoing Surgery
8:15 AM - 8:30 AM	***FRANSIA DE LEON*** - Impact of ATG Dose Reduction on Kidney Transplant Outcomes During the COVID-19 Pandemic
8:30 AM - 8:45 AM	***HENGYUE SONG*** - A biocompatible scaffold engineered with proangiogenic proteoglycan mimetics and loaded with endothelial cells promotes deep burn wound healing
8:45 AM - 9:00 AM	***KHURSHID IRANPUR*** - Inhibitory Receptor TIGIT is a critical regulator of Natural Killer Cell Activation and Cell Death Following Strong Stimulation
9:00 AM - 9:15 AM	**BREAK**
	QUICK SHOT SESSION 1 A LH 2222 | 9:15 AM - 10:15 AM
	MODERATORS – PETER PHAN & TANYA RINDERKNECHT
9:15 AM - 9:25 AM	***LEORA GOLDBLOOM-HELZNER*** - Use of ExoView technology to measure extracellular vesicle surface modification efficiency and inform optimization of carbodiimide crosslinking protocols
9:25 AM - 9:35 AM	***LALITHASRI RAMASUBRAMANIAN*** - Evaluation of Endothelial Progenitor Cell Plasma Membrane as an Anti-thrombotic and Pro-Angiogenic Biomaterial
9:35 AM - 9:45 AM	***FRANSIA DE LEON*** - A Review of Our Center's Renal Allograft Outcomes from Donors After Circulatory Death

SESSIONS IN LH 2222

9:45 AM – 9:55 AM	***SU YEON LEE*** - Gender disparity in pediatric surgery: an evaluation of pediatric surgery conference participation
9:55 AM - 10:05 AM	***SIRJAN MOR*** - Placental Mesenchymal Stem Cells Improve Motor Function in a Rat Unilateral Spinal Cord Contusion Model
10:05 AM - 10:15 AM	***ARYANA RAZMARA*** **-** Inhaled recombinant human IL-15 in Dogs with Naturally Occurring Pulmonary Metastases from Osteosarcoma or Melanoma: A Phase 1 Study of Clinical Activity and Correlates of Response
10:15 AM - 10:30 AM	**BREAK**

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

MODERATORS – BETHANY CUMMINGS & TINA PALMIERI

10:30 AM - 10:45 AM	***DAKE HAO*** - Engineered extracellular vesicles with high collagen-binding affinity present superior in situ retention and therapeutic efficacy in tissue repair
10:45 AM - 11:00 AM	***CHRISTINA THEODOROU*** **-** Evaluation of a Novel Biodegradable Polyurethane Patch for Repair of Diaphragmatic Hernia in a Rat Model: A Pilot Study
11:00 AM - 11:15 AM	***LAUREN PERRY*** **-** Patients with Soft Tissue Sarcomas Harbor an Intratumoral Microbiome Which is Linked with Immune Infiltrate and Prognosis
11:15 AM - 11:30 AM	***DAVID WALLACE*** - Poverty and Frailty in Patients with Burn Injuries: Important but Unrelated
11:30 AM - 11:45 AM	***JEAN DEBÉDAT*** - Cyclopropane fatty acids are bacteria-derived xenolipids displaying binding affinities toward peroxisome proliferator activated receptors α, δ, and γ
11:45 AM - 12:00 PM	***CYRUS SHOLEVAR*** - Tissue resident lung natural killer (NK) cells demonstrate enhanced responses to IL-15 compared to peripheral populations
12:00 PM - 12:30 PM	**LUNCH**
12:30 PM - 1:30 PM	**KEYNOTE SPEAKER PRESENTATION BY DR. KIM BARRETT** *"Surviving and Thriving in Academic Medicine"*

SESSIONS IN LH 2222

	ORAL PRESENTATION SESSION 3 LH 2222 | 1:30 PM - 3:00 PM
	MODERATORS – JONATHAN KOHLER & VICTORIA LYO
1:30 PM - 1:45 PM	***JACQUELYN YU*** **-** Lipid Metabolism Profile Of Human Kidneys During Ex Vivo Normothermic Perfusion
1:45 PM - 2:00 PM	***RAFAEL LOZANO*** - External Validation of the TEMPT Score as a Predictor of Blood Transfusion
2:00 PM - 2:15 PM	***ELAN SHERAZEE*** - Review of Graft Patency in Robotically Assisted Coronary Artery Bypass and Totally Endoscopic Coronary Bypass Surgery
2:15 PM - 2:30 PM	***NICOLE MOORE*** - The Impact of Bariatric Surgery on the Development of Exocrine Pancreatic Insufficiency
2:30 PM - 2:45 PM	***CARA POZOLO*** **-** Improved Follow-Up After Hospital Discharge Does Not Impact 30-Day Readmissions After Vascular Procedures
2:45 PM - 3:00 PM	***ANAMARIA ROBLES*** **–** The Chicken or The Egg: Correlation Of Low Platelets & Post-Injury Acute Respiratory Distress Syndrome
3:00 PM - 3:15 PM	**BREAK**

NOTES:

SESSIONS IN LH 2222

	QUICK SHOT SESSION 2A - LH 2222 | 3:15 PM - 4:25 PM
	MODERATORS – LISA BROWN & MICHAEL CAMPBELL
3:15 PM - 3:25 PM	***ALEXANDRA JOHNS*** **-** Factors influencing length of stay following bariatric surgery
3:25 PM - 3:35 PM	***ISABELLE STRUVE*** **-** Lower coded pediatric trauma patients are exposed to increased rates of cross-sectional imaging despite similar injury severity.
3:35 PM - 3:45 PM	***KAITLIN CLARK*** - Characterization of Extracellular Vesicles Isolated from Canine Placenta-derived Mesenchymal Stem/Stromal Cells
3:45 PM- 3:55 PM	***ANDREA KULINICH*** **-** A Comprehensive Update on Pneumothorax as a Complication of Breast Augmentation
3:55 PM - 4:05 PM	***ANASTASIYA STASYUK*** - Interventions and outcomes in glottic versus multi-level airway stenosis: multi-institutional review
4:05 PM - 4:15 PM	***CYRUS SHOLEVAR*** **-** Building a Successful Hepatic Artery Infusion (HAI) Program: An International Survey of the HAI Consortium Research Network
4:15 PM - 4:25 PM	***NICOLE MOORE***- How Adolescents and Young adults with Incidental Adrenal Tumors Differ from Similar Aged Patients Without Adrenal Tumors
4:30 PM - 4:45 PM	**FINAL REMARKS**
6:00 PM - 7:30 PM	**DINNER & 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 – LUIS GODOY & ROBERT CANTER
9:15 AM - 9:25 AM	***LAUREN PERRY*** - Impact of Pre-existing Psychiatric Disorders on Outcomes after Pancreatic Cancer Surgery
9:25 AM - 9:35 AM	***KARA KLEBER*** - Inhaled IL-15 post amputation for prevention of pulmonary metastasis in dogs with osteosarcoma with assessment of the gut microbiome as a biomarker of response
9:35 AM - 9:45 AM	***JULIA PERSKY*** - Characterization of Natural Killer and Cytotoxic T Cell Immune Infiltrates in Pancreatic Ductal Adenocarcinoma
9:45 AM - 9:55 AM	***DAKE HAO*** - Developing a combinational stem cell-based tissue engineering approach to treat spina bifida before birth
9:55 AM - 10:05 AM	***JENNIFER LOZA*** - Donor Characteristics Associated with Early Allograft Failure in Deceased Donor Kidney Transplantation
10:05 AM - 10:15 AM	***ASHLY RUF*** - Dedicated Acute Care Surgery Operating Room: A Race Against the Clock
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 – CLAIRE GRAVES & ANDREW LI
3:15 PM - 3:25 PM	***ELISE HILL*** - The Power Of Cooperation: A Quantitative Analysis Of The Benefit Of Civilian Partnerships On The Academic Output Of Military Surgeons
3:25 PM- 3:35 PM	***ELAN SHERAZEE*** - Hyperoxia is Not Associated with Early Mortality nor Mid-Term Functional Outcomes After Severe Traumatic Brain Injury
3:35 PM - 3:45 PM	***JENNIFER GEIGER*** -Evaluating a Simulation-Based Serious Illness Communication Workshop Using a Structured Guide in Surgical Residents

3:45 PM - 3:55 PM	***CHAOXING ZHANG*** **-** mRNA vaccine delivery by microneedle patches for treatment of unresectable melanoma
3:55 PM - 4:05 PM	***ANGELICA MARTIN*** - Research Addressing Racial Health Disparities in Cardiothoracic Surgery Represents Only a Small Fraction of Total Major Meeting Peer-reviewed Content
4:05 PM - 4:15 PM	***AMANDA PHARES*** - Revitalizing the Robotic Surgery Curriculum for General Surgery Residents - One Year Follow Up
4:15 PM - 4:25 PM	***RAFAEL LOZANO*** **-** Intraoperative Systemic Heparin Is Safe for Treatment of Blunt Thoracic Aortic Injury with Concomitant Traumatic Brain Injury

Welcome from the Chairs

Welcome to the 33rd Annual Department of Surgery Research Symposium at the University of California, Davis. The Annual Research Symposium is an opportunity to recognize and celebrate the extraordinary research accomplishments of our trainees and faculty who work every day to ensure better outcomes for our patients. While conducting rigorous research is not without challenges, few things are as rewarding as creating and contributing to new knowledge and advancing surgical science.

Our department has rich history in contributing to surgical science and research and we strive to ignite the passion of research in our trainees. Research in the department of surgery is a core value and is made possible by the tireless dedication, commitment, and collaboration of faculty, staff, students, and trainees. Together, we all learn from curiosity and periodically we must step back to reflect on our efforts and celebrate them in a way that invigorates and prepares us to meet the challenges of tomorrow.

Today's symposium is an opportunity to stimulate new ideas and collaborations by highlighting the breadth of research activities happening across the various surgical disciplines. It is important—and refreshing— to occasionally lift our heads, look around, and observe what is happening outside our areas of focus. In doing so we might identify resources that can enhance our own research portfolios as well as find the camaraderie of like-minded peers which can serve as a source of inspiration.

Our program includes oral presentations and quick-shot oral poster presentations that highlight the diverse research in our department. We will award prizes for the top clinical and basic science oral presentations as well as the best quick-shot oral presentation.

We thank you for joining us today in celebration of surgical science and research and helping to advance our field forward.

Sincerely,

Diana L. Farmer, MD, FACS, FRCS
Distinguished Professor and Pearl Stamps Stewart Chair
Chair, Department of Surgery, UC Davis School of Medicine
Surgeon-in-Chief, UC Davis Children's Hospital

Sean Adams, PhD, FTOS
Professor and Vice Chair, Basic Science

Rachael Callcut, MD, MSPH, FACS
Professor and Vice Chair, Clinical Sciences

Tina Palmieri, MD, FACS, FCCM
Professor and Vice Chair, Clinical Research

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

RESEARCH VICE CHAIRS

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

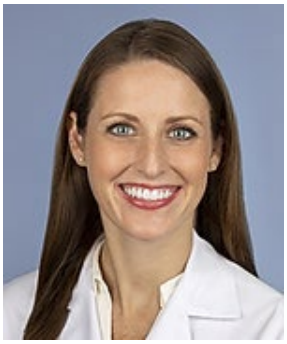
Sean H. Adams, PhD, FTOS
Vice Chair, Basic Research

Rachael A. Callcut, MD, MSPH, FACS
Vice Chair, Clinical Sciences

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

RESEARCH COMMITTEE

Shushmita Ahmed, MD
Foregut, Metabolic, and General Surgery



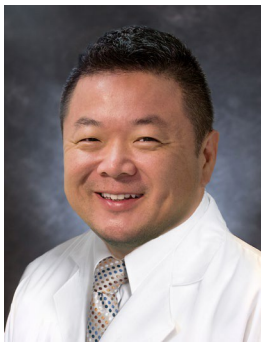
Erin Brown, MD
Pediatric General Surgery

Ian Elliot Brown, MD, PhD
Trauma, ACS

Lisa M. Brown, MD, MAS
General Thoracic Surgery

Robert J. Canter, MD
Surgical Oncology

Bethany Cummings, DVM, PhD
Metabolism and Obesity Researcher

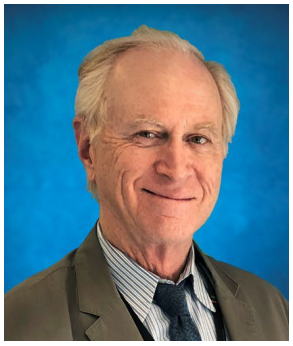


Shinjiro Hirose, MD
Pediatric General Surgery

Misty Humphries, MD, MAS, RPVI
Vascular Surgery

Bob Kiaii, MD
Cardiac Surgery

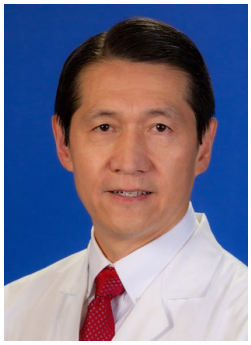
RESEARCH COMMITTEE



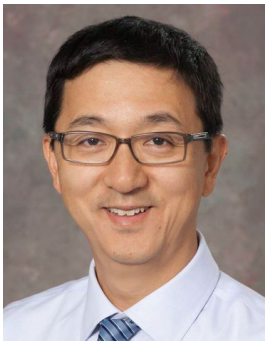
Kent Lloyd, DVM, PhD
Research, Surgery

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

Clifford Pereira, MD
Plastic Surgery and Reconstruction



Lee L.Q, Pu, MD, PhD
Plastic Surgery and Reconstruction



Junichiro Sageshima, MD
Transplant Surgery

Hazem Shamseddeen, MD
Foregut, Metabolic, and General Surgery

Keynote Speaker – Kim E. Barrett, Ph.D

Kim Elaine Barrett, Ph.D., is the Vice Dean for Research and Distinguished Professor of Physiology and Membrane Biology at the UC Davis School of Medicine. Barrett is advancing an innovative vision for the future of research at the School of Medicine that emphasizes collaboration to transform health. She is responsible for implementing key initiatives and fostering partnerships across UC Davis Health and with other schools, centers, and colleagues throughout UC Davis. Barrett also leads the medical school's collaborative efforts to develop UC Davis' Aggie Square research program.

Barrett joined UC Davis Health in 2021 with more than 30 years of notable scientific research and institutional leadership experience. Immediately prior to UC Davis, Barrett was a distinguished professor of medicine at UC San Diego and director of the division of graduate education at the National Science Foundation.

She has received numerous honors and awards for her research, teaching, mentoring, and service activities. Barrett is also an internationally recognized scholar in gastrointestinal physiology and has published extensively. She has received numerous awards for her academic contributions as well as her teaching, administrative skills, and mentoring. These include the 2021 Distinguished Achievement Award for Basic Science from the American Gastroenterological Association.

Barrett is originally from the United Kingdom and earned both her B.Sc. (Medicinal Chemistry, 1979) and her Ph.D. (Biological Chemistry, 1982) from University College, London, England.

