

**UC DAVIS**  
**HEALTH**

**COMPREHENSIVE  
CANCER CENTER**

**29<sup>th</sup> Annual Cancer Research Symposium**  
October 5 and 6, 2023

<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 29th Annual Symposium. In its 29th year, the Annual Symposium event highlights cancer research efforts conducted by our Cancer Center members. Our long-standing symposium 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 will be organized into five main sessions and two poster sessions: Thursday, Session I – Population Sciences and Health Disparities, chaired by Dr. Shehnaz Hussain; Session II – Career Development and Education, chaired by Dr. Frederick Meyers; Session III – Basic/Translational Science, chaired by Dr. Xiao-Jing Wang and Dr. Nicholas Mitsiades; and Friday, Session IV – Community Outreach and Engagement, chaired by Dr. Laura Fejerman and Session V - Clinical Research, chaired by Dr. Megan Daly. Poster sessions will allow cancer-focused investigators to highlight their innovative science.

The keynote presentation in Session I, "Searching for Clues for the Etiology and Risk Disparities of Multiple Myeloma and its Precursor", brings renowned scientist Dr. Wendy Cozen from UC Irvine. Her research focuses on the areas of epidemiology, cancer disparities, and immunology.

Session II will feature a panel on Career Paths in Implementation Science with speakers: Dr. Brittany Garcia, Dr. Ulfat Shaikh, and Dr. Elisa Tong. These outstanding cancer investigators will share their experiences and provide insights for aspiring researchers.

The keynote lecture for Session III will be given by Dr. J. Silvio Gutkind from UC San Diego Moores Cancer Center, whose research exploits the emerging information on dysregulated signaling circuitries and individual genomic and molecular alterations to develop new precision therapies to prevent and treat cancer. His presentation is entitled "Cancer in the New Era of Precision Medicine: Novel Multimodal Targeted and Immunotherapies."

Session IV on Community Outreach and Engagement is a new focus this year. Chaired by Dr. Laura Fejerman, the session will include presentations and a panel on "Insights from Successful Community-Research Partnerships" featuring Dr. Chester Austin from Northern Valley Indian Health and Ysabel Duron with The Latino Cancer Institute, joined by Dr. Julie Dang.

Our final keynote, and the David R. Gandara Lectureship Awardee for Fridays Session V, will be given by Dr. Karen Reckamp from Cedars-Sinai Cancer on the development of novel therapies and biomarkers for lung cancer with an emphasis on targeted therapies. She will speak on "The Future of Lung Cancer Therapy and Pragmatic Trial Designs."

In addition to our keynote and panel speakers, we are highlighting cutting-edge cancer research from UC Davis. For twenty-nine years this event has allowed us to introduce new faculty, feature research by students, and promote programmatic and multidisciplinary interactions.

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,

A handwritten signature in black ink that reads "Primo N. Lara, M.D." The signature is written in a cursive, flowing style.

Primo N. Lara, M.D.

Director, UC Davis Comprehensive Cancer Center

Executive Associate Dean for Cancer Programs

Professor, Division of Hematology and Oncology, Department of Internal Medicine

Codman-Radke Endowed Chair for Cancer Research

# SYMPOSIUM COMMITTEE MEMBERS

Primo N. Lara, M.D.  
Director, UC Davis Comprehensive Cancer Center  
Executive Associate Dean for Cancer Programs  
Professor, Division of Hematology and Oncology, Department of Internal Medicine  
Codman-Radke Endowed Chair for Cancer Research

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., MACP  
Associate Director for Education, Training, and Career Development, UC Davis Comprehensive Cancer Center  
Director, Center for Precision Medicine and Data Sciences  
Professor, Division of Hematology and Oncology, Department of Internal Medicine

Xiao-Jing Wang, M.D., Ph.D.  
Chief Science Officer and Associate Director for Basic Science, UC Davis Comprehensive Cancer Center  
Professor and Robert E. Stowell Endowed Chair in Experimental Pathology, Department of Pathology and Laboratory Medicine

Nicholas Mitsiades, M.D., Ph.D.  
Chief Translational Officer and Associate Director for Translational Research, UC Davis Comprehensive Cancer Center  
Professor and Albert Holmes Rowe Chair of Genetics III Endowed Chair, Division of Hematology and Oncology, Department of Internal Medicine

Laura Fejerman, Ph.D.  
Associate Director for Community Outreach and Engagement, UC Davis Comprehensive Cancer Center  
Professor, Department of Public Health Sciences

Megan Daly, M.D.  
Interim Associate Director for Clinical Research, UC Davis Comprehensive Cancer Center  
Professor, Department of Radiation Oncology

# CANCER CENTER SYMPOSIUM STAFF

Gina Dayton, M.P.A.  
Associate Director for  
Administration

Rachel Rivas  
Research Program and Data  
Analyst

Chelsey Reeves  
Executive Assistant

Ashley Hodel, Ph.D.  
Interim Administrative Director  
for Programs, Planning, and  
Evaluation

Aruna Chetty, M.B.A.  
Shared Resource Administrator

Peggy Martin  
Executive Assistant

Kirsten Asher  
Education Manager

Hanouvi Agbassekou  
Program Coordinator

Rui Wu  
Data System Analyst

Christian Joyce  
Marketing Specialist

# INDEX

Agenda.....	5-7
Oral presentations .....	8-18
Keynote speakers' biographical information .....	9-10
Abstracts of oral presentations (Thursday).....	11-15
Abstracts of oral presentations (Friday).....	16-18
Poster presentations.....	19-51
Poster Index.....	20-23
Poster abstracts (Thursday).....	24-37
Poster abstracts (Friday).....	38-51

# AGENDA

## 29<sup>th</sup> Annual Cancer Research Symposium

**Thursday, October 5, 2023**

Time	Title	Presenter	Location	
8 – 8:30 a.m.	<b>Breakfast</b>		Boardroom Foyer	
8:30 – 8:45 a.m.	Introduction and Welcome	<b>Primo Lara, M.D.</b> Director, UC Davis Comprehensive Cancer Center	Goodnight Auditorium, 1100 Cancer Center	
<b>SESSION I: Population Sciences and Health Disparities</b> Chair: Shehnaz Hussain, Ph.D., Sc.M.				
Time	Title	Presenter	Location	
8:45 – 9:30 a.m.	Keynote Presentation: “Searching for Clues for the Etiology and Risk Disparities of Multiple Myeloma and it’s Precursor”	<b>Wendy Cozen, D.O., M.P.H.</b> Professor, Division of Hematology/Oncology, Department of Medicine, School of Medicine; Department of Pathology, School of Medicine; Department of Epidemiology, School of Population Health; Susan and Henry Samueli College of Health Sciences; Co-Director, Experimental Tissue Resource Leader, Translational Cancer Epidemiology, Chao Family Comprehensive Cancer Center, University of California, Irvine	Goodnight Auditorium, 1100 Cancer Center	
9:30 – 9:45 a.m.	Q&A			
9:45 – 10 a.m.	“Obesity and the Risk of Early-age-onset Colorectal Cancer: Decoding Relationships and the Impact of Bariatric Surgery”	<b>Hisham Hussan, M.D.</b> Associate Professor, Gastroenterology, UC Davis		
10 – 10:05 a.m.	Q&A			
10:05 – 10:20 a.m.	“Utilizing Silicone Wristbands to Detect Environmental Contaminants within the Yurok Tribal Community”	<b>Elisabeth Rose Middleton, Ph.D.</b> Associate Director of Environmental and Climate Justice, Professor and Yocha Dehe Endowed Chair in California Indian Studies, Native American Studies, UC Davis		
10:20 – 10:25 a.m.	Q&A			
10:25 – 10:40 a.m.	“Between Two Worlds: Adolescent and Young Adult Oncology in Latin America”	<b>Elysia Alvarez, M.D., M.P.H.</b> Associate Professor, Department of Pediatrics, UC Davis		
10:40 – 10:45 a.m.	Q&A			
10:45 – 11 a.m.	<b>Break</b>			

## SESSION II: Career Development and Education

### Theme: Implementation Science

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

Time	Title	Presenters	Location
11 – 11:45 a.m.	Panel: “Career Paths in Implementation Science”	<b>Ulfat Shaikh, M.D., M.P.H.</b> Professor, Pediatrics, UC Davis <b>Elisa Tong, M.D., M.A.</b> Professor, Internal Medicine, UC Davis <b>Brittany Garcia, Ph.D.</b> Research Program Manager, Division of General Internal Medicine and Bioethics, UC Davis	Goodnight Auditorium, 1100 Cancer Center
11:45 – 1:15 p.m.	<b>Poster Session &amp; Lunch</b>		Boardrooms, 1101 & 1103 Cancer Center

## SESSION III: Basic and Translational Science

Chairs: Xiao-Jing Wang, M.D., Ph.D. and Nicholas Mitsiades, M.D., Ph.D.

Time	Title	Presenter	Location
1:15 – 1:45 p.m.	Keynote Presentation: “Cancer in the New Era of Precision Medicine: Novel Multimodal Targeted and Immunotherapies”	<b>J. Silvio Gutkind, Ph.D.</b> Distinguished Professor & Chair, Department of Pharmacology, School of Medicine; Associate Director Basic Science, UC San Diego Moores Cancer Center	Goodnight Auditorium, 1100 Cancer Center
1:45 – 2 p.m.	Q&A		
2 – 2:15 p.m.	“Fluorescence Lifetime Imaging in Surgical Oncology”	<b>Laura Marcu, Ph.D.</b> Professor, Biomedical Engineering, UC Davis	
2:15 – 2:20 p.m.	Q&A		
2:20 – 2:35 p.m.	“Epigenetic Alterations Promote Pancreatic Cancer Progression and Metastasis”	<b>Chang-il Hwang, Ph.D., D.V.M.</b> Assistant Professor, Microbiology and Molecular Genetics, UC Davis	
2:35 – 2:40 p.m.	Q&A		
2:40 – 2:55 p.m.	“Metabolic Adaptations in Renal Cell Carcinoma”	<b>Shuchi Gulati, M.D., M.S.</b> Assistant Professor, Hematology and Oncology, UC Davis	
2:55 – 3 p.m.	Q&A		

**End of Day 1**

## Friday, October 6, 2023

Time	Title	Presenter	Location
<b>8 a.m. – 9:30 a.m.</b>	<b>Poster Session and Breakfast</b>		Boardrooms, 1101 & 1103 Cancer Center
<b>SESSION IV: Community Outreach and Engagement</b> Chair: Laura Fejerman, Ph.D.			
9:30 – 10:15 a.m.	Presentation and Panel: “Insights from Successful Community-Research Partnerships”	<b>Ysabel Duron</b> Founder, The Latino Cancer Institute; Member of the National Cancer Advisory Board <b>Gerardo Mackenzie, Ph.D.</b> Associate Professor, Nutrition, UC Davis <b>Julie Dang, M.P.H., Ph.D.</b> Assistant Adjunct Professor, Public Health Sciences Executive Director, Office of Community Outreach and Engagement, UC Davis <b>Chester Austin, M.D.</b> Medical Director, Northern Valley Indian Health	Goodnight Auditorium, 1100 Cancer Center
<b>SESSION V: Clinical Research</b> Chair: Megan Daly, MD			
10:15 – 10:45 a.m.	<b>David R. Gandara</b> <b>Lectureship on Developmental Therapeutics:</b> “The Future of Lung Cancer Therapy and Pragmatic Trial Designs”	<b>Karen Reckamp, M.D., M.S.</b> Director, Division of Medical Oncology; Associate Director, Clinical Research; Clinical Professor, Department of Medicine, Cedars-Sinai Cancer	Goodnight Auditorium, 1100 Cancer Center
10:45 – 11 am	Q&A		
11 – 11:10 am	<b>Break</b>		
11:10 – 11:20 a.m.	“Pulmonary Functional Image-Guided Radiotherapy”	<b>Tokihiro Yamamoto, Ph.D., D.A.B.R.</b> Associate Professor, Radiation Oncology, UC Davis	
11:20 – 11:25 a.m.	Q&A		
11:25 – 11:35 a.m.	“Tobacco and Cancer Quality Outcomes with the UCDCCC Stop Tobacco Program”	<b>Elisa Tong, M.D., M.A.</b> Professor, Internal Medicine, UC Davis	
11:35 – 11:40 a.m.	Q&A		
11:40 – 11:50 a.m.	“Targeted Therapy and Immunotherapy in Lung Cancer: A New World”	<b>Jonathan Riess, M.D., M.S.</b> Associate Professor, Hematology and Oncology, UC Davis	
11:50 – 11:55 a.m.	Q&A		
11:55 – 12:05 p.m.	“A Patient-Centered Approach to Perioperative Care for Patients Undergoing Lung Cancer Resection”	<b>Lisa Brown, M.D., M.A.S.</b> Assistant Professor, General Thoracic Surgery, UC Davis	
12:05 – 12:10 a.m.	Q&A		
12:10 – 12:20 p.m.	Closing Remarks and Poster Awards Announcement	<b>Primo Lara, M.D.</b> Director, UC Davis Comprehensive Cancer Center	
<b>Symposium Close</b>			

# ORAL PRESENTATIONS

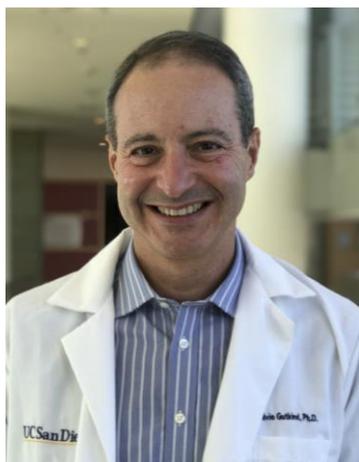
Keynote speaker biographical information: page 9-10  
Abstracts of oral presentations (Thursday): page 11-15  
Abstracts of oral presentations (Friday): page 16-18

## KEYNOTE SPEAKER BIOGRAPHICAL INFORMATION

**Dr. Cozen** is a cancer epidemiologist with a focus on the etiology and epidemiology of hematologic neoplasms. She received her DO from Western University of Health Sciences, had residency training in Pathology at the UCLA West LA VA Medical Center and then obtained an MPH in epidemiology and completed a Preventive Medicine residency at UCLA. She was the Deputy Director of the Los Angeles County Department of Health Services Sexually Transmitted Disease Program for 2 years before moving to academic medicine. She completed an NCI fellowship in cancer epidemiology in the USC Department of Preventive Medicine and joined the faculty building her 25-year research program on the etiology of lymphoma and multiple myeloma with an emphasis on risk disparities and immune-related factors. She recently relocated to UC Irvine and is a tenured professor in the division of hematology and oncology, in the department of medicine, where she continues her research on hematologic neoplasms. She has had continuous grant support since 1998 and has 259 peer-reviewed papers. She is an AAAS fellow for her contributions to lymphoma etiology and served on the American Society of Hematology Scientific Affairs committee. Current areas of interest and funding include tumor microenvironment and host factors in predicting Hodgkin lymphoma in a multiethnic sample, and determinants of MGUS and multiple myeloma, focused on explaining the African American excess risk of these conditions.



**Wendy Cozen, DO, MPH**  
Professor, Division of Hematology/Oncology, Department of Medicine, School of Medicine; Department of Pathology, School of Medicine; Department of Epidemiology, School of Population Health; Susan and Henry Samueli College of Health Sciences; Co-Director, Experimental Tissue Resource Center, Translational Cancer Epidemiology, Chao Family Comprehensive Cancer Center, University of California, Irvine



**J Silvio Gutkind, PhD**  
Distinguished Professor & Chair,  
Department of Pharmacology,  
School of Medicine  
Associate Director Basic Science,  
UC San Diego Moores Cancer  
Center

**Dr. Gutkind** is a Distinguished Professor and Chair, Department of Pharmacology, School of Medicine, and Associate Director for Basic Science at the Moores Cancer Center, University of California San Diego. He received his Ph.D. in pharmacy and biochemistry from the University of Buenos Aires, Argentina, and after his post-doctoral training at the NIMH and NCI, he joined the NIDCR, NIH. He served as the Chief of the Oral and Pharyngeal Cancer Branch, NIDCR, NIH, since 1998 until his recruitment to UCSD in 2015.

His research team is exploiting the emerging information on dysregulated signaling circuitries and individual genomic and molecular alterations to develop new precision therapies to prevent and treat cancer, and to identify novel multimodal strategies to enhance the response to cancer immunotherapies. His research team has pioneered the study of G proteins and G protein coupled receptors in human malignancies. As part of his translation efforts, Dr. Gutkind has led a multi-institutional clinical trial establishing the benefits of treating oral cancer patients with mTOR inhibitors, and he is co-leading a new mTOR-targeting chemoprevention medicine trial in oral premalignancy. His laboratory has recently launched a new effort exploring multimodal precision immunotherapy approaches for cancer prevention and treatment.

His honors include the NIH Merit Award, the Elliot Osserman Award from the Israel Cancer Research Foundation, the Pharmaceutical Research and Manufacturers of America (PhRMA) Research & Hope Award, the Distinguished Scientist Award from the International Association of Dental Research (IADR), 2023 Susan Band Horwitz Award Lecture in Cancer Pharmacology (ASPET Division of Cancer Pharmacology) and the election as the Chair, Division of Molecular Pharmacology, American Society for Pharmacology and Experimental Therapeutics (ASPET). He was elected in 2019 to the National Academy of Medicine, recognizing his team's translational efforts in the area of cancer signaling. He has published over 500 research articles in some of the most prestigious journals and has organized and co-organized multiple national and international meetings and symposia on signal transduction and oral cancer research. He has been a member of many editorial boards of scientific journals and national and international advisory committees, and he has

supervised and mentored many junior investigators, who are now playing leadership roles in multiple institutions in the United States and abroad.

**Dr. Reckamp** is a Clinical Professor in Medicine and Director of the Division of Medical Oncology at Cedars-Sinai Medical Center. She is also the Associate Director of Clinical Research for the Cedars Sinai Cancer, and Medical Oncology Director of the Women's Guild Lung Institute at Cedars Sinai Medical Center.

She received a master's degree in clinical investigation from the department of Biomathematics at UCLA. Dr. Reckamp also serves as the Associate Director of Clinical Research for the Samuel Oschin Comprehensive Cancer Institute (SOCCI). She obtained my medical degree at the University of Chicago, Pritzker School of Medicine in 1998 with AOA distinction, and trained in Internal Medicine at Washington University's Barnes-Jewish Hospital. Dr. Reckamp completed fellowship training in Hematology/Oncology at the David Geffen School of Medicine, UCLA in June 2004, and completed a Master of Science degree in Clinical Research (MSCR).

Dr. Reckamp serves as Chair for the Association of American Cancer Institute's Physician Clinical Leadership Initiative. She leads many phase I, II, and III studies funded by the NCI, internal funds and industry. Dr. Reckamp is a member of ASCO, AACR, International Association for the Study of Lung Cancer, and SWOG. She is vice Chair of the SWOG Lung MAP platform. She participated in the ASCO Leadership Development Program and led the Scientific Committee for metastatic lung cancer for the ASCO annual meeting. Dr. Reckamp has been the past recipient of many honors including American Lung Association, Lung Force Honoree in 2018. She has also authored or co-authored many manuscripts in the field of Thoracic Oncology in high impact journals, including the New England Journal of Medicine and Journal of Clinical Oncology.



**Karen Reckamp, MD, MS**  
Director, Division of Medical Oncology; Associate Director, Clinical Research; Clinical Professor, Department of Medicine, Cedars-Sinai Cancer

# **ABSTRACTS OF ORAL PRESENTATIONS (THURSDAY)**

## **SESSION I: Populations Sciences and Health Disparities**

*Chair: Shehnaz K Hussain, PhD, Sc.M*

### **KEYNOTE LECTURE: SEARCHING FOR CLUES FOR THE ETIOLOGY AND RISK DISPARITIES OF MULTIPLE MYELOMA AND ITS PRECURSOR MGUS: CURRENT STATE OF KNOWLEDGE AND FUTURE DIRECTIONS.**

*Wendy Cozen, DO, MPH, Professor, Division of Hematology/Oncology, Department of Medicine, School of Medicine; Department of Pathology, School of Medicine; Department of Epidemiology, School of Population Health; Susan and Henry Samueli College of Health Sciences; Co-Director, Experimental Tissue Resource Leader, Translational Cancer Epidemiology, Chao Family Comprehensive Cancer Center, University of California, Irvine*

Multiple myeloma is a neoplasm of plasma cells, with approximately 32,000 cases diagnosed in the U.S. annually. Monoclonal gammopathy of undetermined significance (MGUS) is the benign necessary, but not sufficient, precursor for multiple myeloma. Blacks experience 1.5 (men) -2 (women) -fold increased risk of multiple myeloma and 2- (men)- 3 (women)-fold increased risk of MGUS compared to Whites. U.S. Asian Americans experience 50% lower risk of both. Other risk factors include older age and male sex. Common risk variants have been identified by GWAS in Whites explaining 16% heritability, which mostly replicated in Blacks, but do not explain the excess risk in this group (with a caveat of small numbers). Obesity is the most consistently observed risk factor for multiple myeloma, MGUS and progression of MGUS to multiple myeloma, although the majority of studies have been conducted in Whites. Adipose tissue produces plasma cell growth factors providing a possible mechanism. We conducted a study of MGUS risk factors in the Multiethnic Cohort and found the body mass index at cohort entry was positively associated within most racial/ethnic groups, with high and low risk non-IgM MGUS, and with a non-significant 3% increase in IgM MGUS. Previously reported polygenic risk scores (PRS) for MGUS and multiple myeloma were not associated with MGUS or MGUS progression to multiple myeloma in the Multiethnic Cohort. Of note, there were significant differences in isotype distribution among the diverse racial/ethnic groups. Other possible, less studied explanations for the risk difference include environmental and dietary exposures.

