UC DAVIS HEALTH | COMPREHENSIVE CANCER CENTER

31st Annual Cancer Research Symposium

October 9 - 10, 2025

https://health.ucdavis.edu/cancer/research/education-training/symposia.html

FROM THE DIRECTOR

I am pleased to welcome you to the UC Davis Comprehensive Cancer Center's 31st Annual Symposium. The Annual Symposium highlights the best cancer research efforts conducted by our Comprehensive Cancer Center members and brings together the many talents and passions of investigators devoted to solving the problem of cancer across the entire spectrum from prevention to survivorship.

This year's two-day in-person event is organized into six thematic sessions featuring keynote and panel speakers. The program opens on Thursday with a new session - Artificial Intelligence, Data Science, and Cancer - chaired by John McPherson, Ph.D., and includes a keynote address from Vladimir Yarov-Yarovoy, Ph.D., the Associate Director of the UC Davis Center for Precision Medicine and Data Sciences.

Session II on Population Sciences and Cancer Control, chaired by Shehnaz Hussain, Ph.D., Sc.M., features a keynote presentation entitled "Pragmatic Trials of Cancer Center Delivery in Learning Health Systems" from Michael K. Gould, M.D., M.S., Professor and Faculty Director of Research for the Department of Health Systems Science and the Kaiser Permanente Bernard J. Tyson School of Medicine.

Session III on Education, Training, and Workforce Development, chaired by Frederick Meyers, M.D., M.A.C.P., focuses on how scholars are a driving force in innovation and teamwork with a panel of "futurist" scholars and mentors who are taking chances and launching big ideas.

Session IV on Basic Science, chaired by Xiao-Jing Wang, M.D., Ph.D., features Maria Jasin, Ph.D., from Memorial Sloan Kettering Cancer Center, who will present on "Genetic and Genomic Loss Arising from DNA Double-Strand Breaks."

The second day of the symposium starts with Session V on Community Outreach and Engagement, co-chaired by Laura Fejerman, Ph.D., and Julie Dang, Ph.D., M.P.H. The session highlights bidirectionality in action and how our research community benefits from collaborating with our community.

Our final keynote - the David R. Gandara Lectureship Awardee - Dr. Lajos Pusztai, Chief of Breast Medical Oncology, and Professor of Medicine at Yale University, leads Session VI on Clinical Research chaired by Megan Daly, M.D.

In addition to keynote presentations and panel discussions, we are highlighting cutting-edge cancer research from UC Davis in two poster and exhibition sessions.

I am certain that you will find this event to be a remarkably productive experience. Our team looks forward to interacting with you and sharing new knowledge through this forum. Thank you for your continued support.

Sincerely,

Primo N. Lara Jr.

Primo "Lucky" N. Lara, Jr., M.D., F.A.S.C.O.
Director, UC Davis Comprehensive Cancer Center
Distinguished Professor of Medicine
Executive Associate Dean for Cancer Programs
Codman-Radke Endowed Chair for Cancer Research

SYMPOSIUM COMMITTEE

Primo N. Lara, M.D., F.A.S.C.O.
Director, UC Davis Comprehensive Cancer Center
Distinguished Professor of Medicine
Executive Associate Dean for Cancer Programs
Codman-Radke Endowed Chair for Cancer Research

John McPherson, Ph.D.
Deputy Director, UC Davis Comprehensive Cancer Center
Professor, Department of Biochemistry and Molecular Medicine
Chair, Integrative Genetics and Genomics Graduate Program

Shehnaz Hussain, Ph.D., Sc.M.
Associate Director for Population Sciences
UC Davis Comprehensive Cancer Center
Professor, Department of Public Health Sciences

Frederick J. Meyers, M.D., M.A.C.P.
Associate Director for Education, Training, and Workforce Development
UC Davis Comprehensive Cancer Center
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UC Davis Comprehensive Cancer Center
Professor and Robert E. Stowell Endowed Chair in Experimental Pathology, Department of Pathology and Laboratory Medicine

Laura Fejerman, Ph.D.
Associate Director for Community Outreach and Engagement
UC Davis Comprehensive Cancer Center
Professor, Department of Public Health Sciences
Placer Breast Cancer Endowed Chair
Co-Director, Women's Cancer Care and Research Program

Julie Dang, Ph.D., M.P.H.
Assistant Director for Community Outreach and Engagement
UC Davis Comprehensive Cancer Center
Associate Professor, Department of Public Health Sciences

Megan Daly, M.D.
Associate Director for Clinical Research
UC Davis Comprehensive Cancer Center
Professor, Department of Radiation Oncology
Jennifer Rene Harmon Tegley and Elizabeth Erica Harmon Endowed Chair, Cancer Clinical Research

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Program Manager

Krandalyn Goodman, M.P.H.
Program Manager

Hanouvi Agbassekou, M.Ed.
Program Coordinator

Christian Joyce
Marketing Specialist

Rui Wu, M.S.D.S.
Data Systems Analyst

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Thursday, October 9, 2025

Time	Title	Presenter	Location
7:30-8 a.m.	**Breakfast**		
8:00-8:15 a.m.	Introduction and Welcome	Primo Lara, M.D., F.A.S.C.O.	Goodnight Auditorium
SESSION I: Artificial Intelligence, Data Science, and Cancer Chair: John McPherson, Ph.D.			
Time	**Title**	**Presenter**	**Location**
8:15-8:45 a.m.	**Keynote Presentation**: "AI Design of Biologics Targeting Ion Channels"	Vladimir Yarov-Yarovoy, Ph.D.	Goodnight Auditorium
8:45-9 a.m.	Q&A		
9-9:15 a.m.	"AI and Theranostics Digital Twins for Liver Cancer Radioembolization"	Emilie Roncali, Ph.D.	
9:15-9:20 a.m.	Q&A		
9:20-9:35 a.m.	To Be Announced	John Paul Graff, D.O., F.C.A.P., M.A.S.	
9:35-9:40 a.m.	Q&A		
9:40-9:55 a.m.	"AI and Machine Learning Methods for Studying Non-coding Genomic Regions and RNA in Cancer"	Fereydoun Hormozdiari, Ph.D.	
9:55-10 a.m.	Q&A		
10-10:15 a.m.	Break		
SESSION II: Population Sciences and Cancer Control Chair: Shehnaz Hussain, Ph.D., Sc.M.			
Time	**Title**	**Presenter**	**Location**
10:15-10:45 a.m.	**Keynote Presentation**: "Pragmatic Trials of Cancer Care Delivery in Learning Health Systems"	Michael K. Gould, M.D., M.S.	Goodnight Auditorium
10:45-11 a.m.	Q&A		
11-11:15 a.m.	"Ambient and Wildfire PM2.5 and Lung Cancer Survival: The Time is Now"	Surbhi Singhal, M.D.	
11:15-11:20 a.m.	Q&A		
11:20-11:35 a.m.	"Beyond the Flames: Understanding Cancer Risk in California Firefighters"	Shehnaz Hussain, Ph.D., Sc.M.	
11:35-11:40 a.m.	Q&A		
11:40-11:55 a.m.	"Human Papillomavirus (HPV) Ends Here: A Multilevel Clinic-based Intervention to Improve HPV Vaccination Rates"	Julie Dang, Ph.D., M.P.H.	

11:55a.m.-12 p.m.	Q&A	
12-1:15 p.m.	**Poster Session & Lunch**	Education Building, 1st and 2nd Floor breezeways

SESSION III: Education, Training, and Workforce Development
Chair: Frederick Meyers, M.D., M.A.C.P.

Time	Title	Presenter	Location
1:30-2:15 p.m.	"Scholar Centered Models to Promote Innovation and Impact"	**Panelists:** • Theresa Keegan, Ph.D., M.S. • Edward Kim, M.D., Ph.D. • Primo Lara, M.D., F.A.S.C.O. • Jasmin Mah, Ph.D.	Goodnight Auditorium

SESSION IV: Basic Science
Chairs: Xiao-Jing Wang, M.D., Ph.D.

Time	Title	Presenter	Location
2:15-2:45 p.m.	**Keynote Presentation**: "Genetic and Genomic Loss Arising from DNA Double-Strand Breaks"	Maria Jasin, Ph.D.	Goodnight Auditorium
2:45-3 p.m.	Q&A		
3:00-3:15 p.m.	"Biosensor Imaging Reveals the Heterogenous Impact of Targeted Therapies on Tumor and Immune Cells"	John Albeck, Ph.D.	
3:15-3:20 p.m.	Q&A		
3:20-3:35 p.m.	"A Cancer-linked Regulator of GTPASE Signaling Plays a Central Role in Leukocyte Migration"	Sean Collins, Ph.D.	
3:35-3:40 p.m.	Q&A		
3:40-3:55 p.m.	"The Role of PRMT5-mediated Symmetric Arginine Dimethylation in Telomere Biology"	Lifeng Xu, Ph.D.	
3:55-4 p.m.	Q&A		
End of Day 1			

Friday, October 10, 2025

Time	Title	Presenter	Location
8:00-9:15 a.m.	**Poster Session & Breakfast**		Education Building, 1st and 2nd Floor breezeways

Session V: Community Outreach and Engagement
Chairs: Laura Fejerman, Ph.D. and Julie Dang, Ph.D., M.P.H.

9:30-10:15 a.m.	"Community-Based Prostate Cancer Education and Outreach in Sutter County"	Gwen Ford and Avery Braun, D.O.	Goodnight Auditorium

	"Nanoplastic Exposure in Breast Cancer: A Pilot Blood Collection Event and Education Series"	Denise Rose M.S., P.C.C. and Randy Carney, Ph.D.	
	"Cancer Risk Reduction at Free Food Distributions: A Pilot Study"	Eric Spring, M.P.H., Cassandra Nguyen, Ph.D. and Charlotte Kerber, M.S.	
SESSION VI: Clinical Research Chair: Megan Daly, M.D.			
Time	**Title**	**Presenter**	**Location**
10:15-10:45 a.m.	Keynote Presentation: "Pursuing Cure in Breast Cancer"	Lajos Pusztai, M.D., Ph.D.	Goodnight Auditorium
10:45-11:00 a.m.	Q&A		
11:00-11:15 a.m.	"Modeling a Heterogeneous Disease to Identify Common Vulnerabilities"	Janai Carr-Ascher, M.D., Ph.D.	
11:15-11:20 a.m.	Q&A		
11:20-11:35 a.m.	"Development of a Novel Murine Model of Lung Squamous Cell Carcinoma to Serve as a Platform for Discovery of New Therapy Options"	Shiruyeh Schokrpur, M.D., Ph.D.	
11:35-11:40 a.m.	Q&A		
11:40-11:55 a.m.	"Developing Cell-based Immunotherapeutic Models from Patient-derived Head and Neck Squamous Cell Carcinoma"	Siao-Yi Wang, M.D., Ph.D.	
11:55-12:00 p.m.	Q&A		
Symposium Close			

KEYNOTE SPEAKERS

Vladimir Yarov-Yarovoy, Ph.D., earned an M.S. Degree in Physics at the Moscow State University in Moscow, Russia (mentored by Dr. Galina Mironova), and then a Ph.D. Degree in Biochemistry and Molecular Biology at the Oregon Health Science University in Portland, Oregon (mentored by Dr. Keith Garlid). Dr. Yarov-Yarovoy was a postdoctoral fellow in Biophysics (mentored by William Catterall, a member of the National Academy of Sciences) and Computational Biology (mentored by David Baker, the 2024 Nobel Prize in Chemistry Laureate and member of the National Academy of Sciences) at the University of Washington in Seattle, Washington. He then became a Research Assistant Professor in the Department of Pharmacology at the University of Washington. He joined UC Davis as an Assistant Professor in Physiology and Membrane Biology in 2011 and became a full Professor in 2020. He became Associate Director of the Center for Precision Medicine and Data Sciences and Vice Chair of the Department of Physiology and Membrane Biology in 2024. Dr. Vladimir Yarov-Yarovoy's research interests and expertise encompass neuroscience, protein structure, and computational biology. The primary focus of his research group is on the computational design of subtype-specific ion channel modulators, structure-function studies of voltage-gated ion channels, and the development of computational methods for membrane protein structure prediction and design. Recent advances in computational protein design, determination of high-resolution ion channel structures and discoveries of natural peptides that target them with high affinity, set a stage for computational design of novel ion channel modulators.

Michael K. Gould, M.D., M.S., is a pulmonologist and health services researcher with major interests in cancer care delivery, learning healthcare systems (LHS) and implementation science. His research is deeply embedded in the delivery system at Kaiser Permanente Southern California (KPSC), where he conducts both externally funded and operationally focused studies of care delivery for patients with cancer and respiratory disease. His recent work aims to ensure that lung cancer screening is implemented safely and effectively to maximize benefits and minimize harms, leveraging the quality and safety infrastructure of the KPSC health system as a laboratory for innovation and improvement. Dr. Gould has published over 300 scholarly articles, with past research support from the Department of Veterans Affairs, the National Cancer Institute (NCI), the Agency for Healthcare Research and Quality, and the Patient-Centered Outcomes Research Institute (PCORI). He currently serves as Principal Investigator (PI) for the PCORI-funded "Watch the Spot" Trial, a large, multicenter, pragmatic, comparative effectiveness trial of strategies for pulmonary nodule evaluation, and as multiple PI for two NCI-funded studies of lung cancer screening and post-treatment surveillance.

Maria Jasin, Ph.D., is biomedical researcher at Memorial Sloan Kettering Cancer Center in New York, where she holds the William E. Snee Chair in the Developmental Biology Program. In addition to her MSK appointment, she also has an appointment in the Weill Cornell Graduate School of Medical Sciences. Research in her laboratory focuses on DNA recombination and the relationship to the maintenance of genomic integrity and cancer, targeted genome modification, and meiosis. She obtained a Ph.D. from the Massachusetts Institute of Technology and performed postdoctoral research at the University of Zürich and Stanford University before starting her own lab in New York. She is an elected member of the US National Academy of Sciences, the National Academy of Medicine, and the American Academy of Arts and Sciences, and has received a number of prizes in recognition of her work, including the 2019 Shaw Prize in Life Science and Medicine, the 2018 Basser Global Prize for BRCA Research, and, most recently, the 2025 Pearl Meister Greengard Prize recognizing outstanding women in Biomedical Research.

Lajos Pusztai, M.D., Ph.D., is Professor of Medicine at Yale University, Scientific Co-Director of the Center for Breast Cancer at Yale Cancer Center and Co-Leader of the Yale Cancer Center Genomics Genetics and Epigenetics Program. He is also Chair of the Breast Cancer Research Committee of the Southwest Oncology Group (SWOG). Dr. Pusztai received his medical degree from the Semmelweis University of Medicine in Budapest, and his D.Phil. degree from the University of Oxford in England. His research group has made important contributions to establish that estrogen receptor-positive and-negative breast cancers have fundamentally different molecular, clinical and epidemiological characteristics. He has been a pioneer in evaluating gene expression profiling as a diagnostic technology to predict chemotherapy and endocrine therapy sensitivity and have shown that different biological processes are involved in determining the prognosis and treatment response in different breast cancer subtypes. He also made important contributions to clarify the clinical value of preoperative (neoadjuvant) chemotherapy in different breast cancer subtypes and made important contributions to characterize the immune microenvironment of breast cancer. Dr Pusztai is also principal investigator of several clinical trials investigating new drugs, including immunotherapies for breast cancer. Over 25 years of academic career he has mentored many graduate and postgraduate students who subsequently become academic thought leaders. He has published over 450 scientific manuscripts cited in high impact medical journals including the NEJM, JAMA, Journal of Clinical Oncology, Nature Biotechnology, PNAS, Lancet Oncology and JNCI, and was among the top 1% most highly cited investigators in clinical medicine according to a Thomson Reuters report.

ORAL PRESENTATION ABSTRACTS (THURSDAY)

Session I: Artificial Intelligence, Data Science, and Cancer

Chair: John McPhearson, Ph.D.

KEYNOTE LECTURE: AI DESIGN OF BIOLOGICS TARGETING ION CHANNELS

Vladimir Yarov-Yarovoy, Ph.D., Professor and Vice Chair, Department of Physiology and Membrane Biology and Professor, Department of Anesthesiology and Pain Medicine, UC Davis, Sacramento, CA

Voltage-gated sodium (Nav) channels are pivotal in conducting electrical activity in excitable cells and are critical pharmaceutical targets for treating many diseases, including cancer, cardiac arrhythmia, epilepsy, and pain. Despite their significance, challenges such as achieving target selectivity persist in the development of therapeutics targeting Nav channels. Recent progress in deep learning methods has enabled the computational design of protein binders targeting ion channels. These developments coincide with a surge in experimental structural data for Nav channels, providing a rich foundation for computational design efforts. My talks will review recent advancements in computational protein design using deep learning methods, with a focus on their application in designing protein binders to modulate ion channel activity. I will provide a comprehensive overview of the different design scenarios, discuss key structural considerations, and address the practical challenges in developing protein binders targeting Nav channels. By exploring these innovative computational methods, we aim to provide a framework for developing novel strategies that could significantly advance Nav channel pharmacology and lead to the discovery of effective and safe therapeutics for treatment of cancer.

AI AND THERANOSTICS DIGITAL TWINS FOR LIVER CANCER RADIOEMBOLIZATION

Emilie Roncali, Ph.D., Associate Professor, Department of Biomedical Engineering and Department of Radiology

The continued rising mortality and incidence of liver cancer (primary or metastatic) make research on improving its management essential. Transarterial radioembolization is a localized liver cancer treatment that delivers radioactive microspheres to tumors via a catheter inserted in the hepatic arterial tree with the goal maximizing therapeutic efficacy while minimizing damage to healthy liver tissue. Yttrium-90 radioembolizaton accounts for more than annual 10,000 interventions in the U.S. Unfortunately, optimization is challenging due to complex hepatic artery anatomy, variable blood flow, and uncertainty in microsphere transport. The creation of dynamic, patient-specific digital twins may provide a transformative solution to these challenges.
This work outlines a framework for a liver radioembolization digital twin using high-fidelity computational fluid dynamics (CFD) and/or recent physics-informed machine learning approaches. The CFD approach involves blood flow field and microsphere transport calculations in the hepatic arterial tree with individual patient data, which enables personalized treatment planning. Although accurate, traditional CFD is computationally expensive and limits clinical applicability.

To accelerate simulations, physics-informed neural networks (PINNs) and their generative extensions play an increasingly important role. These AI surrogates not only maintain physical fidelity but also support rapid sampling of diverse flow scenarios, facilitating real-time decision support. Together, CFD and physics-informed AI methods form the foundation of dynamic, patient-specific digital twin to optimize radioembolization planning and ultimately improve clinical outcomes.

In this presentation, I will discuss our research on liver digital twins to predict the dose distribution and assist with Y-90 radioembolization treatment planning. Dose verification post-treatment is also a critical step in improving patient care through close monitoring of treatment efficacy and exposure of non-target organs, which we are addressing by imaging the patient post treatment with positron emission tomography.

TO BE ANNOUNCED

John Paul Graff, D.O., F.C.A.P., M.A.S., Associate Professor, Department of Pathology and Laboratory Medicine

AI AND MACHINE LEARNING METHODS FOR STUDYING NON-CODING GENOMIC REGIONS AND RNA IN CANCER

Fereydoun Hormozdiari, Ph.D., Associate Professor, Department of Biochemistry and Molecular Medicine

Non-coding regions of the genome play a critical but underexplored role in cancer. In this talk, I will present two complementary approaches that leverage non-coding genomic regions and non-coding RNA signals for both understanding cancer biology and enabling early detection. First, I will introduce Dr. Nod, a framework for identifying non-coding regulatory driver mutations using tissue-matched enhancer–gene maps. Dr. Nod reveals new enhancer disruptions that alter transcription and dysregulate oncogenes and tumor suppressors. Next, I will present Orion, a generative AI model trained on serum-derived orphan non-coding RNAs (oncRNAs) from over 1,000 individuals with NSCLC. Orion achieves 94% sensitivity and 87% specificity for cancer detection, outperforming existing methods on held-out datasets. Together, these studies highlight the power of non-coding genomic features in both cancer development and non-invasive diagnosis.

SESSION II: Population Sciences and Cancer Control

Chair: Shehnaz Hussain, Ph.D., Sc.M.

KEYNOTE LECTURE: PRAGMATIC TRIALS OF CANCER CARE DELIVERY IN LEARNING HEALTH SYSTEMS

Michael K. Gould, M.D., M.S., Professor and Faculty Director of Research, Department of Health Systems Science, Kaiser Permanente Bernard J. Tyson School of Medicine

In this talk, Dr. Gould will summarize the methods and results of the Watch the Spot Trial, a large, multicenter, technology-enabled, pragmatic clinical trial of less vs. more intensive strategies for CT surveillance in patients with small pulmonary nodules. He will describe challenges and opportunities afforded by the pragmatic design, and review the advantages and disadvantages of using real-world data to improve cancer care delivery.

Rationale: Guidelines for pulmonary nodule surveillance are based on expert opinion and indirect evidence from studies of cancer risk factors.

Methods: This unblinded, cluster-randomized, pragmatic, noninferiority trial compared less versus more intensive surveillance strategies for patients with pulmonary nodules ≤15 mm in diameter, detected incidentally or by screening. Conducted across 14 U.S. healthcare systems, 24 clusters (13 systems and 11 hospitals) were randomized to one of two surveillance protocols modeled after published guidelines. The primary outcome was the proportion of lung cancers measuring >20 mm at diagnosis, with a noninferiority margin of 5 percentage points. Intention-to-treat (ITT), modified ITT, and per-protocol analyses were conducted using mixed-effects logistic regression to adjust for clustering and confounding.

Results: Lung cancer was diagnosed within 27 months of nodule identification in 273 of 17,841 participants (1.5%) in the less intensive study arm and 231 of 16,845 participants (1.4%) in the more intensive arm. Among those with available outcome data, 97 of 267 participants (36.3%) in the less intensive arm and 62 of 224 (27.7%) in the more intensive arm had cancers measuring >20 mm at diagnosis. Less intensive surveillance did not meet noninferiority criteria in ITT (adjusted difference 7.0 percentage points, 95% CI -2.0 to 15.9), modified ITT (4.4 points, 95% CI -4.7 to 13.5), or per-protocol (14.4 points, 95% CI -1.3 to 31.1) analyses.

Conclusions: Small, malignant nodules frequently progressed during surveillance. Trial findings do not support the use of less intensive surveillance for patients with small lung nodules. Clinical Trials Registration: NCT 02623712

AMBIENT AND WILDFIRE PM2.5 AND LUNG CANCER SURVIVAL: THE TIME IS NOW

Surbhi Singhal, M.D., Assistant Professor, Division of Hematology and Oncology

Air pollution is an invisible carcinogen, yet its impact on cancer outcomes is only beginning to be understood. Fine particulate matter (PM2.5) has been linked to lung cancer incidence, but little is known about how chronic and acute exposures shape outcomes after diagnosis. We analyzed survival among patients with newly diagnosed non-small cell lung cancer in the context of both background ambient PM2.5 and wildfire-dominant PM2.5 exposure. Strikingly, patterns of risk were not uniform: never smokers had particularly adverse outcomes at lower chronic levels, while patients receiving immunotherapy experienced a paradoxical survival benefit in the setting of higher wildfire-related exposures. These findings highlight a complex and context-specific relationship between environmental exposures and cancer treatment outcomes. Beyond biology, they underscore the urgency of integrating environmental health into cancer care and the need for public health interventions that extend “precision medicine” to the air our patients breathe.

BEYOND THE FLAMES: UNDERSTANDING CANCER RISK IN CALIFORNIA FIREFIGHTERS

Shehnaz Hussain, Ph.D., Sc.M., Professor, Department of Public Health Sciences, Associate Director for Population Sciences

Firefighters are regularly exposed to known and suspected carcinogens through their work, leading the International Agency for Research on Cancer to designate firefighting as carcinogenic to humans. However, the precise exposures and their mechanisms of action are poorly understood, and effective cancer prevention interventions remain elusive. Compounding the problem of inhaled, ingested, and dermally absorbed carcinogenic combustion emissions, firefighters experience numerous chemical, physical, mental, and behavioral hazards that increase cancer risk including sleep disruption, metabolic imbalances, and stress. In this talk, Dr. Hussain will present baseline data from the California Firefighter Cancer Research Study, a longitudinal cohort study of 2,000 California firefighters established to advance knowledge on understudied cancer risk factors in firefighters.

HUMAN PAPILLOMAVIRUS (HPV) ENDS HERE: A MULTILEVEL CLINIC-BASED INTERVENTION TO IMPROVE HPV VACCINATION RATES

Julie Dang, Ph.D., M.P.H., Associate Professor, Department of Public Health Sciences and Assistant Director, Community Outreach and Engagement

Human papillomavirus (HPV) vaccination is a proven strategy to prevent HPV-related cancers, yet uptake in the United States remains below national targets. To address this gap, we developed and implemented a clinic-based randomized controlled trial of a multilevel intervention aimed at increasing HPV vaccination among patients ages 11–12. The intervention included primary care team training, culturally tailored patient education delivered via MyChart, and follow-up calls from a community health educator compared to standard of care. This approach highlights the potential of multilevel, clinic-based strategies to advance HPV prevention and inform broader implementation efforts.

SESSION III: Education, Training, and Workforce Development

Chair: Frederick Meyers, M.D., M.A.C.P.

SCHOLAR CENTERED MODELS TO PROMOTE INNOVATION AND IMPACT

Scholars are practical and know how to succeed in incremental achievements: write papers, finish experiments, read literature, and advance their disciplinary tools. Importantly, scholars have often been the driving force in innovation and teamwork. In this session we will hear from four speakers who will relate their experiences as scholars and mentors to be "futurists," to take a chance and launch "big ideas." The panel will inspire others to "be the change."

Panelists:

Theresa Keegan, Ph.D., M.S., Professor, Division of Hematology and Oncology

Edward Kim, M.D., Ph.D., Professor, Division of Hematology and Oncology

Primo Lara, M.D., F.A.S.C.O., Director, UC Davis Comprehensive Cancer Center

Jasmin Mah, Ph.D., Postdoctoral Scholar, Department of Molecular and Cellular Biology

SESSION IV: Basic Science

Chairs: Xiao-Jing Wang, M.D., Ph.D.

KEYNOTE LECTURE: GENETIC AND GENOMIC LOSS ARISING FROM DNA DOUBLE-STRAND BREAKS

Maria Jasin, Ph.D., William E. Snee Chair, Developmental Biology Program, Memorial Sloan Kettering Cancer Center

Harnessing DNA double-strand breaks (DSBs) is a powerful approach for gene editing, but it may provoke loss of heterozygosity (LOH), a common feature of tumor genomes. To interrogate this risk, we developed a flow cytometry-based system (Flo-LOH), detecting LOH in ~5% of mouse embryonic and human epithelial cells following a DSB. Inhibition of both nonhomologous end joining (NHEJ) and microhomology-mediated end joining (MMEJ) massively increases LOH in both cell types, although the dependence on individual pathways differs. Multiple mechanisms lead to LOH, including chromosome truncations with de novo telomere addition and whole chromosome loss. LOH spans megabases distal to the DSB, but also frequently tens of megabases centromere proximal. The latter can be explained by breakage-fusion-bridge events resulting in truncated chromosomes; in conjunction with truncations, inverted duplications can also arise, which are common in cancer genomes where they are often termed foldback inversions. In summary, the Flo-LOH system we developed can be a powerful approach to understand factors and mechanisms that lead to LOH.