ORAL PRESENTATIONS

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

MODERATORS
KENT LLOYD & SEPIDEH GHOLAMI

1. **KEWA GAO –** Non-viral gene editing in utero with lipid nanoparticles complexed to mRNA

2. **SEAN JUDGE -** Transcriptome analysis of tumor infiltrating lymphocytes identifies gene signatures associated with immune infiltration and survival in soft tissue sarcoma

3. **SYLVIA CRUZ -** Characterization of the Immune Tumor Microenvironment in Soft Tissue Sarcoma Patients Undergoing Surgery

4. **FRANSIA DE LEON -** Impact of ATG Dose Reduction on Kidney Transplant Outcomes During the COVID-19 Pandemic

5. **HENGYUE SONG -** A biocompatible scaffold engineered with proangiogenic proteoglycan mimetics and loaded with endothelial cells promotes deep burn wound healing

6. **KHURSHID IRANPUR -** Inhibitory Receptor TIGIT is a critical regulator of Natural Killer Cell Activation and Cell Death Following Strong Stimulation

Kewa Gao

Non-viral gene editing in utero with lipid nanoparticles complexed to mRNA

Kewa Gao MD, PhD[1], Jie Li PhD[2], Hengyue Song MD[1,3], Yongheng Wang MS[1,4], Hesong Han PhD[2], Bryan Anggito[4], Qianyu Jin[5], Diana Farmer MD[1], Niren Murthy PhD[2], Aijun Wang PhD[1,4]

[1]Department of Surgery, School of Medicine, University of California, Davis, Sacramento, CA, USA. [2]Department of Bioengineering, University of California, Berkeley, CA, USA. [3]Department of Burns and Plastic Surgery, The Third Xiangya Hospital of Central South University, Changsha, Hunan, China. [4]Department of Biomedical Engineering, University of California, Davis, CA, USA. [5]College of Biological Sciences, University of California, Davis, CA, USA

Abstract

The delivery of mRNA in utero with lipid nanoparticles (LNP) has tremendous potential for treating fetal diseases. However, the in utero tissue tropism of LNP/mRNA complexes is unknown and this limits the development of mRNA based fetal therapeutics. In this report we identified the cells and organs transfected with mRNA/LNP complexes, after in utero delivery, using the Ai9 mouse model accompanied with CRE mRNA delivery. We demonstrate here that LNP/mRNA complexes around 110 nm in size can deliver CRE mRNA in utero to all the major fetal organs, such as the heart, the liver, kidneys, lungs and the gastrointestinal tract with remarkable efficiency and low toxicity. In addition, we analyzed Ai9 mice, treated in utero with LNP/CRE mRNA complexes, 1 day and 4 weeks after birth and demonstrate that muscle cells in the diaphragm (23.33 ± 4.47%) and heart (7.18 ± 2.01%) were edited. These results revealed in utero tissue tropism of LNP/mRNA complexes and highlighted the great potential of LNP for delivering macromolecules to organs outside of the liver for the treatment of a wide variety of diseases. We expect this study to have an impact on the research in the field of gene therapy and beyond.

Sean Judge

Transcriptome analysis of tumor infiltrating lymphocytes identifies gene signatures associated with immune infiltration and survival in soft tissue sarcoma

Sean Judge MD[1], Joshua Bloomstein BS[2], Cyrus Sholevar MD[1], Morgan Darrow MD[3], Kevin Stoffel MS[4], Logan Vick BS[4], Cordelia Dunai PhD[4], Sylvia Cruz BS[2], Aryana Razmara BS[5], Arta Monjazeb MD, PhD[6], Robert Rebhun DVM, PhD[5], William Murphy PhD[4], Robert Canter MD[1]

[1]Division of Surgical Oncology, Department of Surgery, University of California, Davis, Sacramento, CA, USA. [2]School of Medicine, University of California, Davis, Sacramento, CA, USA. [3]Department of Pathology, University of California, Davis, Sacramento, CA, USA. [4]Department of Dermatology, University of California, Davis, Sacramento, CA, USA. [5]School of Veterinary Medicine, University of California, Davis, Davis, CA, USA. [6]Department of Radiation Oncology, University of California, Davis, Sacramento, CA, USA

Abstract

Current T-cell based immunotherapies have been limited in soft tissue sarcomas (STS), while pre-clinical studies have shown evidence of natural killer (NK) cell activity. Since tumor infiltrating lymphocytes are prognostic and predictive of outcomes in the majority of solid tumors, we sought to evaluate the gene expression profile of tumor and circulating lymphocytes as well as tumor cells in STS patients with the goal of identifying unique signatures of immune cell function and tumor-intrinsic drivers of immune infiltration.

We isolated purified blood and tumor-infiltrating CD3-CD56+ NK and CD3+ T cells and CD45- tumor cells from STS patients undergoing surgery. We then evaluated differential gene expression (DGE) of flow-sorted populations by RNA sequencing analysis (RNA-Seq). To evaluate survival differences and validate primary DGE results, we queried the TCGA database to compare outcomes stratified by bulk tumor gene expression.

Sorted intra-tumoral T cells showed significant upregulation of established activating (CD137) and inhibitory genes (TIM-3) compared to circulating T cells. In contrast, intra-tumoral NK cells did not exhibit tumor-specific upregulation of canonical cytotoxic genes, but rather significant DGE in mitogen signaling (DUSP4) and metabolic function (SMPD3, SLC7A5). Tumors with higher lymphocyte infiltration exhibited significantly increased expression of the pro-inflammatory receptor TLR4. TCGA analysis revealed that STS tumors with high TLR4 expression ($P = 0.03$) and low STMN1 expression involved in microtubule polymerization ($P < 0.001$) were associated with significantly improved survival.

Intratumoral NK cells appear to have alterations restricted primarily to metabolic pathways in this cohort of STS patients. Increased immune cell infiltration and improved survival were positively correlated to TLR4 expression and inversely correlated to STMN1 expression within tumors, suggesting possible novel immunotherapeutic targets for STS.

Sylvia Cruz

Characterization of the Immune Tumor Microenvironment in Soft Tissue Sarcoma Patients Undergoing Surgery

Sylvia Cruz[1], Cyrus Sholevar MD[1], Sean Judge MD[1], Morgan Darrow MD[2], Lauren Perry MD[1], Lauren Farley[1], Khurshid Iranpur[1], Cordelia Dunai PhD[3], Shuai Chen PhD[4], Steven Thorpe MD[5], Robert Canter MD[1]

[1]Division of Surgical Oncology, Department of Surgery, University of California Davis School of Medicine, Sacramento, CA, USA. [2]Pathology and Laboratory Medicine, University of California Davis School of Medicine, Sacramento, CA, USA. [3]Dermatology, University of California Davis School of Medicine, Sacramento, CA, USA. [4]Public Health Sciences, University of California Davis School of Medicine, Sacramento, CA, USA. [5]Orthopedic Surgery, University of California Davis School of Medicine, Sacramento, CA, USA

Abstract

Background: Tumor infiltrating lymphocytes (TILs) have been shown to predict survival in soft tissue sarcomas (STS), but the specific contribution of natural killer (NK) and CD8+ T cells to outcomes is undefined. Therefore, we sought to characterize the extent of NK and CD8+ T cell infiltration in STS.

Methods: Prospectively, we evaluated 15 patients using fresh tumor from surgery for flow cytometric analysis. Retrospectively, we evaluated archived tumor tissue from 90 STS patients by immunohistochemistry (IHC) for CD3, CD8, CD45RO, NKp46, TIGIT, MHC-I, and p53. We analyzed metastasis-free survival (MFS) and overall survival (OS) by Kaplan-Meier method.

Results: By flow cytometry, we observed significant variability in CD45+ leukocytes in the STS TME (mean 29±24% of total live cells) with low percentages of tumor-infiltrating CD3-CD56+ NK cells (1.7±1.9% of total live cells and 5.3±3.0% of live CD45+ cells) and CD8+ T cells (1.6±1.6% of total live cells and 29.6±30.5% of live CD45+ cells). By IHC, NK and T cell infiltrates were low (median H score 0, range 0-66.5 and 2.7, range 0-110, respectively). We confirmed a positive correlation between CD8+ T cell infiltration and significantly improved OS ($P<0.05$) and a trend for improved MFS. We also observed a trend for improved OS among patients with higher NKp46 scores ($P=0.07$). MHC-I expression positively correlated with both T and NK cell infiltration ($P<0.05$), whereas TIGIT expression positively correlated with T cell infiltration ($P<0.05$), but not NK infiltration.

Conclusion: Infiltration of NK and CD8+ T cells is overall low in STS patients undergoing surgery but associated with superior OS. Further characterization of the immune infiltrate in STS may yield better biomarkers of prognosis and immune targeting.

Fransia S. De Leon

Impact of ATG Dose Reduction on Kidney Transplant Outcomes During the COVID-19 Pandemic

Fransia S. De Leon BA[1], Peter A. Than MD[1], Kuang-Yu Jen MD[2], Jacquelyn Yu MD[1], Naeem Goussous MD[1], Neal Mineyev MD[1], Junichiro Sageshima MD[1], Richard V. Perez MD[1], Aileen X. Wang MD[3]

[1]UC Davis Department of Surgery, Division of Transplant Surgery, Sacramento, CA, USA. [2]UC Davis Department of Pathology, Sacramento, CA, USA. [3]UC Davis Department of Medicine, Division of Transplant Nephrology, Sacramento, CA, USA

Abstract

Introduction: During the COVID-19 pandemic, many transplant centers modified induction immunosuppression regimens to protect patients. Our center specifically instituted a protocol reduction in anti-thymocyte globulin (ATG) dose up to 33% compared to the pre-pandemic doses for all kidney transplant recipients, with no change in maintenance immunosuppression. We hypothesize that reduced ATG dose will not adversely impact kidney allograft and transplant recipient outcomes.

Methods: We retrospectively reviewed adult patients who received a kidney transplant between January 2019 and December 2019 (pre-pandemic) or between December 2020 and March 2021 (pandemic), with a minimum follow-up of 6 months. The former group was selected as a comparable pre-pandemic cohort as they were treated before the COVID-19 pandemic. Primary outcomes included delayed graft function (DGF), BK viremia, and rejection.

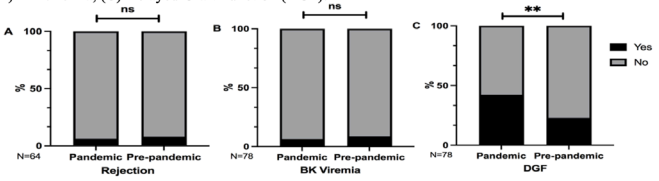
Results: 78 adult kidney transplants were performed during the pandemic and 211 were performed during the pre-pandemic era. Cohort characteristics are depicted on Table 1; primary outcomes are depicted on Figure 1. The rate of biopsy proven rejection (including surveillance and for-cause biopsies) did not increase during the pandemic as compared to the pre-pandemic era (6.3% vs 8.0%, respectively, p=0.8). The rate of BK viremia (>1000 copies/mL) at 3 months was lower in the pandemic era, but not statistically significant (6.4% vs 8.7%, respectively, p=0.6). The rate of DGF was significantly higher during the pandemic compared to pre-pandemic (42.3% vs 22.9%, respectively, p=0.002). No recipients tested positive for COVID-19 within 1-month post-transplant.

Conclusions: Despite the reduction in ATG dose during the pandemic, we found no significant change in the rate of rejection or BK viremia; however, there was a significant increase in the rate of DGF. Future studies should assess the long-term impact of reduced induction immunosuppression on kidney transplant recipients.

Table 1. Cohort Characteristics

	Pre-Pandemic (n=211)	Pandemic (n=78)
cPRA ≥40, n(%)	84(39.8)	17(21.8)
Type of Transplant, n(%)		
Deceased Donor	144(68.2)	74(94.9)
Donation after Circulatory Death	43(29.9)	32(43.2)
Kidney Donor Profile Index, median(IQR)	46(23-65)	61(41-83)
Cold Ischemia Time (hrs), mean +/- SD	16.0(13.0)	19.2(9.6)
Time to Biopsy (days), median (IQR)	90(90-105)	92(87-96)

Figure 1. Primary renal allograft outcomes of the pre-pandemic cohort versus the pandemic cohort. (A) Rejection, (B) BK viremia, (C) Delayed Graft Function (DGF).



Hengyue Song

A biocompatible scaffold engineered with proangiogenic proteoglycan mimetics and loaded with endothelial cells promotes deep burn wound healing

Hengyue Song MD[1,2], Kewa Gao MD, PhD[1], Andrew Li MD[3], Ruiwu Liu PhD[4], Bryan Anggito BS[5], Qianyu Jin BS[6], Kit Lam MD, PhD[4], Alyssa Panitch PhD[5], Diana Farmer MD[1], Aijun Wang PhD[1]

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Abstract

Neovascularization is the key to accelerate wound healing. We have fabricated a multi-functional pro-angiogenic molecule by grafting cyclic peptide LXW7 and collagen-binding peptides (SILY) to a dermatan sulfate (DS) glycosaminoglycan backbone, named DS-SILY-LXW7, and further employed this to functionalize collagen-based scaffolds.

In this study, we established a large-area deep burn model by treating C57BL6/J mice with 65°C hot water for 20 seconds on a 2×3 cm area of dorsal skin which produced 2nd-degree burns approximately equal to 20% of the mouse's total body surface area. The burn wounds were treated with Integra® only, endothelial progenitor cell (EPC) loaded Integra®, DS-SILY-LXW7 modified Integra®, and EPC-loaded DS-SILY-LXW7 modified Integra®. The burn wound size was photographed and measured weekly for a period of 5 weeks post-treatment. The re-epithelialization, wound length, collagen deposition and neovascularization were measured under histologic staining.

EPC loaded DS-SILY-LXW7 modified Integra® scaffolds significantly increased the rate of wound healing at 2-3weeks post-treatment compared to Integra® only group. The re-epithelization, density of functional neovascularization, and collagen density of EPC loaded and DS-SILY-LXW7 modified Integra® group were significantly higher than the Integra® only group at 5 weeks post-treatment. These results suggest that the EPC-loaded LXW7-DS-SILY modified Integra® scaffolds can significantly promote wound healing, enhance neovascularization, re-epithelization, and collagen deposition.

This study provides a promising novel treatment to accelerate deep burn wound healing, thereby reducing the morbidity of open burn wounds, such as insensible fluid losses and infection. Moreover, our scaffolds present the potential for treating large areas of deep burns by reducing and potentially obviating the need for autografting, and its accompanying morbidity, in patients with already limited areas of harvestable skin.

Inhibitory Receptor TIGIT is a critical regulator of Natural Killer Cell Activation and Cell Death Following Strong Stimulation

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Abstract

Background: Natural killer (NK) cells are key lymphocytes of the innate immune system with anti-viral and anti-tumor properties and can rapidly respond to target cells without prior antigen sensitization. Here, we sought to evaluate the role of inhibitory receptor TIGIT to restrain NK responses in vitro and in vivo.

Methods: NK cells were isolated from the spleen, lung, and liver of wild type C57BL/6 mice and aged-matched TIGIT knockout (KO) mice and cultured in vitro with recombinant human interleukin 15 (rhIL-15) and IL-2. The wild type and KO mice were treated in vivo with IL-15 and IL-2. We assessed NK cell frequencies, viability, activation, proliferation, and apoptosis by flow cytometry and cytokine analysis.

Results: NK cells from TIGIT KO mice showed greater proliferation and expansion both in vitro and in vivo with higher Ki67 expression and numbers following acute stimulation. However, by day 7 in vitro, NK cells from TIGIT KO showed lower viability (76±6% vs 92±1%) and fold expansion (0.2±0.2 vs 2.0±0.7) than the WT cells. In vivo, we observed greater NK numbers in the spleen, lungs, and liver of KO mice following IL-15 exposure, peaking on day 4 but remaining elevated on day 8. NK cells from TIGIT KO mice showed significantly higher apoptosis (66 ± 6% vs. 20 ± 6%, $P<0.001$ in vitro and 25±4% vs. 12±2% $P<0.01$ in vivo).

Conclusion: Our results indicate that TIGIT plays a critical role in regulating NK cell responses following cytokine stimulation, suggesting that TIGIT blocking strategies may lead to both greater acute expansion but subsequently greater depletion of NK cells longterm following activation.

