UCDAVIS HEALTH | COMPREHENSIVE CANCER CENTER

30th Annual Cancer Research Symposium

October 10-11, 2024

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 30th Annual Symposium. As it enters its third decade, the Annual Symposium continues to highlight the best cancer research efforts conducted by our Cancer Center members and brings together the many talents and passions of investigators devoted to solving the problem of cancer across the entire spectrum from prevention to survivorship.

This year's two-day in-person event is organized into seven thematic sessions featuring keynote and panel speakers. The program will open on Thursday with Session I, chaired by Dr. David Cooke. This inaugural session will address Inclusion, Diversity, Equality, and Accessibility, and will include an address from Dr. Colmar Figueroa-Moseley, Ph.D., M.P.H. co-chair of the GI Health Equity and Research Development subcommittee of the Southwest Oncology Group.

Session II on Population Sciences and Health Disparities, chaired by Dr. Shehnaz Hussain, features a keynote presentation on "Challenges of Lung Cancer Screening. Are we Up to the Task?" from renowned scientist Dr. Robert Smith with the American Heart Association.

Session III on Career Development and Education, chaired by Dr. Frederick Meyers, will feature a series of short presentations on "Mentoring for Impact" with speakers: Dr. Maxine Umeh Garcia from Stanford University, Dr. Alan Lombard, and Dr. Julie Schweitzer. This outstanding trio will share their experiences and provide insights into the power of mentorship.

Session IV on Basic and Translational Science, chaired by Dr. Xiao-Jing Wang and Dr. Nicholas Mitsiades will feature a keynote address by Dr. Christopher Amos from the Dan L. Duncan Comprehensive Cancer Center at Baylor College of Medicine.

Unique to this year's event is Session V chaired by Dr. Xiao-Jing Wang and focused on the vision for the new basic research program.

Friday will include Session VI with a focus on Community Outreach and Engagement, chaired by Drs. Moon Chen and Elisa Tong. This session will include a panel discussion on "Co-designing Intervention Research Among Native Americans: A Collaborative Academic-Community Grant Application in Progress."

Our final keynote, and the David R. Gandara Lectureship Awardee for Fridays Session VII, will be given by Dr. Edgardo Santos, M.D., F.A.C.P., F.A.S.C.O., the Medical Director for Broward County Florida, Clinical Associate Professor with the Charles E. Schmidt College of Medicine at Florida Atlantic University and leader of the Florida Society of Clinical Oncology (FLASCO) and FLASCO Foundation.

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

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

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

David Tom Cooke, M.D., F.A.C.S.
Associate Director for Inclusivity, Diversity, Equity and Accessibility and Interim Physician-in-Chief,
UC Davis Comprehensive Cancer Center
Professor, Department of Surgery

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

Frederick J. Meyers, M.D., M.A.C.P.
Associate Director for Education, Training, and Career Development,
UC Davis Comprehensive Cancer Center
Distinguished Emeritus Professor of Internal Medicine, Division of Hematology and Oncology, Department of Internal Medicine
Director, Academic Research Careers for Medical Doctors, UC Davis School of 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 Endowed Chair of Genetics Ill, Division of Hematology and Oncology, Department of Internal Medicine

Moon S. Chen, Ph.D., M.P.H.
Professor, Division of Hematology and Oncology, Department of Internal Medicine
Senior Advisor to the Director
UC Davis Comprehensive Cancer Center for Community Outreach and Engagement COE and Population Science

Elisa Tong, M.D., M.A.
Assistant Director for Population Science and Medical Director, Stop Tobacco Program,
UC Davis Comprehensive Cancer Center
Director, Tobacco Cessation Policy Research Center
Professor, Division of General Medicine, Department of Internal Medicine

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

SYMPOSIUM STAFF

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

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

Kirsten Asher
Administrative Manager

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

Hanouvi Agbassekou
Program Coordinator

Christian Joyce
Marketing Specialist

Chelsey Reeves
Executive Analyst

Peggy Martin
Executive Assistant

Rui Wu
Data System Analyst

Samiksha Seshadri
Student Assistant

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30TH ANNUAL CANCER RESEARCH SYMPOSIUM

OCTOBER 10-11, 2024

THURSDAY

7:30 - 8 a.m.	**BREAKFAST**
	SESSION I: INCLUSION, DIVERSITY, EQUITY AND ACCESSIBILITY CHAIR: DAVID TOM COOKE, M.D.
8 - 8:15 a.m.	Introduction and Welcome **Primo Lara, M.D.** Director, UC Davis Comprehensive Cancer Center
8:15 - 9 a.m.	Keynote Presentation: “Improving Diversity and Representativeness in Clinical Trials – The SWOG Experience” **Colmar Figueroa-Moseley, Ph.D., M.P.H.** Co-chair, SWOG GI Health Equity and Research Development Subcommittee, Member, SWOG GI Committee, SWOG Veterans Committee, and SWOG Recruitment and Retention Committee
	SESSION II: POPULATION SCIENCES AND HEALTH DISPARITIES CHAIR: SHEHNAZ HUSSAIN, Ph.D., Sc.M.
9 - 9:30 a.m.	Keynote Presentation: “Challenges of Lung Cancer Screening. Are We Up to the Task?” **Robert Smith, Ph.D.** Senior Vice President, Early Cancer Detection Science, American Cancer Society
9:30 - 9:45 a.m.	Q&A
9:45 - 10 a.m.	“The External Exposome and Cancer: Using Spatial Data to Study Environmental Drivers of Cancer Risk” **Peter James, Sc.D., M.H.S.** Associate Professor, Department of Public Health Sciences and Director, Center for Occupational and Environmental Health
10 - 10:05 a.m.	Q&A

THURSDAY

10:05 - 10:20 a.m. "Flavored Tobacco Sales Restrictions and Youth E-Cigarette Behavior"

Melanie Dove, M.P.H., Sc.D.
Assistant Adjunct Professor, Department of Public Health Sciences

10:20 - 10:25 a.m. Q&A

10:25 - 10:40 a.m. "Geriatric Oncology and Ongoing Supportive Care Clinical Trial"

Alex Fauer Ph.D., R.N., O.C.N.
Assistant Professor, Family Caregiving Institute, Betty Irene Moore School of Nursing

10:40 - 10:45 a.m. Q&A

10:45 - 11 a.m. **BREAK**

SESSION III: CAREER DEVELOPMENT AND EDUCATION
CHAIR: FREDERICK J. MEYERS, M.D., M.A.C.P.

11 - 11:45 a.m. "Mentoring for Impact"

Maxine Umeh Garcia, Ph.D., M.S.
Instructor, Department of Biomedical Data Science, Stanford University

Julie Schweitzer, Ph.D.
Professor, Department of Psychiatry and Behavioral Sciences, Assistant Director for Mentoring, UC Davis Comprehensive Cancer Center

Alan Lombard, Ph.D.
Assistant Professor, Department of Biochemistry and Molecular Medicine and Department of Urologic Surgery, Assistant Research Program Leader, Molecular Oncology Program, UC Davis Comprehensive Cancer Center

11:45 a.m. - 1:15 p.m. **POSTER SESSION and LUNCH**
Education Building, 1st/2nd Floor Foyers

SESSION IV: BASIC AND TRANSLATIONAL SCIENCE
CHAIRS: XIAO-JING WANG, M.D., Ph.D. AND NICHOLAS MITSIADES, M.D., Ph.D.

1:15 - 1:45 p.m. "Integrating Genetics Information for Precision Prevention of Cancer in Diverse Populations"

Christopher Amos, Ph.D.
Professor and Chief, Epidemiology and Population Science Director for the Institute of Clinical and Translational Medicine Associate Director of Quantitative Science, Dan L Duncan Comprehensive Cancer Center Baylor College of Medicine

1:45 - 2 p.m. Q&A

2 - 2:15 p.m. "The Development of a Canine Tumor Genome Atlas: Leveraging Spontaneous Canine Disease to Accelerate Discoveries for Human Cancer"

Christine Toedebusch, D.V.M., Ph.D., Dipl. A.C.V.I.M.
Assistant Professor, Department of Surgical and Radiological Sciences

2:15 - 2:20 p.m. Q&A

2:20 - 2:35 p.m. "Characterization of PARP Inhibitor Response in Prostate Tumor Cells Reveals Drug Tolerant Persistent Phenotype"

Alan Lombard, Ph.D.
Assistant Professor, Department of Biochemistry and Molecular Medicine and Department of Urologic Surgery, Assistant Research Program Leader, Molecular Oncology Program, UC Davis Comprehensive Cancer Center

2:35 - 2:40 p.m. Q&A

THURSDAY

2:40 - 2:55 p.m. "Modeling Tumor Heterogeneity"

Janai Carr-Ascher, M.D., Ph.D.
Assistant Professor in Residence, Department of Hematology and Oncology, Assistant Director, Education, Training, and Career Development, UC Davis Comprehensive Cancer Center

2:55 - 3 p.m. Q&A

3 - 3:15 p.m. **BREAK**

SESSION V: ORGANIZATION OF THE NEW BASIC SCIENCE RESEARCH PROGRAM
CHAIR: XIAO-JING WANG, M.D., Ph.D.

3:15 - 3:30 p.m. "Organization of the New Basic Science Research Program"

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

3:30 - 4 p.m. DISCUSSION

END OF DAY 1

FRIDAY

8 - 9:30 a.m.. **BREAKFAST and POSTER SESSION**
Education Building, 1st/2nd Floor Foyers

SESSION VI: COMMUNITY OUTREACH AND ENGAGEMENT
CHAIRS: MOON S. CHEN, Ph.D., M.P.H. AND ELISA K. TONG, M.D., M.A.

9:30 - 10:15 a.m. Panel: "Co-designing Intervention Research Among Native Americans: A Collaborative Academic-Community Grant Application in Progress"

MODERATORS:

Moon S. Chen, Ph.D., M.P.H.
Professor, Division of Hematology and Oncology, Department of Internal Medicine and Senior Advisor to the Director, UC Davis Comprehensive Cancer Center, Office of Community Outreach and Engagement, and Population Science

Elisa K. Tong, M.D., M.A.
Professor, Division of General Internal Medicine and Bioethics, Department of Internal Medicine, Assistant Director, Population Science and Medical Director, Stop Tobacco Program, UC Davis Comprehensive Cancer Center

PANELISTS:

Judith Surber
Pulitzer Center recognized Native American author, Native Cultural Consultant, Hoopa, CA

Angie Brown B.S.N., P.H.N., C.S.N.
Director of Nursing, K'ima:w Medical Center, Hoopa, CA

Teresa Martens, M.S.N., R.N.
Director, Outreach and Community Health, Northern Valley Indian Health, Chico, CA

FRIDAY

SESSION VII: CLINICAL RESEARCH
CHAIR: MEGAN DALY, M.D.

10:15 - 10:45 a.m.	David R. Gandara Lectureship on Developmental Therapeutics: "What is Next for Patients Whose Tumors Progress After 3rd Generation EGFR TKI?" **Edgardo S. Santos Castillero, M.D., F.A.C.P., F.A.S.C.O.** Medical Director - Broward, Florida The Oncology Institute of Hope and Innovation Clinical Associate Professor/Charles E. Schmidt College of Medicine Florida Atlantic University Vice-President, Florida Society of Clinical Oncology (FLASCO) President, FLASCO Foundation
10:45 - 11 a.m.	Q&A
11 - 11:10 a.m.	**BREAK**
11:10 - 11:25 a.m.	"Lung Cancer in Aging Populations: The Bench, Bedside, and Beyond" **Surbhi Singhal, M.D.** Assistant Professor, Department of Hematology and Oncology
11:25 - 11:30 a.m.	Q&A
11:30 - 11:45 a.m.	"Feasibility Pilot Study of a Standardized Extract of Cultured Lentinula edodes Mycelia (AHCC®) on Quality of Life for Ovarian Cancer Patients on Adjuvant Chemotherapy" **Hui (Amy) Chen, M.D.** Assistant Clinical Professor, Department of Obstetrics and Gynecology
11:45 - 11:50 a.m.	Q&A
11:50 a.m. - 12:05 p.m.	"Combining Immunotherapy, TGF-Beta inhibition and Stereotactic Body Radiation Therapy for the management of Oligometastatic Head and Neck Squamous Cell Carcinoma" **Shyam Rao, M.D., Ph.D.** Associate Professor, Department of Radiation Oncology
12:05 - 12:10 p.m.	Q&A
12:10 - 12:20 p.m.	Closing Remarks and Poster Awards Announcement **Primo Lara, M.D.** Director, UC Davis Comprehensive Cancer Center

ORAL PRESENTATIONS

KEYNOTE SPEAKERS

Dr. Colmar Figueroa-Moseley, Ph.D., M.P.H.

Colmar Figueroa-Moseley, Ph.D., M.P.H., earned his bachelor's in psychology with a minor in music from Carnegie Mellon University. He received his doctorate in psychology at the University of Alabama at Birmingham and his Master of Public Health in Epidemiology from the University of Rochester School of Medicine. Dr. Figueroa-Moseley has held academic and leadership positions at the Centers for Disease Control and Prevention in Atlanta, San Diego State University, the Mayo Clinic (where he was Director of the Office of Community-Engaged Research), the University of Rochester Medical Center, and UC Davis. His research has focused on symptom management of cancer patients, cancer disparities, and the impact physical and social environments have on children and adults.

Dr. Figueroa-Moseley currently sits on the Southwest Oncology Group (SWOG) GI, Veterans, Recruitment and Retention board committees, UC Davis Scientific Review Committee and co-chairs the GI Health Equity and Research Development (HEARD) subcommittee and the DEI Council of the UC Davis Comprehensive Cancer Center. He is also a member of Alpha Phi Alpha's National Surgeon General's Health Disparities committee. Dr. Figueroa-Moseley is a married father of two, whose interests include spending time with family and friends, organic gardening, cooking diverse cross-cultural dishes, and enjoying Latin jazz, R&B, blues, salsa, country, and classical music.

Robert Smith, Ph.D.

Robert Smith, Ph.D., is a cancer epidemiologist and Senior-Vice President, Cancer Screening, and Director, American Cancer Society Center for Early Cancer Detection Science (CECDS). He also is Adjunct Professor of Epidemiology at the Rollins School of Public Health, Emory University School of Medicine, and Honorary Professor, the Wolfson Institute of Preventive Medicine, Barts and The London School of Medicine and Dentistry, Queen Mary University of London.

Dr. Smith received his Ph.D. at the State University of New York at Stony Brook in 1984 and has held positions at the Boston University School of Public Health, the Centers for Disease Control, and the American Cancer Society (ACS). At the ACS he leads the development of cancer screening guidelines, and various research and policy initiatives focused on early cancer detection.

KEYNOTE SPEAKERS

Christopher Amos, Ph.D.

Christopher Amos, Ph.D., is the Director for the Institute of Clinical and Translational Medicine and Associate Director of Population and Quantitative Science with the Dan L. Duncan Comprehensive Cancer Center at Baylor College of Medicine.

Dr. Amos received his undergraduate degree in mathematics from Reed College, and his Ph.D. in biometry from Louisiana State University Medical Center. He was on the faculty at MD Anderson for 19 years before becoming a professor of Family and Community Medicine at the Geisel School of Medicine at Dartmouth in 2012, and then inaugural chair of the new Department of Biomedical Data Science in 2014. He became Director of the Institute for Clinical and Translational Research at Baylor College of Medicine in 2017 with the support of an "established investigator" grant from the Cancer Prevention and Research Institute of Texas.

Dr. Amos is focused on understanding which genes or pathways are causing early-stage lung cancers to relapse, so that patients can be treated more effectively when they are first diagnosed. Utilizing tissues obtained by surgical removal of early-stage lung cancers and following patients during and after treatment, he is working to build a large database linking genetic profiles with clinical outcomes. The biggest difficulty with this type of research is patient follow-up, because patients may have surgery in one hospital but subsequent treatment somewhere else. To this end, he is establishing collaborations to facilitate linking genetic profiles with clinical data.

Dr. Amos has very recently moved to the University of New Mexico, where he serves as the Associate Director for Population Science and Cancer Prevention and the Director of Data Science Initiatives.

Edgardo S. Santos Castillero, M.D., F.A.C.P., F.A.S.C.O.

Edgardo S. Santos Castillero, M.D., F.A.C.P., F.A.S.C.O., practices at The Oncology Institute (TOI) of Hope and Innovation, is Clinical Associate Professor at Charles E. Schmidt College of Medicine/Florida Atlantic University. Edgardo S. Santos Castillero, MD, FACP, FASCO practices at The Oncology Institute (TOI) of Hope and Innovation and is Clinical Associate Professor at Charles E. Schmidt College of Medicine/Florida Atlantic University. Dr. Santos is the Medical Director at Broward County, Florida for TOI, Vice-President of Florida Society of Clinical Oncology (FLASCO), President of the FLASCO Foundation, member of the Membership Committee as well as Editorial Group member IASLC Lung Cancer News (ILCN) of the International Association for the Study of Lung Cancer (IASLC), member of the Evidence-based Medicine Committee, Head and Neck Guideline Advisory Group and member of the 2023 and 2024 ASCO-SEP Item Writing Task Force for the American Society of Clinical Oncology (ASCO). Dr. Santos earned his M.D. in 1994 at the University of Panama, School of Medicine, Republic of Panama. He completed his internship and residency training in Internal Medicine at Jackson Memorial Medical Center, University of Miami School of Medicine. Then, he went on to complete his fellowship in Hematology/Oncology at the Sylvester Comprehensive Cancer Center, Miami, Florida.

He was selected “Best Fellow” in Hematology/Oncology Division as well as the Department of Medicine in 2003 and was a recipient of “The Spirit Award” by the American Cancer Society. Dr. Santos has authored or co-authored more than 100 manuscripts in peer-reviewed journals and serves as reviewer for several scientific publications. His focus and expertise in on lung cancer diagnosis, management, and research.

Dr. Santos is a former faculty member of University of Miami Miller School of Medicine, Miami, Florida where he held an academic rank as an Associate Professor of Medicine (2008-2012) and Tulane University Health Sciences Center, New Orleans, Louisiana (2004-2008). Dr. Santos has occupied several administrative, educational, and research leadership positions including Tulane University Principal Investigator at Southwest

Oncology Group (SWOG), Associate Scientific Director of Tulane Cancer Center's Office of Clinical Research, Associate Director of the Fellowship Programs (Tulane University and University of Miami), Chief of the Hematology/Oncology Section at the Southeast Louisiana Veterans Healthcare System, Chair of the Committee Research Advisory Board, Co-Leader of Clinical Research for the Louisiana Cancer Research Consortium, Co-Leader of the Head and Neck Cancer Program at Sylvester Cancer Center, Medical Director of Cancer Research at Lynn Cancer Institute/Boca Raton Regional Hospital, Medical Director of Research Services at Florida Precision Oncology/Genesis Care US and member of the Global Lung Cancer Committee/Genesis Care, among others. He is an active member of ACP, ASCO, ASH, AACR, ESMO, IASLC, OLA, and ILBS.

ORAL PRESENTATION ABSTRACTS (THURSDAY)

SESSION I: Inclusion, Diversity, Equality, and Accessibility

Chair: David Tom Cooke, M.D.

KEYNOTE LECTURE: IMPROVING DIVERSITY AND REPRESENTATIVENESS IN CLINICAL TRIALS – THE SWOG EXPERIENCE

Colmar Figueroa-Moseley, Ph.D., M.P.H., Co-chair, Southwest Oncology Group (SWOG) GI Health Equity and Research Development Subcommittee, Member, SWOG GI Committee, SWOG Veterans Committee, and SWOG Recruitment and Retention Committee

The session features keynote speaker Dr. Colmar Figueroa-Moseley, Ph.D., M.P.H., co-chair of the Southwest Oncology Group (SWOG) GI Subcommittee. This 35-minute keynote, followed by a 10-minute audience question and answer session, will focus on the critical importance of diversity and inclusion in clinical trials to address disparities in cancer prevention, detection, treatment, and outcomes. Dr. Figueroa-Moseley will highlight the journey of SWOG's Health Equity and Research Development (HEARD) initiative, and its efforts to increase underrepresented populations' participation in clinical trials.

SESSION II: Populations Sciences and Health Disparities

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

KEYNOTE LECTURE: CHALLENGES OF LUNG CANCER SCREENING. ARE WE UP TO THE TASK?

Robert Smith, Ph.D., Senior Vice President, Cancer Screening, Director, American Cancer Society Center for Early Cancer Detection Science, Adjunct Professor of Epidemiology, Emory University Rollins School of Public Health, Atlanta, GA

Despite gains in disease control associated with tobacco control, after many decades lung cancer still is the leading cause of cancer death in the U.S. At the turn of this century, the potential for a successful strategy to detect lung cancer sufficiently early to influence outcomes was demonstrated, guidelines followed, but more than 10 years after the initiation of enabling features to promote screening (guidelines, insurance coverage, conventional health promotion, etc.), the uptake of lung cancer screening has been discouragingly slow. To measurably reduce lung cancer deaths through early detection, there is an urgent need to correct a number of missteps in the roll out of lung cancer screening, ranging from overly restrictive eligibility criteria to failure to understand the challenges in reaching a unique target group.

THE EXTERNAL EXPOSOME AND CANCER: USING SPATIAL DATA TO STUDY ENVIRONMENTAL DRIVERS OF CANCER RISK

Peter James, Sc.D., M.H.S., Associate Professor, Department of Public Health Sciences and Director, Center for Occupational and Environmental Health

Research on environmental drivers of cancer risk is dominated by studies of single exposures in isolation; however, we are exposed to multiple risk (and resilience) factors simultaneously every day. The field of environmental epidemiology has made a shift towards studying the external exposome, or the totality of all exposures across the life course, to estimate how multiple exposures contribute to chronic disease risk, including cancer. In this presentation

FLAVORED TOBACCO SALES RESTRICTIONS AND YOUTH E-CIGARETTE BEHAVIOR

Melanie Dove, M.P.H., Sc.D., Assistant Adjunct Professor, Department of Public Health Sciences

E-cigarettes are the most used tobacco product, with 85% of youth reporting a preference for flavored e-cigarettes. Youth who use e-cigarettes are three times more likely to initiate cigarette smoking, which causes 20% of all cancers. To address this challenge, Flavored Tobacco Sales Restrictions (FTSRs) are implemented, which decrease the availability and sales of tobacco products (including e-cigarettes) in retail stores. We examined the association between seven cities with local FTSRs implemented in 2018/2019 and e-cigarette use among high school students in the California Bay Area. Methods: We analyzed data from the California Healthy Kids Survey using a difference-in-differences (D-I-D) strategy. We compared pre- and post-policy changes one year after FTSR implementation in current and ever e-cigarette use among students attending school in a city with a FTSR (exposed) (n=20,832) versus without (unexposed) (n=66,126). Other outcomes included ever marijuana use in an e-cigarette and ease of access to e-cigarettes. Separate analyses were conducted for students in cities with low and high tobacco retailer density. Results: Overall, local FTSRs in the California Bay Area were not associated with a change in youth e-cigarette use one-year post-implementation. However, among students with low tobacco retailer density, FTSRs were associated with a reduction in ease of access to e-cigarettes. Among students with high retailer density, FTSRs were associated with an increase in ease of access to e-cigarettes and current use. Conclusions: Flavor restrictions had positive impacts on youth e-cigarette access in low, but not high tobacco retailer density cities. From a health equity perspective, our results underscore how flavor restrictions may have uneven effects among vulnerable groups.