BIOSENSOR IMAGING REVEALS THE HETEROGENOUS IMPACT OF TARGETED THERAPIES ON TUMOR AND IMMUNE CELLS

John Albeck, Ph.D., Professor, Department of Molecular and Cellular Biology

Modern cancer therapy targets the molecular mechanisms of both tumor and immune cells, in an effort to impair pro-tumorigenic behavior such as proliferation and enhance anti-tumorigenic behavior such as immune-induced cell death. However, the populations of both tumor and immune cells within the cancer microenvironment are known to be highly heterogeneous, with variation driven by non-genetic factors that cannot be easily detected by sequencing. To address this potential obstacle to effective therapy, we have developed a live-cell imaging approach that allows cellular metabolic and signaling activities to be tracked at single cell resolution. This

platform allows for combinations of three or four biosensors at a time to detect parameters including ATP concentration, ADP/ATP ratio, glycolytic intermediates, and AMPK, AKT, mTOR and ERK kinase signaling. With this approach, we observe that targeted therapies induce a wide range of dynamic activities, which impact gene expression and cellular phenotypes. Our collaborative efforts currently focus on detecting and suppressing adaptation to EGFR inhibitors in lung cancer cells and on screening potential suppressors of glycolysis in renal carcinoma cells.

A CANCER-LINKED REGULATOR OF GTPASE SIGNALING PLAYS A CENTRAL ROLE IN LEUKOCYTE MIGRATION

Sean Collins, Ph.D., Associate Professor, Department of Microbiology and Molecular Genetics

Immune cells follow chemoattractant signals to reach sites of injury and infection to target their responses. Their ability to migrate persistently allows them to navigate around obstacles and cover long distances during this process. Stable cell polarity, which defines cell front and rear domains, is critical for persistent migration. To understand the signaling that underlies this process, we conducted a focused CRISPR interference screen and identified Arhgap30 as a negative regulator of Rho GTPase signaling that is critical for leukocyte polarity and migration. This protein has also been implicated as suppressing or promoting cancer progression in different contexts, but its mechanistic role in cell migration has been unclear. Using genetic experiments and live-cell imaging, we are characterizing the dynamic role of Arhgap30 in maintaining and directing persistent cell migration.

THE ROLE OF PRMT5-MEDIATED SYMMETRIC ARGININE DIMETHYLATION IN TELOMERE BIOLOGY

Lifeng Xu, Ph.D., Associate Professor, Department of Microbiology and Molecular Genetics

Telomerase is essential for telomere maintenance and cellular immortality. In human cells, a critical step in telomerase maturation occurs within Cajal bodies (CBs). CBs are membrane-less organelles enriched in small nuclear RNAs, including scaRNAs, and proteins bearing symmetrically dimethylated arginine (SDMA) residues. PRMT5, a type II protein arginine methyltransferase, plays a central role in RNA processing and splicing by methylating key spliceosome components and coilin, the major structural scaffold of CBs. Recently, we identified TCAB1, a WD40-repeat protein and integral component of the telomerase complex, as a selective reader of SDMA modifications. I will present our latest findings on the role of PRMT5-mediated SDMA modification in telomere maintenance and its clinical implications.

ORAL PRESENTATION ABSTRACTS (FRIDAY)

Session V: Community Outreach and Engagement

Chairs: Laura Fejerman, Ph.D., and Julie Dang, Ph.D., M.P.H.

The Office of Community Outreach and Engagement at the UCDCCC has implemented a strong infrastructure to support bidirectional engagement between the Center's researchers and community-based organizations (CBOs) in the catchment area. In this session we will highlight three pilot projects, shared from both the CBO and researchers' perspectives, that illustrate the collaborative relationships we hope to foster in order to advance innovative research.

Presenting Partners:

COMMUNITY-BASED PROSTATE CANCER EDUCATION AND OUTREACH IN SUTTER COUNTY

Gwen Ford, Executive Director, Connecting Cultures Collaborative, Inc.
Avery Braun, D.O., Assistant Clinical Professor, Department of Urologic Surgery

NANOPLASTIC EXPOSURE IN BREAST CANCER: A PILOT BLOOD COLLECTION EVENT AND EDUCATION SERIES

Denise Rose M.S., P.C.C., Chair of Board of Directors, Thriving Pink
Randy Carney, Ph.D., Associate Professor, Department of Biomedical Engineering

CANCER RISK REDUCTION AT FREE FOOD DISTRIBUTIONS: A PILOT STUDY

Eric Spring, M.P.H., Food Access Programs Manager, Sacramento Food Bank & Family Services
Cassandra Nguyen, Ph.D., Assistant Professor of Cooperative Extension, Department of Nutrition
Charlotte Kerber, M.S., Graduate Candidate, Department of Public Health Sciences

SESSION VI: Clinical Research

Chair: Megan Daly, M.D.

KEYNOTE LECTURE: PURSUING CURE IN BREAST CANCER

Lajos Pusztai, M.D., Ph.D., Chief of Breast Medical Oncology, Professor of Medicine, Breast Cancer Program, Yale Medical Oncology

Breast cancer survival has improved substantially over the past 20 years. I will review how new treatment strategies including neoadjuvant chemotherapy followed by response guided adjuvant treatment led to improvements in outcome, discuss the emerging controversy around pathologic complete response rate as early surrogate for drug efficacy, and highlight some of the ongoing trials that could change practice in this treatment setting along with the new questions that they inevitably will generate. I will also discuss the next generation challenge of how to reduce breast cancer mortality in low risk patients (stage I/II), who account for greater than 60% of all annual breast cancer death, and would like to plant the idea that it is time to design curative intent trials for some forms of stage IV breast cancers.

MODELING A HETEROGENEOUS DISEASE TO IDENTIFY COMMON VULNERABILITIES

Janai Carr-Ascher, M.D., Ph.D., Assistant Professor, Division of Hematology and Oncology and Assistant Professor in Residence, Department of Orthopaedic Surgery

High-grade complex karyotype sarcomas are a heterogeneous group of tumors with a uniformly poor prognosis. Within complex karyotype sarcomas, there are innumerable genetic changes but identifying those that are clinically relevant has been challenging. To address this, the lab has focused on generating new models of common sarcoma subtypes. Through this system, we have identified new therapeutic opportunities.

DEVELOPMENT OF A NOVEL MURINE MODEL OF LUNG SQUAMOUS CELL CARCINOMA TO SERVE AS A PLATFORM FOR DISCOVERY OF NEW THERAPY OPTIONS

Shiruyeh Schokrpur, M.D., Ph.D., Assistant Professor, Division of Hematology and Oncology

Lung cancer is the leading cause of cancer deaths worldwide and in the United States. Lung squamous cell carcinoma (LSCC) accounts for nearly one quarter of all cases. Metastatic patients with this condition can expect treatment with chemotherapy, immunotherapy, or a combination of both. Despite these treatments, nearly half will fail to respond, and the overall survival (OS) rate is less than 1.5 years. There is a critical need for new treatment modalities to improve response rates and OS for these patients. Genetically engineered murine models (GEMM) are invaluable tools in the preclinical development of novel therapy options. Alterations in phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha (PIK3CA), SRY-box transcription factor 2 (Sox2), and tumor protein p53 (TP53) commonly occur in clinical LSCC. We leveraged our expertise in murine tumor modeling to generate the TPS mouse strain, under which PIK3CA H1047R, Sox2 overexpression, and TP53 R172H are expressed in a tissue-specific manner in Clara cells, a type implicated in the origin of lung cancer. This model generates widespread primary lung tumors within four months, with half of all animals developing tumors. Immunohistochemical staining confirms Sox2 expression, phosphorylation of S6 downstream of PIK3CA/Akt/ mechanistic target of rapamycin kinase (mTOR) activation, and squamous cell marker tumor protein p63 (TP63). Lung tissues inclusive of tumors have been analyzed using digital spatial profiling and identify genes highly expressed in tumor tissues. We also isolated tumors from one of our GEMM animals to generate cell lines to be easily assessed in vitro for drug sensitivity. From these, we developed the TPS SCM cell line, which showed expected phosphorylation of Akt, Sox2, and GFP expression by Western Blot. These cells were implanted into NOD SCID (NOD.CB17-Prkdcscid/NCrCrl) immunocompromised mice subcutaneously and yielded palpable tumors following two to three months. Immunohistochemical staining confirmed TP63, Sox2, and GFP expression in tumors that grew from the TPS line. In vitro viability studies reveal susceptibility to novel autophagy inhibitors. These findings underscore the potential of our models to discover new therapeutics and possible targets for further research in lung squamous cell carcinoma.

DEVELOPING CELL-BASED IMMUNOTHERAPEUTIC MODELS FROM PATIENT-DERIVED HEAD AND NECK SQUAMOUS CELL CARCINOMA

Siao-Yi Wang, M.D., Ph.D., Assistant Professor, Division of Hematology and Oncology

Recurrent or metastatic (R/M) head and neck squamous cell carcinoma (HNSCC) patients have a poor prognosis with median overall survival between six and 15 months. Recently, immune checkpoint inhibitors alone or in combination with chemotherapy have become standard of care for R/M HNSCC. However, response rates range between 17-36% and a vast majority of patients progress while on treatment. Adoptive cellular therapy has become an exciting method to treat malignant disease, but success for HNSCC has been limited. This is most likely due to the unique immunosuppressive tumor microenvironment (TME) in HNSCC. Patient-derived xenograft (PDX) models of HNSCC have been generated to preserve tumor heterogeneity in human disease and replicate the TME. However, PDX models rely on an immunodeficient host for tumor growth, which is suboptimal for evaluating immunotherapies. In these studies, we implanted PDX tumors from HNSCC patients in mice engrafted with human hematopoietic stem cells (HSCs) to generate the first humanized HNSCC-specific model for cellular therapy. We used a high-resolution spatial profiling platform to evaluate the tumors and

demonstrate the presence of human immune cell components of the TME. Gene expression analysis on a single-cell level confirmed the presence of tumor associated macrophages (TAMs), myeloid-derived suppressor cells (MDSCs), and regulatory T cells (Tregs). In addition, we detect a diverse population of T cells and assess expression of genes associated with immune effector function and proliferation. This model is currently being used to evaluate the effects of the TME on chimeric antigen receptor (CAR) T cells and autologous tumor infiltrating lymphocytes (TIL) therapy. It is expected that these studies will expand our understanding of interactions between therapeutic T cells and HNSCC tumors, leading to the development of future therapies with improved efficacy.

POSTER AND EXHIBIT ABSTRACTS (THURSDAY)

(Listed alphabetically by the last name of the presenting author.)

PT-01: DIET-INDUCED MICROBIOME ALTERATIONS ACCELERATE HEAD AND NECK SQUAMOUS CELL CARCINOMA PROGRESSION IN MURINE MODELS

Anastasia E. Abello, Graduate Student[1,3], Yu-Jui Yvonne Wan[1,3], Andrew C. Birkeland[2,3], Karleen Meiklejohn[1], Jack Goon[1,3], and Xiao-Jing Wang[1,3]
[1]Department of Pathology and Laboratory Medicine, UC Davis, Sacramento, CA; [2]Department of Otolaryngology Head and Neck Surgery, UC Davis, Sacramento, CA; [3]UC Davis Comprehensive Cancer Center, Sacramento, CA

Head and Neck Squamous Cell Carcinoma (HNSCC) is associated with high morbidity and mortality. A Western Diet (WD) has been shown to promote cancer progression by inducing inflammation and immunosuppression. We developed an SCC murine cell line derived from a gain-of-function KrasG12D mutation and deletion of the Smad4 tumor suppressor in keratin (K15)-positive stem cells, closely mimicking the clinical progression of HNSCC tumors. The SCC cells were orthotopically implanted into the buccal mucosa of mice. The mice started their respective diets on the day of tumor implantation, receiving either regular chow or WD. Saliva samples were collected weekly. At endpoint, tumors, saliva, cecum content, and plasma were collected for analysis. Metabolomic profiling, 16S rRNA sequencing, spatial transcriptomics, and immunostaining were performed on samples to elucidate mechanisms contributing to SCC progression. Oral tumor-bearing mice on a WD exhibit more aggressive tumor progression, as indicated by increased tumor volume and histopathological analysis, compared to those on a regular diet. Tumors in the WD group display an increased presence of cancer stem cell signatures relative to controls. Spatial transcriptomics revealed reduced macrophages and fibroblasts in the stroma of WD tumors, indicating diet-induced changes in the TME. Additionally, saliva samples from WD tumor-bearing hosts reveal distinct metabolite profiles of both host and microbial origin. Our findings indicate that a WD promotes a tumor-supportive microenvironment in HNSCC by altering the TME and metabolomic landscape, underscoring diet as a modifiable factor in HNSCC progression and a potential therapeutic target. (Supported by Diversity Supplement under HNSCC SPORE.)

PT-02: EX VIVO FLUORESCENCE LIFETIME IMAGING FOR CANCER CLASSIFICATION IN HEAD AND NECK SURGICAL SPECIMENS

Mohamed Abul Hassan, Project Scientist[1,4], Karleen M Meiklejohn[2], Dorina Gui[2], Andrew Birkland[3,4], Laura Marcu[1,4]
[1]Department of Biomedical Engineering, UC Davis, Davis, CA; [2]Department of Pathology and Laboratory Medicine, UC Davis, Sacramento, CA; [3]Department of Otolaryngology-Head & Neck Surgery, UC Davis, Sacramento, CA; [4]UC Davis Comprehensive Cancer Center, Sacramento, CA

Accurate intraoperative margin assessment in head and neck (H&N) cancer surgery remains a significant clinical challenge, often contributing to incomplete resections and local recurrence. This study presents a machine learning framework leveraging ex vivo fluorescence lifetime imaging (FLIm) for tissue classification in H&N surgical specimens from the oral cavity and oropharynx. Using a point-scanning fiber-based FLIm system, each scan generates point-wise optical data encompassing average fluorescence lifetime, intensity ratios, and Laguerre coefficients across three spectral channels. The x–y location of each point is spatially registered to a corresponding white light image, enabling spatially localized tissue characterization.
Classification models were developed to distinguish malignant from benign tissue using features extracted from each FLIm point. Both point-level and sample-level predictions were evaluated, with all outcomes validated against standard histopathology. To enhance model robustness under potential label noise inherent to clinical tissue handling, we employed a data-centric learning strategy incorporating label pruning and confidence-based filtering. This approach yielded a high classification performance, achieving an area under the ROC curve (AUC) of 0.94 for cancer vs. benign discrimination.

Our results demonstrate the potential of FLIm-based classification as a rapid, label-free adjunct to histopathology, offering real-time feedback for surgical guidance. Integration of this optical platform into the clinical workflow could help reduce dependence on frozen sections, streamline intraoperative decision-making, and improve oncologic outcomes in head and neck cancer care.

PT-03: FLUORESCENCE LIFETIME SENSITIVITY TO IMMUNE INFILTRATION DURING GLIOMA RESECTION SURGERY

Alexandra C. Adams, Postdoctoral Scholar[1], Alba Alfonso-Garcia[1,4], Silvia Noble Anbunesan[1,4], Lisanne Kraft[1], Julien Bec[1], Han Sung Lee[2], Orin Bloch[3,4], Laura Marcu[1,3,4]
[1]Department of Biomedical Engineering, UC Davis, Davis, CA; [2]Department of Pathology and Laboratory Medicine, UC Davis, Sacramento, CA; [3]Department of Neurological Surgery, UC Davis, Sacramento, CA; [4]UC Davis Comprehensive Cancer Center, Sacramento, CA

Background: Glioblastoma multiforme (GBM) represents the most aggressive brain tumor with a 6% 5-year survival rate. Up to 30% of the tumor cellular mass comprises tumor-associated macrophages, and high macrophage burden correlates with poor prognosis and chemotherapy resistance. However, current inflammatory cell detection relies on histopathology. Fluorescence lifetime imaging (FLIm) provides label-free intraoperative brain tumor identification and can differentiate immune cell phenotypes. This study assesses whether FLIm is sensitive to both tumor and immune cell infiltration during craniotomy in vivo.

Method: A total of 402 surgical margins were measured from 67 patients undergoing craniotomy with FLIm (470/28nm fluorescence emission). Microbiopsies were obtained and analyzed by clinical histopathologist, recording tumor cellularity, and immune cell presence. Median fluorescence lifetime values per margin were tested using linear mixed-effects regression.

Results: Fluorescence lifetime increased, independent of tissue type or tumor cellularity, in the presence of inflammatory cells. This was statistically significant in white matter (estimate: 0.57ns, p=<0.0001), and showed trending effects in cortex (estimate: 0.52ns, p=0.1), although limited by small sample size (cortex without/with inflammatory cells: n=80/4). The model demonstrated strong discriminatory capability, explaining 44% of fluorescence lifetime variance.

Conclusion: GBM's poor prognosis is partly attributed to immune suppression, yet current intraoperative assessments cannot characterize immune populations in-situ. We demonstrate fluorescence lifetime to reliably detect inflammatory cell infiltration in vivo during craniotomy. Our findings establish FLIm as a label-free, in-situ tool capable of identifying tumors with inflammatory cell infiltration during surgery, providing immediate information that could both diagnose and guide therapeutic decisions.

PT-04: BRD2 UPREGULATION AS A PAN-CANCER ADAPTIVE RESISTANCE MECHANISM TO BET INHIBITION

Suyakarn Archasappawat, Graduate Student[1,2], Juliette Jacques[1], EunJung Lee[1], Chang-il Hwang[1,2]
[1]Department of Microbiology and Molecular Genetics, UC Davis, Davis, CA; [2]UC Davis Comprehensive Cancer Center, Sacramento, CA

Bromodomain and extraterminal motif (BET) inhibitors, such as JQ1, are promising cancer therapeutics that target epigenetic regulators, particularly BRD4. However, resistance to BET inhibitors limits their clinical utility, necessitating a better understanding of adaptive mechanisms. We identified BRD2 upregulation as a conserved response to BET inhibition across multiple cancer types and hypothesized that BRD2 compensates for BRD4 loss, sustaining essential transcriptional programs during treatment. Consistent with this, BRD2 knockdown sensitized cancer cells to BET inhibitors in vitro, and combining BRD2 depletion and JQ1 treatment significantly impaired tumor growth in vivo. At the chromatin level, BRD2 and BRD4 ChIP-seq analysis of pancreatic cancer cells showed consistent BRD4 loss from chromatin after JQ1 treatment, while BRD2 displacement differed by sensitivity. Resistant cells maintained higher BRD2 occupancy than sensitive cells, suggesting a link between

BRD2 retention and drug response. To dissect the underlying mechanism of BRD2 upregulation upon BET inhibition, we analyzed co-expression networks and observed that NFYA is co-expressed with BRD2 across diverse tissues and cancer types. Consistently, NFYA binds the BRD2 promoter. NFYA depletion abrogated BRD2 upregulation upon BET inhibitor treatment, indicating that NFYA is required for BRD2 induction following BET inhibition. Collectively, our findings establish BRD2 as a critical mediator of adaptive resistance to BET inhibitors in pan-cancer and identify NFYA as a novel transcriptional regulator of this process. Co-targeting BRD2 or its regulatory network offers a rational strategy to enhance the durability and efficacy of BET-based therapies.

PT-05: DEVELOPMENT OF PHOTOACOUSTIC NANOSENSOR FOR THE DETECTION OF GRANZYME B IN RESPONSE TO NATURAL KILLER CELL IMMUNOTHERAPY

Brendan R. Barlow, Graduate Student[1], Tasneem Mukarrama[1], Anika Kulkarni[1,2], Ana Sandoval-Castellanos[1], Ruiwu Liu[3], Myeongsoo Kim[4], Robert J. Canter[1,5], Jinhwan Kim[1,2,5]
[1]Department of Surgery, School of Medicine, UC Davis, Sacramento, CA; [2]Department of Biomedical Engineering, UC Davis, Davis, CA; [3]Department of Biochemistry and Molecular Medicine, UC Davis, Sacramento, CA; [4]Wallace H. Coulter Department of Biomedical Engineering, Georgia Institute of Technology and Emory University School of Medicine, Atlanta, GA; [5]UC Davis Comprehensive Cancer Center, Sacramento, CA

Introduction: Adoptive natural killer (NK) cell therapy holds significant potential as an off-the-shelf cancer immunotherapy. Yet noninvasive, real-time assessment of the infused NK cell activity within the tumor micro environment (TME) remains unexplored. To address this barrier, we have engineered a gold nanoparticle-based photoacoustic nanosensor that responds to the enzyme granzyme B (GzmB), a key cytotoxic protease released by activated NK cells. Integrated with noninvasive ultrasound-guided photoacoustic (US/PA) imaging, the nanosensor enables longitudinal monitoring of NK cell activity within the TME.
Methods: Gold nanospheres (GNSs) were coated with a GzmB-cleavable peptide sequence to induce GzmB-responsive PA signal changes. The sensitivity and selectivity of the nanosensor was assessed by incubating the sensor with known concentrations of GzmB and other catalytic enzymes, followed by measuring PA signal changes. The function of the nanosensor in response to GzmB released by NK cells was assessed by co-incubation of soft tissue sarcoma cell lines and NK-92, followed by measuring PA signal.

Results: When incubated with soft tissue sarcoma cell lines treated with NK-92 cells, our nanosensor produced a measurable shift in PA signal. No PA signal changes occurred in the presence of untreated sarcoma cells or NK-92 only, indicating the nanosensor was specifically responding to the presence of GzmB from cytotoxic NK cells in the environment.

Conclusion: These results show that our GzmB nanosensor can detect NK cell activity in vitro, which could serve as a valuable tool for real-time, noninvasive monitoring of adoptive NK cell therapy with further in vivo testing.

PT-06: TARGETING CANINE BLADDER CANCER WITH NIMBOLIDE, A NEEM (AZADIRACHTA INDICA) LIMONOID

Neelu Batra, Associate Specialist[1,2], Conner N. Suen[1,3,7], Avani R. Durve[1,3], Ustat Kaur[1,4], Kenneth A Iczkowski[5,7], Robert B Rebhun[6,7], Christopher A. Lucchesi[1,3,7], Paramita M. Ghosh[1,2,3,7]
[1]VA Northern California Health Care System, Mather, CA; [2]Department of Biochemistry and Molecular Medicine, UC Davis, Sacramento, CA; [3]Department of Urologic Surgery, UC Davis, Sacramento, CA; [4]Department of Neurobiology, Physiology and Behavior, UC Davis, Davis, CA; [5]Department of Pathology and Laboratory Medicine, UC Davis, Sacramento, CA; [6]Department of Surgical and Radiological Sciences, UC Davis, Davis, CA; [7]UC Davis Comprehensive Cancer Center, Sacramento, CA

The 5-year relative survival rate for Bladder Cancer (BlCa) patients with distant metastases is about 9% (1). Hence, novel and innovative therapies for metastatic BlCa are required. Dogs were found to develop muscle-invasive BlCa (MIBC) spontaneously and 10% progress to distant metastases at the time of diagnoses (2). Currently most dogs with MIBC are treated with non-steroidal anti-inflammatory drugs (NSAIDs); however, <25%

respond to them (3). Our quest was to identify low-cost natural compounds of low toxicity that can be used in dogs. Nimbolide, a limonoid extracted from Neem leaves, was found to have anti-tumor effects in human BlCa cell lines (4). Hence, we tested whether this natural product will be effective in two canine BlCa lines –K9TCC-PU-AXC (AXC), that formed tumors in nude mice and K9TCC-PU-Pu (PuPu), which did not (5). Nimbolide was more effective in suppressing proliferation in PuPu cells (IC50 = 0.656 μM) compared to AXC cells (IC50 = 1.2 μM). Flow cytometric analysis showed that AXC did not undergo apoptosis in response to nimbolide whereas PuPu did; however, nimbolide caused autophagy in both cells. On the other hand, nimbolide prevented epithelial mesenchymal transition (EMT) and migration in AXC, but not in PuPu cells. These effects of nimbolide were not seen in human dermal fibroblasts, underlining the specificity and selectivity of nimbolide. Based on these results, we intend to develop nimbolide as a therapeutic tool in the treatment of canine BlCa in future studies.

PT-07: HIGH VARIATION OF INPATIENT ADMISSION RATES BETWEEN HOSPITALS FOR CANCER-ASSOCIATED PULMONARY EMBOLISM IN CALIFORNIA

Ann Brunson, Research Data Analyst[1], Kavya Babu[1], Anjlee Mahajan[1], Oyebimpe Adesina[1], Ted Wun[1,2]
[1]Center for Oncology Hematology Outcomes Research and Training (COHORT), Division of Hematology and Oncology, UC Davis, Sacramento, CA; [2]UC Davis Comprehensive Cancer Center, Sacramento, CA

Introduction: Patients with pulmonary embolism (PE) at low risk for 30-day mortality by the Pulmonary Embolism Severity Index (PESI) can be safely managed as outpatients. However, it is unknown if this applies to cancer patients.

Methods: Using California Cancer Registry data linked with statewide emergency department (ED) and hospitalization data, we identified adults with active cancer and PE seen in EDs between 2009-2018. The primary outcome was admission to the hospital. We used descriptive statistics and multivariable hierarchical regression to predict inpatient admission.

Results: We identified 17798 PEs among 14763 patients with active cancer. Among the 325 facilities analyzed, the median admission rates decreased over time: 88.9% in 2009-2011, 80.6% in 2012- 2014, and 73.9% in 2015-2019. In the hierarchical models, facilities accounted for 17.5% of the variability in the admission rate. Urban (odds ratio [OR] 2.64, 95% confidence internal [CI] 2.11-3.30) and non-Kaiser teaching hospitals (OR 2.59, CI 1.87-3.60) were more likely to admit patients compared to Kaiser facilities. Metastatic cancer (OR 1.12, CI 1.02-1.22), concurrent proximal DVT (OR 3.81, CI 3.22-4.52), and recent major surgery (OR 1.39, CI 1.25-1.55) were associated with increased likelihood of admission. Compared to patients with private insurance, those with Medicare (OR 8.52, CI 7.50-9.67) and other public insurance (OR 2.35, CI 2.03-2.71) were more likely admitted, whereas uninsured patients were less likely admitted (OR 0.68, CI 0.49-0.94).

Conclusions: There was wide variation between hospitals in admission rates for patients with CA-PE, suggesting local practice patterns in addition to risk score are contributing factors.