### **OBESITY AND THE RISK OF EARLY-AGE-ONSET COLORECTAL CANCER: DECODING RELATIONSHIPS AND THE IMPACT OF BARIATRIC SURGERY**

*Hisham Hussan, MD, Associate Professor, Gastroenterology, UC Davis*

Obesity will soon surpass smoking and alcohol as a leading cause of preventable cancer in the United States and worldwide. The risk of colorectal cancer (CRC) is increased by 30% with obesity. Early-onset obesity-related cancers (cancers diagnosed <50 years) are also rising in the U.S., possibly due to rising obesity rates. Notably, using a nationally representative sample, our data identify a greater and earlier body fatness in adults with early-onset colorectal, other gastrointestinal, and uterine cancers than later-onset cancers. In parallel, the utilization of bariatric surgery expanded as a successful treatment option in adults with severe obesity who fail conservative weight loss approaches. Nowadays, about 250,000 adults have bariatric surgery yearly in the U.S., and this number will likely increase. Bariatric surgery can improve early-life obesity, per our data. However, studies do not show an effect on early-onset CRC. Further, our in-depth evaluation of sex differences has uncovered a 60% significant reduction in CRC risk post-Roux-en-Y gastric bypass (RYGB) in females compared to controls with severe obesity, while CRC risk was suggestively increased in males post-RYGB. In our presentation we discuss the microbiome patterns after RYGB that are potentially implicated in CRC risk. Future studies are needed to validate and understand the impact of these microbiome changes on CRC risk after bariatric surgery.

## **UTILIZING SILICONE WRISTBANDS TO DETECT ENVIRONMENTAL CONTAMINANTS WITHIN THE YUROK TRIBAL COMMUNITY**

*Elisabeth Rose Middleton, PhD, Associate Director of Environmental and Climate Justice, Professor and Yocha Dehe Endowed Chair in California Indian Studies, Native American Studies, UC Davis*

This collaborative study between the Yurok Tribe and UC Davis deploys silicone wristbands as passive sampling devices to obtain data on personal chemical exposures of tribal members. Our collective goal is to address Yurok Tribal members' concerns regarding everyday exposure on tribal lands. Tribal members who participate will receive an individual report of the contaminants found on their wristbands. After removing all identifiable information from the data, the project team will create informational graphics and handouts to disseminate findings to the Tribe. Data on contaminant exposure from the wristbands may correlate with other UCD-Yurok collaborative studies to detect and identify contaminants in soil and water, thus creating a more complete dataset on environmental contaminants and pathways of exposure affecting Tribal members.

## **BETWEEN TWO WORLDS: ADOLESCENT AND YOUNG ADULT ONCOLOGY IN LATIN AMERICA**

*Elysia Alvarez, MD, MPH, Associate Professor, Department of Pediatrics, UC Davis*

There are over 1 million new cancer diagnoses each year in adolescent and young adults (AYA: ages 15-39) worldwide, with most of these diagnoses occurring in low-and middle-income countries (LMIC). There is evidence in high-income countries (HIC) of disparities in outcomes in this age group, that is often referred to as the "AYA gap," including specific psychosocial challenges, poor access to specialist oncology care, and static survival rates over the last few decades for some cancers. Various strategies to overcome these disparities are underway in many HIC. However, global data on care delivery and outcomes for AYAs are scarce, but a similar "AYA gap" has been documented in some LMIC. To address this issue in Latin American LMIC, we are working to understand barriers and facilitators to delivery care for AYA patients in LMIC in Latin America. In addition, we will use this information to develop guidelines for culturally informed models of care. This study is critical to deepen our understanding of factors impacting AYA care from the perspective of various key stakeholders and the patient care experience, including the development of resource adapted, culturally informed models of care that address the unique challenges this group and their medical providers face in delivering optimal care. The results of this study will inform AYA inclusion in national cancer control plans in LMIC in Latin America and identify potential models of AYA cancer care that can accelerate progress to improve AYA survival globally.

# Session II: Career Development and Education

Chair: Frederick Meyers, MD, MACP

## **THEME: CAREER PATHS IN IMPLEMENTATION SCIENCE**

Implementation Science and Systems based improvement of care and population health are recognized as critical steps in cancer research. Today's symposium highlights three different investigators journey to funding in cancer implementation science.

## **USING IMPLEMENTATION SCIENCE TO CROSS THE QUALITY CHASM**

*Ufat Shaikh, MD, MPH, Professor, Pediatrics, UC Davis*

It takes 17 years to turn 14% of original research into services that are routinely provided in community settings. It may take even longer to de-adopt unnecessary practices. This presentation shares how implementation science can shorten the gap between research and practice, improve health outcomes, and control health care costs.

## **TOBACCO CESSATION AND POLICY PROJECTS FOR IMPLEMENTATION SCIENCE**

*Elisa Tong, MD, MA, Professor, Internal Medicine, UC Davis*

Tobacco is the leading preventable cause of death and there is strong evidence that cessation treatment improves health outcomes. Despite this strong evidence, there are still important gaps in the implementation of tobacco cessation and policy especially at the system level. Advancing implementation science includes identifying barriers and facilitators, testing new strategies, and disseminating best practices. Examples of research projects include a population-based survey analysis demonstrating factors influencing Latino Medi-Cal smokers being advised less than non-Latino counterparts, a randomized controlled trial testing a health system's proactive outreach strategy, and a tobacco learning collaborative for improving quality metrics.

A new opportunity is the cancer center's Tobacco Cessation Policy Research Center (TCPRC), a 4-year award funded by the Tobacco-Related Disease Research Program, that will also offer new research and training opportunities. The TCPRC's mission for advancing tobacco cessation policy in California is to build capacity for health care access, promote excellence in health care delivery, facilitate health care and community engagement, and achieve equity in health plan coverage. The TCPRC's goals are to generate evidence that can support tobacco cessation policy adoption and implementation, to collaborate with community and policy stakeholders for optimizing policy impacts, and to develop the pipeline of researchers for sustaining the TCPRC mission.

## **NON-TRADITIONAL PATHWAY TO A CAREER AS AN INDEPENDENT RESEARCHER**

*Brittany Garcia, PhD, Research Program Manager, Division of General Internal Medicine and Bioethics, UC Davis*

Dr. Garcia will discuss her personal, non-traditional career pathway to a target career as an independent researcher. She will provide details relating to her funding experience, mentor team, and the mentorship and career development plans to further expand her research skills and portfolio.

# SESSION III: Basic/Translational Science

Chair: Xiao-Jing Wang, MD, PhD and Nicholas Mitsiades, MD, PhD

## **KEYNOTE LECTURE: CANCER IN THE NEW ERA OF PRECISION MEDICINE: NOVEL MULTIMODAL TARGETED AND IMMUNOTHERAPIES**

*J. Silvio Gutkind, PhD, Distinguished Professor & Chair, Department of Pharmacology, School of Medicine; Associate Director Basic Science, UC San Diego Moores Cancer Center*

We will focus on the development of novel multimodal targeted and immunotherapies. Recent studies will be presented investigating the mechanisms by which genetic mutations in Gαq proteins initiate uveal and cutaneous melanoma, and the therapeutic potential of co-targeting the Hippo and ERK signaling pathways. We showed that the persistent activation of the PI3K/mTOR signaling circuitry is one of the most frequent dysregulated signaling mechanism in oral cancer. We will discuss studies targeting mTOR for oral cancer prevention and treatment, and recently launched efforts aimed at achieving durable responses in oral cancer patients by the development of novel multimodal immunotherapies.

## **FLUORESCENCE LIFETIME IMAGING IN SURGICAL ONCOLOGY**

*Laura Marcu, PhD, Professor, Biomedical Engineering, UC Davis*

This presentation reviews the development of clinically-compatible fluorescence lifetime imaging (FLIM) technology and applications in surgical oncology. Emphasis is placed on the integration of FLIM in surgical workflow and the potential of this approach to improve surgical decision-making during neurosurgical procedures and trans-oral robotic surgery (TORS). Current results demonstrate the utility of FLIM-derived parameters detecting tissue biochemical and metabolic characteristics to sense infiltrative brain cancer at the resection margins and to distinguish oral and oropharyngeal cancer in real-time from surrounding normal tissue in patients in-situ during TORS. Our findings suggest that label-free FLIM-based tissue assessment, characterized by simple, fast and flexible data acquisition and display, could find applications in a variety of surgical procedures.

## **EPIGENETIC ALTERATIONS PROMOTE PANCREATIC CANCER PROGRESSION AND METASTASIS**

*Chang-il Hwang, PhD, DVM, Assistant Professor, Microbiology and Molecular Genetics, UC Davis*

Pancreatic cancer is the third leading cause of cancer-related deaths in the United States with a 5-year survival rate of only 12%, the lowest among all common cancers. Pancreatic ductal adenocarcinoma (PDAC) is the most common and challenging form of pancreatic cancer due to its highly metastatic nature. Key driver mutations such as oncogenic mutations of *KRAS* and loss-of-function mutations in *TP53* are known to promote formation of pancreatic intraepithelial neoplasia (PanIN) lesions, ultimately leading to the development of PDAC. While no recurrent mutation responsible for PDAC metastasis has yet been identified, an increasing amount of evidence suggests that epigenetic alterations (e.g., enhancer activity, chromatin accessibility and/or DNA methylation) are responsible for the late stage of disease progression in PDAC. Previously, various transcription factors (TFs) have been shown to reshape the epigenetic landscape, thereby conferring aggressive characteristics, and leading to a molecular subtype switch from the progenitor to the squamous subtype. In this context, we provide an example of EN1, a homeodomain TF, which represses its target genes through direct binding to gene enhancers and promoters, implicating roles in the activation of MAPK pathways and the acquisition of mesenchymal properties. Additionally, we present compelling evidence that PDAC progression is accompanied by recurrent DNA methylation changes, which might be further exploited for PDAC diagnostics and therapeutics in the future.

## **METABOLIC ADAPTATIONS IN RENAL CELL CARCINOMA**

*Shuchi Gulati, MD, MS, Assistant Professor, Hematology and Oncology, UC Davis*

Genomic modifications and transcriptomic gene signatures have been studied both in the metastatic setting as well as in localized kidney cancer. However, these signatures lack prospective validation. A single scoring system, transcriptomic signature or genomic classifier, is unlikely to accurately define prognosis in RCC. When viewed in the context of metabolism, worse survival in ccRCC has been shown to correlate with upregulation of pentose phosphate pathway genes (G6PH, PGLS, TALDO and TKT), fatty acid synthesis genes (ACC and FASN), and PI(3)K pathway enhancing genes (MIR21). Better survival correlates with upregulation of AMPK complex genes, multiple Kreb's cycle genes and PI(3)K pathway inhibitors (PTEN, TSC2). There is also evolving evidence that metabolic reprogramming drives progression in ccRCC, and a specific "metabolic phenotype" defines aggressive cancers. Additionally, this phenotype in cancer cells may also influence components of the tumor microenvironment, such as immune cells, and ultimately influence therapeutic responses in kidney cancer. We aim to further elucidate these phenotypes and hence lay the foundation for an understanding of how metabolic pathways influence the prognosis and possibly the therapeutic impact of contemporary treatments in kidney cancer.

# ABSTRACTS OF ORAL PRESENTATIONS (FRIDAY)

## SESSION IV: Community Outreach and Engagement

*Chair: Laura Fejerman, PhD*

### THE ROAD TO COMMUNITY ENGAGEMENT - RESPECT, TRUST AND COLD, HARD CASH!

*Ysabel Duron, Founder, The Latino Cancer Institute; Member of the National Cancer Advisory Board*

The growing demand for researchers to engage with community in research, instead of just checking the box, has become the stuff of academic papers in community based participatory research. But these papers stop short of reflecting the lived experience and realistic Point of View (POV) of the community-based agencies (CBOs) tasked to become research partners. Or maybe CBOs are just too polite!

Ysabel Duron, the Founder and Executive Director of The Latino Cancer Institute, a cancer survivor, a 23-year patient advocate, a serial engager in research and, most recently, a presidential appointee to the National Cancer Advisory Board at the NCI, will take up the challenge in addressing this topic.

Hopefully, the award-winning veteran TV newscaster and former journalist, won't scare you away, but will provide a pathway for developing long, respectful, and productive community partnerships that serve both researcher and community.

### TIME, TRUST, TRANSPARENCY: BUILDING AND SUSTAINING COMMUNITY COLLABORATIONS

*Julie Dang, MPH, PhD, Assistant Adjunct Professor, Public Health Sciences; Executive Director, Office of Community Outreach and Engagement, UC Davis*

The University of California, Comprehensive Cancer Center's Office of Community Outreach and Engagement has spent over a decade building and nurturing community relationships to assess and address the cancer burden among diverse and underrepresented populations of our catchment area. These partnerships have led to many collaborations over the years, not only to increase cancer awareness, prevention, and control in the community but also to build capacity and facilitate community engaged research. Our ability to approach and engage the community stems from the time we have devoted to earning the trust of the community by being flexible and transparent. While this process is unique for each community, we found that by using bilingual and bicultural health educators to provide tailored outreach and education and through partnering with local, trusted, community-based organizations we can connect with communities. Here, we describe our strategies, lessons learned, and share opportunities for increasing community engagement throughout the cancer research and control continuum. Our approaches and community networks can be harnessed to foster bidirectional community-academic partnerships that can help inform research and institutional priorities, advance cancer health equity, and improve community and population health.

### PANEL: INSIGHTS FROM SUCCESSFUL COMMUNITY-RESEARCH PARTNERSHIPS

- **Ysabel Duron**, Founder, The Latino Cancer Institute; Member of the National Cancer Advisory Board
- **Chester Austin, MD**, Medical Director, Northern Valley Indian Health
- **Gerardo Mackenzie, PhD**, Associate Professor, Nutrition, UC Davis
- **Julie Dang, MPH, PhD**, Assistant Adjunct Professor, Public Health Sciences; Executive Director, Office of Community Outreach and Engagement, UC Davis

# SESSION V: Clinical Research

*Chair: Megan Daly, MD*

## **DAVID R. GANDARA LECTURESHIP ON DEVELOPMENTAL THERAPEUTICS: THE FUTURE OF LUNG CANCER THERAPY AND PRAGMATIC TRIAL DESIGNS**

*Karen Reckamp, MD, MS, Director, Division of Medical Oncology; Associate Director, Clinical Research; Clinical Professor, Department of Medicine, Cedars-Sinai Cancer*

Therapies for lung cancer have evolved and patients are living longer with precision oncology treatment options available for many. Despite advances, improving survival and quality of life remains a major goal. Trials in the past decade have become more complex often limiting the types of participants, which result in studies with conclusions that are not necessarily applicable to the general population. Novel trial designs and outreach mechanisms are needed to increase inclusion in trials. The NCTN Pragmatica-Lung trial represents a novel design that decreases burden on clinical research staff and reduces eligibility barriers to increase participant diversity in trials.

## **PULMONARY FUNCTIONAL IMAGE-GUIDED RADIOTHERAPY**

*Tokihiro Yamamoto, PhD, DABR, Associate Professor, Radiation Oncology, UC Davis*

Thoracic radiotherapy (RT) is integral to the management of thoracic cancers, although it is limited by substantial pulmonary toxicity. For example, symptomatic radiation pneumonitis is a clinically important toxicity after thoracic RT. Pneumonitis is also caused by an immune checkpoint inhibitor (ICI). Symptomatic pneumonitis occurs in 35-43% of patients with locally advanced non-small cell lung cancer receiving the current standard-of-care, chemo-RT combined with consolidation ICI, and severe pneumonitis occurs in 3-18%. Pneumonitis is associated with poor survival in lung cancer patients treated with RT. A major obstacle to improving the therapeutic ratio in patients receiving thoracic RT is the lack of a strategy to reduce pulmonary toxicity. Pulmonary functional image-guided RT is a new strategy that preferentially avoids irradiating normally functioning lung regions, which has the potential to reduce pulmonary toxicity. There is a growing body of evidence for its feasibility, safety, and potential clinical benefit in reducing toxicity. This presentation will present the current and emerging pulmonary functional imaging methods based on computed tomography (CT), positron emission tomography (PET), and magnetic resonance imaging (MRI), and provide a review of the current evidence for functional image-guided thoracic RT.

## **TOBACCO AND CANCER QUALITY OUTCOMES WITH THE UC DCCC STOP TOBACCO PROGRAM**

*Elisa Tong, MD, MA, Professor, Internal Medicine, UC Davis*

Tobacco treatment and cessation is a critical factor for improving cancer care outcomes but widespread implementation for cancer centers has been difficult. Since 2017, the UCD Comprehensive Cancer Center's Stop Tobacco Program (SToP) has been integrating tobacco treatment into cancer care and building a sustainable program to increase reach. This work builds upon "UC Quits" which connected the 5 UC health systems with electronic referral orders to our free state quitline housed at UCSD. SToP is part of the National Cancer Institute's Cancer Center Cessation Initiative and helped launch the American College of Surgeons' Commission on Cancer tobacco quality improvement projects "Just ASK" in 2022 and "Beyond ASK" in 2023 for community cancer programs.

Over the past 5 years, SToP has more than doubled the reach of tobacco treatment among cancer patients. In partnership with UCD Health Management Education, SToP has worked with cancer clinic staff to improve referrals for comprehensive treatment, which includes 1:1 counseling and cessation medication. SToP has also developed proactive outreach strategies outside of the clinic encounter, identifying patients who do not yet have a tobacco status or documented assistance. These strategies are being shared across the UCD and other health systems, through the CA Quits' Tobacco Learning Collaborative, to improve tobacco quality metrics for the state's Quality Incentive Pool program. These strategies will also prepare UCD and the UC Lung Cancer Consortium for the new 2024 lung cancer screening quality metric.

## **TARGETED THERAPY AND IMMUNOTHERAPY IN LUNG CANCER: A NEW WORLD**

*Jonathan Riess, MD, MS, Associate Professor, Hematology and Oncology, UC Davis*

Targeted therapies and immunotherapy have revolutionized the treatment of lung cancer. We now have targeted therapies for more than 9 different oncogene driven subsets of lung cancer, often associated with lung cancers in never smokers. Moreover, immune checkpoint inhibitors have improved survival mainly in non-oncogene driven lung cancers. This presentation will highlight research from UC Davis investigators in the thoracic oncology program that have contributed to these major advances.

## **A PATIENT-CENTERED APPROACH TO PERIOPERATIVE CARE FOR PATIENTS UNDERGOING LUNG CANCER RESECTION**

*Lisa Brown, MD, MAS, Assistant Professor, General Thoracic Surgery, UC Davis*

Patients undergoing thoracic surgery are the least likely to be on opioids before surgery but have the highest rate of new persistent opioid use after surgery compared to other surgical cohorts. Notably, 10-26% of opioid naïve lung cancer resection patients become new persistent opioid users. There were an estimated 238,340 new cases of lung cancer in 2023, 100,140 (42%) of whom may undergo surgery based on cancer stage. Given the magnitude of this problem, improvements in patient-centered opioid management strategies are needed to reduce new persistent opioid use after thoracic surgery. Efforts to decrease opioid use have been focused on prescriber education and guidelines rather than patient education for pain management and opioid use. Regardless of surgical approach, approximately 25% of patients undergoing thoracic surgery develop chronic postsurgical pain. Patients do not know what to expect after surgery regarding pain and how to manage it including effective opioid use which balances achieving pain control while minimizing side effects and new persistent opioid use. This presentation will focus on the evidence for pain, its management, and opioid use in patients undergoing lung cancer resection and potential solutions to these problems.