GERIATRIC ONCOLOGY AND ONGOING SUPPORTIVE CARE CLINICAL TRIAL

Alex Fauer, Ph.D., R.N., O.C.N., Assistant Professor, Betty Moore School of Nursing

It is surprising how few clinical trials address the post-treatment needs of older adult cancer survivors. More cancer survivors are living long into their late decades than ever before, often with the presence of multiple chronic health conditions and burdensome physical and psychosocial symptoms. Given that comorbidity and geriatric syndromes are a risk factor for mortality, the integration of geriatric assessments in cancer survivorship care is critical for patients in the “older- old” (70-80) and “oldest old” (80+) age groups. Geriatric assessment is a necessary component of survivorship care; adults age 85 and older are the fastest group of cancer survivors, and often need to navigate shifts in goals of care. Evidence for the efficacy of geriatric assessment in evaluating patients at risk for adverse outcomes outside of cancer care has grown through randomized trials and meta-analyses, but clinical trials to develop and test models of care that reduce the risk of adverse outcomes in older cancer survivors are disproportionately funded less often. objective of this pilot supportive care trial is to evaluate the feasibility of the practical geriatric assessment and navigation intervention facilitated by a community health worker (CHW) and improve functional status and psychosocial outcomes in community-dwelling older adult cancer survivors.

Session III: Career Development and Education

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

MENTORING FOR IMPACT

Mentorship plays an outsized role in the success of scholars, at all stages of our carers. Mentorship is a complicated dyad, with responsibilities for success on both the mentor and mentee. Mentorship covers may domains: professional, personal, career guidance, coaching, and often cannot be accomplished by one mentor, rather by a mentoring family. This session explores several successful strategies that the attendee will be able to take away and test in their own environment.

PRESENTERS:

Maxine Umeh Garcia, Ph.D., M.S., Instructor, Department of Biomedical Data Science, Stanford University

After transferring to UC Merced from a community college, Dr. Maxine Umeh Garcia received her B.S. in Developmental Biology with a minor in Psychology. During the last year of her undergrad, Maxine was invited to do research in studying nervous system development. Because of this research experience, Maxine decided to stay at UC Merced to pursue her master's in quantitative and systems biology. Immediately after graduating, she started her Ph.D. at UC Davis, where her research centered on triple negative breast cancer, due to its high incidence in women of African ancestry. After completing her Ph.D. in Biochemistry, Molecular, Cell and Developmental Biology with an emphasis in Translational Research, Maxine became a postdoctoral fellow (and now Instructor) at Stanford University in the Department of Neurosurgery. Dr. Umeh Garcia's research leverages systems-level approaches to investigate the tumor microenvironment (TME) of breast cancer brain metastases, including profiling of cancer tissues and human cerebrospinal fluid. Using her background in bench research, data science, and translational research; as an independent researcher, Dr. Umeh Garcia plans to investigate how spatial organization and cell-cell interactions in brain metastases impacts disease progression and therapeutic resistance. Additionally, as a women and underrepresented minority, Dr. Umeh Garcia is keenly interested mentoring women and underrepresented students, and in developing strategic approaches to increasing diversity in biomedical sciences and academic research.

Julie Schweitzer, Ph.D., Professor, Department of Psychiatry and Behavioral Sciences and Assistant Director for Mentoring, UC Davis Comprehensive Cancer Center

Dr. Julie Schweitzer is a clinical psychologist and cognitive neuroscientist and Professor in the Department of Psychiatry and Behavioral Sciences and the MIND Institute. She has a lengthy history of funding from the NIH and other federal agencies as principal investigator for her research in ADHD, autism and substance use disorders. Dr. Schweitzer is active in supporting research workforce development and training translational scientists across UC Davis Health and serves in a directorship role for the Mentoring Academy for Research in Cancer (MARC), assistant director for Education, Training, and Career Development for the UC Davis Comprehensive Cancer Center, Director of the CTSC's Mentoring Academy for Research Excellence (MARE) and its Mentored Clinical Research Training Program.

Alan Lombard, Ph.D., Assistant Professor, Department of Biochemistry and Molecular Medicine and Department of Urologic Surgery and Assistant Research Program Leader, Molecular Oncology Program, UC Davis Comprehensive Cancer Center

Dr. Alan Lombard is an Assistant Professor focused on characterizing prostate tumor cell therapeutic response, with the goal of understanding and targeting mechanisms of tumor progression and the development of treatment resistance. Alan received his bachelor's degree from Rensselaer Polytechnic Institute and his doctorate from UC Davis studying in the lab of Dr. Maria Mudryj where he studied mechanisms of progression of both prostate and bladder tumors. Dr. Lombard remained at UC Davis after graduation and went on to specialize in prostate cancer as a postdoctoral scholar in the lab of Dr. Allen Gao and now he likes to say that he's becoming an "Aggie lifer." Through the support of the UC Davis family, Dr. Lombard has won several awards, including a Department of Defense postdoctoral training fellowship and most recently, a K01 career

development award from the NCI. He was also named as a CAMPOS scholar in 2022. Dr. Lombard is excited to pay it forward working not only to better understand cancer and its treatment, but also to train the next generation of diverse scientists. He serves the UC Davis community in several ways and is committed to creating a more diverse and inclusive environment here on campus.

SESSION IV: Basic/Translational Science

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

KEYNOTE LECTURE: INTEGRATING GENETICS INFORMATION FOR PRECISION PREVENTION OF CANCER IN DIVERSE POPULATIONS

Christopher Amos, Ph.D., Professor and Chief, Epidemiology and Population Science Director for the Institute of Clinical and Translational Medicine Associate Director of Quantitative Science, Dan L. Duncan Comprehensive Cancer Center Baylor College of Medicine

Precision medicine approaches are widely adopted for cancer therapy, but how relevant are they for cancer prevention? We have been conducting very large genomic studies to identify risk factors for lung cancer. These analyses have identified selected genetic loci that confer very high risks for developing lung cancer that occur at high prevalence in selected populations. For these populations, a targeted screening approach may be warranted, that includes these individuals in addition to standard screening based primarily on smoking behavior. Our genetic analyses have also identified the impact that genetic factors have on smoking behavior and difficulty with smoking cessation. Clinical trials considering these variants have documented that a precision approach to smoking cessation is effective. Because adherence to CT screening for high-risk individuals (based on ethnicity, smoking and family history) have not been very effective alternative strategies that use blood-based biomarkers may be effective in identifying high-risk individuals and further motivation them towards screening. I present results from our studies of protein biomarker studies. Additionally, polygenic risk scores may also identify individuals at high risk. The development of polygenic risk scores results from the increasingly precise genetic information we are obtaining from studies of large populations of individuals. While many polygenic risk scores have been developed, fewer studies have focused on understanding how to integrate data from diverse populations and present findings to diverse participants. This presentation describes methods for calibrating and scaling PRS scores when data from distinct populations have been used to construct PRS, particularly when the majority of participants have been identified as European and other minorities are underrepresented. We describe an alternative approach to PRS construction that integrates genetic information from diverse populations to create a single approach to scoring results, for application in participants at elevated risks for lung cancer. Finally, we discuss the value of aligning the goals and process of PRS development with the interests of the target audience. Our findings suggest that the target audience for PRS is receptive to receiving findings but education messaging around risk needs to be carefully developed.

THE DEVELOPMENT OF A CANINE TUMOR GENOME ATLAS: LEVERAGING SPONTANEOUS CANINE DISEASE TO ACCELERATE DISCOVERIES FOR HUMAN CANCER

Christine Toedebusch, D.V.M., Ph.D., Dipl. A.C.V.I.M., Assistant Professor, Department of Surgical and Radiological Sciences

The UC Davis Comprehensive Cancer Center has a long-standing partnership with the UC Davis School of Veterinary Medicine. Together, we have advanced the study of naturally occurring cancer in companion animals that can inform the diagnosis and treatment of human cancers. However, key gaps persist in our understanding of the molecular features of most canine cancers. Through support of the Comprehensive Cancer Center, our team of investigators from the UC Schools of Medicine and Veterinary Medicine aim to bridge these gaps through 1) the characterization of the genetic, transcriptomic, and immune landscape of common and deadly canine cancers, and 2) utilize these data to create a publicly available database, Canine Tumor Genome Atlas (CTGA), that will inform investigators across disciplines on the appropriate use of the dog as a translational model for human cancer.

CHARACTERIZATION OF PARP INHIBITOR RESPONSE IN PROSTATE TUMOR CELLS REVEALS DRUG TOLERANT PERSISTENT PHENOTYPE

Alan Lombard, Ph.D., Assistant Professor, Department of Urologic Surgery and Department of Biochemistry and Molecular Medicine and Assistant Research Program Leader, Molecular Oncology Research Program, UC Davis Comprehensive Cancer Center

PARP inhibition is significantly improving how we manage advanced prostate cancer. Despite this progress, resistance and progression remain inevitable. Our findings reveal that response to PARP inhibition may be characterized as drug tolerant persistence, which could be a path toward development of treatment insensitivity. We seek to understand and target the drug tolerant persistent phenotype to improve treatment efficacy and improve patient outcomes.

MODELING TUMOR HETEROGENEITY

Janai Carr-Ascher, M.D., Ph.D., Assistant Professor in Residence, Division of Hematology and Oncology, Department of Internal Medicine and Assistant Director, Education, Training, and Career Development, UC Davis Comprehensive Cancer Center

The Carr-Ascher lab focuses on sarcomas, a heterogeneous group of connective tissue cancers. Clinically, this array of diseases is treated similarly with varying outcomes. The presentation will focus on the new models the lab has created to study sarcoma development and metastasis. These new tools can be used to better understand this heterogeneous disease and identify new therapeutic opportunities.

Session V: Organization of the New Basic Science Research Program

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

FACILITATED DISCUSSION

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

ORAL PRESENTATION ABSTRACTS (FRIDAY)

SESSION VI: Community Outreach and Engagement

Chairs: Moon S. Chen, Ph.D., M.P.H. and Elisa Tong, M.D., M.A.

CO-DESIGNING INTERVENTION RESEARCH AMONG NATIVE AMERICANS: A COLLABORATIVE ACADEMIC-COMMUNITY GRANT APPLICATION IN PROGRESS

This year's COE Symposium features "live" interactions of the ongoing community engagement and outreach processes that UC Davis faculty are involved in their collaboration with two Tribal Federally Qualified Health Centers (TFQHCs) in a R01 to be submitted to NIH in October 2024. The Moderators: Moon Chen and Elisa Tong (MPIs) will contextualize the significance of the research being proposed; Native cultural leader Judith Surber will offer a cultural perspective of resilience; and Panelists: Angie Brown and Teresa Martens will respectively introduce their TFQHCs: K'ima:w Medical Center in Hoopa and Northern Valley Indian Health in Chico. Following that overview, panelists will invite audience interactions on topics such as the community's consideration and perspectives on collaborating with academic researchers; specific differences between the demands of working in TFQHCs and preparing a grant application to NIH; and challenges, rewards, and recommendations.

MODERATORS:

Moon S. Chen, Ph.D., M.P.H., *Professor, Division of Hematology and Oncology, Department of Internal Medicine and Senior Advisor to the Director, UC Davis Comprehensive Cancer Center for COE and Population Science*

Elisa K. Tong, M.D., M.A., *Professor, Division of General Internal Medicine and Bioethics, Department of Internal Medicine, Assistant Director, Population Science and Medical Director, Stop Tobacco Program, UC Davis Comprehensive Cancer Center*

PANELISTS:

Judith Surber, Pulitzer Center recognized Native American author, Native Cultural Consultant, Hoopa, CA

Angie Brown B.S.N., P.H.N., C.S.N., Director of Nursing, K'ima:w Medical Center, Hoopa, CA

Teresa Martens, M.S.N., R.N., Director, Outreach and Community Health, Northern Valley Indian Health, Chico, CA

UC Davis **N**ative **A**merican **C**ommercial **T**obacco and lung cancer **I**ntervention **S**tudy (**NACTIONS**)

Research Team
Moon S. Chen, Ph.D., M.P.H., Contact PI (MPI)
Elisa K. Tong, M.D., M.A., Medical PI (MPI)
David T. Cooke, M.D., Interim Physician-in-Chief
Miriam Nuño, Ph.D., Biostatistician

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Amy Sage, M.D.

SESSION VII: Clinical Research

Chair: Megan Daly, M.D.

DAVID R. GANDARA LECTURESHIP ON DEVELOPMENTAL THERAPEUTICS: WHAT IS NEXT FOR PATIENTS WHOSE TUMORS PROGRESS AFTER 3RD GENERATION EGFR TKI?

Edgardo Santos, M.D., F.A.C.P., F.A.S.C.O., Medical Director - Broward, Florida, The Oncology Institute of Hope and Innovation, Clinical Associate Professor/Charles E. Schmidt College of Medicine, Florida Atlantic University, Vice-President, Florida Society of Clinical Oncology (FLASCO), President, FLASCO Foundation

Since 2008 when IPASS study showed superiority of gefitinib, first generation EGFR TKI, over chemotherapy, we started our journey to improve the quality and potency of these agents. It was not until 2018 when osimertinib, a third generation TKI, proved to be superior to first generation EGFR TKIs (erlotinib and gefinitib). The FLAURA study reported an improved progression-free survival, and later it showed an overall survival advantage.

The FLAURA study established osimertinib as the preferred and category 1 EGFR TKI by the NCCN guidelines. This guideline recommendations still prevail nowadays, despite acquired resistance to EGFR TKI is an inevitable phenomenon. Nonetheless, advances in molecular medicine and technology to assess for genomic aberrations (e.g., next generation sequencing) in both tissue and blood specimens have allowed us to understand more and elucidate some acquired mechanisms of resistance to these agents.

Some mechanisms of resistance will be discussed in this lecture. However, recent advances in terms of first line therapy for patients whose tumors harbor EGFR sensitive mutations are making our treatment selection more complicated and decision made at first line will impact subsequent lines of therapy as well as mechanism of resistance. Two landmark studies FLAURA-2 and MARIPOSA have challenged clinicians in their treatment decision when they face a lung cancer EGFR mutation positive patient in clinic. Recently, at ESMO 2024, mechanism of resistance to the combination of amivantamab/lazertinib was reported, providing novel insights on how these tumor cells behave under the pressure of this potent and dual inhibition. Moreover, on September 19, 2024, the US FDA approved for the first time ever a regimen for Osimertinib progressors based on the results of MARIPOSA-2 study.

This lecture will briefly discuss the background and platform of initial therapy for patients with EGFR positive tumors, and then dissect the avalanche of efforts made in recent years to fight against EGFR TKI resistance from EGFR-dependent mechanisms (e.g., novel EGFR mutations), EGFR-independent mechanism (e.g., bypass track), histologic transformation, and other. Our lecture will finish with future direction and promising ongoing studies. One of them is the use of antibody-drug conjugates as well as brief discussion on the drug tolerant persister state concept and how to use it as potential therapeutic development.

LUNG CANCER IN AGING POPULATIONS: THE BENCH, BEDSIDE, AND BEYOND

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

As the U.S. and California population ages, lung cancer care for older adults presents unique challenges and opportunities. This presentation will explore advances in preclinical models, immunotherapy, and personalized treatment approaches tailored to aging populations. From bench to bedside and beyond, it will highlight how new discovering in oncology are shaping the future of lung cancer care for older adults. Drawing on research from UC Davis investigators, the talk will examine how biomarker-driver therapies, clinical trials, and patient-centered care models are improving outcomes for older adults with lung cancer.

FEASIBILITY PILOT STUDY OF A STANDARDIZED EXTRACT OF CULTURED LENTINULA EDODES MYCELIA (AHCC®) ON QUALITY OF LIFE FOR OVARIAN CANCER PATIENTS ON ADJUVANT CHEMOTHERAPY

Hui (Amy) Chen, M.D., Assistant Clinical Professor, Department of Obstetrics and Gynecology

Background: Ovarian cancer is a deadly gynecologic malignancy, with most cases diagnosed at advanced stages. Quality of life for women with ovarian cancer is not only affected by their disease but also the symptoms caused by the treatment, which includes radical debulking surgery and chemotherapy. More than 60% of gynecologic patients in the United States are using integrative medicine therapies to help with their symptoms. One intriguing approach is AHCC®, the mycelia of the Lentinula edodes or shiitake mushroom. In pre-clinical and small clinical studies, AHCC® has been shown to modulate the immune system, such as upregulating CD4 and CD8 T-lymphocytes and increasing cytokines IFN-γ and -β function, while alleviating side effects associated with chemotherapy, such as nausea and neutropenia. The objective of this study is to evaluate the effects of AHCC® on health related quality of life (HRQOL) and immune function for ovarian cancer patients undergoing chemotherapy. Methods: This is a single-institution pilot feasibility randomized clinical trial of 20 patients with newly diagnosed ovarian cancer who have undergone initial surgery and require adjuvant chemotherapy. English or Spanish-speaking adult patients with Stage I-IV ovarian cancer requiring platinum and taxane adjuvant chemotherapy are eligible. Participants are randomized 1:1 to 3 grams of AHCC® or placebo while receiving chemotherapy. To test for feasibility testing, 50 eligible patients with ovarian cancer will be screened and approached for participation. We will evaluate the time needed to recruit 20 subjects to our pilot clinical trial. We will also be evaluating adherence to treatment and subject perception of acceptability to participate in a supplement clinical trial while managing the burdens of chemotherapy. To measure HRQOL, participants complete validated patient reported outcomes assessments throughout the study. To evaluate the side effects and toxicities of chemotherapy, laboratory values and symptoms will be collected from the electronic medical record. Finally, blood samples collected at baseline and end of the trial will evaluate up and downregulation of immune cell components and function using single cell and bulk RNA sequencing and flow cytometry. This trial began enrollment in October 2023. To date, 27 ovarian cancer patients have been identified. 19 participants were eligible for the trial. Currently six participants have been consented for the study. Three participants have completed their chemotherapy and one is currently undergoing treatment. Clinicaltrials.gov registration: NCT05763199

COMBINING IMMUNOTHERAPY, TGF-BETA INHIBITION AND STEREOTACTIC BODY RADIATION THERAPY FOR THE MANAGEMENT OF OLIGOMETASTATIC HEAD AND NECK SQUAMOUS CELL CARCINOMA

Shyam Rao, M.D., Ph.D., Associate Professor, Department of Radiation Oncology

Management of recurrent and metastatic head and neck squamous cell carcinoma is challenging due to lack of effective therapies. We will present UCDCC311, a Phase IB study of Losartan, Pembrolizumab and Stereotactic Body Radiation Therapy (SBRT) in patients with locoregionally recurrent, refractory, or oligometastatic head and neck squamous cell carcinoma.

POSTER PRESENTATIONS AND EXHIBITS

Poster and Exhibit Index:

Poster and Exhibit Abstracts:

Poster and exhibit session (Thursday): 11:45 am – 1:15 pm

Poster and exhibit session (Friday): 8:00 am – 9:30 am

POSTER PRESENTATIONS AND EXHIBITS (THURSDAY)

PT-01 Metabolic Risk Factors and Survival in Patients with Glioblastoma
Presenter: John Paul Aboubechara

PT-02 Characterization of a Novel Small Molecule Ligand of Prohibitin 1, LLS133, which Promotes Chemosensitivity in Castration Resistant Prostate Cancer
Presenter: Rebecca Armenta

PT-03 Metastatic Recurrences among California AYA Patients Diagnosed with Seven Common Cancers, 2006-2018
Presenter: Ann Brunson

PT-04 Rhogefs Gone Rhogue: Investigating the Mechanisms by which PDZ-Rhogef Drives Cancer Cell Migration
Presenter: Matthew Braga

PT-05 Immunomodulatory Effects of RANKL Blockade with Denosumab on Cancer Patients
Presenter: Hewitt Chang

PT-06 Feasibility Pilot Study of a Standardized Extract of Cultured Lentinula Edodes Mycelia (AHCC®) on Quality of Life for Ovarian Cancer Patients on Adjuvant Chemotherapy
Presenter: Hui (Amy) Chen

PT-07 Design and Optimization of Chimeric Antigen Receptor Nanolipoprotein for Immunotherapy
Presenter: Joshua Claxton

PT-08 Transformable Peptide Nanoparticle with Doxorubicin Pro-Drug for Bladder Cancer Targeted Therapy
Presenter: Zhaoqing Cong

PT-09 Characterizing PARP Inhibitor and AR Pathway Inhibitor Responses in Advanced Prostate Cancer
Presenter: Bryan Correa Gonzalez

PT-10 Naphthalene Forms DNA Adducts in Mouse Lung and Liver after Oral Exposure
Presenter: Morgan Domanico

PT-11 Capacity Building for Geriatric Oncology and Cancer Survivorship Clinical Trials: Engagement with Survivors and Promotores De Salud
Presenter: Alex Fauer

PT-12 Characterizing Drug-induced Transcriptional Programs in Ovarian Cancer
Presenter: Jaskaran Halait

PT-13 Identification of MTAP-Deficiency Regulatory Genes via DNA Methylation in Lung Adenocarcinoma: Potential Biomarkers and Therapeutic Targets
Presenter: Ssu-Wei Hsu

PT-14 Short-Term Dietary Intervention Impacts Anti-PD-1 Treatment Outcome of HCC
Presenter: Ying Hu

PT-15 Treatment Differences for Premenopausal Women with a Triple Negative Secondary vs Primary Breast Cancer
Presenter: Ana Isabel Jacinto

PT-16 Olfactomedin-Like 3 Neutralization Extended Survival in a Mouse Model of Glioblastoma
Presenter: Daniela Jimenez

PT-17 Fluorescence Lifetime Signatures of Colorectal Polyps: A Feasibility Study
Presenter: Lisanne Kraft

PT-18 The Role of Shroom3 Downstream of Wnt/Planar Cell Polarity Signaling in Breast Cancer Metastasis
Presenter: Julie Learn

PT-19 Characterization of Carboplatin-Induced DTP Cells and Identification of Effective Oncology Drugs in Ovarian Cancer
Presenter: Meirong Liang

PT-20 Single Arm Study to Assess the Immune Effects of Fermented Wheat Germ (FWG) Nutritional Supplementation in Patients with Advanced Malignancies Being Treated with Standard of Care Checkpoint Inhibitor-Based Therapy - A Trial in Progress
Presenter: Reed Serena Ling

PT-21 Evaluating Molecular Biomarker Testing and Systemic Treatments among Patients with Stage IV NSCLC
Presenter: Fran Maguire

PT-22 Engineering CAR-T Cells for Improved Cancer Targeting Using Nanolipoparticle Protein Delivery
Presenter: Jillian McCool

PT-23 Non-Invasive Skin Sampling for Improved Melanoma Diagnosis Using Adhesive Patches: Optimization of RNA Isolation
Presenter: Marin Melloy

PT-24 Characterizing Delays in Rectal Cancer Care
Presenter: Miquell Miller

PT-25 Integrin Alpha 4 Expression as a Marker for Response to Immune Checkpoint Inhibitors (or to a Novel CTLA-4 Inhibitor ONC-392)
Presenter: Dennis Montoya

PT-26 Mechanistic and Phenotypic Insights into Temporal and Dosage-Dependent Responses to PARP Inhibition in Advanced Prostate Cancer
Presenter: Love Moore

PT-27 The California Firefighter Cancer Research Study (CAFF-CRS): Cohort Profile and Baseline Assessment of Metabolic, Occupational
Presenter: Tony Nguyen

PT-28 Utilization of Antibody Targeted Perfluorocarbon Nanoparticles for Multiplexed 19F MRI of Tumor-Associated Macrophages
Presenter: Lauren Ohman

PT-29 Development of Surface-Enhanced Raman Probes for the Detection of Heterogenous Cancer Biomarkers
Presenter: Samantha Ono

PT-30 Elucidating the Metal-Dependent Activities of Oxytocin in the Breast Cancer Cell Line
Presenter: Jennifer Park