PT-08: CHARACTERIZING ROS-ASSOCIATED CYTOTOXICITY IN EMERGING NECROSIS-INDUCING COMPOUNDS

Noemi Castro, Graduate Student[1], Michelle Hu[1], Anastasia Berg[1], Ruiwi Liu[1,2], Kit Lam[1,2], and Kermit Carraway[1,2]
[1]Department of Biochemistry and Molecular Medicine, UC Davis, Sacramento, CA; [2]UC Davis Comprehensive Cancer Center, Sacramento, CA

Drug resistance leading to cancer recurrence poses a particularly challenging barrier to clinical disease management. Since tumor cells commonly activate anti-apoptotic pathways that cause caspase-dependent pathways to malfunction, cellular resistance to apoptosis is perhaps the most critical factor contributing to the therapeutic failure of conventional and targeted therapeutic agents. Consequently, subpopulations of apoptosis-resistant cells, such as cancer stem cells (CSCs), persist after therapy to seed primary tumor recurrence and metastatic lesions, even after complete remission. The overarching goal of this project is to develop novel drugs

that exploit the process of lysosome-dependent cell death, a programmed necrotic cell death mechanism, in suppressing CSC-mediated triple-negative breast cancer. We have previously observed that hexamethylene amiloride (HMA), a derivative of the FDA-approved diuretic amiloride, is cytotoxic in vitro and ex vivo toward cultured cells from a variety of tumor types but not non-transformed cells. HMA also suppresses primary and metastatic tumor outgrowth in vivo. It can act on breast tumor cells regardless of subtype, proliferative status, or species of origin. HMA engages a potent caspase- and autophagy-independent programmed necrotic death mechanism in tumor cells that alters lysosome structure, dysregulates lipid synthesis, leads to lysosomal membrane permeabilization, and acts efficiently toward therapy-resistant CSC-related subpopulations. Although some specifics of the mechanism remain unknown, we examine how the formation of reactive oxygen species is crucial to the induction of necrosis and the potency of HMA and other amiloride derivatives.

PT-09: INTERROGATING THE ROLE OF CD101 AS A NOVEL IMMUNE CHECKPOINT IN HEAD AND NECK CANCER

Brenna Champlin, Medical Student[1], Jack Goon[2,6], Andrew Birkeland[3,6], X.J. Wang[4,6], Shiruyeh Schokrpur[5,6]
[1]UC Davis School of Medicine, Sacramento, CA; [2]Department of Pathology and Laboratory Medicine, UC Davis, Sacramento, CA; [3]Department of Otolaryngology – Head and Neck Surgery, UC Davis, Sacramento, CA;, [4]Department of Pathology and Laboratory Medicine, UC Davis, Sacramento, CA; [5]Division of Hematology and Oncology, UC Davis, Sacramento, CA; [6]UC Davis Comprehensive Cancer Center, Sacramento, CA

Immune checkpoint blockade (ICB) has transformed treatment for head and neck squamous cell carcinoma (HNSCC), yet most patients fail to derive durable benefit. Emerging evidence suggests that CD101, an inhibitory immune marker expressed on multiple immunosuppressive immune cell subsets, may be a potential regulator of resistance to ICB. We seek to investigate the role of CD101 as a novel biomarker and therapeutic target in HNSCC. We first evaluated CD101 protein expression in archival head and neck tumor specimens using single-cell RNA sequencing (sc-RNA-seq) to identify the cell types expressing the highest levels of this marker. We found that CD8+ T cells, monocytes, macrophages, regulatory T cells and dendritic cells exhibited the highest levels of CD101 across immune cells in human HNSCC and the murine A223 model. We plan to utilize preclinical models of squamous cell carcinoma in CD101 knockout mice to determine whether loss of CD101 enhances responsiveness to anti-PD-L1 therapy. Tumor growth, survival, and immune infiltrate composition will be assessed. Furthermore, we will utilize digital spatial profiling to evaluate clinical head and neck sample regions with highest expression of CD101 for correlation with gene profiles consistent with immunosuppression. Collectively, this work proposes CD101 as a conserved regulator of immune suppression and resistance to ICB, with potential to stratify patients for immunotherapy and guide the development of combinatorial treatment strategies. Findings may extend beyond HNSCC and reshape how we identify and overcome immunotherapy resistance.

PT-10: Z-SPECTRA LINEWIDTH BROADENING AND EXCHANGE RATE CHANGE AS A TOOL FOR HYDROXYL (-OH) CEST MRI ANALYSIS

Md Saiful I. Chowdhury, Postdoctoral Scholar[1,2], Sakunrat Prompalit[1], Yanyu Huang[2], Menghuan Tang[2], Yuanpei Li[2,3], Felipe Godinez[1,3]
[1]Department of Radiology, UC Davis, Sacramento, CA; [2]Department of Biochemistry and Molecular Medicine, UC Davis, Sacramento, CA; [3]UC Davis Comprehensive Cancer Center, Sacramento, CA

Introduction- A higher exchange rate of hydroxyl (-OH) proton-containing Chemical exchange saturation transfer (CEST) MRI agents makes their detection difficult at low field MRI using an asymmetry-based approach. Linewidth broadening (Δω) on the Z-spectra from the direct water saturation (WASSR peak) and exchange rate (kex) mapping could be a solution for the -OH containing agents in place of asymmetry. Natural hydroxyl (-OH) CEST agents are generally safe and biodegradable.

Method- DSPE-PEG2K-NH2 amine was coupled with lysine(K) and Maltobionic Acid molecules to make the amphiphilic CEST agent with exchangeable -OH its polar head and was integrated into liposomal nanoparticles. Aqueous solutions of MA at different concentrations and pH were prepared. CEST MRI scans were completed

using Bruker BioSpec 7T MRI. A change in full width at half maxima (FWHM) was used to measure the linewidth broadening. An orthotropic CT-2A (GFP/Luc) orthotopic glioma tumored mouse model in the brain has been established and studied for Δω and Kex.

Results- Z-spectra at five B1 fields were collected. The omega plot method was used to obtain Kex values (around 1000 Hz) for MA-containing liposomes. A proportional increase in Δω with the concentration of -OH proton was found at 7T. A significant change in linewidth broadening was observed between tumor and non-tumor regions with and without CEST agents.

Discussion and conclusion- Linewidth change and Kex mapping of CEST agents containing -OH can give valuable insights for MRI analysis. Adding MA to the polar head of amphiphilic lipids provides GLUT1 targeting alongside the Warburg effect.

PT-11: CHARACTERIZING RESPONSE TO PARP INHIBITOR TREATMENT COMBINATION IN ADVANCED PROSTATE CANCER

Bryan Correa Gonzalez, Undergraduate Student[1,3], Akshaya Karthikeyan[1], Love A. Moore[1,3], Anamitra Bhaumik[1], Ethan Sandoval[1], Alan P. Lombard[2,3]
[1]Department of Biochemistry and Molecular Medicine, UC Davis, Sacramento, CA; [2]Department of Urologic Surgery, UC Davis, Sacramento, CA; [3]UC Davis Comprehensive Cancer Center, Sacramento, CA

Combining poly (ADP-ribose) polymerase inhibitors (PARPis) with androgen receptor pathway inhibitors (ARPis) has improved management of metastatic castration-resistant prostate cancer (mCRPC) but questions remain regarding the current clinical landscape and how these agents work in combination. Our work suggests previous exposure to an ARPi does not preclude a benefit from combination treatment, but that the effect is greatest in ARPi-naïve cells. Despite a decrease in cellular viability, morphological and biochemical analysis of treated cells reveals a largely cytostatic response. Transcriptomic analysis suggests current hypotheses explaining the mechanism of combination efficacy may be incomplete. Our data do not support that ARPis induce significant BRCAness nor that PARPis reduce AR activity. Given that ARPi and PARPi combination may be less effective post ARPi exposure, we sought an alternative which may be more effective in this setting. Our work suggests that PARPis induce a robust, ATM-driven DNA damage response, and that co-targeting ATM elicits a synergistic reduction in cellular viability. Co-inhibition of ATM and PARP is much more effective than ARPi containing combinations in models of ARPi-resistant mCRPC. Our work suggests that 1) ARPi and PARPi combinations may be most effective earlier in the treatment paradigm, 2) more work is needed to understand ARPi and PARPi combination efficacy, and 3) ATM inhibition may be better in combination with a PARPi in more advanced settings. More work is needed to understand how these drugs work together and when best to administer them given the rapidly evolving prostate cancer treatment paradigm.

PT-12: RARE BUT REAL: A CASE SERIES OF METASTATIC MENINGIOMA WITH SYSTEMIC INVOLVEMENT

Alexander Del Bosque, Graduate Student[1], Muhammad Sulman, Medical Student[2], John Paul Aboubechara[1,4], Orwa Aboud[3,4]
[1]Department of Neurology, UC Davis, Sacramento, CA; [2]School of Medicine, UC Davis, Sacramento, CA; [3]Department of Neurological Surgery,UC Davis, Sacramento, CA; [4]UC Davis Comprehensive Cancer Center, Sacramento, CA

Background: Meningiomas are typically benign, slow-growing tumors originating from the meninges arachnoid cells. Most meningiomas stay in the cranial or spinal regions, but less than 1% metastasize outside the Central Nervous System (CNS), mainly Grade 2/3 cases, spreading to the lungs, liver, and pleura. Data is limited due to rarity. We present a case series from our institution.

Methods: From 2012-2024, we conducted a retrospective review of patients with brain tumors from our EMR database. We found 2888 patients with meningiomas. Six of whom developed metastatic meningiomas. Clinical

data, including imaging, biopsy results, and surgical outcomes, were reviewed, focusing on genomic details, histopathology, disease progression, and treatment.

Results: Among the six patients with metastatic meningiomas, two had Grade 2 atypical meningiomas, and four had Grade 3 anaplastic meningiomas. Metastases occurred to the scalp and orbit (1
case), parotid gland (1 case), vertebra (3 cases), liver (1 case), lungs (1 case) and neck (1 case). Imaging (CT, MRI, PET-CT) and follow-up biopsies confirmed meningioma origin of metastases except in one patient. These patients received multiple surgical resections, chemotherapy, targeted therapy (everolimus, Ixazomib, and tazemetostat), and localized radiation. Mutations in MTAP, BRACA-1 associated protein-1, CDKN2A/B, and H3K27me3 were noted during the molecular analysis. Despite aggressive treatment, three patients experienced disease progression and died, while the others showed partial response to therapy. Survival averaged 110 months from diagnosis, dropping to 26 months post-metastasis despite aggressive treatment.

Conclusion: Extra CNS metastatic meningiomas, while rare, pose significant diagnostic and therapeutic challenges. High-grade meningiomas are more likely to metastasize; early detection of metastatic spread is challenging. Our findings highlight the need for close follow-up and vigilance for distant metastasis, especially in recurrent or high-grade meningiomas with distinct mutations.

PT-13: LATE EFFECTS IN ADOLESCENT AND YOUNG ADULT SURVIVORS OF COLORECTAL CANCER

Diego Del Toro Rivera, Graduate Student[1,11], Qian Li[2], Anne C. Kirchhoff[3,4], Renata Abrahão[2,11], Ann Brunson[2], Jessica Chubak[5,6], Erin E. Hahn[7], Alex Zhornitskiy[2,11], Chun Chao[7], Hazel B. Nichols[8], Candice A. Sauder[2,11], Kathryn J. Ruddy[9,10] Theresa H.M. Keegan[2,11]
[1]Department of Internal Medicine, UC Davis, Sacramento, CA; [2]Department of Public Health Sciences, UC Davis, Sacramento, CA; [3]Department of Pediatrics, University of Utah, Salt Lake City, UT; [4]Huntsman Cancer Institute, University of Utah, Salt Lake City, UT; [5]UCLA, [6]Kaiser Permanente Washington Health Research Institute, Seattle, WA; [7]Department of Research and Evaluation, Kaiser Permanente Southern California, Pasadena, CA; [8]Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina, Chapel Hill, NC; [9]Dana-Farber Cancer Institute, Boston, MA; [10]Department of Oncology at Mayo Clinic, Rochester, MN; [11]UC Davis Comprehensive Cancer Center, Sacramento, CA

Introduction: Colorectal cancer (CRC) incidence is increasing among adolescents and young adults (AYA, 15-39 years), resulting in a growing number of CRC survivors at-risk for late effects from their cancer treatment or late medical conditions (late effects). However, there are limited studies examining late effects in this population.

Methods: We examined clinical and sociodemographic factors associated with late effects among AYAs diagnosed with CRC from 2006-2018 who survived ≥2 years. Data were obtained from statewide California and Utah Cancer Registries linked to hospitalization, emergency department, and ambulatory surgery databases. We present 5-year cumulative incidence of seven late effects and examine associations between survivor characteristics with each late effect using Cox proportional hazard regression.

Results: Among 3,508 survivors, the incidence was highest for liver (7.12%), cardiovascular (6.46%), and respiratory (6.14%) diseases. Non-Hispanic Black (vs non-Hispanic White) survivors had a higher risk for venous thromboembolism (VTE) (Hazard Ratio (HR)=2.65, 95% confidence interval (CI):1.55-4.55) and renal disease (HR=2.75, CI=1.51-4.99). Survivors with public (vs private/military) insurance at diagnosis/initial treatment had a greater risk of cardiovascular (HR=1.54, CI=1.18-2.01), VTE (HR=1.86, CI=1.25-2.76), respiratory (HR=1.40, CI=1.06-1.86), and renal (HR=1.70, CI=1.14-2.54) diseases, and second cancer (HR=1.83, CI=1.29-2.61). Those with stage IV (vs stage I) and who received chemotherapy had a greater risk of VTE and liver disease; risk of renal disease was higher among those who received radiation.

Conclusions: Findings from this study identify CRC survivors at higher risk for late effects, highlighting the need for early detection and improved follow-up care for these populations.

Research reported in this publication was supported by the National Cancer Institute of the National Institutes of Health under Award Number P01CA233432 and 3P01CA233432-05S1.

This research was supported by the Utah Cancer Registry, which is funded by the National Cancer Institute's SEER Program (Contract HHSN261201800016I), the US Center for Disease Control and Prevention's National Program of Cancer Registries (Cooperative Agreement No. NU58DP007131). Partial support for all UPDB datasets is provided by the University of Utah, Huntsman Cancer Institute and the Huntsman Cancer Institute Cancer Center Support grant (NCI P30 CA42014). Research was also supported by the NCRR grant, "Sharing Statewide Health Data for Genetic Research" (R01 RR021746, G. Mineau, PI) with additional support from the Utah Department of Health and the University of Utah.

The collection of cancer incidence data used in this study was supported by the California Department of Public Health pursuant to California Health and Safety Code Section 103885; Centers for Disease Control and Prevention's (CDC) National Program of Cancer Registries, under cooperative agreement 5NU58DP006344; the National Cancer Institute's SEER Program under contract HHSN261201800032I awarded to the University of California, San Francisco, contract HHSN261201800015I awarded to the University of Southern California, and contract HHSN261201800009I awarded to the Public Health Institute.

PT-14: UNDERSTANDING THE ROLE OF TUMOR SUPPRESSOR GENE ARID1A IN GASTRIC CANCER DEVELOPMENT AND THERAPEUTIC RESPONSE

Jasmine Diaz, Junior Specialist[1], Nicole B. Halmai[1], Alexa Morales Arana[1,2], Hongyong Zhang[1], Paul C. Lott[1], Ana Estrada-Florez[1], Luis G. Carvajal-Carmona[1,2,3]
[1]Genome Center, UC Davis, Davis, CA; [2]Department of Biochemistry and Molecular Medicine, UC Davis, Sacramento, CA [3]UC Davis Comprehensive Cancer Center, Sacramento, CA

Gastric cancer (GC) is a leading cause of cancer-related deaths worldwide. While more recent incidence and mortality rates have dropped, GC remains a significant cause of health disparities for many underserved and under-resourced communities in the US, including racial and ethnic minorities. Despite a high minority cancer burden, few FDA-approved targeted therapies are available for GC. This can be partially explained by limited availability of cancer genomic data and patient-derived models from diverse populations, which hamper therapeutic target identification and drug efficacy studies. To address this, our group has spearheaded two patient-derived xenograft and organoid development and trial centers to generate and characterize preclinical models of GC that are representative of the patient population. Genomic sequencing of a Latino GC cohort revealed over 30% of tumors harbored pathogenic mutations in the tumor suppressor gene, ARID1A. This is comparable to frequencies observed in TCGA, suggesting that ARID1A may be a bona fide driver of GC. ARID1A functions within the SWI/SNF (BAF) chromatin remodeling complex to regulate chromatin accessibility. We performed Cut-and-Run and RNA-Seq to identify chromatin-mediated alterations in gene expression in Latino patient-derived organoids with ARID1A mutations vs those with wildtype ARID1A, and in normal gastric organoids that we engineered with ARID1A knockout mutations using CRISPR/Cas9 compared unedited normal gastric organoids. Analyses revealed significant alterations in multiple signaling pathways implicated in cancer proliferation and migration. To investigate sensitivity to inhibitors targeting altered pathways, we then performed drug response screens in these models with targeted inhibitors against PARP enzymes (PARPi) and PI3K/Akt (PI3Ki, AKTi) pathway. Results revealed varied vulnerability against individual targeted inhibitors, which we are actively testing in combination for greater efficacy. These studies address critical knowledge gaps in ARID1A-related tumor biology and may inform precision medicine approaches in an underserved and disproportionately affected population.

PT-15: CD57 IS PROGNOSTIC FOR HEAD AND NECK SQUAMOUS CELL CARCINOMA PATIENTS TREATED WITH RADIATION THERAPY, WHICH INDUCES CANCER CELL IMMUNOGENICITY IN PRECLINICAL MODELS

Jack B. Goon, Graduate Student[1,4], Hanne T. Lind[1,4], John D. Aleman[1,2], Zachary R. Wilcox[3]; Xiao-Jing Wang[1,2,4]
[1]Department of Pathology and Laboratory Medicine, UC Davis, Sacramento, CA; [2]Department of Pathology, University of Colorado Anschutz Medical Campus, Aurora, CO; [3]Department of Chemistry, Stony Brook University, Stony Brook, NY; [4]UC Davis Comprehensive Cancer Center, Sacramento, CA

Advanced head and neck squamous cell carcinoma (HNSCC) patients have poor prognosis in part due to insufficient anti-tumor immune responses. Radiation therapy (RT) is a promising combination partner for immune checkpoint inhibitors (ICIs) to treat HNSCC due to its inflammatory properties, though underlying mechanisms are only partially understood. To investigate which pre-treatment tumors successfully respond to RT, we investigated The Cancer Genome Atlas HNSCC database which revealed that pre-treatment expression of CD57, a marker for natural killer (NK) cell maturation, positively correlated with overall survival in RT-treated patients. To investigate potential mechanisms behind this, we employed two immune-competent mouse models to study NK cell responses +/- RT: one which responds to RT with increased survival (responder), and one which does not (non-responder). We conducted in vitro experiments where cell lines from both models were treated +/- 10 Gray RT and rested for 48 hours prior to either single cell RNA sequencing (scRNAseq) or co-culture with syngeneic mouse splenocytes. scRNAseq revealed that RT increased the expression of ligands for the activating receptor NKG2D in the responder cells, as well as Irf3 transcription factor activity. These changes were not observed in the non-responder cells. Co-culture experiments revealed that RT induced NK cell activation against responder cells as determined by CD107A surface expression. These studies support the prognostic value of mature NK cell infiltration in HNSCC tumors to be treated with RT and show that RT can improve cancer cell immunogenicity, which may underly the prognostic value of NK cells.

PT-16: TOWARD PRECISION NANOMEDICINE FOR GLIOMA: STICK-LNPS FACILITATE SEQUENTIAL TARGETING ACROSS THE BLOOD-BRAIN BARRIER AND TUMOR

Yanyu Huang, Associate Specialist[1], Menghuan Tang[1], Qiufang Zong[1], Ruohao Fan[1], Nhung Au[1], Kelsey Racacho[1,2], Saiful Islam Chowdhury[1,2], Tzu-Yin Lin[1,2], Yuanpei Li[1,2]
[1]Department of Biochemistry and Molecular Medicine, UC Davis, Sacramento, CA; [2]UC Davis Comprehensive Cancer Center, Sacramento, CA

Glioma is one of the most aggressive and lethal brain tumors, marked by poor prognosis and resistance to conventional therapies. To address the challenges of drug delivery across the blood–brain barrier (BBB) and to achieve deep tumor penetration, we develop a novel lipid-based nanoplatform—Sequential Targeting In CrosslinKing (STICK) lipid nanoparticles (LNPs). These LNPs are constructed by lysine-branched lipids conjugated with maltobionic acid (MA, targets Glut1 on the BBB) and 3-(propionamido)phenylboronic acid (PAPBA, targets glioma cells), respectively. Vincristine (VCR), a chemotherapeutic agent with limited BBB permeability, was chosen as a model drug and encapsulated into STICK-LNPs via microfluidic synthesis, yielding uniform, stable, and scalable NPs. We evaluate the therapeutic efficacy and safety of free VCR and its nanoformulations—MA-LNPs@VCR, PAPBA-LNPs@VCR, and STICK-LNPs@VCR—in an orthotopic CT-2A glioma mouse model. Tumor progression is monitored using bioluminescence imaging and magnetic resonance imaging, while systemic toxicity is evaluated via histological analysis of major organs. Among all tested groups, STICK-LNPs@VCR demonstrates the most potent anti-glioma effects, significantly reducing tumor burden and prolonging survival. Importantly, all LNP formulations, including STICK-LNPs@VCR, exhibit no observable toxicity in major organs. These results highlight the advantages of dual-ligand targeting via MA and PAPBA, which synergistically enhance BBB penetration and glioma-specific localization. Overall, STICK-LNPs@VCR represents a safe and effective therapeutic platform with strong potential to overcome CNS drug delivery barriers and improve glioblastoma treatment outcomes.

PT-17: DETERMINING AGE-DEPENDENT DIFFERENCES IN BREAST CANCER TUMORIGENESIS DRIVEN BY CELLULAR AND MOLECULAR CHANGES IN THE TUMOR MICROENVIRONMENT

Ava Jessen, Graduate Student[1], Cesar Morfin[1,2], Nosisa Ncube[1], Thomas Ambrosi[1,2], Gabriela Loots[1,2]
[1]Department of Orthopaedic Surgery, UC Davis, Sacramento, CA; [2]UC Davis Comprehensive Cancer Center, Sacramento, CA

Breast cancer (BCa) is the second leading cause of cancer death in women in the USA. Approximately 20-30% of cases will develop metastatic BCa, characterized by highly aggressive tumorigenesis and therapeutic resistance. The formation of the pro-metastatic niche is mediated by two cell types in the tumor

microenvironment: immune cells and cancer-associated fibroblasts (CAFs) that release signaling molecules with the ability to remodel the extracellular matrix to support metastasis. The average age at the time of BCa diagnosis is 62, yet most animal research is carried out in young mice.

To elucidate the age-dependent contributions of the stromal environment to tumorigenesis and metastasis, E0771Luc cells were orthotopically implanted into young (6-10 weeks old) and old (22-month-old) female C57BL/6 mice. Tumor growth and in-vivo imaging to track metastasis was assessed 2x/week. Non-cancerous tissues along with primary and metastatic tumors were collected for histological assessment and spatial transcriptomics to compare immune and CAF populations between young and old mice. We found old mice to develop tumors 2-3x faster and had a higher metastatic burden than young mice. Additionally, we observed more immune infiltration in tumors of young mice, while primary tumors from the old mice were more fibrotic and had fewer immune cells. Further transcriptomic assessment will help determine what cell populations are significantly different and what cells in the stromal environment promote immune suppression. Identifying immune modulatory factors that affect immune therapy efficacy will help inform future immune checkpoint inhibitor intervention to improve therapeutic outcomes in women with aggressive breast tumors.

PT-18: PATIENT AND FAMILY-CENTERED CARE IN PEDIATRIC TRAUMA RECOVERY: A VOLUNTEER'S PERSPECTIVE FROM UC DAVIS MEDICAL CENTER

Amreen Kaur, Volunteer, UC Davis Medical Center, Sacramento, CA

As a volunteer in the Labor and Delivery and Burn Units at UC Davis Medical Center—and as a survivor of a traumatic car accident in 2022—I have developed a unique perspective on the role of trauma-informed, patient- and family-centered care in pediatric recovery. This poster explores how healthcare teams at UC Davis support not only the physical but also emotional and psychological healing of young patients and their families, especially in high-stress units such as burn care and neonatal/pediatric wards. Drawing from personal observations, volunteer experiences, and conversations with patients and staff, I identify key care practices that foster resilience, trust, and comfort—such as family integration in treatment decisions, play therapy, culturally sensitive care, and continuity of care.

I also propose a framework for future research to evaluate how volunteer programs and non-clinical support teams can enhance pediatric outcomes through empathy-driven care. By connecting personal narrative with current pediatric care models, this project highlights the value of lived experience and volunteer integration in supporting holistic recovery, especially in institutions serving trauma or cancer patients. The insights shared here may inform broader practices across pediatric care and community recovery strategies.

PT-19: PATIENT-DERIVED 3D BIOPRINTED TUMOROIDS ENABLE FUNCTIONAL IMMUNE AND DRUG RESPONSE PROFILING

Ustat Kaur, Undergraduate Student[1,3], Cayla Divodi[1], Neelu Batra[1,2], Conner N. Suen[1,3,4], Avani R. Durve[1,3], Paramita M. Ghosh[1,2,4], Christopher A. Lucchesi[1,4]
[1]VA Northern California Health Care System, Mather, CA; [2]Department of Biochemistry and Molecular Medicine, UC Davis, Sacramento, CA; [3]Department of Urologic Surgery, UC Davis, Sacramento, CA; [4]UC Davis Comprehensive Cancer Center, Sacramento, CA

Traditional tumor models—such as 2D cultures, animal models, and organoid systems—often fail to capture the complexity of the human tumor microenvironment (TME), limiting their utility in predicting immunotherapy outcomes. We have developed a patient-specific, 3D-bioprinted tumor platform that incorporates primary tumor cells, autologous immune cells, and stromal elements within a physiologically relevant extracellular matrix (ECM). This model recapitulates key features of the TME ex vivo, enabling functional assessment of therapeutic response.

Fresh tumor specimens and matched blood samples are processed immediately following surgical resection. Tumor cells are suspended in a collagen-based bioink and bioprinted into 96-well plates as 3D tumoroids.

Autologous PBMCs, drug treatments (e.g., androgen deprivation therapy for prostate cancer, immune checkpoint inhibitors for bladder cancer), and other modulators are then added. After 6 days of co-culture, cytostatic effects are measured by changes in tumoroid size and morphology, while cytotoxic effects are quantified using live/dead imaging and immune-mediated killing assays.

This platform enables direct observation of immune cell infiltration, cytokine dynamics, and tumor response in a patient-matched context. For prostate cancer, it can distinguish androgen-responsive from castration-resistant disease. In muscle-invasive bladder cancer (MIBC), it allows functional assessment of immune checkpoint inhibitor efficacy. The system is scalable, supports high-throughput screening, and can integrate multimeric analyses, offering a powerful tool for precision oncology.