# **POSTER PRESENTATIONS**

## Poster Index:

Thursday poster presentations: page 20-21

Friday poster presentations: page 22-23

## Poster Abstracts:

Thursday poster abstracts: page 24-37

Friday poster abstracts: page 38-51

Thursday poster session: 11:45 am – 1:15

pm Friday poster session: 8 am – 9:30 am

## **THURSDAY POSTER PRESENTATIONS (INDEX)**

- 1. A Central Role of the Aryl Hydrocarbon Receptor (AhR) in the Tumor Microenvironment of Breast Cancer**  
*Presenter: Christoph Vogel*
- 2. Force-Induced Recruitment of LIM Proteins along Actin and Keratin Fibers**  
*Presenter: Dah Som Kim*
- 3. Engrailed-1 Promotes Pancreatic Cancer Metastasis**  
*Presenter: Reno Jihao Xu*
- 4. Force-Dependent Proximal Biotinylation Surrounding Actin Filaments in Live Cells**  
*Presenter: Agustina Diener*
- 5. A Western-Style Mimicking High-Fat Diet Causes Changes in Adipose Tissue and Promotes Early-Stage Pancreatic Carcinogenesis in a KC Mouse Model**  
*Presenter: Aya Ead*
- 6. Heterogeneous MHC Class I Expression Alters Response to Radiation and Anti-PD-L1/Anti-TGF**  
*Presenter: Hanne Lind*
- 7. Harnessing ADAR Editing for Transformative Chemotherapeutic Advances**  
*Presenter: Prince Salvador*
- 8. Next-Generation Anti-Androgen Therapies Enhance PARP Inhibitor Efficacy in Advanced Prostate Cancer**  
*Presenter: Alan P. Lombard, PhD*
- 9. Dual Targeting of HSP70 and AURKA Improves Treatment in Neuroendocrine Prostate Cancer**  
*Presenter: Pengfei Xu*
- 10. Markers of Bone Metabolism and Overall Survival in Men with Bone-Metastatic Hormone Sensitive Prostate Cancer (HSPC): A Subset Analysis of SWOG S1216, a Phase III Trial of Androgen Deprivation with or without Orteronel**  
*Presenter: Primo N. Lara Jr.*
- 11. Optimization of Non-Commercial CAR-T Cell Manufacturing Processes: Achieving Early Cell Harvest and Fresh Infusion for Enhanced Cost-Efficiency and Expedited Delivery**  
*Presenter: Jordan Pavlic, MA*
- 12. A Comparison of in vivo Tumor-Homing Abilities of Placental-Derived and Bone Marrow-Derived Mesenchymal Stromal Cells in High-Risk Neuroblastoma**  
*Presenter: Kathleen E. Doyle*
- 13. Novel Bio-Engineered MicroRNA Therapy for High-Risk Neuroblastoma**  
*Presenter: Maria Sutter*
- 14. Adjuvant Everolimus in Patients (Pts) with Localized Non-Clear Cell Renal Cell Carcinoma (RCC): Subgroup Analysis from the EVEREST Trial (SWOG S0931)**  
*Presenter: Shuchi Gulati*
- 15. Chemically Optimizing Amiloride to Generate Highly Effective Derivatives that Selectively Target Triple-Negative Breast Cancer Stem Cells**  
*Presenter: Noemi Castro*

16. **Recent Advances in the Management of Metastatic Prostate Cancer: Opportunities for Improving Patient Care**  
*Presenter: Reggie Fan*
17. **Bioengineered siRNA Agents for Research and Therapy**  
*Presenter: Neelu Batra*
18. **Characterizing Persistent Poverty and Cancer Incidence in the UC Davis Cancer Center Catchment Area**  
*Presenter: Arti Parikh-Patel*
19. **The Impact of a Perioperative Nutrition Protocol in Reducing Hospital Acquired Malnutrition in Patients with Esophageal Cancer**  
*Presenter: Amanda Allen, MS, RD, CSSD, CNSC*
20. **Association between Wildfire PM2.5 and Cancer Stage at Diagnosis**  
*Presenter: Mariela Alaniz*
21. **Descriptive Epidemiology of Canine and Feline Cancer in California, United States from 2000 to 2019**  
*Presenter: Ruwini Rupasinghe*
22. **Engaging Diverse and Underserved Communities through “Community Conversations on Cancer (C3)”**  
*Presenter: Neha Singh, BS*
23. **Facilitators and Barriers to Adapting a Hereditary Breast Cancer Education Program for Spanish-Speaking Hispanic/Latinx Individuals in Federally Qualified Health Centers: Rapid Evaluation Study Using the Consolidated Framework for Implementation Research**  
*Presenter: Laura Adame*
24. **Association of HPV Status with Depressive Symptoms in HNC Patients**  
*Presenter: Soroush Ershadifar*
25. **FLIm-based In Vivo Classification of Residual Cancer in the Surgical Cavity during Transoral Robotic Surgery**  
*Presenter: Mohamed A. Hassan*
26. **A Bayesian Machine Learning Approach for Predicting Atypical Lipomatous Tumors From MR Radiomics**  
*Presenter: Felipe Godinez*

## **FRIDAY POSTER PRESENTATIONS (INDEX)**

1. **Investigating the TGF- $\beta$ /MUC4 Signaling Axis in Platelet-Circulating Tumor Cell Interactions during Breast Cancer Metastasis**  
*Presenter: Savannah Free*
2. **Investigating the Role of Wnt/PCP Signaling in the Reprogramming of Energy Metabolism in Breast Cancer**  
*Presenter: Liliana Loza Sanchez*
3. **Cancer EVs Drive a Microglia-Mediated Inflammatory Response in a New Mixed Cortical Cell Culture Model**  
*Presenter: Rachel R. Mizenko*
4. **Adapting Two-Component Signaling Pathways for Engineering Human Cells**  
*Presenter: Sean R. Collins*
5. **Production and Use of Recombinant miRNAs to Dissect the Intrinsic Differences in miRNA Biogenesis and Functions**  
*Presenter: Yimei Wang*
6. **Recombinant Mir-7-5P Effectively Inhibit NSCLC Cell Viability Through Regulating Mitochondrial Function**  
*Presenter: Gavin M. Traber*
7. **Metabolic Risk Factors and Outcomes in Patients with Glioblastoma**  
*Presenter: John Paul Aboubechara, PhD*
8. **Meclizine Is Much More mTORC1-Selective Than Rapamycin and Dose Dependently Kills Glioblastoma Stem Cells**  
*Presenter: Alexey Tomilov*
9. **A New Vulnerability to BET Inhibition Due to Enhanced Autophagy in BRCA2-Deficient Pancreatic Cancer**  
*Presenter: Suyakarn Archasappawat*
10. **Efficacy of Different let-7 Isoforms in the Modulation of Target Gene Expression in HCC Cells**  
*Presenter: Joseph Cronin*
11. **Disrupting  $\beta$ -2 Adrenergic Receptor Signaling Triggers Glioma Cell Death and Down-Regulates Survivin**  
*Presenter: Orli Algranatti*
12. **Use of Recombinant MicroRNAs as Antimetabolites to Inhibit Human Non-Small Cell Lung Cancer**  
*Presenter: Meijuan Tu*
13. **A Multi-Ethnic Population-Based Study of Multiple Myeloma Disparities: Results From a Recruitment Pilot**  
*Presenter: April Vang*
14. **Late Venous Thromboembolism in Adolescent and Young Adult Cancer Survivors: A Population-Based Analysis from the VOICE Study**  
*Presenter: Renata Abrahão*

15. **Development of HPV Awareness and Prevention Education Materials for Hispanic/Latinx Community Health Educators**  
*Presenter: Charlotte Bergheimer*
16. **Characterization of Carcinogenic Constituents of Domestic Wells in Northern and Central California**  
*Presenter: Vida Sánchez*
17. **Disparities in Breast Cancer Stage at Diagnosis and Quality of Cancer Care in California by Source of Health Insurance**  
*Presenter: Nuen Tsang Yang*
18. **Early Recognition and Prompt Intervention of Immunotherapy-Induced Adrenal Insufficiency in Cancer Patients: A Case Series and A Prospective Multidisciplinary Workflow**  
*Presenter: Ashley Trane*
19. **Cancer Incidence among Armenians in California**  
*Presenter: Ani Movsisyan Vernon*
20. **A Trim37 Risk Variant rs57141087 Contributes to Triple-Negative Breast Cancer Onset and Progression in African American Women**  
*Presenter: Rachisan Djake Tihagam*
21. **Transcriptome-Wide Study of Tumor Samples from Peruvian Women Identifies Dysregulated Pathways in Luminal Tumors Typically Associated with More Aggressive Disease**  
*Presenter: Chenghuiyun Xu*
22. **Synthesis, Radiolabeling, and Preclinical Evaluation of Hyaluronan Conjugates for PET Imaging and Dual Targeting to CD44 and Integrin  $\alpha\beta6$**   
*Presenter: Hua Zhang*
23. **Preclinical Evaluation of a Dimer Peptide Targeting Integrin  $\alpha\beta6$**   
*Presenter: Ryan Davis*
24. **FIBI: Novel Slide-Free Microscopy That Can Be Better Than the H&E Gold Standard**  
*Presenter: Richard Levenson*
25. **Enhancing Ovarian Cancer Diagnostics: Integrating Raman Tag Labeling with ML-Enabled SERS of Extracellular Vesicles for Improved Transparency and Precision**  
*Presenter: Qing He*
26. **A Dosimetric Comparison of Y-90 Radioembolization, Stereotactic Body Radiation Therapy and HDR Brachytherapy for Treatment of Liver Cancer**  
*Presenter: Kajetan Wysoczynski*

# THURSDAY POSTER PRESENTATIONS (ABSTRACTS)

## <<1>> A CENTRAL ROLE OF THE ARYL HYDROCARBON RECEPTOR (AHR) IN THE TUMOR MICROENVIRONMENT OF BREAST CANCER

C. Sweeney, S. Kado, K. Bein, C. Vogel

<sup>1</sup>Department of Biochemistry & Molecular Medicine, School of Medicine, University of California, Davis, CA 95817, USA

<sup>2</sup>Center for Health and the Environment, University of California, One Shields Avenue, Davis, CA 95616, USA

<sup>3</sup>Department of Environmental Toxicology, University of California, One Shields Avenue, Davis, CA 95616, USA

Air pollution and occupational exposure studies have reported positive associations with the risk of developing breast cancer. Air pollution and ambient particulate matter (PM) contain a complex mixture of compounds, including polycyclic aromatic hydrocarbons (PAHs) and various metals (e.g., iron, nickel, copper), which may modulate immune responses and stimulate progression of breast cancer. The aryl hydrocarbon receptor (AhR) is known as a sensor of environmental exposure to pollutants and may act as a critical player in tumor promotion. Here, we tested the role that AhR plays in mammary tumorigenesis by regulating molecular markers and cellular processes which are critically involved in carcinogenesis in the PyMT mouse model. The exposure to PM shortened tumor-free survival and increased tumor burden in PyMT mice. Positron emission tomography (PET) imaging revealed early lesions at mammary glands after treatment with PM. Furthermore, using PET imaging we were able to detect metastasis in the lungs. The PM-induced growth of mammary tumors and metastasis was associated with accumulation of tumor associated myeloid cells (TAMCs). The data are indicating the presence and accumulation of TAMCs in mammary tumors of PyMT mice which is further stimulated by PM exposure. The presence and accumulation of TAMs is supported by a significant increase of mRNA markers including CCAAT/Enhancer-Binding Protein beta (C/EBP $\beta$ ), cyclooxygenase (COX)-2, Arg1, and IDO-1 characteristic for immunosuppressive TAMCs in mammary tumors. Our data indicate that exposure to traffic-related PM activates AhR signaling and creates a tumor-promoting microenvironment enabling the development of breast cancer and metastasis.

## <<2>> FORCE-INDUCED RECRUITMENT OF LIM PROTEINS ALONG ACTIN AND KERATIN FIBERS

Dah Som Kim<sup>1</sup>, Joleen S. Cheah<sup>1</sup>, Tzu-Wei Gabriella Lai<sup>1</sup>, Karen X. Zhao<sup>1</sup>, Yuh-Ru Julie Lee<sup>2</sup>, Cole J. Armstrong<sup>1</sup>, Skylar Foust<sup>1</sup>, Volkmar Heinrich<sup>1</sup>, Su Hao Lo<sup>3</sup>, Soichiro Yamada<sup>1</sup>

<sup>1</sup>Department of Biomedical Engineering, University of California, Davis

<sup>2</sup>Department of Plant Biology, University of California, Davis

<sup>3</sup>Department of Biochemistry and Molecular Medicine, University of California, Davis

The cytoskeleton of epithelial cells is constantly exposed to physical stimuli during embryogenesis, tissue regeneration, and cancer development. Selected members of the LIM domain containing protein family, known to be involved in tumorigenesis, cancer progression, and metastasis, have been shown to bind directly to force-bearing actin fibers using its LIM domain. Interestingly, two members of the LIM protein family, LMO1 and LIMK1, with only two LIM domains, co-localized with keratin filaments and cten, a focal adhesion protein implicated in cancer that also accumulates along force-bearing keratin fibers, rather than actin fibers. To investigate whether LMO1 and LIMK1 proteins bind directly or indirectly to the keratin filaments, we developed an in vitro force-dependent protein interaction assay using recombinant His-tagged keratin 8 and keratin 18 and a microneedle to apply strain. GFP-tagged LMO1 and LIMK1 proteins were selectively recruited along the force-bearing keratin filament bundles but not GFP proteins. Hence, LMO1 and LIMK1 with two LIM domains bind directly to keratin fibers in a force-induced manner. Under the force-bearing conditions, the densely packed keratin filaments may expose cryptic binding sites for mechano-sensing proteins such as LMO1 and LIMK1. These results show that LIM mechano-sensing extends beyond the actin cytoskeleton, and may provide novel insights into the force-regulated dynamics between the cytoskeleton and LIM proteins and their role in cancer.

### <<3>> ENGRAILED-1 PROMOTES PANCREATIC CANCER METASTASIS

*Jihao Xu<sup>1</sup>, Jae-Seok Roe<sup>2,3</sup>, EunJung Lee<sup>1,3,4</sup>, Claudia Tonelli<sup>3,4</sup>, Tim D.D. Somerville<sup>3</sup>, Melissa Yao<sup>3,4</sup>, Joseph P. Milazzo<sup>3</sup>, Herve Tiriach<sup>3,4</sup>, Anna M. Kolarzyk<sup>5</sup>, Esak Lee<sup>5</sup>, Jean L. Grem<sup>6</sup>, Audrey J. Lazenby<sup>6</sup>, James A. Grunkemeyer<sup>6</sup>, Michael A. Hollingsworth<sup>6</sup>, Paul M. Grandgenet<sup>6</sup>, Alexander D. Borowsky<sup>7</sup>, Youngkyu Park<sup>3,4</sup>, Christopher R. Vakoc<sup>3</sup>, David A. Tuveson<sup>3,4,#</sup>, Chang-Il Hwang<sup>1,8,9,#</sup>*

<sup>1</sup>Department of Microbiology and Molecular Genetics, University of California, Davis, Davis, CA 95616, USA

<sup>2</sup>Department of Biochemistry, Yonsei University, Seoul 03722, South Korea

<sup>3</sup>Cold Spring Harbor Laboratory, Cold Spring Harbor, NY 11724, USA

<sup>4</sup>Lustgarten Foundation Pancreatic Cancer Research Laboratory, Cold Spring Harbor, NY 11724, USA

<sup>5</sup>Nancy E. and Peter C. Meinig School of Biomedical Engineering, Cornell University, Ithaca, NY, 14853 USA

<sup>6</sup>Department of Medicine, University of Nebraska Medical Center, Omaha, NE 68198, USA

<sup>7</sup>Department of Pathology, School of Medicine, University of California, Davis, Sacramento, CA 95817, USA.

<sup>8</sup>University of California, Davis, Comprehensive Cancer Center, Sacramento, CA 95817, USA.

<sup>9</sup>Lead Contact

Engrailed-1 (EN1) is a critical homeodomain transcription factor (TF) required for neuronal survival, and EN1 expression has been shown to promote aggressive forms of triple negative breast cancer. Here, we report that EN1 is aberrantly expressed in a subset of pancreatic ductal adenocarcinoma (PDA) patients with poor outcomes. EN1 predominantly repressed its target genes through direct binding to gene enhancers and promoters, implicating a role in the acquisition of mesenchymal cell properties. Gain- and loss-of-function experiments demonstrated that EN1 promoted PDA transformation and metastasis in vitro and in vivo. Our findings nominate the targeting of EN1 and downstream pathways in aggressive PDA.

### <<4>> FORCE-DEPENDENT PROXIMAL BIOTINYLATION SURROUNDING ACTIN FILAMENTS IN LIVE CELLS

*Agustina Diener<sup>1</sup>, Hikaru Katan<sup>2</sup>, Yurina Araki<sup>3</sup>, Volkmar Heinrich<sup>4</sup>, Soichiro Yamada<sup>4</sup>*

<sup>1</sup>Biomedical Engineering University of California Davis

<sup>2</sup>Kyoto University

<sup>3</sup>Osaka Prefecture University

<sup>4</sup>Biomedical Engineering University of California Davis

Mechano-transduction is the process by which a cell senses, integrates, and converts mechanical stimuli into biochemical signals, thereby regulating cell adhesion and cell behavior as well as cancer progression. Yet, the molecular details of this process are not well understood. Upon physical stimulation, actin filaments are thought to recruit vital regulatory proteins to initiate mechano-transduction, but the comprehensive list of proteins surrounding the “tensed” actin network has not been described. To identify force-dependent protein interactions surrounding actin filaments, we fused TurboID, a promiscuous biotin ligase, with F-tractin, an actin filament binding sequence. Using purified biotinylated samples from control and stretch conditions, our preliminary mass spectrometry analysis identified over thousands of proteins and these proteins were ranked based the proximity to the tensed actin filaments. As expected, Zyxin and ABLIM1, LIM proteins which are known to bind to strained actin filaments, and ACTN1, an actin binding protein that is known to interact with zyxin, were identified as proximal to the tensed actin network. Interestingly, LATS1, a tumor suppressor, was also among the top candidates, but currently not known to be a part of mechano-transduction. In live-cell imaging analysis, LATS1 proteins appear to partially colocalize with the keratin network upon cell stretch, demonstrating close proximity of the actin and keratin network under force-bearing conditions. The analysis of other promising candidates is in progress. By identifying force-dependent protein interactions, we will better understand the molecular basis of mechano-transduction, and may uncover the potential role of mechano-transduction in cancer.

## <<5>> A WESTERN-STYLE MIMICKING HIGH-FAT DIET CAUSES CHANGES IN ADIPOSE TISSUE AND PROMOTES EARLY-STAGE PANCREATIC CARCINOGENESIS IN A KC MOUSE MODEL

*Aya Ead, Joanna Wirkus, Gerardo G. Mackenzie  
Department of Nutrition, University of California, Davis*

Multiple preclinical studies have indicated a link between high-fat and high-sugar diets on the acceleration of pancreatic carcinogenesis, in the context of obesity. However, the impact of diets resembling the omega-6 to omega-3 fatty acid ratio (FA) in a Western-style diet, remains unclear. Our aim was to determine the impact of a high-fat diet with a ratio of 10 parts omega-6 FA to each omega-3 FA, on early stages of pancreatic carcinogenesis in a genetically engineered LSL- KrasLSL-G12D; Ptf1aCre/+ (KC) model of pancreatic cancer, with an emphasis on evaluating the contribution of the mesenteric adipose tissue (MAT). Cohorts of male and female KC mice (N = 6-8 mice per sex) were randomly assigned to either a control diet (CD) group or a high-fat diet (HFD) group and fed their diets until three months of age. After eight weeks on their diets, HFD-fed mice had significantly higher body weight, fat mass, and elevated serum leptin levels. Furthermore, HFD-fed mice had increased acinar-to-ductal metaplasia, associated with increased PCNA expression, ERK phosphorylation and immune cell expression compared to CD-fed mice. Metabolomic analysis of the MAT revealed that HFD-fed mice had significant upregulation of alpha-linolenic acid metabolism and biosynthesis of unsaturated FAs. HFD-fed mice had significantly higher levels of alpha-linolenic acid and linoleic acid and lower levels of myristic acid, palmitoleic acid, alpha tocopherol, and 1,5-anhydroglucitol, many of which have been linked to proliferative pathways. In summary, a HFD accelerates pancreatic carcinogenesis through a multifaceted mechanism, including effects on the tumor and surrounding adipose depots.