PT-31 Investigating Metabolic Sensitivity and Organization of Renal Cell Carcinoma: To Enhance Effective Therapies and Patient Survival.
Presenter: Madhura Patankar

PT-32 Targeting P300/CBP to Inactivate Cancer-Associated Fibroblasts and Suppress Pancreatic Cancer Growth
Presenter: Duc Pham

PT-33 Signal Detection with Chemical Exchange Saturation Transfer (CEST) MRI
Presenter: Sakunrat Prompalit

PT-34 Missing Data Methods for Evaluating Breast Cancer Outcomes
Presenter: Lihong Qi

PT-35 Advancing Evidence of the Associations Between Specific Benign Breast Diagnoses and Future Breast Cancer Risk
Presenter: Olivia Sattayapiwat

PT-36 Identifying Force-Dependent Interactions Surrounding Actin Filaments in Live Cells
Presenter: Yibo Shi

PT-37 A Novel Autophagy Inhibitor Overcomes Cisplatin Resistance in Head and Neck Cancer
Presenter: Yaping Shiau

PT-38 Impact of Wildfire-Dominated PM2.5 on Non-Small Cell Lung Cancer Survival in California
Presenter: Surbhi Singhal

PT-39 HSP70 Leverages STUB1 to Modulate N-Myc Protein Turnover in Lethal Prostate Cancer
Presenter: Pengfei Xu

ET-01 UC Davis Comprehensive Cancer Center Shared Resources
Presenters: Aruna Chetty, Kent Lloyd, and Ben Spencer

ET 02 National User Resource for Biological Accelerator Mass Spectrometry
Presenter: Bruce Buchholz

POSTER PRESENTATIONS AND EXHIBITS (FRIDAY)

PF-01 Chemotherapy-Induced Peripheral Neuropathy in Children, Adolescents and Young Adults with Cancer and Medicaid Insurance in California
Presenter: Renata Abrahao

PF-02 A Pilot Study of Intratumoral SD-101 (Toll-Like Receptor 9 Agonist), Nivolumab, and Radiotherapy for Treatment of Chemotherapy-Refractory Metastatic Pancreatic Adenocarcinoma
Presenter: Ebaa Al-Obeidi

PF-03 Investigating the Role of BRD2 in Resistance to BET Inhibitors in Pancreatic Cancer
Presenter: Suyakarn Archasappawat

PF-04 Hexamethylene Amiloride-Mediated Induction of Lysosomal Membrane Permeabilization
Presenter: Rhea Bains

PF-05 Chemically Optimizing Amiloride to Generate Highly Effective Derivatives that Selectively Target Triple-Negative Breast Cancer Stem Cells
Presenter: Noemi Castro

PF-06 Innovative Strategies for Targeted Neuroblastoma Therapy: Integrating Mirna Therapeutics with Nanoparticle Delivery
Presenter: Samiha Chohan

PF-07 Efficacy of Individual Let-7-5p Isoforms in the Modulation of Target Gene Expression in HCC Cells
Presenter: Joseph Cronin

PF-08 Investigating the Longitudinal Efficacy and Resistance Mechanisms of Anti-PD-1 Therapy in a Murine NSCLC Model Using Single-Cell and Spatial Transcriptomics
Presenter: Oscar Davalos

PF-09 MARCKS in Macrophages Contributes to Lung Cancer Progression
Presenter: Anjolie Doan

PF-10 ANGEL2 Modulates Enfortumab Vedotin Chemosensitivity in Muscle Invasive Bladder Cancer
Presenter: Avani Durve

PF-11 Fluorescence Lifetime Imaging with Protoporphyrin IX for Differentiating between Cancer and Healthy Tissues in Spontaneously Occurring Canine Oral Squamous Cell Carcinoma
Presenter: Stephanie Goldschmidt

PF-12 Single-Cell Resolution Impact of Radiation Therapy on Murine Squamous Cell Carcinomas In-Vitro Reveals Its Complicated Role in Regulating Immunity
Presenter: Jack Goon

PF-13 Leveraging Key Informant Interviews and Focus Groups to Inform Intervention Development: The Healthy Cervix Program (HEALIX)
Presenter: Ramneek Kahlon

PF-14 Impact of Primary Care Initiated Lung Cancer Screening Program: The VANCHCS Experience
Presenter: Guneet Kaleka

PF-15 Characterization of PARP Inhibitor Response in Prostate Tumor Cells Reveals Drug Tolerant Persistent Phenotype
Presenter: Akshaya Karthikeyan

PF-16 Distinct Domains of Tensin 3 and Cen Interact Directly with Force-Bearing Keratin Filaments
Presenter: Dah Som Kim

PF-17 Leukocyte Lmmunoglobulin-Like Receptor (LILRB2)-Targeted JTX-8064 plus Tanti-PD1 Inhibitor JTX-4014 (Pimivalimab) in Immune-Checkpoint Inhibitor (ICI)-Pretreated Patients (Pts) with Advanced or Metastatic Renal Cell Cancer (Mrcc): Results from the Multi-Stage Phase 1-2 INNATE Trial
Presenter: Primo Lara

PF-18 IGFBP3 Signaling Promotes Resistance to Next-Generation Antiandrogens Therapeutics in Advanced Prostate Cancer
Presenter: Amy Leslie

PF-19 IGFBP3 Promotes Taxane-Olaparib Cross Resistance in Advanced Prostate Cancer
Presenter: Kristina Leslie

PF-20 Deep Interactive Learning-Based Segmentation of Canine Oral Squamous Cell Carcinoma and Melanoma in Histopathological Slides for Enhanced Tumor Detection
Presenter: Zihan(Tom) Li

PF-21 Investigating the Role of Wnt/PCP Signaling in the Reprogramming of Energy Metabolism in Breast Cancer
Presenter: Liliana Loza Sanchez

PF-22 Studying T Cell Memory Phenotypes in CART Cell Therapy for B Cell Lymphoma
Presenter: Jennifer Mayo

PF-23 Portable and Automated Sampler to Monitor VOC Exposures of Firefighters Actively Fighting Wildland Urban Interface Fires
Presenter: Mitchell McCartney

PF-24 Reporting of Race and Ethnicity in Pediatric Oncology Clinical Trials: A Scoping Review
Presenter: Alexa Morales Arana

PF-25 Cancer Incidence in Persistent Poverty Areas of California by Race/Ethnicity
Presenter: Ani Movsisyan Vernon

PF-26 Optimizing CAR-T Cell Therapy: Reducing Manufacturing Time and Examining T Cell Memory Phenotypes in B Cell Lymphoma
Presenter: Jordan Pavlic

PF-27 Challenges in Recruiting for a Randomized Controlled Intervention to Increase Lung Cancer Screening
Presenter: Lucy Rios

PF-28 Genetic Screen for the Identification of TP53 Mutants that Can Be Functionally Restored by APR-246
Presenter: Anais Saunders

PF-29 Significance of ANGEL2 Expression on Cisplatin Chemoresistance in Muscle Invasive Bladder Cancer
Presenter: Conner Suen

PF-30 The Heparin-Binding Domain of VEGF165 Directly Binds to Integrin Avβ3 and VEGFR2/KDR D1: A Potential Mechanism of Negative Regulation of VEGF165 Signaling by Avβ3
Presenter: Yoko Takada

PF-31 Bladder Cancer Cells Exposed to Wildfire Smoke Exhibit Signs of Epithelial-Mesenchymal Transition
Presenter: Aayush Verma

PF-32 Reduced Efficacy of Fractionated Radiotherapy in Obese Mice
Presenter: Logan Vick

PF-33 The Role of Macrophages in Conferring Antiandrogen Resistance and Immune Evasion in Castration-Resistant Prostate Cancer
Presenter: Leyi Wang

PF-34 Non-Activated and IL-7 Cultured CD19-Specific CAR T Cells Are Enriched in Stem Cell Phenotypes and Functionally Superior
Presenter: Siao-Yi Wang

PF-35 A Retrospective Case Series of Myasthenia Gravis Associated with Immune Checkpoint Inhibitors
Presenter: Ge Xiong

PF-36 LX1 Targets Androgen Receptor Variants and AKR1C3 to Overcome Therapy Resistance in Advanced Prostate Cancer
Presenter: Shu Ning

PF-37 Impact f Health Insurance on Cancer Care: A Quality Measures Analysis in California, 2014–2021
Presenter: *Nuen Tsang (Matt) Yang*

PF-38 Perception of Environmental Cancer Risk Factors among Residents of the UCDCCC Catchment Area
Presenter: Marissa Bashore

PF-39 Nanoparticle CEST MRI Visualization
Presenter: Saiful Chowdhury

EF-01 UC Davis Comprehensive Cancer Center Shared Resources
Exhibitors: Aruna Chetty, Kent Lloyd, and Ben Spencer

POSTER AND EXHIBIT ABSTRACTS (THURSDAY)

<<PT-01>> METABOLIC RISK FACTORS AND SURVIVAL IN PATIENTS WITH GLIOBLASTOMA

John Paul Aboubechara, Resident Physician[1,2], Orwa Aboud[1,2,3]

[1]Department of Neurology, UC Davis, Sacramento, CA; [2]Department of Neurologic Surgery, UC Davis, Sacramento, CA; [3]UC Davis Comprehensive Cancer Center, Sacramento, CA

Altered cellular metabolism is a hallmark of cancer. Systemic metabolic dysregulation has been associated with the pathogenesis of cancer, including glioblastoma. In particular, the metabolic syndrome has been found to increase the risk of developing various systemic cancers, but it is not known how often the metabolic syndrome occurs in patients with glioblastoma or how it affects their clinical outcomes. This study retrospectively investigates the prevalence and impact of metabolic syndrome, and its component risk factors, on survival in patients with glioblastoma IDH-wild type. Seventy three patients who received treatment for glioblastoma at UC Davis between 2018-2024 have been included. Metabolic syndrome prevalence prior to diagnosis was 41% (30/73), higher than the prevalence of 33% in the general population. Patients with metabolic syndrome showed a trend towards reduced overall survival. A significant dose-response association was found between the number of metabolic risk factors and overall survival (p=0.03). Hyperglycemia demonstrated worsened survival (p=0.04), aligning with prior studies. Obesity, hypertension, and dyslipidemia were not significantly associated with survival. These findings highlight the therapeutic potential for targeting systemic metabolic dysregulation, and hyperglycemia in particular, in patients with glioblastoma.

<<PT-02>> CHARACTERIZATION OF A NOVEL SMALL MOLECULE LIGAND OF PROHIBITIN 1, LLS133, WHICH PROMOTES CHEMOSENSITIVITY IN CASTRATION RESISTANT PROSTATE CANCER

Rebecca B. Armenta, Graduate Student, Pharmacology and Toxicology Graduate Group[1], Neelu Batra[2], Aayush Verma[1], Avani Durve[1], Shreya Indulkar[3], Huanyao Gao[3], Leiwei Wang[3], Christopher A. Lucchesi[4,6], Ruiwu Liu[2,6], Maria Mudryj[5,6], Paramita M Ghosh[1,2,4,6]

[1]VA Northern California Health Science Center, Mather, CA; [2] Department of Biochemistry and Molecular Medicine, UC Davis, Davis, CA; [3]Department of Molecular Pharmacology and Experimental Therapeutics, Mayo Clinic, Rochester, MN; [4]Department of Urological Surgery, UC Davis, Sacramento, CA; [5]Department of Microbiology and Medical Immunology, UC Davis, Sacramento, CA; [6]UC Davis Comprehensive Cancer Center, Sacramento, CA

Prostate cancer (PCa) remains a significant challenge, with 15-20% of patients experiencing recurrence within five years post-treatment. The recurrent disease is predominantly driven by androgen signaling, and while androgen deprivation therapy (ADT) is initially effective, resistance often develops, leading to castration-resistant prostate cancer (CRPC). Prohibitin proteins (PHB1 and PHB2), initially thought to be tumor suppressors, have been implicated in the progression of PCa, with their roles differing between hormone-sensitive and castration-resistant stages. We have developed LLS133, a novel benzimidazole-based small molecule, which induces cytotoxicity in CRPC cells, including C4-2B and 22Rv1 at low doses (IC50~0.5 µM). Investigation of the targets of LLS133 showed that it directly binds PHB1, which heterodimerizes with PHB2 to form an active complex. In vivo studies confirmed LLS133's low toxicity and a high half-life of 16.2 hours. Further, we show that LLS133 induced the nuclear translocation and increased transcription of PHB1 and PHB2, which associated with improved survival in PCa patients. Additionally, LLS133 was found to enhance the effectiveness of cabazitaxel, a chemotherapeutic agent, in resistant PCa cells. RNA-seq analysis further showed that LLS133 inhibited cell cycle progression while promoting steroid biosynthesis. These results suggest that LLS133 could be a valuable therapeutic option for CRPC, particularly in cases where resistance to conventional treatments has developed, offering a new avenue for improving patient outcomes.

<<PT-03>> RHOGEFS GONE RHOGUE: INVESTIGATING THE MECHANISMS BY WHICH PDZ-RHOGEF DRIVES CANCER CELL MIGRATION

Matthew Braga, Graduate Student, Biochemistry, Molecular, Cellular, and Developmental Biology Graduate Group[1], Alexandra Calderon[1], Jennifer Cash[1,2], Sean Collins[1,2]

[1]Department of Molecular and Cellular Biology, UC Davis, Davis, CA; [2]UC Davis Comprehensive Cancer Center, Sacramento, CA

The Rho guanine-nucleotide exchange factor (RhoGEF) PDZ-RhoGEF (PRG) mediates cell migration downstream of G-protein coupled receptors (GPCRs) through activation of the RhoA GTPase and is implicated in invasiveness and metastasis in various cancers. PRG is altered in over 30% of breast cancers and over 25% of lung cancers, making it an appealing molecular target for therapeutics. While it activates RhoA through its catalytic core, the activity of PRG is regulated by multiple accessory domains that sensitize it to inputs such as G-protein signaling. The subcellular localization of PRG is also tightly regulated by interactions with binding partners, including GPCRs. However, the molecular mechanisms that control localized PRG activity downstream of specific GPCRs to drive cancer cell migration are unclear. The objective of this project is to investigate these regulatory mechanisms. We hypothesize that PRG exists in an autoinhibited state until multiple inputs cooperate to localize and activate it, forming signaling scaffolds that control a cell migratory response downstream of GPCRs. We are using integrative structural biology methods, including SAXS, XL-MS, and cryo-EM to examine the structural basis of PRG regulation by its accessory domains. To investigate recruitment and activation dynamics of PRG, we are using live-cell imaging and synthetic GPCRs that directly engage the PRG pathway to observe changes in the subcellular localization of PRG and in overall cell morphology. The results of this project will provide insights into the mechanisms of PRG regulation, and this will inform the rational design of therapeutics against PRG to combat metastatic cancer.

<<PT-04>> METASTATIC RECURRENCES AMONG CALIFORNIA AYA PATIENTS DIAGNOSED WITH SEVEN COMMON CANCERS, 2006-2018

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Background: While cancer treatment continues to improve for adolescents and young adults (AYAs), metastatic recurrence remains one of the leading causes of death. Historically, cancer registries have not collected recurrence data after initial cancer diagnosis, making it difficult to estimate incidence and outcomes of metastatic recurrences.

Methods: Seven first primary cancers diagnosed in AYAs (15-39 years) from 2006-2018 were identified from the California Cancer Registry. Metastatic recurrence was identified from statewide hospitalization, emergency department and ambulatory surgery encounters. Among patients with stage I-III, metastatic recurrence was identified from International Classification of Diseases (ICD) -9/ICD-10 disease codes ≥6 months after cancer diagnosis or a cancer-related cause of death. We calculated the cumulative incidence (CMI) of metastatic recurrence, overall and by stage at diagnosis. We estimated overall survival using the Kaplan-Meier method.

Results: Among 49,020 patients, 9.5% had metastatic recurrence. The 5-year CMI was higher for sarcoma (25.1%) and colorectal (22.1%), intermediate for cervical (16.7%) and breast (14.8%), and lowest for melanoma (5.6%), testicular (5.5%) and thyroid (1.3%) cancers. The CMI increased with later stage at diagnosis, with the highest CMI for stage III sarcoma (47.9%) and cervical (42.2%) cancer. Overall survival was better among patients with metastatic disease at diagnosis (vs metastatic recurrence) for all sites except testicular, melanoma, and thyroid cancers (for which there was no survival difference).

Conclusions: Our findings suggest metastatic recurrences occur among a substantial proportion of AYAs. Future work is needed to understand differences and mitigate risk factors for poor outcomes following metastatic recurrence in AYA cancer survivors.

<<PT-05>> IMMUNOMODULATORY EFFECTS OF RANKL BLOCKADE WITH DENOSUMAB ON CANCER PATIENTS

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Denosumab is a fully human monoclonal antibody that binds receptor activator of nuclear factor-κB ligand (RANKL), blocking RANK binding. Cancer patients routinely receive denosumab to reduce the incidence of skeletal-related events by regulating bone turnover through controlling osteoclast recruitment, development, and activity. These interactions also regulate medullary thymic epithelial cells, which when inhibited results in reduced thymic negative selection of T cells and could enhance the generation of tumor-specific T cells. We examined whether administering denosumab modulates circulating immune cells in cancer patients. Blood was collected from 23 prostate cancer patients and 3 renal cell carcinoma patients, all with advanced disease, prior to and during denosumab standard-of-care treatment. Using high-dimensional mass cytometry, we found that denosumab treatment alone induced modest effects on circulating immune cell frequency and activation. Additionally, there were minimal changes in the circulating T-cell repertoire and the frequency of new thymic emigrants with denosumab treatment. However, when we stratified patients by treatment with chemotherapy and/or steroids, patients receiving these concomitant treatments showed significantly greater immune modulation, such as a broad induction of CTLA-4 and TIM3 expression in circulating lymphocytes and some monocyte populations. These findings suggest that denosumab treatment alone has modest immunomodulatory effects, but when combined with conventional cancer treatments, can lead to the induction of immunologic checkpoints. Further studies of the immunomodulatory effects of chemotherapy and steroids without denosumab would be critical in understanding the contribution of different treatments.

<<PT-06>> FEASIBILITY PILOT STUDY OF A STANDARDIZED EXTRACT OF CULTURED LENTINULA EDODES MYCELIA (AHCC®) ON QUALITY OF LIFE FOR OVARIAN CANCER PATIENTS ON ADJUVANT CHEMOTHERAPY

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Background: Quality of life for women with ovarian cancer is affected by both their disease and the treatment. Two-thirds of gynecologic patients in the United States are using integrative medicine to improve their symptoms. AHCC®, the mycelia of shiitake mushrooms, has been shown to upregulate CD4 and CD8 T-lymphocytes and increase IFN-γ and -β while alleviating chemotherapy side effects in pre-clinical and small clinical studies.

Objective: To evaluate the effects of AHCC® on health related quality of life (HRQOL) and immune function for ovarian cancer patients undergoing chemotherapy.

Methods: This is a pilot feasibility randomized trial of newly diagnosed ovarian cancer patients undergoing chemotherapy after surgery. Participants are randomized 1:1 to AHCC® or placebo. HRQOL will be measured by validated assessments. Side effects from chemotherapy will be collected from the electronic medical record. Immune cell components and function will be evaluated using RNA sequencing and flow cytometry. For feasibility testing, all women with ovarian cancer will be approached for participation over 12 months. We will evaluate the time needed to recruit 20 participants. We will also evaluate adherence to treatment and acceptability of participating in a supplement clinical trial.

Results: To date, 14 of the 18 ovarian cancer patients identified have been eligible. Four participants have been consented and one is undergoing recruitment. Three have completed their chemotherapy.

Conclusion: Based on this pilot study, a larger randomized trial of AHCC® may be feasibly performed to evaluate its impact on quality of life and cancer outcomes for women with ovarian cancer.

<<PT-07>> DESIGN AND OPTIMIZATION OF CHIMERIC ANTIGEN RECEPTOR NANOLIPOPROTEIN FOR IMMUNOTHERAPY

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Generating chimeric antigen receptor (CAR) proteins would be highly desirable for both structural biology and for designing and optimizing CAR constructs for cancer therapy. However, CAR proteins contain highly insoluble transmembrane domains, and as they contain a single chain antibody and may be difficult to synthesize. NanoLipoprotein particles (NLPs), discoidal nanoparticles comprised of a lipid bilayer and an apolipoprotein, can solubilize transmembrane proteins and promote proper folding while preserving function. We used cell-free expression to synthesize CAR-CD19-28z receptor and ∆49Apolipoprotein A1 scaffold in the presence of lipids and optimized the production of the CAR-NLP complex using a series of temperature and lipid screens to determine the ideal environment that optimized expression, purity and solubility. We found that a cell free reaction at 20˚C for 24 hours improved protein solubility from <10% to 82% solubilized CAR protein. The association between the CAR-CD1928z receptor and the NLP was confirmed by nickel affinity purification using a His tag on the ∆49Apolipoprotein A1, which formed the supporting membrane protein scaffold. Once we established the complex, we tested solubility and functionality using CART-specific antibody binding assays. CAR T-specific antibody binding assays included Western and Dot Blots. We further demonstrate schematically how we can go from generation through function characterization and application in under three days. Overall, this represents the first demonstration of soluble, functional CAR formulations within NLPs, which may provide a versatile tool for studying target engagement and a provide a platform for the design of next generation of CAR constructs in the future.

<<PT-08>> TRANSFORMABLE PEPTIDE NANOPARTICLE WITH DOXORUBICIN PRO-DRUG FOR BLADDER CANCER TARGETED THERAPY

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Bladder cancer (BC) remains a significant health concern, necessitating the development of innovative therapeutic approaches. In this study, we present a novel strategy utilizing BC cell surface receptor-mediated transformable peptide nanoparticles, in which the prodrug leucine- doxorubicin (Leu-DOX) and PLZ4 ligand were linked by a β-sheet forming peptide sequence KLVFF, to enhance the efficacy of drug delivery while minimize toxicity. These transformable peptides self-assemble into nanoparticles which exhibit high specificity for bladder tumor tissues through the specific recognition of αvβ3 integrin on the surface of BC cells via PLZ4, a ligand discovered by one bead one compound (OBOC) combinatorial library method. Upon binding to αvβ3 integrin, the nanoparticles undergo a transformation process facilitated by ligand-receptor interaction, forming

nanofibrils on the cancer cell surface, followed by gradual uptake by the cancer cells. The precursor prodrug of doxorubicin was released in response to the overexpression of matrix metallopeptidase 9 (MMP9) enzyme in the tumor microenvironment and inside the endosomes of the tumor cells, leading to effective tumor cell elimination. Notably, the precursor prodrug remains inactive in normal tissues, which lack the MMP9 enzyme, thereby significantly lowering the risk of doxorubicin toxicity in healthy tissues. This innovative therapeutic approach has the potential to improve drug accumulation in bladder tumor tissue, enhance drug uptake by tumor cells, minimize drug toxicity, and ultimately augment the anti-tumor efficacy. The findings could have substantial implications for the development of targeted therapies of BC, offering a promising avenue for improved patient outcomes.