QUICK SHOT PRESENTATIONS

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

MODERATORS
PETER PHAN & TANYA RINDERKNECHT

1. **LEORA GOLDBLOOM-HELZNER -** Use of ExoView technology to measure extracellular vesicle surface modification efficiency and inform optimization of carbodiimide crosslinking protocols

2. **LALITHASRI RAMASUBRAMANIAN -** Evaluation of Endothelial Progenitor Cell Plasma Membrane as an Anti-thrombotic and Pro-Angiogenic Biomaterial

3. **FRANSIA DE LEON -** A Review of Our Center's Renal Allograft Outcomes from Donors After Circulatory Death

4. **SU YEON LEE** - Gender disparity in pediatric surgery: an evaluation of pediatric surgery conference participation

5. **SIRJAN MOR -** Placental Mesenchymal Stem Cells Improve Motor Function in a Rat Unilateral Spinal Cord Contusion Model

6. **ARYANA RAZMARA** - Inhaled recombinant human IL-15 in Dogs with Naturally Occurring Pulmonary Metastases from Osteosarcoma or Melanoma: A Phase 1 Study of Clinical Activity and Correlates of Response

Leora Goldbloom-Helzner

Use of ExoView technology to measure extracellular vesicle surface modification efficiency and inform optimization of carbodiimide crosslinking protocols

Leora Goldbloom-Helzner MSE[1,2], Rachel Mizenko BS[2], Dr. Priyadarsini Kumar PhD[1], Dr. Randy Carney PhD[2], Dr. Diana Farmer MD[1], Dr. Aijun Wang PhD[1,2]

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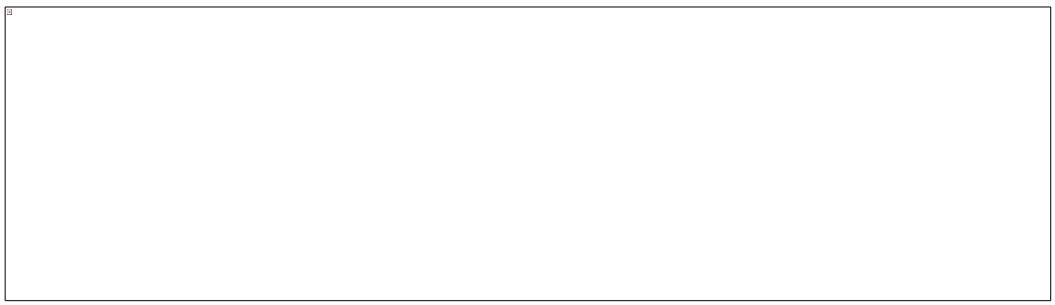
Abstract

Introduction: Extracellular vesicles (EVs) derived from placental mesenchymal stromal cells (PMSCs) have the potential to provide neuroprotection at sites of injury. We have engineered these EVs with a myelin-targeting aptamer, LJM-3064, to improve EV targeting across the blood brain barrier and increase therapeutic remyelination in vivo. Although this work has shown preliminary success, current technology has not been used to measure conjugation efficiency on a single EV level. In this study, ExoView R100 was used to determine conjugation efficiency of FITC-labeled aptamer-modified EVs (Apt-EVs) and informed optimization efforts to improve surface modification.

Methods: PMSC-EVs were modified with a 5'FAM 3'carboxyl group LJM-3064 aptamer using EDC/sNHS bioconjugation. Nanoparticle tracking analysis (NTA) measured EV size fluctuations after surface modification. ExoView characterized colocalized expression of EV markers (CD9, CD63, CD81) on a single EV scale and measured conjugation of LJM-3064 on EVs by dividing LJM-3064+ EVs by the total number of EVs counted on ExoView chips.

Results: PMSC-EV size remained within 50-100nm for both unmodified and modified EVs, trending to only slightly larger diameters for Apt-EVs. Using ExoView, we saw normal EV expressions of CD9, CD63, and CD81 and measured a ~4-fold increase in aptamer conjugation efficiency (**Figure 1**) by changing parameters such as incubation times and quenching steps in the conjugation protocol.



Conclusion: This initial study uses ExoView technology to further characterize PMSC-EVs by adding a new parameter to measure surface modification efficiency. With this efficiency, researchers will be able to determine the degree of conjugation required to see a significant therapeutic effect in vivo. Our future experiments will begin the iterative process to improve surface conjugation while assessing the functional effects of Apt-EVs.

Lalithasri Ramasubramanian

Evaluation of Endothelial Progenitor Cell Plasma Membrane as an Anti-thrombotic and Pro-Angiogenic Biomaterial

Lalithasri Ramasubramanian[1,2,3], Dr. Diana Farmer M.D[1,2], Dr. Aijun Wang PhD[1,2,3]

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Abstract

Introduction: Endothelial progenitor cells (EPCs) are immature precursors to endothelial cells that regulate hemostasis and angiogenesis partially due to their membrane surface proteins. The therapeutic functions of the EPC membrane can potentially be leveraged as a standalone therapy by isolating plasma membrane components and applying it singularly as a new biomaterial. Here we show that isolated EPC membranes retain significant biological activity specific for hemostasis and angiogenesis and can be used as a biomaterial for the design of membranous nanoparticles.

Methods: Plasma membranes were isolated from umbilical cord blood-derived EPCs using differential ultracentrifugation. Tandem mass spectrophotometry was used to characterize the proteomic profile of isolated membranes. Functional properties were evaluated by assessing membrane biological activity for hemostasis. Membrane fractions were synthesized into nanovesicles and characterized for physical and pro-angiogenic properties.

Results: Preliminary proteomic analysis detected the presence of ~2835 proteins in 2245 clusters. AMP production studies showed that CD39, an EPC surface marker that modulates platelet activity, remained biologically active and successfully hydrolyzed ADP into AMP. The membrane fractions were then synthesized into ~100 nm homogenous plasma membrane nanovesicles which remained hydrodynamically stable at physiological conditions for over 15 days. When treated with these vesicles, human umbilical vein endothelial cells (HUVEC) showed an increase in migration and proliferation.

Conclusions: EPC membranes were successfully isolated and shown to retain bioactive proteins that can modulate characteristic hemostatic and angiogenic functions. This presents the opportunity for the use of EPC membrane as a natural biomaterial for the design of drug delivery vehicles that can be tailored for specific therapeutic functions.

Fransia S. De Leon

A Review of Our Center's Renal Allograft Outcomes from Donors After Circulatory Death

Fransia S. De Leon BA[1], Aileen X. Wang MD[2], Kuang-Yu Jen MD[3], Naeem Goussous MD[1], Jacquelyn Yu MD[1], Jennifer Loza BS[1], Neal M. Mineyev MD[1], Junichiro Sageshima MD[1], Richard V. Perez MD[1], Peter A. Than MD[1]

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Abstract

Introduction: Strategies to address the shortage of organs include the use of kidneys from expanded criteria donors (ECD) and donors after circulatory death (DCD). These categories are often under-utilized due to associated complications, such as delayed graft function (DGF) and primary non-function (PNF). Thus, we aim to identify factors that may influence DCD kidney transplantation outcomes, such as rates of DGF and PNF.

Methods: We retrospectively reviewed adult patients (ages ≥18) undergoing kidney transplantation from DCD donors between July 2016 and July 2021. Factors that may contribute to the development of DGF and PNF were examined, including patient demographics, donor terminal creatinine (Cr) > 2.0, warm ischemia time (WIT), cold ischemia time (CIT), kidney donor profile index (KDPI), and use of hypothermic kidney perfusion (kidney pumping). Significance is defined as $p< 0.05$.

Results: 357 adult patients were transplanted with DCD kidneys, 146(40.9%) were female, with a median age of 57(46.0- 65.0). Of these, 6.2% developed PNF and 54.6% developed DGF. No significant differences in recipient age, ethnicity, and gender were found between kidney transplants that resulted in PNF or DGF. A significantly greater proportion of Black patients were found to have DGF (p=0.02) but there was no significant increase in the progression to PNF. WIT, CIT, and KDPI did not differ among patients who developed DGF and PNF. Lack of kidney pumping was significantly associated with increased DGF (p=0.02) (Table 1).

Conclusions: We found no significant donor or recipient characteristics to account for the observed cases of PNF. As our center performs protocol renal allograft time zero biopsies and maintains an archive of histology slides, we plan to examine histologic changes in the DCD allografts that may help to predict kidneys at risk for PNF. Further studies are needed to examine factors that may contribute to the higher rates of DGF in Black patients.

Table 1. Factors that contribute to DGF and PNF in DCD kidney transplantation

		Primary Non-Function			Delayed Graft Function		
		No (n=335)	Yes (n=22)		No (n=162)	Yes (n=195)	
WIT, median(IQR)mm				NS			NS
		24.0(19.0-41.0)	25.0(19.0-41.0)		23.5(18.3-38.5)	25.0(19.8-41.3)	
CIT, median(IQR)hr				NS			NS
		24.6(18.9-31.5)	29.0(23.2-34.3)		24.3(18.6-31.6)	25.2(19.7-32.5)	
KDPI>85%, n(%)				NS			NS
	No	309(92.2)	21(95.5)		152(93.8)	178(91.3)	
	Yes	26(7.8)	1(4.5)		10(6.2)	17(8.7)	
Pumped Kidney				NS			0.02
	No	50(14.9)	3(13.6)		16(9.9)	37(19.0)	
	Yes	285(85.1)	19(86.4)		146 (90.1)	158(81.0)	
Donor Terminal Lab Cr >2.0				NS			NS
	No	314(93.7)	20(90.9)		151(93.2)	183(93.8)	
	Yes	21(6.3)	2(9.1)		11(6.8)	12(6.2)	

Su Yeon Lee

Gender disparity in pediatric surgery: an evaluation of pediatric surgery conference participation

Su Yeon Lee MD, Sirjan Mor MS, Abd-Elrahman Said Hassan MD, Diana Farmer, Erin Brown MD

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Abstract

Intro: In pediatric surgery, women now represent more than half of all fellowship applicants but remain under-represented in academic and leadership positions. Leadership in academic conferences is a factor considered for academic advancement. Underrepresentation of women in academic surgical conferences has been demonstrated in other subspecialties, but it has not been studied in-depth for pediatric surgery.

Methods: This retrospective, descriptive study analyzes conference participation from American Pediatric Surgical Association and American Academy of Pediatrics- Surgery subsection annual conference programs from 2010 to 2021. Moderator, lecturer, panelist, and research presenter sex was collected. The primary outcome measure was proportion of female participants in each role. Mann-Kendall trend test was conducted to assess for significance.

Results: Across 17 meetings, a total of 320 session were examined. Overall, mean women participation in all roles increased from 2010 to 2021. There was a significant increase in proportional female representation in leadership role as moderator (21% to 38%, p=0.01) and a trend towards significance for lecturer or panelist (20% to 34%, p=0.07). Female participation in podium research presentation demonstrated the largest proportional increase over time with 2.7-fold increase (25% to 68%, p=0.02). In 2010, 64% of sessions were moderated by all men with zero female moderators; this decreased to 21% in 2021 (p=0.01).

Conclusion: Gender representation in pediatric surgery conferences has improved over the last decade with significantly fewer sessions with only male moderators. Women now represent the majority of podium research presenters. However, women still only make up 1/3 of leadership roles at these conferences. Further efforts should be made to address increasing leadership opportunities for woman in pediatric surgery academic conferences.

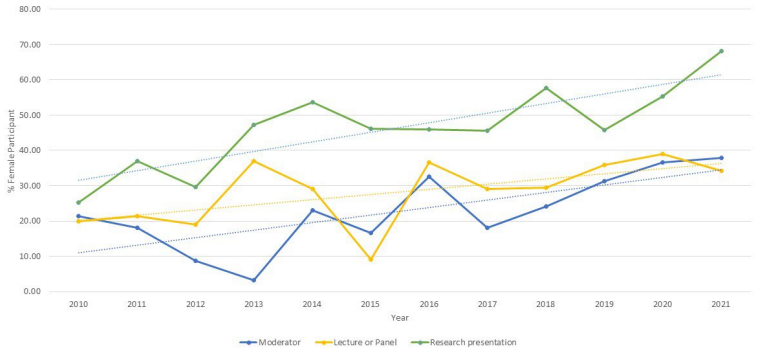

Figure 1. Trends in the proportion of female participants in moderator, lecture or panel, and research presentation roles at pediatric surgery conferences from 2010 to 2021.

Sirjan Mor

Placental Mesenchymal Stem Cells Improve Motor Function in a Rat Unilateral Spinal Cord Contusion Model

Sirjan Mor M.S.[1], Dr. Edwin Kulubya M.D.[2], Mounika Bhaskara M.S.[1], Zachary Paxton B.S.[1], Christopher Pivetti M.S.[1], Dr. Priyadarsini Kumar Ph.D.[1], Samantha Avallone B.S.[1], Dr. Aijun Wang Ph.D.[1], Dr. Diana Farmer M.D.[1]

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Abstract

Introduction: Placental mesenchymal stem cells (PMSCs) are a promising avenue of treatment in spinal cord injury due to their neuroprotective and angiogenic properties. In addition, extracellular vesicles (EVs) released from these stem cells are an attractive cell-free therapeutic approach. Extracellular vesicles are approximately 150 nm vesicles released by placental mesenchymal stem cells that contain the proteins, miRNAs and other cargo of the cells themselves – and are hypothesized to help in spinal cord injury the same way as placental mesenchymal stem cells.

Methods: The *in vivo* studies included injured rats that underwent a laminectomy at C5, followed by a unilateral spinal cord injury (SCI), and uninjured rats that underwent a laminectomy at C5, but did not sustain an SCI. The injured groups were then treated with either an extracellular matrix (ECM) patch alone, an ECM patch with PMSCs or an ECM patch with PMSC-EVs. Motor function tests and histological analysis were used to determine the efficacy of our PMSC and PMSC-EV treatment.

Results: SCI rats treated with PMSCs and PMSC-EVs show *significantly greater* motor recovery compared with SCI rats treated with ECM only. IBB Scoring showed that rats that received 1st trimester PMSC-ECM (P=0.017) and 1st trimester PMSC-EV-ECM (P=0.015) had significantly improved ipsilateral forelimb motor function after injury.

Conclusions: PMSCs and their extracellular vesicles provide a novel therapeutic approach for spinal cord injury and especially improve motor recovery through white matter preservation.

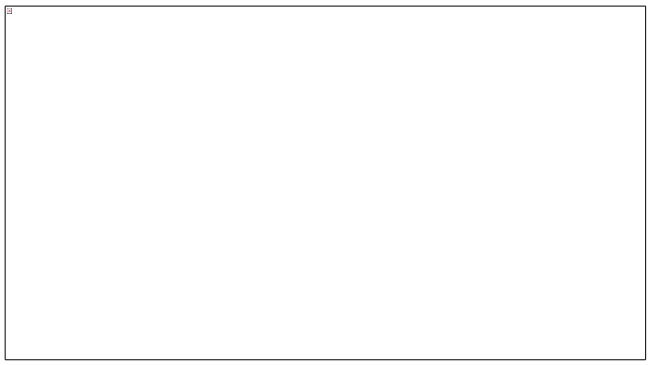

Figure 1: Motor data taken every week, for 8 weeks, using the Irvine, Beatties and Bresnahan (IBB) Forelimb Recovery Scale. Higher scores correlate with better performance. Different colors represent different experimental groups.