## <<6>> HETEROGENEOUS MHC CLASS I EXPRESSION ALTERS RESPONSE TO RADIATION AND ANTI-PD-L1/ANTI-TGF

*H.T. Lind<sup>1</sup>, S. Half<sup>2</sup>, A. Strait, S. Chen, C.D. Young<sup>2</sup>, P. Owens<sup>2</sup>, Xiao-Jing Wang<sup>1</sup>  
<sup>1</sup>University of California, Davis  
<sup>2</sup>University of Colorado Anschutz Medical Campus, Aurora, CO*

Squamous cell carcinoma (SCC) is often marked by an immunosuppressive tumor microenvironment (TME) which represses the anti-tumor immune response. Radiation has previously been shown to modify the TME and engage an anti-tumor immune response. In this study, we investigated the therapeutic strategy of priming murine SCC tumors radiation to modify tumor-immune interactions in murine models, followed in combination with by checkpoint inhibitor treatment. We transplanted two tumor cell lines (A223 or P029) derived from two spontaneous SCCs of K15.Kras12D/Smad4<sup>-/-</sup> mice to syngeneic mouse recipients and subjected them to RT plus PD-L1/TGF

## <<7>> HARNESSING ADAR EDITING FOR TRANSFORMATIVE CHEMOTHERAPEUTIC ADVANCES

*Prince Salvador, Erin Doherty, Hannah Brinkman, Victorio Jauregui-Matos, Peter Beal*

The Adenosine Deaminase Acting on RNA (ADAR) enzyme family converts adenosine to inosine in duplex RNA, and through the delivery of guide RNAs, can be directed to edit specific adenosine sites. Our goal is to harness the potential of RNA editing through ADAR enzymes through well-designed guide strands and extensive RNA library screenings. Up to this point, ADAR editing has been primarily targeted to disease-causing termination codons. However, ADARs also have the ability deaminate adenosines in lysine codons, which are highly conserved in protein kinases. Using proto-oncogene tyrosine protein kinase Src (SRC) mRNA as a model, ADAR2's action on lysine codons generates an inactivating arginine codon—a known protein kinase mutation. Our efforts involve testing diverse chemically modified guide oligonucleotides to enhance in vitro and in cellulo editing efficiency. We observed a four-fold increase in ADAR1 editing at a lysine site in SRC mRNA with the sugar analogue ribopyridine-2-one. Significantly, we also demonstrate that strategically placed locked nucleic acids (LNAs) can control bystander editing in vitro. Encouraged by these outcomes, we are simultaneously pursuing the enablement RNA editing events at two chemotherapeutically relevant sites within

both ADAR1 isoforms' mRNA: ADAR1p110 dimerization helix and ADAR1p150 start codon using an established library screening method. These targeted interventions aim to disrupt hyper-editing, fine-tune protein expression, and shed light on RNA editing's potential as a chemotherapeutic strategy.

## <<8>> NEXT-GENERATION ANTI-ANDROGEN THERAPIES ENHANCE PARP INHIBITOR EFFICACY IN ADVANCED PROSTATE CANCER

*Alan P. Lombard, PhD<sup>1,2</sup>; Love A. Moore<sup>1,3</sup>; Bryan Correa Gonzalez<sup>1,2</sup>; Christopher P. Evans, MD<sup>1</sup>; Allen C. Gao, MD PhD<sup>1</sup>*

<sup>1</sup>*Urologic Surgery, UC Davis*

<sup>2</sup>*Biochemistry and Molecular Medicine, UC Davis*

<sup>3</sup>*GGI Graduate Group, Urologic Surgery, UC Davis*

Background: PARP inhibitors (PARPi) have improved advanced prostate cancer management. However, questions remain regarding optimal clinical integration. Here, we sought to better understand PARPi treatment sequencing and to further define the mechanism of action underlying their combination with next-generation anti-androgen therapies (NGAT).

Methods: LN-OlapR/2B-OlapR olaparib resistant cell lines were generated from LNCaP and C4-2B cells through chronic exposure to olaparib. Cell viability assays determined response to androgen receptor directed therapies and combination treatments with a PARPi. RNA-sequencing, gene set enrichment analysis (GSEA), and qPCR assessed the PARPi resistant phenotype and treatment response. Western blots assay DNA-damage response.

Results: PARPi resistant models respond to NGAT's similarly as parental cells suggesting no cross-resistance with PARPi's. However, RNA-sequencing suggests the advent of lineage plasticity with neuroendocrine features in 2B-OlapR cells. Since early evidence of lineage switching may preclude durable NGAT responses, we hypothesized that combining a PARPi with a NGAT upfront may be more beneficial. Combining the NGAT abiraterone with a PARPi is significantly more effective than monotherapy. Mechanistically, we present evidence that synergy may depend partly on a class effect of NGAT's to reduce DNA repair and replication capacity. In line with this hypothesis, we show that all tested NGAT's work with olaparib.

Conclusions: Our data support successes of the PROpel, TALAPRO-2, and MAGNITUDE clinical trials and add insight into the mechanism underlying the efficacy of combining PARPi's with NGAT's. Our data suggest any NGAT may work with a PARPi and that there may be clinical flexibility in design of these regimens.

## <<9>> DUAL TARGETING OF HSP70 AND AURKA IMPROVES TREATMENT IN NEUROENDOCRINE PROSTATE CANCER

*Pengfei Xu<sup>1</sup>, Joy C. Yang<sup>1</sup>, Bo Chen<sup>1</sup>, Shu Ning<sup>1</sup>, Leyi Wang<sup>1</sup>, Christopher Nip<sup>1</sup>, Allen C. Gao<sup>1</sup>, Jason Gestwick<sup>2</sup>, Christopher P. Evans<sup>1</sup>, Chengfei Liu<sup>1</sup>*

<sup>1</sup>*Department of Urologic Surgery, University of California Davis*

<sup>2</sup>*Department of Pharmaceutical Chemistry, University of California, San Francisco*

Background: Neuroendocrine prostate cancer (NEPC) is the most aggressive type of prostate cancer with no effective treatment. Therefore, there is an urgent need to develop novel therapeutic strategies. Aurora kinase A (AURKA) prevents N-Myc from degradation. The AURKA inhibitor alisertib inhibits NEPC tumor growth by disrupting N-Myc signaling; however, it has recently failed in a phase II clinical trial for prostate cancer. In this study, we tested the synergy between the novel HSP70 allosteric inhibitor JG231 and alisertib in NEPC models.

Methods: RT-PCR, western blotting, and immunohistochemistry were used to determine the expression of NEPC related genes in different prostate cancer cell lines and PDX tumors. A co-immunoprecipitation assay was performed to determine the ubiquitination levels. RNA sequencing was employed to determine the changes in gene programs regulated by JG231 in NEPC cells. The effects of JG231 and alisertib on cell proliferation were examined in NEPC cell lines and PDX organoid models.

Results: PC3, CWR22Rv1, H660, LuCaP93, and LuCaP173.1 PDX tumors had significantly increased expression of N-Myc and neuroendocrine markers. Knockdown of HSP70 by siRNA or using the HSP70

inhibitor JG231 significantly inhibited the growth of NEPC models, leading to a combination effect with alisertib ( $p < 0.001$ ). Mechanistically, JG231 blocked neuroendocrine-related signaling pathways and inhibited N-Myc expression in NEPC cells.

Conclusions: JG231, a novel HSP70 inhibitor, improved the treatment efficacy of the AURKA inhibitor alisertib against NEPC by regulating N-Myc protein homeostasis.

Source of Funding: This work was supported in part by grants NIH/NCI R37CA249108 (C, Liu) and R01CA251253 (C, Liu).

## <<10>> **MARKERS OF BONE METABOLISM AND OVERALL SURVIVAL IN MEN WITH BONE-METASTATIC HORMONE SENSITIVE PROSTATE CANCER (HSPC): A SUBSET ANALYSIS OF SWOG S1216, A PHASE III TRIAL OF ANDROGEN DEPRIVATION WITH OR WITHOUT ORTERONEL**

*Primo N. Lara Jr.<sup>1</sup>, Edward Mayerson<sup>2</sup>, Erik Gertz<sup>3</sup>, Catherine Tangen<sup>2</sup>, Amir Goldkorn<sup>8</sup>, Marta van Loan<sup>3</sup>, Maha Hussain<sup>4</sup>, Shilpa Gupta<sup>6</sup>, Jingsong Zhang<sup>7</sup>, Mamta Parikh<sup>1</sup>, Przemyslaw Twardowski<sup>5</sup>, David I. Quinn<sup>8</sup>, Michael LeBlanc<sup>2</sup>, Ian Thompson<sup>9</sup>, and Neeraj Agarwal<sup>10</sup>*

<sup>1</sup>University of California Davis Comprehensive Cancer Center, Sacramento, CA

<sup>2</sup>SWOG Statistical Center, Seattle, WA

<sup>3</sup>US Department of Agriculture, Western Human Nutrition Research Center, University of California Davis, Davis, CA

<sup>4</sup>Northwestern University, Chicago, IL

<sup>5</sup>St. John's Cancer Institute, Providence Health, Santa Monica, CA

<sup>6</sup>Cleveland Clinic, Cleveland, OH

<sup>7</sup>Moffit Cancer Institute, Tampa Bay, FL

<sup>8</sup>USC Norris Comprehensive Cancer Center, Los Angeles, CA

<sup>9</sup>Christus Santa Rosa Health System, San Antonio, TX Health, San Antonio, TX

<sup>10</sup>Huntsman Cancer Institute, Salt Lake City, UT

**Background:** Circulating biomarkers of bone metabolism are significantly associated with overall survival (OS) in men with advanced prostate cancer. In the SWOG S1216 phase III trial, we showed that elevated bone biomarkers are significantly associated with an increased risk of death in hormone sensitive prostate cancer (HSPC) regardless of the status of bone metastases, identifying three risk groups with differential OS outcomes based on bone biomarker status. Here we report the association of bone biomarkers with OS in men with HSPC and documented skeletal metastases as part of a planned subset analysis of S1216.

**Methods:** Bone resorption [C-telopeptide (CTx); Pyridinoline (PYD)] and bone formation markers [C-terminal collagen propeptide (CICP); bone alkaline phosphatase (BAP)] were assessed from in blood from men with bone metastatic HSPC. Patients were randomly divided into training (n=238) and validation (n=475) sets. In the training set, recursive partitioning that maximizes discrimination of OS was used to identify the dichotomous cut-point for each biomarker and for a combination of biomarker split points to define prognostic groups. In the validation set, Cox proportional hazards models were used to assess the impact of biomarkers on OS, adjusted for patient and tumor characteristics.

**Results:** Of 1,279 men, 713 had both baseline bone metastases and evaluable bone biomarkers. Patient characteristics were similar between the overall population and the subset with bone metastases. Elevated levels of CICP, CTX, and PYD were strongly prognostic for OS. Hazard ratios (95% CI) for OS adjusted for treatment arm and baseline clinical variables were: BAP – 1.31 (0.93, 1.84),  $p=0.12$ ; CICP – 1.58 (1.09, 2.29),  $p < 0.02$ ; CTx – 1.55 (1.12, 2.15),  $p=0.008$ ; and PYD – 1.66 (1.27, 2.217),  $p=0.0002$ . There was no evidence of interaction between elevated biomarkers and treatment (all  $p > 0.2$ ). Recursive partitioning algorithms identified four groups of patients with differential OS outcomes based on bone biomarkers, adjusted for baseline clinical variables, with median OS ranging from 2.3 years (highest risk group) to 7.5 years (lowest risk group).

**Conclusions:** In this planned S1216 subset analysis of men with HSPC and bone metastases, elevated serum markers of bone metabolism were significantly associated with worse OS. Bone biomarker levels alone and in combination with patient and tumor characteristics identify unique subsets of men with differential OS outcomes.

**<<11>> OPTIMIZATION OF NON-COMMERCIAL CAR-T CELL MANUFACTURING PROCESSES: ACHIEVING EARLY CELL HARVEST AND FRESH INFUSION FOR ENHANCED COST-EFFICIENCY AND EXPEDITED DELIVERY**

*Jordan Pavlic, MA; Brian Fury, MA; Dane Coleal-Bergum, MA; Jeannine Logan White, MS; Jan Nolta, PhD UC Davis*

There is currently a high cost associated with Chimeric Antigen Receptor T-Cell (CAR-T cell) therapy, which has shown promising results in treating various hematologic malignancies. To address the cost issue, several academic programs in the United States have their own non-commercial CAR-T cell clinical trials aimed at developing cost-effective CAR-T cell platforms. However, further optimization of the manufacturing process is necessary to reduce costs and expedite the delivery of CAR-T cell therapy. The current standard manufacturing process utilizing platforms such as Miltenyi's CliniMACS Prodigy® takes up to 12 days, but the studies that we have recently completed optimize areas of CAR-T cell manufacturing that allow for cells to be harvested as early as Day 8, with the possibility of infusing the manufactured cell product fresh rather than cryopreserved. Given the potentially short survival time for patients post-recurrence, expedited and cost-effective manufacturing strategies are critical for improving patient outcomes.

**<<12>> A COMPARISON OF IN VIVO TUMOR-HOMING ABILITIES OF PLACENTAL-DERIVED AND BONE MARROW-DERIVED MESENCHYMAL STROMAL CELLS IN HIGH-RISK NEUROBLASTOMA**

*Kathleen Doyle, MD<sup>1</sup>; Maria Sutter, BS<sup>2</sup>; Abd-Elrahman Hassan, MD<sup>1</sup>; Monica Rodriguez, BS<sup>2</sup>; Priyadarsini Kumar, PhD<sup>2</sup>; Erin Brown, MD<sup>3</sup>*

<sup>1</sup>Department of Surgery, University of California-Davis, Sacramento, California, USA

<sup>2</sup>Surgical Bioengineering Laboratory, Department of Surgery, University of California-Davis, Sacramento, California, USA

<sup>3</sup>Department of Surgery, Division of Pediatric Surgery, University of California-Davis, Sacramento, California, USA.

Background: Neuroblastoma is the most common extracranial malignancy in children <5 years old. Survival remains poor in high-risk disease. Mesenchymal stromal cells (MSCs) have innate tumor-homing properties and may represent novel cellular delivery vehicles. We compared in vivo homing abilities of placental-derived MSCs (PMSCs) and bone marrow-derived MSCs (BM-MSCs) in a neuroblastoma orthotopic xenograft model. Methods: 26 mice underwent orthotopic implantation of neuroblastoma cells (cell line NB1643) into the adrenal gland. Tumor growth was monitored with ultrasound. Mice underwent intraperitoneal injection of 5x10<sup>6</sup> GFP- and luciferin-labeled MSCs (PMSC n=13, BM-MSC n = 13). MSC migration was serially monitored with in vivo imaging system (IVIS) up to 72 hours (n=5 each group) or 7 days (n=8 each group) post-MSC injection. Ex vivo imaging was performed on adrenal masses and select organ tissues. Immunohistochemistry (IHC) was performed to assess the presence of MSCs within tissues.

Results: Bioluminescence confirmed migration of MSCs to the adrenal gland in vivo. Signal persisted until day 7 although radiance decreased over time. Ex vivo IVIS demonstrated bioluminescence signal in adrenal tumors but not within other organs. There was no significant difference in average tumor radiance between PMSC and BM-MSC mice (p=0.74). IHC confirmed presence of PMSCs and BM-MSCs within the tumor.

Conclusion: Both PMSCs and BM-MSCs migrated to neuroblastoma tumors in vivo and bioluminescent signals indicated persistence up to 7 days. There was no significant difference between the homing capabilities of PMSCs compared to BM-MSCs, indicating that both have potential to act as a drug delivery vehicles.

## <<13>> NOVEL BIO-ENGINEERED MICRORNA THERAPY FOR HIGH-RISK NEUROBLASTOMA

*Maria Sutter, BS<sup>1</sup>; Kathleen Doyle, MD<sup>2</sup>; Monica Rodriguez, BS<sup>1</sup>; Meijuan Tu, PhD<sup>3</sup>; Neelu Batra, PhD<sup>3</sup>; Priyadarsini Kumar, PhD<sup>1</sup>; Aiming Yu, PhD<sup>3</sup>; Erin Brown, MD<sup>4</sup>*

<sup>1</sup>*Surgical Bioengineering Laboratory, Department of Surgery, University of California-Davis, Sacramento, California, USA*

<sup>2</sup>*Department of Surgery, University of California-Davis, Sacramento, California, USA*

<sup>3</sup>*Department of Biochemistry and Molecular Medicine, UC Davis School of Medicine, Sacramento, CA 95817, USA*

<sup>4</sup>*Department of Surgery, Division of Pediatric Surgery, University of California-Davis, Sacramento, California, USA*

**Introduction:** Neuroblastoma is a common pediatric cancer with poor outcomes for patients with high-risk disease. MicroRNAs (miRs) are small RNAs that control post-transcriptional gene regulation. Dysregulation of certain miRs is linked to tumorigenesis and treatment resistance in neuroblastoma. miR-34a-5p and miR-124-5p have been identified as downregulated miRs in neuroblastoma and are potential targets for therapeutics. We investigated the effects of bioengineered miR-34a-5p and miR-124-5p on neuroblastoma cell viability in vitro.

**Methods:** Neuroblastoma cell line SH-SY5Y was seeded at 12,000 cells/well and transfected with bioengineered miR-34a-5p and miR-124-3p using lipofectamine 3000 (LP) transfection agent. Neuroblastoma cells were seeded with miR concentrations of 25nM. Wells containing SH-SY5Y cells alone, cells with LP only, and cells with a non-specific miR sequence (LSA) served as controls. Cells were monitored for 7 days and cell viability was measured using an MTT assay.

**Results:** Neuroblastoma cells SH-SY5Y treated with bioengineered miR-34a-5p and miR-124-5p demonstrated reduced cell viability of 39.4% and 39.6%, respectively. This was a two-fold reduction in cell viability compared to LP controls, but a 1.2-fold reduction over LSA controls. When assessing transfection efficacy, approximately 20% of SH-SY5Y cells were successfully transduced with miRs.

**Conclusions:** Bioengineered miR-34a-5p and miR-124-5p effectively reduced neuroblastoma cell viability in vitro, supporting the potential of miRs as targeted therapeutic agents for neuroblastoma. Effects may be limited by the transfection efficiency of neuroblastoma cells. Further in vitro studies to improve transfection rates and testing with other cell lines are ongoing. Future directions include in vivo testing in an orthotopic neuroblastoma model.

## <<14>> ADJUVANT EVEROLIMUS IN PATIENTS (PTS) WITH LOCALIZED NON-CLEAR CELL RENAL CELL CARCINOMA (RCC): SUBGROUP ANALYSIS FROM THE EVEREST TRIAL (SWOG S0931)

*Shuchi Gulati, MD, MS<sup>1</sup>; Catherine Tangen, DrPH<sup>2</sup>; Christopher W. Ryan, MD<sup>3</sup>; Ulka N. Vaishampayan, MD<sup>4</sup>; Brian M. Shuch, MD<sup>5</sup>; Pedro Barata, MD<sup>6</sup>; Deepak K. Pruthi, MD<sup>7</sup>; Cristiane Bergerot, PhD<sup>8</sup>; Abhishek Tripathi, MD<sup>9</sup>; Ian M. Thompson, MD<sup>10</sup>; Primo N. Lara Jr., MD<sup>1</sup>; Sumanta K. Pal, MD<sup>9</sup>*

<sup>1</sup>*UC Davis Comprehensive Cancer Center, Sacramento, CA*

<sup>2</sup>*SWOG Statistics and Data Management Center, Seattle, WA*

<sup>3</sup>*Oregon Health and Science University Knight Cancer Institute, Portland OR*

<sup>4</sup>*University of Michigan Rogel Cancer Center, Ann Arbor, MI*

<sup>5</sup>*University of California Los Angeles, Los Angeles, CA*

<sup>6</sup>*Tulane Univ Health Sciences Center, New Orleans, LA*

<sup>7</sup>*University of Texas Health San Antonio, San Antonio, TX*

<sup>8</sup>*Centro de Cancer de Brasilia Instituto Unity de Ensino e Pesquis, Brasilia DF, Brazil*

<sup>9</sup>*City of Hope Comprehensive Cancer Center, Duarte, CA*

<sup>10</sup>*Christus Santa Rosa Health System, San Antonio, TX*

**Background:** In the phase-III SWOG 0931 (EVEREST) trial, adjuvant treatment with mTOR inhibitor, everolimus, yielded disease-free survival (DFS) and overall survival (OS) hazard ratios (HR) of 0.85 (95% CI 0.71-1.00) and 0.90 (95% CI 0.71-1.13) respectively, in pts with resected, localized RCC. We sought to evaluate the efficacy of everolimus in the non-clear cell subsets.

Methods: 1545 adult pts with treatment-naïve, non-metastatic, fully-resected RCC at intermediate high- (pT1 G3-4 N0 to pT3a G1-2 N0) or very high-risk (pT3a G3-4 to pT4 G-any or N+) for recurrence were randomized 1:1 to 54 weeks of everolimus or placebo within 12 weeks of nephrectomy. Exploratory analyses of RFS and OS in the chromophobe (ch) and papillary (pap) subgroups were performed.

Results: A total of 99 eligible pts had chRCC; 109 had papRCC. Fewer pts completed all 54 weeks of everolimus in each subgroup compared to placebo (49% vs. 74% in ChRCC; 46% vs. 71% in papRCC). With a median follow-up of 76 months, RFS was not improved with everolimus than with placebo in the chRCC (5-year RFS 79% vs. 77%; HR, 0.89; 95% CI, 0.37 to 2.13; P=0.79) or in the papRCC cohort (5-year RFS 62% vs. 70%; HR 1.19; 95% CI, 0.61 to 2.33, p=0.61).

Conclusion: Non-clear cell histology accounted for a considerable proportion (~13%) of EVEREST.

Postoperative everolimus did not improve RFS compared with placebo among patients with pap or chRCC.

Results from the study do not support the adjuvant use of everolimus for non-clear cell RCC after surgery.