<<PT-09>> CHARACTERIZING PARP INHIBITOR AND AR PATHWAY INHIBITOR RESPONSES IN ADVANCED PROSTATE CANCER

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Combining poly (ADP-ribose) inhibitors (PARPis) with androgen receptor inhibitors (ARPis) has proven successful in the treatment of metastatic castration-resistant prostate cancer (mCRPC). However, much remains unclear about its efficacy and progression following the combination. Does prior exposure to an ARPi preclude response to combination therapy? Can ARPi synergize with PARPi and promote a synthetic lethal effect? Previous work suggested a dual response to PARP inhibition including apoptosis and a drug-tolerant persistent (DTP) state. These cytostatic persisters may facilitate progression and development of resistance. In this study we aimed to analyze how the addition of ARPi would affect the response to PARPis, potentially overcoming the DTP state following PARP inhibition. To study the response to the combination we used models of treatment naïve mCRPC, C4-2B, and ARPi resistant mCRPC, AbiR and MDVR. Our data suggests that the combination remains efficacious regardless of prior exposure to an ARPi, although the treatment naïve cells have a greater response. Morphological analysis shows a persisting cytostatic population bypassing treatment-induced cell death, suggesting the combination is not synthetic lethal, but instead further promotes the DTP state seen under PARP inhibition monotherapy. Evaluating biochemical expression through markers known to respond to PARP inhibition corroborates a minimal amount of apoptosis occurring under combinatorial treatment. Further analysis of the response to combination therapy is required, as flow cytometry analyzing cell cycle dynamics has yielded unexpected results. Future studies involve further characterizing the response to PARPi and ARPi combinations and searching for novel strategies to enhance their efficacy.

<<PT-10>> NAPHTHALENE FORMS DNA ADDUCTS IN MOUSE LUNG AND LIVER AFTER ORAL EXPOSURE

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Naphthalene is a ubiquitous environmental pollutant to which humans are exposed through combustion events or by consumption of contaminated food or water. Chronic exposure to naphthalene vapor increases tumor formation in respiratory epithelium of rodents. Bioactivated naphthalene has been shown to form stable DNA adducts (a potential genotoxic mechanism) in mouse airway explants, but it is unclear if this occurs in vivo, as ex vivo explants do not fully recapitulate a complex multi-organ system. We hypothesized that naphthalene is capable of adducting to DNA in vivo and that DNA adduct quantity would vary by duration after exposure due to the impact of DNA repair. Wild-type C57BL/6 mice were exposed to 50 mg/kg 14C-labeled naphthalene or vehicle (corn oil) via oral gavage. Lung and liver were collected at four post-exposure timepoints (2, 4, 24 & 72 hours), then DNA was extracted and analyzed using accelerator mass spectrometry to measure quantities of covalent naphthalene-DNA adducts. Aligned ranks transformation analysis of variance (ART-ANOVA) demonstrated levels of naphthalene-DNA adducts in lung and liver are greatest at 2 or 4 hours after exposure,

and significantly decrease by 24 or 72 hours (P< 0.05). However, even at 72 hours post-exposure, DNA adduct levels remain elevated in mouse lung (both sexes) and female liver compared to control tissue. In conclusion, naphthalene-DNA adducts are detectable in vivo in mouse lung and liver after oral exposure. The persistence of naphthalene-DNA adducts at 72 hours post-exposure is concerning, as these adducts likely evaded DNA repair and may lead to mutagenesis.

<<PT-11>> CAPACITY BUILDING FOR GERIATRIC ONCOLOGY AND CANCER SURVIVORSHIP CLINICAL TRIALS: ENGAGEMENT WITH SURVIVORS AND PROMOTORES DE SALUD

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Introduction: Clinicians and policymakers around the globe have advocated for expanded access to cancer survivorship care. In an effort to address greater treatment burdens and morbidity, survivorship has been increasingly delivered in community settings by Promotores (Community Health Workers). Promotores are trusted bridges between communities and health systems. In some states, like California, promotores' services are eligible for reimbursement by public insurance (Medicaid).

Objective: Enlist promotores and survivor stakeholders for the refinement, training, and pilot implementation of a behavioral clinical trial for older adult cancer survivors. Foster partnership with community-based organization (Visión y Compromiso) promotores, trained in health education and prevention.

Methods: We convened two focus groups with promotores (n = 17) and three interviews with older adult survivor stakeholders. Next a community health worker training for the intervention was held involving didactic and case study informed by the qualitative findings. Qualitative analysis used descriptive and deductive content analysis.

Results: Qualitative analyses affirmed the validity of the protocol including the research questions, community health worker skillsets, and institutional resources. The intervention was ultimately designed to be delivered in English and Spanish, combining geriatric assessment, education, and problem-solving strategies.

Conclusions: Engaging with promotores and survivor stakeholders led to a feasible launch of the pilot study. The Tailored Assessment in Geriatric Oncology and Survivorship (TANGOS) study activated in March 2024, and is a registered clinical trial (NCT#06125145). A larger efficacy trial may be warranted later.

<<PT-12>> CHARACTERIZING DRUG-INDUCED TRANSCRIPTIONAL PROGRAMS IN OVARIAN CANCER

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Despite being the third-most common gynecologic cancer, cancers of the ovary and fallopian tube remain the most deadly of this disease type, with a five-year survival rate of 50.8%. High rates of recurrence and developed resistance to first-line, platinum-based therapies is largely to blame for these clinical outcomes. Recent work has implicated multiple cell types as potential culprits for these negative trends, including cancer stem cells and drug-tolerant persister cells. This study is part of a larger body of work attempting to identify and characterize these cell types, with the ultimate aim of developing targeted therapies against them. The first-line, platinum-based agent carboplatin was administered to three ovarian cancer cell lines (OVCAR3, OVSAHO, and SKOV3), with cells then being harvested at 6 hours, 48 hours, and 14 days for single-cell RNA sequencing. The resulting data was analyzed through the Seurat and Monocle 3 R toolkits. These analyses reveal a non-uniform transcriptional response of carboplatin-treated cells at the 6-and-48-hour timepoints, suggesting the development of distinct cell subpopulations following exposure to treatment.

<<PT-13>> IDENTIFICATION OF MTAP-DEFICIENCY REGULATORY GENES VIA DNA METHYLATION IN LUNG ADENOCARCINOMA: POTENTIAL BIOMARKERS AND THERAPEUTIC TARGETS

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Lung cancer is a major contributor to cancer-related deaths worldwide, with methylthioadenosine phosphorylase (MTAP) deficiency observed in approximately 30% of cases. However, the regulatory mechanisms of MTAP deficiency, particularly those involving DNA methylation, remain largely unclear. In this study, we utilized The Cancer Genome Atlas (TCGA) lung adenocarcinoma (LUAD) dataset to identify genes regulated by DNA methylation in MTAP-deficient LUAD. Through the overlap of differentially expressed genes in MTAP-deficient LUAD and those with differential DNA methylation patterns, we identified several genes, including GPR56, DLK1, HOTAIR, HOXC13, HOXC4, SOX11, STAP2, TFAP2D, VAX1, and VAX2, which are induced by MTAP-deficiency-regulated DNA methylation. These genes are involved in various cellular functions, such as cell signaling (GPR56), differentiation (DLK1, HOXC13, HOXC4), transcription regulation (HOTAIR, TFAP2D), neural development (VAX1, VAX2), and tumor progression (SOX11, STAP2). Additionally, CRMP1, a gene known to be a suppressor of epithelial-mesenchymal transition (EMT), invasion, and metastasis, was identified as inhibited by MTAP-deficiency-related DNA methylation. The identification of these genes suggests that MTAP deficiency in lung cancer is associated with specific epigenetic modifications that influence gene expression and contribute to tumor development and progression. These findings highlight potential novel biomarkers and therapeutic targets for MTAP-deficient lung cancer. Further studies are needed to clarify the mechanisms by which MTAP deficiency modulates DNA methylation and its role in lung cancer pathogenesis.

<<PT-14>> SHORT-TERM DIETARY INTERVENTION IMPACTS ANTI-PD-1 TREATMENT OUTCOME OF HCC

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Hepatocellular carcinoma (HCC) is a solid tumor with limited treatment options, and immunotherapy has shown disappointing results. No biomarkers currently predict treatment efficacy, leading to unnecessary treatments with side effects but no benefits. This study aims to understand the mechanisms behind anti-PD-1 resistance in HCC.

To achieve this, research focused on orthotopic HCC models in immunocompetent mice, where tumors develop in the liver, better replicating the gut microbiota's influence on liver inflammation via the gut-liver axis. Using this model, we found that diet during anti-PD-1 treatment affects HCC outcomes. Therapy was effective only in mice fed a healthy control diet (CD), while those on a Western diet (WD) or high-fat diet (HFD) showed no response.

Transcriptomic profiling revealed that CD/HCC mice had enriched interferon (IFNα and IFNγ) signaling and the allograft rejection pathway. IFNα, crucial for innate immunity, promotes dendritic cell maturation, while IFNγ is mainly produced by T cells, including CD8+ cytotoxic and CD4+ Th1 cells. Further studies revealed that IFNα, but not IFNγ, could treat anti-PD-1 non-responders (WD/HCC), highlighting its potential role in overcoming resistance.

In summary: (1) Diet significantly alters the immune landscape of HCC; (2) IFNα is crucial for anti-PD-1 responsiveness; (3) A short-term healthy diet improves anti-PD-1 treatment outcomes.

<<PT-15>> TREATMENT DIFFERENCES FOR PREMENOPAUSAL WOMEN WITH A TRIPLE NEGATIVE SECONDARY VS PRIMARY BREAST CANCER

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Background: Women diagnosed with a secondary triple negative breast cancer (TNBC) have worse breast cancer specific survival (BCSS) compared to those diagnosed with a primary TNBC. Treatment approaches to secondary TNBC may need to differ from that for primary TNBC, but currently there are no guidelines. Therefore, we aim to identify the treatments used for secondary TNBC and how they differ from primary TNBC treatment in premenopausal women.

Methods: This is a population-based, retrospective cohort study of women aged 15-50 years, diagnosed from 2003 to 2019 with either a primary TNBC (N= 9220) or secondary TNBC (N=682), defined as a new TNBC after any prior cancer. Data was obtained from the California Cancer Registry. Multivariable logistic regression was used to compare treatment between women with secondary vs. primary TNBC. Results are presented as adjusted odds ratios (OR) and 95% confidence intervals (CI).

Results: Women with a secondary TNBC were two-times more likely to be treated with a mastectomy (vs lumpectomy) than women with a primary TNBC [OR 2.01 (CI: 1.61, 2.50)]. Those with a secondary TNBC were less likely to be treated with neoadjuvant (vs. adjuvant) chemotherapy [OR 0.61 (CI: 0.49, 0.77)]. Additionally, chemotherapy use was higher for primary TNBC, but most secondary TNBCs were treated with non-anthracycline based regimens with cyclophosphamide, methotrexate, fluorouracil being most common [OR 4.66 (CI: 2.55, 8.50)].

Conclusion: Differences in treatment, specifically the timing and type of chemotherapy used for secondary TNBC, could be associated with worse BCSS, suggesting the need for further exploration.

<<PT-16>> OLFACTOMEDIN-LIKE 3 NEUTRALIZATION EXTENDED SURVIVAL IN A MOUSE MODEL OF GLIOBLASTOMA

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Glioblastoma (GBM) is a devastating and lethal primary brain tumor. The immunosuppressed tumor microenvironment is a major obstacle to the development of effective therapies. Our laboratory and others have shown that the novel secreted glycoprotein, olfactomedin-like 3 (OLFML3), contributes to microglia-mediated immunosuppression and GBM growth. In this current study, we tested the hypotheses that intratumoral neutralization of OLFML3 will 1) extend survival in a syngeneic GBM mouse model and 2) this effect is mediated through increased anti-tumor immunity. The anti-OLFML3 neutralizing and IgG control antibodies were generated in collaboration with Evitria AG (Zurich, Switzerland). Briefly, anti-mouse OLFML3 rat monoclonal antibodies (clone 9F8) were produced in Chinese hamster ovarian cells and IgG purified. Continuous intratumoral delivery of an OLFML3 neutralizing antibody extended median survival time in GL261 GBM mice (16.5 days, n=6 vs. 12 days, n=6 IgG control; p = 0.03). Ongoing experiments are being conducted to define the immune cell type composition, specifically interrogating glioma associated microglia/macrophages (GAM) and T cell populations, and their molecular signatures across treated and untreated tumors. Identifying

shifts in immune cell populations can identify the mechanism of action for this novel therapeutic target and will provide insight for clinical translation to human and canine brain tumor patients.

<<PT-17>> FLUORESCENCE LIFETIME SIGNATURES OF COLORECTAL POLYPS: A FEASIBILITY STUDY

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Colorectal cancer is the third most diagnosed cancer and the second leading cause of cancer-related deaths worldwide. A critical problem in the early detection of colorectal cancer is that conventional methods (e.g., white light endoscopy) may not readily distinguish malignant from benign tissue in real-time. We hypothesize that normal colorectal tissue, pre-cancer, and cancerous lesions display distinct autofluorescence properties due to differences in metabolism and structure that can be resolved with interventional fluorescence lifetime imaging (FLIm).

In this study, in vivo intraluminal FLIm imaging was performed on 16 patients before tissue collection, as part of the standard of care. The resected specimens were diagnosed via standard histopathological evaluation. The study was approved by the University of California, Davis Institutional Review Board (IRB), and all patients provided informed consent before participation.

We show FLIm contrast between polyps and adjacent tissue. All hyperplastic polyps in the dataset (n=7) had an increase in lifetime at 390nm (coefficient of variance, cv=0.9), and mostly shorter lifetimes at 470nm and 540nm. Tubular adenomas (n=33) consistently showed average lifetimes shorter than normal surrounding tissue (cv<2) for all spectral bands, and sessile serrated adenomas (n=7) showed less consistent trends and had a high coefficient of variance (cv=3.1 at 540 nm, and cv=38.3 at 390nm). These results point at the metabolic heterogeneity between polyp types.

FLIm shows potential as an optical biopsy method for colorectal screening by augmenting biochemical information in real time and in situ during colonoscopy procedures.

<<PT-18>> THE ROLE OF SHROOM3 DOWNSTREAM OF WNT/PLANAR CELL POLARITY SIGNALING IN BREAST CANCER METASTASIS

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The 5-year survival rate for patients diagnosed with metastatic breast cancer (BC) remains below 30%, highlighting the need to better understand the molecular mechanisms driving BC metastasis to develop more effective therapeutic strategies in the future. Wnt/Planar Cell Polarity (Wnt/PCP) is a non-canonical Wnt pathway that promotes global directional cues to produce locally polarized cell behavior, leading to increased cell motility, survival, and proliferation. Core Wnt/PCP components are frequently upregulated in aggressive BCs and our lab has demonstrated a role for Wnt/PCP signaling in mediating BC cell motility and metastasis. However, understanding of the mechanistic underpinnings linking core Wnt/PCP components to the cytoskeletal rearrangements that promote cell motility is limited. In a phosphoproteomics screen to identify proteins differentially phosphorylated in response to Wnt/PCP pathway activation in BC cells, our lab identified the protein Shroom3. Shroom3 is an actin binding protein critical for cytoskeletal rearrangements that promote cell and tissue morphogenesis during development and has previously been placed downstream of Wnt/PCP signaling. I hypothesize that Shroom3 is recruited to the leading edge of migrating BC cells upon Wnt/PCP pathway activation where it then recruits its binding partners, including ROCK and myosin II, to promote

actomyosin cytoskeletal rearrangements, facilitating BC cell motility and metastasis. I will assess the role of Shroom3 in Wnt/PCP-mediated BC cell motility and investigate Wnt/PCP-mediated regulation of Shroom3 localization and phosphorylation. This study will for the first time evaluate the contribution of Shroom3 to cancer progression and enhance our understanding of how Wnt/PCP signaling promotes BC metastasis.

<<PT-19>> CHARACTERIZATION OF CARBOPLATIN-INDUCED DTP CELLS AND IDENTIFICATION OF EFFECTIVE ONCOLOGY DRUGS IN OVARIAN CANCER

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Drug-tolerant persister (DTP) cells are key contributors to cancer recurrence and chemotherapy resistance, necessitating the creation of in vitro models for effective drug screening. However, their characteristics and specific role in high-grade serous ovarian cancer (HGSOC) require further elucidation. This study focuses on characterizing DTP cells in HGSOC induced by carboplatin and identifies effective oncology drugs against them. We utilized both carboplatin-sensitive (OVCAR3, CaOV3) and carboplatin-resistant (OVSAHO, OVCAR4) cell lines, inducing DTP cells through carboplatin treatment. Gene expression profiles were analyzed using sc-RNAseq and UMAP clustering. Our findings indicate that OVSAHO cells enter a reversible DTP state, with significant growth suppression upon carboplatin, yet growth resumes following drug withdrawal. Morphologically, DTP cells appear enlarged and flattened, with increased cell body size, nuclei, and lysosomal content. Notably, the compound BAQ13, which combines lysosomotropic properties with autophagy inhibition, was found to disrupt lysosomal integrity in OVCAR3 and OVSAHO DTP cells. Additionally, drug screenings revealed that these DTP cells are particularly sensitive to the BCL2 inhibitor ABT-263 and VCP inhibitors. This study broadens our comprehension of carboplatin-induced DTP cells and proposes new therapeutic strategies to target these persistent cells in ovarian cancer.

Acknowledgment: We extend our gratitude to all the members of the Lam Lab and Li Lab for their invaluable support and contributions to this research.

<<PT-20>> SINGLE ARM STUDY TO ASSESS THE IMMUNE EFFECTS OF FERMENTED WHEAT GERM (FWG) NUTRITIONAL SUPPLEMENTATION IN PATIENTS WITH ADVANCED MALIGNANCIES BEING TREATED WITH STANDARD OF CARE CHECKPOINT INHIBITOR-BASED THERAPY - A TRIAL IN PROGRESS

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The bridge between Allopathic Medicine (AM) and Complementary Medicine (CM), optimized for patients benefit, may facilitate the ability to provide less toxic, alternative approaches to Oncology care. Approximately 33% of adults use some form of CM, and many promising approaches that utilize CM are abandoned due to a paucity of well-designed clinical trials which will potentially deprive cancer patients of less toxic and less expensive approaches to cancer therapy. This ongoing pilot study is enrolling patients with malignancies that utilize CPI-based therapy and exemplifies this “bridge” research which has potential to enhance current evidence that Fermented Wheat Germ (FWG) can increase Checkpoint Inhibitor-based therapy (CPi) therapeutic response by modulating the host immune response and gut microbiota. Our protocol design utilizes what we are calling the Four Pillars of Successful CM Oncology Trials: 1) studying a CM that has been demonstrated to be safe, 2) defining a specific primary objective (i.e. NK-cell killing activity gut microbiome analysis, 3) employing validated quality of life questionnaires, 4) conducting complete capture of all symptoms.

Preliminary data does not include analysis of samples, however, in n=13 whom completed the study compared to 20 with similar variance on CPi without FWG, a significant difference (p = 0.01) in treatment satisfaction was shown by Fisher ordinal logistic regression. Additionally, several FWG subjects have reported improved digestion and one asked to continue the FWG after trial.

A supplement like FWG offers an opportunity for the kind of quality CM oncology trials needed to form this AM-CM bridge.

<<PT-21>> EVALUATING MOLECULAR BIOMARKER TESTING AND SYSTEMIC TREATMENTS AMONG PATIENTS WITH STAGE IV NSCLC

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Background: Lung cancer is the leading cause of cancer-related death. Novel targeted therapies for non-small cell lung cancer (NSCLC) harboring specific genetic alterations (i.e., EGFR, ALK, etc.) have dramatically improved outcomes. The evidence-based standard is for all patients diagnosed with stage IV NSCLC to undergo molecular testing to inform treatment selection, but the testing rate is unknown.

Methods: We quantified rates of molecular testing (EGFR and ALK) among patients with stage IV NSCLC in the California Cancer Registry (CCR) diagnosed 2021 to 2022, when molecular testing information became available. We determined first-line systemic treatments using text fields from the CCR. Multivariable logistic regression was used to examine characteristics associated with testing receipt.

Results: We identified 9,930 patients with median age 71 years. Most were non-Hispanic White (53.0%), and fewer than half had private insurance (44.8%). 38.7% of the cohort received EGFR or ALK molecular testing. Patients with older age, male sex, low socioeconomic status (SES), higher comorbidity, and not treated at NCI-designated cancer centers were less likely to be tested. Asian/ Pacific Islander patients and those diagnosed in 2022 (vs. 2021) were more likely to be tested. Approximately 74% of patients positive for either marker received targeted treatments.

Conclusion: In this population-based study, fewer than half of patients received standard of care molecular testing for Stage IV NSCLC. The decreased likelihood of testing for patients residing in low SES neighborhoods suggests possible financial and educational barriers. More research is needed to evaluate biomarker testing among this patient group.

<<PT-22>> ENGINEERING CAR-T CELLS FOR IMPROVED CANCER TARGETING USING NANOLIPOPARTICLE PROTEIN DELIVERY

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While personalized cancer therapies using Chimeric Antigen Receptor T cells (CAR-T) have improved the survival rates of some blood cancers, current technologies to manufacture CAR-T cells are expensive and time-consuming. Our group has developed a unique transgene-free manufacturing strategy for CAR-T engineering, where a CAR protein enveloped in a nanolipoprotein particle (NLP) is used to deliver the CAR protein to human T cells in vitro. To test the viability of this CAR-T engineering strategy, we first treated human T cells with CAR-NLP particles in the presence of immune activating reagents. This resulted in detectable CAR uptake in >50% of T cells at 24 hours as measured by flow cytometry. Cell viability remained high during CAR-NLP dosing (>80%), indicating low toxicity associated with delivery of the CAR protein. Treated T cells were stained with a fluorescent CD19 protein to test if integration of the CAR protein was successful. CD19

staining on CAR-NLP treated cells was comparable to positive antibody controls while cells treated with the vehicle (empty NLPs) showed very low CD19 binding, indicating that CAR-NLP treated T cells can bind the target ligand specific to the engineered CAR construct. These data indicate that delivery of a CAR protein encased in an NLP may be a viable cell engineering strategy. Overall, this approach does not require genetic modifications of cells and can be performed in <24 hours. Thus, we believe it could enable faster, cheaper, and safer engineering of CAR-T cells to better treat cancers.

<<PT-23>> NON-INVASIVE SKIN SAMPLING FOR IMPROVED MELANOMA DIAGNOSIS USING ADHESIVE PATCHES: OPTIMIZATION OF RNA ISOLATION

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Introduction: Melanoma is the deadliest form of skin cancer, responsible for 80% of skin cancer-related deaths. Early, accurate diagnosis is crucial for patient survival. Current diagnostic methods rely on invasive skin biopsies, and only a subset of biopsied lesions are malignant.This study aimed to develop a non-invasive, adhesive patch-based diagnostic method for melanoma.

Objectives: We aimed to optimize a RNA isolation protocol from epidermal keratinocytes using adhesive patches to detect melanoma.

Methods: An IRB-approved study was conducted with samples collected from healthy, non-lesional skin using two different adhesive patch types (D-101 DSquame and ARCare90068), with 20 consecutive patches pressed to the same site followed by RNA isolation. RNA was disrupted from the patches using either ultrasound sonication or skin scraping and then isolated using silica-membrane spin column technology. RNA quality and quantity were assessed using nanodrop spectrophotometer and bioanalyzer. RT-qPCR evaluated the expression of epidermal keratinocyte genes KRT10 and FLG2.

Results: DSquame adhesive patches and RNA disruption via ultrasound sonication yielded better RNA quality, although RNA amounts were too low to quantify accurately. RT-qPCR analysis showed consistent and reliable expression of KRT10 and FLG2, validating the effectiveness of the optimized protocol.

Conclusion: The optimized protocol using DSquame patches and ultrasound sonication as a disruption technique improves RNA isolation from epidermal keratinocytes. This non-invasive method has the potential to enhance melanoma diagnosis by providing an alternative to traditional skin biopsies. Future studies will focus on incorporating additional biomarkers to further refine the assay’s diagnostic accuracy.