Aryana Razmara

Inhaled recombinant human IL-15 in Dogs with Naturally Occurring Pulmonary Metastases from Osteosarcoma or Melanoma: A Phase 1 Study of Clinical Activity and Correlates of Response

Robert Rebhun[1], Daniel York[1], Sylvia Cruz[2], Sean Judge[2], Aryana Razmara[2], Lauren Farley[2], Rachel Brady[3], Eric Johnson[1], Jenna Burton[4], Jennifer Wilcox[1], Luke Wittenburg[1], Kevin Woolard[5], Cordelia Dunai[6], Susan Stewart[7], Ellen Sparger[6], Sita Withers[8], Alicia Gingrich[2], Katherine Skorupski[1], Sami Al-Nadaf[1], Amandine LeJeune[1], William Murphy[6], Michael Kent[1], Robert Canter[2]

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Abstract

Although recombinant human interleukin-15 (rhIL-15) has generated much excitement as an immunotherapeutic agent for cancer, activity in human clinical trials has been modest to date, in part due to the risks of toxicity with significant dose escalation. Since pulmonary metastases are a major site of distant failure in human and dog cancers, we sought to investigate inhaled IL-15 in dogs with naturally occurring lung metastases from osteosarcoma (OSA) or melanoma. We hypothesized a favorable risk/benefit profile given the concentrated delivery to the lungs with decreased systemic exposure. We performed a Phase I trial of inhaled rhIL-15 in dogs with gross pulmonary metastases using a traditional 3+3 cohort design. A starting dose of 10 mg twice daily x 14 days was used based on human, non-human primate, and murine studies. We enrolled 21 dogs with 18 dogs reaching the 28-day response assessment to be evaluable. At dose level 5 (70 mg), we observed 2 DLTs, thereby establishing 50 mg BID x 14 days as the MTD and recommended phase 2 dose. We observed 1 complete response > 1 year, 1 partial response with resolution of multiple target lesions, and 5 stable disease for an overall clinical benefit rate of 39%. Pharmacokinetic analysis revealed detectable and sustained plasma rhIL-15 levels between 1- and 6-hours post-nebulization. Decreased baseline lymphocyte counts prior to treatment were significantly associated with clinical benefit. Cytotoxicity assays of banked peripheral blood mononuclear cells revealed significant increases in peak cytotoxicity against canine melanoma and OSA targets which correlated with overall survival. In this first-in-dog clinical trial of inhaled rhIL-15, we observed promising clinical activity when administered as monotherapy for 14 days. These data have significant clinical and biological implications for both dogs and humans with refractory lung metastases and support exploration of combinatorial therapies using inhaled rhIL-15.

QUICK SHOT PRESENTATIONS

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

MODERATORS
ROBERT CANTER & LUIS GODOY

1. **LAUREN PERRY** - Impact of Pre-existing Psychiatric Disorders on Outcomes after Pancreatic Cancer Surgery

2. **KARA KLEBER** - Inhaled IL-15 post amputation for prevention of pulmonary metastasis in dogs with osteosarcoma with assessment of the gut microbiome as a biomarker of response

3. **JULIA PERSKY** - Characterization of Natural Killer and Cytotoxic T Cell Immune Infiltrates in Pancreatic Ductal Adenocarcinoma

4. **DAKE HAO** - Developing a combinational stem cell-based tissue engineering approach to treat spina bifida before birth

5. **JENNIFER LOZA** - Donor Characteristics Associated with Early Allograft Failure in Deceased Donor Kidney Transplantation

6. **ASHLY RUF** - Dedicated Acute Care Surgery Operating Room: A Race Against the Clock

Lauren Perry

Impact of Pre-existing Psychiatric Disorders on Outcomes after Pancreatic Cancer Surgery

Lauren Perry MD[1], Kara Kleber MD[1], Ganesh Rajasekar MPH[2], Miriam Nuño PhD[2], Richard Bold MD, MBA[1]

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[2]Department of Public Health Sciences, Division of Biostatistics, University of California Davis, Sacramento, CA, USA

Abstract

Introduction: Prior research has indicated that psychiatric illnesses negatively influence outcomes following surgery. Given the substantial morbidity of pancreatic resections, determining whether psychiatric comorbidities are associated with poorer outcomes is valuable for preoperative risk stratification. We hypothesized that patients with pre-existing mood disorders would have worse outcomes after undergoing resection for localized pancreatic cancer.

Methods: We performed a retrospective cohort analysis of patients diagnosed with resectable pancreatic adenocarcinoma from the Surveillance, Epidemiology, & End Results database merged with Medicare data. Patients were classified with a pre-existing mood disorder if they had depressive or anxiety disorder diagnosis or were prescribed any medication used for the treatment these disorders within 6 months before their surgery date.

Results: 208 (16%) of 1,305 patients had a pre-existing mood disorder. Presence of a mood disorder had no impact after pancreatic resection regarding length of stay (12.9 vs. 13.2 days, p=0.75), 30-day complications (26% vs. 22%, p=0.31), 30-day readmissions (26% vs. 21%, p=0.1), 30-mortality (3% vs. 4%, p=0.35), or 90-day mortality (8% vs. 9%, p=0.79); only an increased 90-day readmissions rate (42% vs. 31%, p=0.001) was observed. No effect on adjuvant chemotherapy receipt (62.5% vs. 69.2%, p=0.06) or survival (24-months, 43% vs. 39%, p=0.44) was observed.

Conclusion: In this analysis, pre-existing mood disorders influenced 90-day readmissions after pancreatic resection, but not other postoperative or oncologic outcomes. These findings suggest that patients with pre-existing mood disorders should be offered appropriate treatment for early-stage pancreatic cancer and be expected to have outcomes similar to patients without mood disorders.

Kara Kleber

Inhaled IL-15 post amputation for prevention of pulmonary metastasis in dogs with osteosarcoma with assessment of the gut microbiome as a biomarker of response

Kara Kleber[1], Aryana Razmara[2], Sean Judge[1], Lauren Farley[1], Khurshid Iranpur[1], Ryan Nielsen[1], Michael Kent[2,1], Robert Rebhun DVM[1,2], Robert Canter MD[1]

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Abstract

Background: In a phase I trial of dogs with pulmonary osteosarcoma (OSA) metastases, we have shown a response rate of 11% and a clinical benefit rate of 37% following inhaled (IH) IL-15. Therefore, we sought to determine the clinical benefit of adjuvant IH IL-15 in combination with standard therapy for localized disease. Given advances in human medicine using gut microbiome as a predictor of treatment response, we sought to evaluate canine gut microbiome with outcomes.

Methods: We prospectively enrolled dogs with OSA undergoing amputation and chemotherapy for non-metastatic disease in a phase II trial. Subjects received 2 weeks of IH rhIL-15 post amputation and pre-chemotherapy. Prospective stool and tissue samples were collected and microbiome data analyzed with respect to clinical response. Our primary endpoint was the proportion of dogs without progression at 15 weeks post amputation, hypothesizing a reduction in the risk of metastasis formation from 40% to 20% using IH IL-15. Secondary outcomes were survival, evidence of immune response, and microbiome diversity, abundance, and composition.

Results: Over 8 months, we have enrolled 18 dogs of a planned 40, 17 or which completed immunotherapy with no adverse events reported. Preliminary clinical outcomes data are encouraging, suggesting a reduction in metastasis formation with respect to historical controls. Among subjects, 21 stool samples have been collected from 7 patients before, during, and after IL-15 and from 7 controls. DNA recovery from microbiome samples was 57±12.7 ng/mL for stool, and 48.5±11.2 for tumor. Post IL-15 stool samples showed decreased DNA yields (44.9±19.3 ng/mL) which was not statistically significant (P=0.82). DNA sequencing and bioinformatic analysis are ongoing.

Conclusion: Preliminary data suggest a favorable effect of adjuvant IH IL-15 in dogs with OSA undergoing amputation and chemotherapy. Novel microbiome studies may yield insights into biomarkers of response and resistance.

Julia Persky

Characterization of Natural Killer and Cytotoxic T Cell Immune Infiltrates in Pancreatic Ductal Adenocarcinoma

Julia Persky BS[1,2], Sylvia M Cruz BS[1,2], Sean J Judge MD[2], Cyrus J Sholevar MD[2], Sepideh Gholami MD[2], Richard J Bold MD[2], Anthony N Karnezis MD, PhD[3], Karen E Matsukuma MD, PhD[3], Morgan A Darrow MD[3], Robert J Canter MD[2]

[1]University of California Davis School of Medicine, Sacramento, CA, USA. [2]Division of Surgical Oncology, Department of Surgery, University of California Davis, Sacramento, CA, USA. [3]Pathology and Laboratory Medicine, University of California Davis, Sacramento, CA, USA

Abstract

Background: Pancreatic ductal adenocarcinoma (PDAC) is characterized by a poor prognosis and resistance to systemic therapies including immunotherapy. Although PDAC has been linked to low T cell infiltrates, the contribution of natural killer (NK) cells has received less attention. Our objective was to evaluate immune parameters in PDAC, including NK cells, to determine if NK cells associate with patient outcomes.

Methods: We analyzed tumors from 93 PDAC patients treated from 2012–2020. Predictor variables included tumor infiltrating lymphocytes (TILs), T cell markers (CD3, CD8, CD45RO), NK markers (NKp46), and NK inhibitory markers (TIGIT and MHC-I). TILs were scored from 0-3, and immune markers were scored from 0-300. Primary outcome variables were metastasis-free survival (MFS) and overall survival (OS).

Results: Mean age was 70, 55% were female, and mean tumor size was 3.1±1.1cm. 89% involved the pancreatic head, and 63% were lymph node positive. The majority of patients received adjuvant therapy. With a median follow up of 24 months, median survival was 35 months. Median TIL infiltration was 1.1, and 50% were 0 or 1. Mean CD3 score was 20.6±17.4, and mean NKp46 score was 3.1±3.9. Although there was strong positive correlation between T cell and NK cell scores (CD3/NKp46 $P=0.005$, $r=0.3$; CD45RO/NKp46 $P<0.0001$, $r=0.7$), neither T nor NK cell infiltration were associated with MFS or OS. Similarly, there was a tight positive correlation between MHC-I expression and all T cell markers (CD3, CD8 and CD45RO+), but not with NKp46 nor with survival outcomes (MFS/OS, $P>0.05$). TIGIT expression was also low (mean 30.8±21.9).

Conclusion: NK and T cell infiltrates are overall low in PDAC and do not associate with oncologic outcomes. Further characterization of the immune infiltrate in PDAC, including inhibitory signals and suppressive cell types, may yield better biomarkers of prognosis and immune targeting in this refractory disease.

Dake Hao

Developing a combinational stem cell-based tissue engineering approach to treat spina bifida before birth

Dake Hao PHD[1], Christopher Pivetti MS[1], Su Yeon Lee MD[1], Robert Gresham BS[2], Abd-Elrahman Hassan MD[1], Priyadarsini Kumar PHD[1], Edwin Kulubya MD[1], Jordan Jackson MD[1], Juan-Maria Lopez BS[1], Rodrigo Somoza PHD[3], Arnold Caplan PHD[3], Kent Leach PHD[2], Diana Farmer MD[1], Aijun Wang PHD[1]

[1]Center for Surgical Bioengineering, University of California, Davis, Sacramento, CA, USA. [2]Department of Orthopaedic Surgery, University of California, Davis, Sacramento, CA, USA. [3]Department of Biology, Case Western Reserve University, Cleveland, OH, USA

Abstract

Introduction: Previously, we demonstrated in utero treatment with placenta-mesenchymal stem cells (PMSCs) prevented hind limb paralysis at birth in the fetal sheep spina bifida (SB) model via a neuroprotection mechanism. However, the observed motor recovery appears to be transient, with motor function decreasing over time. We found they developed severe kyphosis and adjacent spinal cord compression due to the lack of bone. Thus, we proposed to develop a combinational bioengineered scaffold will protect neurons in the spinal cord and provide structural support to the spine and mechanical protection to its underlying fragile spinal cord.

Methods: The PMSCs were isolated and characterized by using flow cytometry, ELISA, neuroprotective assay and histological analysis. Endochondral bone formation of PMSC-seeded scaffolds were evaluated by using lentiviral transduction, In Vivo Imaging System (IVIS), micro-CT and histological analysis. The combinational bioengineered scaffold was constructed with a neuroprotective layer and a bone regenerative layer. The sheep motor function was evaluated by using the Sheep Locomotor Rating (SLR) scale.

Results: We obtained a thousand million PMSCs from 30 mg placental villus tissue within 21 days, and the PMSCs possessed strong neuroprotective, chondrogenic and osteogenic capacities. The PMSC-seeded scaffold showed strong endochondral bone formation in a mouse subcutaneous model and a fetal sheep spinal bone defect model. The combinational bioengineered scaffold could restore the normal motor function of the SB sheep and maintain it for longer compared to the motor function of the SB sheep treated with our previous single neuroprotective approach.

Conclusion: This novel combinational treatment approach will protect neural tissue and regenerate bone to preserve locomotor recovery in the long term, which will open the door to a new therapeutic option for SB and other neurodegenerative disorders, bone disorders and spinal cord injury.

Jennifer Loza

Donor Characteristics Associated with Early Allograft Failure in Deceased Donor Kidney Transplantation

Jennifer Loza BS[1], Jacquelyn Yu MD[2], Junichiro Sageshima MD[1], Peter Than MD[1], Naeem Goussous MD[1], Neal Mineyev MD[1], Richard Perez MD[1]

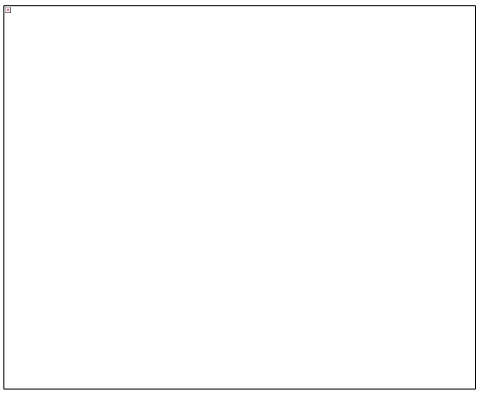
[1]UC Davis, Transplant Surgery, Sacramento, CA, USA. [2]UC Davis, General Surgery, Sacramento, CA, USA

Abstract

Introduction: While certain donor characteristics from deceased donor kidney transplantation are known to be predictive of delayed graft function (DGF), it is unclear whether these same characteristics are associated with early allograft failure (EAF). In this study, we analyze donor characteristics associated with DGF to determine their associations with EAF.

Methods: We reviewed recipient outcomes and donor characteristics of single kidney transplantation from deceased donors at our institution from January 2005 through April 2021. Recipients of previous or multiple organ transplantation were excluded. Univariate analysis of donor characteristics using chi-square and Student's *t*-test was performed for the primary endpoint of EAF within 90 days of transplantation.

Results: During this period, 2429 patients with a median (range) age of 56 years (11 months-82 years) received single kidney transplantation from deceased donors. Of this cohort, 76 patients had EAF. There were no patient deaths with a functioning allograft within 90 days of transplantation. We found that increased donor age, Kidney Donor Risk Index (KDRI), and cold ischemia time (CIT), as well as kidneys recovered after circulatory death (DCD), and a donor history of hypertension or diabetes were significantly associated with EAF. However, donor sex, weight, height, terminal serum creatinine, BUN, and use of machine perfusion were not significantly associated with EAF (Table 1).



Conclusion: This study identified unmodifiable donor characteristics associated with EAF, suggesting changes in donor selection may impact the rate of EAF. Minimizing CIT duration, the only modifiable risk factor associated with EAF, may offer an opportunity to decrease the rate of EAF in the future.

Ashly Ruf

Dedicated Acute Care Surgery Operating Room: A Race Against the Clock

Dr Ashly C Ruf MD, Dr Lauren E Coleman MD, Dr Elan A Sherazee MD, Dr Nicholas F Antonino MD, Dr. Rachael A Callcut MD, MSPH, FACS, Dr. Scott A Zakaluzny MD FACS

University of California-Davis, Sacramento, CA, USA

Abstract

Objective: Assess the impact a dedicated Acute Care Surgery (ACS) operating room has on time to operation, length-of-stay, and overnight cases through a Simulated Operating Room (SOR) Model.

Background: Timing of ACS cases is critical to reduce morbidity and optimize patient flow. However, there is little data to show how dedicated operating rooms for urgent cases effect OR wait times

Methods: ACS Patients requiring urgent surgery at a tertiary-referral-center from February-to-June 2021 were tracked in real-time as part of a quality improvement project. We applied real time operative case length data into a SOR Model allowing for only one case to occupy the SOR at a time. Real time and SOR OR wait times, lengths-of-stay, afterhours operations, and surgeries starting within booking priority target windows; were compared.