## <<15>> CHEMICALLY OPTIMIZING AMILORIDE TO GENERATE HIGHLY EFFECTIVE DERIVATIVES THAT SELECTIVELY TARGET TRIPLE-NEGATIVE BREAST CANCER STEM CELLS

*Noemi Castro, Michelle Hu, Anastasia Berg, Ruiwi Liu, Kit S. Lam, Kermit L. Carraway III*

*Department of Biochemistry and Molecular Medicine and UC Davis Comprehensive Cancer Center, UC Davis School of Medicine, 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 conferring therapeutic failure to both 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 in cases of apparent complete clinical response. The overarching goal of this project is to develop novel drugs that exploit the process of lysosome-dependent cell death, one of the programmed necrotic cell death mechanisms, in suppressing CSC-mediated triple-negative breast cancer recurrence and metastasis. We have previously observed that hexamethylene amiloride (HMA), a derivative of the FDA-approved potassium-sparing diuretic amiloride, is cytotoxic in vitro and ex vivo toward cultured cells derived from a variety of tumor types but not non-transformed cells, and suppresses primary and metastatic tumor outgrowth in vivo. HMA acts on breast tumor cells regardless of subtype, proliferative status, or species of origin, engages a potent caspase- and autophagy-independent programmed necrotic death mechanism in tumor cells, and acts efficiently toward therapy-resistant CSC-related subpopulations. Moreover, we have observed that derivatives of amiloride modified at its C(5) amine exhibit a strong relationship between the hydrophobicity (logP) of the drug and cancer cell-specific cytotoxicity. Here we will exploit these findings to develop and characterize three novel amiloride derivatives and assess their ability to suppress tumor growth, recurrence, and metastasis.

## <<16>> RECENT ADVANCES IN THE MANAGEMENT OF METASTATIC PROSTATE CANCER: OPPORTUNITIES FOR IMPROVING PATIENT CARE

*Mr. Reggie Fan<sup>1</sup>, Dr. Chong-Xiang Pan<sup>2</sup>, Dr. Nicholas Mitsiades<sup>3</sup>*

<sup>1</sup>*California Northstate University Master of Pharmaceutical Sciences student*

<sup>2</sup>*Brigham and Women's Hospital*

<sup>3</sup>*UC Davis Medical Center*

Prostate cancer (PC) is the most commonly diagnosed cancer and second leading cause of cancer death in men in the United States. While advanced PC remains incurable, there have been significant improvements in the management of patients with metastatic castration-resistant PC (CRPC) since 2016, with novel Androgen Receptor (AR) antagonists, PARP inhibitors, immunotherapies, and Prostate Specific Membrane Antigen (PSMA)-targeted agents becoming available. Increasingly, Precision Oncology, guided by analysis of the tumor's DNA, RNA and other biomarkers, has been applied for the clinical management of PC. Here, we present the case of an 80-year-old patient who died of metastatic CRPC in June 2017, within 10 months after

initial diagnosis. Next-generation sequencing (NGS) analysis provided insight into the molecular drivers and the evolution of this aggressive PC, with aberrations in the AR, EGFR, MYC, CDK6, CDK12, and PTCH1 genes identified. In just six years since then, impressive developments in the field of Precision Oncology and PC management have led to novel treatment opportunities, both as standard-of-care and as molecularly guided clinical trials, that were not available to this particular patient in 2017. This presentation will summarize new diagnostic and treatment options, their clinical benefit, limitations, and emerging treatment opportunities relevant to this case. We propose that NGS testing can provide significant benefits for PC patients, and should be performed early and subsequently repeated longitudinally throughout the clinical course of the disease.

## <<17>> BIOENGINEERED SIRNA AGENTS FOR RESEARCH AND THERAPY

*Neelu Batra, Mei-Juan Tu, Ai-Ming Yu*

RNA research and therapy relies primarily on the use of RNA agents chemically engineered. Although they are designed to serve as biosimilars, RNA analogs synthesized in vitro and decorated with extensive artificial modifications at various locations differ largely from natural RNAs comprised of minimal posttranscriptional modifications and folded in vivo in their structures, physicochemical properties, biological activities, and safety profiles. In this study, we aimed to use our innovative tRNA/pre-miRNA-based RNA bioengineering technology to achieve in vivo fermentation production of biologic siRNA agents (BioRNA/siRNAs). Herein we show a high-level heterogenous overexpression (accounting for >50% of total bacterial RNA) of 10 target BioRNA/siRNA molecules at 100% success rate, yielding 10-40 mg BioRNA/siRNA per liter bacterial culture with high purity ( $\geq 98.5\%$ ) and low endotoxin ( $< 1.5$  EU/ $\mu$ g RNA). Further studies demonstrated that target siRNAs (e.g., PD-L1-siRNA) are specifically released from BioRNAs (BioRNA/PD-L1-siRNA) in human NSCLC cells to effectively reduce the protein levels of targeted genes (PD-L1) to about 70-80%. We also employed a PD-1/PD-L1 blockade bioassay to validate the efficacy of our BioRNA/PD-L1-siRNA, and our results showed that BioRNA/PD-L1-siRNA can efficiently downregulate human PD-L1 in the engineered CHO cells and sharply change the PD-1/PD-L1 interaction reporter signals. These promising results pave the way for a new avenue in the development of biologic siRNA therapeutics. By harnessing the potential of bioengineered siRNA agents, we aim to advance the field of siRNA-based therapeutics and offer new and alternative opportunities for treating various diseases.

## <<18>> CHARACTERIZING PERSISTENT POVERTY AND CANCER INCIDENCE IN THE UC DAVIS CANCER CENTER CATCHMENT AREA

*Arti Parikh-Patel<sup>1</sup>, Ani Movsisyan Vernon<sup>1</sup>, Brenda Hofer<sup>1</sup>, Theresa H.M. Keegan<sup>1,2</sup>, Shehnaz Hussain<sup>3</sup>*

<sup>1</sup>California Cancer Reporting and Epidemiologic Surveillance Program, University of California Davis Comprehensive Cancer Center

<sup>2</sup>Center for Oncology Hematology Outcomes Research and Training (COHORT) and Division of Hematology and Oncology, University of California Davis School of Medicine

<sup>3</sup>Department of Public Health Sciences, School of Medicine and Comprehensive Cancer Center, University of California, Davis

Background: The USDA Economic Research Service defines persistent poverty areas (PPAs) as those where greater than 20% of the population has lived below the poverty level for the past 30 years. Residents living in PPAs have increased cancer risk due to multiple factors related to environment, lifestyle, and healthcare access. The objective of this analysis was to characterize cancer incidence and late-stage diagnosis among individuals with screen-detectable cancers living in PPAs within the UC Davis Comprehensive Cancer Center (UCDCCC) catchment area.

Methods: Individuals diagnosed with invasive breast, cervical, colorectal, lung, melanoma, oropharyngeal, or prostate cancer from 2006-2019 residing within the 19 county UCDCCC catchment area were identified in the California Cancer Registry. Patients were designated as living in a PPA based on their residential census tract at diagnosis. Descriptive statistics, including age-adjusted incidence rates and proportion of late-stage diagnoses, were calculated by cancer type.

Results: A total of 10,928 out of 199,930 (5.5%) patients with the cancers of interest in the catchment area were identified as living in a PPA. In UCDCCC's catchment area, 9.2% (93/1,013) of census tracts met the definition of PPA. Patients living in PPAs had significantly higher cervical (11.7/100,000 vs. 7.3/100,000) and lung (63.0/100,000 vs. 53.2/100,000) cancer incidence than those living in non-PPAs. Patients residing in PPAs had higher proportions of late-stage diagnosis for all cancer types studied ( $p < 0.05$ ).

Conclusion: More granular study of the underlying reasons for the observed cancer disparities is needed. Targeted interventions to improve early detection in UCDCCC PPAs should be implemented.

### <<19>> THE IMPACT OF A PERIOPERATIVE NUTRITION PROTOCOL IN REDUCING HOSPITAL ACQUIRED MALNUTRITION IN PATIENTS WITH ESOPHAGEAL CANCER

*Amanda Allen MS, RD, CSSD, CNSC; Erin Nella, RD, CNSC; Daniel Black, Danielle Baham, MS, RD; Luis Godoy, MD; Lisa Brown, MD, MAS, FACS; David Cooke, MD, FACS*  
*UC Davis Health Departments of Food & Nutrition Services and Thoracic Surgery*

Background: Enhanced Recovery After Surgery (ERAS) protocols, which include several nutrition optimization components, have been found to reduce postoperative complications among many surgical populations including patients receiving esophagectomy. Malnutrition is the result of nutrition insufficiency and is known to be an independent risk factor for postoperative complications, making identification and prevention an utmost priority. At our institution, barriers to adequate nutrition delivery with a heightened incidence of hospital acquired malnutrition have been identified in patients undergoing esophagectomy. A Perioperative Nutrition Protocol including immunonutrition was created to improve nutrition delivery with a goal of reducing hospital acquired malnutrition.

Methods: This quality improvement initiative included a retrospective chart review of the outcomes pre- and post-implementation of a Perioperative Nutrition Protocol including immunonutrition supplementation. Data were obtained from February 2019 to July 2023 before ( $n=23$ ) and after ( $n=46$ ) protocol implementation. We compared nutritional and clinical outcomes in the pre- and post-intervention groups.

Results: Following protocol implementation 70% of preoperative patients were screened for nutrition risk, 65% received preoperative carbohydrate loading beverage, and 63% received preoperative immunonutrition supplementation. Postoperatively, time to initiate enteral nutrition (EN) reduced from an average of 57 hours to 17 hours, average percentage of energy needs met increased from 57% to 74%, average percentage of protein needs met increased from 54% to 80%, and incidence of hospital acquired malnutrition reduced from 60% to 15%.

Conclusion: A Perioperative Nutrition Protocol with immunonutrition can be successfully implemented and can reduce incidence of hospital acquired malnutrition.

Acknowledgements: Jessica Harvey MA, PA-C; Sarah Holmes MA, PA-C; Valerie Kuderer, RN, OCN

### <<20>> ASSOCIATION BETWEEN WILDFIRE PM2.5 AND CANCER STAGE AT DIAGNOSIS

*Tracy Hysong<sup>1</sup>, Mariela Alaniz<sup>1</sup>, Sean M. Raffuse<sup>2</sup>, Theresa H. Keegan<sup>1</sup>, Irva Hertz-Picciotto<sup>1</sup>, Shehnaz K. Hussain<sup>1</sup>*

<sup>1</sup>Department of Public Health Sciences

<sup>2</sup>Air Quality Research Center

Introduction: A growing concern is the increased risk for cancer development, progression, and treatment response associated with wildfire particulate matter (PM)<sub>2.5</sub> exposure. Prior studies have focused on etiology; thus, little is known about the cancer promoting effects of wildfire PM<sub>2.5</sub>.

Methods: We identified all incident cancers diagnosed 1/1/2017-12/31/2020 using the California Cancer Registry. Daily PM<sub>2.5</sub> was estimated over the same period. Random forests regression was used to fuse diverse datasets (official air quality monitoring, satellite observations, meteorological modeling, predictive smoke modeling, and low-cost sensor networks [PurpleAir]) to produce a consensus estimate of PM<sub>2.5</sub> for each centroid of a 1-square kilometer grid across California. We used home address at the time of cancer diagnosis to map each patient to the nearest centroid. Nonparametric Wilcoxon tests and Kruskal-Wallis

ANOVA were used to test differences between the mean PM2.5 daily concentrations and stage at diagnosis (I,II,III, and IV) over the 1, 3 and 6 months preceding the date of cancer diagnosis by cancer site. Results: 781,382 patients were diagnosed with cancer, 97% of which had adequate geocoding for mapping. For several cancer sites, including lung, prostate, bladder, and breast cancer, we observed a significant association between increasing PM2.5 concentrations and later stage. Associations were most pronounced for exposures captured over the 1-month preceding cancer diagnosis. Conclusion: Stage at diagnosis was associated with wildfire PM2.5 exposure. In future analyses, we will examine the effects of wildfire PM2.5 on cancer survival, adjusting for biological and sociodemographic risk factors.

## <<21>> DESCRIPTIVE EPIDEMIOLOGY OF CANINE AND FELINE CANCER IN CALIFORNIA, UNITED STATES FROM 2000 TO 2019

*Ruwini Rupasinghe<sup>1</sup>, Jose Manuel Díaz Cao<sup>1,2</sup>, Michael Kent<sup>3</sup>, Beatriz Martínez-López<sup>1</sup>*

<sup>1</sup>*Center for Animal Disease Modeling and Surveillance (CADMS), Department of Medicine and Epidemiology, School of Veterinary Medicine, University of California, Davis, California, USA*

<sup>2</sup>*Department of Animal Pathology, Universidade de Santiago de Compostela, Galicia, Spain*

<sup>3</sup>*Center for Companion Animal Health, Department of Surgical and Radiological Sciences, School of Veterinary Medicine, University of California, Davis, California, USA*

We assessed the distribution and epidemiological characteristics of nine major cancer types in dogs and cats, utilizing a subset of hospital records from the Veterinary Medical Teaching Hospital in California from 2000 to 2019. Sarcoma, carcinoma, lymphoid neoplasia (LN), mast cell tumor (MCT), and melanoma were statistically evaluated by multivariable logistic regression with a p-value  $\leq 0.05$  considered statistically significant. The dataset contained 150,063 total patients (79.9% dogs and 20.1% cats) with 26,883 patients diagnosed with cancer (18.1% dogs and 17.0% cats). Cats had more LN (34.1% vs 14.6%) and carcinoma (30.4% vs 20.7%), but less sarcoma (42.2% vs 61.6%) compared to dogs. Older age and being spayed/neutered were significant for any cancer (except carcinoma) in dogs while being male was significant for sarcoma and LN in dogs. Older age was the only significant risk factor for canine carcinoma and any cancer in cats. Interaction effects were identified in dogs between neuter status and gender for sarcoma, LN, and MCT, while age was correlated with gender and neuter status for sarcoma and melanoma, respectively. Odds ratios between spayed/neutered and intact dogs were higher in females than males with sarcoma (OR=1.38;95%CI=1.25,1.54 vs OR=1.10;95%CI=1.02,1.17), LN (OR=1.43;95%CI=1.17,1.75 vs OR=1.04;95%CI=0.91,1.18), and MCT (OR=1.92;95%CI=1.46,2.54 vs OR=1.22;95%CI=1,1.48). Male dogs were more likely to have LN if intact (OR=1.59;95%CI=1.27,1.99), while female dogs were to have MCT if spayed (OR=1.28;95%CI=1.16,1.41). Here, the data was limited to a single veterinary hospital; thus, a cancer registry would offer a more comprehensive picture of cancer epidemiology in dogs and cats.

## <<22>> ENGAGING DIVERSE AND UNDERSERVED COMMUNITIES THROUGH “COMMUNITY CONVERSATIONS ON CANCER (C3)”

*Neha Singh, BS<sup>1</sup>; Alexandra Gori, BS<sup>1</sup>; Bao Her, MHA<sup>1</sup>; Laura Adame, BS<sup>1</sup>; Laura Fejerman, MSc, PhD<sup>1,2</sup>; Julie Dang, MPH, PhD<sup>1,2</sup>*

<sup>1</sup>*University of California, Davis Comprehensive Cancer Center, Office of Community Outreach and Engagement*

<sup>2</sup>*University of California, Davis, Department of Public Health Sciences*

Background: In response to the National Cancer Institute’s call for cancer centers to address catchment area population cancer concerns, the UC Davis Comprehensive Cancer Center’s (UCDCCC) Office of Community Outreach and Engagement (OCOE) implemented Community Conversations on Cancer (C3s) to inform the creation of health education materials, outreach, and training activities for the community, as well as to establish bidirectional relationships between the community and UC Davis researchers.

Methods: Participants were recruited through convenience sampling within UCDCCC community partners’ networks. PowerPoint presentations were developed, featuring county/community specific cancer rates and

behavioral risk factors. A facilitator's guide was used to engage community members through group discussions on their cancer-related experiences. Qualitative data from these conversations were analyzed using thematic analysis.

Results: A total of 9 C3s were conducted with non-profits, community-based organizations, federally qualified health centers, and religious institutions in 8 catchment area counties. There were approximately 130 participants, of self-reported Asian, Non-Hispanic White, and Hispanic/Latino racial and ethnic background. Sessions revealed community members voicing similar concerns including: air pollution, insurance, transportation barriers, limited cancer screening opportunities due to geographic barriers, the role of education in informed cancer decision-making, and the desire for providers to have ongoing cancer-related training to keep up-to-date with trends and practices.

Conclusions: C3s allowed diverse and underserved community members to express their cancer needs and opinions. C3s helped the UCDCCC OCOE to identify concerns as well as inspire cancer center investigators to develop projects and bidirectional relationships to address them.

Acknowledgements: Cancer Center Support Grant, National Cancer Institute

### **<<23>> FACILITATORS AND BARRIERS TO ADAPTING A HEREDITARY BREAST CANCER EDUCATION PROGRAM FOR SPANISH-SPEAKING HISPANIC/LATINX INDIVIDUALS IN FEDERALLY QUALIFIED HEALTH CENTERS: RAPID EVALUATION STUDY USING THE CONSOLIDATED FRAMEWORK FOR IMPLEMENTATION RESEARCH**

*Charlotte L. Bergheimer, MS<sup>1&</sup>; Bao Her, MHA<sup>2&</sup>; Laura Adame, BS<sup>2</sup>; Alyssa Reed, MPH<sup>2</sup>; Jesus A. Bastian, BS<sup>3</sup>; Melanie Gallegos-Campos, BS<sup>3</sup>; Sara G. Ashley, BS<sup>3</sup>; Brittany D. Clary, BS<sup>3</sup>; Laura Fejerman, PhD, MSc<sup>1,2,\*</sup>; Julie H.T. Dang, PhD, MPH<sup>1,2,\*</sup>*

<sup>1</sup>*Department of Public Health Sciences, University of California, Davis*

<sup>2</sup>*University of California Davis Comprehensive Cancer Center*

<sup>3</sup>*University of California, Davis, Undergraduate Program*

<sup>&</sup>*Co-First authors*

<sup>\*</sup>*Co-Senior authors*

Background: Awareness about hereditary breast and ovarian cancer (HBOC) and genetic testing is lower in Hispanic/Latinx (H/L) than non-Hispanic white individuals in the United States. This study aimed to identify factors that hinder or facilitate effective implementation of a comprehensive and culturally appropriate hereditary breast cancer education and risk identification program for Spanish-speaking H/L people in two federally qualified health center (FQHC) systems.

Methods: Semi-structured interviews with stakeholders from the participating FQHCs were conducted, audio-taped, and transcribed verbatim. Rapid qualitative analysis using the Consolidated Framework for Implementation Research (CFIR) identified facilitators and barriers to HBOC education and risk identification in each FQHC, informing an adapted program implementation strategy.

Results: Stakeholder interviews (n=11) generated five common barriers and two common facilitators to implementing the HBOC education and risk identification program in these FQHCs. Barriers included: provider time constraints; lack of standard workflow to ask patients HBOC questions; follow-up and tracking referred HBOC patients; provider and staff training; and patient insurance influence on genetic counseling referral locations. Facilitators shared among FQHCs: program's alignment with their model of care, values, and mission; and the program's support among FQHC leaders.

Conclusions: The CFIR-driven evaluation revealed important factors influencing the implementation of an adapted HBOC education and risk identification program for Spanish-speaking H/L individuals at FQHCs. Although the program has organizational support, identified barriers must be considered in implementation recommendations, including standardization of workflows and patient navigation. Using barriers and facilitators to inform implementation strategies can improve program access and future expansion.

## <<24>> ASSOCIATION OF HPV STATUS WITH DEPRESSIVE SYMPTOMS IN HNC PATIENTS

*Soroush Ershadifar, BS; Beverly Garber, ANP-C; Andrew Birkeland, MD; Marianne Abouyared, MD  
UC Davis Otolaryngology*

**Introduction:** Patients with head and neck cancer (HNC) are at an increased risk of developing depression. The goal of this research project was to assess the relationship between human papillomavirus (HPV) status and age among HNC patients with developing depressive symptoms during surveillance visits.

**Methods:** This study was a retrospective analysis at a tertiary care center of patients with head and neck cancer who completed a Patient Health Questionnaire (PHQ)-2 screening during surveillance visit.

**Results:** 110 patients were identified. The majority of the patients were male (n=66, 60%) with a mean age of 66.5 years old (range 16-94, SD = 13.8). 88.2% of the patients included in the study had no history of psychiatric diagnosis prior to the PHQ screening. Among the patients, 15 (13.6%) scored  $\geq 3$  on the PHQ-2 screening and were identified as the high-risk group while the rest of the patients scored  $< 3$  on the PHQ-2 questionnaire and stratified as the low-risk group. 26 patients (23.6%) were identified with HPV-positive lesions, of which 22 were in the low-risk group and 4 were in the high-risk group. Univariate analysis revealed statistically significant difference in mean age across high-risk (mean= 62.7, SD = 12.9) and low-risk (mean = 66.7, SD =13.7) PHQ scoring group. A chi-square test of independence examining HPV-status and PHQ score grouping found no statistically significant ( $p < 0.05$ ) association between the variables. On multivariate logistic regression, age was found to be statistically significant predictor of high-risk PHQ status with odds ratio (OR) of 0.96 (95% CI: 0.92-1.00) while HPV status was not a predictor of being in the high-risk PHQ group (OR 1.35, 95 CI: 0.38 - 4.71).