PT-20: NET-MEDIATED B CELL REPROGRAMMING DRIVES IMMUNOSUPPRESSIVE TUMOR PROGRESSION IN ADVANCED OSCC

Yao Ke, Postdoctoral Scholar[1], Jack Brent Goon[1,6], John Aleman[2], Khoa A Nguyen[2], Scott Simon[3], Sean R. Collins[4,6], Yuanpei Li[5,6], Christian D. Young[2], and Xiao-Jing Wang[1,6]
[1]Department of Pathology and Laboratory Medicine, UC Davis, Sacramento, CA; [2]Department of Pathology, School of Medicine, University of Colorado, Anschutz Medical Campus, Aurora, CO; [3]Department of Biomedical Engineering, UC Davis, Davis, CA; [4]Department of Microbiology and Molecular Genetics, UC Davis, Davis, CA; [5]Department of Biochemistry and Molecular Medicine, UC Davis, Sacramento, CA; [6]UC Davis Comprehensive Cancer Center, Sacramento, CA

Oral squamous cell carcinoma (OSCC), the most prevalent subtype of head and neck squamous cell carcinoma (HNSCC), often progresses from premalignant lesions yet is diagnosed at an advanced stage in over 70% of patients, with a five-year survival rate declining from 87% (early-stage) to 39% (advanced-stage). A critical barrier to early intervention is the limited understanding of mechanisms that promote an immunosuppressive tumor microenvironment (TME). Recent studies implicate neutrophils and neutrophil extracellular traps (NETs) in driving tumor progression. Our preliminary data show that neutrophils in OSCC lesions predominantly undergo NETosis, a unique cell death process that releases chromatin fibers complexed with granular proteins. Elevated local NET burden is associated with more advanced OSCC. Co-transplantation of OSCC cells with neutrophils in immunocompetent mice accelerated tumor growth and promoted a NET-rich TME enriched with tumor-infiltrating B cells (TIBs). Transcriptomic analysis of The Cancer Genome Atlas (TCGA) supports these findings, where high NET gene signatures predict worse survival in HNSCC. Human single-cell RNA sequencing data reveal functional associations between neutrophils and B-cell subsets, with plasma-like B cells enriched in NET-low TMEs. Targeting the PI3Kγ pathway to inhibit neutrophil recruitment and NET formation significantly reduced disease severity and shifted TIBs toward an antibody-producing phenotype. We hypothesize that NET-mediated B cell recruitment and reprogramming contribute to immunosuppressive TME formation and OSCC progression. This project aims to define the spatial and mechanistic links between NETosis and B cell modulation, providing insights for early intervention in advanced OSCC.

PT-21: DIFFERENCES IN THE GENOMIC AND IMMUNOLOGIC LANDSCAPE BETWEEN PROSTATE CANCERS DIAGNOSED IN AFRICAN AMERICAN VS WHITE PATIENTS: RESULTS FROM A MULTIMODAL REAL-WORLD DATABASE

Tu C. Le, Medical Student[1], Nicholas Mitsiades[2,3]
[1]School of Medicine, UC Davis, Sacramento, CA; [2]Division of Hematology and Oncology; [3]UC Davis Comprehensive Cancer Center, Sacramento, CA

Introduction: Racial disparities in prostate cancer (PCa) can be attributed to socioeconomic and environmental factors. However, underlying biological differences may also contribute to disease progression and prognosis.

Methods: We identified 945 African American (AA) and 4,132 White men with PCa who underwent tumor tissue next-generation sequencing as part of the TEMPUS real-world nationwide database (Chicago, IL). Clinical

features, biomarker, immune cell infiltration profiles, somatic and germline alterations were compared between groups.

Results: Clinically, AA men with either localized (stage I–III) and advanced PCa (stage IV) were diagnosed at a younger age than White men (61 vs. 67 years and 64 vs. 68 years, respectively). AA patients also had higher tumor mutation burden (TMB) and more TMB-high cases (≥10 mutations/Mb), although the latter did not reach statistical significance. Immune profiling highlighted a more activated immune landscape in AA patients, with AA tumors having greater B-cell (↑26%) and NK-cell infiltration (↑9%), and higher neutrophils (↑18%) with lower Treg levels (↓22%). We also observed an elevated M2/M1 ratio in AA PCa tumors, suggesting a shift to a tumor-promoting microenvironment. SPOP, CDK12, and BRAF mutations were more prevalent in AA men, whereas PTEN mutations, TP53 mutations, and TMPRSS2-ERG fusions were less common. Conversely, germline testing showed a higher single nucleotide variant burden in White patients.

Conclusions: Elevated TMB, along with distinct immune and genomic features, may contribute to earlier onset and more aggressive PCa biology in AA men, highlighting the need for personalized treatment strategies and greater AA representation in studies.

PT-22: THE ROLE OF SHROOM3 DOWNSTREAM OF WNT/PCP SIGNALING IN BREAST CANCER METASTASIS

Julie Learn, Graduate Student[1], Kacey VanderVorst[1], Kermit Carraway[1,2]
[1]Department of Biochemistry and Molecular Medicine, UC Davis, Sacramento CA; [2]UC Davis Comprehensive Cancer Center, Sacramento, CA

The 5-year survival rate for patients diagnosed with metastatic breast cancer (BC) remains below 30%, highlighting the need to better understand the molecular mechanisms driving BC metastasis to develop more effective therapeutic strategies in the future. Wnt/Planar Cell Polarity (Wnt/PCP) is a non-canonical Wnt pathway that promotes global directional cues to produce locally polarized cell behavior, leading to increased cell motility, survival, and proliferation. Core Wnt/PCP components are frequently upregulated in aggressive BCs and our lab has demonstrated a role for Wnt/PCP signaling in mediating BC cell motility and metastasis. However, understanding of the mechanistic underpinnings linking core Wnt/PCP components to the cytoskeletal rearrangements that promote cell motility is limited. In a phosphoproteomics screen to identify proteins differentially phosphorylated in response to Wnt/PCP pathway activation in BC cells, our lab identified the protein Shroom3 (Shrm3). Shrm3 is an actin binding protein critical for cytoskeletal rearrangements that promotes cell and tissue morphogenesis during development and has previously been placed downstream of Wnt/PCP signaling. This study aims to investigate the role and mechanisms of Shrm3 in mediating actomyosin cytoskeletal rearrangements that drive BC cell motility and metastasis downstream of Wnt/PCP signaling. This study will for the first time evaluate the contribution of Shrm3 to cancer progression, enhancing our understanding of how Wnt/PCP signaling promotes BC metastasis.

PT-23: INDUCTION OF CUPROPTOSIS COMBINED WITH ANTI-PD-L1 IMPROVES ANTI-TUMOR RESPONSE IN HNSCC MURINE MODEL

Ivan Lu, Graduate Student[1], Jin Zhang[2,3], John D. Aleman[1], Xiao-Jing Wang[1,3]
[1]Department of Pathology and Laboratory Medicine, UC Davis, Sacramento, CA; [2]Department of Surgical and Radiological Sciences, UC Davis, Davis, CA; [3]UC Davis Comprehensive Cancer Center, Sacramento, CA

Head and neck squamous cell carcinoma (HNSCC) is the sixth most common cancer worldwide, with a 66% 5-year survival rate that drops to 40% upon metastasis. Despite therapeutic advances, prognosis remains poor due to immunotherapy resistance and an immunosuppressive tumor microenvironment (TME). Recent studies suggest that cuproptosis, a novel copper-dependent regulated cell death (RCD) pathway, may enhance anti-tumor immunity in murine cancer models such as melanoma. RCD has been shown to heavily influence the immunogenicity of tumors and modulate local inflammation in the TME. In this study, we used elesclomol

complexed with copper(II) (eles-Cu) to induce cuproptosis in SCC. Preliminary experiments showed that eles-Cu selectively killed murine SCC cells while sparing splenocytes. Based on this, we hypothesized that eles-Cu could enhance anti-tumor effects in combination with anti-PD-L1 immunotherapy in an immunocompetent A223 SCC mouse model by promoting immune-mediated cytotoxicity. First, we confirmed that elesclomol alone induced dose-dependent SCC cell death, and Cu(II) conjugation further increased cytotoxicity in-vitro. Subsequently in-vivo, tumors were established subcutaneously and treated with eles-Cu ± anti-PD-L1 via intraperitoneal injection. After a two-week treatment course, tumors receiving combination therapy showed significant reduced tumor volume relative to the negative control. These findings suggest that cuproptosis may enhance immunotherapy efficacy in HNSCC and underscore the need to further investigate how it modulates tumor immunogenicity—particularly through factors released by dying cells in the TME. (This study was funded by CO HNC SPORE P50-CA261605.)

PT-24: NANOBODY-BASED TARGETING OF OSTEOSARCOMA CANCER STEM CELLS

Nathan Martinez, Junior Specialist[1], Liming Zhao[2], Charles K.F.[2], Thomas H. Ambrosi[1,3]
[1]Department of Orthopaedic Surgery, UC Davis, Sacramento CA; [2]Division of Plastic and Reconstructive Surgery, Stanford University, Palo Alto CA; [3]UC Davis Comprehensive Cancer Center, Sacramento, CA

Osteosarcoma (OS) is the most common malignant tumor in the skeletal system. Cancer stem cells (CSCs) make up a small population of cells with stem cell-like properties that drive tumor growth, but their identity remains mostly elusive. Antibody-drug conjugates (ADCs) utilize antibodies to deliver therapeutic drugs to tumor cells. ADCs have been tested for OS but have been shown to be inefficient, likely due to the inability to penetrate the very dense extracellular matrix of OS. Nanobodies are a promising alternative due to their significantly smaller size. As proof of concept, the OS cell line SAOS2 was engineered to express GFP protein on the cell membrane. Nanobodies recognizing GFP were produced that selectively targeted GFP+ OS cells in mixed cultures with non-GFP cells in vitro. Importantly, the same nanobodies were also able to specifically home to GFP+ SAOS2-derived tumors in vivo after systemic injection. To identify specific markers for CSCs, we based our investigation on the skeletal stem cell (SSC), a skeletal tissue-specific bone-, cartilage-, and stroma-forming cell type. Using patient-derived xenograft (PDX) cell lines and primary tissue samples, we tracked clonal dynamics of OS CSCs and characterized the OS niches via spatial transcriptomics. We found putative CSCs that share both tumor and SSC characteristics as identified by single-cell RNA-sequencing. The target cell surface markers were conjugated with doxorubicin and will be tested for anti-OS efficacy in vivo. In summary, we provide proof of concept that nanobodies can be used to specifically target OS CSCs.

PT-25: GENERATION OF A HIGH-RESOLUTION TAM AND CAF SINGLE CELL MAP OF THE TUMOR MICROENVIRONMENT TO IMPROVE IMMUNE CHECKPOINT THERAPIES

Cesar Morfin, Postdoctoral Scholar[1,2], Ava Jessen[1], Nosisa Ncube[1], Gabriela Loots[1,2]
[1]Department of Orthopaedic Surgery, UC Davis, Sacramento, CA; [2]UC Davis Comprehensive Cancer Center, Sacramento, CA

Immune checkpoint inhibitors (ICIs) have transformed cancer therapy by enhancing immune recognition and elimination of cancer cells. However, many patients remain unresponsive because their tumors have poor immune cell infiltration, a state known as a “cold” tumor microenvironment (TME) that fails to mount an effective antitumor response. In contrast, ‘hot’ TMEs, rich in immune populations, are more responsive to ICIs.
scRNA-seq and spatial transcriptomics have advanced our understanding of TME complexity, yet key tumor-associated macrophage (TAM) and cancer-associated fibroblast (CAF) subpopulations remain poorly defined. Distinguishing stable subtypes from transient states remains a major challenge, limiting our ability to target these cells therapeutically.

To address this, we developed a strategy to fluorescently label and enrich TAM and CAF populations using transgenic mouse models. For TAMs, we use LysM-Cre; Ai9 (dT) mice; a well-established myeloid-specific system. In our EO771 breast cancer allograft model, we found large dT+ and F4/80+ myeloid populations in the primary tumor. For CAFs, we propose using Col6a1 as a pan-CAF marker. Our scRNA-seq data, along with

others, show Col6a1-3 are more broadly expressed than classical markers like Pdgfra and Acta2. Protein analysis also reveals stronger Col6a1 expression in stromal-rich and stromal-poor regions. We are generating Col6a1-Cre; Ai9 mice to enable CAF enrichment and characterization.

This lineage-labeling strategy should enable >80% enrichment of TAMs and CAFs, supporting high-resolution single-cell mapping. These data will inform TAM/CAF hierarchies and provide mechanistic insights into tumor immunogenicity and ICI responsiveness.

PT-26: UNVEILING BREAST CANCER VASCULAR NETWORKS: POTENTIAL SYNERGY OF FIBI SLIDE-FREE MICROSCOPY AND TOPOLOGICAL DATA ANALYSIS

Jazmin Orozco, Laboratory Assistant[1,3], Nathan Anderson[1], Shael Brown[2], Jacob Hertz[1], Richard Levenson[1,3]
[1]Department of Pathology and Laboratory Medicine, UC Davis, Sacramento, CA; [2]Kintsugi Analytics, Montreal, CA; [3]UC Davis Comprehensive Cancer Center, Sacramento, CA

Fluorescence-imitating brightfield imaging (FIBI) is a new type of slide-free microscopy that creates images similar to those in H&E-stained slides, but within minutes from tissue acquisition. FIBI images, because they don't rely on 5-micron sections, improve capture of longitudinal structural features relevant to cancer biology. These include blood vessels within and surrounding tumors, which often differ from those associated with normal or non-neoplastic tissues. Topological data analysis (TDA) is a relatively novel mathematical tool that may prove useful for detailed study of such vascular features in cancer. For example, persistent homology—a technique within TDA—can analyze loops, branches, and connections. The goal of this study is to compare blood vessel structures seen in FIBI and H&E images using paired tissue specimens of breast cancer, and include TDA-based metrics, to investigate: a) whether FIBI indeed is useful for vessel characterization; and b) whether it outperforms standard H&E-stained slide-based approaches. We imaged a series of anonymized breast cancer specimens using both H&E- and FIBI approaches. Vascular structures were then annotated manually using QuPath tools, and the segmented vessel overlays subjected to TDA analysis. Preliminary results suggest that FIBI images reveal blood vessels, including capillaries, more clearly, and with extended longitudinal features than with H&E images. In the future, FIBI, perhaps in combination with TDA, may provide faster and more detailed images for cancer diagnosis and therapeutic guidance.

PT-27: METABOLOMIC PROFILING IN HUMAN GLIOMAS

Vihar Patel, Assistant Professor[1], John Paul Aboubechara[2,11], Yin Liu[3,11] Oliver Fiehn[4,11], Lina A Dahabiyeh[4,5], Ruben Fragoso[6,11], Jonathan W. Riess[7,11], Rawad Hodeify[8], Orin Bloch[9,11], Orwa Aboud[10,11]
[1]Department of Pathology, UC Davis, Sacramento, CA; [2]Department of Neurology, UC Davis, Sacramento, CA; [3]Department of Ophthalmology, UC Davis, Sacramento, CA; [4]West Coast Metabolomics Center, UC Davis, Davis, CA; [5]Department of Pharmaceutical Sciences, School of Pharmacy, The University of Jordan, Amman, Amman Governorate, Jordan; [6]Department of Radiation Oncology, UC Davis, Sacramento, CA; [7]Division of Hematology and Oncology, UC Davis, Sacramento, CA; [8]Department of Biotechnology, School of Arts and Sciences, American University of Ras Al-Khaimah, United Arab Emirates; [9]Department of Neurological Surgery, UC Davis, Sacramento, CA; [10]Department of Neurological Surgery, UC Davis, Sacramento, CA; [11]UC Davis Comprehensive Cancer Center, Sacramento, CA

Background: Glioblastoma is a metabolically diverse and aggressive brain tumor. We used untargeted metabolomics and unsupervised analysis to define metabolic subtypes within IDH-wildtype glioblastoma and to identify features shared with IDH-mutant glioma.

Methods: Brain tissue from IDH-wildtype glioblastoma (n = 38), IDH-mutant astrocytoma, Grade 4 (n = 5), and non-neoplastic controls (n = 20) underwent untargeted metabolomic profiling. Partial Least Squares Discriminant Analysis (PLS-DA) was followed by k-means clustering. ANOVA was used to identify metabolites significantly altered between groups. Heatmaps visualized group-level differences, and pathway enrichment was performed using MetaboAnalyst 6.0.

Results: K-means clustering revealed three distinct metabolic subtypes within IDH-wildtype glioblastoma. Cluster 1 showed increased galactose and sucrose metabolism. Cluster 2 was characterized by elevated fructose metabolism, primarily driven by sorbitol accumulation. Cluster 3 demonstrated increased pyruvate metabolism, glutathione metabolism, and amino acid pathways including alanine, aspartate, and glutamate metabolism. 2-hydroxyglutarate (2HG) was dramatically elevated 130-fold in IDH-mutant gliomas, while hypotaurine was highly abundant in both glioblastoma and IDH-mutant glioma. Additional metabolites elevated in both tumor types included citric acid, glutamic acid, maltotriose, glycine, and 3-aminoisobutyric acid.

Conclusion: Metabolomic profiling identified three distinct subtypes of IDH-wildtype glioblastoma with unique metabolic signatures and revealed shared metabolic features between glioblastoma and IDH-mutant glioma. These results highlight the potential for metabolic classification to improve understanding of tumor biology and guide therapeutic strategies in glioma.

PT-28: TARGETING PLXND1 USING RNA BIOENGINEERING TECHNOLOGIES AND CUSTOMIZED LIPID NANOPARTICLES IN ADVANCED PROSTATE CANCER

Huan Qu, Postdoctoral Scholar[1], Menghuan Tang[2], Qiufang Zong[2], Sohaib Mahri[2], Pengfei Xu[1], Joy C. Yang[1], Fan Wei[1], Junwei Zhao[2], Meijuan Tu[2], Neelu Batra[2], Leyi Wang[1,3], Allen C. Gao[1,4], Kit Lam[2,4], Marc Dall'Era[1,4], Aiming Yu[2,4], Yuanpei Li[2,4], Chengfei Liu[1,3,4]
[1]Department of Urologic Surgery, UC Davis, Sacramento, CA; [2]Department of Biochemistry and Molecular Medicine, UC Davis, Sacramento, CA; [3]Graduate Group in Integrative Pathobiology, UC Davis, Davis, CA; [4]UC Davis Comprehensive Cancer Center, Sacramento, CA

PLXND1 (Plexin D1) is an 'undruggable' transmembrane receptor protein that plays crucial roles in driving neural lineage plasticity and enzalutamide resistance in prostate cancer. siRNA therapy holds great promise for cancer treatment by selectively silencing disease-driving genes but faces challenges such as instability, poor cellular uptake, and off-target effects. Here, we leverage an innovative RNA bioengineering platform based on a natural tRNA scaffold to stabilize and deliver PLXND1 siRNAs in a highly efficient and biocompatible manner via customized lipid nanoparticles (LNPs). We constructed the corresponding BioRNA/PLXND1-siRNA expression plasmids through molecular cloning using a tRNA/pre-miRNA-mir-34a scaffold. We purified the BioRNA-siPLXND1 molecule, and quality control analysis confirmed high yield, excellent purity, and low endotoxin levels. We also tested its functions in vitro. BioRNA-siPLXND1 effectively reduced both PLXND1 RNA and protein levels. Importantly, BioRNA-siPLXND1 significantly inhibited cell proliferation, colony formation, and organoid growth. Moreover, we developed two LNP formulations using different lipid components (DOPE or DOTAP) to load BioRNA-siPLXND1. LNP-DOTAP showed higher transfection efficiency in prostate cancer cells but greater toxicity in normal cells compared to LNP-DOPE. LNP-DOPE-loaded BioRNA-siPLXND1 remained stable in vitro for 7 days and effectively suppressed PLXND1, inhibited proliferation, and induced death in neuroendocrine prostate cancer patient-derived xenograft organoids. In vivo, LNP-DOPE was well tolerated and accumulated in tumors within 2 hours, persisting up to 4 days. Biodistribution analysis revealed predominant tumor retention by day 7, supporting LNP-DOPE as a safe, targeted BioRNA-siPLXND1 delivery system for prostate cancer treatment.

PT-29: BIOMARKER-BASED CHARACTERIZATION OF CANINE HEPATOCELLULAR CARCINOMA

Esandi Kurulugama, Junior Specialist[1], Resmi Ravindran[1], Tamar Cohen-Davidyan[2], Yutong Ji[1], Dongguang Wei[1,2,3], Yvonne Wan[1,3], William Culp[2,3], Imran Khan[1]
[1]Department of Pathology and Laboratory Medicine, UC Davis, Sacramento, CA; [2]Department of Surgical and Radiological Sciences, UC Davis, Davis, CA; [3]UC Davis Comprehensive Cancer Center, Sacramento, CA

Hepatocellular carcinoma (HCC) accounts for approximately 75–85% of primary liver cancers in humans. In dogs, HCC is the most common primary liver malignancy, comprising 35–60% of all hepatic tumors. While our laboratory has developed mouse models that facilitated the development of novel HCC therapies, canine HCC offers a spontaneously occurring and clinically relevant model for studying human HCC. However, the molecular and immunological landscape of canine HCC remains insufficiently defined. This study aims to characterize

naturally occurring canine HCC to identify biomarkers and explore therapeutic targets applicable to both veterinary and human HCC. Samples were obtained from client-owned dogs (n=14) diagnosed with HCC who underwent surgical resection at the UC Davis Veterinary Medical Hospital. For each case, paired tumor and adjacent non-tumor liver tissues, as well as plasma, were collected. Additionally, plasma samples from age- and sex-matched healthy control dogs (n =14) were included for comparative analysis. Characterization of HCC was conducted using histopathology, immunohistochemistry for galectin-1, cytokine profiling, transcriptomics, proteomics, and untargeted metabolomics. Preliminary findings (n=8) suggest that Galectin-1 expression is upregulated in HCC tumor tissues. Results from the ongoing cytokine profiling, transcriptomic, and metabolomic analyses aim to elucidate tumor-associated immune and metabolic alterations will be presented. Comparative assessments with established mouse models and publicly available human HCC datasets are underway to evaluate cross-species comparisons.

Our preliminary findings support the utility of canine HCC as a relevant comparative model for human HCC. The integration of molecular, immunological, and clinical data from canine, murine, and human HCC highlights shared biomarkers and potential therapeutic targets.

PT-30: COMBINATION OF BIOENGINEERED MICRORNA AND CHEMOTHERAPEUTICS SHOWED ENHANCED THERAPEUTIC EFFICIENCY FOR HIGH-RISK NEUROBLASTOMA IN VIVO

Ana Sandoval-Castellanos, Postdoctoral Scholar[1], Yunyoung Lee[1], Albatool Alkhazal[1], Meijuan Tu[2], Aiming Yu[2,4], Jinhwan Kim[1,3,4] and Erin Brown[1,4]
[1]Department of Surgery, UC Davis, Sacramento, CA; [2]Department of Biochemistry and Molecular Medicine, UC Davis, Sacramento, CA; [3]Department of Biomedical Engineering, UC Davis, Davis, CA; [4]UC Davis Comprehensive Cancer Center, Sacramento, CA

High-risk neuroblastoma (HRNB) has a poor prognosis, and current chemotherapy regimens result in severe side effects. Recent studies have demonstrated that microRNAs (miRs, small noncoding RNAs) play a key role in tumor development and progression. Here, using in vitro and in vivo HRNB models, we investigated the potential of combining miR-based therapy with chemotherapeutics to enhance efficacy while reducing chemotherapy-associated toxicity.

HRNB cell lines were used to evaluate the pro-apoptotic and synergistic effects of miRs (miR-124-3p and miR-34a-5p) in combination with cisplatin in vitro. Subcutaneous xenograft HRNB models were used for in vivo. Once tumors reached adequate volume, mice received intratumoral miR-124-3p or miR-34a-5p and intravenous cisplatin, followed by tumor growth monitoring. At the endpoint, mice were euthanized and samples collected for histological and blood analysis.
In vitro, HRNB cell lines treated with both miRs and cisplatin showed a significantly decreased cell viability, compared to cisplatin treatment only. In vivo HRNB subcutaneous xenograft models showed that combination therapy with miRs and cisplatin led to a marked reduction in tumor size, surpassing even the efficacy observed with a double dosage of cisplatin alone, demonstrating synergistic potential compared to cisplatin monotherapy.

The combination of miRs and cisplatin, in our in vitro and in vivo models, demonstrated enhanced therapeutic efficacy, suggesting the potential for reducing the chemotherapy dosage, which is particularly valuable in pediatric oncology. This observed synergy highlights the need for further investigation into miR-based combination therapies as a promising therapeutic strategy for children with HRNB.

PT-31: ORGANIZER NETWORK - THE EMERGING POSTEMBRYONIC GROWTH CONTROL SYSTEM

Charles Shang, Clinical Professor, Eye Center, UC Davis, Sacramento, CA

Organizers are small groups of cells which control growth and differentiation of a larger region. Organizers are the singular points of morphogen gradient field and bioelectric field. They can be activated by subtle stimuli causing long lasting growth control effects and potentially therapeutic effects. The organizer model of postembryonic growth control suggests that a network of organizers continues to exist after embryogenesis and

regulate growth, regeneration and physiology. Organizers tend to locate at the extreme points of body surface curvature or tissue interface curvature (e.g. concave, convex and saddle points). Growing evidence is supporting that acupoints originate from the organizers. The corollaries and predictions of this model have confirmed:

1. Organizers have local maximum electrical conductance and current density.
2. Boundaries in growth control have high electric conductance with high density of gap junctions.
3. The growth control boundaries are the separatrices of morphogen gradient and bioelectric field.
4. Some morphogens and organizers continue to function after embryogenesis
5. Acupuncture (perturbation at likely organizers) has been shown to have extensive growth control effects as predicted.

The bioelectrical field of the organizers/acupoints can change as part of early signal transduction of a pathological process and can be used for diagnosis and prognosis. The existence of singularity in growth control system indicates that small perturbation at organizers can cause major, long lasting systemic change - offering a convenient and potentially cost-effective way of manipulating the growth control system for cancer prevention and therapy.

PT-32: SPATIAL TRANSCRIPTOME ANALYSIS OF THE KERATINOCYTE MICROENVIRONMENT IN MELANOMA

Angela Soghomonian, Graduate Student[1], Claire Williams[2], Nicholas Love[1], Maayan Baron[3], Maija Kiuru[4,5]
[1]Department of Dermatology, UC Davis, Sacramento, CA; [2]Bruker Spatial Biology, Seattle, WA; [3]Zephyr AI, Tysons Corner, VA; [4]Division of Clinical Dermatology and Pathology, UC Davis, Sacramento, CA; [5]UC Davis Comprehensive Cancer Center, Sacramento, CA

Melanoma, one of the deadliest forms of skin cancer, can be cured if detected early. Accurate diagnosis is difficult for some melanomas due to their resemblance to benign moles (melanocytic nevi). This challenge can result in misdiagnosis, leading to an increase in morbidity and mortality. In its early stages, melanoma is confined to the outermost epithelial layer of the skin (epidermis). However, the role of epidermal keratinocytes in the initiation and progression of melanoma is not well understood. Likewise, their potential as a diagnostic or therapeutic target is largely unexplored. In this study, we used single-cell spatial transcriptomics to profile the expression of ~6000 genes within 147,541 individual cells of the keratinocyte microenvironment of 7 melanocytic tumors (3 invasive melanomas, one melanoma in situ, one dysplastic nevus, one common nevus) and one basal cell carcinoma. For each sample, sections containing both lesional and adjacent non-lesional epidermal tissue were analyzed. Differential gene expression analysis of the lesional and non-lesional keratinocyte niches revealed a high expression of damage associated molecular patterns (DAMPs) S100A7, S100A8, and S100A9 and wound-associated keratins (KRT6B and KRT6C) in the microenvironment of melanoma and basal cell carcinoma, but not nevi. Furthermore, upregulation of DSC2, DYNLL1, LCN2 and RAB11A was unique to the keratinocyte microenvironment of melanoma. Our results highlight the gene signatures of the keratinocyte microenvironment responding to melanoma growth and the potential to identify biomarkers and therapeutic targets in this keratinocyte population.