<<PT-24>> CHARACTERIZING DELAYS IN RECTAL CANCER CARE

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Introduction: Timely coordination of rectal cancer treatment is essential, and the standard of care is within 60 days. Identifying patients with delays to definitive treatment and characterizing barriers to care is imperative for targeted interventions. Our study seeks to characterize delays in treatment initiation based on sociodemographic variables and staging.

Methods: A retrospective review of rectal cancer patients from 2013-2023 was conducted. Patients were segmented based on time-to-treatment, defined as time from initial biopsy to definitive treatment (chemotherapy, radiation, surgery). Descriptive statistics and chi-square analyses were conducted analyzing patients with time-to-treatment < 60 days versus > 60 days with respect to patient demographic data and completion of staging (CT, MRI). A multivariate binary logit model was conducted with significant variables from the univariate model.

Results: There were 328 patients with 129/328 (39.3%) patients with time-to-treatment > 60 days. Median duration from biopsy to staging with CT and MRI was 14 and 33 days, respectively. Chi-square analyses revealed age (p=.008), insurance type (p=.02), and MRI completion (p=.016) were significantly associated with

time-to-treatment. The multivariate model revealed that patients with Medicare (p=.047) and patients who received an MRI (p=.03) were significantly associated with delays in treatment initiation.

Conclusion: Our analysis revealed patients with Medicare were significantly associated with delays in definitive treatment. Staging MRIs were also associated with delays in treatment initiation. This indicates a need for intervention for prompt coordination of rectal cancer care and to reduce the time between biopsy and definitive treatment.

<<PT-25>> INTEGRIN ALPHA 4 EXPRESSION AS A MARKER FOR RESPONSE TO IMMUNE CHECKPOINT INHIBITORS (OR TO A NOVEL CTLA-4 INHIBITOR ONC-392)

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Background: Integrins mediate interactions between cells and induce signaling that can regulate migration, activation, and proliferation, particularly in the immune system. Here, we examine the dynamics of integrin expression in immune cells as potential markers for a successful immune response during cancer immune-blockade therapy.

Methods: We generated both single-cell RNAseq (n = 20) and bulk RNAseq (n = 44) transcriptional profiles from blood immune cells isolated before and after ONC-392 (a novel CTLA-4 inhibitor) treatment mainly lung cancer patients as part of the PRESERVE-001 study (NCT04140526).

Results: We then performed a cell-specific differential analysis of the 138,444 cells from the scRNAseq data, before and after treatment, across the major immune subsets. ITGA4 expression significantly increased after treatment in responders patients (n = 7) in CD4+ T central memory cells (TCM), T regulatory, and CD8+ T effector memory cells. In contrast, ITGA4 decreased or was not significantly changed in NR patients (n = 3) in the same cell types. Furthermore, ITGA4 expression with CD4+ TCM correlated with genes enriched for cell activation pathways. A ITGA4-high cell cluster of CD4 TCM was found to uniquely express PRF1, GZMA, and KLRB1, suggesting a cytotoxic CD4 T cell phenotype.

Conclusion: We show that integrins are significantly associated with a successful response to immunotherapy blockade in this small exploratory cohort. ITGA4 has previously been shown to be an important marker of antigen-specific T cell activation and our data here suggests it may be a marker for tumor-specific T cell activation in the context of immunotherapy response.

<<PT-26>> MECHANISTIC AND PHENOTYPIC INSIGHTS INTO TEMPORAL AND DOSAGE-DEPENDENT RESPONSES TO PARP INHIBITION IN ADVANCED PROSTATE CANCER

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Background: Poly ADP-ribose polymerase (PARP) inhibition effectively treats prostate cancer (PCa) by inducing DNA damage and cell death through synthetic lethality. However, drug resistance inevitably develops, necessitating the study of short- and long-term effects. Responses to PARP inhibition in PCa vary from cytostasis to cell death, with the impact of different dosages and durations underexplored. This study examines how temporal and dosage variations of Olaparib (Ola) influence PCa cell phenotypes and identifies mechanisms and therapeutic targets to address vulnerabilities following PARP inhibition.

Methods: C4-2B cells were treated with 0 μM, 1 μM, and 5 μM Olaparib for 1 and 5 days. RNA sequencing (RNA-seq), cell growth assays, microscopy, and western blotting were used to identify pathway alterations and putative vulnerabilities.

Results: After 1 day, RNA-seq revealed a dominant p53-mediated cell cycle arrest driven by ATM. By day 5, cells exhibited significant morphological changes, stress-induced phenotypes, and indicators of epithelial-mesenchymal transition (EMT). Fatty acid metabolism alterations, minimal initially, became prominent by day 5, indicating a shift towards a stress-resistant phenotype. These findings suggest that prolonged PARP inhibition leads to metabolic adaptations and the survival of a resistant subpopulation.

Conclusion: PARP inhibition induces distinct cellular and metabolic changes based on dosage and duration. Acute exposure triggers p53-mediated cell cycle arrest, while prolonged treatment results in stress responses and metabolic shifts that promote cell survival, underscoring the need for combination therapies to address both immediate and long-term effects.

<<PT-27>> THE CALIFORNIA FIREFIGHTER CANCER RESEARCH STUDY (CAFF-CRS): COHORT PROFILE AND BASELINE ASSESSMENT OF METABOLIC, OCCUPATIONAL

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Introduction: Cancer is the leading cause of death among California firefighters (CA-FFs), yet the precise determinants are poorly understood, and effective preventive interventions remain elusive. CA-FF experience numerous chemical, physical, mental, and behavioral hazards that initiate and promote cancer. CAFF-CRS was established to further elucidate these risks.

Methods:Firefighters in the Sacramento area were recruited between Feb-May, 2024 and completed a baseline blood donation, body composition testing, vitals and clinical lab testing, nutritional assessment, and numerous validated questionnaires. Additionally, participants were asked to continuously wearing a study-issued Fitbit to measure sleep, heart rate, and activity.

Results: A total of 385 firefighters were enrolled (mean age, 38 years; female, 5%; Asian, 7%, Black of African American, 4%, White, 86%, American-Indian, 4%, Hispanic or Latino, 13%). Tobacco and alcohol use were prevalent and varied according to rank, 47% of firefighters ever used smokeless tobacco and 29% of fire captains or chiefs used alcohol 3+ days/week. Poor sleep quality was prevalent; all participants had greater sleep disturbance compared to a reference U.S. population. Several indicators of metabolic unhealth were observed and were highest among fire captains or chiefs including: 37% obesity (BMI ≥ 30),18% pre-diabetes/diabetes (HbA1c ≥ 5.7 %), 19% high cholesterol (≥ 240 mg/dL), and 37% stage II hypertension (>140 />90 mmHg).

Conclusions:Cancer risk factors are prevalent among firefighters. Future analyses will examine risk factors in relation to epigenetic and inflammation markers to improve our understanding of biological mechanisms and prevention strategies to reduce cancer in firefighters.

<<PT-28>> UTILIZATION OF ANTIBODY TARGETED PERFLUOROCARBON NANOPARTICLES FOR MULTIPLEXED 19F MRI OF TUMOR-ASSOCIATED MACROPHAGES

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Tumor-associated macrophages (TAMs) play important roles in the progression of cancer, adapting a spectrum of tumoricidal (M1) or tumor promoting (M2) phenotypes. Historically, lower M1/M2 ratio or high macrophage density correlated to lessened survival chances, but emerging research suggests that these links to survival depend on tumor type. Current diagnostic techniques miss heterogeneity and are highly invasive, therefore we propose using 19F magnetic resonance imaging (MRI) for noninvasive imaging of the TAM environment. 19F MRI has high SNR and provides quantitative analysis of contrast agent concentration. Furthermore, it permits imaging of multiple biomarkers, through the assigning of discrete identifiers to agents by using perfluorocarbons (PFC) with unique chemical shifts, which can be discriminated through imaging. We identified M1 biomarkers (CD40, CD86), M2 biomarkers (CD204, CD206) and pan-macrophage marker (CD68) for multiplexed 19F MRI.

We synthesized perfluorocarbon nanoemulsions (PFC-NE), incorporating a copper-free click component for post-emulsification conjugation of a targeting antibody, and measured stability over 130 days. Particles show loss of ~30% [fluorine] with no significant change in size. We demonstrated targeting to CD68 by clicking azide-labeled anti-CD68 Fab to PFC-NE. On RAW 264.7 cells, we saw significantly higher uptake in targeted-NE to control-NE. For preliminary multiplexed 19F MRI, we show the ability to image fluorine signals only 8 ppm apart, and quantify [fluorine] for two distinct fluorine signals in solution by imaging mixtures of two PFC.

Future work will continue targeting for each biomarker of interest and eventually utilize this platform for elucidation of TAM phenotype in different tumor models.

<<PT-29>> DEVELOPMENT OF SURFACE-ENHANCED RAMAN PROBES FOR THE DETECTION OF HETEROGENOUS CANCER BIOMARKERS

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Molecular biomarkers are powerful indicators of disease, often detecting abnormalities at early stages before visible changes or more serious symptoms occur. Due to the extreme heterogeneity in composition and temporospatial arrangement of molecules in cancerous tissues, disease diagnosis and prognosis can be challenging when relying on a single biomarker. Thus, the rapid and accurate detection of multiple biomarkers in single samples is of utmost clinical importance. Optical multiplexing is a potential strategy for simultaneous detection of multiple biomarkers in a sample, however translation of traditional fluorescence-based multiplexing techniques from the lab to the clinic is difficult due to limitations in the number of unique laser channels in an instrument and the availability of non-overlapping fluorescent tags. To address these limitations, we aim to expand the multiplexing capabilities of surface-enhanced Raman spectroscopy (SERS) through the development of a modular library of polyyne-containing small molecules. Alkynes (molecules containing the functional group C□C) have been shown to produce signal in the biologically silent Raman region, offering a high signal-to-noise ratio. Furthermore, increased polyyne (conjugated alkyne) length systematically red shifts Raman signal, enabling multiplexing in this spectral window. Polyynes are notoriously unstable and difficult to solubilize, hindering their development into SERS probes. We seek to optimize the synthesis of polyyne Raman reporter molecules, and investigate how additional functional groups influence their Raman shift, stability, and solubility. By diversifying our polyyne library, we intend to expand the spectroscopic toolbox to increase the number of biomarkers that can be simultaneously identified for the improved detection of cancer.

<<PT-30>> ELUCIDATING THE METAL-DEPENDENT ACTIVITIES OF OXYTOCIN IN THE BREAST CANCER CELL LINE

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Oxytocin, a nine-amino-acid hormone peptide known for its role in reproduction and childbirth, has fascinated researchers for its diverse biological functions. Early studies suggested the effect of metal ions on oxytocin's activities, but the molecular details underlying its interaction with metal ions remains unclear. In 2023, our group discovered that oxytocin binding with copper and zinc affects the activation of mitogen-activated protein kinase (MAPK) signaling in kidney cell lines. We hypothesize that extracellular metal-bound oxytocin modulates the interaction of the oxytocin receptor, thereby altering the activation of MAPK pathways. Based on this observation, we aim to broaden our understanding of the metal-dependent biological effects of oxytocin by examining MAPK signaling activation, oxytocin receptor (OXTR) expression, and cell migration in a triple-negative breast cancer (TNBC) cell line—an aggressive subtype of breast cancer lacking estrogen, progesterone, and human epidermal growth factor receptor 2. Previous research has shown that oxytocin inhibits cell proliferation, and OXTR may serve as a promising therapeutic target in TNBC. However, the impact of metal-bound oxytocin complexes on TNBC remains unexplored. Our preliminary data indicate that MAPK signaling activation, OXTR expression, and cell migration rates vary depending on the specific metal ion or metal-bound oxytocin complex introduced to the TNBC cell line. Through this investigation, we aim to elucidate the mechanistic role of metal-bound oxytocin in cancer biology, potentially uncovering new therapeutic strategies for TNBC.

<<PT-31>> INVESTIGATING METABOLIC SENSITIVITY AND ORGANIZATION OF RENAL CELL CARCINOMA: TO ENHANCE EFFECTIVE THERAPIES AND PATIENT SURVIVAL

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Background: Renal cell carcinoma (RCC) tumors are metabolically dysfunctional, often resulting from loss of von-Hippel Lindau (VHL) and consequent upregulation of hypoxia-inducible factors (HIF1/2), transcriptional regulators of glycolysis. Current therapies, including immune checkpoint inhibitors and tyrosine kinase inhibitors, have shown improvements in the outcomes of RCC patients. However, targeting RCC metabolism remains an unexploited critical area for innovation.

AIM: We aim to investigate mechanisms of metabolic adaptation in RCC cell lines (VHL mutant) and primary human tumor cells. Using a novel biosensor-based technique, we aim to identify the dependence of glycolytic flux on cells on tyrosine kinase, PI3K, mTOR, and HIF signaling, employing both standard-of-care and investigational pathway inhibitors.

Methods: We generated immortalized 786-O RCC cells stably expressing biosensors for the activity of glycolysis and the AMPK pathway. Data from live cells treated with metabolic inhibitors were collected and analyzed using our MATLAB-based pipeline. We have also extended the analysis to primary cells collected from nephrectomy specimens and matched metastatic biopsy samples. Effects of inhibitors on metabolism will be quantified and compared to their impact on tumor cell survival.

Results and Conclusion: Our single-cell data show that 786-O cells vary in their usage of OXPHOS and glycolysis. We also noted very modest effects of the inhibitors tested on glycolytic kinetics, suggesting that the anti-tumor mechanisms of existing inhibitors do not involve potent inhibition of glycolysis. We are currently expanding the library of compounds to identify additional compounds that will serve as potential leads for metabolically active therapies.

<<PT-32>> TARGETING P300/CBP TO INACTIVATE CANCER-ASSOCIATED FIBROBLASTS AND SUPPRESS PANCREATIC CANCER GROWTH

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Pancreatic cancer (PDAC) remains the third-leading cause of cancer-related death in the U.S. with only 13% of five-year survival rate in patients. PDAC is marked with a dense tumor-surrounding fibrous stroma, which only supports tumor growth but also significantly hinders the delivery of chemotherapies. This stroma is mainly contributed by cancer-associated fibroblasts (CAFs), which have not been targeted successfully for therapy due to the presence of multiple subtypes with distinct transcriptional profiles and functional roles. Thus, it is necessary to comprehensively understand the maturation of quiescent pancreatic stellate cells (PSCs) into different PDAC CAF subtypes, including myofibroblasts (myCAFs) and inflammatory fibroblasts (iCAFs). Interestingly, a line of evidence has shown the plasticity and interchangeability of CAF subtypes, suggesting the involvement of epigenetic regulations in CAF maturation. Our preliminary ATAC sequencing data on in vitro models of pancreatic myCAFs and iCAFs showed that CAF differentiation could be mediated through chromatin accessibility. Here, we showed evidence suggesting the potential role of P300/CBP in CAF epigenetic regulation. Inhibiting P300/CBP with A485 significantly suppressed the expression of pancreatic CAFs and converted them morphologically back to quiescent PSC state. Moreover, A485 treatment in co-cultures of pancreatic cancer organoids and PSCs resulted in a reduced cancer organoid growth, implicating a disruption of the mutual support reported between cancer cells and CAFs. This study suggests a novel strategy to target CAFs in tumor microenvironment for enhanced PDAC treatment.

<<PT-33>> SIGNAL DETECTION WITH CHEMICAL EXCHANGE SATURATION TRANSFER (CEST) MRI

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CEST is a potential tool to detect MRI contrast agents and tumor acidity. Liable protons of amide or amine bonds can be exchanged with water protons to transfer a signal reduction (saturation), leading to a decrease in water signal as CEST contrast. In this work, we develop the data processing pipeline for CEST using Iopromide and liposome as CEST agent samples and test the pipeline on in-vivo imaging of mice with brain tumors.

CEST images were acquired on a Bruker Imager using a turbo spin echo sequence. Saturation transfer was generated for the offset frequency range of [-10,+10] ppm in 0.5 ppm increments for iopromide and liposome samples and offset frequency range of [-6,+6] ppm in 0.2 ppm increments for mouse imaging. The WASSR concept is adopted to correct for the shift in all voxels independently. CEST spectra inside the desired ROI are averaged and fitted to the Lorentzian function. Then, we evaluated magnetization transfer ratio asymmetry (MTRasym) and generated CEST maps.

B0 correction improves homogeneity throughout an entire image. For CEST contrast agents, the Lorentzian fitted line and MTRasym show that iopromide saturation occurs at about 1.1 ppm, 4.2 ppm, and 5.7 ppm. Liposome saturation is not significantly observed, but it could be at around 2.4 ppm. For mouse images, the amplitude of the mean CEST spectrum from the tumor region is slightly higher than the normal brain tissue. However, with changes in acquisition parameters such as field strength, we should repeat the experiment to confirm tumor detection. In addition, B1 heterogeneity corrections and denoise need to be investigated.

Acknowledgement: This work is supported by the UC Davis Comprehensive Cancer Center with funds from the NCI's Paul Calabresi K12 program 5K12CA138464-12.

<<PT-34>> MISSING DATA METHODS FOR EVALUATING BREAST CANCER OUTCOMES

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Missing data is common in cancer research. Handling missing data improperly may generate misleading results. Multiple imputation (MI) is popular for addressing this issue. In this pilot study, we explored whether using auxiliary dataset(s) additional to the study dataset can improve MI performance. We investigated how survival differed by race/ethnicity among women with screen detected cancers in the Breast Cancer Surveillance Consortium, adjusting for stage. Both race/ethnicity and stage had missing values in the study and the full cohort (study+auxiliary datasets). Mode of cancer detection also had missing values in the auxiliary dataset. We implemented MI for these missing variables and compared various models using the study dataset only and the full cohort. Preliminary results show that Black women had significantly higher risk for mortality than White women, even after adjusting for stage and age-at-diagnosis. All models had similar trends for the parameter estimates and significance for Black women, although incorporating auxiliary dataset in MI along with imputing the missing mode of detection generated a much smaller P value (0.003 vs 0.02/0.03 for other models) and narrower 95% confidence interval (CI length 0.55 vs 0.68/0.69). This model also shows that more advanced stages increased the risk of mortality significantly with narrower CIs. These results indicate that using auxiliary datasets may increase the precision of the estimate for Black women and provide initial evidence that incorporating auxiliary datasets into the study dataset might improve MI performance with less bias and more efficiency, warranting comprehensive investigations of this important issue in cancer research.

<<PT-35>> ADVANCING EVIDENCE OF THE ASSOCIATIONS BETWEEN SPECIFIC BENIGN BREAST DIAGNOSES AND FUTURE BREAST CANCER RISK

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The risk of cancer associated with many specific benign breast diseases (BBD) have not been extensively studied, especially those histologically deemed low risk (typically absent of atypia). We identified 131,834 benign breast biopsies performed between 1994-2022 from pathology databases within 7 Breast Cancer Surveillance Consortium registries. Pathological terms were grouped into 40 BBD diagnoses and descriptors by two breast pathologists. For comparison, we identified 1,737,109 women without a prior breast biopsy and a negative or benign screening mammography assessment (American College of Radiology BI-RADS 1 or 2) from the same registries. We used Cox proportional hazards model to estimate hazard ratios (HR) associated with BBD diagnoses and descriptors. The most common BBD diagnoses were fibrocystic changes (28.1%), fibroadenoma (24.1%), usual ductal hyperplasia (15.0%), and fibrosis (15.0%). Apocrine metaplasia, columnar cell lesions, sclerosing adenosis, and papillomatosis occurred >80% of the time with other BBDs. Compared with women without a prior breast biopsy, women with histologic diagnoses in absence of atypia were at higher risk of invasive breast cancer (HR=1.99, 95% confidence interval (CI): 1.92-2.06) and ductal carcinoma in situ (DCIS) (HR=2.54, 95% CI: 2.38-2.72). Among low-risk diagnoses, multiple papillomas had the strongest association with invasive breast cancer (HR=2.64, 95% CI: 1.56, 4.46) and DCIS (HR=5.43, 95% CI: 2.91, 10.15). Having radial scar, columnar cell lesions, or phyllodes tumor did not increase the risk of invasive cancer but did increase the risk of DCIS (HRs ranged from 1.83-2.82). These findings provide strong support of elevated risk of breast cancer following benign biopsy.

<<PT-36>> IDENTIFYING FORCE-DEPENDENT INTERACTIONS SURROUNDING ACTIN FILAMENTS IN LIVE CELLS

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Cancer cells are constantly exposed to mechanical stress from surrounding cells and extracellular matrix. While cancer cells sense and respond to mechanical stress, the molecular details of this mechano-transduction are not well understood. Actin filaments are thought to be a molecular force sensor that recruits other proteins upon physical stimulation, but the comprehensive list of force-dependent actin binding proteins has not been described. Using TurboID, a promiscuous biotin ligase, fused with F-tractin, an actin filament binding sequence of IPTKA, we sought to identify the binding partners of actin filaments in cells exposed to mechanical stimuli. Purified biotinylated proteins from control and stretch conditions were ranked based on the proximity to the strained actin filaments. As expected, zyxin and ABLIM1, LIM proteins which are known to actin filaments in a force-dependent manner, and ACTN1, an actin binding protein and a zyxin binding partner, were identified as proximal to the strained actin network. Interestingly, KANK1, a focal adhesion protein and tumor suppressor, was also among the top candidates. In live-cell imaging analysis, KANK1 re-localized to strained actin filaments, but distinct from that of zyxin. Truncation analysis of KANK1 sequence suggests that KANK1-talin interaction is responsible for this unique recruitment to the strained actin filaments. Our analysis will lead to a better understanding of the molecular basis of force-induced protein interactions and may uncover the potential role of KANK1-dependent mechano-transduction in cancer.

<<PT-37>> A NOVEL AUTOPHAGY INHIBITOR OVERCOMES CISPLATIN RESISTANCE IN HEAD AND NECK CANCER

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Head and neck cancers have a high recurrence rate, often due to the development of resistance to cisplatin-based chemotherapy. This resistance is primarily due to upregulated autophagy in cancer stem cells and lysosomal drug sequestration, which allows cancer cells to survive despite chemotherapy. Our study introduces BAQ13, a novel lysosomotropic bisaminoquinoline (BAQ) autophagy inhibitor designed to disrupt autophagy and lysosomal integrity in cancer cells. BAQ13 demonstrates potent anticancer activity by effectively targeting cisplatin-sensitive and -resistant head and neck cancer cell lines. It reduced cell migration and invasion and overcame cisplatin resistance. In cell-derived and patient-derived xenograft models, BAQ13 significantly decreases tumor size, retards lung metastasis, and extends survival, especially in combination with cisplatin. Mechanistically, BAQ13 enhances cisplatin cytotoxicity by regulating oxidative stress production, modulating calcium transportation, and disrupting lysosomal drug sequestration. These actions release cisplatin into the cytosol, increasing its efficacy in killing cancer cells. These findings suggest that BAQ13 holds significant promise as a therapeutic strategy for improving outcomes in head and neck cancer patients by overcoming chemotherapy resistance.

<<PT-38>> IMPACT OF WILDFIRE-DOMINATED PM2.5 ON NON-SMALL CELL LUNG CANCER SURVIVAL IN CALIFORNIA

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Introduction: Wildfires emit hazardous substances, including fine particles ≤2.5 μm (PM2.5). PM2.5 exposure has been associated with lung cancer risk, which is the leading cause of cancer-related death. However, the impact of wildfire-dominated PM2.5 on non-small cell lung cancer (NSCLC) survival is unknown.