**Conclusions:** Our analysis indicates that HPV status is not associated with self-reported depression symptomatology during surveillance visits. Furthermore, age of the patients (being younger) is a significant predictor for higher depressive symptoms independent of HPV status. Our study underscores the importance of depression screening in younger patients with HPV-positive lesions despite having more favorable outcomes.

## <<25>> FLIM-BASED IN VIVO CLASSIFICATION OF RESIDUAL CANCER IN THE SURGICAL CAVITY DURING TRANSORAL ROBOTIC SURGERY

*Mohamed A. Hassan<sup>1</sup>, Brent Weyers<sup>1</sup>, Julien Bec<sup>1</sup>, Jinyi Qi<sup>1</sup>, Dorina Gu<sup>2</sup>, Arnaud Bewley<sup>3</sup>, Marianne Abouyared<sup>3</sup>, Gregory Farwell<sup>4</sup>, Andrew Birkland<sup>3</sup> and Laura Marcu<sup>1</sup>*

<sup>1</sup>Department of Biomedical Engineering, University of California, Davis

<sup>2</sup>Department of Pathology and Laboratory Medicine, University of California, Davis

<sup>3</sup>Department of Otolaryngology – Head & Neck Surgery, University of California, Davis

<sup>4</sup>Department of Otorhinolaryngology – Head & Neck Surgery, University of Pennsylvania

Incomplete surgical resection with residual cancer left in the surgical cavity is a potential sequelae of Transoral Robotic Surgery (TORS). To minimize the risk of residual cancer in the surgical cavity, TORS surgeons rely on in- traoperative frozen sections analysis (IFSA) to locate and remove the remaining tumor; this process, however, leads to false negatives and is time-consuming. Mesoscopic fluorescence lifetime imaging (FLIm) of tissue fluorophores (i.e., collagen and metabolic co-factors NADH and FAD) emission has demonstrated the potential to demarcate the extent of head and neck cancer in patients under- going surgical procedures of the oral cavity and the oropharynx. Here, we demon- strate the first label-free FLIm-based classification model to identify residual cancer in the surgical cavity of the oropharynx. The model only used FLIm data from healthy surgical cavity tissue for training due to highly imbalanced label representation in the cavity and classified the residual tumors as an anomaly. FLIm data from N=22 patients undergoing upper aerodigestive oncologic surgery were used to train and validate the classification model using leave-one-patient- out cross-validation. Our approach identified all patients with positive surgical margins (N=3) confirmed by pathology. Furthermore, the proposed method re- ported a point-level sensitivity of 0.75 across optically interrogated tissue surface and a specificity of 0.78 for all N=22 patients. The results indicate that the FLIm- based classification model can identify residual cancer by directly imaging the surgical cavity, potentially enabling intraoperative surgical guidance for TORS.

## <<26>> A BAYESIAN MACHINE LEARNING APPROACH FOR PREDICTING ATYPICAL LIPOMATOUS TUMORS FROM MR RADIOMICS

*F. Godinez<sup>1</sup>, A. Roy<sup>3</sup>, Y. Abdelhafez<sup>1</sup>, N. Yuan<sup>4</sup>, Q. Ng<sup>1</sup>, C. Bateni<sup>1</sup>, J. Qi<sup>4</sup>, M. Guindan<sup>2</sup>, L. Nardo<sup>1</sup>*

<sup>1</sup>*Department of Radiology, University of California Davis*

<sup>2</sup>*Department of Biostatistics, University of California Los Angeles*

<sup>3</sup>*The Indian Statistical Institute, Kolkata, India*

<sup>4</sup>*Department of Biomedical Engineering, University of California Davis*

**Introduction:** Atypical lipomatous tumors (ALTs) are hard to differentiate from simple lipomas on MRI and an excision biopsy is frequently required to establish this distinction. Here we explore a non-invasive way to perform diagnosis using machine learning (ML) approach. The aim is to benchmark the classification performance of ALT predictor model-based ML with Bayesian additive regression trees (BART) driven by MRI radiomics.

**Methods:** At a single institution, T1-MRI images were collected from 229 patients with suspected ALT, an excisional biopsy (including MDM2 analysis) confirmed the diagnosis of either ALT or simple lipoma. A total of 1132 radiomics features were extracted from each image using the pyRadiomics software. The ML model was implemented using the BARTmachine tool. The ML was benchmarked using data subsets for training (70%) and testing (30%). Based on the BART output confusion matrix, the sensitivity, specificity, accuracy, false positive rate, misclassification rate, positive predictive value, and negative predictive value were computed. The process was repeated 500 times to generate statistical metrics.

**Results:** The result for the performance metrics are shown in table 1. The accuracy using the data subsets for training and testing was, 0.84 (SD=0.04) for the BART model.

**Discussion:** The aim of this work is to distinguish benign lipomas from well differentiated liposarcomas using an ML model. Given the current performance, this prediction might be used to inform the radiologist's decision, especially with equivocal readings, thus improving overall accuracy.

**Conclusion:** The BART machine learning model is capable of accurately classifying ALTs from simple lipomas.

# FRIDAY POSTER PRESENTATIONS (ABSTRACTS)

## <<1>> INVESTIGATING THE TGF- $\beta$ /MUC4 SIGNALING AXIS IN PLATELET-CIRCULATING TUMOR CELL INTERACTIONS DURING BREAST CANCER METASTASIS

*Savannah Free<sup>1</sup>, Kermit Carraway III<sup>1</sup>, Ronald Li<sup>2</sup>*

<sup>1</sup>UC Davis Dept of Biochemistry and Molecular Medicine, UC Davis Comprehensive Cancer Center

<sup>2</sup>UC Davis School of Veterinary Medicine, Surgical and Radiological Sciences Dept

Despite improvements in breast cancer treatment, patients with advanced metastatic disease face a 5-year survival rate of only 30%. Effective treatment will require a greater understanding of the mechanisms of the metastatic cascade and identification of novel targets essential to this process. Circulating breast tumor cells (CTCs) in the bloodstream rely on the physical protection and chemical signals of platelets to survive and seed metastatic lesions. One such chemical signal is transforming growth factor beta (TGF- $\beta$ ), which, after secretion by platelets, has been shown to modulate CTC gene expression and behavior. Significantly, TGF- $\beta$  has also been shown to upregulate expression of the cell-surface glycoprotein Mucin-4 (MUC4). MUC4 has been consistently implicated in breast cancer metastasis, with upregulated expression observed in patient metastases relative to primary tumors, and five-fold fewer lung metastases observed in a MUC4-knockout mouse model of metastatic breast cancer relative to wild-type. Importantly, MUC4 knockout results in significantly decreased platelet-CTC interactions in a mouse model—offering a possible explanation for MUC4-mediated metastatic enhancement—but the mechanism whereby this occurs is not known. These findings suggest a model wherein platelet-secreted TGF- $\beta$  upregulates CTC-MUC4 during vascular transit, reinforcing platelet-CTC interaction and generating a positive feedback loop, thereby enhancing metastatic cell survival. Through a thorough in vitro and in vivo investigation of the platelet-secreted TGF- $\beta$ /CTC-MUC4 axis, this project seeks to characterize the role of MUC4 in platelet-CTC interactions, elucidating a novel means by which metastasizing cells survive and illuminating a potential new therapeutic target for metastatic breast cancer.

## <<2>> INVESTIGATING THE ROLE OF WNT/PCP SIGNALING IN THE REPROGRAMMING OF ENERGY METABOLISM IN BREAST CANCER

*Liliana Loza Sanchez, Kacey VanderVorst, Courtney A. Dreyer, Julie Learn, Kermit L. Carraway*  
*Biochemistry, Molecular, Cellular and Developmental Biology Graduate Group*

Breast cancer is the most prevalent cancer affecting women, and the 5-year survival rate for women diagnosed with metastatic breast cancer remains below 30%. For breast tumors to progress and ultimately result in metastatic disease, large increases in energy demands must be met. Tumors gain bioenergetic versatility by undergoing metabolic reprogramming through the upregulation of glycolytic and oxidative phosphorylation (OXPHOS) activity, and through alterations in mitochondrial biogenesis and degradation (mitophagy). However, the signal transduction pathways critical to sustaining the high levels of ATP production remain largely undefined. The non-canonical Wnt/planar cell polarity (Wnt/PCP) signaling pathway has been implicated in promoting tumor cell migration and metastasis in diverse tumor types. Our laboratory has reported that the Wnt/PCP-specific transmembrane protein Vangl mediates breast cancer collective migration and metastasis. Further, our recent proteomics and metabolomics studies indicate that Vangl1 regulates the expression of critical components in the OXPHOS pathway in vivo and in vitro, and that the Wnt/PCP ligand Wnt5a alters the phosphorylation of proteins involved in mitochondrial biogenesis and mitophagy. Thus, I propose that Wnt/PCP signaling regulates the reprogramming of energy metabolism to drive cell proliferation and motility in breast cancer. This will be tested by investigating the contribution of Wnt/PCP signaling to OXPHOS activity and the regulation of mitochondrial biogenesis and mitophagy in breast cancer. This study will promote our understanding of Wnt/PCP involvement in breast cancer progression and provide new insights into the mechanisms contributing to cancer metabolic reprogramming.

### **<<3>> CANCER EVS DRIVE A MICROGLIA-MEDIATED INFLAMMATORY RESPONSE IN A NEW MIXED CORTICAL CELL CULTURE MODEL**

*Rachel R Mizenko<sup>1</sup>, Hyehyun Kim<sup>1</sup>, Erkin Seker<sup>2</sup>, Randy P. Carney<sup>1</sup>*

*<sup>1</sup>Department of Biomedical Engineering, University of California, Davis, Davis, California, USA*

*<sup>2</sup>Department of Electrical and Computer Engineering, University of California, Davis, Davis, California, USA*

Metastatic niche formation in the brain is hypothesized to be mediated in part by cancer-derived EV interaction with CNS cells. However, models to study this interaction often lack cell-to-cell signaling that may mediate metastasis, such as neuroinflammation. Here, we employ primary rat cortical tri-culture (neurons, astrocytes, microglia) and contrasting co-culture (without microglia) to compare interactions of EVs from breast cancer cells (MDA-MB-231) to their brain-tropic variant (231-Br) in an inflammation-competent model.

EVs were isolated via differential ultracentrifugation and characterized via nanoparticle tracking analysis, flow cytometry, and interferometric imaging. Cultures were prepared from rat-pup neocortices and seeded in chambered coverslips. For cellular uptake,  $2 \times 10^{11}$  EVs were fluorescently labeled and incubated in cultures for 4 hrs. Cells were immunostained and imaged by confocal microscopy. For studying cytokine profile, EVs were incubated for 24 hrs, and conditioned media was analyzed for cytokines.

231-Br EVs were taken up by neurons and astrocytes at similar levels in co- and tri-culture. MDA-MB-231 EV uptake was not significant compared to controls. Autofluorescence obscured potential uptake by microglia. Despite non-significant uptake, MDA-MB-231 EVs resulted in the highest increase in inflammatory cytokines (e.g., MCP-1 and MIP-1 $\alpha$ ) in tri-culture. Though 231-Br EVs had similar cytokine trends, these increases were not significant compared to controls.

These results suggest that evading microglia could be important to EV-mediated metastasis, with EVs from brain-metastatic cells having more uptake in other cells and causing less inflammation. This work highlights that microglia inclusion is important to understanding the interaction of metastatic EVs within the CNS.

### **<<4>> ADAPTING TWO-COMPONENT SIGNALING PATHWAYS FOR ENGINEERING HUMAN CELLS**

*Diana Sernas, Shashank Shastry, Aditi Thambala, Alexandra Calderon, Sabrina Truong, Yubai Sun, Sean R. Collins*

*Department of Microbiology & Molecular Genetics, UC Davis, Davis, CA 95616*

Emerging immunotherapy approaches based on engineering immune cells have shown exciting promise for treating cancer. As a prominent example, chimeric antigen receptors allow modified T cells to detect and kill cancer cells. However, these strategies are still limited by a lack of efficacy against many solid tumor types and dangerous side effects from excessive immune responses and unintended targeting of normal cells. The creation of molecular tools to make the activity of engineered cells more specific could address these challenges. We are developing two-component systems (TCS) as a flexible platform for adding sensing and signal integration capabilities to focus the activity of engineered immune cells. TCS are ubiquitous in bacteria and have evolved to sense a multitude of environmental conditions, including metabolites and small molecules associated with inflammation. TCS pathways have a compact size and use biochemical modifications orthogonal to those of mammalian pathways, which make them ideal candidates for insulated sensing pathways. As a proof of principle, we are testing the function of TCS pathways that respond to light, reactive oxygen species, and nitric oxide in HEK293 cells. Ultimately, we plan to connect sensing of tumor- or inflammation-associated ligands with transcriptional or signaling outputs that could be used to limit immune activity in healthy regions of the body and/or sensitize responses at tumor locations. This work has been funded in part by a UC Davis Cancer Center Support Grant.

## **<<5>> PRODUCTION AND USE OF RECOMBINANT MIRNAS TO DISSECT THE INTRINSIC DIFFERENCES IN MIRNA BIOGENESIS AND FUNCTIONS**

*Yimei Wang, Meijuan Tu, Neelu Batra, Aiming Yu*

*Department of Biochemistry and Molecular Medicine, UC Davis School of Medicine*

MicroRNAs (miRNAs) are small non-coding RNAs that control posttranscriptional gene regulation by acting on the 3'-untranslated region of target transcripts. Many miRNAs have been shown to act as tumor suppressors or oncogenes while being down- or up-regulated in cancer. Additionally, some miRNAs regulate specific drug metabolizing enzymes and transporters to modulate drug metabolism, disposition, efficacy or toxicity. While one miRNA (e.g., hsa-miR-491, or miR-491) might be processed to both 5p and 3p in cells, one is usually the predominant form (hsa-miR-491-5p). Therefore, reports on the trivial species without denoting 5p or 3p have caused many confusions and distractions. In this study, we aimed to delineate the differences in miRNA biogenesis and functions in hepatocellular carcinoma (HCC) cells by taking advantage of our unparalleled RNA molecular bioengineering technology to generate model recombinant miR-491-5p, -3p, and pre-miR-491 molecules. To this end, we have heterogeneously overexpressed targeted recombinant miR-491-5p, -3p and pre-miR-491 and purified each biologic RNA (BioRNA) to high purity (>98% by HPLC). Furthermore, we have validated the release of miR-491-5p and -3p strands from individual BioRNAs in human HEK293 and Hep3B cells. We will further compare the levels of miR-491-5p and -3p in HCC cells using RNA-seq techniques and define their effects on the expression of ATP-binding cassette (ABC) transporters, which are critical for cancer drug transport and multidrug resistance. In addition, we will critically define the subsequent impact on drug disposition and chemosensitivity of HCC cells that is expected to offer insight into developing new therapies to improve HCC treatment.

## **<<6>> RECOMBINANT MIR-7-5P EFFECTIVELY INHIBIT NSCLC CELL VIABILITY THROUGH REGULATING MITOCHONDRIAL FUNCTION**

*Gavin M. Traber, Mei-Juan Tu, Neelu Batra, Colleen Yi, Ai-Ming Yu*

*Department of Biochemistry and Molecular Medicine, UC Davis School of Medicine, Sacramento, CA, USA*

Non-Small Cell Lung Cancer (NSCLC) makes up 84% of all lung cancer cases and lack of effective treatment options contribute to low survival rates. RNA interfering (RNAi) microRNA (miRNA or miR) provides researchers with an alternative to modulate gene expression to combat disease. Of these, the level of tumor suppressive miR-7-5p (miR-7) is reduced in NSCLC. Notably, miR-7 downregulates genes important in mitochondrial function including EGFR and VDAC1, and it is a putative regulator of mitochondrial gene AGK. Reintroduction of miR-7-5p has been reported to inhibit NSCLC progression, however the miRNA mimics used in those studies are chemically synthesized in vitro with extensive modifications that may trigger immunogenic and off-target responses. By contrast, our laboratory has developed a novel technology to bioengineer RNAi agents (BioRNA) in vivo to preserve the natural physiochemical properties of endogenous miRNAs. Using this technology, we aim to develop BioRNA/miR-7 as an anticancer agent that functions through endogenous RNAi mechanisms to reduce cancer cell viability by regulating mitochondrial function. Thus far, we successfully produced and purified leucyl and glycyl human tRNA versions of BioRNA/miR-7, established the effects of BioRNA/miR-7 to reduce cell viability, validated the processing of glycyl tRNA-BioRNA/miR-7 (BioRNAGly/miR-7-5p) to target miR-7-5p in NSCLC cells, assessed the function BioRNAGly/miR-7 to regulate known target gene expression, and established the effects of BioRNAGly/miR-7 on mitochondrial function. Together, our BioRNA technology alongside our preliminary data suggests that miR-7 plays an important role in mitochondrial function, and that BioRNAGly/miR-7 may be developed as a new therapeutic for NSCLC treatment.

## <<7>> METABOLIC RISK FACTORS AND OUTCOMES IN PATIENTS WITH GLIOBLASTOMA

*John Paul Aboubechara<sup>1</sup>, Orwa Aboud<sup>1,2,3</sup>*

<sup>1</sup>*Department of Neurology, University of California, Davis, Sacramento, CA*

<sup>2</sup>*Department of Neurological Surgery, University of California, Davis, Sacramento, CA*

<sup>3</sup>*University of California Davis, Comprehensive Cancer Center*

The purpose of this study is to test the hypothesis that the metabolic syndrome is a risk factor for developing glioblastoma and is associated with worse survival outcomes.

A retrospective cohort study was conducted, consisting of patients at a single institution. Clinical records from 40 patients with glioblastoma IDH wild type were reviewed as part of this interim analysis—with plans to analyze 80 patients by study completion. Records included the patient's diagnosis, progression free survival, overall survival, treatment, tumor molecular characteristics, blood pressure, body mass index, medications, and laboratory data.

Our results demonstrate a trend that patients with the metabolic syndrome have worse overall survival compared to those who do not (16.7 months vs 8.1 months;  $p=0.069$ ). Interestingly, hypertension ( $p=0.007$ ), hyperglycemia ( $p = 0.044$ ), and dyslipidemia ( $p = 0.041$ ) were negatively associated with survival, while BMI was not. Furthermore, there was a significant negative association between overall survival and the number of metabolic risk factors that patients accumulate (i.e. BMI, HTN, etc.) ( $p=0.0038$ ). However, our results demonstrate the prevalence of metabolic syndrome in GBM patients to be 30%, which is less than that of the general population, 35%.

These interim results suggest that the metabolic syndrome is associated with worse survival in patients with glioblastoma IDH wild type, but that it is not a risk factor in the development of this cancer. These results support other work that has implicated metabolic dysregulation in the pathogenesis of glioblastoma.

## <<8>> MECLIZINE IS MUCH MORE MTORC1-SELECTIVE THAN RAPAMYCIN AND DOSE DEPENDENTLY KILLS GLIOBLASTOMA STEM CELLS

*Alexey Tomilov, Claire Montgomery, Sundeep Dugar, Gino Cortopassi*

mTORC1 is an appealing cancer drug target. First mTORC1 inhibitor Rapamycin is used in more than 1000 clinical trials, and ~40 for the Glioblastoma. However, Rapamycin is not completely specific and inhibits mTORC2 resulting in side effects. We screened FDA-approved drugs for mTORC1 inhibitors, and Isolated Meclizine, as novel non Rapalog mTORC1 specific inhibitor that directly bind mTOR protein and specifically inhibit the activity of only mTORC1, but not mTORC2. Meclizine represents a class of "old" safe drugs piperazines that were prescribed for several decades. Therefore, we identified a potential repurposed indication for piperazines – the specific mTORC1 inhibition.

Meclizine applied alone in concentrations that it reaches in plasma during normal dosing, or in combination with standard of care killed patient-derived GBMSC much more potently than Standard-of-Care Temozolomide. Moreover, Meclizine was recently shown by NIA's Interventions multisite double-blinded Testing Program to significantly extend lifespan in mice, and as suggested by the program, the extended longevity could result from reduced tumorigenesis.

Given the enhanced mTORC1 specificity of Meclizine vs Rapamycin, and very low side-effect profile of Meclizine, we suggest a clinical trial in Glioblastoma could be designed with Meclizine alongside Standard of Care resection and temozolomide therapy.