PT-33: BIDIRECTIONAL CROSSTALK OF RESIDENT BONE CELLS AND METASTATIC PROSTATE CANCER

Maxwell A. Tracy, Graduate Student[1], Kristina V. Wells[1], Damian C. Genetos[1,2]
[1]Department of Anatomy, Physiology, and Cell Biology, UC Davis, Davis, CA; [2]UC Davis Comprehensive Cancer Center, Sacramento, CA

Prostate cancer (PCa) is the most prevalent form of cancer for males. While localized cases of PCa have high rates of survival, metastatic cases are characterized by higher morbidity and mortality by a large margin. PCa commonly establishes secondary tumors within bone, as the osteogenic niche provides a synergistic space for PCa to both reside in and grow. This cancer growth in bone is accompanied by excess bone growth (termed osteoblastic lesions), wherein bone resident cells and PCa will interact to direct aberrant formation of bone,

further exacerbating the lesion and therefore impacting patient outcomes. The exact mechanisms of how this occurs, and what consequential molecular factors are at play, have not been fully characterized. To address this gap, we are carrying out in vitro experiments to initially assess paracrine effects between cell types, measuring migration changes in PCa and apoptotic induction in osteoblasts and osteocytes. Due to the known mechanosensitivity of resident bone cells, especially osteocytes, we will also assess whether mechano-stimulation of osteoblasts or osteocytes modulates their impact upon PCa. Further identification of candidate factors will be done by utilizing gene expression data from osteoblasts and osteocytes following PCa conditioned media treatment, with candidate genes functionally assessed after. This work ultimately seeks to identify novel drivers of bone lesion development, with a focus on probing the effects that biologically relevant stimuli have on this axis of resident bone cell and PCa crosstalk.

PT-34: METASTATIC HEAD AND NECK SQUAMOUS CELL CARCINOMA-DERIVED EXTRACELLULAR VESICLES FACILITATE PRE-METASTATIC NICHE CONDITIONING IN THE LUNGS

Lan-Chi Vo, Graduate Student[1,3], Rachel Mizenko[2], Jack Goon[1,3], Randy P. Carney[2,3], Xiao-Jing Wang[1,3]
[1]Department of Pathology and Laboratory Medicine, UC Davis, Sacramento, CA; [2]Department of Biomedical Engineering, UC Davis, Davis, CA; [3]UC Davis Comprehensive Cancer Center, Sacramento, CA

Head and neck squamous cell carcinoma (HNSCC) is associated with high morbidity and mortality. While the current standard of care is effective for early-stage disease, outcomes for recurrent or metastatic HNSCC remain poor, and current molecular biomarkers fail to predict or prevent metastasis. Recent studies suggest that tumor-derived extracellular vesicles (EVs) facilitate formation of a pre-metastatic niche in distant secondary organs in other cancer types. Here, we utilize immunocompetent SCC murine models to determine whether HNSCC-derived EVs contain proteins reflective of their parent cells and assess their role in promoting metastasis. EVs were isolated from non-metastatic and metastatic SCC cell lines using differential centrifugation, ultrafiltration, and size exclusion chromatography (SEC). Preliminary proteomic analysis indicated that EVs derived from metastatic SCC cells are enriched in integrins α2, α3, β1, and β6 compared to EVs from non-metastatic cells. Metastatic SCC-derived EVs also carried increased levels of chemokines CXCL-1, 2, 3, and 5, which are involved in granulocyte chemotaxis. Gene ontology analysis revealed that metastatic SCC-derived EVs were enriched in multiple pathways associated with cancer metastasis, including regulation of cell migration and regulation of blood vessel remodeling. In vivo, mice pre-treated with metastatic SCC-derived EVs for three weeks before i.v. injection of non-metastatic SCC cells showed increased lung blood vessels with perivascular $CD11b^+$ cells compared to the control group. These results suggested that EVs may also play a role in promoting angiogenesis, leading to greater infiltration of myeloid cells recruited through integrin and chemokine signaling. (Supported by CO HNC SPORE P50-CA261605.)

PT-35: DIETARY OMEGA-3 POLYUNSATURATED FATTY ACIDS PREVENT OBESITY AND OBESITY-ASSOCIATED INFLAMMATION: IMPLICATIONS FOR CANCER RISK REDUCTION

Yige Wang, Graduate Student[1], Nan Jing[1], Jun Yang[2], Guodong Zhang[1,3]
[1]Department of Nutrition, UC Davis, Davis, CA; [2]Department of Entomology and Nematology, UC Davis, Davis, CA; [3]UC Davis Comprehensive Cancer Center, Sacramento, CA

Objectives: Obesity is a well-established risk factor for multiple cancers, largely through chronic low-grade inflammation and metabolic dysfunction. While omega-3 polyunsaturated fatty acids (ω-3 PUFAs) have shown promise in reducing obesity and inflammation, the molecular mechanisms remain incompletely understood. This study aimed to investigate how dietary ω-3 PUFAs modulate obesity-related inflammation and metabolic pathways, with a particular focus on lipid mediators that may influence cancer risk.

Methods: We treated C57BL/6 mice with a low-fat diet, a high-fat diet, or omega-3 PUFA-enriched high-fat diets, then the development of obesity, adipose inflammation and dysfunction, and other metabolic disorders were studied. In addition, we used LC-MS/MS-based lipidomics, which can analyze >100 lipid metabolites, to study how omega-3 PUFA intake modulates obesity-associated lipid metabolism.

Results: Dietary administration of omega-3 PUFA reduced obesity development in a dose-dependent manner, illustrating the anti-obese effects of omega-3 PUFAs. LC-MS/MS lipidomics showed that omega-3 intake significantly altered the profiles of lipid metabolites in tissues, with cytochrome P450-derived omega-3 fatty acid epoxides showing the most pronounced increase.

Conclusions: Our studies support the anti-obese effects of dietary omega-3 PUFAs. Furthermore, the lipidomics analysis suggests that omega-3 epoxides may play a key role in the health benefits of omega-3 PUFAs.

Funding Sources: This research is supported by a new faculty start-up grant from the University of California Davis (to G.Z.).

PT-36: MUTATIONAL LANDSCAPE OF MELANOCYTIC TUMORS FROM PATIENTS WITH RASOPATHIES

Alexis E. Willy, Graduate Student[1], Laura J. Young[1], Summer Meyer[1], Jennifer Tavernetti[1], Elanee Simmons[1], Katherine A. Rauen[2] John D. McPherson[3,5], Maija Kiuru[1,4,5]
[1]Department of Dermatology, UC Davis, Sacramento, CA; [2]Department of Pediatrics, UC Davis, Sacramento, CA; [3]Department of Biochemistry and Molecular Medicine, UC Davis, Sacramento, CA; [4]Department of Pathology and Laboratory Medicine, UC Davis, Sacramento, CA; [5]UC Davis Comprehensive Cancer Center, Sacramento, CA

RASopathies, such as Neurofibromatosis 1 (NF1), Cardio-facio-cutaneous Syndrome (CFC), and Costello Syndrome (CS), are genetic syndromes characterized by germline pathogenic variants in genes of the RAS pathway. These syndromes are multi-systemic, often presenting with a distinctive cutaneous phenotype. The RAS pathway is also frequently mutated in sporadic melanocytic nevi and melanoma, with the BRAF p.V600E somatic mutation present in approximately 80% of melanocytic nevi in the population. Despite this, additional somatic mutations of the RAS pathway in melanocytic tumors from RASopathy patients, and its implications for melanoma risk, remains unexplored. In this study, we investigated the mutational landscape of melanocytic nevi in patients with NF1, CFC, CS, and controls. Whole exome sequencing was performed with tumor-normal or tumor-only analysis on 50 nevi (29 common, 21 dysplastic) from 50 patients (3 NF1, 3 CFC, 1 CS, 43 controls). A BRAF p.V600E somatic variant was found in 66% of the control nevi. In comparison, only 28.6% of the RASopathy nevi harbored a BRAF p.V600E somatic variant. The RASopathy nevi harbored significantly more melanoma-associated variants in RAS and cancer genes compared to controls (Mann-Whitney U =115.0. p = 0.0032). Tumor mutation burden did not significantly differ between RASopathy patients and controls (Mann-Whitney U = 144, p = 0.83), suggesting comparable mutational loads across groups. This study explored the mutational landscape of melanocytic nevi from patients with RASopathies and controls and found increased somatic mutation burden in RAS pathway genes in RASopathy-associated nevi, leading to more insight into melanoma risk in RASopathies.

PT-37: IMMUNE RESPONSE PATHWAYS REWIRING IN THE TRANSITION TO ENZALUTAMIDE RESISTANCE AND NEURAL LINEAGE PLASTICITY IN PROSTATE CANCER

Pengfei Xu, Postdoctoral Scholar[1], Huan Qu[1], Joy C. Yang[1], Fan Wei[1], Junwei Zhao[2], Menghuan Tang[2], Leyi Wang[1,3], Christopher Nip[1], Allen C. Gao[1,4], Kit Lam[2,4], Marc Dall'Era[1,4], Yuanpei Li[2,4], Chengfei Liu[1,3,4]
[1]Department of Urologic Surgery, UC Davis, Sacramento, CA; [2]Department of Biochemistry and Molecular Medicine, UC Davis, Sacramento, CA; [3]Graduate Group in Integrative Pathobiology, UC Davis, Davis, CA; [4]UC Davis Comprehensive Cancer Center, Sacramento, CA

Treatment induced neuroendocrine prostate cancer (t-NEPC) represents a highly aggressive form of advanced prostate cancer. t-NEPC is mainly caused by lineage plasticity transformation of adenocarcinoma after long-term androgen deprivation therapy or androgen receptor (AR) signaling inhibitor treatment, such as enzalutamide. However, the molecular mechanisms underlying its transition, particularly the response to immune signaling pathways, remain poorly defined. Here, we demonstrate that immune-related pathways, including IFNγ, IFNα, IL-6-JAK-STAT3, and inflammatory responses, are significantly suppressed in NEPC patent compared to castration-resistant prostate cancer (CRPC) patient samples. Mechanistically, enzalutamide-resistant and NEPC

cells exhibited marked impairment in IFNγ and IL6 signaling, while enzalutamide treatment at early stages paradoxically enhanced IFNγ and IL6 responsiveness in prostate cancer cells. Transcriptomic profiling revealed that early enzalutamide treatment upregulated E2F target genes alongside IFNα/IFNγ and JAK/STAT pathways activation, suggesting a coordinated transcriptional reprogramming. Notably, early-stage enzalutamide-treated cells remained highly sensitive to IFNγ and IL6 stimulation and exhibited increased susceptibility to STAT1 inhibition by fludarabine, while resistant cells lost this sensitivity. These findings highlight the dynamic regulation of immune-related signaling during prostate cancer progression and suggest that early combination therapy with enzalutamide and STAT pathway inhibitors may delay or prevent the evolution of neural lineage plasticity and resistance.

PT-38: RACIAL INEQUITIES IN PROVIDER-INITIATED LUNG CANCER SCREENING DISCUSSIONS AMONG CURRENT AND FORMER SMOKERS

Ya Yang, Graduate Student[1], Heejung Bang[1], Melanie Dove[1,3], Elisa Tong[2,3]
[1]Department of Public Health Sciences, UC Davis, Sacramento, CA; [2]Department of Internal Medicine, UC Davis, Sacramento, CA; [3]UC Davis Comprehensive Cancer Center, Sacramento, CA

Background: Lung cancer screening (LCS) via low-dose computed tomography (LDCT) can reduce mortality through early detection. However, conversations between providers and eligible patients remain uncommon, particularly among racial and ethnic populations. To help reduce race/ethnic disparities, LCS eligibility was expanded in 2021 to include adults aged 50–80 with at least a 20 pack-year smoking history. This study examines racial and ethnic differences in provider-initiated discussions about LCS among U.S. adults aged 50-80 with a smoking history.

Methods: This cross-sectional study used national data from the 2020–2024 Health Information National Trends Survey (HINTS). The sample included adults aged 50-80 with current or former smoking history (n = 1,185). The outcome was whether a provider discussed LCS in the past year. Logistic regression examined associations between race/ethnicity and provider-initiated discussions, controlling for sociodemographic and health-related covariates.

Results: Hispanics had significantly lower odds of reporting a LCS discussion compared to non-Hispanic Whites (AOR = 0.46, 95% CI: 0.24–0.89). Males (AOR = 1.42, 95% CI: 1.01–2.02), those with four or more provider visits (AOR = 1.67, 95% CI: 1.17–2.39), and those with depression (AOR = 1.49, 95% CI: 1.03–2.16) had higher odds of reporting LCS discussions. Former smokers were less likely than current smokers to report such discussions (AOR = 0.26, 95% CI: 0.17–0.38).

Conclusion: Despite expanded eligibility, disparities persist in provider-initiated conversations about LCS, especially for Hispanics. Because the dataset lacked smoking history, future research should collect this information to assess if disparities stem from lower pack-years among Hispanics.

PT-39: FUNCTIONAL INVERSION OF CIRCADIAN REGULATOR REV-ERBA LEADS TO TUMORIGENIC GENE REPROGRAMMING

Yatian Yang, Assistant Project Scientist[1], Xiong Zhang[1], Demin Cai[1], Xingling Zheng[1], Xuan Zhao[2], Eva Corey[3], Ronald M. Evans[2], Hong-Wu Chen[1,4]
[1]Department of Biochemistry and Molecular Medicine, UC Davis, Sacramento, CA; [2]Gene Expression Laboratory, Salk Institute for Biological Studies, La Jolla, CA; [3]Department of Urology, University of Washington, Seattle, WA; [4]UC Davis Comprehensive Cancer Center, Sacramento, CA

Profound functional switch of key regulatory factors may play a major role in homeostasis and disease. Dysregulation of circadian rhythm (CR) is strongly implicated in cancer with mechanisms poorly understood. We report here that the function of REV-ERBα, a major CR regulator of the orphan nuclear receptor subfamily, is dramatically altered in tumors in both its genome binding and functional mode. Loss of CR is linked to a functional inversion of REV-ERBα from a repressor in control of CR and metabolic gene programs in normal tissues to a

strong activator in different cancers. Through changing its association from NCoR/HDAC3 corepressor complex to BRD4/p300 coactivators, REV-ERBα directly activates thousands of genes including tumorigenic programs such as MAPK and PI3K-Akt signaling. Functioning as a master transcriptional activator, REV-ERBα partners with pioneer factor FOXA1 and directly stimulates a large number of signaling genes, including multiple growth factors, receptor tyrosine kinases, RASs, AKTs, and MAPKs. Moreover, elevated REVERBα reprograms FOXA1 to bind new targets through a BRD4-mediated increase in local chromatin accessibility. Pharmacological targeting with SR8278 diminishes the function of both REV-ERBα and FOXA1 and synergizes with BRD4 inhibitor in effective suppression of tumorigenic programs and tumor growth. Thus, our study revealed a functional inversion by a CR regulator in driving gene reprogramming as an unexpected paradigm of tumorigenesis mechanism and demonstrated a high effectiveness of therapeutic targeting such switch.

PT-40: CIRCADIAN REGULATOR REV-ERBA IS A MASTER REGULATOR OF TUMOR LINEAGE PLASTICITY AND AN EFFECTIVE THERAPEUTIC TARGET

Xiong Zhang, Postdoctoral Scholar[1], Yatian Yang[1], Eva Corey[2], Hong-Wu Chen[1,3]
[1]Department of Biochemistry and Molecular Medicine, UC Davis, Sacramento, CA; [2]Department of Urologic Surgery, University of Washington, Seattle, WA; [3]UC Davis Comprehensive Cancer Center, Sacramento, CA

Epigenetic and transcriptional dysregulation plays a fundamental role in tumor lineage plasticity (LP). However, the underlying mechanisms, especially for the initial events of LP development, are still poorly understood. Here, we report that in progression of prostate cancer from adenocarcinoma to treatment-induced neuroendocrine prostate cancer (t-NEPC), anti-AR signaling inhibitors (ARSIs) reprogram the function of a circadian regulator/nuclear receptor REV-ERBα by switching its target gene programs from kinase signaling and metabolic programs to programs of LP, which includes neurogenesis, stem cell and epithelial to mesenchymal transition (EMT) as well as over fifteen LP drivers including POU3F2/BRN2, ASCL1, FOXA2, ONECUT2 and MYCN. Mechanistically, REV-ERBα directly binds at promoters of LP genes. Loss of REV-ERBα potently inhibits NEPC cell growth and abolishes the expression of LP drivers and gene programs. Pharmacological inhibition of REV-ERBα exhibits high potency in blocking the growth of NEPC tumors including patient-derived xenografts. Our findings reveal that therapy-induced LP development entails a coordinated induction of a network of LP drivers and that REV-ERBα is a novel master regulator of the network and a promising therapeutic target for treatment of advanced prostate cancer such as NEPC.

ET-01: COMPREHENSIVE CANCER CENTER SHARED RESOURCES

Aruna Chetty, Shared Resource Administrator, Dan Port, Marketing Specialist, UC Davis Comprehensive Cancer Center, Sacramento, CA

The Shared Resources provide the UC Davis research community with centralized access to specialized scientific expertise, consultation, assistance, infrastructure, and equipment necessary to conduct cutting-edge cancer research. Through Cancer Center Support Grant funding arrangements, Cancer Center members conducting cancer research receive subsidies for and priority access to services from eight Shared Resources and one developing Shared Resource.

POSTER AND EXHIBIT ABSTRACTS (FRIDAY)

(Listed alphabetically by the last name of the presenting author.)

PF-01: PLASMA LIPIDOMICS AS A NOVEL LIQUID BIOPSY APPROACH FOR GLIOBLASTOMA

John Paul Aboubechara, Resident[1,2], Yin Liu[2,10], Oliver Fiehn[,3] Lina A. Dahabiyeh[4], Ruben Fragoso[,5,10], Han Sung Lee[6], Jonathan W. Riess[,7,10], Rawad Hodeify[8], Orin Bloch[9,10], and Orwa Aboud[9,10]
[1]Department of Neurology, UC Davis, Sacramento, CA; [2]Department of Ophthalmology, UC Davis, Sacramento, CA; [3]West Coast Metabolomics Center, UC Davis, Davis, CA; [4]Department of Pharmaceutical Sciences, School of Pharmacy, The University of Jordan, Amman, Amman Governorate, Jordan; [5]Department of Radiation Oncology, UC Davis, Sacramento, CA; [6]Department of Pathology, UC Davis, Sacramento, CA; [7]Division of Hematology and Oncology, UC Davis, Sacramento, CA; [8]Department of Biotechnology, School of Arts and Sciences, American University of Ras Al-Khaimah, United Arab Emirates; [9]Department of Neurological Surgery, UC Davis, Sacramento, CA, [10]UC Davis Comprehensive Cancer Center, Sacramento, CA

Glioblastoma is an aggressive brain tumor that invariably recurs despite treatment, partly due to metabolic adaptations, including altered lipid metabolism. This study in-vestigates plasma lipidomic profiles in glioblastoma patients to explore their potential as a liquid biopsy for disease monitoring. Plasma samples were collected from 36 patients with histopathologically-confirmed IDH wild-type glioblastoma at four treatment stages: Pre-Surgery (n=36), Post-Surgery (n=32), Pre-Radiation (n=28), and Post-Radiation (n=17). Untargeted lipidomics analysis was performed using liquid chromatography-high resolution mass spectrometry (LC-HR-MS/MS. Plasma lipidomic signatures differed sig-nificantly across treatment stages. Specifically, the lipidomic profile prior to surgery was distinct from those at subsequent stages, demonstrating increased compound abundance of numerous lipids prior to surgery that are decreased at subsequent stages, including linolenic acid (fold change 2.58, p=4.21x10-11), behenic acid (fold change 2.09, p=9.3x10-10), and linolenic acid (fold change 4.44, p=5.83x10-6). Random Forest modeling could predict pre-surgical samples with 85.7% accuracy. Plasma lipidomics shows promise as a liquid biopsy approach for monitoring glioblastoma treatment. The distinct lipidomic profile observed prior to surgery suggests potential for early detection.

PF-02: INCIDENCE OF CHRONIC MEDICAL CONDITIONS IN ADOLESCENT AND YOUNG ADULT SURVIVORS OF HEMATOLOGIC MALIGNANCIES IN CALIFORNIA, 2006–2020

Renata Abrahão, Assistant Professional Researcher[1,12], Andrew B. Smitherman[2], Candice A. M. Sauder[3,12], Kathryn J. Ruddy[4], Hazel B. Nichols[5], Jessica Chubak[6] Anne C. Kirchhoff[7], Larry Kushi[8], Erin E. Hahn[9,10], Theresa H.M. Keegan[11,12]
[1]Center for Oncology Hematology Outcomes Research and Training (COHORT), Division of Hematology and Oncology, UC Davis, Sacramento, CA; [2]Division of Pediatric Hematology-Oncology, Lineberger Comprehensive Cancer Center, University of North Carolina School of Medicine, Chapel Hill, NC; [3]Division of Surgical Oncology, UC Davis, Sacramento, CA; [4]Department of Oncology, Mayo Clinic, Rochester, MN; [5]Department of Epidemiology, University of North Carolina, Gillings School of Global Public Health, Chapel Hill, NC; [6]Kaiser Permanente Washington Health Research Institute, Seattle, WA; [7]Department of Pediatrics and Huntsman Cancer Institute, University of Utah, Salt Lake City, UT; [8]Division of Research, Kaiser Permanente Northern California, Pleasanton, CA; [9]Department of Research and Evaluation, Kaiser Permanente Southern California, Pasadena, California; [10]Kaiser Permanente Bernard J. Tyson School of Medicine, Pasadena, CA; [11]Department of Public Health Sciences, Sacramento, CA; [12]UC Davis Comprehensive Cancer Center, Sacramento, CA

Background: Survivors of adolescent and young adult (AYA) hematologic malignancies face elevated risks of chronic medical conditions. We assessed the cumulative incidence (CMI) and incidence rate ratios (IRRs) of several conditions among cancer survivors compared to a matched non-cancer cohort.

Methods: We used data from Kaiser Permanente (KP) Northern and Southern California to identify AYAs (15–39 years) diagnosed with Hodgkin lymphoma (HL), non-Hodgkin lymphoma (NHL), acute myeloid leukemia (AML), or acute lymphoblastic leukemia (ALL), from 2006–2020 who survived ≥2 years after diagnosis. A non-cancer cohort was matched 10:1 by age, sex, diagnosis year, and KP site. We estimated CMI for each condition,

accounting for death as a competing risk, and used multivariable Poisson regression to estimate IRRs, adjusting for age, sex, and race/ethnicity.

Results: Among 2,624 survivors (42% HL, 40% NHL, 9% AML, 9% ALL; median follow-up of 5.9 years), the 10-year CMI was 43.9% for any condition and 16.1% for ≥2 conditions (vs. 22.4% and 4.4% in the matched cohort). Survivors had 2.7- and 4.8-times higher rates of developing 1 and ≥2 conditions, respectively. IRRs ranged from 1.5 for respiratory disease to 36.8 for venous thromboembolism (VTE). Highest IRRs were for VTE and renal disease, followed by cardiovascular disease and diabetes. In lymphoma patients, risk was higher with regional/distant vs. localized disease. Elevated IRRs were observed across demographic and socioeconomic groups.

Conclusions: AYA survivors of hematologic malignancies face substantial risk for chronic conditions. Long-term surveillance and targeted interventions are warranted to improve outcomes and reduce premature mortality.

PF-03: A PILOT STUDY OF INTRATUMORAL SD-101 (TOLL-LIKE RECEPTOR 9 AGONIST), NIVOLUMAB, AND RADIOTHERAPY FOR TREATMENT OF CHEMOTHERAPY-REFRACTORY METASTATIC PANCREATIC ADENOCARCINOMA

Ebaa Al-Obeidi, Assistant Professor[1], Justin A. Chen[2], Jasmine C. Huynh[3], Arta M. Monjazeb[5], May T. Cho[4], Edward J. Kim[5]
[1]Division of Hematology and Oncology, UC Davis, Sacramento, CA; [2]Veterans Affairs Palo Alto Health Care, Palo Alto, CA; [3]Washington Cancer Center, UC San Fransisco, Fremont, CA; [4]Replimune; [5]UC Davis Comprehensive Cancer Center, Sacramento, CA

Background: Immunotherapy has revolutionized care for various solid organ malignancies but not yet for pancreatic cancer. This pilot study assessed the combination of SD-101, a toll-like receptor 9 agonist that is injected intratumorally to increase immunogenicity in the tumor microenvironment; localized radiation; and the checkpoint inhibitor nivolumab

Methods: Six patients with chemotherapy-refractory, liver-metastatic pancreatic adenocarcinoma were enrolled. SD-101 is injected intratumorally into a liver metastasis on days 1, 8, 15, 29. Localized radiation (6-10 Gy) to the injected lesion was given on days 1, 3, 5, 8, and 10. Nivolumab was given at 240 mg every 2 weeks starting day 2 until progression or unacceptable toxicity. Primary objective was to evaluate safety and tolerability, defined as ≥5 patients reaching day 29 without experiencing grade ≥3 treatment-related toxicity.

Results: The patients enrolled were heavily pre-treated and had received a median of 3 prior lines of therapy. Four of the 6 patients received at least one cycle of the experimental treatment. The most common treatment-related adverse events (TRAE) were lymphopenia, anemia, and aspartate aminotransferase elevation. The most common grade 3 TRAE was lymphopenia. 50% of the patients had progressive disease and 50% were non-evaluable (2 withdrew from study after developing rapidly progressive symptomatic metastases, 1 withdrew due to sepsis and was transitioned to hospice).

Conclusions: Intratumoral injection of SD-101 was feasible. The primary endpoint of safety could not be assessed as two patients did not receive the first cycle of therapy. Future directions include analyzing biospecimens for biomarkers of immune response.

PF-04: FACILITATING TRANSCRIPTIONAL CONDENSATES: HOW KSHV LANA AND K-RTA PROMOTE BRD4 PHASE SEPARATION

Chris Amaya Bautista, Undergraduate Student[1], Jonna Espera[1], Tomoki Inahaki[1], Chie Izumiua[1], Yoshihiro Izumiya[1,2]
[1]Department of Dermatology, UC Davis, Sacramento, CA; [2]UC Davis Comprehensive Cancer Center, Sacramento, CA

Liquid-liquid phase separation (LLPS) enables transcription factors to form membraneless condensates that concentrate regulatory proteins and enhance gene expression. These regulate frequencies of transcription at the recruited sites. BRD4, for example, forms "enhancer dots" which are essential for transcriptional regulation. LANA and K-Rta are KSHV transcription factors that are essential for viral latency and reactivation. However, their LLPS properties remain poorly understood.