Methods: We identified all incident NSCLC patients (N=36,047) in the California Cancer Registry between 2017-2020. We used random forests regression to produce a daily PM2.5 estimate for each centroid of a 1-square kilometer grid across California. We averaged PM2.5 exposures over the 6 months preceding cancer diagnosis based on home address. Cox-proportional hazards regression was used to quantify the hazard ratio (HR) for death from any cause following cancer diagnosis associated with PM2.5 concentration. We adjusted for patient demographics, comorbidity, smoking status, rural/urban residence, and stage at diagnosis.

Results: In the total cohort, a 10 μg/m³ increase in PM2.5 concentration was associated with 12% increased hazard of death (HR=1.12; 95% confidence interval (CI) 1.03-1.22) in never smokers, but not former/current smokers (HR=1.01; 95% CI 1.00-1.12). The association with PM2.5 was more pronounced among stage IV (HR=1.14; 95% CI 1.03-1.25) than stage I (HR 1.08; 95% CI 0.80-1.47) or Stage II/III (HR=1.09; 95% CI 0.89-1.34) never smokers.

Conclusion: In this large cohort of patients with NSCLC, wildfire-dominated PM2.5 exposure was independently associated with increased risk of death, particularly among people with stage IV NSCLC who never smoked. Our findings show a heightened susceptibility to wildfires among these patients, requiring further public health or clinical intervention among these susceptible individuals.

<<PT-39>> HSP70 LEVERAGES STUB1 TO MODULATE N-MYC PROTEIN TURNOVER IN LETHAL PROSTATE CANCER

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Background: Imbalances in protein homeostasis (proteostasis) are associated with a wide range of diseases, including neurodegeneration and tumorigenesis. Prostate cancer has proven to be a key model for understanding how proteostasis regulates tumor progression. Neuroendocrine prostate cancer (NEPC) is the most aggressive type of prostate cancer with no effective treatment. The amplification of N-Myc (encoded by MYCN) is a key modification of NEPC. However, it has proven challenging to identify therapeutic strategies that reduce N-Myc transcriptional activity or levels owing to the presence of intrinsically disordered functional domains and lack of enzymatically active sites. In this study, we sought to take a different approach and identify the molecular chaperones involved in N-Myc proteostasis.

Methods: N-Myc was knocked down by siRNA. Cell proliferation and N-Myc expression were assessed using cell viability assays and Western blotting, respectively. Rapid immunoprecipitation pull-down assays followed by label-free mass spectrometry were used to identify N-Myc-binding proteins. Co-immunoprecipitation (Co-IP) and Proximity Ligation Assay (PLA) were performed to detect the interaction between HSP70 and STUB1 with N-Myc. In vitro ubiquitination assays were conducted to detect the ubiquitination of N-Myc. Site-directed mutagenesis (SDM) was used to construct N-Myc, STUB1, and ubiquitination deletion or point mutation plasmids. Cycloheximide (CHX) chase assays were employed to examine the half-life of N-Myc.

Results: Knockdown of N-Myc by siRNA significantly inhibited the growth of H660, UCDCaP-CR, and CWR22Rv1 cells. A total of 779 proteins were identified as N-Myc-binding proteins. Among them, several HSP70 family proteins, such as HSPA1B (HSP70), HSPA6, and HSPA8 (HSC70), were the most enriched. The HSP70/STUB1 complex interacted with N-Myc and regulated N-Myc protein turnover. This interaction appeared to occur at a degron 'SELILKR' in N-Myc. The K416 and K419 of N-Myc seem to be sites for ubiquitination by STUB1, where it added K11-linked polyubiquitin chains for further proteasome degradation.

Conclusions: The HSP70 interacts with N-Myc at a conserved binding motif and regulates N-Myc protein turnover through STUB1.

<<ET-01>> UC DAVIS COMPREHENSIVE CANCER CENTER SHARED RESOURCES

Aruna Chetty[1,4], Kent Lloyd[2,4], and Ben Spencer[3,4]

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

<<ET-02>> NATIONAL USER RESOURCE FOR BIOLOGICAL ACCELERATOR MASS SPECTROMETRY

Bruce Buchholz, Staff Scientist[2], David Baliu-Rodriguez[1], Heather Enright[1], Mike Malfatti[1], Esther Ubick[1], Dorothy You[1], Jun Jiang[2], Ted Ognibene[2], Graham Bench[2]

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The National User Resource for Biological Accelerator Mass Spectrometry at Lawrence Livermore National Laboratory provides ultra-sensitive isotopic analysis (primarily Carbon-14) by accelerator mass spectrometry (AMS) for NIH-funded and other researchers. It is the only User Resource of its type in the United States and leverages >30 years of expertise in the development and application of AMS in broad-based biomedical research. AMS is a specialized and unique type of mass spectrometry that provides absolute quantitation of radiocarbon and relevant other isotopes with limits of detection in real samples on the order of a few attograms/mg sample. The technology enables a deeper understanding of the etiology of human health concerns by (1) enabling the ability to quantify pharmacokinetics and other molecular endpoints directly in humans; (2) offering the ability to conduct quantitative studies using biologics such as proteins or lipids; and (3) enabling more relevant studies of metabolic pathways in health and disease through the use of much lower, more biologically-relevant, concentrations of metabolic substrates in cells and intact organisms. The User Resource has three goals: (1) provide high throughput, ultra-sensitive 14C analysis for the NIH user community ; (2) improve the efficiency of ultra-sensitive 14C analysis through installation of new interfaces to our AMS systems, improvements in ion source efficiency and upgrades to our data analysis codes; and (3) increase the accessibility and visibility of ultra-sensitive 14C measurements for the biomedical research community by training new investigators and expanding its user base of researchers requiring ultra-sensitive 14C analysis.

POSTER AND EXHIBIT ABSTRACTS (FRIDAY)

<<PF-01>> CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHY IN CHILDREN, ADOLESCENTS AND YOUNG ADULTS WITH CANCER AND MEDICAID INSURANCE IN CALIFORNIA

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Background: Peripheral neuropathy is a common and potentially debilitating effect of chemotherapy. Limited information exists on its incidence among young cancer survivors.

Purpose: To examine the association between chemotherapy and the development of peripheral neuropathy in children (<15 years), adolescents and young adults (AYAs, 15–39) with common cancers.

Methods: Using Medicaid data linked to the California Cancer Registry, hospitalization and emergency department data, we identified 418 children diagnosed with Hodgkin lymphoma (HL) or non-Hodgkin lymphoma (NHL) and 6,028 AYAs with HL, NHL, female breast, colorectal (CRC) or testicular cancer during 2005–2017. Patients were classified as receiving specific neurotoxic versus non-neurotoxic agents identified in Medicaid claims.

Results: Of 6,446 patients, 55% received neurotoxic drugs and 16% developed peripheral neuropathy during a median follow-up of 4.8 years from cancer diagnosis. In multivariable Cox models adjusted for sociodemographic factors and diabetes, across all cancer sites, the hazard of peripheral neuropathy was approximately 2 to 9.5-fold higher among patients who received neurotoxic chemotherapy. The agents with the strongest association with peripheral neuropathy were brentuximab (alone or with other neurotoxic drugs) for HL (Hazard Ratio [HR]=9.5), brentuximab for NHL (alone or with vinca alkaloids, HR=7.0), paclitaxel for breast cancer (HR=4.0); oxaliplatin for CRC (HR=3.5), and cisplatin and etoposide for testicular cancer (HR=2.1).

Conclusions: Our study revealed a high incidence of peripheral neuropathy in a socioeconomically disadvantaged population of young cancer survivors, highlighting the importance of monitoring patients receiving neurotoxic agents. Further development of cancer treatment regimens that reduce neurotoxicity and maintain efficacy is needed.

<<PF-02>> A PILOT STUDY OF INTRATUMORAL SD-101 (TOLL-LIKE RECEPTOR 9 AGONIST), NIVOLUMAB, AND RADIOTHERAPY FOR TREATMENT OF CHEMOTHERAPY-REFRACTORY METASTATIC PANCREATIC ADENOCARCINOMA

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

Methods: Six patients with chemotherapy-refractory, liver-metastatic pancreatic adenocarcinoma were enrolled. SD-101 is injected intratumorally into a liver metastasis on days 1, 8, 15, 29. Localized radiation (6-10 Gy) to the injected lesion was given on days 1, 3, 5, 8, and 10. Nivolumab was given at 240 mg every 2 weeks

starting day 2 until progression or unacceptable toxicity. Primary objective was to evaluate safety and tolerability, defined as ≥5 patients reaching day 29 without experiencing grade ≥3 treatment-related toxicity.

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

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

<<PF-03>> INVESTIGATING THE ROLE OF BRD2 IN RESISTANCE TO BET INHIBITORS IN PANCREATIC CANCER

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Resistance to Bromodomain and Extraterminal (BET) inhibitors remains a significant challenge in the treatment of various cancers, including pancreatic ductal adenocarcinoma (PDAC). This study investigates the role of BRD2 in mediating resistance to BET inhibitors, with a particular focus on the adaptive mechanisms that emerge following treatment. Our findings demonstrate that BET inhibitor treatment, such as with JQ1, leads to the upregulation of BRD2 at both the transcriptional and protein levels in PDAC. Importantly, BRD2 knockdown via shRNA sensitizes these cells to BET inhibitors, indicating that BRD2 may play a crucial role in the development of resistance. To further explore the molecular mechanisms involved, we performed CUT&RUN-seq experiments targeting BRD2, BRD4, and the histone modification H3K27ac in PDAC cell lines treated with JQ1. Our analysis revealed distinct chromatin binding patterns and transcriptional changes associated with BRD2 upregulation, suggesting that BRD2 may compensate for the inhibition of BRD4, thereby contributing to the resistance phenotype. These results enhance our understanding of BRD2's role in BET inhibitor resistance and may inform future therapeutic strategies aimed at overcoming this challenge in PDAC and potentially other BRD2-overexpressing cancers.

<<PF-04>> HEXAMETHYLENE AMILORIDE-MEDIATED INDUCTION OF LYSOSOMAL MEMBRANE PERMEABILIZATION

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Hexamethylene amiloride (HMA) is a cationic amphiphilic drug that has been linked to selectively targeting tumor cells and inducing cancer cell death. A gap exists in the use of current cancer therapies (including chemotherapy, radiation, and immunotherapy), which each have a plethora of side effects and demonstrate ineffectiveness in individual cases for tumors that have developed immunity. In conjunction with the common cancer therapeutics currently in use, HMA has the capacity to become a novel therapy with minimal side effects. This project intends to uncover the mechanism by which HMA induces cell necrosis and whether this mechanism could be via the induction of membrane permeabilization. Through cell fluorescence microscopy on HMA-treated breast cancer cell lines, HMA-induced necrosis via lipid peroxidation can be colocalized to the lysosome, mitochondria, and/or plasma membrane. Quantification of lipid peroxidation pre and post-treatment as well as cross-correlation with the mentioned organelles in the cells treated allow for conclusions to be drawn about how HMA truly works. Further analysis of HMA and its cytotoxic effects have the potential for optimized drug development, so that it may be used as a cancer therapeutic and aid in the fight against drug-resistant tumors.

<<PF-05>> CHEMICALLY OPTIMIZING AMILORIDE TO GENERATE HIGHLY EFFECTIVE DERIVATIVES THAT SELECTIVELY TARGET TRIPLE-NEGATIVE BREAST CANCER STEM CELLS

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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 conventional and targeted therapeutic agents. Consequently, subpopulations of apoptosis-resistant cells such as cancer stem cells (CSCs) persist after therapy to seed primary tumor recurrence and metastatic lesions, even after complete remission. The overarching goal of this project is to develop novel drugs that exploit the process of lysosome-dependent cell death, one of the programmed necrotic cell death mechanisms, in suppressing CSC-mediated triple-negative breast cancer. We have previously observed that hexamethylene amiloride (HMA), a derivative of the FDA-approved diuretic amiloride, is cytotoxic in vitro and ex vivo toward cultured cells from a variety of tumor types but not non-transformed cells 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 that alters lysosome structure, dysregulates lipid synthesis, leads to lysosomal membrane permeabilization, and acts efficiently toward therapy-resistant CSC-related subpopulations. Moreover, we have observed that amiloride derivatives modified at its C(5) amine exhibit a strong relationship between the hydrophobicity 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 disrupt lipid metabolism and suppress tumor growth.

<<PF-06>> INNOVATIVE STRATEGIES FOR TARGETED NEUROBLASTOMA THERAPY: INTEGRATING MIRNA THERAPEUTICS WITH NANOPARTICLE DELIVERY

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Neuroblastoma (NB), a neural crest progenitor cell derived tumor, is the most frequently occurring childhood tumor and most patients are diagnosed with high-risk NB. High-risk NB has a survival rate of less than 50% underscoring the need for a novel therapy. The significant challenges with NB treatment are due to tumor heterogeneity and limited treatment efficacy which result in poor prognosis and outcomes for children diagnosed with this cancer. This proposal aims to address therapeutic challenges in a high-risk NB treatment through optimization of a nanoparticle encapsulated delivery of microRNAs (miRNAs) to NB cells. Our study focuses on investigating the effect of two specific miRNAs, miR-34 and miR-124 which are known for their tumor-suppressive roles and potential therapeutic effects in NB.

Our project aims to optimize polymer nanoparticle formulations for efficient miRNA loading, evaluate the impact of miRNAs on reporter gene expression in NB cells, and assess the potential synergy between miRNAs and chemotherapeutics in suppressing NB cell growth. We hypothesize that optimized formulations will enhance miRNA loading efficiency, delivery of miR-34 and miR-124 will downregulate reporter gene expression in NB reporter cell lines and that miRNA-loaded nanoparticle cotreatment with chemotherapeutics will sensitize NB cells to chemotherapeutics will sensitize NB cells to chemotherapeutics and inhibit cell growth more than chemotherapy alone.

Various techniques such as gel electrophoresis, dynamic light scattering, zeta potential measurements, electron microscopy, fluorescence microscopy, and flow cytometry will be utilized to characterize the miRNA-loaded nanoparticle complexes and their effects on NB cells. This project is expected to span eight months with milestones including optimization of nanoparticle formulation for efficient miRNA loading, establishment of

a stable reporter gene NB cell line, and evaluation of miRNA-based suppression and inhibition of NB cell growth.

We hypothesize that by optimizing nanoparticle formulations for delivering miRNAs to NB cell lines they should demonstrate enhanced miRNA loading capacity compared to initial formulations. Establishment of stable reporter gene NB cell lines expressing GFP and luciferase will enable the assessment of reporter gene expression modulation by miRNAs. The introduction of miRNA via lipofectamine transfection or nanoparticle delivery should result in observable changes in reporter gene expression levels. Treatment of NB cell lines with miR-124 or miR-34 delivered via lipofectamine transfection or via miRNA-loaded nanoparticles (polyplexes) is anticipated to lead to a reduction in cell proliferation compared to untreated cells. This research holds promise for advancing NB treatment by learning more about the effects of these specific miRNAs on NB cell growth and it contributes to the future goal of using mesenchymal stem cells as drug delivery vehicles carrying miRNA treatment to NB cells in vivo in future studies.

<<PF-07>> EFFICACY OF INDIVIDUAL LET-7-5P ISOFORMS IN THE MODULATION OF TARGET GENE EXPRESSION IN HCC CELLS

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Multidrug resistance (MDR) is a major barrier in the treatment of hepatocellular carcinoma (HCC) and other cancers and is characterized by the overexpression of efflux transporters such as ABCC1-5 that are critical to the absorption, distribution, metabolism, and excretion (ADME) processes of chemotherapeutic drugs. Endogenous microRNA (miRNA) are small noncoding RNAs that are critical posttranscriptional regulators of a wide variety of cellular processes, capable of targeting multiple mRNA transcripts to modulate drug transport and disease progression. The let-7-5p miRNA family consists of several unique isoforms that have demonstrated potential in previous experiments inhibiting HCC viability and negatively regulating the expression of ADME genes implicated in MDR. To further elucidate the therapeutic potential and efficacy of individual let-7-5p isoforms against HCC, a novel in vivo fermentation based, RNA bioengineering approach was used to produce unique biologic let-7-5p miRNAs (BioRNA/let-7-5p) in high yield. This study identified suitable liver cell line models to study potential modulation of several protein levels (ABC transporters ABCC1-5 and oncogenic, RNA-binding protein LIN28B) by let-7-5p isoforms. Additionally, this study employed selective stem loop RT-qPCR methods to validate the processing of novel bioengineered miRNA let-7-5p (BioRNA/let-7-5p) molecules to respective let-7-5p isoforms in human liver cells. Finally, western blot analysis was utilized to elucidate the impact of individual BioRNA/let-7-5p agents on the protein outcomes of ABCC5 and LIN28B in HCC cells. These results demonstrating downregulation of ABCC5 following BioRNA/let-7-5p treatment will inform the direction of future study exploring rational combination with chemotherapies in HCC.

<<PF-08>> INVESTIGATING THE LONGITUDINAL EFFICACY AND RESISTANCE MECHANISMS OF ANTI-PD-1 THERAPY IN A MURINE NSCLC MODEL USING SINGLE-CELL AND SPATIAL TRANSCRIPTOMICS

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Lung cancer is the leading cause of cancer-related deaths globally, with non-small cell lung cancer (NSCLC) comprising ~85% of cases, often diagnosed at advanced stages with limited treatment options. Anti-programmed cell death protein 1 (anti-PD-1) immunotherapy is a first-line treatment for patients without tumor-driving gene mutations, but only 15-20% of NSCLC patients respond positively. Responders may develop primary or acquired resistance, leading to cancer progression. This study uses a murine lung cancer cell line representative of NSCLC, derived from a genetically engineered mouse model expressing KrasG12D and P53-/flox mutations in club cells. After establishing the cell line, cells were subcutaneously injected into

immunocompetent C57BL/6 mice and treated with anti- PD-1 therapy for 3 weeks. Tumor growth curves showed a significant size reduction in anti- PD-1-treated tumors compared to the IgG isotype control group ($p < 0.045$). To assess tumor microenvironment dynamics, single-cell RNA sequencing and spatial transcriptomics were performed during and after anti-PD-1 treatment. Samples were collected at 1- and 3-weeks during treatment, and 3 weeks post-treatment. Single-cell RNA sequencing revealed changes in immune recruitment, while relapsed tumors exhibited elevated myeloid gene expression and a shift to a fibrotic phenotype post-therapy. Supporting the fibrotic phenotype, we observed high expression of Spp1 in the malignant cells. These findings suggest initial responsiveness to anti-PD-1 therapy, followed by significant microenvironmental changes. This study underscores the translational potential of our oncogenic cell line in understanding NSCLC and its response to anti-PD-1 therapy.

<<PF-09>> MARCKS IN MACROPHAGES CONTRIBUTES TO LUNG CANCER PROGRESSION

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Lung cancer is one of the leading causes of death in the United States, with more than 130,000 deaths per year. We identified MARCKS, myristoylated alanine-rich c-kinase substrate, as a potential therapeutic target for lung cancer, where its phosphorylation increases tumorigenesis and cancer cell migration. MARCKS also exhibited abundant expression in tumor-associated macrophages (TAMs) which have garnered attention for their involvement in cancer progression. To understand the function of MARCKS in TAMs in lung cancer development, the differential expressed genes (DEGs) in MARCKS-expressing TAMs from lung cancer scRNAseq analysis were used for DAVID pathway enrichment. The enriched pathways included Efferocytosis pathway which created a tumor-favorable microenvironment, several interleukin pathways, IL10, IL4, IL13, and IL6, and CD163 mediating anti-inflammatory responses, which are involved in macrophage polarization towards an M2-like (anti-inflammation) phenotype, and CCR5 chemokine receptor binding pathway which promoted cancer proliferation and migration. Furthermore, the identification of the pathway, negative regulation of T cell-mediated immune response to tumor cells, suggested MARCKS in TAMs may also play a role in tumor immune evasion. In summary, MARCKS-expressing TAMs play a pivotal role in lung cancer progression, influencing tumor microenvironment and immune evasion mechanisms, highlighting its potential as a therapeutic target.

<<PF-10>> ANGEL2 MODULATES ENFORTUMAB VEDOTIN CHEMOSENSITIVITY IN MUSCLE INVASIVE BLADDER CANCER

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Enfortumab vedotin (EV) administered with pembrolizumab is anticipated to be a first line treatment against muscle invasive bladder cancer (MIBC) as it increases overall survival to current platinum-based treatments. However, only ~30% of patients that receive EV treatment achieve complete response. Consequently, there is an unmet need to understand the mechanisms driving EV resistance. EV is an antibody-drug conjugate that binds to NECTIN4 which delivers monomethyl auristatin E (MMAE), a cytotoxin, to kill the tumor. However, clinical data shows NECTIN4 is not ubiquitously expressed in MIBC, making EV ineffectual in these patients. Furthermore, in certain tumors with NECTIN4, EV is also ineffective highlighting the necessity to better understand the drivers of EV resistance. Herein, we demonstrate that the efficacy of EV, and its MMAE warhead, is directly correlated to the expression of the protein ANGEL2. Cell viability assays illustrate that EV is ineffective in NECTIN4 expressing SW780 ANGEL2-null cells, whereas wildtype (WT) cells were highly sensitive. Further, assays on WT and ANGEL2-null cells treated with MMAE monotherapy demonstrate a significantly reduced efficacy in cells with loss of ANGEL2 at physiological concentrations. 10X Genomics Visium analysis of two MIBC patients demonstrated that NECTIN4 is not ubiquitously expressed throughout

the tumor. We demonstrate that loss of ANGEL2 is inversely associated with EV sensitivity. Thus, we hypothesize that ANGEL2 may serve as a prognostic biomarker identifying resistance to EV due to modulation of NECTIN4 and MMAE drug sensitivity.

<<PF-11>> FLUORESCENCE LIFETIME IMAGING WITH PROTOPORPHYRIN IX FOR DIFFERENTIATING BETWEEN CANCER AND HEALTHY TISSUES IN SPONTANEOUSLY OCCURRING CANINE ORAL SQUAMOUS CELL CARCINOMA

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To date, there is no non-invasive pre-operative or intraoperative diagnostic capable of accurately delineating neoplastic and healthy tissues in the oral cavity of dogs. Surgical safety margins are employed to ensure removal of all potential non-visible neoplastic cells, yet this compromises healthy tissue and introduces substantial functional complications. Despite the attempt to achieve safety margins, local recurrence rates are reported in up to 28% of canine oral squamous cell carcinoma (SCC) and remains as the 3rd highest positive surgical margin rate amongst human cancers. Fluorescence lifetime imaging (FLIm) with autofluorescence has been utilized intraoperatively for human SCC with good success. The aim of this study was to evaluate diagnostic accuracy of Protophoryin IX (PpIX) compared to autofluorescence lifetime measurements to differentiate between cancer and healthy tissues in a spontaneous large animal model of disease. The mechanistic drivers of changes in visual PpIX appearance and spectral signatures were evaluated by looking at the enzymes of the heme biosynthetic pathway and nanostring spatial transcriptomics.

<<PF-12>> SINGLE-CELL RESOLUTION IMPACT OF RADIATION THERAPY ON MURINE SQUAMOUS CELL CARCINOMAS IN-VITRO REVEALS ITS COMPLICATED ROLE IN REGULATING IMMUNITY

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Immunotherapy may be more efficacious in combination with radiation therapy (RT), though the limitations of this combination remain under-studied. While RT induces immune-stimulatory genes like classical class I HLA, it has also been shown to induce immune-regulatory HLA-E expression, which binds to NKG2A/CD94 on T and NK lymphocytes. The mechanisms by which RT may induce HLA-E expression in a cancer-intrinsic manner are unknown. To investigate this phenomenon, we employ 2 mouse models of squamous cell carcinoma (SCC). A223 previously responded to RT + immunotherapy, while P029 did not. We treated both cell lines in-vitro with 10 Gray RT, allowed cells to incubate for 48 hours, and conducted single-cell RNA sequencing. In a biased analysis, both immune-activating and inhibiting ligands increased in expression in A223 but not P029, highlighting the complicated role of RT in modulating antitumor immunity. Both NKG2D ligands and the murine HLA-E homologue, Qa-1, increased in expression in A223 but not P029. In an unbiased analysis, RT induced an inflammatory cell state in A223 and to a lesser degree in P029. Broad transcriptional trends were observed by gene set analysis, hinting at signaling differences that may be responsible for the differential responses to RT. Ultimately, these results provide rationale for investigating anti-NKG2A or anti-HLA-E therapy in combination with RT, which would hopefully tilt the scale towards immune stimulation. Further research should verify how Qa-1 surface expression changes with RT and how that might be regulated.