## <<9>> A NEW VULNERABILITY TO BET INHIBITION DUE TO ENHANCED AUTOPHAGY IN BRCA2-DEFICIENT PANCREATIC CANCER

*Suyakarn Archasappawat<sup>1,2,\*</sup>, EunJung Lee<sup>1,\*</sup>, Keely Ji<sup>1,\*</sup>, Jocelyn Pena<sup>3</sup>, Virneliz Fernandez-Vega<sup>3</sup>, Ritika Gangaraju<sup>4</sup>, Nitin Sai Beesabathuni<sup>4</sup>, Martin Jean Kim<sup>1</sup>, Qi Tian<sup>1</sup>, Priya Shah<sup>1,4</sup>, Louis Scampavia<sup>3</sup>, Timothy Spicer<sup>3</sup>, Chang-Il Hwang<sup>1,5,#</sup>*

<sup>1</sup>Department of Microbiology and Molecular Genetics, University of California, Davis, CA

<sup>2</sup>Graduate Group in Integrative Pathobiology, University of California, Davis, CA

<sup>3</sup>UF Scripps Biomedical Research High-Throughput Screening Center, Department of Molecular Medicine, Scripps Florida, Jupiter, FL

<sup>4</sup>Department of Chemical Engineering, College of Engineering, University of California, Davis, CA

<sup>5</sup>University of California Davis Comprehensive Cancer Center, Sacramento, CA

\*These authors contributed equally to this work: *Suyakarn Archasappawat, EunJung Lee, Keely Ji*

Pancreatic ductal adenocarcinoma (PDAC) is the third leading cause of cancer-related deaths in the United States. Around 10% of pancreatic cancer diagnoses are thought to be familial pancreatic cancer (FPC). BRCA2 gene with pathogenic variants has been identified as one of the genes closely associated with FPC. Personalized medicine approaches tailored towards FPC mutation profiles could improve patient outcomes. We performed high-throughput drug screening using isogenic mouse Brca2 knockout (KO) and control PDAC cells. JQ1, a bromodomain and extra-terminal domain protein (BET) family inhibitor, preferentially induced cytotoxicity in Brca2 KO cells. JQ1 significantly decreased cell viability of Brca2 KO cells in vitro and suppressed growth of Brca2 KO tumors in vivo compared to the controls. The RNA-seq showed that JQ1 treatment resulted in upregulation of the gene sets associated with macroautophagy. Multi-orthogonal autophagy assays including live cell imaging of fluorescence-based autophagy reporter also supported that Brca2 KO cells had a constitutively higher basal level of autophagic activities compared to the controls, and JQ1 further induced autophagic flux in Brca2 KO cells. Moreover, blocking autophagy process by pharmacological inhibition or knocking down essential autophagy genes rescued JQ1-induced cell death in Brca2 KO cells, indicating that the increased autophagy is responsible for JQ1-mediated cell death in Brca2 KO cells. Overall, we found that BRCA2 deficiency elevated autophagic flux, and extensive autophagy was further activated by BET inhibition, culminating in autophagy-dependent cell death in Brca2-deficient PDAC. Our findings suggest that BET inhibition could be a promising therapeutic strategy for treating BRCA2-deficient PDAC.

## <<10>> EFFICACY OF DIFFERENT LET-7 ISOFORMS IN THE MODULATION OF TARGET GENE EXPRESSION IN HCC CELLS

*Joseph Cronin, Mei-Juan Tu, Ai-Ming Yu*

MicroRNAs are a large family of noncoding RNAs that control posttranscriptional regulation of target genes through interacting with their transcripts. Endogenous miRNAs serve as critical epigenetic regulators of many cellular processes, including those integral to drug transport and disease progression. Our previous studies have demonstrated the potential of miRNA replacement therapy, which reintroduces miRNA species that are commonly downregulated or lost in cancer such as the let-7-5p miRNA family. This family consists of several isoforms that differ slightly in their mature sequence. Studies have shown that let-7 miRNA replacement therapy can inhibit hepatocellular carcinoma (HCC) tumor progression by modulating the expression of specific oncogenes such as Lin28B. Prior experiments also revealed that let-7c-5p can directly target and downregulate ABCC5, an efflux drug transporter that is commonly overexpressed in HCC and implicated in multidrug resistance. To further elucidate the therapeutic potential and define the efficacy of individual let-7-5p isoforms, the current study utilized a novel in vivo fermentation based, RNA bioengineering approach to produce fully humanized biologic let-7-5p miRNAs (BioRNA/let-7-5p) in high yield. All BioRNA/let-7-5p isoforms similarly downregulated protein level of Lin28B, with BioRNA/let-7d-5p demonstrating the strongest and most consistent downregulation across three HCC cell lines. Additionally, HCC cells treated with BioRNA/let-7-5p agents demonstrated lower ABCC5 protein levels with small differences between individual isoforms. These results illustrate the differences of let-7-5p family isoforms in the regulation of target gene expression in HCC

cells, providing insight into how target complementarity and regulatory strength may affect the anticancer potency of individual miRNA isoforms.

### <<11>> **DISRUPTING B-2 ADRENERGIC RECEPTOR SIGNALING TRIGGERS GLIOMA CELL DEATH AND DOWN-REGULATES SURVIVIN**

*Orli Algranatti, Undergraduate Student; James Michael Angelastro, PI*

Epidemiological studies showed that  $\beta$ -adrenergic antagonists caused a low incidence of several cancer types. Glioblastoma highly expresses  $\beta$ -2-adrenergic receptors. GBM accounts for 50% of central nervous system cancers. After standard-of-care therapeutic intervention, there is a survival time of 15 months. Our goal is to develop a translational therapy that will trigger the death of GBM cells while preserving healthy cells.

Salmeterol xinafoate is a biased agonist that activates the G-protein pathway. Biased agonists activate signaling through the G-protein or the  $\beta$ -arrestin pathway of G-protein coupled receptors. Dose-response experiments were performed using  $\beta$ 1 and  $\beta$ 2-adrenergic receptor antagonists and biased  $\beta$ 2-adrenergic receptor agonists to determine loss of glioma cell viability in three glioma cell lines. Western immunoblotting was used to gauge salmeterol xinafoate-mediated dose-response decrease of survivin in the three glioma cell lines. Epoxomicin was used to inhibit the proteasome complex.

Disrupting  $\beta$ -2-adrenergic receptor signaling by salmeterol xinafoate leads to cell death of glioma cells by sparing healthy neuron-glia cells using similar doses. Survival of glioma cells appears to be regulated by the  $\beta$ -arrestin pathway. Antagonists have been shown to promote glioma cell death. It was also discovered that salmeterol xinafoate down-regulates survivin through the proteasome complex in glioma cell lines.

Promising results show loss of viability and disrupting survivin expression in glioma cells, allows FDA-approved drug salmeterol xinafoate to be forwarded to the clinic. Repurposing this drug for GBMs may be combined with the current standard-of-care chemotherapies to enhance more significant loss of tumor volume and increase patient survival.

### <<12>> **USE OF RECOMBINANT MICRORNAS AS ANTIMETABOLITES TO INHIBIT HUMAN NON-SMALL CELL LUNG CANCER**

*Yixin Chen, Mei-Juan Tu, Zhenzhen Liu, Neelu Batra, Ai-Ming Yu*

*Department of Biochemistry and Molecular Medicine, UC Davis School of Medicine, Sacramento, CA 95817, USA*

Lung cancer remains the leading cause of cancer deaths worldwide. Very recently, we have established a novel technology to produce bioengineered miRNA agents for the study of cancer biology and new therapies. After experimental screening of unique recombinant miRNAs produced in vivo, three lead antiproliferative miRNAs against human NSCLC cells, miR-22-3p, miR-9-5p, and miR-218-5p, were revealed to target folate metabolism by bioinformatic analyses. Recombinant miR-22-3p, miR-9-5p, and miR-218-5p were shown to regulate key folate metabolic enzymes to inhibit folate metabolism and subsequently alter amino acid metabolome in NSCLC A549 and H1975 cells. Isotope tracing studies further confirmed the disruption of one-carbon transfer from serine to folate metabolites by all three miRNAs, inhibition of glucose uptake by miR-22-3p, and reduction of serine biosynthesis from glucose by miR-9-5p and -218-5p in NSCLC cells. With greater activities to interrupt NSCLC cell respiration, glycolysis, and colony formation than miR-9-5p and -218-5p, recombinant miR-22-3p was effective in reducing tumor growth in two NSCLC patient-derived xenograft mouse models without causing any toxicity. In conclusion, our results demonstrated that bioengineered miR-22-3p, miR-9-5p, and miR-218-5p act on the folate cycle to suppress NSCLC cell metabolic capacity and exhibit strong antiproliferation activities, which shall provide new insights into developing antimetabolite RNA therapies.

## <<13>> A MULTI-ETHNIC POPULATION-BASED STUDY OF MULTIPLE MYELOMA DISPARITIES: RESULTS FROM A RECRUITMENT PILOT

Angelica Perez<sup>1,2</sup>, April Vang<sup>1,4</sup>, Juanita Elizabeth Quino<sup>1</sup>, Ana Estrada<sup>1</sup>, Eric Stewart<sup>3</sup>, Rosemary Cress<sup>3</sup>, Luis G. Carvajal-Carmona<sup>1,2,3</sup>

<sup>1</sup>UC Davis Genome Center

<sup>2</sup>UC Davis Comprehensive Cancer Center

<sup>3</sup>Cancer Registry of Greater California

<sup>4</sup>UC Davis Graduate Statistics Studies

To understand multiple myeloma (MM) incidence and survivorship disparities, we established the Precision MEDicine, EqUity and Disparities Research in MultipLe MyeLoma (MEDULLA) study. Our study contacted 400 MM patients reported to the Cancer Registry of Greater California (CRGC) between 2013-2018 with 100 adults each from racial/ethnic groups: Blacks, Whites, Latinos, and Asians with MM diagnosis. Data collection included variables reported to the CRGC, a self-administered survey, and biospecimen saliva collection. The survey focused on demographics, risk factors, cancer treatment, family history, quality of life, and social determinants of health. We also used census tract level features obtained by the American Community Survey 2007-2011. A total of 95 patients participated in the survey (overall response rate = 24%). We perform univariate and multivariable logistic regression with age and sex kept as covariates. These methods were stratified by Whites and Non-Whites separately.

The highest response received was from Whites at 44.2%, with significantly lower rates in all minority groups (<20% for all groups). Response rates were higher for patients living in areas with higher median annual incomes and education. For every 10% increase in the proportion of individuals having a college degree, responding to the survey increased by 1.17 units for minorities in that neighborhood (p=0.07). In conclusion, we found significantly lower participation rates among minority groups, with socio-economic factors affecting response rates. We suggest that future studies develop community-focused and culturally tailored strategies to understand MM etiology and survivorship in such populations.

## <<14>> LATE VENOUS THROMBOEMBOLISM IN ADOLESCENT AND YOUNG ADULT CANCER SURVIVORS: A POPULATION-BASED ANALYSIS FROM THE VOICE STUDY

Renata Abrahão<sup>1</sup>, Qian Li<sup>1</sup>, Ann Brunson<sup>1</sup>, Hazel B. Nichols<sup>2</sup>, Chun Chao<sup>3,4</sup>, Judy Li<sup>1</sup>, Kathryn Ruddy<sup>5</sup>, Jessica Chubak<sup>6</sup>, Candice Sauder<sup>7,8</sup>, Marcio Malogolowkin<sup>9</sup>, Lawrence Kushi<sup>10</sup>, Erin Hahn<sup>3,4</sup>, Karen Wernli<sup>3,6</sup>, Ted Wun<sup>1</sup>, Theresa Keegan<sup>1</sup>

<sup>1</sup>Center for Oncology Hematology Outcomes Research and Training (COHORT), Division of Hematology and Oncology, University of California Davis Comprehensive Cancer Center, Sacramento, CA

<sup>2</sup>University of North Carolina Gillings School of Global Public Health, Chapel Hill, NC

<sup>3</sup>Department of Health Systems Science, Kaiser Permanente Bernard J. Tyson School of Medicine, Pasadena, CA

<sup>4</sup>Department of Research and Evaluation, Kaiser Permanente Southern California, Pasadena, CA

<sup>5</sup>Department of Oncology, Mayo Clinic, Rochester, MN

<sup>6</sup>Kaiser Permanente Washington Health Research Institute, Seattle, WA

<sup>7</sup>Division of Surgical Oncology, Department of Surgery, University of California Davis, Sacramento, CA

<sup>8</sup>University of California Davis Comprehensive Cancer Center, Sacramento, CA

<sup>9</sup>Department of Pediatrics, Division of Pediatric Hematology/Oncology, University of California Davis School of Medicine, Sacramento, CA

<sup>10</sup>Division of Research, Kaiser Permanente Northern California, Oakland, CA

Introduction: Venous thromboembolism (VTE), a common complication in cancer patients, occurs more often during the initial phase of treatment. However, information on VTE beyond the first two years after diagnosis ('late VTE') is scarce, particularly in young survivors.

Methods: We examined the risk of, and factors associated with late VTE among adolescents and young adults (AYA, 15–39 years) diagnosed with cancer (2006–2018) who survived ≥2 years. Data were obtained from the California Cancer Registry linked to hospital discharge summaries. We used non-parametric models and Cox proportional hazard regression for analyses.

Results: Of 59,343 survivors, 927 (1.6%) developed late VTE. Most VTEs were pulmonary embolism (PE, 48%) or PE associated with deep venous thrombosis (11%). The hazard of VTE was higher among those who had active cancer, including progression from lower stages to metastatic disease (Hazard Ratio (HR)=10.44, 95% confidence interval (CI): 8.91–12.25), second primary cancer (HR=2.58, CI:2.01–3.30), or metastatic disease at diagnosis (HR=2.47, CI:1.91–3.19). The hazard of late VTE was increased among survivors who underwent a hematopoietic cell transplant, those who received radiotherapy, with a history of VTE, public insurance (vs private), and non-Hispanic Black/African American race/ethnicity (vs non-Hispanic White). Compared to patients with thyroid cancer, patients with leukemias, lymphomas, sarcoma, melanoma, colorectal, breast and cervical cancers had a higher VTE risk.

Conclusions: VTE risk remained elevated  $\geq 2$  years following cancer diagnosis in AYA survivors. Active cancer is a significant risk factor for VTE; thus, late VTE should prompt evaluation for recurrence or secondary malignancy.

## <<15>> DEVELOPMENT OF HPV AWARENESS AND PREVENTION EDUCATION MATERIALS FOR HISPANIC/LATINX COMMUNITY HEALTH EDUCATORS

*Charlotte Bergheimer, Daisy Montoya, Laura Adame, Jesus Bastian, Najila Dabbagh, Yelitza Campos, Laura Fejerman, University of California, Davis*

The human papillomavirus (HPV) is the most common sexually transmitted infection in the United States. Although there is no cure for HPV infections, implementation of highly effective preventable measures (screening tests and HPV vaccination) has reduced the incidence of HPV-related cancers. Despite these interventions, the Hispanic/Latinx (H/L) community continues to experience high incidences of HPV infections and some of its related cancers. H/L underutilization of these preventative health services can be explained by low health literacy levels and language barriers. To address these determinants, the program 'Mas Vale Prevenir' aims to develop culturally and linguistically appropriate HPV related cancer prevention educational materials to train community health educators (Promotores) in educating the Californian H/L community. Consistent with a continuous stakeholder engagement approach, we conducted two focus groups with Promotores (N=12) which were analyzed using qualitative methodology (Thematic Analysis). We identified insights related to pre-determined themes: learning preferences (e.g., use medical terminology) and opinions related to content (e.g., liked narrative format, relatability) as well as to emerging themes: importance of content (e.g., normalizing the material, H/L-specific statistics) and the role of Promotores (e.g., bridge between doctors and community). Results from the focus groups analysis were used to refine materials in an iterative manner. Engaging H/L Promotores in the development of health educational materials is essential for their effectiveness as community educators. The next step is to evaluate the effectiveness of the 'Mas Vale Prevenir' program in changing HPV related preventative behavior within the H/L community and reducing HPV related cancer health disparities.

## <<16>> CHARACTERIZATION OF CARCINOGENIC CONSTITUENTS OF DOMESTIC WELLS IN NORTHERN AND CENTRAL CALIFORNIA

*Dr. Jasquelin Peña<sup>1</sup>, Dr. Shehnaz Hussain<sup>2</sup>, Dr. Irva Hertz-Picciotto<sup>2</sup>, Dr. Thomas Young<sup>1</sup>, Espe Vielma<sup>3</sup>, Shosha Capps<sup>4</sup>, Tracy Hysong<sup>2</sup>, Kyounglim Kang<sup>1</sup>, Vida Sánchez<sup>5</sup>*

<sup>1</sup>*UC Davis Civil and Environmental Engineering*

<sup>2</sup>*UC Davis Public Health Sciences*

<sup>3</sup>*Environmental Justice Coalition for Water*

<sup>4</sup>*UC Davis Environmental Health Sciences*

<sup>5</sup>*UC Davis*

**Introduction:** Groundwater provides 40–60% of California's water supply. Due to their decentralized nature and high cost of testing, domestic well water quality is not regulated in California. Many well users rely on hydrologic models for information about their water quality but there remains a need for an integrated approach that combines place-based quantitative analysis with cancer risk assessment and community engagement.

**Methods:** Our pilot study aims to build relationships and science literacy with private well water users through compensated community sampling of California well water and provision of quantitative reports including 22 constituents (e.g. nitrate, arsenic, uranium, among others). Additionally, the pilot study seeks to investigate the impacts of seasonality, land use, and climate change phenomena (e.g. wildfire, drought, floods) on California groundwater water quality. Participants (n=100) were recruited in collaboration with our community partner, the Environmental Justice Coalition for Water. Chemical analyses were performed at UC Davis and used to generate water quality measurements and to assess potential public health risks and resources for remediation.

**Results:** Of the 57 samples tested, none had exceedances of Primary MCLs, 28% had at least one constituent exceedance of Secondary MCLs, and all had at least one constituent exceedance of PHGs (e.g. Lead (57/57), Uranium (28/57), Arsenic (12/57), Cadmium (11/57)).

**Next Steps:** This study will help study participants assess the health risks of their well water and provides the infrastructure to scale up to a larger groundwater quality monitoring program.

## <<17>> DISPARITIES IN BREAST CANCER STAGE AT DIAGNOSIS AND QUALITY OF CANCER CARE IN CALIFORNIA BY SOURCE OF HEALTH INSURANCE

*Nuen Tsang Yang<sup>2</sup>, Frances B. Maguire<sup>2</sup>, Brenda M. Hofer<sup>2</sup>, Allyn M. Fernandez<sup>2</sup>, Theresa Keegan<sup>1,2,3</sup>, Shehnaz K. Hussain<sup>1,2</sup>, Arti Parikh-Patel<sup>2</sup>*

<sup>1</sup>*Department of Public Health Sciences, University of California Davis, Davis, CA, USA*

<sup>2</sup>*California Cancer Reporting and Epidemiologic Surveillance Program, University of California Davis Comprehensive Cancer Center, Sacramento, CA, USA*

<sup>3</sup>*Department of Internal Medicine, Division of Hematology and Oncology, University of California Davis, Davis, CA, USA*

**Background:** Breast cancer (BC) ranks as a leading cause of cancer-related mortality among women in the United States. Addressing disparities in BC care is crucial for improving cancer outcomes. This study investigates disparities in stage at diagnosis and quality of cancer care linked to health insurance utilizing the most recent data available from the California Cancer Registry (CCR).

**Methods:** Women newly diagnosed with BC (2014-2020) were identified in CCR. Health insurance at diagnosis/initial treatment was categorized as private insurance, Medicare, Medi-Cal, other public insurance, and uninsured and AJCC stage at diagnosis was categorized as 0, I or II (early stage) and III or IV (late stage). The Commission on Cancer quality measure assessed the percentage of breast-conserving surgeries (BCS) performed among women diagnosed with early-stage disease. Analyses were stratified by health insurance and age at diagnosis.

**Results:** Among 226,043 women with BC, uninsured and Medi-Cal insured had the largest percentage of late stage disease at diagnosis for the 19-64 (20.5% Medi-Cal and 22.1% uninsured vs. 10.5% private) and the ≥65 (16.0% Medi-Cal and 17.1% uninsured vs. 9.4% private) age groups. Medi-Cal patients and the uninsured with early-stage disease were less likely to have BCS compared with privately insured for both 19-64 (58.5% Medi-

Cal and 58.5% uninsured vs. 63.2% private) and ≥65 (59.6% Medi-Cal and 60.6% uninsured vs. 70.8% private) age groups.

Conclusions: Our study underscores significant disparities in the stage at which BC patients are diagnosed and the care they receive based on their source of health insurance.

### <<18>> **EARLY RECOGNITION AND PROMPT INTERVENTION OF IMMUNOTHERAPY-INDUCED ADRENAL INSUFFICIENCY IN CANCER PATIENTS: A CASE SERIES AND A PROSPECTIVE MULTIDISCIPLINARY WORKFLOW**

*Ashley Trane, MD; Aili Guo, MD; Tianhong Li MD, PhD  
UC Davis Hospital*

Background: Immune checkpoint inhibitors (ICIs) have significantly improved the prognosis of multiple malignancy types. Unfortunately, they can result in immune-related adverse events (irAEs). In a systemic review, approximately 10% of patients treated with ICIs developed an ICI associated endocrinopathy, including adrenal insufficiency. The initial diagnosis of immunotherapy induced adrenal insufficiency and subsequent encounters for adrenal crisis often occur in hospital settings. However, the early recognition and prompt management of irAEs requires a complex coordination of care across multiple specialties, especially hospitalized patients. We aim to present a proposed multidisciplinary approach to improve time to diagnosis and improved outcomes in our cancer patients with immunotherapy induced adrenal insufficiency.