Results: 310 patients met inclusion criteria. Using the SOR, there was a decrease in time to operation from 18.2hrs to 9.1hrs ($p<0.05$) for all ACS cases including cholecystectomies (23hrs to 9hrs), appendectomy (8hrs to 5hrs), and incision and drainages (11hrs to 6hrs), all $p<0.05$. When assessing subgroups, patients with surgical case request requiring urgent intervention within 12hrs and 24hrs priority were more reliably able to start their procedures within their target windows (16hrs vs 8hrs and 31hrs vs 13hrs, respectively; $p<0.05$). Additionally, afterhours operations decreased from 165 to 91 ($p<0.05$). Length-of-stay was shorter, but not statistically significant (248hrs vs 238hrs; $p>0.05$).

Conclusion: A dedicated operating room for ACS patients, as demonstrated by a SOR Model, reduces the time to operation, afterhours cases, improves patient throughput and OR metrics.

ORAL PRESENTATIONS

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

MODERATORS
TINA PALMIERI & BETHANY CUMMINGS

1. **DAKE HAO -** Engineered extracellular vesicles with high collagen-binding affinity present superior in situ retention and therapeutic efficacy in tissue repair

2. **CHRISTINA THEODOROU -** Evaluation of a Novel Biodegradable Polyurethane Patch for Repair of Diaphragmatic Hernia in a Rat Model: A Pilot Study

3. **LAUREN PERRY -** Patients with Soft Tissue Sarcomas Harbor an Intratumoral Microbiome Which is Linked with Immune Infiltrate and Prognosis

4. **DAVID WALLACE -** Poverty and Frailty in Patients with Burn Injuries: Important but Unrelated

5. **JEAN DEBÉDAT -** Cyclopropane fatty acids are bacteria-derived xenolipids displaying binding affinities toward peroxisome proliferator activated receptors α, δ, and γ

6. **CYRUS SHOLEVAR -** Tissue resident lung natural killer (NK) cells demonstrate enhanced responses to IL-15 compared to peripheral populations

Dake Hao

Engineered extracellular vesicles with high collagen-binding affinity present superior in situ retention and therapeutic efficacy in tissue repair

Dake Hao PHD[1], Lu Lu PHD[1], Hengyue Song MD[1], Yixin Duan PHD[2], Jianing Chen BS[1], Randy Carney PHD[3], Jian-Jian Li PHD[2], Ping Zhou PHD[4], Jan Nolta PHD[4], Kit Lam PHD, MD[5], Kent Leach PHD[6], Diana Farmer MD[1], Alyssa Panitch PHD[3], Aijun Wang PHD[1]

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Abstract

Introduction: Although stem cell-derived extracellular vesicles (EVs) have remarkable therapeutic potential for numerous diseases, the therapeutic efficacy of EVs is hindered by their poor retention and short half-life after transplantation. Here, we developed a new generation of collagen-binding EVs (SILY-EVs) by covalently conjugating a collagen-binding peptide SILY to EVs, which were proposed to bind to collagen backbone of the extracellular matrix (ECM) to form the EV-ECM complex to prolong their in situ retention and therapeutic efficacy after transplantation.

Methods: SILY was conjugated to the surface of mesenchymal stem cell (MSC)-derived EVs by using click chemistry to construct SILY-EVs. Nanoparticle tracking analysis (NTA) and transmission electron microscopy (TEM) were used to characterize the SILY-EVs. Fluorescence imaging (FLI), MTS assay, ELISA assay and real-time polymerase chain reaction (RT-PCR) were used to evaluate the collagen binding and biological functions of SILY-EVs in vitro. In a mouse hind limb ischemia model, the In Vivo Imaging System (IVIS), laser doppler perfusion imaging (LDPI), micro-CT and FLI were used to determine the SILY-EV retention, blood perfusion and tissue regeneration.

Results: In vitro, the SILY conjugation significantly enhanced EV adhesion on collagen surface and maintained the EVs' biological functions. In the mouse hind limb ischemia model, SILY-EVs achieved longer retention, inhibited inflammatory response, and significantly augmented muscle regeneration and revascularization compared to the unmodified EVs.

Conclusion: With the advance of enriched resource of collagen in all human tissue and organs, the SILY-EVs hold promise to promote the therapeutic efficacy of EV-mediated treatment in a wide range of clinical diseases. Moreover, the SILY-EVs possess superior potential for functionalizing collagen-based biomaterials and delivering therapeutic agents in regenerative medicine.

Christina Theodorou

Evaluation of a Novel Biodegradable Polyurethane Patch for Repair of Diaphragmatic Hernia in a Rat Model: A Pilot Study

Christina Theodorou[1], Alan Taylor[2], Su Yeon Lee[1], Huikang Fu[2], Christopher Pivetti[1], Chaoxing Zhang[1], Anastasiya Stasyuk[1], Dake Hao[1], Priyadarsini Kumar[1], Diana Farmer[1], Jun Liao[2], Erin Brown[1], Yi Hong[2], Aijun Wang[1]

[1]UC Davis Medical Center. [2]Department of Bioengineering, UT Texas at Arlington

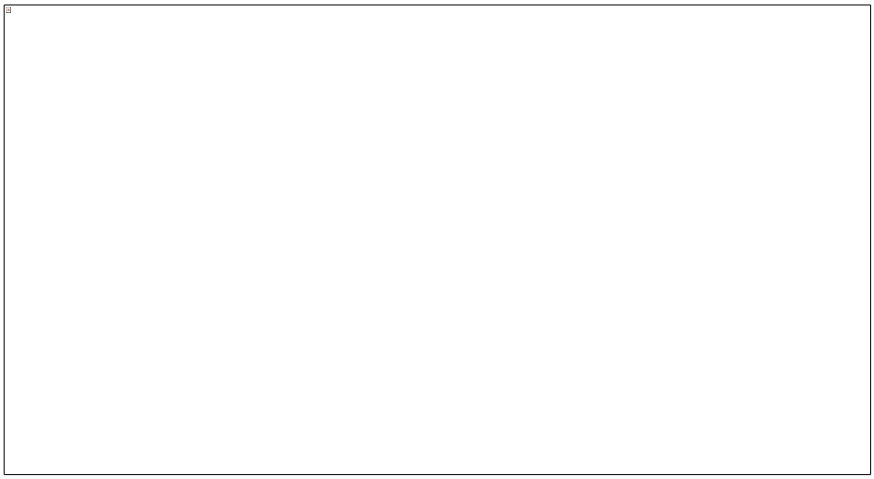
Abstract

Introduction: Congenital diaphragmatic hernia (CDH) repair is an area of active research. Large defects requiring patches have a recurrence rate of up to 50%. We designed a novel biodegradable polyurethane (PU)-based elastic patch that matches the mechanical properties of native diaphragm muscle. We compared the PU patch to a non-biodegradable Gore-Tex (polytetrafluoroethylene) patch.

Methods: A nanofibrous PU patch was synthesized from polycaprolactone, hexadiisocyanate and putrescine by electrospinning. Rats underwent 4mm diaphragmatic hernia (DH) creation via laparotomy followed by immediate repair with Gore-Tex (n=6) or novel PU (n=6) patches. Six rats underwent sham laparotomy without DH creation/repair. Diaphragm function was evaluated by fluoroscopy at 1 and 4 weeks. At 4 weeks, animals underwent gross inspection for recurrence and histologic evaluation for inflammatory reaction.

Results: There were no recurrences. Gore-Tex had limited diaphragm rise compared to sham at 4 weeks (1.2mm vs 2.8mm, p=0.004), but no difference was found between PU and sham (1.8mm vs 2.8mm, p=0.14). There were no differences between PU and Gore-Tex at any time point. PU had thicker granulation tissue around the patch on the thoracic side compared to Gore-Tex (0.65mm vs 0.36mm, p=0.004). However, there was no difference on the abdominal side (0.36mm PU vs 0.13mm Gore-Tex, p=0.08).

Conclusion: The novel PU patch allowed for greater diaphragmatic excursion compared to Gore-Tex. There was increased inflammation with PU. Further work is needed to evaluate long-term functional outcomes and further optimize the properties of the novel PU patch in vitro and in vivo.



Lauren Perry

Patients with Soft Tissue Sarcomas Harbor an Intratumoral Microbiome Which is Linked with Immune Infiltrate and Prognosis

Lauren Perry MD[1], Kara Kleber MD[1], Sylvia Cruz BS[1], Sean Judge MD[1], Morgan Darrow MD[2], Louis Jones MD[3], Ugur Basmaci BS[1], Nikhil Joshi PhD[4], Matthew Settles PhD[4], Blythe Durbin-Johnson PhD[4], Alicia Gingrich MD[1], Arta Monjazeb MD[5], Janai Carr-Ascher MD[6], Steven Thorpe MD[7], William Murphy PhD[8], Jonathan Eisen PhD[9], Robert Canter MD[1]

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Abstract

Introduction: Groundbreaking studies have linked the gut microbiome with anti-tumor immune responses, and mounting evidence has demonstrated intratumoral microbiomes, including in soft tissue sarcomas (STS). We sought to characterize the intratumoral and gut microbiome in STS patients undergoing preoperative radiotherapy (RT) and surgery, hypothesizing the presence of a distinct intratumoral microbiome with potentially clinically significant microbial signatures.

Methods: We prospectively obtained tumor and stool samples from adult patients with non-metastatic STS using a strict sterile collection protocol to minimize contamination. Metagenomic classification was used to estimate abundance using genus and species taxonomic levels across all classified organisms, and data were analyzed with respect to clinicopathologic factors.

Results: Fifteen patients were enrolled. Four (27%) patients developed metastases, and 3 (20%) died from disease progression. Despite overwhelming human DNA (>99%) intratumorally, we detected a small, consistent proportion of bacterial DNA (0.02-0.03%) in all tumors. In patients with metastases, *Piscirickettsia* (P=0.002) and *Respirovirus* (P=0.04) were differentially abundant in the pre-RT tumor microbiome. Most DNA from stool samples was represented by bacterial DNA (>50%). Notably, one patient's tumor microbiome exhibited a greater relative abundance of viral DNA (>90%) at both time points compared to all other patients. Metagenomic analysis demonstrated exclusivity of human herpesvirus 6B in the patient's tumor, with enrichment of NK cells in the TME (>50% of immune infiltrate).

Conclusion: We prospectively demonstrate the presence of a measurable intratumoral microbiome in STS patients at multiple time points. Our data suggest that the STS tumor microbiome at diagnosis has prognostic significance which does not clearly link with the gut microbiome. Additional studies are warranted to further assess the clinical impact of these findings.

David Wallace

Poverty and Frailty in Patients with Burn Injuries: Important but Unrelated

Dr David Wallace MD MSc FRCSC, Ms Ketura Sloan RN AG-ACNP, Ms Deborah Williams RN BSN, Dr Jason Heard MD, Dr David Greenhalgh MD FACS, Dr Tina Palmieri MD FACS FCCM, Dr Soman Sen MD FACS, Dr Kathleen Romanowski MD FACS

UC Davis, Sacramento, CA, USA

Abstract

Purpose: The purpose of this study was to determine the relationship of frailty and poverty in burn patients and their association with patient outcomes.

Methods: A retrospective chart review from 2009-2018 of patients >50 years admitted to an ABA verified burn center with acute burn injuries was completed. Standard clinical variables were collected. Frailty scores were assigned using the Canadian Study of Health and Aging Clinical Frailty Scale (scored 1-7). Frailty was dichotomized with scores >5 being frail. Poverty data were obtained using zip / US census data. Poverty level was categorized according to whether a patient came from a zip code that had >20% of people living in poverty. Univariate and multivariate analyses examined the relationship between frailty and poverty, as well as each variable independently on mortality and length of stay (LOS).

Results: 953 patients were included. Mean frailty score was 3.8 and mean poverty was 17.3. The overall mortality rate was 8.8%. Univariate analysis showed non-survivors had significantly higher chances of living in poverty (p=0.02), and were more likely to have frailty scores of 5 or greater compared to survivors. There was no significant correlation between poverty and frailty (p=0.08).Multivariate logistic regression confirmed relationship between poverty and mortality (OR 0.47 95% CI 0.25-0.89) and frailty and mortality (OR 2.9 95%CI 1.4-5.8). It also demonstrated that the combined variable of frailty and poverty was not significantly associated with mortality (Wald $\chi 2$ 2.0, p=0.15). Neither poverty (p=0.26) nor frailty (p=0.52) were associated with LOS. Both poverty and frailty were associated with a patient's disposition destination (p=0.03; p<0.0001).

Conclusion: Poverty and frailty each independently predict mortality and discharge destination in burn patients >50, but they are not associated with LOS, and do not show a significant association with each other, nor a combined effect on mortality.

Jean Debédat

Cyclopropane fatty acids are bacteria-derived xenolipids displaying binding affinities toward peroxisome proliferator activated receptors α, δ, and γ

Dr Jean Debedat PharmD/PhD, Dr Trina Knotts PhD, Dr Sean Adams PhD

Center for Alimentary and Metabolic Sciences (CAMS), Department of Surgery, University of California Davis, Sacramento, CA, USA

Abstract

Gut bacteria produce a myriad of molecules daily, many of which can affect the host's physiology. An example of bacteria-derived "xenometabolites" are cyclopropane fatty acids (CpFA) in which bacterial enzymes introduce a cyclopropane ring into the backbone of unsaturated fatty acids (FAs). CpFAs, such as lactobacillic and dihydrosterculic acids, have been identified in food items as well as in human adipose, serum, and liver. We recently discovered two novel CpFAs that are the precursors of the most abundant plasma medium-chain acylcarnitine in humans, supporting the idea that CpFAs are naturally occurring components of the human lipidome like "classic" FAs, although little is known about their bioactivities. The presence of the methylene bridge(s) in CpFAs structurally induces a bend similar to unsaturated FAs, suggesting that CpFAs might bind PPAR α, γ, and δ nuclear receptors that are critical to metabolic regulation in liver, adipose and elsewhere. Using molecular modeling methods in silico (Maestro-Schrödinger), we demonstrated that the CpFAs display significant binding potential to all three PPARs, with binding energies similar to those of PPAR-selective ligands (fenofibrate, rosiglitazone). These results are consistent with a recent paper demonstrating that lactobacillic acid binds PPARγ. Furthermore, it was reported that the treatment of hepatocytes and adipocytes with a C17 CpFA resulted in the up-and down-regulation of metabolism genes in a pattern consistent with PPARγ antagonism. As such, this in silico study and the extant literature support the idea that CpFAs can target PPARs and thus serve as metabolically-relevant signals from the gut microbiota. We are currently performing dedicated binding and reporter assays to confirm, as well as in vitro bioactivity studies. Our work suggests that "non-self" xenolipids impact important components of the host physiology (inflammation, metabolism) and could be interesting targets of dedicated interventions.

Cyrus Sholevar

Tissue resident lung natural killer (NK) cells demonstrate enhanced responses to IL-15 compared to peripheral populations

Cyrus Sholevar[1], Sean Judge[1], Ryan Nielsen[1], Lauren Farley[1], Khurshid Iranpur[1], Cordelia Dunai[2], Aryana Razmara[3], Morgan Darrow[4], David Cooke[5], Erin Brown[6], Robert Rebhun[3], William Murphy[7], Robert Canter[1]

[1]University of California Davis, Surgical Oncology. [2]University of Liverpool. [3]University of California Davis, Veterinary Medicine. [4]University of California Davis, Department of Pathology. [5]University of California Davis, Division of General Thoracic Surgery. [6]University of California Davis, Division of Pediatric Surgery. [7]University of California Davis, Hematology/Oncology

Abstract

In dogs with osteosarcoma pulmonary metastases, we have demonstrated that inhaled interleukin 15 (rhIL-15), a cytokine that activates lung natural killer (NK) cells, is associated with a clinical benefit of 37% suggesting that lung NK cells can be targeted for anti-tumor effects. Thus, we set out to evaluate the phenotype and function of resting and rhIL-15-stimulated lung NK cells using murine and human models.

We isolated spleen, liver, and lung NK cells from C57BL/6 and BALB/C mice for in vitro assessment of NK cell phenotype, function, and apoptosis with and without rhIL-15. In vivo, we exposed mice to increasing doses of rhIL-15, measuring proliferation, cytotoxicity, and apoptosis of splenic, liver, and lung NK cells. Human blood and non-tumor lung specimens were obtained from patients, and NK cells were analyzed before and after short term rhIL-15 co-culture for phenotype and function.