<<PF-13>> LEVERAGING KEY INFORMANT INTERVIEWS AND FOCUS GROUPS TO INFORM INTERVENTION DEVELOPMENT: THE HEALTHY CERVIX PROGRAM (HEALIX)

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Background: Disparities in cervical cancer outcomes affect Hispanic/Latinx communities despite the availability of effective cervical cancer screening and prevention tools. The goal of the study was to prepare for the implementation of a community clinic health-educator (CHE) and navigator based cervical cancer education, prevention, and screening intervention, tailored to Spanish-speaking individuals at a federally qualified health center (FQHC).

Methods: We conducted 11 semi-structured interviews with FQHC staff and 2 focus groups with patients during pre-implementation. Rapid qualitative analysis was utilized to analyze the interviews and focus groups. The Consolidated Framework for Implementation Research (CFIR) identified barriers and facilitators to cervical cancer screening and human papillomavirus (HPV) vaccination. Focus group participants reviewed patient facing intervention materials and provided feedback on usability, informing the intervention methodology.

Results: Clinic staff identified barriers such as lack of transportation, low health literacy, and limited knowledge of cervical cancer as reasons for high non-compliance with preventative behaviors. Facilitators included: the availability of a clinic reporting data tool, strong patient-provider relationships, and HEALIX's alignment with the FQHC's mission. Meanwhile, focus groups emphasized materials being clear and concise.

Conclusions: Academic-clinic partnerships for implementation of evidence-based interventions in FQHCs requires an understanding of individual and institutional barriers and facilitators to build effective programs. Results of this study informed the design and implementation of the HEALIX program, which aims to remove barriers to cervical cancer screening and HPV vaccination for patients, as well as leverages the alignment between the program and the clinic goals for collaboration as implementation moves forward.

<<PF-14>> IMPACT OF PRIMARY CARE INITIATED LUNG CANCER SCREENING PROGRAM: THE VANCHCS EXPERIENCE

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Introduction: Despite the known benefits of low dose CT scan (LDCT) in improving the survival of lung cancer patients through early diagnosis, screening rates remain low across the United States. To address the need for improved lung cancer screening (LCS), a primary care-based LCS program was initiated at the VA Northern California Health Care System (VANCHCS) in 2017. We conducted this retrospective study to evaluate the impact of LCS program on the stage of lung cancer diagnosis between 2012 and 2022.

Methods: Eligible Veterans were screened by primary care providers who ordered LDCT scans. A dedicated LCS coordinator reviewed the Lung-RAD reports and coordinated diagnostic workups with relevant specialists. The Chi-square test was conducted to assess the difference in screening rates across all and different race groups.

Results: Between 2012 and 2022, 1073 Veterans were diagnosed with lung cancer at VANCHCS. While the total number of lung cancer cases diagnosed per year remained stable, there was a notable increase in the proportion of patients diagnosed at stage I and a decrease in stage IV over time. Before 2017, the average percentages of patients diagnosed at stage 1 and stage 4 were 23.6% and 44.1% respectively. However, from 2018 to 2022, the average percentages increased to 38.3% for stage 1 and decreased to 34.8% for stage 4.

Conclusions: The primary care provider-initiated LCS program at VANCHCS has enhanced the clinical implementation of lung cancer screening. Further studies are needed to address the disparities in screening rates, particularly among Black and Hispanic Veterans, and to evaluate the impact of this LCS program on cancer-specific mortality at VANCHCS.

<<PF-15>> CHARACTERIZATION OF PARP INHIBITOR RESPONSE IN PROSTATE TUMOR CELLS REVEALS DRUG TOLERANT PERSISTENT PHENOTYPE

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Background: PARP inhibitors (PARPi) have improved management of prostate cancer, but acquired resistance remains inevitable. Drug tolerant persistence (DTP) is characterized by a small population of tumor cells which survive treatment through transient acquisition of insensitivity. DTP cells are not intrinsically resistant but may slowly proliferate, allowing for mutation accumulation, development of resistance, and progression. Characterization of drug tolerant persistence and mechanisms enabling a DTP state under PARP inhibition remain unknown in prostate cancer.

Methods: Viability assays determined efficacious doses of olaparib and rucaparib in PARPi sensitive C4-2B metastatic castration-resistant prostate cancer cells and the C4-2B abiraterone-resistant derivative cells, AbiR. Various assays were used to characterize response to olaparib and rucaparib. RNA-seq determined the transcriptomic profile of PARPi DTP cells.

Results: C4-2B and AbiR response to olaparib and rucaparib is heterogeneous, characterized by cell death and cytostasis. Despite prolonged exposure to high dose PARPi, we observe a small minority of cells which persist, display varying altered morphologies, and altered cell cycle dynamics. C4-2B and AbiR cells exposed to high PARPi dosing for 9 days followed by drug holiday regain normal, parental cell morphology and become re-sensitized to treatment in line with acquisition of a DTP phenotype. RNA-seq reveals transcriptomic characteristics of drug tolerant persistence including increased mutability, altered metabolism, and cell identity changes.

Conclusions: Our data suggest that transient, drug tolerant persistence may mediate survival of a minority of tumor cells. Future efforts will characterize this phenotype further and investigate vulnerabilities that target survivors to improve treatment efficacy.

Acknowledgements: NCI K01 (K01CA262351) (APL), NIH eMCDB T32 (AK)

<<PF-16>> DISTINCT DOMAINS OF TENSIN 3 AND CTEN INTERACT DIRECTLY WITH FORCE-BEARING KERATIN FILAMENTS

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Cellular response to mechanical force is crucial for cell proliferation, their barrier functions, and cancer progression. The tensin family, implicated in cancer development and metastasis, are critical phosphoproteins involved in cytoskeletal regulation by directly linking actin filaments to integrin receptors. Interestingly, the tensin family's interaction with the cytoskeletal network extends beyond actin filaments. Tensin 3 and tensin 4 (also known as cten) rapidly accumulate along tensed keratin fibers in epithelial cells, suggesting that keratin fibers, known for their role in the structural integrity of epithelial cells, are also active participants in mechanotransduction pathways. Notably, the highly conserved C-terminal Src Homology 2 (SH2) and

phosphotyrosine-binding (PTB) domains are dispensable for the force-sensitivity of tensin 3 and cten. Instead, the force-induced accumulation relies on distinct regions: unique alpha-helical structures in the central region of tensin 3 and disordered regions in the N-terminal domain of cten. To further investigate whether tensin 3 and cten proteins bind directly or indirectly to the force-bearing keratin filaments, we developed an in vitro force-dependent protein interaction assay using recombinant keratin 8 and keratin 18 and a microneedle to apply strain. Importantly, GFP-tagged force-sensitive regions of tensin 3 and cten proteins selectively and directly bind to the force-bearing keratin filament bundles in vitro. These results collectively demonstrate that distinct domains of tensin 3 and cten interact directly with force-bearing keratin intermediate filaments. Unraveling the molecular details of the tensin proteins' force sensitivity may provide insights into how mechanical forces regulate tumorigenesis and metastasis.

<<PF-17>> LEUKOCYTE IMMUNOGLOBULIN-LIKE RECEPTOR (LILRB2)-TARGETED JTX-8064 PLUS THE ANTI-PD1 INHIBITOR JTX-4014 (PIMIVALIMAB) IN IMMUNE-CHECKPOINT INHIBITOR (ICI)-PRETREATED PATIENTS (PTS) WITH ADVANCED OR METASTATIC RENAL CELL CANCER (MRCC): RESULTS FROM THE MULTI-STAGE PHASE 1-2 INNATE TRIAL

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Background. Disease progression following treatment of mRCC pts with ICI-based therapy (tx) is nearly universal, warranting evaluation of novel immunotherapeutic approaches. LILRB2 is an immune checkpoint molecule expressed primarily in cells of myeloid origin (e.g., monocytes/macrophages). Inhibition of LILRB2 reprograms macrophages from an immunosuppressive (M2) to an immunostimulatory (M1) phenotype. JTX-8064 is a humanized monoclonal antibody that binds to LILRB2, blocking its interaction with MHC1 molecules. Preclinical studies suggest that JTX-8064 can overcome anti-PD(L)1 resistance mechanisms. Here we report the results of an expansion cohort of previously-treated mRCC pts in INNATE, a multi-stage phase 1-2 trial of JTX-8064 in combination with anti-PD1 agents in solid tumors.

Methods. Pts with pathologically-confirmed clear cell mRCC progressing on or after anti-PD(L)1 tx in the most recent prior line, acceptable end-organ function, and ECOG PS 0-1 were treated with JTX-8064 700 mg and JTX-4014 500 mg IV q3 weeks. Primary endpoint was overall response rate (ORR); secondary endpoints were safety, disease control rate (DCR), progression-free survival (PFS), and overall survival (OS). A Simon 2-stage design (n=10+19) was employed where ORR >= 20% was deemed to be of further interest versus null hypothesis of ORR <= 5%, with alpha=0.05.

Results. 31 pts were enrolled, with median age of 64 years (range 38-85); 84% males; 16% Hispanic; 93% White; 45% PS=0; 71% one prior tx line. Of 28 pts evaluable for response, 1 CR, 1 PR, 14 SD (6 SD >= 6 months), and 11 PD were seen for an ORR of 7% and DCR of 54%. Median PFS was 4 months (95%CI: 2, 6.8); 12-month OS was 75% (95%CI: 55,88). Tx-related adverse events (AE) of all grades were reported in 11 pts (45%), most commonly fatigue (16%) and diarrhea (10%). Only 4 protocol-related G3-4 AEs were reported: thrombocytopenia (G4); diplopia, diarrhea, and bradycardia (all G3). Three on-study deaths (hypotension; cardiorespiratory arrest; and unknown) were deemed unrelated to protocol tx.

Conclusions. While ORR did not meet the protocol-defined efficacy target, evidence of anti-tumor activity was seen in ICI pre-treated mRCC pts with combination JTC-8064 + JTX-4014. Treatment was reasonably well-tolerated. Identification and evaluation of clinical and molecular phenotypes most likely to benefit from LILRB2-targeted therapies are warranted.

<<PF-18>> IGFBP3 SIGNALING PROMOTES RESISTANCE TO NEXT-GENERATION ANTIANDROGENS THERAPEUTICS IN ADVANCED PROSTATE CANCER

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Next-generation antiandrogen therapeutics (NGATs) have irrefutably improved the survival of prostate cancer patients. However, treatment resistance to NGATs remains a clinical challenge for men with castration-resistant prostate cancer (CRPC). The molecular mechanisms underlying resistance to NGAT remain confounding. Insulin growth factor binding protein 3 (IGFBP3) is associated with prostate cancer tumorigenesis and progression. It is known that IGFBP3 induces sphingosine kinase (SphK1) activation subsequently inducing sphingosine-1-phosphate (S1P) production. Previously, we found that IGFBP3 is necessary for PARP inhibitor (PARPi) resistance in acquired resistant models (OlapR cells). We hypothesize that IGFBP3 is required for acquired and intrinsic NGAT resistance. We discovered that IGFBP3 expression was increased in CRPC patients' post-enzalutamide treatment compared to those before treatment. We hypothesize that IGFBP3 is required for acquired and intrinsic NGAT resistance. This study found that IGFBP3 was upregulated in NGAT resistant models (MDVR, AbiR, ApalR, DaroR, 42D, 42F, and 22Rv1 cells) using transcriptomics. We found that NGAT resistant models highly express IGFBP3 and Sphingosine-1-Kinase (SphK1) using qPCR and western blot. SphK1 is a lipid kinase that phosphorylates sphingosine to form sphingosine-1-phosphate (S1P) metabolite which promotes tumor survival and resistance. We discovered high levels of IGFBP3 and S1P secretion in the resistant models. We found that inhibition of IGFBP3/SphK1 decreased both SphK1 expression and S1P secretion. Mechanistically, IGFBP3 activated the Sphingolipids pathway to promote survival and subsequently enforce the growth factor signaling to enhance cell proliferation. Our findings demonstrate that targeting the IGFBP3/SphK1 signaling axis enhances our ability to resensitizes resistant CRPC to NGAT therapeutics.

<<PF-19>> IGFBP3 PROMOTES TAXANE-OLAPARIB CROSS RESISTANCE IN ADVANCED PROSTATE CANCER

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Taxanes, PARP inhibitors (PARPi), and next-generation antiandrogen therapies (NGATs) are the main classes of drugs used to treat castration-resistant prostate cancer (CRPC). The 1st – generation and 2nd – generation taxanes, Docetaxel and Cabazitaxel, have vastly improved the survival of metastatic CRPC patients. Unfortunately, therapeutic resistance hinders the treatment of patients with advanced, lethal prostate cancer. Previously, we chronically exposed C4-2B CRPC cells to Docetaxel (TaxR) and Cabazitaxel (CabR) to create acquired Taxane-resistant models. Both TaxR and CabR display robust resistance to their respective taxanes, Docetaxel and Cabazitaxel. We established that TaxR cells are not only intra cross-resistant to Cabazitaxel but also display inter cross-resistance to the PARPi, Olaparib. We discovered the Insulin Growth Factor Binding Protein 3 (IGFBP3) was upregulated in the acquired Olaparib-Resistant (OlapR) cells and that silencing IGFBP3 expression re-sensitized the OlapR models to PARP inhibition. Next-generation sequencing revealed that IGFBP3 expression was increased 2.4-fold and 13.7-fold in TaxR and CabR cells, respectively. We hypothesize that IGFBP3 mediates cross-resistant phenotype between Taxanes and Olaparib in the Taxane-resistant models. Using qPCR, we verified that IGFBP3 mRNA levels are upregulated in the resistant cells. The western blot revealed that TaxR and CabR express high levels of IGFBP3 protein in comparison to C4-2B cells. We used RNA interference (RNAi) to inhibit the expression of IGFBP3. Our cell growth assays showed that silencing IGFBP3 via siRNA in the CabR cells decreased cell proliferation which promoted Cabazitaxel sensitivity. Our findings demonstrated that inhibiting IGFBP3 aids in Taxane sensitivity in the resistant setting.

<<PF-20>> DEEP INTERACTIVE LEARNING-BASED SEGMENTATION OF CANINE ORAL SQUAMOUS CELL CARCINOMA AND MELANOMA IN HISTOPATHOLOGICAL SLIDES FOR ENHANCED TUMOR DETECTION

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Management of oral cancers, such as squamous cell carcinoma (SCC) and melanoma, involves surgical resection aimed at achieving negative margins. Pathologists play a crucial role during these procedures by identifying cancerous cells in histological slides from excised tissue. However, in situ margin assessment during surgery faces challenges, including time-consuming section preparation, diagnostic errors due to artifacts, limited tissue coverage, and high stress on pathologists under time constraints. These issues can lead to variability in accuracy and the risk of incomplete resection, underscoring the need for innovative solutions to improve intraoperative pathology. Deep learning has proven effective in analyzing digitized hematoxylin and eosin (H&E)-stained histopathology slides, enhancing cancer detection and morphological analysis. In this study, we propose using Deep Learning (DL) to segment canine oral squamous cell carcinoma and melanoma from H&E-stained slides, leveraging a pre-trained model from canine cutaneous cancer segmentation. The model demonstrated strong performance on canine oral cancer data, significantly reducing annotation time while maintaining high segmentation accuracy. Our findings lay the groundwork for future research into AI applications in veterinary oncology, where resources are often more limited compared to human healthcare. This study aims to advance AI-driven techniques in veterinary pathology and contribute to the growing field of canine oral cancer research.

<<PF-21>> INVESTIGATING THE ROLE OF WNT/PCP SIGNALING IN THE REPROGRAMMING OF ENERGY METABOLISM IN BREAST CANCER

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Breast cancer is the second leading cause of cancer death in women worldwide, 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.

<<PF-22>> STUDYING T CELL MEMORY PHENOTYPES IN CART CELL THERAPY FOR B CELL LYMPHOMA

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Advancements in CAR-T cell therapy have demonstrated significant potential in cancer treatment by enhancing T-Cell targeting of cancer cells via genetic modification. A study at UC Davis focused on CAR-T cell therapy for B cell lymphoma and achieved an 85% response rate and a 78% remission rate out of 17 patients. Our research aims to investigate T cell memory phenotypes, cytoxic T central memory cells (TCM), cytotoxic T effector memory cells (TEM), helper TCM cells, and helper TEM cells. Preliminary results indicate a possible correlation between reduced levels of helper T memory cells and adverse clinical outcomes.

<<PF-23>> PORTABLE AND AUTOMATED SAMPLER TO MONITOR VOC EXPOSURES OF FIREFIGHTERS ACTIVELY FIGHTING WILDLAND URBAN INTERFACE FIRES

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Firefighters in California who routinely fight fires at the wildland urban interface (WUI) are exposed to carcinogens like volatile organic compounds (VOCs) generated by combustion. Yet, firefighters lack tools that monitor VOC exposures to derive data-driven protective strategies and reduce cancer risks. Through a collaboration between researchers at UC Davis and the Los Angeles County Fire Department (LACoFD), our team has developed a portable, battery-operated sampler to automatically collect environmental VOC samples while firefighters actively combat WUI fires. Devices are mounted onto the firetruck and take a “set it and forget it” approach, automatically engaging at predetermined sampling frequencies and durations through multiple days of firefighting activities, requiring minimal interaction by firefighting personnel. Each sampler contains 4 sorbent-packed micro-preconcentrator chips, allowing collection and preservation of four separate environmental samples from a single charge for subsequent offline analysis. Analytical methods target PAHs, PCBs, brominated flame retardants, organophosphates, pesticides, and other VOCs of concern. The sampler has been tested during fire training sessions and will be deployed by LACoFD in the upcoming 2024-25 wildfire season. Through continued partnerships with LACoFD, we aim to deploy devices and correlate firefighting activities with high incidents of VOC exposure to recommend interventions and decrease cancer risk among California firefighters. In the next design iteration, the sampler will contain a portable chemical detector chip that can measure VOC exposures in real time.

<<PF-24>> REPORTING OF RACE AND ETHNICITY IN PEDIATRIC ONCOLOGY CLINICAL TRIALS: A SCOPING REVIEW

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The consistent reporting of race and ethnicity in clinical trials is critical for ensuring equitable health outcomes and enhancing the applicability of research across diverse populations. However, research has shown there is a gap between policy and practice with regard to race and ethnicity reporting in clinical research. This study aims to assess the frequency and patterns of race and ethnicity reporting in pediatric oncology clinical trials.

We conducted a scoping review of U.S. and international pediatric oncology clinical trials published between 2013 and 2022. Only studies with cancer-directed therapy as the main focus and a majority of pediatric patients (under 18 years old) were included. Using Covidence, a systemic review management tool, 6,386 studies were imported for screening, of which 5,205 studies were excluded based on title and abstract. A total of 1,045 full-text articles were assessed for eligibility, and 572 studies met the inclusion criteria. Currently, data extraction is underway from the eligible studies, focusing on study design and participant demographics, with particular attention to race and ethnicity reporting.

The findings from this scoping review will inform future research efforts by highlighting the need for standardized reporting practices in pediatric oncology clinical trials. By improving the consistency and transparency of race and ethnicity data, researchers can better address disparities in cancer treatment and outcomes among diverse pediatric populations. This review underscores the importance of including comprehensive demographic information in clinical trial reporting to ensure that all patient groups are adequately represented.

<<PF-25>> CANCER INCIDENCE IN PERSISTENT POVERTY AREAS OF CALIFORNIA BY RACE/ETHNICITY

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Background: While several studies have examined the relationship between living in persistent poverty areas (PPAs) and adverse cancer outcomes, the relationship between PPAs in California and disparities in cancer incidence rates and trends by race/ethnicity are unknown.

Purpose: Understand the impact of poverty on the cancer burden in California.

Methods: PPAs are defined as census tract of residence at time of diagnosis with a poverty rate of at least 20 percent for approximately 30 years. Using California Cancer Registry data, we identified patients diagnosed with 16 common cancers between 2006-2020. We compared incidence rates (AAIRs), rate ratios (RRs), and average annual percent changes (AAPCs) among patients in PPAs and non-PPAs by race/ethnicity.

Results: Of the 2,493,936 patients, 162,538 (6.5%) lived in PPAs. Across all racial/ethnic groups, AAIRS of cervical and liver cancers were significantly higher among patients in PPAs. Among non-Hispanic/Latina Whites, cervical cancer significantly decreased only in non-PPAs (AAPC=-2.0). Incidence of colorectal cancer and non-Hodgkin lymphoma among Hispanic/Latinos increased significantly in PPAs (AAPC=0.4, 1.2). Thyroid cancer incidence among Black/African Americans significantly increased in PPAs (AAPC=4.7). Among

American Indian patients, significant increases were observed for most cancers in non-PPAs, although trends for many cancers could not be calculated in PPAs due to small numbers.

Conclusion: Populations living in PPAs of California would benefit from public health interventions. Our findings of higher AAIRs of cervical and liver cancers across all racial/ethnic groups among patients in PPAs call for additional research to appropriately distribute cancer prevention resources to reduce the observed disparities.

<<PF-26>> OPTIMIZING CAR-T CELL THERAPY: REDUCING MANUFACTURING TIME AND EXAMINING T CELL MEMORY PHENOTYPES IN B CELL LYMPHOMA

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Chimeric Antigen Receptor T cell (CAR-T) therapy has revolutionized oncology by enabling T-cells to target cancer cells effectively. Our study at UC Davis (IND 26979) on CAR-T therapy for B cell lymphoma achieved an 85% response rate and 78% remission rate among 17 patients. Building on these results, we aimed to refine CAR-T therapy by analyzing T cell memory phenotypes and optimizing the manufacturing process.

Traditionally, CAR-T cell manufacturing takes 12 days, followed by a 3-week cryopreservation hold, delaying patient treatment and increasing costs. Our study reduced the manufacturing time to 8 days with fresh cell infusion, maintaining efficacy and safety. We compared the traditional 12-day process with our 8-day protocol, evaluating Vector Copy Number, Replication Competent Lentivirus Levels, anti-CD19 CAR transduction efficiency, and cell viability. Our cohort of 3 patients showed a 100% manufacturing success rate for the 8-day process, comparable to the 12-day process. Patients treated with the 8-day protocol demonstrated a 100% survival rate and reduced treatment costs.

Implementing fresh cell infusion allows patients to receive cells 3 weeks sooner. This innovation led to an FDA-approved process amendment, marking a significant advancement in CAR-T therapy. We also examined T cell memory phenotypes to assess their relationship with clinical outcomes. Initial findings suggest a correlation between depleted helper T memory cells and adverse outcomes.

Our study shortens treatment time, reduces costs, and enhances the understanding of immune responses in CAR-T therapy, potentially improving access and advancing personalized medicine for B cell lymphoma patients.