Methods: We evaluated a case series of 8 patients treated with ICIs at the UC Davis Comprehensive Cancer Center for an underlying malignancy and were subsequently admitted for complications related to ICI-induced adrenal insufficiency.

Results: In our single institution case series, we noted a delay to diagnosis, a delay to initiation of stress dose steroids, and/or subtherapeutic glucocorticoid dosing. There was a wide variation within their hospital courses thus demonstrating a need for a multidisciplinary workflow to standardize treatment.

Conclusion: As early intervention of immunotherapy induced adrenal insufficiency can decrease morbidity and decreased hospitalization times, we propose a multidisciplinary workflow approach to the early detection and initiation of increased glucocorticoid dosing.

### <<19>> **CANCER INCIDENCE AMONG ARMENIANS IN CALIFORNIA**

*Ani Movsisyan Vernon<sup>1,2</sup>, Jeffrey S. Hoch<sup>1,3,4</sup>, Laura Fejerman<sup>1,2</sup>, Theresa H.M. Keegan<sup>1,2,5</sup>*

<sup>1</sup>Department of Public Health Sciences, University of California Davis, Davis, CA, USA

<sup>2</sup>UC Davis Comprehensive Cancer Center, University of California Davis Medical Center, Sacramento, CA, USA

<sup>3</sup>Division of Health Policy and Management, Department of Public Health Sciences, University of California, Davis, CA 95616, USA

<sup>4</sup>Center for Healthcare Policy and Research, University of California, Davis, CA 95616, USA

<sup>5</sup>Division of Hematology and Oncology, Center for Oncology Hematology Outcomes Research and Training, UC Davis School of Medicine, Davis, CA, USA

Background: California is home to the largest population of Armenians in the United States. However, Armenians have historically been categorized with non-Hispanic White (NHW) or other race groups in population databases, which has likely masked cancer incidence patterns in this population. This is the first population-based study considering cancer incidence among Armenians in California.

Methods: We used the Armenian Surname List (ASL) and birthplace information in the California Cancer Registry to identify Armenians with cancer diagnosed during 1988-2019. We calculated proportional incidence ratios (PIR) for the top ten most frequent cancers among Armenian men and women, with NHW men and women as the comparison group.

Results: There were 27,212 cancer diagnoses among Armenians in California, 13,754 among males and 13,458 among females. Armenian males had a significantly higher proportion of stomach (PIR=2.39), bladder (PIR=1.53), colorectal (PIR=1.29), lung (PIR=1.16), leukemia (PIR=1.16), liver and intrahepatic bile duct

(PIR=1.19), and kidney (PIR=1.11) cancers, and a significantly lower proportion of prostate (PIR=0.84) cancer. Armenian females had a significantly higher proportion of stomach (PIR=3.24), thyroid (PIR=1.47), colorectal (PIR=1.29), pancreatic (PIR=1.20), leukemia (PIR=1.20), non-Hodgkin's lymphoma (PIR=1.15), and ovarian (PIR=1.14) cancers, and a significantly lower proportion of lung (PIR=0.49) cancer.

Discussion: We observed higher proportions of several cancers among Armenians compared with NHWs, particularly stomach cancer, which may relate to diet or exposure to harmful environmental agents. Further research is needed to understand and address risk factors leading to higher proportions of specific cancers among Armenians in California.

## <<20>> A TRIM37 RISK VARIANT RS57141087 CONTRIBUTES TO TRIPLE-NEGATIVE BREAST CANCER ONSET AND PROGRESSION IN AFRICAN AMERICAN WOMEN

*Rachisan Djake Tihagam, Song Lou, Kammi Liu, Arjun Tushir Singh, Sanchita Bhatnagar  
Department of Medical Microbiology and Immunology, University of California Davis School of Medicine,  
University of California Comprehensive Cancer Centre, Davis, CA 95616, USA.*

TNBC incidence is disproportionately higher in African American (AA) women compared to other races, signifying racial disparity (1, 2). Whether earlier onset or advanced-stage at the time of diagnosis, an aggressive tumor phenotype is a characteristic feature of TNBC in AA women (3-5). Consequentially, a 5-year survival rate for TNBC in AA patients is only 14% compared to 36% in non-African American women (3). Although disparities in treatment, co-morbid disease, and access to health care contribute to poor prognosis (2, 6-8), a race-specific biological component to TNBC disparity cannot be ruled out. We have previously discovered an epigenetic regulator called TRIM37, which we described as a novel breast cancer oncoprotein (9-11) and metastatic driver (12). Our preliminary investigations identified a genetic link between TRIM37 and AA ethnicity. Through a small-screen candidate-based screen, we have identified an association between TRIM37 expression and rs57141087, with AA women more likely to carry the risk allele in healthy, cancer-free breast tissue. Mechanistically, we find that the risk allele of rs57141087 modulates promoter-enhancer interaction to upregulate TRIM37 transcriptionally and contributes to tumorigenesis. Together, we uncovered that higher TRIM37 expression in the breast of AA women triggers TNBC onset and predisposes them to accelerated progression.

## <<21>> TRANSCRIPTOME-WIDE STUDY OF TUMOR SAMPLES FROM PERUVIAN WOMEN IDENTIFIES DYSREGULATED PATHWAYS IN LUMINAL TUMORS TYPICALLY ASSOCIATED WITH MORE AGGRESSIVE DISEASE

*Chenghuiyun Xu<sup>1</sup>, Valentina A. Zavala<sup>1</sup>, David Rocke<sup>1,5</sup>, Xiaosong Huang<sup>1</sup>, Sandro Casavilca-Zambrano<sup>2</sup>, Jeannie Navarro-Vásquez<sup>2</sup>, Ruddy Liendo-Picoaga<sup>2</sup>, Monica Calderón<sup>2</sup>, Guillermo Valencia<sup>2</sup>, Henry Gómez<sup>2</sup>, Patricia Rioja<sup>2</sup>, Carlos A. Castañeda<sup>2</sup>, Zaida Morante<sup>2</sup>, Silvia P. Neciosup<sup>2</sup>, Hugo A. Fuentes<sup>2</sup>, Julio E. Abugattas<sup>2</sup>, Jose M. Cotrina<sup>2</sup>, Katia Roque<sup>2</sup>, Jule Vásquez<sup>2</sup>, Luis Mas<sup>2</sup>, Marco Gálvez-Nino<sup>2</sup>, Jovanny Zabaleta<sup>3</sup>, Tatiana Vidaurre<sup>2</sup>, Laura Fejerman<sup>1,4</sup>*

<sup>1</sup>Department of Public Health Sciences, University of California Davis, Davis, CA, USA

<sup>2</sup>Instituto Nacional de Enfermedades Neoplásicas, Lima, Peru

<sup>3</sup>Department of Pediatrics and Stanley S. Scott Cancer Center LSUHSC, New Orleans, LA, USA

<sup>4</sup>UC Davis Comprehensive Cancer Center, University of California Davis, Davis, CA, USA

<sup>5</sup>Department of Biomedical Engineering, University of California Davis, Davis, CA, USA

Purpose: Breast cancer incidence and outcomes differ by US census racial/ethnic category. Since large-scale genetic studies of human disease are predominately focused on populations of European ancestry, little is known about breast cancer molecular biology in Hispanic/Latinos, especially those with high Indigenous American ancestry. This can widen cancer health disparities due to suboptimal translation of discoveries into clinical practice or public health policy. To improve cancer health outcomes for Hispanic/Latinos, we aim to describe the relevant pathways for breast cancer subtype differentiation in breast cancer patients from Peru, who have high Indigenous American ancestry.

Results: Transcriptomic pathway analysis showed that most of the significantly changed pathways were similar to those previously described such as upregulation of high proliferation pathways in LumB, HER2, and Basal tumors, and a strong dependency on the estrogen pathway for LumA. The top 20 significantly changed pathways show some unique findings: the eukaryotic translation initiation, eukaryotic translation elongation, and ribosome pathways are upregulated in Basal and LumB, compared to HER2 tumors, which is unexpected for LumB subtype given that these pathways are associated with uncontrolled proliferation of cancer cells and poor outcomes. After adjusting for ancestral proportions, even more pathways that are associated with poor prognosis are significantly upregulated when comparing LumB to HER2 subtype.

Conclusions: We identified novel pathways associated with breast cancer subtypes in individuals with high Indigenous American ancestry from Peru which suggests a more aggressive profile of Luminal subtypes in the studied samples from Peru. This has implications for treatment and survival.

## <<22>> SYNTHESIS, RADIOLABELING, AND PRECLINICAL EVALUATION OF HYALURONAN CONJUGATES FOR PET IMAGING AND DUAL TARGETING TO CD44 AND INTEGRIN $\alpha\beta 6$

*Hua Zhang<sup>1</sup>, Tanushree Ganguly<sup>1</sup>, Rebecca Harris<sup>2</sup>, Ryan A. Davis<sup>1</sup>, Sven H. Hausner<sup>2</sup>, Aaron M. Mohs<sup>3,4</sup>, Julie L. Sutcliffe<sup>1,2,5\*</sup>*

<sup>1</sup>Department of Biomedical Engineering, University of California, Davis, CA

<sup>2</sup>Department of Internal Medicine, Division of Hematology & Oncology, University of California, Davis, CA

<sup>3</sup>Department of Pharmaceutical Sciences, College of Pharmacy, University of Nebraska Medical Center, Omaha, NE

<sup>4</sup>Fred and Pamela Buffett Cancer Center, University of Nebraska Medical Center, Omaha, NE

<sup>5</sup>Center for Molecular and Genomic Imaging, University of California, Davis, CA

Hyaluronan (HA) is an attractive construct for the development of agents for cancer imaging and drug delivery due to its targeting capability to CD44, a cancer cell marker, and its excellent biocompatibility [1]. Our goal was to develop HA-constructs for PET imaging and for dual targeting of CD44 and the integrin  $\alpha\beta 6$ , an epithelial cancer specific receptor [2]. HA, with a molecular weight (MW) range of 10 - 200 kDa, was modified by first sulfo-dibenzocyclooctyne (DBCO)-PEG-NH<sub>2</sub>, then N<sub>3</sub>-DOTA or DOTA-Orn(N<sub>3</sub>)- $\alpha\beta 6$ -BP to yield HAMW-DOTA or HAMW-[ $\alpha\beta 6$ -BP-DOTA], respectively. The HA constructs were radiolabeled with copper-64 (radiochemical purity >85%) and evaluated in vitro for binding and internalization using DX3puro $\beta 6$  (CD44+ $\alpha\beta 6$ +) and DX3puro (CD44+ $\alpha\beta 6$ -) cells. [<sup>64</sup>Cu]Cu-[HAMW-DOTA] showed low binding (<12%) and internalization (<3%) to DX3puro $\beta 6$  and DX3puro cells, while [<sup>64</sup>Cu]Cu-[HAMW-[ $\alpha\beta 6$ -BP-DOTA]] showed a high binding (58 - 66%) and internalization (48 -51% of total radioactivity) to the DX3puro $\beta 6$  cells. [<sup>64</sup>Cu]Cu-HA200k-[ $\alpha\beta 6$ -BP-DOTA] showed the best  $\alpha\beta 6$ -selectivity, and therefore was evaluated in vivo in mice bearing paired DX3puro $\beta 6$  and DX3puro cell xenograft tumors. [<sup>64</sup>Cu]Cu-HA200k-[ $\alpha\beta 6$ -BP-DOTA] showed high accumulation in liver and spleen (~30% ID/g), and some accumulation in both tumors (~0.8% ID/g) by PET and biodistribution. In conclusion, hyaluronan was successfully modified to develop HA-constructs for PET imaging and for dual targeting of CD44 and the integrin  $\alpha\beta 6$ . The synthetic strategy reported here could be further explored to study the pharmacokinetics of other HA constructs.

Acknowledgements: We thank the CMGI staff at UC Davis for help with animal studies, and the NIH U01CA217665 for financial support.

1. Choi, K.Y., et al., Advanced Materials, 2019.

2. Hausner, S.H., et al., Clinical cancer research, 2019.

## <<23>> PRECLINICAL EVALUATION OF A DIMER PEPTIDE TARGETING INTEGRIN AVB6

*Ryan A. Davis<sup>1</sup>, Tanushree Ganguly<sup>1</sup>, Rebecca Harris<sup>2</sup>, Sven H. Hausner<sup>2</sup>, and Julie L. Sutcliffe<sup>1,2,3</sup>*

<sup>1</sup>*Department of Biomedical Engineering*

<sup>2</sup>*Department of Internal Medicine, Division of Hematology/Oncology*

<sup>3</sup>*Center for Molecular and Genomic Imaging, University of California Davis, CA, USA*

The integrin  $\alpha\beta6$  is an epithelial cell surface receptor that is over-expressed on many cancers but has limited expression on normal tissues, making it an important target for imaging and therapy.<sup>1</sup> With the goal to evaluate avidity-based enhanced tumor accumulation and improved pharmacokinetics, the integrin  $\alpha\beta6$  Binding Peptide ( $\alpha\beta6$ -BP)<sup>1</sup> was dimerized and radiolabeled with copper-64 to produce the [64Cu]Cu DOTA-dimer. It was evaluated in vitro for cell binding to DX3puro $\beta6$  ( $\alpha\beta6$  +), BxPC-3 ( $\alpha\beta6$  +) and DX3puro ( $\alpha\beta6$  -) cells and in vivo by PET/CT imaging and biodistribution in mice bearing a BxPC-3 xenograft tumor. The [64Cu]Cu DOTA-dimer was produced in an overall yield of 27% and was radiolabeled in >98% radiochemical purity. It exhibited high stability in human serum (24 h >97%), but degraded rapidly in mouse serum (1 h 90%, 4 h 72%, 24 h 15%). The [64Cu]Cu DOTA-dimer showed  $\alpha\beta6$ -dependent cell binding (DX3puro $\beta6$  60.4 $\pm$ 1.7%; BxPC-3 53.2 $\pm$ 2.9%; DX3puro 4.4 $\pm$ 0.5%), similar to the [64Cu]Cu DOTA-monomer. In PET/CT imaging and biodistribution the [64Cu]Cu DOTA-dimer showed good tumor accumulation that reached a maximum of 5.7% ID/g at 24 h, 3.5-fold higher than the [64Cu]Cu DOTA-monomer (1.6% ID/g).<sup>2</sup> However, the pharmacokinetic data also revealed >1.8-10-fold higher accumulation and retention in clearance organs compared to the [64Cu]Cu DOTA-monomer (% ID/g, 24 h, dimer vs monomer: the kidneys 103.4 vs 10.2, the liver 6.9 vs 1.3, and the gastrointestinal tract 4.9 vs 1.7).<sup>2</sup> Overall, in the case of the  $\alpha\beta6$ -BP, while increasing tumor uptake, dimerization did not result in an improved pharmacokinetic profile.

References: 1Clin Cancer Res, 2019, 25, 1206. 2Mol Pharmaceutics, 2021, 18, 4437.

Acknowledgements: A special thank you to the funding agencies for their support; this research was funded by National Institute of Health, grants number R01CA199725 and R50CA211556-01. We would also like to thank Sarah Tam from the CMGI for animal study support including compound injection and PET/CT imaging.

## <<24>> FIBI: NOVEL SLIDE-FREE MICROSCOPY THAT CAN BE BETTER THAN THE H&E GOLD STANDARD

*Richard Levenson, Farzad Fereidouni, Nithya Ganti, Nathan Anderson*

Light microscopy of tissue biopsies remains the central technique in diagnosis and management of cancers as well as other diseases. The brightfield (transmission) optical design of today's clinical microscopes requires optically thin slices of tissue mounted onto glass slides.

Our laboratory is developing a slide-imaging technique termed fluorescence imitating brightfield imaging, or FIBI. FIBI is a non-destructive technique that captures high-resolution microscopy images directly from the face of unsectioned, briefly stained tissue specimens. With FIBI, whole-slide-like images can be captured within a few minutes that directly resemble conventional brightfield histology. Color normalization can be used to enhance the resemblance. At the same time, images also contain additional features that includes surface topology, greater continuity of linear structures such as blood vessels, and contrast that can highlight macromolecular species that are not well visualized with H&E alone. This presentation will highlight some of these features that are visible with FIBI that may be hard or impossible to discern on standard slides. These include elastin, clearly highlighted in FIBI. Others are elements that are eliminated during the sample preparation process, such as edema and fat, remain intact on FIBI images. Finally, surface topology, displayed by intestinal villi, for example, is obliterated in thin sections, but can be clearly appreciated with FIBI.

Conclusion: While FIBI is capable of recapitulating standard histology for routine diagnostics, it can also reveal novel or inapparent tissue components and structures that may help inform cancer research and other basic biology questions.

**<<25>> ENHANCING OVARIAN CANCER DIAGNOSTICS: INTEGRATING RAMAN TAG LABELING WITH ML-ENABLED SERS OF EXTRACELLULAR VESICLES FOR IMPROVED TRANSPARENCY AND PRECISION**

*Qing He<sup>1</sup>, Hanna J. Koster<sup>1</sup>, Justin O'Sullivan<sup>2</sup>, Samantha G. Ono<sup>2</sup>, Tatu Rojalin<sup>1</sup>, Rachel R. Mizenko<sup>1</sup>, Hannah J. O'Toole<sup>1</sup>, Marie C. Heffern<sup>2</sup>, Randy P. Carney<sup>1</sup>*

<sup>1</sup>University of California, Davis, Department of Biomedical Engineering

<sup>2</sup>University of California, Davis, Department of Chemistry

Liquid biopsy utilizing machine learning (ML)-enabled surface-enhanced Raman scattering (SERS) of extracellular vesicles (EVs) presents significant potential in the realm of cancer screening due to its inherent advantages, including minimal invasion, early detection, high throughput, and cost-effectiveness. However, its widespread clinical adoption is hampered by the opaque 'black box' nature of ML algorithms. In this study, we aimed to enhance transparency and trust by amalgamating ML-enabled SERS profiling of EVs by using a novel Raman tag labeling assay specific to ovarian cancer EV biomarkers (CA-125, CA-19-9, HE4). Results underscored that Raman tags, linked to cancer biomarkers, significantly enhanced the interpretability of the SERS data. Notably, SERS outperformed ELISA of the same markers, and SERS spectra from cancer-afflicted patients showed a pronounced Raman tag signal of corresponding cancer biomarkers, in contrast to the subtler signals in the control groups. Further, integrating the Raman tag signature data enhanced the classification accuracy, sensitivity, and specificity across all nine ML models evaluated. Among them, the support vector machine (SVM) model stood out, achieving an exemplary performance with accuracy, sensitivity, and specificity rates all reaching up to 95%. This research underscores the potential of combining Raman tags with ML-enabled SERS to offer a more transparent, effective, and precise approach to ovarian cancer diagnosis.

**<<26>> A DOSIMETRIC COMPARISON OF Y-90 RADIOEMBOLIZATION, STEREOTACTIC BODY RADIATION THERAPY AND HDR BRACHYTHERAPY FOR TREATMENT OF LIVER CANCER**

*Kajetan Wysoczynski, Brahim Mehadji, Peter Park, Jon Hunt, Stanley Benedict, Emilie Roncali*  
UC Davis Biomedical Engineering, Radiology, Radiation Oncology

Liver cancer treatment is a high-impact clinical area. More insight is required to choose between modalities. This study compares dose distribution and conformity of several treatment planning methods, including Y-90 microsphere radioembolization, stereotactic body radiation therapy (SBRT), and HDR brachytherapy. Five patients with hepatocellular carcinoma underwent Y-90 treatment, then a PET / CT scan. Radioembolization dosimetry was based on the PET scan and contours delineated on CT images. Four-fraction plans using a conventional SBRT linac with 5 mm leaf width. Single-fraction HDR brachytherapy plans were simulated with a maximum of 5 catheters. Dose distributions were compared for several organs based on dose-volume histograms. Y-90 radioembolization allows for delivery of the highest local dose - 82% of tumor volume received 100 Gy, where SBRT had a 75 Gy maximum. Brachytherapy allows for high conformity in smaller tumors; in one patient, at least 99% of the tumor volume received 34 Gy, but there was a hotspot of 199 Gy at 3% volume. Dose should be maximized for the target and minimized for healthy tissue. Brachytherapy allows for high dose delivery, but is only appropriate for small tumors. SBRT delivers the most homogeneous dose distribution to the tumor, with a maximum rarely exceeding 125% of prescription. Y-90 data showed localized doses of up to 900 Gy to the tumor, but careful planning and well-vascularized tumors are needed for successful treatment. All three studied modalities are viable for liver cancer treatment. In future studies, biologically effective dose will be considered and proton therapy will be included.

THANK YOU TO OUR PLATINUM EVENT SPONSORS

**sanofi**

***REGENERON***®

**UCDAVIS**  
**HEALTH**

**COMPREHENSIVE**  
**CANCER CENTER**