Compared to mouse spleen and human blood, there was a higher proportion of NK cells in baseline mouse (2.5 fold higher, $P<0.05$) and a trend in human (1.25 fold higher, $P=0.08$) lung samples. Lung NK cells had higher expression of activation markers CD69 (mouse, human) and HLA-DR (human), but lower expression of the inhibitory receptor TIGIT. Co-culture with rhIL-15 resulted in greater upregulation of Ki67 on lung NK cells in both mouse and human ($P<0.05$). In murine models, rhIL-15 resulted in upregulation of Ki67 and lower upregulation of TIGIT in lung NK cells compared to spleen NK. Subset analysis of tissue resident CD49a+ lung NK cells showed similar results in both species. After co-culture with rhIL-15, human lung NK cells showed greater activation and proliferation and lower apoptosis than blood NK cells.

Taken together, our results suggest that lung NK cells harbor a more active baseline phenotype and preferential stimulation after rhIL-15 compared to circulating NK cells. Targeting of lung NK cells may be a viable therapeutic strategy in patients with lung metastases.

ORAL PRESENTATIONS

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

MODERATORS
VICTORIA LYO & JONATHAN KOHLER

1. **JACQUELYN YU -** Lipid Metabolism Profile Of Human Kidneys During Ex Vivo Normothermic Perfusion

2. **RAFAEL LOZANO -** External Validation of the TEMPT Score as a Predictor of Blood Transfusion

3. **ELAN SHERAZEE -** Review of Graft Patency in Robotically Assisted Coronary Artery Bypass and Totally Endoscopic Coronary Bypass Surgery

4. **NICOLE MOORE -** The Impact of Bariatric Surgery on the Development of Exocrine Pancreatic Insufficiency

5. **CARA POZOLO -** Improved Follow-Up After Hospital Discharge Does Not Impact 30-Day Readmissions After Vascular Procedures

6. **ANAMARIA ROBLES –** The Chicken or The Egg: Correlation Of Low Platelets & Post-Injury Acute Respiratory Distress Syndrome

Jacquelyn Yu

Lipid Metabolism Profile Of Human Kidneys During *Ex Vivo* Normothermic Perfusion

Jacquelyn Yu MD[1], Ivonne Palma BS[2], Sean Adams PhD[3], Junichiro Sageshima MD[2], Peter Than MD[2], Richard Perez MD[2]

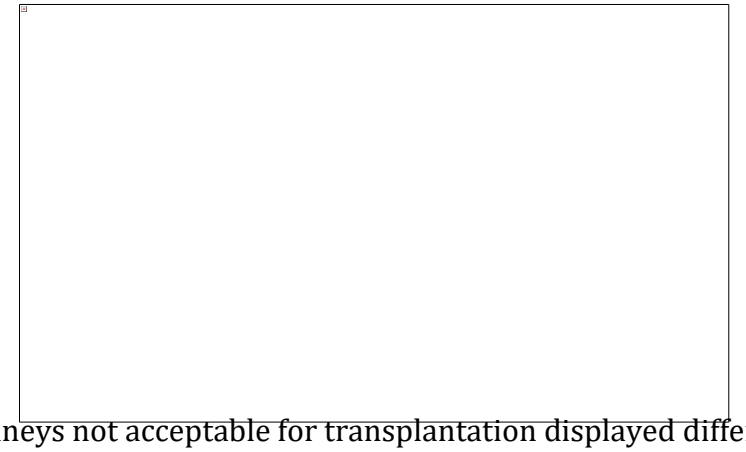
[1]UC Davis, General Surgery, Sacramento, CA, USA. [2]UC Davis, Transplant Surgery, Sacramento, CA, USA. [3]UC Davis, Center for Alimentary and Metabolic Science, Sacramento, CA, USA

Abstract

Introduction: The kidney is a highly metabolic organ and lipids are an important energy source. In this study, we examined the lipid profiles of discarded human kidneys placed on *ex vivo* normothermic perfusion (EVNP) to discern trends in lipid metabolites and associations with renal function.

Methods: Eight human kidneys deemed unsuitable for transplantation were placed on EVNP with oxygenated packed red blood cells for 12 hours. Markers of kidney perfusion, function and injury were monitored, and kidney cortex tissue samples were obtained for lipid metabolomics analysis.

Results: Two groups emerged with 4 kidneys termed “good performers” and the other 4 kidneys termed “poor performers", where the former group compared to the latter had higher urine output and renal flow, and lower resistance and urinary neutrophil gelatinase-associated lipocalin. The good performers had lower initial triglyceride (TG) levels that slightly increased in the first 30 minutes of EVNP, followed by a large increase up to 8 hours. The poor performers had higher initial TG levels with an early decrease followed by a gradual increase (Figure). Overall, TGs decreased while long-chain acylcarnitines increased in the first 30 minutes, which may represent early TG mobilization to yield fatty acids and in turn, acylcarnitines. In addition, the good performers had lower initial ceramide levels followed by a decrease in the first 30 minutes, while poor performers demonstrated the opposite. As ceramides are a metabolite implicated in mitochondrial dysfunction, this may suggest that the poor performers had markers of increased cellular toxicity.



Conclusion: High-risk kidneys not acceptable for transplantation displayed different levels of function on EVNP coincident with alterations in tissue lipid profiles. Our findings suggest that kidneys destined to perform poorly on EVNP have higher baseline triglycerides and ceramides, which may be indicative of abnormal fat metabolism in the tissue.

Rafael Lozano

External Validation of the TEMPT Score as a Predictor of Blood Transfusion

Dr Rafael Lozano MD[1], Leonardo Graeff[2], Dr Anamaria Robles MD[1], Richa Kalamdani[2], Ashli Barnes[2], Jason Li[2], Haradeen Dhillon[2], Dr Anthony Calabro Ph.D[2], Randi Mcnulty[2], Dr Lucy Kornblith MD[3], Dr Rachael Callcut MD, MPH[1]

[1]UC Davis Medical Center, General Surgery, Sacramento, CA, USA. [2]UC Davis Medical Center, Trauma Research, Sacramento, CA, USA. [3]UC San Francisco, General Surgery, San Francisco, CA, USA

Abstract

Introduction: Most prediction tools for transfusion rely on total anatomic injury burden. This limits their utility for early activation of massive transfusion protocols in the setting of occult injury. TEMPT (Trauma Early Mortality Prediction Tool) was created as an abbreviated injury score (AIS) independent tool for emergency department (ED) use. External validation of prediction tools is the gold standard, and this study is the first external validation of TEMPT for prediction of transfusion of red blood cell (RBC) transfusion.

Methods: A prospective cohort of high-level trauma activations aged>=18 years old were enrolled in the Precision Approaches to Resuscitation in Trauma (PART III) study if a blood sample was obtained with intravenous access on presentation. The enrolling center did not participate in the original TEMPT study, representing a validation site. Demographics, injury characteristics, labs, transfusion data, and outcomes were collected. A TEMPT score (0 to 6) was calculated for each patient using the initial ED value for each component (presence of TBI, age>=59.5 years, base excess>=-4.35, partial thromboplastin time (PTT)>=31.5, INR>=1.25, temperature<=36.25 degrees Celsius). Multiple logistic regression was performed with R statistical package for predictors of RBC transfusion.

Results: From March 21-Feb 22, 102 patients were enrolled. Median age was 44 (IQR 30-61), 82% were male, 68% suffered blunt trauma, 30% had an ISS>15, and 53% required ICU admission. RBC transfusion occurred in 32% of the cohort, 88% (n=29/33) receiving RBCs in the first 6 hours. TEMPT scores ranged from 0 to 5 with no patient having a positive value for all 6 components. TEMPT was a strong predictor of RBC transfusion, increasing probability of RBC transfusion for each score point (p=0.009, Figure).

Conclusion: TEMPT is an easy-to-use tool for early identification of patients likely to need PRBC transfusion and is independent of the need for an AIS.

Elan Sherazee

Review of Graft Patency in Robotically Assisted Coronary Artery Bypass and Totally Endoscopic Coronary Bypass Surgery

Elan Sherazee MD, Timothy Guenther MD, Bob Kiaii MD

UC Davis

Abstract

Introduction: Robotically assisted coronary artery bypass grafting surgery (RACABG) avoids the morbidities of a sternotomy and cardiopulmonary bypass and is becoming increasingly popular. Robotically assisted minimally invasive direct CABG (RMIDCAB) and totally endoscopic CABG (TECAB) have been shown to have similar patency rates compared to conventional CABG (Left internal mammary artery patency: 98%, 95%, 88% at 5, 10 and 15 years, respectively). A systematic review was performed to evaluate graft patency and clinical outcomes in patients who underwent RACABG.

Methods: A systematic review of studies reporting graft patency after RACABG was performed using PubMed, Google Scholar, and Embase.

Results: Between June 1998 and August 2018, 4,344 patients underwent RACABG, either by RMIDCAB (2,662) or TECAB (1,682) approach. Both cohorts were evaluated with post operative CTA or angiogram at similar rates (TECAB 70% vs RMIDCAB 69%). The average graft patency at short- (<1 month), mid- (<5 years) and long-term (≥5 years) follow up was 97.6%, 95.3% and 94.2% for RMIDCAB, respectively and 98%, 95.6% and 93.7% for TECAB, respectively. Rates of 30-day mortality, conversion to sternotomy and post op reintervention for an occluded graft were 0.3%, 1.5% and 1.6%, respectively.

Conclusion: RACABG has comparable patency rates to conventional CABG with a low rate of reintervention. Short term patency rates are well documented in the literature; however, there are only a few studies reporting on the mid- and long-term outcomes. Although the initial data is very encouraging, further investigation is warranted to further assess this minimally invasive technique for surgical coronary artery revascularization.

Nicole Moore

The Impact of Bariatric Surgery on the Development of Exocrine Pancreatic Insufficiency

Dr. Nicole Moore MD[1], Ms. Alexis Chirco[2], Dr. Trevor Plescia MD[1], Ms. Barbara Jachniewicz NP[1], Dr. Mohamed Ali MD[1], Dr. Victoria Lyo MD, MTM[1]

[1]UC Davis Medical Center, Sacramento, CA, USA. [2]UC Davis, Sacramento, CA, USA

Abstract

Introduction: Gastrointestinal symptoms such as diarrhea, bloating, abdominal pain, and nausea are common after bariatric surgery (BS) and can lead to a significant morbidity. Exocrine pancreatic insufficiency (EPI), infection, medication side effect, dumping syndrome, and bacterial overgrowth can all lead to such symptoms. The frequency and outcomes of EPI after BS are not well understood. We investigated the prevalence and outcomes of EPI over 18 years at a tertiary bariatric referral center.

Methods: Records of patients treated with primary or revisional BS from 2002–2020 were reviewed. Demographics, symptoms, labs, and treatment outcomes were collected for patients suspected of EPI or underwent Fecal Elastase testing (FE-1). EPI diagnosis was defined as positive FE-1 testing or improvement with empiric pancreatic enzyme replacement therapy (PERT).

Results: Of 3,489 patients, 262 (7.5%) were suspected of having EPI and 191 were tested via FE-1 (171, 89.5%) or empirically treated (20, 10.5%). EPI was diagnosed in 80 (41.9%) patients: 69 (86.3%) after Roux-en-Y gastric bypass (RYGB), 7 (8.8%) after biliopancreatic diversion-duodenal switch or jejunoileal bypass (BPD-DS/JIB), 4 (5.0%) after sleeve gastrectomy (SG). Therapeutic PERT was given to 66 patients diagnosed with EPI: 57 (86.4%) had improvement in symptoms. Patients diagnosed with EPI were more likely to have RYGB and BPD-DS versus SG (48.3%, 70.0% vs 17.4%, $p<0.01$ Chi square), and no patients with AGB had EPI.

Symptoms prompting FE-1 testing included: diarrhea (91.5%), abdominal pain (50.2%), nausea (28.7%), bloating (12.6%), and excessive flatulence (6.9%). No symptoms were significantly associated with EPI diagnosis by Chi square analysis.

Conclusion: A high index of suspicion for EPI in bariatric patients with gastrointestinal complaints is recommended, especially following RYGB. Further work to define symptoms prompting work-up, optimal treatment, and prevention is necessary.

Cara Pozolo

Improved Follow-Up After Hospital Discharge Does Not Impact 30-Day Readmissions After Vascular Procedures

Dr. Cara Pozolo MD, Christina Philip MS, BSN, RN-BC, Dr. Austin Holmes MD, Dr Matthew Mell MD

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Abstract

Objective: We sought to evaluate the integration of an automated patient contact system with a standardized process for inpatient discharge for successful transition to outpatient care.

Methods: All patients who underwent procedures with the vascular surgery service from April 2021 through October 2021 were discharged using a process improvement (PI) protocol and compared with a historical control cohort discharged from May 2018 through July 2019. The PI protocol included standardized in-person discharge instructions by a vascular nurse coordinator and early follow-up visits. For both cohorts patients received an automated phone call from a third-party vendor (CipherHealth, New York, NY), with an option to escalate to a clinical nurse. Primary outcomes were unplanned readmission within 30 days of discharge and time from discharge to follow-up visit.

Results: A total of 469 patients who received an automated call (1.4 ± 1.0 days) after discharge were analyzed (271 control vs 198 PI). No significant change in 30-day readmission rates was observed. Request for escalation to clinical nurse was significantly decreased after intervention (28.0% control vs 16.7% PI; p=0.004). Escalation was associated with increased 30-day readmission (8.6% vs 20.1%; p=0.001) for all patients. Two-thirds of readmissions occurred before scheduled post-discharge visit. The median interval from discharge to follow-up visit was markedly improved with PI (24 days [IQR 14-33] vs 16 days [IQR 11-32]; p=0.007).

Conclusions: Restructuring the discharge process decreased escalation to clinical staff from the automated post-discharge phone call and improved time to follow-up. Readmission rates remained unchanged despite these efforts and was increased for patients requesting escalation. These findings support the benefit of a structured discharge approach for post-discharge transition of care and suggest that other actionable factors are required to decreased readmission after vascular procedures.

Anamaria Robles

THE CHICKEN OR THE EGG: CORRELATION OF LOW PLATELETS & POST-INJURY ACUTE RESPIRATORY DISTRESS SYNDROME

Anamaria Robles MD[1], Richa Kalamdani BS[1], James Ross MD[1], Lucy Kornblith MD[2], Rachael Callcut MD MSPH[1]

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Abstract

Introduction: Pathophysiologic origins of post-injury Acute Respiratory Distress Syndrome (ARDS) remain elusive. Platelet transfusion has been proposed as a possible mechanism. The lung has recently been shown to be the key site of primary platelet biogenesis and sequestration. The interaction between initial thrombocytopenia, lung platelet production post-injury, and ARDS is undefined. This study investigates the correlation of platelet counts, ARDS risk, and platelet recovery in the first 7 days post-injury.

Methods: Secondary data analysis was performed of a prospective cohort of highest-level activations who were followed for 28 days. Demographics, injury characteristics, labs, and outcomes were collected. ARDS was defined prospectively using Berlin criteria including adjudicated radiographs. Correlation (Pearson's) between ISS, daily lowest platelet count, and ARDS was assessed. Logistic regression was performed.

Results: 2003 patients were enrolled with 10.3% (n=207) developing ARDS. ARDS patients had higher median age, lower GCS, higher ISS, more likely to be thrombocytopenic and hypotensive on presentation (Table). Overall median platelet count across the first 7 days was lower in the ARDS patients (p<0.0001). Platelet recovery as measured by total counts appeared to begin at day 7 with higher daily median counts compared with day 1-6 (p<0. 05), and no day 7 difference between groups (p=NS). Lower platelet count in the first 7 days and ISS were independent predictors of ARDS (Table).