We investigated whether LANA and K-Rta undergo LLPS individually or in combination with interacting partners. Recombinant EGFP-CHD4, EGFP-KRta, mBFP LANA, mCherry-BRD4, and mCherry CHD4 were expressed in insect cells using a baculovirus system and purified. LLPS was assessed under conditions (10% PEG, 1mM DTT, 150 mM NaCl, Tri-HCl [pH7.5]). Negative controls included EGFP, mBFP, and mCherry alone.

We found that EGFP-K-Rta and mCherry-BRD4 formed phase-separated condensates independently across tested concentrations (0.7uM, 0.14uM, 0.07uM), whereas mBFP-LANA failed to self-aggregate. However, LANA readily underwent LLPS when co-incubated with either K-Rta or BRD4, suggesting interaction-driven condensate formation.

To determine which domains of LANA mediate LLPS, we examined two deletion mutants: one lacking acidic repeats and one lacking the CHD4 interaction motif. The acidic mutant retained the ability to form LLPS with BRD4, while the LANAΔCHD4 mutant failed to form condensates with BRD4, indicating that the CHD4 binding site is critical for interaction-driven LLPS.

These findings suggest that LANA relies on multiple interaction motifs to undergo LLPS, facilitating the formation of transcriptional hubs. This cooperative mechanism may regulate KSHV gene expression during latency and reactivation.

PF-05: DEVELOPING A COMMUNITY CANCER PREVENTION ACADEMY FOR NATIVE COMMUNITY HEALTH REPRESENTATIVES

Marissa Bashore, Health Education Supervisor[1], Nicole Halmai[2], Mayra Sandoval[1], Julie HT Dang[1,3]
[1]Office of Community Outreach and Engagement, UC Davis Comprehensive Cancer Center, Sacramento, CA; [2]Department of Biochemistry and Molecular Medicine, UC Davis, Sacramento, CA; [3]Department of Public Health Sciences, UC Davis, Sacramento, CA

Community Health Representatives (CHRs) are vital to cancer prevention and navigation in American Indian and Alaska Native (AI/AN) communities. In 2022, CHRs in California gained the ability to bill for services through Medi-Cal, creating an opportunity to expand training and capacity. In collaboration with the California Rural Indian Health Board (CRIHB), the Office of Community Outreach and Engagement (OCOE) at UC Davis Comprehensive Cancer Center developed a tailored Community Cancer Prevention Academy to support CHRs in delivering cancer education.

Following a review of evidence-based Native community trainings and expert feedback, OCOE hosted a one-day, in-person Academy on February 12, 2025, with 21 CHRs and Native clinic staff attending. Topics included: Cancer in California (data focused on AI/AN populations); Cancer Prevention: Risk Factors and Screenings; Cancer Research and Clinical Trials (emphasizing Native participation and data sovereignty); and Community Cancer Education. Sessions were interactive and culturally grounded.

Post-training evaluations showed 100% of participants were satisfied with the content, presenters, and resources, and felt the training was relevant to their roles. All indicated they would apply what they learned to their work. The Academy strengthened partnerships with CRIHB and Indian Health Services (IHS), leading to two additional CHR trainings planned for July (Sacramento) and August (San Diego) 2025. A joint community-science research funding application with CRIHB was also submitted in May 2025.

This initiative highlights the power of culturally responsive, community-driven programming to empower CHRs and advance cancer prevention in Native communities.

PF-06: SINGLE-CELL ANALYSIS REVEALS MARCKS-DRIVEN CROSSTALK IN TUMOR-ASSOCIATED MACROPHAGES AS A MEDIATOR OF LUNG CANCER PROGRESSION AND IMMUNOSUPPRESSION

Jenna Berton, Undergraduate Student[1], Ssu-Wei Hsu[1], Ching-Hsien Chen[1,2]
[1]Department of Internal Medicine, UC Davis, Sacramento, CA; [2]UC Davis Comprehensive Cancer Center, Sacramento, CA

Lung cancer remains the leading cause of cancer-related mortality worldwide, with 1.8 million deaths annually. MARCKS (myristoylated alanine-rich c-kinase substrate) has previously been identified as a potential therapeutic target for lung cancer and is highly expressed not only in cancer cells but also in tumor-associated macrophages (TAMs). To investigate the role of MARCKS in TAMs, we analyzed single-cell RNA sequencing data from lung cancer patients (GSE131907), and found that MARCKS may contribute to M2-like polarization and immune evasion in TAMs. Using CellChat, we observed that MARCKS-expressed TAMs, MARCKS(+), exhibited increased outgoing and incoming signalling interactions compared to MARCKS(-) TAMs. Notable outgoing signals included CCL, MIF, SPP1, VEGF, TNF, TGFB, CALCR, and SN, while incoming signals included TGFB, TNF, ITGB2, CCL, SPP1, VISFATIN, ANGPTL, and CSF. Interestingly, only MARCKS(+) TAMs were able to receive the TGFB signaling, a key driver of M2-like polarization. Furthermore, MARCKS(+) TAMs uniquely secreted SPP1 and MIF, which are associated with tumor progression and were not observed in MARCKS(-) TAMs. SPP1-CD44 engagement drives metastasis, chemotherapy resistance, and immune evasion of cancer cells and also promotes fibroblast differentiation to cancer-associated fibroblasts (CAFs) while influencing T cell exhaustion. MIF binding to CD74-CXCR4 facilitates immune evasion by recruiting the Treg and impairs NK cell chemotaxis and functions. These findings highlight MARCKS-driven alterations in cell-cell communication that contribute to lung cancer progression, including metastasis, immune evasion, and tumor growth. Overall, identifying these pathways provides insight into potential biomarkers and therapeutic targets for lung cancer.

PF-07: EFFECTS OF RADIATION THERAPY COMBINED WITH TGF-B AND PD-L1 BLOCKADE ON THE TUMOR MICROENVIRONMENT IN A MURINE HEAD AND NECK SQUAMOUS CELL CARCINOMA MODEL

Hewitt Chang, Medical Student[1], Ivan Lu[2], John Aleman[3], Xiao-Jing Wang[4,5]
[1]School of Medicine, UC Davis, Sacramento, CA; [2]Immunology Graduate Program, UC Davis, Davis, CA; [3]Cancer Biology Program, Anschutz Medical Campus, University of Colorado, Aurora, CO; [4]Department of Pathology and Laboratory Medicine, UC Davis, Sacramento, CA; [5]UC Davis Comprehensive Cancer Center, Sacramento, CA

Head and neck squamous cell carcinoma (HNSCC) represented the 6th most common cancer globally in 2022, and patients with recurrent or metastatic HNSCC respond poorly to therapy options or have subsequent disease progression and eventual death from the disease. Thus, there remains a need for further therapy options for recurrent or metastatic HNSCC patients. One approach to this issue is the dual inhibition of transforming growth factor-beta (TGF-β) and the PD-1/PD-L1 axis. We examined whether treatment with radiation therapy (RT) and TGF-β and PD-L1 blockade in a syngeneic HNSCC mouse model impacts the immune landscape within the tumor microenvironment. Tumors were collected from C57BL/6 mice under the following treatment conditions: untreated, RT + control antibody, RT + bintrafusp alfa, and RT + losartan + anti-PD-L1. Using immunohistochemistry staining, we found minimal changes in the density of myeloid cells, macrophages, natural killer cells, T-cells, and B-cells when comparing the treatment groups. However, when looking at apoptosis-mediated cell death, we observed an increase in the amount of cleaved caspase 3 staining in tumors treated with either RT + bintrafusp alfa or RT + losartan + anti-PD-L1. This finding suggests that dual blockade of TGF-β and the PD-1/PD-L1 axis can lead to increased cell death within the tumor. Further studies to examine what mediates the increased cell death would be critical in understanding how losartan and anti-PD-1 or anti-PD-L1 immunotherapy can be used in combination for patients with recurrent, refractory, or oligometastatic HNSCC.

PF-08: INTERLEUKIN 15 STIMULATION AUGMENTS MYELOID-DERIVED SUPPRESSOR CELL IMMUNOSUPPRESSION IN CROSS-SPECIES MODELS OF SARCOMA

Yeji Cho,Graduate Student[1], Cyrus J. Sholevar[1], Makan Karimzadeh[1], Megan Purl[1], Tasneem Mukarrama[1], Robert J. Canter[1,2]
[1]Division of Surgical Oncology, UC Davis, Sacramento, CA; [2]UC Davis Comprehensive Cancer Center, Sacramento, CA

Myeloid-derived suppressor cells (MDSCs) are a heterogenous immune cell population expanded in cancer, with immunosuppressive effects on natural killer (NK) and T cells, inhibiting antitumor immunity. Cytokine immunotherapy with interleukin 15 (IL-15) has shown promise in human and canine bone and soft tissue sarcoma. Although IL-15 is classically associated with heightened NK and T cell antitumor response, MDSC expression of IL-15 receptor alpha may be associated with shorter disease-free intervals in dogs receiving IL-15 for osteosarcoma (OSA). This study sought to characterize the effects of pre-conditioning MDSCs in vitro with IL-15 in cross-species models. Murine MDSCs (CD11b+ Gr1+) were isolated from OSA-bearing BALB/c splenocytes and pre-treated +/- IL-15, then cultured with wild-type splenocytes (anti-CD3/28 stimulated). NK and CD8 T cell phenotype and function were evaluated by flow cytometry. At 1:1 responder-to-suppressor (R:S) ratio, MDSCs significantly inhibited NK and CD8 T cell proliferation, with suppression increased following IL-15 pre-treatment. Human MDSCs were differentiated in vitro from peripheral blood CD33+ cells with IL-6 and GM-CSF stimulation, then pre-treated +/- IL-15. MDSCs were cultured with donor-matched CD33- PBMCs (anti-CD3/28 and IL-2 stimulated) then evaluated by flow cytometry. At 1:1 R:S, MDSCs significantly inhibited NK and T cell proliferation (cell count, Ki67), activation (CD69), and cytotoxicity (GZMB), and effects were greater following IL-15 pre-treatment of MDSCs. The IL-15 / IL-15 receptor alpha axis is a novel mechanism of MDSC function with potential pro-tumor effects. Better understanding of this pathway is likely to have translational impact in cancer and autoimmunity.

PF-09: BONE MARROW FIBROSIS IN PATIENTS WITH HISTORY OF A MYELOPROLIFERATIVE NEOPLASM EVALUATED USING DUET (DUAL-MODE EMISSION AND TRANSMISSION) MICROSCOPY

Elham Vali Betts, Associate Professor[1], Nate Anderson[1], Richard Levenson[1,3], Farzad Feredouni[2,3], Ananya Datta Mitra[1,3]
[1]Department of Pathology and Laboratory Medicine, UC Davis, Sacramento, CA; [2]Department of Pathology and Laboratory Medicine, Emory University School of Medicine, Atlanta, GA; [3]UC Davis Comprehensive Cancer Center, Sacramento, CA

Introduction: Myeloproliferative neoplasms are a group of disorders characterized by progressive fibrosis in the bone marrow, where hematopoietic cells are gradually replaced by scar tissue. In this group, primary myelofibrosis (PMF) serves as the prototype example of relentless progression of marrow fibrosis leading to bone marrow failure.

Masson's trichrome is the most widely used histochemical stain for evaluating collagen fibrosis on histological sections, but it is prone to significant inter- and intra-laboratory variability and lacking specificity for collagen deposits; thus, impairing both visual assessment and quantitative image analysis. We describe here Dual-mode Emission Transmission microscopy (DUET), a novel simple microscopy technique that can highlight collagen distribution without special stains, as it works on existing hematoxylin & eosin (H&E) slides by generating color contrast for various tissue elements using its fluorescence mode. This is accomplished without relying on complicated optics or additional histochemical or immuno¬histochemical staining.

Methods: Slides from patients with PMF prepared with H&E and Masson's trichrome stains were reviewed and initially scanned using a commercial brightfield scanner at 20x. H&E slides were further scanned at 20x using a DUET scanner. Two pathologists reviewed and graded the fibrosis. Regions of interest were selected for qualitative assessments and select fields were run through machine-learning algorithms trained to segment collagenous from non-collagenous regions. The results from DUET were compared to pathologist's evaluation of fibrosis.

Findings and conclusion: With DUET we demonstrated specificity and sensitivity equivalent to traditional evaluation using trichrome for identification of collagen deposits. Segmentation using machine-learning algorithms showed promise.

PF-10: EXAMINING HEALTH DISPARITIES IN THE USE OF HEMATOPOIETIC CELL TRANSPLANTS FOR HIV-LYMPHOMA

Kurt Anthony David, Graduate Student[1,11], Ann Brunson[2], Alex Fauer[1,11], Sarah Schoenfeld[3], Shuai Chen[4,11], Roland Zepf[5], Laura Fejerman[6,11], Jeffery Auletta[7,8,9,] Christa Meyer[7], Lori Muffly[10], Lindsay Morton[3], Sheryl Catz[1], Theresa Keegan[2,11]
[1]Betty Irene Moore School of Nursing, UC Davis, Sacramento, CA; [2]Center for Oncology Hematology Outcomes Research and Training (COHORT), Division of Hematology and Oncology, UC Davis, Sacramento, CA ; [3]Radiation Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Department of Health and Human Services, Bethesda, MD; [4]Division of Biostatistics, UC Davis, Sacramento, CA; [5]School of Nursing Community Health Systems, UC San Francisco, San Francisco, CA; [6]Department of Public Health Sciences, UC Davis, Sacramento, CA; [7]Center for International Blood and Marrow Transplant Research, National Marrow Donor Program, Minneapolis, MN; [8]Division of Hematology/Oncology/BMT, Nationwide Children's Hospital, Columbus, OH; [9]Division of Infectious Diseases, Nationwide Children's Hospital, Columbus, OH; [10]Division of Blood and Marrow Transplantation and Cellular Therapy, Stanford University, Palo Alto, CA; [11]UC Davis Comprehensive Cancer Center, Sacramento, CA

Introduction: Despite people with HIV being at an increased risk of lymphoma, they are less likely to receive cancer treatment. While hematopoietic cell transplant(HCT) is a potentially curative treatment in the non-HIV population, the likelihood of receiving an HCT for HIV-lymphoma is unknown.

Methods: We identified lymphoma patients 18-79 years of age at diagnosis from the California Cancer Registry, linked to statewide hospitalization and Center for International Blood and Marrow Transplant Registry databases(1991-2016). Among HIV lymphoma patients, cumulative incidence calculated HCT utilization over time and a multivariate Cox proportional hazards regression model characterized factors associated with HCT use. Regression models evaluated complications, hospital use, and survival between HIV and matched non-HIV(1:3) lymphoma patients with HCT.

Results: Among HIV lymphoma patients(n=6,258), the incidence of HCT at 60 months increased from 1.9%(95CI: 1%-3.5%) in <1997 to 7.2%(95 CI: 5.6%-9%) in >2006. Factors associated with lower HCT use included older age (HR 0.98, 95 CI: 0.96-0.99), low socioeconomic status (HR 0.38, 95 CI: 0.25-0.59), single/unmarried (0.5, 95 CI: 0.34-0.73), and public insurance (0.64, 95 CI: 0.44-0.93). Among 140 matched HIV and 409 non-HIV lymphoma patients with HCT, there were no significant differences in acute renal or liver complications, sepsis/ infections, or hospital use within 90 days following HCT. Two-year overall survival following HCT was similar(73% HIV vs 69% non-HIV; p>0.05).

Conclusion: Among the largest population of HCTs in people with HIV, our findings identify low utilization of and barriers to HCT use and suggest that HCT use is both safe and effective.

PF-11: ANGEL2 LOSS FUELS BLADDER CANCER PROGRESSION THROUGH METABOLIC REPROGRAMMING AND STROMAL ACTIVATION

Avani Durve, Undergraduate Student[1], Neelu Batra[1], Conner Suen[1,4], Ustat Kaur[1], Brie Fielder[1], Cecilia Giulivi[2], Paramita Ghosh[1,3,4], Christopher Lucchesi[1,3,4]
[1]Department of Urologic Surgery, UC Davis, Sacramento, CA; [2]Department of Molecular Biosciences, UC Davis, Davis, CA; [3]Sacramento Veterans Affairs Medical Center, Mather, CA; [4]UC Davis Comprehensive Cancer Center, Sacramento, CA

ANGEL2 is a 2′,3′-cyclic phosphatase involved in tRNA processing. Recent findings suggest that its expression may have prognostic relevance in bladder cancer. ANGEL2-deficient T24 bladder cancer cells exhibit elevated

expression of epithelial-mesenchymal transition (EMT) and stemness-associated markers relative to wild-type (WT) controls, indicating a shift toward a more aggressive tumor phenotype.

Co-culture experiments using immortalized human bladder fibroblasts (hTERT-transduced and mCherry-labeled) demonstrated increased fibroblast proliferation when cultured with ANGEL2-null T24 cells compared to WT counterparts. Flow cytometry gating on mCherry-positive fibroblasts revealed upregulation of cancer-associated fibroblast (CAF) markers, including RGS5, α-SMA, and CD140 (PDGFRβ), in fibroblasts co-cultured with ANGEL2-deficient tumor cells. These findings suggest that loss of ANGEL2 in tumor cells promotes fibroblast-to-CAF transition and may contribute to a more tumor-permissive microenvironment.

Metabolically, ANGEL2-null cells displayed reduced mitochondrial mass as measured by citrate synthase activity, along with altered oxidative phosphorylation capacity assessed via Seahorse analysis. Treatment with FCCP confirmed a reduced reserve respiratory capacity in ANGEL2-deficient cells, while sensitivity to the glycolysis inhibitor JX06 further supported a metabolic reprogramming toward glycolytic dependence. All experiments were performed in triplicate, and observed trends were statistically consistent across biological replicates. Together, these results indicate that ANGEL2 loss promotes tumor aggressiveness through both cell-intrinsic metabolic shifts and modulation of the stromal microenvironment. A synthetic enthalpy approach that targets glycolytic activity in ANGEL2 knockout cells may be used to address the metabolic shifts associated with the loss of ANGEL2.

PF-12: DESIGN, DEVELOPMENT, AND EVALUATION OF GENE THERAPEUTICS SPECIFIC TO KSHV-ASSOCIATED DISEASES

Jonna Espera, Assistant Specialist[1], Tomoki Inagaki[1], Kang-Hsin Wang[1], Somayeh Komaki[1], Sonali Nair[1,2], Ryan R. Davis[3], Ashish Kumar[1], Ken-ichi Nakajima[1,5], Yoshihiro Izumiya[1,4,5]
[1]Department of Dermatology, UC Davis, Sacramento, CA; [2]Department of Medical Health Science, Touro University California, Vallejo, CA; [3]Department of Pathology and Laboratory Medicine, UC Davis, Sacramento, CA; [4]Department of Biochemistry and Molecular Medicine, UC Davis, Sacramento, CA; [5]UC Davis Comprehensive Cancer Center, Sacramento, CA

Kaposi's sarcoma-associated herpesvirus (KSHV) is the causative agent of Kaposi's sarcoma (KS) and two human lymphoproliferative diseases: primary effusion lymphoma and AIDS-related multicentric Castleman's disease. KSHV-encoded latency-associated nuclear antigen (LANA) is expressed in KSHV-infected cancer cells and is responsible for maintaining viral genomes in infected cells. Thus, LANA is an attractive target for therapeutic intervention for KSHV-associated diseases.

Here, we devised a cancer gene therapy vector using the adeno-associated virus (AAV), which capitalizes the LANA's function to maintain terminal repeat (TR) containing circular genome in latently infected cells and the TR's enhancer function for KSHV inducible gene promoters. By including two TR copies with a lytic inducible gene promoter (TR2-OriP), we prepared an AAV vector, which expresses an engineered thymidine kinase (TK) selectively in KSHV-infected cells. Ganciclovir (GCV), an anti-herpesvirus drug, effectively eradicated multiple KSHV-infected cells that include iPSC-derived epithelial colony-forming cells, but not non-KSHV-infected counterparts in the presence of AAV8-TR2-OriP-TK. In addition, AAV8-TR2-OriP-TK prevents KSHV virion production from reactivated cells, spreading KSHV infections from reactivated cells. Anti-cancer drugs, known to reactivate KSHV, stimulated TK expression from the vector and, therefore, synergized with AAV8 TR2-OriP-TK to induce KSHV-infected cancer cell death. Finally, the AAV8-TR2-OriP-TK with GCV completely diminished KSHV-infected cancer cells in the xenograft tumor model. The new cancer gene therapeutics should augment the current clinical protocol for KS.

PF-13: INVESTIGATING FRIZZLED7-DRIVEN REGULATION OF VANGL1 IN WNT/PCP SIGNALING IN BREAST CANCER

Savannah Free, Graduate Student[1,2], Courtney Dreyer[1] Kermit Carraway[1,2]
[1]Department of Biochemistry and Molecular Medicine, UC Davis, Sacramento, CA; [2]UC Davis Comprehensive Cancer Center, Sacramento, CA

Wnt/Planar Cell Polarity (Wnt/PCP) signaling is a non-canonical developmental pathway reactivated during tumorigenesis in many cancers, where it promotes tumor aggressiveness and correlates with poor prognosis (Hatakeyama et al., 2014). Vangl1, a transmembrane scaffolding protein whose activity is unique to Wnt/PCP signaling, is an important site for assembly of protein complexes which drive cytoskeletal rearrangement at the leading edge of migratory cells, supporting metastasis (Dreyer et al., 2023). Vangl1 has been shown to interact with the Wnt/PCP transmembrane receptor Frizzled7 both inter-cellularly—to promote polarity and establish epithelial organization—and, more recently, intra-cellularly—to drive localized signaling events which promote migration. However, the relationship between Vangl1 and Frizzled7 is not fully understood.

We recently found that Vangl1 undergoes a Frizzled7-dependent post-translational modification, evident from a mobility shift on SDS-PAGE upon Frizzled7 overexpression. Biochemical assays revealed this is a phosphorylation event that:

1. Requires Vangl1's C-terminal PDZ-binding motif,
2. Occurs independently of Wnt5a (the presumed ligand driving Wnt/PCP signaling), and
3. Persists despite mutation of two candidate phosphorylation sites—leaving the true sites unknown.

To investigate functional consequences, we performed Vangl1 immunoprecipitation-mass spectrometry (IP-MS) with and without Frizzled7 expression. The results identified several Vangl1 interactors—both known and novel—whose binding is altered by Frizzled7. These findings suggest Frizzled7 may regulate Vangl1 function through phosphorylation-dependent modulation of its protein interactions.

PF-14: PROVIDER PERSPECTIVES ON LUNG CANCER SCREENING: A COALITION-LED SURVEY ON PROVIDER BARRIERS TO RECOMMENDING SCREENING AND KNOWLEDGE OF UPDATED USPSTF GUIDELINES

Lucy Rios, Graduate Student[1,10], Alexandra Gori, Community Outreach and Engagement Coordinator[10], Britany Lundberg[2], Michael Mair[3], Tana Toll[3], Christina Fantozzi[4], Jodi Bobbitt[4], Vivian Leong[4], Brooks Novi[5], Sarah Cheung[6], Pleshette Robertson[7], Valarie Scruggs[7], Tammy Harrod[8], Julie HT Dang[1,10], Elisa Tong[9,10]
[1]Department of Public Health Sciences, UC Davis, Sacramento, CA; [2]Department of Internal Medicine and Psychiatry, UC Davis, Sacramento, CA; [3]Dignity Health Cancer Institute, Carmichael, CA; [4]Sutter Health, Sacramento, CA; [5]Genentech, Sacramento, CA; [6]Department of Public Health, Sacramento County, Sacramento, CA; [7]The SOL Project, Sacramento, CA; [8]WellSpace Health, Sacramento, CA; [9]Department of Internal Medicine, UC Davis, Sacramento, CA' [10]UC Davis Comprehensive Cancer Center, Sacramento, CA

Introduction: California ranks below the national average in lung cancer screening (LCS) rates. To help address these low-screening rates within the Sacramento region, the Love Your Lungs: Sacramento Lung Health Coalition (LYL) - comprised of organizations across Sacramento County - developed and administered a survey to healthcare providers. The survey aimed to identify the top three barriers to referring eligible patients for LCS and to assess their knowledge of the updated screening guidelines.

Methods: Healthcare providers who were practicing in the Sacramento metropolitan area and provided care to patients ages 50 - 80 were asked to complete a 12-question survey between May - July 2025 to assess primary barriers to referring eligible patients, and knowledge about LCS guidelines. Healthcare provider and health system responses were compared using t-tests and $\chi 2$ tests.

Results: Preliminary data indicate that n=51 eligible healthcare providers across four health systems completed the survey. The top three selected barriers to making a LCS recommendation to eligible patients were: time

constraints or competing priorities 74% (26/35), EMR alert does not show up 66% (23/35), and insurance coverage 34% (12/35). Participants showed highest knowledge on pack-year criteria (100%) and lowest on correctly answering family history which is not part of eligibility (51%) when assessed for their knowledge of current LCS guidelines.

Conclusion: These preliminary findings highlight key system-level and logistical barriers to LCS referrals among healthcare providers in Northern California. Insights from this survey will guide the LYL coalition in prioritizing targeted interventions. These efforts aim to increase LCS rates in the region.

PF-15: INTERNATIONAL DAY OF LIGHT: ENHANCING BIDIRECTIONAL COMMUNITY ENGAGEMENT IN CANCER RESEARCH THROUGH LIGHT-BASED TECHNOLOGIES

Bao Her, Community Outreach and Engagement Coordinator[1], Marissa Bashore[1], Julie Dang[1,2,6], Laura Fejerman[1,2,6], Randy Carney[3,5,6], Laura Marcu[3,5,6], Andrew Birkeland[4,6], Silvia Anbunesan[3], Jinhwan Kim[3,6]
[1]Office of Community Outreach and Engagement, UC Davis Comprehensive Cancer Center, Sacramento, CA; [2]Department of Public Health Sciences, UC Davis, Sacramento, CA; [3]Department of Biomedical Engineering, UC Davis, Davis, CA; [4]Department of Otolaryngology, UC Davis, Sacramento, CA; [5]National Center for Interventional Biophotonic Technologies, UC Davis, Sacramento, CA; [6]UC Davis Comprehensive Cancer Center, Sacramento, CA

Background: The Cancer Centers Support Grant (CCSG) emphasizes that Cancer Center's research programs must illustrate how community outreach and engagement of communities result in high-impact science. This approach ensures bidirectionality, a two-way exchange that catalyzes activities to drive relevant research and to improve cancer prevention and outcomes. In response, the UCDCCC's Biotechnology Program with the National Center for Interventional Biphotonic Technologies partnered with the Office of Community Outreach and Engagement (OCOE) and hosted International Day of Light, an interactive event showcasing light-based technologies for community partners from the catchment area. Such events are crucial, as community engagement can support the full research process, enabling community members to inform and shape scientific efforts.

Methods: Three demonstrations were led by its respective researchers whose light-based presentations were reviewed and vetted by OCOE to ensure community appropriateness. With OCEO's guidance, researchers refined community-tailored questions on usability, accessibility and relevance which guided community input and feedback.