Conclusion: ARDS risk persists in the first week and is correlated with persistently lower platelet counts. Sequestration and decreased primary lung platelet production may be factors in the persistent thrombocytopenia.

	ARDS (n = 207)	No ARDS (n = 1796)	*p*
Age, median (IQR)	44 (28 to 59)	36 (26 to 53)	0.0003
Male sex, (%)	82.6%	81.6%	0.7763
Glasgow Coma Scale score, median (IQR)	3 (3 to 5)	13 (3 to 15)	<0.0001
Initial SBP <=90 mmHg	11.6%	6.2%	0.0065
Blunt Injury, %	85.0%	54.3%	<0.0001
Initial Platelet counts,			
Median (IQR), in thousands	166 (104 to 229)	232 (178 to 287)	0.3113
% with count < 150 in thousands	41.5%	14.2%	<0.0001
Injury severity score, median (IQR)	30 (25 to 41)	10 (1 to 25)	<0.0001(W)
% with score < 15	10.1%	62.4%	<0.0001(F)
% with 15 ≤score <25	12.1%	12.4%	
% with score >=25	77.8%	25.3%	
Logistic multiple regression	OR ARDS	95% CI	
Platelet count (every 10,000 increase)	0.936	(0.918-0.955)	
ISS (each 5 point increase)	1.357	(1.292-1.425)	

QUICK SHOT PRESENTATIONS

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

MODERATORS
MICHAEL CAMPBELL & LISA BROWN

1. **ALEXANDRA JOHNS** - Factors influencing length of stay following bariatric surgery

2. **ISABELLE STRUVE** - Lower coded pediatric trauma patients are exposed to increased rates of cross-sectional imaging despite similar injury severity

3. **KAITLIN CLARK** - Characterization of Extracellular Vesicles Isolated from Canine Placenta-derived Mesenchymal Stem/Stromal Cells

4. **ANDREA KULINICH** - A Comprehensive Update on Pneumothorax as a Complication of Breast Augmentation

5. **ANASTASIYA STASYUK** - Interventions and outcomes in glottic versus multi-level airway stenosis: multi-institutional review

6. **CYRUS SHOLEVAR** - Building a Successful Hepatic Artery Infusion (HAI) Program: An International Survey of the HAI Consortium Research Network

7. **NICOLE MOORE**- How Adolescents and Young adults with Incidental Adrenal Tumors Differ from Similar Aged Patients Without Adrenal Tumors

Alexandra Johns

Factors influencing length of stay following bariatric surgery

Dr. Alexandra Johns MD[1], Dr. Shushmita Ahmed MD[2], Dr. Marcoandrea Giorgi MD[3], Dr. Victoria Lyo MD[2], Dr. Mohamed Ali MD[2]

[1]University of California, Davis, Department of General Surgery, Sacramento, CA, USA. [2]University of California, Davis, Division of Foregut, Metabolic, and General Surgery, Sacramento, CA, USA. [3]Brown Surgical Associates, Bariatric Surgery, Providence, RI, USA

Abstract

Background: Enhanced recovery after surgery (ERAS) protocols have been applied following laparoscopic Roux-en-Y gastric bypass (RYGB) and laparoscopic sleeve gastrectomy (SG) to facilitate discharge as early as the first post-operative day (POD 1). This study aims to identify preoperative and intraoperative predictors prolonging length of stay beyond POD 1 following RYGB and SG between 2010 and 2015.

Methods: A retrospective analysis of a prospectively maintained database was analyzed at a single academic institution. Data collected included weight, comorbidities, intra-operative findings, length of hospitalization, and 30-day complications. Univariate and multivariate analyses were used to identify predictors of hospital stay beyond POD 1.

Results: Consecutive patients underwent RYGB (n=647) or SG (n=310). The majority of RYGB patients (57.2%) and SG patients (71.3%) required hospitalization beyond POD 1. For SG, only body mass index (BMI) greater than 50 kg/m2 was associated with hospitalization beyond POD 1. On multivariate analysis, insulin-dependent diabetes (OR 2.0, 95% CI: 1.1 to 3.6), decreased functional status (OR 2.0, 95% CI: 1.0 to 4.1), and additional procedures performed along with the index case (OR 1.5, 95% CI: 1.0 to 2.2) were significant predictors of hospitalization beyond POD 1 in RYGB patients. BMI was not a predictor of prolonged stay after RYGB. There were no differences in 30-day complications between patients who were discharged on POD 1 versus those discharged after POD 1 for both RYGB (7.2% vs 4.6%, p = 0.16) and SG (3.4% vs 4.8%, p = 0.65).

Conclusions: Discharge on POD 1 is a safe option for select patients. Only BMI greater than 50 kg/m2 predicted extended hospital stay for patients undergoing SG. Several factors correlate with extended stay after RYGB, including comorbidities and functional status. Pre-habilitation in these patients may mitigate these factors to reduce delays in postoperative discharge.

Isabelle Struve

Lower coded pediatric trauma patients are exposed to increased rates of cross-sectional imaging despite similar injury severity.

Isabelle Struve MD, Jonathan Kohler MD, Minna Wieck MD, Erin Brown MD, Shinjiro Hirose MD, Payam Saadai MD

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

Abstract

Introduction: Our hypothesis is that there is an increased rate of cross sectional imaging in lower coded pediatric trauma patients compared to the higher coded patients.

Methods: This is a retrospective study from 2017 to 2021 at a Level 1 Trauma Center using the UC Davis trauma registry database. All pediatric trauma patients aged less than 18 years old who were coded as traumas (911, 922, 933) were included. Trauma transfers were excluded. Demographics including age, gender, injury mechanism, injury severity score (ISS), hospital length of stay, and rates of cross sectional imaging of the head, cervical spine, and abdomen were assessed. Data were analyzed using a simple chi-squared test.

Results: A total of 1458 patients were analyzed. 911 pediatric trauma patients (n=528) underwent cross sectional imaging of the head, cervical spine, and abdomen at rates of 70%, 54%, and 58% respectively. The mean ISS for 911 patients was 13.9. 922 pediatric trauma patients (n=434) underwent cross sectional imaging of the head, cervical spine, and abdomen at rates of 65%, 27%, and 34% respectively. The mean ISS for 922 patients was 7.6. 933 pediatric trauma patients (n=496) underwent imaging of the head, cervical spine, and abdomen at rates of 65%, 44%, and 58%, respectively. The mean ISS for 933 patients was 7.5. There was no significant association between the presence of head CT imaging and trauma code. There was a significant association between the presence of imaging of the cervical spine and abdomen and trauma code ($p=0.0003$ and $p<0.00001$, respectively) given the same ISS.

Conclusions: Despite the same ISS, 922 pediatric trauma patients had decreased rates of cross sectional imaging of the cervical spine and abdomen compared to 933 pediatric trauma patients. The next steps include multivariable analysis, determining the rates of clinically significant positive findings, and calculating the cost and radiation exposure differences amongst differently coded patients.

Kaitlin Clark

Characterization of Extracellular Vesicles Isolated from Canine Placenta-derived Mesenchymal Stem/Stromal Cells

Kaitlin Clark MA[1,2], Ashley Amador BS[1], David Wang BS[3,2], Gabriela Rivas BS[1], Dr. Diana Farmer MD[1,2], Dr. Aijun Wang PhD[1,2]

[1]University of California, Davis, Sacramento, CA, USA. [2]Shriner's Hospital for Children, NorCal, Sacramento, CA, USA. [3]University of California, Davis, USA

Abstract

Mesenchymal stem cells (MSCs) are of key interest for the treatment of many central nervous system (CNS) disorders due to their potent immunomodulatory and regenerative properties shown in several species. However, the mechanism of action (MOA) by MSCs has not been well elucidated. Placenta-derived MSCs (PMSCs) possess unique robust neuroprotective and immunomodulatory properties. Interest in using cell free therapeutics has increased, namely utilizing the MSC secretome and bioactive factors. Extracellular vesicles (EVs) are nano-sized particles containing bioactive molecules which mediate intercellular communication and may be clinically advantageous for CNS disorders. Companion animals are an underutilized model to evaluate cell-free therapies as they suffer from diseases comparable to human disease. The goal of this study is to isolate and characterize canine PMSC-EVs (cPMSC) for future studies to evaluate therapeutic applications in large animal models.

cPMSC-EVs were isolated by adapting a sequential ultracentrifugation approach used currently for human PMSC-EVs. Characterization of canine PMSC-EVs was established by western blots and nanoparticle tracking analysis (NTA). It was found that cPMSCs yield on average 5e5 EVs per day, with a size distribution of 124nm and an Zeta potential of -19mV. cPMSC-EVs were positive for Alix and TSG101 and negative for calnexin. These results suggest canine PMSC-EVs can be effectively isolated and further optimization of functional assays is ongoing. It has been reported cPMSC MOA of immunomodulation differs from adult tissue sources of MSCs, however there has yet to be detailed characterization of cPMSC-EVs. Successful isolation and characterization of cPMSC-EVs will lay the foundation for further development of PMSC-EVs as a novel regenerative therapy for treating canine CNS disorders. Furthermore, functional studies of cPMSC-EVs will support the development of PMSC-derived regenerative therapy for human diseases.

Andrea Kulinich

A Comprehensive Update on Pneumothorax as a Complication of Breast Augmentation

Andrea Kulinich B.S.[1], John Mark B.S.[1], Dr. John Osborn M.D[2], Dr. David Sahar MD, FACS[2], Dr. Lee L.Q Pu M.D, Ph.D, FACS[2]

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Abstract

Background: The frequency of pneumothorax as a complication of breast surgery was unknown until a survey of members of the California Society of Plastic Surgeons (CSPS) was completed in 2002. The response rate of the survey was 50%, and the incidence of pneumothorax seemed to be more common than generally appreciated with 1 out 3 surgeons experiencing at least one pneumothorax in their career. A review of the literature determined that no study has attempted to examine the actual incidence of pneumothorax in breast augmentation surgery since the above study.

Methods: An online survey was sent to members of the CSPS in 2020, inquiring about their experience with this complication. A retrospective chart review was completed, in which breast augmentation procedures performed over a 6-year period by 4 plastic surgeons at the UC Davis Health System were screened for pneumothorax. A literary search of the PubMed/MEDLINE database was performed. Data on breast augmentations complicated by pneumothoraces were obtained from the American Association of Accreditation of Ambulatory Surgical Facilities (AAAASF) for the year 2019.

Results: The updated CSPS survey response rate was 18.3%. Out of the 55 respondents, 25 reported a total of 43 pneumothoraces throughout their careers. In the retrospective chart review performed at UC Davis Health, no pneumothoraxes were identified. In the literature search, a total of 11 patients who underwent breast augmentation between 2005 and 2021 experienced a pneumothorax. AAAASF found an incidence of 0.000031% (3 out of 97,495) for pneumothorax for 2019.

Conclusion: The literature review indicated that possible risk factors for pneumothorax include low BMI and heavy smoking among others. This study found that 2 in 5 members of the CSPS had at least one patient who experienced a pneumothorax. Future studies should aim to replicate results in aesthetic centers that perform high-volume breast augmentation procedures.

Anastasiya Stasyuk

Interventions and outcomes in glottic versus multi-level airway stenosis: multi-institutional review

Shambavi Rao[1], Grant Gochman[2], Anastasiya Stasyuk[3], Kychelle Del Rosario[1], Daniel Cates[4], Lyndsay Madden[5], VyVy Young[2]

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Abstract

Introduction: Airway stenosis – particularly multi-level – presents complex management challenges. This study assessed rates of tracheostomy, decannulation, and number of surgeries required in patients with posterior glottic stenosis (PGS), multi-level airway stenosis (MLAS), and bilateral vocal fold paralysis (BVFP).

Methods: Airway stenosis patients treated between 2016 - 2021 at three tertiary medical centers were identified. Demographics, etiology of stenosis, medical comorbidities, and patient reported outcome measures (PROMs) were collected.

Results: 158 patients (84 women, mean age 56.98+/-15.5 years) were identified (54 PGS, 38 MLAS, 66 BVFP). 72.3% required tracheostomy, including 72.2%, 86.8%, and 63.6% in these groups, respectively. Decannulation rates were 43.6%, 21.2% and 32.5% in these groups, respectively. Patients with MLAS had higher rates of tracheostomy than BVFP ($p<0.05$). However, decannulation rates were not different between groups ($p>0.05$). MLAS required more surgeries (mean 4.0+/-3.9) than PGS (2.4+/-2.2, $p=0.02$) or BVFP (1.0+/-1.8, $p<0.0001$). Mean PROMs scores at latest follow-up were abnormal: 15.4+/-12.2 (Dyspnea Index), 19.9+/-12.2 (Voice Handicap Index-10), and 9.67+/-11.1 (Eating Assessment Tool-10). Co-morbidities present included body mass index >30 (41.4%), diabetes (31.8%), pulmonary disease (50.7%), gastroesophageal reflux disease (39.4%), autoimmune disease (22.9%), and tobacco use history (55.2%).

Conclusions: Airway stenosis is a challenging clinical problem that negatively impacts patients' quality of life and often requires numerous surgeries. PGS more frequently requires tracheostomy compared to BVFP, but patients can often decannulate successfully. Patients with multi-level stenosis have lower decannulation rates and require more surgeries than glottic stenosis alone; these patients would benefit from earlier and/or more aggressive intervention.

Cyrus Sholevar

Building a Successful Hepatic Artery Infusion (HAI) Program: An International Survey of the HAI Consortium Research Network

Cyrus Sholevar[1], Michael Cavnar[2], Tara Ghalambor[1], Michael Lidsky[3], Ismael Dominguez[4], Paul Karanicolas[5], Ryan Merkow[6], Skye Mayo[7], Flavio Rocha[7], Ryan Fields[8], Bas Groot Koerkamp[9], Adam Yopp[10], Henrik Petrowsky[11], Michael D'Angelica[12], Sepideh Gholami[1]

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Abstract

Introduction: Despite encouraging oncologic outcomes, widespread implementation of hepatic arterial infusion (HAI) therapy has faced multiple barriers. By querying members of the recently established international HAI Consortium Research Network (HCRN), this survey aims to identify important elements and challenges in establishing a successful HAI program.

Methods: Using SurveyMonkey™, a 17-question survey assessing perceived factors required for establishing a successful program was developed by 12 HCRN surgical oncologists. Content analysis was used to code textual responses, and the frequency of categories was calculated. For rank-order questions, scores were generated by calculating average ranking for each answer choice.

Results: Twenty-eight HCRN surgical oncologists responded to the survey. Implementation time varied, with 53.8% requiring less than a year, and up to 3 years for the rest. Most programs (n=17, 60.7%) became active in the past 5 years (32.1% from 2016-2018 and 28.6% from 2019-2021). Team members from 51% of new programs participated in on-site training at a high-volume center. Medical and surgical oncology were ranked most important for building a program (average rank scores 7.96 and 6.59/8, respectively). Administrative or regulatory approval was required at half of the institutions. The top 3 challenges faced when building a program were related to regulatory approval, device/equipment access, and drug (FUDR) access (average rank scores 6.65, 6.33, and 6.25/9, respectively).

Conclusion: Widespread development of successful programs outside of historically established centers is feasible and requires a multidisciplinary team. Future collaborative efforts are critical for sustainability of safe/effective new programs and execution of multicenter clinical trials in HAI.

Nicole Moore

How Adolescents and Young adults with Incidental Adrenal Tumors Differ from Similar Aged Patients Without Adrenal Tumors

Dr. Nicole Moore MD, Mr. Satninderdeep Bhatti MPH, Dr. Claire Graves MD, Dr. Michael Corwin MD, Dr. Michael Campbell MD FACS

UC Davis Medical Center, Sacramento, CA, USA

Abstract

Introduction: The incidence of adrenal incidentalomas (AIs) increases with age. The tumor types and prevalence of metabolic disorders in adolescents and young adults (AYA) with AIs has not been well evaluated.

Methods: Single institution, case control study of AYA patients (age 15 – 40 years) with AIs compared to similar aged patients [CEG1] without an AI identified using a radiology keyword search with subsequent chart review.

Results: We identified 51 AYA patients with an AI with a mean age of 32 years (15 – 40 years). The mean tumor size was 2.9 cm (0.7 – 9 cm) and was comprised of 34 (66.7%) adrenocortical adenomas, 7 (13.7%) radiographically indeterminate tumors, 5 (9.8%) cases of adrenal hemorrhage, 3 (5.9%) malignancies, 1 (2%) ganglioneuroma and 1 (2.0%) myelolipoma. Nineteen (37.3%) AYA patients received at least a partial functional evaluation with 1 (2.0%) patient having a pheochromocytoma. On univariate analysis, AYA patients with an AI had a higher body mass index (32.6 vs 28.2, p=0.01) and were more likely to have diabetes (27.5% vs 12.2%, p=0.01), hypertension (37.3% vs 10.9%, p < 0.01), and hyperlipidemia (19.6% vs 7.1%, p=0.01) when compared to similar aged patients without an AI (n=156).

Conclusions: Similar to older patients, AYA patients with AIs predominately have adrenocortical adenomas. Clinicians should consider evaluating AYA patients with AIs for diabetes, hypertension and hyperlipidemia, along with AI functional workup, given the high prevalence of these metabolic disorders in this group of patients.

QUICK SHOT PRESENTATIONS

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

MODERATORS
ANDREW LI & CLAIRE GRAVES

1. **ELISE HILL** - The Power Of Cooperation: A Quantitative Analysis Of The Benefit Of Civilian Partnerships On The Academic Output Of Military Surgeons

2. **ELAN SHERAZEE** - Hyperoxia is Not Associated with Early Mortality nor Mid-Term Functional Outcomes After Severe Traumatic Brain Injury

3. **JENNIFER GEIGER** -Evaluating a Simulation-Based Serious Illness Communication Workshop Using a Structured Guide in Surgical Residents

4. **CHAOXING ZHANG** - mRNA vaccine delivery by microneedle patches for treatment of unresectable melanoma

5. **ANGELICA MARTIN** - Research Addressing Racial Health Disparities in Cardiothoracic Surgery Represents Only a Small Fraction of Total Major Meeting Peer-reviewed Content

6. **AMANDA PHARES** - Revitalizing the Robotic Surgery Curriculum for General Surgery Residents - One Year Follow Up

7. **RAFAEL LOZANO** - Intraoperative Systemic Heparin Is Safe for Treatment of Blunt Thoracic Aortic Injury with Concomitant Traumatic Brain Injury

Elise Hill

The Power Of Cooperation: A Quantitative Analysis Of The Benefit Of Civilian Partnerships On The Academic Output Of Military Surgeons

Dr. Elise Hill MD[1], Dr. Ian Valerio MD, MS, MBA[2]

[1]University of California at Davis, Department of Surgery, Sacramento, CA, USA. [2]Massachusetts General Hospital, Plastic and Reconstructive Surgery, Boston, MA, USA

Abstract

Introduction: Military-civilian partnerships are crucial to maintaining the skills of active-duty surgeons and sustaining readiness. There have been no publications to date that report the quantitative effect of these partnerships on an important aspect of the surgical vocation, academic research. To address this question, the H-indices of active-duty surgeons with a civilian affiliation were compared to those without.

Methods: De-identified rosters of active-duty military surgeons were obtained confidentially through each branch Consultant. H-indices were found on Scopus. Graduation dates and hospital affiliations were identified via public Doximity, LinkedIn profiles, and through hospital biographies. Of 283 initial surgeons, 18 were ultimately excluded, leaving 265 for final analysis.

Results: The mean H-index for the total population is 4.31, with an average of 11.95 documents per surgeon. Military surgeons without a civilian association have a mean H-index of 3.27 versus 5.62 in those with such an affiliation. This pattern is also seen in average number of publications, at 7.89 and 17.09 articles. When further stratified by branch, Air Force surgeons have H-indices of 5.12 and 2.36 with and without a civilian affiliation, respectively. The Army surgeons follow a similar pattern, with H-indices of 6.56 versus 4.24 for those with and without affiliations.

Conclusion: Civilian affiliations are associated with higher academic output, as measured by H-index, for active-duty military surgeons. This association is statistically significant and holds when categorized by branch and when controlling for years since medical school graduation. Given this, the military should continue to seek out and nurture these relationships.

Elan Sherazee

Hyperoxia is Not Associated with Early Mortality nor Mid-Term Functional Outcomes After Severe Traumatic Brain Injury

Elan Sherazee MD[1], Samy Ramadan MD[1], Ashly Ruf MD[1], Rafael Lozano MD[1], Hope Moore MD[1], Ryan Martin MD[1], Gregory Jurkovich MD[1], Jennifer Thornton PhD[2], Scott Zakaluzny MD[1]

[1]UC Davis. [2]Clinical Investigation Facility

Abstract

Introduction: Patients who sustain traumatic brain injuries (TBI) are frequently administered high levels of supplemental oxygen which results in hyperoxia—a phenomenon that is poorly defined and has controversial clinical relevance. We performed a retrospective study with the hypothesis that hyperoxia after severe TBI, as measured by either tissue oxygen saturation (SpO2) or partial pressure of arterial oxygenation (PaO2), affects mortality.

Methods: Our institution's trauma database was screened for adult patients that sustained a severe TBI and required mechanical ventilation for at least 48hrs. SpO2 and PaO2 results from arterial blood gases over the initial 48 hour hospitalization were averaged. Hyperoxia was defined as SpO2>97% or PaO2>200mmHg and normoxia was defined as SpO2 90 to 97% or PaO2 60 to 200mmHg. The primary outcome was in-hospital mortality. Functional outcomes were assessed with Glasgow Outcome Scale- Extended (GOSE). GOSE <4 was defined as a poor outcome and ≥4 a good outcome. A multivariable regression model was created and included variables age, ISS, sex, and admission GCS.

Results: Between 2010 and 2019, 584 patients met inclusion criteria for analysis. When patients were stratified by mean SpO2: 81.3% were hyperoxic, 16.1% were normoxic. When the same cohort was stratified instead by mean PaO2: 20.4% were hyperoxic, 78.4% were normoxic. Hyperoxia as determined by either SpO2 or PaO2 levels was not significantly associated with mortality nor GOSE outcomes in either univariate (unadjusted) nor multivariable (adjusted) analyses.

Conclusion: Hyperoxia as defined by mean SpO2 or mean PaO2 is not associated with in-hospital mortality nor short-term functional outcomes in ventilated patients with severe TBI. Further research is needed to investigate if monitoring brain oxygenation with SpO2 produces noninferior outcomes compared to PaO2.

Jennifer Geiger

Evaluating a Simulation-Based Serious Illness Communication Workshop Using a Structured Guide in Surgical Residents

Dr. Jennifer Geiger MD, MPH[1], Dr. Eleanor Curtis MD, MVPM[2], Dr. Nathan Fairman MD, MPH[3], Ganesh Rajasekar MPH[4], Dr. Misty Humphries MD, MAS[5]

[1]UC Davis, Department of Sugery, Sacramento, CA, USA. [2]UC Davis, Division of Trauma, Acute Care Surgery and Surgical Critical Care, Sacramento, CA, USA. [3]UC Davis, Department of Psychiatry and Behavioral Sciences, Sacramento, CA, USA. [4]UC Davis, Department of Surgery, Sacramento, CA, USA. [5]UC Davis, Division of Vascular Surgery, Sacramento, CA, USA

Abstract

Introduction: Serious illness communication is a core surgical competency, but formal training in residency is limited. The aim of this study was to pilot a skills-practice workshop for surgical residents introducing an evidence-based tool called the Serious Illness Conversation Guide (SICG).

Methods: General surgery residents from UC Davis participated in a two-hour training that included role-play with standardized patients and interdisciplinary clinician facilitators on December 14, 2021. Pre-post-surveys measured participants' self-efficacy in serious illness communication and relevant subtasks. Paired surveys were compared using the Wilcoxon signed rank test. Secondary outcomes included satisfaction with the training and acceptability measures of the SICG. A three-month follow-up survey is pending.

Results: Thirty-three residents attended the workshop. Using 24 matched pre-post surveys, resident self-efficacy in conducting goals of care conversations for patients with serious illness was greater after the workshop, with a significant median [IQR] difference in confidence level of 20% [10, 30] between paired observations ($p < 0.001$). Significant positive pre-post differences were seen across all communication subtasks. Overall satisfaction was high and nearly all (n = 21) residents reported they would recommend the training to colleagues. Residents generally liked the SICG; 74% strongly agreed it is suitable for use in surgical patients and 65% strongly agreed they intend to use it in clinical practice.

Conclusions: Surgical trainees at a tertiary institution report improved self-efficacy in serious illness communication immediately following a workshop using a structured guide. Participants perceived the SICG is an acceptable tool for facilitating serious illness conversations with surgical patients. These preliminary findings support future implementation and evaluation of the training's impact on objective skill acquisition and patient-reported outcomes.

Chaoxing Zhang

mRNA vaccine delivery by microneedle patches for treatment of unresectable melanoma

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Abstract

Introduction: About 13.4% of patients with a high-risk primary melanoma will experience disease recurrence within 2 years. Gene therapy is a medical approach that treats or prevents disease by correcting the underlying genetic problem. Ideally, localized delivery across the skin and sustained release of mRNA vaccine to the site of resection could prevent the recurrence of melanoma. In this work, mRNA vaccine was packaged in lipid nanoparticles first. Then biocompatible and biodegradable microneedle patches loaded with drugs that facilitate the painless localized delivery of mRNA vaccine was developed for the treatment of unresectable melanoma.

Methods: RAW264.7 (macrophage) and B16 (melanoma) cells were co-cultured to recapitulate the interplay between tumor-associated macrophages and melanoma in human. RNA-seq was used to identify upregulated genes in co-culture. Lipid nanoparticles (LNPs) were prepared and characterized for mRNA loading. Polyvinyl alcohol (PVA)-based microneedle patch was fabricated via solvent casting and characterized. The mechanical strength of needle tip and drug delivery efficiency were evaluated ex vivo in porcine skin tissue and mouse skin tissue.

Results: 10 out of 12489 genes were upregulated more than a hundred-fold in co-culture. Cytokines induced by macrophages were revealed by RNA-seq and confirmed by imaging. LNPs-microneedle platform loaded with mRNA vaccine was successfully established and the drug delivery efficiency and function were proved in vitro and ex vivo.

Conclusion: LNPs-microneedle platform is promising for localized mRNA delivery to treat melanoma and other skin diseases. We will further evaluate it in mouse animal model in vivo.

Angelica Martin

Research Addressing Racial Health Disparities in Cardiothoracic Surgery Represents Only a Small Fraction of Total Major Meeting Peer-reviewed Content

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Abstract

Purpose: Heart and lung disease are leading factors affecting morbidity and mortality in African Americans and Latinos. Given this disparity, we sought to determine how often this topic is presented at the most relevant United States annual cardiothoracic surgery meetings.

Methods: Specialty-specific annual meeting abstract books from 2015 to 2021 were queried. We included The Society of Thoracic Surgeons (STS), American Association for Thoracic Surgery (AATS), Western Thoracic Surgical Association (WTSA), and the Southern Thoracic Surgical Association (STSA). Abstract titles and content with the following keywords and phrases: racial health disparities, race, racism, racial bias, institutional racism, and health disparities were counted as a racial health disparity abstract. The proportion of racial health disparity abstracts was calculated as well as the proportion of abstracts that resulted in manuscript publication.

Results: A total of 3,664 abstracts were presented at cardiothoracic surgery annual meetings between 2015 and 2021. Of those, only 0.98% (33/3,664) abstracts presented contained at least one of the keywords or phrases. The breakdown amongst the individual meetings during this period was as follows: STS 1.3% (20/1,501), AATS 0.71% (9/1,274), WTSA 0.65% (2/309) and the STSA 0.34% (2/580). Of these abstracts, the percentage that went on to publication in the meeting-associated journal were; STS 50% (10/20), AATS 56% (3/8), WTSA 50% (1/2) and the STSA 0% (0/2). This, however, only represents 0.38% (14/3,664) of the total number of abstracts presented.

Conclusions: Abstracts on racial health disparities in cardiothoracic surgery represent only a very small fraction of total meeting peer-reviewed content. There is a significant gap in research to identify and develop best practice strategies to address these disparities and mitigate structural racism within the care of underserved patients with cardiothoracic diseases.

Amanda Phares

Revitalizing the Robotic Surgery Curriculum for General Surgery Residents - One Year Follow Up

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Abstract

Introduction: Robotic surgery is a key minimally invasive technique in general surgery. Many surgical residencies offer robotic surgery curricula that prepare residents for independent practice. We previously presented the results of a needs assessment survey for the revitalization of our robotic surgery curriculum for general surgery residents. Utilizing the results, we developed a new curriculum at our institution. We hypothesized that this new curriculum would lead to improved experience in robotic surgery training.

Methods: We developed a new robotic surgery curriculum for general surgery residents based on published best practices and deficits identified in our needs assessment survey. At the end of the academic year, all clinical general surgery residents at a single institution and all faculty who perform robotic surgery at any affiliated training sites were surveyed using the two previously created surveys to assess experience in robotic surgery training. All responses were anonymous and descriptive statistics were performed to compare the outcomes to those of the former curriculum.

Results: The response rates for residents and faculty were 46% (33/72) and 44% (8/18). Awareness of the curriculum increased in both residents (53% to 97%) and faculty (70% to 88%). Engagement in all aspects of the curriculum increased, with increase in residents participating as a bedside assistant from 77% to 88% and operating on the console from 28% to 52%. Faculty incorporation of residents as a bedside assistant at least half of the time increased from 43% to 60% and as console surgeons from 29% to 60%. Faculty-reported inadequate resident preparation decreased from 40% to 17%.

Conclusions: These results demonstrate that our new robotic curriculum is having a positive impact on robotic surgery training for our residents.

Rafael Lozano

Intraoperative Systemic Heparin Is Safe for Treatment of Blunt Thoracic Aortic Injury with Concomitant Traumatic Brain Injury

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Abstract

Introduction: Grading blunt thoracic aortic injuries (BTAI) is key for reporting and treating this condition, but provides no guidance for the use of intraoperative heparin in the setting of traumatic brain injury (TBI). We evaluated the impact of intraoperative systemic heparinization after thoracic endovascular aneurysm repair (TEVAR) for patients with TBI. We compared University of Washington (UW) and Society of Vascular Surgery (SVS) grading systems.

Methods: We reviewed patients admitted with BTAI from 2011 to 2021. Data included injury grading, demographics and concomitant injuries. Primary outcome was progression of TBI after TEVAR. Additional outcomes were time to repair, mortality, and concordance of the two grading systems.

Results: The cohort comprised 174 patients, three excluded for death on arrival. The mean age was 46 ± 19 years, 68% men, median ISS was 34 (IQR 26- 45). Median door to repair time was 19 hours (IQR 11-39 hours), 79% got systemic heparin. Strong agreement was seen between the scoring systems (kappa=.84). Treatment adhered to guidelines for 87%-89% of patients. 63% of patients were repaired (all TEVAR). Time to repair was delayed for TBI patients (TABLE; p=.002). Heparin was used in a majority of TBI patients, but was used less frequently than for those without TBI (TABLE; p<.001). Overall mortality was 8% (12.5% with BTAI observed vs. 5.5% with BTAI treated, p=.09), no BTAI-related deaths. Repair after 48 hours did not decrease mortality (5.0% vs. 5.6%; p=.9). Progression of TBI after TEVAR was not seen with intra-operative systemic heparin use (4.6% with vs. 6.7% without, p=.87). Mean follow-up after TEVAR was 7.9 ± 11.7 months; 97.0% of repaired patients had resolution.

Conclusions: Use of systemic heparin during TEVAR for BTAI appears to be safe in selected patients with TBI. UW BTAI grading system captures patients requiring surgical intervention compared with SVS. Clinical expertise remains key to determine optimal management.

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