Results: 18 community partners participated, providing real-time feedback. Post-survey results revealed that 82.4% strongly agreed the event was valuable, featuring clear presentations, recognition of their input, and new insights gained into light-based technologies. The event also facilitated a new relationship between a community partner and researcher, expanding opportunities for community-engaged research.

Conclusions: International Day of Light was well received and successfully promoted bidirectionality, trust-building, and collaboration between researchers and the community. This open house model offers a promising approach for other research programs to adopt, aiming to enhance community engagement and to improve research relevance and impact.

PF-16: NOTCH PATHWAY MUTATIONS AND RESISTANCE TO ANTI-PD-1 IMMUNOTHERAPY IN CLEAR CELL RENAL CELL CARCINOMA

Longxiaotian Zhang, High School Student,[1], Ssu-Wei Hsu[1], Ching-Hsien Chen[1,2]
[1]Division of Nephrology, UC Davis, Sacramento, CA; [2]UC Davis Comprehensive Cancer Center, Saramento, CA

Kidney cancer remains a significant cause of cancer-related mortality worldwide. Although immune checkpoint inhibitors (ICIs) have transformed the treatment landscape, particularly anti-PD-1 immunotherapy in clear cell renal cell carcinoma (ccRCC), many patients exhibit primary resistance. This study investigates pre-treatment

tumor characteristics associated with resistance to nivolumab, focusing on gene-level disruptions in immune signaling. We analyzed RNA sequencing data from 28 treatment-naïve tumor samples, stratified by clinical response. Transcriptomic and pathway-level comparisons between responders and non-responders revealed distinct differences in immune-related signaling. Notably, pathway enrichment analysis using DAVID identified significant upregulation of the NOTCH signaling pathway in non-responders. Within this pathway, we uncovered evidence of multiple NOTCH1 mutations, including the t(7;9)(NOTCH1:M1580_K2555) translocation, PEST domain truncations, and HD domain point mutations. These alterations lead to persistent activation of the NOTCH1 intracellular domain (NICD), driving not only cancer cell proliferation, invasion, and metastasis, but also reshaping the tumor immune microenvironment. Specifically, persistent NICD signaling was associated with $CD8^+$ T cell exhaustion, M2-like macrophage polarization, and regulatory T cell (Treg) recruitment—hallmarks of an immunosuppressive phenotype. These findings implicate aberrant NOTCH signaling as a critical mechanism of resistance to PD-1 blockade in ccRCC. Targeting the NOTCH pathway may enhance ICI efficacy and improve patient outcomes. Our study provides a rationale for integrating NOTCH pathway biomarkers into therapeutic decision-making and underscores the potential of combinatorial strategies to overcome immune resistance.

PF-17: NUCLEOPLASMIC MACROMOLECULAR CROWDING REGULATES METASTATIC POTENTIAL IN PANCREATIC DUCTAL ADENOCARCINOMA VIA NESPRIN-3

Chang-il Hwang, Associate Professor[1,3], Reno Jihao Xu[1,3], Minh Duc Pham[1, 3], Gant Luxton[2], Dan Starr[2,3]
[1]Department of Microbiology and Molecular Genetics, UC Davis, Davis, CA; [2]Department of Molecular and Cellular Biology, UC Davis, Davis, CA; [3]UC Davis Comprehensive Cancer Center, Sacramento, CA

Pancreatic ductal adenocarcinoma (PDAC) remains one of the deadliest cancers, characterized by aggressive progression, high metastatic potential, and 13.5% of a 5-year survival rate. While genetic and molecular drivers of PDAC have been extensively studied, the role of biophysical factors such as nucleoplasmic macromolecular crowding (NMC) in tumor progression and metastasis remains poorly understood. Here, we investigate the contribution of NMC to PDAC aggressiveness using genetically encoded multimeric nanoparticles (GEMs) as intracellular crowding sensors in 3D organoid models of PDAC. We observed significant differences in NMC between murine primary tumor- and metastasis-derived PDAC organoids, suggesting a link between nuclear crowding and metastatic phenotype. Transcriptomic analysis revealed upregulation of nesprin-3, an outer nuclear membrane protein that connects the nucleoskeleton to the cytoskeleton (LINC complex), in metastasis-derived organoids. Functional perturbation of nesprin-3 disrupted NMC and reduced the metastatic potential of PDAC organoids in vitro, indicating that nesprin-3 is a key regulator of nuclear biophysics and metastatic behavior. These findings highlight the importance of biophysical properties of the nucleoplasm, bridging genetic and mechanical determinants of metastasis. Our study suggests that targeting nuclear mechanotransduction pathways may represent a novel therapeutic avenue in PDAC.

PF-18: TOWARDS THE DEVELOPMENT OF A NANOPARTICLE-MICROBUBBLE SONOPORATION THERAPY FOR THE EARLY DETECTION AND DIAGNOSIS OF PANCREATIC DUCTAL ADENOCARCINOMAS

Naren Krishna Jegan, Undergraduate Student[1], Sourabh Mehta[2], Suresh Thangudu[2], Ramasamy Paulmurugan[2]
[1]Department of Biochemistry and Molecular Medicine; [2]The Canary Center at the Stanford School of Medicine, Palo Alto, CA; [3]UC Davis Comprehensive Cancer Center, Sacramento, CA

Pancreatic cancers (PC) is one among the deadly form of cancers with a 5-year survival rate around 10%. Globally, close to 460,000 individuals die from the 496,000 diagnosed with PC's over a 5-year period. Most patients are diagnosed at a very late stage, where the tumor has metastasized or where surgery is inoperable, leaving low efficiency of treatment. Claudin-18.2 (CLDN18.2), an isoform of the Claudin-18 membrane protein, was found to have significantly higher expression in PDAC samples in comparison to healthy tissue, making it an attractive biomarker for developing targeted therapies.

In this project, we aim to construct a nanoparticle for a nanoparticle-microbubble sonoporation therapy for enhanced We will construct multi-layer lipid nanoparticles that will house the PDAC first-line chemotherapeutic combination FOLFIRINOX. These nanoparticles will also be functionalized with caffeic acid, known for its reactive-oxygen-species (ROS) seeking and anti-inflammatory properties, and 4-carboxyphenylboronic acid, which targets overexpressed sialic acid in the glycoalyx. Finally, these nanoparticles will be decorated with a peptide targeter specific for the CLDN18.2 membrane protein.

PF-19: AN IN-VITRO CYTOTOXICITY EVALUATION OF TRIPLE NEGATIVE BREAST CANCER CELLS THROUGH PFAS 'FOREVER CHEMICAL' EXPOSURE

Sehej S. Johal, Undergraduate Student[1], Michael L. Goodson[2], David S. Guzman[1], Allison K. Ehrlich[1], Michele A. La Merrill[1,3]
[1]Department of Environmental Toxicology, UC Davis, CA; [2]Department of Anatomy, Physiology, & Cell Biology, UC Davis, CA; [3]UC Davis Comprehensive Cancer Center, Sacramento, CA

Per- and polyfluoroalkyl substances (PFAS) are pervasive environmental pollutants found in household items such as non-stick cookware and food packaging material. The International Agency for Research on Cancer classifies PFOA as carcinogenic to humans (Group 1), based on evidence of epigenetic alterations in exposed humans. Moreover, PFOS is classified as possibly carcinogenic to humans (Group 2B). Thus, industries are introducing alternative PFAS. Currently, replacement PFAS, such as hexafluoropropylene oxide trimer acid (HFPO-TA) and hexafluoropropylene oxide tetrameric acid (HFPO-TeA), remain largely untested toxicologically. We investigated the effects of HFPO-TA and HFPO-TeA on the viability of human Hs578T triple-negative breast cancer cells. Hs578T cells were exposed to concentrations of 10 µM, 1 µM, 100 nM, and 10 nM of HFPO-TA and HFPO-TeA over 48 hours. Toxicity was assessed by membrane integrity, and both compounds showed toxicity at various concentrations. Within 12h, HFPO-TA and HFPO-TeA significantly decreased Hs578T cell viability at 10 nM. Within 12h and 24h, HFPO-TA, but not HFPO-TeA, significantly reduced cell viability at 1 µM. These cytotoxic levels align with HFPO-TA concentrations found in human serum (median: 2.93 ng/mL ~ 5.47 nM). These results indicate that HFPO-TA may be cytotoxic at levels typically found in humans. Whether these PFAS could be considered as chemotherapeutics would depend, in part, on cytotoxicity testing of non-cancerous human cells at similar concentrations. We exposed differentiated U-937 human macrophages to HFPO-TA and HFPO-TeA and observed similar cytotoxic effects. This suggests that their toxicity is non-selective and utilizing them as chemotherapeutic agents is likely not plausible.

PF-20: REGIONAL B7-H3 CAR CELL THERAPY AND LIVER-DIRECTED RADIATION FOR PANCREATIC CANCER LIVER METASTASES

Sean J. Judge, Associate Professor[1,5], Megan C. Purl[1], Alexandria Shick[1], Makan Karimzadeh[1], Cyrus Sholevar[1], Tasneem Mukarrama[1], Natalie Liu[1], Marshall L. Lammers[1], Jinhwan Kim[1,5], Edward Kim[2,5], Arta Monjazeb[3,5], William J. Murphy[2,4,5], Robert J. Canter[1,5]
[1]Department of Surgery, UC Davis, Sacramento, CA; [2]Division of Hematology and Oncology, UC Davis, Sacramento, CA; [3]Department of Radiation Oncology, UC, Davis, Sacramento, CA; [4]Department of Dermatology, UC Davis, Sacramento, CA; [5]UC Davis Comprehensive Cancer Center, Sacramento, CA

Background: Pancreatic ductal adenocarcinoma (PDAC) is a lethal disease characterized by early liver metastases. Chimeric antigen receptor (CAR) modified cells (T and NK) have been largely unsuccessful in PDAC and other solid tumors, despite success in hematologic malignancies. Limitations in homing and engraftment of CAR cells into the solid tumor microenvironment may limit clinical efficacy. Regional CAR cell delivery and liver-directed radiation may improve this therapy against PDAC liver metastases. We investigated the impact of regional delivery and radiation therapy (RT) on B7-H3 CAR T cells.

Methods: Human PANC-1 cells were treated with radiation in vitro and in vivo using a liver-only metastatic model and assessed for expression of B7-H3 and NKG2D activating ligands MICA/MICB. B7-H3 CAR T cells were generated and assessed by flow cytometry and killing assays against PANC-1 cells treated with or without 4 Gy

RT. CD8 T cells were transferred into NSG mice via tail vein (IV) or portal vein (PV) injection and engrafted cells were isolated and assessed by flow cytometry.

Results: Following exposure to 4 Gy RT, PANC-1 cells in vitro exhibit a significant increase in expression of B7-H3 and MICA/MICB. More so, this is also detected in vivo following liver-directed RT of liver-only metastases in mice. Following 4 Gy liver-directed RT, PANC-1 liver metastases had significantly increased percent expression of B7-H3 and MFI of MICA/MICB, compared to non-radiated controls. Cytotoxicity of B7-H3 CAR T cells against PANC-1 cells was further increased when PANC-1 cells were pre-treated with 4 Gy RT in vitro. Human CD8 T cells were isolated from the liver of mice 24 hours after injection by either PV or IV. When administered by PV, CD8 T cells isolated from the liver showed significantly higher expression of tissue resident marker CD69 compared to IV administration.

Conclusions: RT increases expression of both B7-H3 and NKG2D activating ligands MICA/MICB on PANC-1 cells in vitro and this is recapitulated in vivo following liver-directed RT. These RT-induced changes result in greater B7-H3 CAR T cell killing. CD8 T cells administered by portal vein are enriched in the tissue resident marker CD69 within the liver, suggesting route of administration may impact engrafting T cells. Overall, liver-directed RT and regional CAR T administration may be a strategy to target PDAC liver metastases.

PF-21: INTRA-TUMORAL TIGIT BLOCKADE AS A STRATEGY FOR NK-BASED IMMUNOTHERAPY IN OSTEOSARCOMA

Makan Karimzadeh, Postdoctoral Scholar[1], Marshall L Lammers[1], Cyrus J. Sholevar[1], Natalie M Liu[1], Megan C. Purl[1], Ryan N. Nielsen[2], Michael K Sheng[2], Arta M Monjazeb[3,4], William J. Murphy[2,4], Sean J. Judge[1,4], Robert J. Canter[1,4]
[1]Division of Surgical Oncology, Department of Surgery, UC Davis, Sacramento, CA; [2]Department of Dermatology, UC Davis, Sacramento, CA; [3]Department of Radiation Oncology, UC Davis, Sacramento, CA; [4]UC Davis Comprehensive Cancer Center, Sacramento, CA

TIGIT is a key regulator of NK and T cell function and marks exhausted cells in cancer patients. However, clinical trials using systemic TIGIT blocking antibodies have shown little benefit as monotherapy. Recent preclinical work by our lab and others have shown that peripheral TIGIT+ NK cells can paradoxically be hyper functional when compared TIGIT- subsets. We sought to understand the impact of tissue compartment on TIGIT expressing NK cell phenotype and function in murine models of osteosarcoma (OSA). Splenic and tumor-infiltrating NK cells from K7M2 OSA BALB/c mice (n=11) were flow phenotyped and separately stimulated with PMA for 4-hours to measure CD107a expression. In parallel, mice were treated with intra-peritoneal (IP) TIGIT block, intra-tumoral (IT) TIGIT block or isotype control. Overall, intra-tumoral TIGIT+ NK cells were more dysfunctional when compared to TIGIT-, expressing significantly less CD107a following PMA stimulation. In contrast, spleen derived TIGIT+ NK cells were hyper-functional. Following IP TIGIT block, IT NK cells increased expression of CD107a compared to controls, while splenic derived NK cells showed decreased CD107a expression. Local IT blockade had no effect on peripheral TIGIT+ hyper-functionality, while reinvigorating IT NK cells. IT TIGIT block also led to significant tumor growth delay and improved mouse survival. Taken together, our results suggest that TIGIT blocking antibodies have disparate effects on peripheral and tumor NK compartments, and intra-tumoral treatment maintains peripheral functionality while reinvigorating tumor-infiltrating NK cells. These findings support site-directed TIGIT block administration as a strategy for immunotherapy in OSA patients.

PF-22: CHARACTERIZATION OF PARP INHIBITOR RESPONSE IN PROSTATE TUMOR CELLS REVEALS DRUG TOLERANT PERSISTER PHENOTYPE

Akshaya Karthikeyan, Graduate Student[1], Jose Torres-Gonzalez, Medical Student[2], Bryan Correa-Gonzalez[3], Love Moore[4], Anamitra Bhaumik[5], Ethan Sandoval[3], Alan Paul Lombard[1,6]
[1]Department of Urologic Surgery, UC Davis, Sacramento, CA; [2]School of Medicine, UC Davis, Sacramento, CA; [3]Department of Systems and Synthetic Biology, UC Davis, Davis, CA; [4]Department of Biochemistry and Molecular Medicine, UC Davis, Sacramento, CA; [5]Department of Neurobiology, Physiology, and Behavior, UC Davis, Davis, CA; [6]UC Davis Comprehensive Cancer Center, Sacramento, CA

Background: PARP inhibitors (PARPi) have improved prostate cancer management, but progression is inevitable. Drug tolerant persistence (DTP) is characterized by a minority of tumor cells which survive treatment and drive failure through transient acquisition of insensitivity. Elucidating and targeting DTP vulnerabilities will provide therapeutic strategies to combat disease progression.

Methods: Viability assays, western blots, and various additional assays determined treatment responses in PARPi sensitive C4-2B metastatic castration-resistant prostate cancer cells and C4-2B abiraterone-resistant derivative AbiR cells. DTP and DTEP models were developed through prolonged PARPi exposure. NGS profiled DTP and DTEP cells. Clinical stage ATM inhibitors were tested for their effects in combination with PARPis.

Results: C4-2B and AbiR response to olaparib and rucaparib is heterogeneous, characterized by cell death and cytostasis. C4-2B and AbiR cells exposed to high PARPi dosing for 9 days followed by drug holiday regain normal, parental cell morphology and become re-sensitized to treatment in line with acquisition of a DTP phenotype. Prolonged exposure to PARPi resulted in drug tolerant expanded persisters (DTEPs) that show less sensitivity to PARP inhibition. DTP and DTEPs display increased phospho-ATM levels suggesting activation of the cell cycle checkpoint. Utilization of ATM inhibitors both prevents DTEP formation and resensitizes DTEPs to PARP inhibition.

Conclusions: Our data suggest that transient, drug tolerant persistence may mediate survival of a minority of tumor cells. ATM inhibition may be used to prolong time to progression or to treat progressive disease. Future studies will focus on translating these strategies.

PF-23: IMPLEMENTING CULTURALLY TAILORED HUMAN PAPILLOMAVIRUS (HPV) VACCINE EDUCATION IN CHINESE-AMERICAN COMMUNITIES: THE HPV CANCER FREE INITIATIVE (HPV/CF)

Elina Kuang, Undergraduate Student[1], Laura Adame[2], Daisy Montoya[2], Julie H. T. Dang[1,2,3], Laura Fejerman[1,2]
[1]Department of Public Health Sciences, UC Davis, Sacramento, CA; [2]UC Davis Comprehensive Cancer Center, Sacramento, CA; [3]Division of Health Policy and Management, UC Davis, Sacramento, CA; [4]

Human papillomavirus (HPV) can cause six types of cancer, including over 99% of cervical cancer cases. Although the HPV vaccine can prevent more than 90% of HPV-related cancers, awareness and vaccination rates remain disproportionately low among Chinese-American communities. Nearly half of Asian-American women in California have never heard of HPV. Asian-American adolescents have lower HPV vaccination rates than their non-Hispanic White peers, with limited awareness and health literacy cited as primary barriers.
Using a continuous stakeholder engagement approach, a culturally tailored HPV vaccine education initiative was designed and implemented in collaboration with Chinese language schools and a Sacramento-based free clinic serving low-income Chinese populations. The PEARL framework, (i.e., Plain language and understandability; Explicit data, statistics, and graphs; Affirmative framing; Representative content; and Local connection) guided the adaptation of educational materials. Bilingual brochures and educational presentations that reflect cultural values, linguistic needs, and community-identified concerns were co-developed. Informal needs assessments and community feedback revealed barriers to HPV awareness, including limited English proficiency, stigma around sexual health, and misconceptions such as HPV only affecting women or unnecessary vaccination for those not sexually active.

These insights guided the content and framing of the materials to ensure accessibility and cultural relevance. The initiative strengthened engagement, fostered open dialogue, and addressed key gaps in HPV knowledge among parents and caregivers. Community response indicated increased trust in the information presented and greater willingness to discuss HPV prevention.

This work demonstrates the value of culturally specific, community-driven outreach in increasing HPV vaccination rates and promoting cancer prevention.

PF-24: COMPARING CANCER MORTALITY SMOKE-ATTRIBUTABLE FRACTION UNDERESTIMATION AND "EVERYTHING CAUSES CANCER APPEARANCES" INFLATION BY CONVENIENCE-DRIVEN NON-RESPONSE AND/OR SMOKING MISCLASSIFICATION BIASES IN COHORT AND REGISTRY VERSUS TIME-SERIES-BASED STUDIES

Bruce Leistikow, Professor Emeritus, Department of Public Health Sciences, UC Davis, Sacramento, CA

Background. For convenience, cohort studies generally omit pre-occupied dying, chain, and similar smokers (nonresponse bias) and misclassify covert and similar smokers as "never smokers." Registry and time-series methods minimize the former and both biases, respectively. So I compared California male overall cancer mortality smoking-attributable (SA) fraction (SAF) (CAMaleCaMortSAF) underestimation for 2017-2019 and, conversely, "Other factors! Unknowns!" overestimation across those SAF estimation methodologies.

Methods. The three CAMaleCaMortSAFs were calculated via published 1. Global Burden Of Disease (GBD) cohort-based and 2. registry SA divided by overall GBD cancer death counts for 2017-2019 and 3. the lung+trachea (CaLungTr)/overall cancer 1980-2021 age-standardized mortality rate (ASMR) Stata regression time-series-based averaged 2017-2019 CAMaleCaMortSAFs using published 1914 CaLungTr ASMRs as unexposed.

Results. CA male annual cancer mortality ASMRs and smoke exposures (active plus all other smoking, as measured by their annual CaLungTr ASMRs), were steeply (slope 1.99 (95% confidence interval 1.94-2.04) and tightly (R2=0.994) associated after autocorrelation adjustment. That, registry, and GBD SA deaths suggested 2017-2019 CAMaleCaMortSAFs of 39.9% (sensitivity range 35.4%-42.2%), 24.4%, and 20.7%, respectively.

Discussion. Male CaLungTr and overall cancer mortality ASMR trends are nearly perfectly (R2=0.994) and steeply associated in California, and, previously, elsewhere. Estimated CAMaleCaMortSAFs remain high, especially so for registry and time-series methods that avoid cohort nonresponse and also smoking misclassification biases, respectively. Those biases likely grossly deflate cohort CAMaleCaMortSAFs globally and inflate the "Other factors! Unknowns!" misattributions that maintain industry sales, profits, and deaths, per experts.

PF-25: IMPACT OF DEEP LEARNING-BASED IMAGE DENOISING ON LESION DETECTABILITY IN POSITRON EMISSION TOMOGRAPHY

David Melnichuk, Undergraduate Student[1], Reimund Bayerlein[1,2], Siqi Li[2,3], Ramsey Badawi[1,2,3]
[1]Department of Biomedical Engineering, UC Davis, Davis, CA; [2]Department of Radiology, UC Davis, Sacramento, CA; [3]UC Davis Comprehensive Cancer Center, Sacramento, CA

Lesion detectability is a vital metric for oncologic diagnostics, crucial for determining the specificity and sensitivity of cancer detection in positron emission tomography (PET) images. The goal of this study is the investigation of lesion detectability in PET images under various conditions before and after the application of a deep learning (DL)-based image denoiser. To that end PET images with three different noise levels and four distinct tumor-to-background ratios (TBR), ranging from 1.5 to 3, were investigated. Lesion-specific list-mode data were simulated and combined with original patient data prior to image reconstruction, ensuring a precise in-vivo ground truth. To emulate different noise levels PET list-mode data was down-sampled by factors of 1/8th , 1/16th and 1/32nd , respectively. These images are then denoised using a 3D Denoising Diffusion Probabilistic Model (3D DDPM), a trained deep learning model that predicts and reconstructs a low-noise image from higher-noise data. In this study we analyze under various conditions how accurately lesions are preserved in the model predictions. Lesion detectability was quantitatively assessed using a numerical model observer, specifically the channelized Hotelling observer with three channels, and the results were expressed through the area under the receiver operating characteristic curve (AROCC). PET image denoising and quantitative analysis are currently in progress. At the symposium, a comprehensive quantitative comparison of lesion detectability with and without the application of the DL-based denoiser will be presented.

PF-26: EXPRESSION DYNAMICS OF LACTYLATION TARGETS ACROSS TUMOR STAGE AND GRADE IN CLEAR CELL RENAL CELL CARCINOMA

Ayan Naveed, Undergraduate Student[1,2], Ssu-Wei Hsu[1], Longxiaotian Zhang[2], Jun Rao[1], Ching-Hsien Chen[1,2,3]
[1]Division of Nephrology, Department of Internal Medicine, UC Davis, Sacramento, CA; [2]Division of Pulmonary and Critical Care Medicine, UC Davis, Sacramento, CA; [3]UC Davis Comprehensive Cancer Center, Sacramento, CA

Lactylation, a recently characterized post-translational modification driven by the glycolytic byproduct lactate, has been implicated in tumor proliferation, metabolic reprogramming, and invasion. To elucidate its role in clear-cell renal cell carcinoma (ccRCC), we integrated TCGA PanCancer Atlas RNA-seq and clinical data taken from 512 ccRCC patients, then filtered for several hundred experimentally validated lactylation targets and analyzed their mean expression across both tumor stages (I–IV) and grades (G1–G4). We observed a clear, stage-dependent up-regulation of cell-cycle regulators (CCNA2, CCNB1, MKI67, TOP2A) and translation machinery (RPL/RPS families, EEF1A1, EEF2), along with chaperones (HSPA5, HSP90B1) and antioxidant enzymes (PRDX1, PRDX6), mirroring enhanced proliferation, protein synthesis, and stress adaptation in advanced tumors. Mesenchymal and cytoskeletal markers (VIM, FSCN1, ACTN1) also increased with stage and grade, consistent with epithelial–mesenchymal transition. Key metabolic enzymes exhibited divergent patterns: TCA cycle subunits SDHA–D peaked at intermediate stages and grades before declining, whereas IDH1/2 rose monotonically with both stage and grade; the water channel AQP1 was progressively down-regulated in higher stages and grades, suggesting altered osmoregulation and metabolism. Other targets—such as the RNA-binding protein RALY—increased steadily, and housekeeping genes (ABCE1, ABCF1, AACS) showed relatively modest changes. These coordinated, stage- and grade-specific expression trajectories highlight lactylation substrates as biomarkers of ccRCC progression and underscore lactate-driven protein modification as a potential therapeutic axis.

PF-27: CHROMATIN ACCESSIBILITY DIFFERENTIATES CANCER ASSOCIATED FIBROBLAST SUBTYPES IN PANCREATIC CANCER

Minh Duc Pham, Graduate Student,[1,2], Kedi Huang[1], Chang-il Hwang[1,2]
[1]Department of Microbiology and Molecular Genetics, UC Davis, Sacramento, CA; [2]UC Davis Comprehensive Cancer Center, Sacramento, CA

Pancreatic ductal adenocarcinoma (PDAC) remains the deadliest cancer with only 13% of five-year survival rate in patients. However, effective administration and drug delivery of have been limited due to the dense fibrotic stroma in PDAC tumor microenvironment (TME), majorly contributed by cancer-associated fibroblasts (CAFs). Unfortunately, targeting CAFs to enhance PDAC treatment has not yet been successful due to the lack of understanding in CAF heterogeneity and plasticity. Previous scRNA-seq studies revealed different CAF subtypes with diverse phenotypes and functions but the underlying mechanisms of CAF activation remain unclear. Interestingly, CAFs do not genetically differ from their origins, and they are interconvertible depending on external factors and signaling cues. These suggest that CAFs are characterized by their cellular states rather than an end-of-point differentiation. Therefore, we hypothesized that CAFs activation is regulated by epigenetic reprogramming. Using ATAC-seq and innovative PDAC organoid-CAF co-culture models, we revealed distinct chromatin accessibility profiles of two major CAF subtypes, myofibroblasts (myCAFs) and inflammatory fibroblasts (iCAFs) in vitro. Gained differentially accessible regions were identified across genomes, located not only at promoters but also at enhancers, and they were highly associated with expression signatures of each subtype. In line with this, analysis on snATAC-seq of the fibroblast population within PDAC tumor tissues also confirmed distinct chromatin accessibility profiles of different CAF subtypes. Overall, our study demonstrates the epigenetic basis of CAFs plasticity both in vitro and in vivo, suggesting a novel therapeutic strategy of epigenetically targeting CAFs to remodel the PDAC TME and improve treatment outcomes in PDAC patients.

PF-28: A NOVEL APPROACH TO TRIPLE-NEGATIVE BREAST CANCER: PIP5K1 INHIBITION AS A STRATEGY TO SUPPRESS PI3K/AKT AND PLC PATHWAYS

Kelsey Racacho, Graduate Student[1,3], Xiaoyun Zhao[1], Rodolfo Villa[1,3], Tzu-Yin Lin[2,3], Yuanpei Li[1,3]
[1]Department of Biochemistry and Molecular Medicine, UC Davis, Sacramento, CA; [2]Department of Internal Medicine, UC Davis, Sacramento, CA; [3]UC Davis Comprehensive Cancer Center, Sacramento, CA

Triple-negative breast cancer (TNBC) is one of the most difficult breast cancer subtypes to treat and currently lacks targeted therapies or a definitive cure. While chemotherapies and immunotherapies have been developed to combat TNBC, their efficacy is limited. One of the key tumor-promoting pathways in TNBC is the phosphatidylinositol 3-kinase/protein kinase B (PI3K/AKT) signaling cascade. Although some AKT-targeting therapies exist, they are typically used in combination regimens or as second-line treatments. A critical upstream enzyme in this pathway is phosphatidylinositol 4-phosphate 5-kinase 1 (PIP5K1), a lipid kinase that generates phosphatidylinositol 4,5-bisphosphate (PIP2), the substrate for both PI3K and phospholipase C (PLC). Through this dual role, PIP5K1 regulates both PI3K/AKT and PLC signaling, the latter of which produces key secondary messengers, inositol triphosphate (IP3) and diacylglycerol (DAG). Notably, there are currently no FDA-approved inhibitors of PIP5K1, representing an untapped therapeutic opportunity. We have developed a novel small-molecule inhibitor (SMI 299) targeting PIP5K1, which shows threefold greater toxicity and greater inhibition of phosphorylated AKT compared to two existing preclinical PIP5K1 inhibitors. Moving forward, we aim to: (1) assess cellular toxicity and pathway inhibition, (2) evaluate intrinsic cell death and potential off-target effects following our SMI treatment, and (3) investigate the toxicity and therapeutic efficacy of our SMI 299 in vivo. We hypothesize that PIP5K1 inhibition via SMI 299 will suppress tumor growth and progression by simultaneously disrupting the PI3K/AKT and PLC pathways in both in vitro and in vivo TNBC models. This novel therapeutic strategy may address a critical treatment gap in TNBC by offering enhanced specificity and efficacy.

PF-29: ENGAGING DIVERSE AND UNDERSERVED COMMUNITIES THROUGH CANCER AWARENESS TRAINING AND EDUCATION (EDUCATE)

Laura Adame, Community Outreach and Engagement Coordinator[1], Neha Singh, Community Outreach and Engagement Coordinator[1], Bao Her[1], Alexandra Gori[1], Julie HT Dang[1,2], Laura Fejerman[1,2]
[1]Office of Community Outreach and Engagement, UC Davis Comprehensive Cancer Center, Sacramento, CA; [2]Department of Public Health Sciences, UC Davis, Sacramento, CA

Background: The UC Davis Comprehensive Cancer Center's Office of Community Outreach and Engagement (OCOE) serves a 19-county catchment area of 5.1 million residents, where cancer screening rates remain below 80%. To promote screening and vaccination, OCOE implemented EDUCATE (Engaging Diverse and Underserved Communities in Cancer Awareness Training and Education), providing education on screenable and vaccine-preventable cancers and modifiable behavioral risk factors.

Methods: Participants were recruited through convenience sampling in partnership with OCOE's community partners. OCOE delivered cancer site specific presentations that addressed signs and symptoms, risk factors, and screening guidelines. Informed consent and pre-surveys were collected before the sessions, and post-surveys and evaluations were administered afterward to assess participants' willingness to adopt cancer preventative behaviors.

Results: From 10/25/2024 to 5/1/2025, 22 educational sessions were conducted. A total of 153 participants completed pre- and post-surveys with the majority being female (81%); aged 60+ (54%) and insured (95%). At baseline, 47% of age-eligible participants were adherent with cancer screenings and hepatitis B vaccinations. In the post-survey, 52% of age-eligible participants reported intending to undergo cancer screening and vaccination within the next year, while 21% did not specify their intentions. 63% planned to improve diet and physical activity, and 84% planned to share the information they learned with others.

Conclusion: While EDUCATE provided cancer screening education and risk reduction strategies, intent to get screened remained low. Educational materials should be modified to assist individuals with behavioral intent and decision making to get cancer screenings.

Acknowledgements: Cancer Center Support Grant, National Cancer Institute

PF-30: RATES AND FACTORS ASSOCIATED WITH RECEIPT OF FIRST-LINE SYSTEMIC THERAPY FOR NEWLY DIAGNOSED STAGE IV NON-SMALL CELL LUNG CANCER (NSCLC): A POPULATION-BASED STUDY

Surbhi Singhal, Assistant Professor[1,4], Theresa H.M. Keegan[2,3,4], Jonathan W. Riess[1,4], Arti Parikh-Patel[2], Brenda M. Hofer[2], Shehnaz Hussain[3,4], Frances B. Maguire[2]
[1]Division of Hematology and Oncology, Department of Medicine, UC Davis, Sacramento, CA; [2]California Cancer Reporting and Epidemiologic Surveillance Program, Sacramento, CA; [3]Center for Oncology Hematology Outcomes Research and Training (COHORT), Division of Hematology and Oncology, UC Davis, Sacramento, CA; [4]UC Davis Comprehensive Cancer Center, Sacramento, CA

Introduction: Lung cancer is the leading cause of cancer-related death. Despite substantial therapeutic advances, improvements in population-level outcomes have been limited. Delayed clinical presentation partially contributes to suboptimal outcomes. Among individuals diagnosed with stage IV NSCLC, some present too clinically deconditioned to initiate treatment. We aimed to define the rate of systemic therapy receipt among individuals newly diagnosed with stage IV NSCLC and to identify factors associated with treatment.

Methods: This population-based cohort study used records from the California Cancer Registry to identify patients newly diagnosed with stage IV NSCLC between 2016 and 2022. Multivariable logistic regression was used to examine characteristics associated with receipt of systemic treatment.

Results: Among 36,623 identified patients, 15,481 (42%) did not receive systemic treatment. We identified several characteristics associated with no systemic treatment: age 65-79 (versus 20-49) (odds ratio [OR] 3.24, 95% confidence interval [CI] 2.77-3.79), age ≥80 (OR 7.42, 95% CI 6.30-8.72), American Indian (versus non-Hispanic White) race/ethnicity (OR 1.44, 95% CI 1.10-1.90), residence in the lowest (versus highest) tertile of neighborhood socioeconomic status (SES) (OR 1.75, 95% CI 1.65-1.87), and Medicaid (versus private) insurance (OR 1.66, 95% CI 1.52-1.80).

Conclusions: These findings demonstrate significant variation in systemic treatment for newly diagnosed Stage IV NSCLC, which may reflect differences in treatment access as well as late presentation precluding therapy. Improving lung cancer outcomes at a population-level will require targeted strategies to support treatment among older adults, patients who identify as American Indian, residents of lower SES neighborhoods, and individuals with Medicaid insurance.

PF-31: PATHWAY ANALYSIS OF NIMBOLIDE FOR IMMUNOTHERAPEUTIC APPLICATION IN NON-MUSCLE INVASIVE BLADDER CANCER

Conner Suen, Undergraduate Student[1,3], Neelu Batra[1], Avani Durve[1], Ustat Kuar[1], Christopher Lucchesi[1,3], Paramita Ghosh[2,3]
[1]Department of Urologic Surgery, UC Davis, Rancho Cordova, CA; [2]Department of Biochemistry and Molecular Medicine, UC Davis, Sacramento, CA; [3]UC Davis Comprehensive Cancer Center, Sacramento, CA

Background: As of 2025, approximately 85,000 new cases of bladder cancer were reported in the U.S., with ~75% classified as non-muscle-invasive bladder cancer (NMIBC). The standard treatment for NMIBC is intravesical Bacillus Calmette–Guérin (BCG), a live attenuated strain of Mycobacterium bovis that recruits immune cells to target tumor cells. However, a global BCG shortage has created an urgent need for alternative therapies. Our lab is investigating Nimbolide, a naturally derived liminoid from the neem tree, as a potential replacement.

Methods: To evaluate Nimbolide's therapeutic potential, we used high-throughput 3D bioprinted tumoroid models incorporating patient-derived tumor cells and the K9TCC-AXC/PuPu canine bladder cancer cell lines. We combined RNA-seq, qPCR, and flow cytometry to assess drug-induced cytotoxicity and immune modulation.

Results: Treatment with Nimbolide increased PBMC recruitment and tumor cell death in the 3D tumoroid platform. Gene expression analysis revealed multiple altered immune-related pathways, including downregulation of MUC16, a known inhibitor of Natural Killer (NK) cell activity that facilitates immune evasion. This suggests that Nimbolide may potentiate anti-tumor immunity through modulation of the tumor microenvironment. These results support the continued development of Nimbolide as a chemo-immunotherapeutic for NMIBC, particularly in the context of the ongoing BCG shortage.

PF-32: THE DIMORPHISM OF THE MULTINUCLEATED GIANT CELLS OF GLIOMAS

Muhammad Sulman, Medical Student[1], John Paul Aboubechara[2,3]
[1]School of Medicine, UC Davis, Sacramento, CA; [2]Department of Neurology, UC Davis, Sacramento, CA; [3]UC Davis Comprehensive Cancer Center, Sacramento, CA

Gliomas are highly aggressive brain tumors with limited treatment options and a poor prognosis. Despite extensive research into their molecular characteristics, their ultrastructural basis of pathogenesis remains largely unexplored. In this study, we aim to elucidate the nature of the multinucleated giant cells (MNGCs) within IDH1-wt glioblastoma (GBM) and IDH1-mutant astrocytoma; thus, shedding light on their types, ontogenies, morphologies, prevalence, significance, and potential impact on tumor progression and treatment resistance. Utilizing transmission electron microscopy (TEM), we examined 30 tumors (18 IDH1-wt GBMs and 12 IDH1-mt astrocytomas) and found that they share two types of MNGCs . Type 1 is formed by the fusion of several tumor cells. Type 2 seems to be produced by tumor fibrillar cells filled with intermediate filaments (IF) and lipids through two processes, either by cell fusion or by the immigration of naked nuclei to a larger IF-filled tumor cell. Both MNGC types lack bounding membranes, and their mitochondria had degenerate inner membranes and were occasionally filled with lipids. Our results showed that MNGC is not as rare as has been speculated; we found them in 43% of the studied cases and in a wide age range from 26 to 60. The two MNGC types occurred solely or in combination in both types of gliomas. Furthermore, MNGCs appear non-proliferative; and therefore, their contribution to tumorigenesis and metastasis is not yet fully resolved.

PF-33 EVALUATION OF VASCULAR EXPRESSION OF PD-L1 AND B7-H3 IN BREAST CANCER USING CONTRAST-ENHANCED ULTRASOUND IMAGING AND EX VIVO VALIDATION

Yash Tipirneni, Undergraduate Student[1,3], Arutselvan Natarajan[2], Jihye Baek[2], Jeremy Dahl[2], Ramasamy Paulmurugan[2]
[1]Department of Animal Biology, UC Davis, Davis, CA; [2]Department of Radiology, Stanford Canary Center, Palo Alto, CA; [3]UC Davis Comprehensive Cancer Center, Sacramento, CA

Immune checkpoint (IC) biomarkers such as PD-L1 and B7-H3 promote tumor immune evasion and are often upregulated in triple-negative breast cancer (TNBC). While immunohistochemistry (IHC) and fluorescence-activated cell sorting (FACS) are standard techniques to quantify these markers, both require invasive biopsies and can yield inaccurate results due to tumor heterogeneity. This study evaluates contrast-enhanced ultrasound (CEUS) with targeted microbubbles (TMBs) as a non-invasive method to detect vascular expression of PD-L1 and B7-H3 in vivo, with validation by IHC and FACS. Biotinylated antibodies for PD-L1 and B7-H3 were conjugated to streptavidin-coated microbubbles and injected into transgenic TNBC mice. CEUS measured differential targeted enhancement (DTE) before and after burst imaging. Tumors were then processed for IHC and FACS. TMB-CEUS showed significantly higher DTE values for PD-L1 (19.0 ± 1.9, $p = 0.001$) and B7-H3 (6.3 ± 1.3, $p = 0.02$) compared to non-targeted controls (1.8 ± 1.4). IHC confirmed elevated PD-L1 (50.8% ± 20.0, $p = 0.03$) and B7-H3 (50.6% ± 15.5, $p = 0.02$), while FACS showed increased expression of B7-H3 (50.1% ± 8.8, $p = 0.007$) and CD31 (13.8% ± 1.3, $p = 0.003$). PD-L1 levels trended higher in FACS but were not statistically significant. These findings support TMB-CEUS as a promising alternative to biopsy-based methods for evaluating immunotherapy eligibility and provide a foundation for clinical translation in cancer diagnostics.

PF-34: MICROGLIA AND MACROPHAGES AT THE BRAIN-TUMOR BORDER HAVE ENRICHED EXPRESSION OF INTERFERON GAMMA AND COMPLEMENT SIGNALING IN NATURALLY OCCURRING CANINE BRAIN METASTATIC MELANOMA: INSIGHT INTO THE MECHANISM(S) OF MELANOMA BRAIN METASTASIS FROM MAN'S BEST FRIEND

Christine Toedebusch, Associate Professor[4,5], Kulani T. Simafranca-Narte[1], Cliff G. Tepper[2] , Ryan G. Toedebusch[4,5], Stephanie Y. Liu[3] , Ryan R. Davis[3] , Michael S. Kent[1,5]
[1]Department of Surgical and Radiological Sciences, UC Davis, Davis, CA; [2]Tandem BioSolutions, Inc., West Sacramento, CA; [3]Genomics Shared Resource, Sacramento, CA; [4]Department of Molecular Biosciences, UC Davis, Davis, CA; [5]UC Davis Comprehensive Cancer Center, Sacramento, CA

Brain metastasis is the leading cause of death for melanoma patients, yet mechanisms of melanoma brain metastasis (MBM) are incompletely understood, and treatment options are often ineffective. MBM develops in approximately 40% of dogs with naturally occurring melanoma and may provide a complementary model for therapeutic investigation. It is likely that both the primary tumor and brain microenvironment contribute to MBM. Therefore, the aim of this study was to characterize the tumor and tumor microenvironment across tissues between dogs with MBM and non-brain melanoma metastases. Utilizing the Nanostring GeoMX Digital Spatial Profiler (DSP) platform and the Canine Cancer Atlas panel, we performed spatial transcriptomics on primary tumors (n=6), metastatic lymph nodes (n-6), and patient-matched brain with MBM (n=3) or without MBM (n=3). We segmented by cell type to include malignant melanocytes (PNL2), microglia/macrophages (IBA1), and lymphocytes (CD3) prior to Illumina sequencing. The results demonstrated that MBM-associated microglia/macrophages were molecularly distinct from those in brain tissue without metastases. We further identified distinct gene expression profiles in IBA1+ cells across the tumor core, tumor border, and peritumoral normal brain locations. Specifically, tumor border IBA1+ cells had increased expression of interferon-inducible genes (BST2, GLUL, LRP1) and complement genes (C3, C1QA, C1QB) compared to tumor core IBA1+ cells ($p<0.0001$). As interdependent pathways, interferon and complement signaling may cooperate to promote metastasis through development of the pre-metastatic niche and immune regulation in MBM. Our continued analysis will inform future studies using naturally occurring canine melanoma as a preclinical model for human MBM.

PF-35: GERMLINE BUB1B MUTATION: A NOVEL GENETIC DRIVER FOR MELANOMA AND MULTIPLE EPITHELIAL MALIGNANCIES

Tram T. Tran, Medical Student[1], Laura J. Young[1], Maha Kazmi[1], Jessica R. Terrell[1], Marin P. Melloy[1,2], Elanee Michelle Simmons[1], Katherine A. Rauen[3], Daniela Martiniuc[4], Hidetoshi Mori[5], Alexander Borowsky[5,7], John D. McPherson[6,7], and Maija Kiuru[4,7,8]
[1]School of Medicine, UC Davis, Sacramento, CA; [2]University of Minnesota Medical School, Minneapolis, MN; [3]Department of Pediatrics, UC Davis, Sacramento, CA; [4]Hereditary Cancer Program, UC Davis Comprehensive Cancer Center, Sacramento, CA; [5]Department of Pathology and Laboratory Medicine, UC Davis, Sacramento, CA; [6]Department of Biochemistry and Molecular Medicine, UC Davis, Sacramento, CA; [7]Deparrtment of Dermatology, UC Davis, Sacramento, CA; [8]UC Davis Comprehensive Cancer Center

Although numerous melanoma predisposition syndromes have been identified, many remain genetically unexplained. Whole exome sequencing revealed a novel germline mutation, BUB1B c.2316C>G (p.Tyr772Ter), in a patient with multiple primary malignancies, including melanoma, breast, thyroid, and lung cancers, and an extensive family history of cancer. This truncating mutation likely leads to haploinsufficiency of the spindle assembly checkpoint protein, BUBR1, encoded by BUB1B, supported by reduced protein levels by immunofluorescence in tumor and non-malignant tissues compared with controls ($p < 0.0001$) and evidence of genomic instability, including increased premature chromatid separation in primary patient leukocytes (6.4% vs. normal ≤2%). Somatic mutation analysis of melanoma samples revealed concurrent mutations in established melanoma drivers, such as NRAS and CDKN2A, underscoring the multifactorial nature of tumorigenesis. RNA sequencing highlighted downregulation of genes implicated in the PI3K-Akt pathway and integrin binding, pathways critical to oncogenesis. This study establishes BUB1B as a putative novel melanoma predisposition

gene and contributes to understanding the role of mitotic checkpoint defects in hereditary cancer syndromes. Further investigation into BUB1B mutations in cancer predisposition and tumorigenesis may also reveal therapeutic and prognostic insights, enhancing clinical management for at-risk individuals.

PF-36: IMMUNE PROFILING REVEALS RICH POPULATIONS OF ACTIVATED TISSUE RESIDENT T CELLS IN HUMAN AND MOUSE ADRENAL GLANDS

Jay Uppuluri, Medical Student[1], Natalie M. Liu[1], Karleen M. Meiklejohn[2], Marshall J. Lammers[1], Cyrus J. Sholevar[1], Megan C. Purl[1], Sean J. Judge[1,3], Claire E. Graves[1], Michael J. Campbell[1,3], Robert J. Canter[1,3]
[1]Department of Surgery, UC Davis, Sacramento, CA; [2]Department of Pathology and Laboratory Medicine, UC Davis, Sacramento, CA; [3]UC Davis Comprehensive Cancer Center, Sacramento, CA

Background: The adrenal glands are an important site of cancer metastasis with poor response rates to immunotherapy. Given limited data characterizing the adrenal immune microenvironment, we sought to evaluate the adrenal gland's role as a potential immune-privileged site that is resistant to immunotherapy.

Method: We collected matched non-tumor bearing adrenal tissue and peripheral blood from adrenalectomy patients. We also collected adrenal glands from C57BL/6 and BALB/C mice for cross-species analysis. Fresh samples were processed into single cell suspensions to assess immune phenotype and function.

Results: In 10 adrenalectomy patients, we observed that adrenal CD45+ live cells contained a notable population of CD3+ T cells (20.2%) that was similar to peripheral blood (17.3%). Adrenal T cells exhibited an increased expression of checkpoint marker PD-1 on both CD4+ and CD8+ T cells compared to peripheral blood (40% and 50% increase, respectively, $P < 0.05$). C57BL/6 and BALB/C mouse adrenal glands showed analogous results, with higher T cell expression of PD-1 when compared to splenic T cells ($P < 0.05$). Human adrenal CD4+ and CD8+ T cells also exhibited increased expression of activation marker CD69 (60% and 70% increase, respectively, compared to peripheral blood T cells, $P<0.05$).

Conclusion: Our analysis shows that adrenal tissue harbors a T cell rich population with increased expression of PD-1 and CD69 compared to peripheral blood. These findings suggest that the adrenal gland harbors a distinct population of tissue resident T cells which are not classically exhausted despite high PD-1 expression.

PF-37: LOCAL GENETIC ANCESTRY AND SPECTRUM OF PATHOGENIC VARIANTS AMONG BREAST CANCER RARE MUTATION CARRIERS FROM LIMA, PERU

Luqi Wang, Graduate Student[1,6], Xiaosong Huang[1], Paul Lott[2], Elad Ziv[3], Susan L. Neuhausen[4], Tatiana Vidaurre[5], Laura Fejerman[1,6]
[1]Department of Public Health Sciences, UC Davis, Sacramento, CA; [2]UC Davis Genome Center, Davis, CA; [3]Department of Medicine, UC San Francisco, San Francisco, CA; [4]Department of Population Sciences, City of Hope Comprehensive Cancer Center, Duarte, CA; [5]Department of Medical Oncology, Instituto Nacional de Enfermedades Neoplasicas, Lima, Peru; [6]UC Davis Comprehensive Cancer Center, Sacramento, CA

Breast cancer genetic testing can guide risk-reduction and early detection among healthy women and treatment in patients. Genetic predisposition to breast cancer remains understudied in women of Indigenous American genetic ancestry. In this study, we conducted whole exome sequencing on 11 high and moderate penetrance genes in 1,359 breast cancer patients from Lima, Peru. A total of 72 germline pathogenic/likely pathogenic (P/LP) variants were identified in 104 (7.65%, 104/1,359) women. The genes with the highest prevalence of P/LP variants were BRCA1 (1.77%), BRCA2 (1.47%), ATM (1.47%), PALB2 (1.18%), and CHEK2 (0.96%), with other genes adding up to 1.02%. The mutation spectrum exhibited unique patterns in the Peruvian breast cancer patients. Recurrent mutations were identified across multiple susceptibility genes, without evidence of increased shared identity by descent among those carrying recurrent mutations. Compared to women without P/LP variants, P/LP variant carriers were more likely to have a first-degree family history of breast cancer (18.3% vs. 7.1%, $p < 0.05$), to be diagnosed at a younger age (46.4 vs. 49.1 years, $p = 0.007$), to present with poorly differentiated or undifferentiated tumors (76.9% vs. 51.0%, $p < 0.05$), and to have triple-negative breast cancer

(26.0% vs. 13.3%, p = 0.003). An enrichment of European local ancestry at BRCA1 P/LP variant locus in carriers was observed compared to non-carriers, suggesting a gap in available knowledge about P/LP status of variants within non-European chromosomal segments in the BRCA1 gene. These findings highlight the importance of including diverse populations in genetic studies to uncover population-specific risk alleles that may be missed in predominantly European-based research.
Acknowledgements: We would like to thank the Peruvian Genetics and Genomics of Breast Cancer Study (PEGEN-BC) study participants, and the Placer Breast Cancer Endowed Chair for making this study possible.

PF-38: ESTROGENIC PREVENTION OF LHRHA-INDUCED BONE LOSS

Kristina Wells, Graduate Student[1], Damian Genetos[1,2]
[1]Department of Anatomy, Physiology and Cell Biology, UC Davis, Davis, CA; [2]UC Davis Comprehensive Cancer Center, Sacramento, CA

Introduction: Prostate cancer (PCa) proliferation is driven by androgens like testosterone and dihydrotestosterone (DHT). Androgen deprivation therapy (ADT), via luteinizing hormone releasing hormone agonists (LHRHa) or orchiectomy (ORX) is standard of PCa care. These treatments may induce bone loss, as bone uses sex hormones like testosterone and 17β-estradiol (E2) to maintain homeostasis. Our study investigates how LHRHa affects bone tissue and if bone mass can be restored via DHT or E2 supplementation.

Methods: 6-month-old C57BL/6J male mice were injected with leuprolide acetate or vehicle monthly for 14 weeks. On week 10, slow-release pellets containing placebo, E2, or DHT—an androgen that cannot be aromatized into estrogen—were implanted. A separate group underwent ORX on week 1. Bone mass, mechanical properties, and cellular mechanism were evaluated.

Results: LHRHa and ORX reduced femoral trabecular and cortical microarchitecture vs. vehicle. Only ORX reduced femoral ultimate load vs vehicle. There is no difference in osteoclast number or surface in any condition.

LHRHa-treated mice supplemented with E2 increased femoral trabecular and cortical bone and increased ultimate load relative to LHRHa+placebo. LHRHa+E2 increased osteoclast number and surface vs. LHRHa+placebo. LHRHa+DHT did not alter any parameter.

Discussion: LHRHa and ORX cause bone loss. Only ORX reduces strength. Patients with ORX may be more susceptible to fracture. E2–but not DHT–improves bone mass, strength, and increases remodeling 4 weeks post-treatment. E2 may spare bone mass for patients on LHRHa. Remodeling associates with greater PCa bone metastasis. Future studies should evaluate the consequences of E2 on bone metastasis.

PF-39: THE ASSOCIATION OF MASS MEDIA EXPOSURE AND UTILIZATION OF BREAST AND CERVICAL CANCER SCREENING IN GHANA

Ya Yang, Gradudate Student[1,3], Charlotte Kerber[1,3], Joseph Adu[2]
[1]Department of Public Health Sciences, UC Davis, Sacramento, CA; [2]Department of Nursing, Toronto Metropolitan University, Toronto, Canada; [3]UC Davis Comprehensive Cancer Center, Sacramento, CA

Background: Breast and cervical cancers are leading contributors to the public health burden affecting women in Ghana. While a few studies have examined how sociodemographic factors influence screening uptake, limited research has explored the role of media exposure in shaping women's decisions to seek these preventive measures. This study examines the association between mass media exposure and the utilization of breast and cervical cancer screening among Ghanaian women.

Methods: This cross-sectional study utilized national data from the 2022 Ghana Demographic and Health Survey (GDHS). The analysis included 10,316 women aged 15 to 49. The primary outcomes assessed whether respondents had ever received breast or cervical cancer screening. The main exposures of interest included

Internet use, mobile phone ownership, television ownership, and radio ownership. Two logistic regression models were used to examine the association between mass media exposure and the uptake of breast and cervical cancer screening.

Results: Women who reported using the Internet demonstrated significantly higher odds of undergoing breast cancer screening (AOR = 1.29, 95% CI: 1.13–1.48). However, Internet use was not statistically significant for cervical cancer screening (AOR = 1.23, 95% CI: 0.99–1.54). Mobile phone ownership was associated with breast cancer screening (AOR = 1.31, 95% CI: 1.10–1.56) but not with cervical cancer screening (AOR = 1.24, 95% CI: 0.92–1.68). Television ownership and radio exposure were not significant predictors of breast or cervical cancer screening uptake.

Conclusion: Mass media exposure, particularly through the Internet and mobile phones, was associated with breast cancer screening uptake but not cervical cancer. Our study suggests that future public health campaigns could leverage evolving digital communication technologies to increase breast cancer screening uptake, especially in developing countries like Ghana.

EF-01: COMPREHENSIVE CANCER CENTER SHARED RESOURCES

Aruna Chetty, Shared Resource Administrator, Dan Port, Marketing Specialist, UC Davis Comprehensive Cancer Center, Sacramento, CA

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