<<PF-27>> CHALLENGES IN RECRUITING FOR A RANDOMIZED CONTROLLED INTERVENTION TO INCREASE LUNG CANCER SCREENING

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Introduction: Lung cancer is the most fatal of all cancers, but of the four US Preventive Services Task Force (USPSTF) recommended cancer screenings, lung cancer screening (LCS) is the least utilized. Nationally, the median LCS rate is 5.0%. We are conducting a prospective, randomized clinical trial to test two interventions associated with increasing the completion of LCS among eligible UC Davis ambulatory patients over usual

care. In this preliminary report, we identify the ongoing challenges in recruiting eligible patients during the first 5 months of this clinical trial involving 503 patients.

Methods: We conducted key informant interviews with providers, patients who completed LCS, and age-eligible patients who smoked to qualitatively identify patient-centered factors that facilitate and impede participation in LCS. These findings informed the randomization of two interventions: (a.) Navigator-guided intervention alone and (b.) Navigator-guided intervention plus a LCS awareness video linked to the electronic patient-physician portal to increase LCS compared to a usual care control clinic arm.

Results: Our initial findings indicate that [1] 8.3% (42/503) of patients have a current cancer diagnosis and are presumably in treatment and excluded from further outreach for LCS; and [2] 87.7% (314/358) of those remaining patients contacted, were not eligible due to not meeting USPSTF recommendations. After all the other eligibility requirements were assessed, only 12.3% (44/358) of the reachable patients were determined to meet LCS eligibility criteria. Among patients whose eligibility was verified, the two arms of Navigator-guided interventions resulted in a LCS rate of 45% (20 scheduled or screened/44 eligible).

<<PF-28>> GENETIC SCREEN FOR THE IDENTIFICATION OF TP53 MUTANTS THAT CAN BE FUNCTIONALLY RESTORED BY APR-246

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TP53, often referred to as the guardian of the genome, is one of the most frequently mutated genes in human cancers. Some cancer sub-types, such as non-small cell lung cancer and high grade serous ovarian cancer, have TP53 mutation rates reaching up to 56% and 96%, respectively. Given its multi-faceted role in human cancers, there have been several efforts to therapeutically target mutant p53. APR-246 binds mutant p53, promotes thermodynamic stabilization of the protein, allowing it to regain wild-type-like conformation and consequentially, WT-like functionality. However, there has yet to be a systematic functional genomic screening of APR-246 rescuable p53 mutants. To address this critical gap we have performed functional genetic screenings using a pooled TP53 mutagenesis library containing ~8,000 amino acid variants, spanning the entirety of the TP53 gene. Following stable transduction of this library into p53-null NSCLC and HGSOC cell lines, we performed functional screenings against sublethal doses of APR-246. NGS of the untreated and treated cell population allows for comparison of variant representation and determination of APR-246-sensitive p53 mutants. Analysis of our screenings has revealed a pool of 38 “hit” mutants which are both significantly depleted following treatment and are clinically relevant mutations which occur in the patient population. We have chosen the top 5 mutants, C141Y, T155I, G245C, G266V, and P278R, for functional follow up studies. Identifying which p53 mutants are able to be rescued by APR-246, allows us to gain actionable clinical insight into what patient population may benefit most from treatment with the drug.

<<PF-29>> SIGNIFICANCE OF ANGEL2 EXPRESSION ON CISPLATIN CHEMORESISTANCE IN MUSCLE INVASIVE BLADDER CANCER

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Background: Cisplatin is a common chemotherapy for muscle invasive bladder cancer, but has an efficacy of approximately 40%. Understanding the mechanisms behind chemotherapeutic resistance to cisplatin would lead to improved treatment. We accumulated evidence to show that the protein ANGEL2 modulates isoform expression of an oncogenic transcription factor, FOXM1. FOXM1 isoforms have oncogenic traits and lead to epithelial-to-mesenchymal transition (EMT).

Methods: We utilized LC-MS/MS, 10x Genomics Visium Spatial Gene Expression system (10GVSGE), RNA-seq, cell culture, and cell viability counts with cisplatin treatment to determine how loss of ANGEL2 contributes to cisplatin resistance and EMT in muscle invasive bladder cancer. Cell models used were from the T24 bladder cancer cell line.

Results: The 10xGVSGE system analyzed two tumors varying in ANGEL 2 and FOXM1 expression levels. The results, paired with drug response analyses tested on patient derived cell lines, showed an inversely proportional relationship between ANGEL2 and FOXM1. The tumor with low ANGEL2 and high FOXM1 expression had cisplatin resistance. Clinical data showed lower survival rates for patients with bladder cancer who had this expression ratio. ANGEL2 knockout cells in vitro had upregulation of FOXM1 isoforms and EMT biomarkers, regardless of cisplatin treatment. Furthermore, these cells also became resistant to cisplatin. The TCGA Pan-Cancer dataset presented an inverse correlation between ANGEL2 and FOXM1 expression ((r) = -0.302, p = <0.0001).

Conclusion: Our research shows ANGEL2 expression modulates the production of FOXM1 isoforms. This suggests that the ANGEL2 protein acts as a prognostic biomarker for cisplatin sensitivity in bladder cancer patients.

<<PF-30>> THE HEPARIN-BINDING DOMAIN OF VEGF165 DIRECTLY BINDS TO INTEGRIN αvβ3 AND VEGFR2/KDR D1: A POTENTIAL MECHANISM OF NEGATIVE REGULATION OF VEGF165 SIGNALING BY αvβ3

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VEGF-A is a key cytokine in tumor angiogenesis and a major therapeutic target for cancer. VEGF165 is the predominant isoform of VEGF-A, and it is the most potent angiogenesis stimulant. VEGFR2/KDR domains 2 and 3 (D2D3) bind to the N-terminal domain (NTD, residues 1–110) of VEGF165. Since removal of the heparin-binding domain (HBD, residues 111–165) markedly reduced the mitogenic activity of the growth factor, it has been proposed that the HBD plays a critical role in the mitogenicity of VEGF165. Here, we report that αvβ3 specifically bound to the isolated VEGF165 HBD but not to VEGF165 NTD. Based on docking simulation and mutagenesis, we identified several critical amino acid residues within the VEGF165 HBD required for αvβ3 binding, i.e., Arg123, Arg124, Lys125, Lys140, Arg145, and Arg149. We discovered that VEGF165 HBD binds to the KDR domain 1 (D1) and identified that Arg123 and Arg124 are critical for KDR D1 binding by mutagenesis, indicating that the KDR D1-binding and αvβ3-binding sites overlap in the HBD. Full-length VEGF165 mutant (R123A/R124A/K125A/K140A/R145A/R149A) defective in αvβ3 and KDR D1 binding failed to induce ERK1/2 phosphorylation, integrin β3 phosphorylation, and KDR phosphorylation and did not support proliferation of endothelial cells, although the mutation did not affect the KDR D2D3 interaction with VEGF165. Since β3-knockout mice are known to show enhanced VEGF165 signaling, we propose that the binding of KDR D1 to the VEGF165 HBD and KDR D2D3 binding to the VEGF165 NTD are critically involved in the potent mitogenicity of VEGF165. We propose that binding competition between KDR and αvβ3 to the VEGF165 HBD endows integrin αvβ3 with regulatory properties to act as a negative regulator of VEGF165 signaling.

<<PF-31>> BLADDER CANCER CELLS EXPOSED TO WILDFIRE SMOKE EXHIBIT SIGNS OF EPITHELIAL-MESENCHYMAL TRANSITION

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Firefighters are at a significantly higher risk of developing mesothelioma and bladder cancer (BICa) due to occupational exposure to carcinogens. The mortality risk from BICa among firefighters is 5.7 times higher than the general population, underscoring the urgent need to understand the chemical exposures they face during fires and training. Substances like soot, polycyclic aromatic hydrocarbons, and PFAS are major contributors to BICa. Smoke exposure can irritate urothelial cells in the bladder, leading to tumor formation. Epithelial-to-mesenchymal transition (EMT), can be triggered by chronic inflammation, promoting tumorigenesis. Using mice exposed to smoke conditions, we measured mRNA expression levels of TWIST1, OCT4, and E-cadherin through qPCR analysis, assessed T24 cell morphology after exposure to smoke-infused media, and conducted scratch assays to compare cell motility rates induced by various chemical irritants. We show that murine tumor cells exposed to different smoke-infused media have significantly enhanced EMT marker expression (TWIST and OCT4), increased metabolic activity, and increased wound healing properties, indicating high cell migration and the occurrence of EMT. Our studies also suggest that cells exposed to smoke-infused media exhibit signs of EMT, a process that can contribute to oncogenesis. We hypothesize that firefighters exposed to specific smoke irritants are at a heightened risk of developing BICa. To mitigate this risk, it is crucial to identify and prioritize combustible training materials that pose the lowest risk of inducing BICa.

<<PF-32>> REDUCED EFFICACY OF FRACTIONATED RADIOTHERAPY IN OBESE MICE

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Clinical data demonstrate that obese cancer patients are more resistant to radiotherapy and have higher rates of recurrence. Although a growing number of cancer patients are obese, and obesity is linked to poor outcomes with radiotherapy, little is understood about how obesity impacts the efficacy of radiotherapy. To interrogate this preclinically control and diet induce obese (DIO) mice were used (Generated by feeding 4-6-week-old, genetically identical, inbred C57BL/6 mice with a high-fat diet consisting of 60% kcal from fat (DIO) or a control diet consisting of 10% fat (control) until 6 months of age). These mice were then implanted with syngeneic tumors (B16F0, 3LL, or MC38) in the hind leg. When tumors reached 5mm in diameter mice were treated with fractionated radiotherapy (12Gy delivered in daily 4Gy fractions X 3 days) using a 2cm electron cutout to treat the tumor + margin only. We observed that fractionated radiotherapy (4Gy x 3) significantly reduced the growth of B16F0 tumors by about three-fold in control mice compared to untreated controls. Radiotherapy failed to significantly reduce tumor size in DIO mice (compared to unirradiated DIO), although the treated tumors trended towards being modestly smaller. Additionally, tumors in the DIO + RT group were significantly larger than the tumors in the control + RT group. Initial mechanistic studies suggest increased tumor proliferation, immune dysfunction, as well as increased baseline DNA repair mechanisms including yH2AX in DIO mice may induce the observed radio-resistance.

<<PF-33>> THE ROLE OF MACROPHAGES IN CONFERRING ANTIANDROGEN RESISTANCE AND IMMUNE EVASION IN CASTRATION-RESISTANT PROSTATE CANCER

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Introduction: Prostate cancer management commonly involves androgen deprivation therapy (ADT); however, resistance and relapse remain significant challenges. The tumor microenvironment, particularly immune cell populations, plays a crucial role in disease progression and therapy resistance. This study investigates the interactions between prostate cancer cells and macrophages, focusing on the roles of Tumor-Associated Macrophages (TAMs) and their impact on therapeutic resistance and tumor progression. We evaluated the effects of ADT on immune cell populations, analyzed RNA sequencing data from co-cultures of MycCaP cells with macrophages, and examined the influence of different macrophage subtypes on cancer cell behavior.

Methods: Macrophages were isolated and differentiated into M0 macrophages, then polarized to M1 and M2 phenotypes, using bone marrow cells from FVB/NJ mice. A clonogenic assay was conducted to assess the effects of interactions between MycCaP cells and M0, M1, and M2 macrophages, both with and without enzalutamide. M2 macrophages were then co-cultured with MycCaP cells, followed by cell sorting and RNA sequencing to compare changes before and after interaction.

Results: The relapsed MycCaP tumors showed a significant increase in the populations of TAMs and myeloid-derived suppressor cells (MDSCs) without changes in T cell infiltration. Co-culturing MycCaP cells with macrophages led to resistance against enzalutamide. RNA sequencing revealed that MycCaP cells modulate macrophages toward an M2 phenotype. Furthermore, M2 macrophages promoted epithelial-mesenchymal transition (EMT) in MycCaP cells, enhanced tumor growth, and reduced CD8+ T cell populations.

Conclusion: The interaction between MycCaP cells and macrophages, particularly the polarization to an M2 phenotype, contributes to therapy resistance and aggressive tumor behavior. These findings underscore the importance of targeting the tumor microenvironment and macrophage polarization to improve therapeutic strategies for prostate cancer.

<<PF-34>> NON-ACTIVATED AND IL-7 CULTURED CD19-SPECIFIC CAR T CELLS ARE ENRICHED IN STEM CELL PHENOTYPES AND FUNCTIONALLY SUPERIOR

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CD19-specific chimeric antigen receptor (CAR) T cells have demonstrated impressive responses in patients with relapsed and refractory B cell malignancies. However, many patients relapse or fail to respond to CD19 CAR T cells, demonstrating the need to improve its efficacy and durability. Current protocols for generating CAR T cells involve T cell activation through CD3 stimulation to facilitate efficient CAR transfer followed by ex vivo expansion with exogenous cytokines to obtain adequate cell numbers for treatment. Both T cell activation and expansion inevitably lead to terminal differentiation and replicative senescence, which are suboptimal for therapy. Interleukin-7 (IL-7) was previously shown to allow for lentiviral transduction of T cells in the absence of activation. In these studies, we utilized IL-7 to generate CD19 CAR T cells without stimulating CD3. Non-activated and IL-7 cultured (NICE) CD19 CAR T cells were enriched with the memory T stem cell population (TSCM), retained novel markers of stemness, had lower expression of exhaustion markers, and increased proliferative potential. Furthermore, our findings are consistent with engraftment of NICE CD19 CAR T cells and demonstrate a superior therapeutic response in both intraperitoneal and subcutaneous in vivo B cell lymphoma models. These results suggest that NICE CD19 CAR T cells may improve outcomes for B cell malignancies and warrant clinical evaluation.

<<PF-35>> A RETROSPECTIVE CASE SERIES OF MYASTHENIA GRAVIS ASSOCIATED WITH IMMUNE CHECKPOINT INHIBITORS

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Introduction: Immune checkpoint inhibitor (ICI) therapy is a revolutionary cancer treatment. However, it could lead to neuromuscular complications including myasthenia gravis (MG).

Objective: Characterize the clinical features of ICI associate MG

Mentods: From Jan 2020 to Jan 2024,1388 patients received ICIs at our institution. Twelve cases with neuromuscular complications after initiation of ICI therapy were identified.

Results: The patients' mean age was 64.7 years, nine of twelve were men. The most common cancer was renal cell carcinoma (33.3%). The most commonly used ICI was Nivolumab (41.7%). Four cases underwent dual ICIs. The time range from initial ICI to symptom onset was 3 days to 32 weeks. Two cases had Guillain Barre syndrome, one had chronic sensorimotor axonal polyneuropathy, one had Bell's palsy. Eight patients had clinical diagnosis of MG. Two had positive acetylcholine receptor antibodies. Three of the MG cases presented with overlap myositis, two MG cases had myocarditis and myositis, one MG case had myocarditis and hepatitis. Five patients with MG received electrophysiological study: 4 demonstrated myopathy, two exhibited decrements to low frequency repetitive stimulation test, one of which also showed myopathic changes. High-dose steroids, IV immunoglobulin, pyridostigmine were the most commonly used treatments. Despite mild to moderate clinical improvement (62.5%), the mortality for ICI-related MG was 58.3%.

Summary/Conclusion: The ICI case series indicates: the rates of positive MG antibodies and of abnormal repetitive nerve stimulation responses are lower than in spontaneously occurring MG; overlap syndromes are common in ICI associated MG, along with increased mortality.

<<PF-36>> LX1 TARGETS ANDROGEN RECEPTOR VARIANTS AND AKR1C3 TO OVERCOME THERAPY RESISTANCE IN ADVANCED PROSTATE CANCER

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Background: The development of resistance to current standard-of-care treatments, such as androgen receptor (AR) targeting therapies, remains a major challenge in the management of advanced prostate cancer. There is an urgent need for new therapeutic strategies targeting key resistant drivers such as AR variants like AR-V7 and steroidogenic enzymes such as AKR1C3 to overcome drug resistance and improve outcomes for patients with advanced prostate cancer. We have designed, synthesized, and characterized a novel class of LX compounds targeting both the AR/AR-Variants and AKR1C3 pathways.

Methods: A library of the LX compounds was designed and synthesized according to structure-based computer modeling. The effects of the lead LXs on the expression and activity of AR/AR-variants and AKR1C3 were evaluated. RNA-seq was performed on the lead LXs. Resistant cell sublines generated from C4-2B cells resistant to enzalutamide (MDVR), apalutamide (ApalR), darolutamide (DaroR), or abiraterone (AbiR) were treated with LX1 or their respective antiandrogen. Mice bearing VCaP xenograft tumors and LuCaP35CR PDX tumors were treated with LX-1 and effects on tumor growth were assessed.

Results: Molecular docking studies and in vitro experiments demonstrated that LX compounds effectively bind to the AKR1C3 active site and inhibit AKR1C3 enzymatic activity. LX1 was also shown to reduce AR/AR-V7 expression and downregulate their target genes, inducing G0/G1 arrest in anti-androgen-resistant cell lines. LX1 treatment reduced tumor volumes and decreased intratumoral testosterone in both xenograft tumor and PDX models. LX1 effectively inhibited the conversion of androstenedione into testosterone in tumor-based ex vivo enzyme assays. Moreover, LX1 synergized with enzalutamide and abiraterone as well as docetaxel,

suggesting its potential to enhance the anti-tumor activity of these standard therapies in resistant prostate cancer. Furthermore, LX1 improved enzalutamide treatment in resistant prostate cancer tumor models.

Conclusions: Our study unveils the dual effect of LX compounds, especially LX1 in reducing intratumoral testosterone and AR and AKR1C3 signaling, along with its synergy with standard therapies in resistant models, underscores its potential as a valuable treatment option for advanced prostate cancer.

PF-37 IMPACT OF HEALTH INSURANCE ON CANCER CARE: A QUALITY MEASURES ANALYSIS IN CALIFORNIA, 2014–2021

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Background: Historical disparities in the quality of cancer care by health insurance type have been well-documented. The Affordable Care Act's implementation in 2014 significantly altered the insurance landscape in California, expanding coverage to more residents, yet its impact on quality of cancer care is unknown.

Methods: We analyzed data from the California Cancer Registry, including 631,010 patients diagnosed between 2014 and 2021 with bladder, breast, cervical, colon, endometrial, gastric, lung, ovarian, and rectal cancer. Five insurance categories (Private, Medicare, Medicaid, Other public, and Uninsured) and 15 Commission on Cancer (CoC) quality of care (QOC) measures were included. The QOC measures assess concordance with CoC established treatment guidelines, including recommended chemotherapy, radiation, and/or surgery. Multivariable logistic regression models were used to assess the association between insurance type and each QOC measure, adjusting for age, sex, race/ethnicity, socioeconomic status, and stage at diagnosis.

Results: Patients with Medicaid, Medicare, or no insurance had lower odds of adherence with QOC measures compared to those with private insurance for breast cancer (OR=0.45; 95% CI: 0.26-0.77 to OR=0.96; 95% CI: 0.93-0.98), colon cancer (OR=0.49; 95% CI: 0.45-0.54 to OR=0.92; 95% CI: 0.88-0.96), and ovarian cancer (OR=0.64; 95% CI: 0.45-0.91 to OR=0.81; 95% CI: 0.72-0.92). For endometrial cancer, only patients with Medicaid had lower odds of adherence with QOC measures. (OR=0.78; 95% CI: 0.65-0.94). Patients with Medicare were less likely to be adherent for bladder (OR=0.78; 95% CI: 0.62-1.00) and lung cancer (OR=0.90; 95% CI: 0.83-0.97).

Conclusions: This study highlights the continued disparities in the quality of cancer care by health insurance type in California, despite broader access to insurance coverage. Efforts to address these disparities may improve treatment outcomes and reduce cancer-related morbidity and mortality.

Acknowledgements: The collection of cancer incidence data used in this study was supported by California Department of Public Health as part of the statewide cancer reporting program mandated by the California Health and Safety Code Section 103885; the National Cancer Institute's Surveillance, Epidemiology and End Results Program under contracts awarded to the Cancer Prevention Institute of California, the University of Southern California, and the Public Health Institute; and the Centers for Disease Control and Prevention's National Program of Cancer Registries, under agreement awarded to the California Department of Public Health.

<<PF-38>> PERCEPTION OF ENVIRONMENTAL CANCER RISK FACTORS AMONG RESIDENTS OF THE UCDCCC CATCHMENT AREA

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Background: A cross-sectional survey was conducted to assess prevalence and perceptions of cancer risk factors and concerns, cancer screening behaviors, healthcare access, health outcomes, and inequities across a representative sample of households within the UCDCCC 19-county catchment area to identify opportunities for future research, public health intervention, and policy development. This analysis focused on concerns regarding local air quality and its potential impact on cancer risk.

Methods: The survey utilized an address-based sampling design with a stratified random sample of 25,000 addresses into 16 strata, oversampling for rural and minority populations. The response rate for the 24,050 households with valid addresses was 8.3%, resulting in 2,008 completed surveys. Nonresponse-adjusted weights were applied to ensure representativeness, aligning oversampled groups with their actual population share. Multivariable logistic regression including covariates such as age, racial/ethnic identity, education, occupation, marital status, household size, English proficiency, health care coverage, and cancer history, weighted to account for complex survey design, was fitted to binary outcomes derived from responses to four specific concerns about air quality: (1) wildfire smoke, (2) industrial air pollution, (3) air pollution's impact on food safety, and (4) air pollution's effect on water safety. Each outcome was coded as a binary variable, indicating whether the respondent was concerned or not. The model calculated odds ratios (OR) and 95% confidence intervals (CI).

Results: Most catchment area residents (62%) were concerned about the impact of wildfire smoke on cancer risk, with elevated concern among individuals not in the workforce (OR: 1.64, 95% CI: 1.02, 2.64). Also, 44% of residents were concerned about the impact of industrial air pollution, which was also elevated among unemployed individuals (OR: 5.38, 95% CI: 1.46, 19.77) and residents with no healthcare insurance or only non-private sources other than Medicare, Medi-Cal, TRICARE, or VA/Military (OR: 2.61, 95% CI: 1.12, 6.08). Individuals who self-identified as Non-Hispanic Asian and Black showed significantly higher concern about air pollution's impact on water safety (OR: 3.14, 95% CI: 1.49, 6.64 and OR: 4.43, 95% CI: 1.55, 12.67, respectively), and Single/Never Married individuals expressed more concern compared to married individuals (OR: 2.46, 95% CI: 1.21, 5.01). Concerns about food safety due to air pollution were not significantly linked to sociodemographic factors, although a trend towards increased concern was observed among those with limited English proficiency ($p = 0.11$).

Conclusions: Sociodemographic factors such as racial/ethnic identity, marital status, and employment status significantly influence concerns about air pollution and its health risks. These insights can guide public health interventions to address the specific needs and concerns of catchment area residents.

Acknowledgements: We gratefully acknowledge the funding provided by the UC Davis Comprehensive Cancer Center, which made this survey possible. Special thanks go to the staff at the Office of Community Outreach and Engagement for their invaluable efforts in organizing and coordinating the survey in collaboration with Westat. Their dedication was essential to the successful execution of this study.

<<PF-39>> NANOPARTICLE CEST MRI VISUALIZATION

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Introduction: Lipid nanoparticles with CEST (Chemical Exchange Saturation Transfer) contrast may serve to target tumors in MR imaging. Here, we present the development of a novel lipid nanoparticle with CEST contrast capabilities.

Methods: Liposomal nanoparticles were made by mixing an amphiphilic lipid with other lipids (DPPC, Cholesterol) using thin film hydration and extrusion. DSPE-PEG^{2K}-NH_2 amine was coupled with lysine (K) amino acid molecules to make the amphiphilic CEST agent with exchangeable amine and amide protons in its polar head. Mass spectrometry (MS) was used to confirm its molecular weight. ^{1}H NMR was acquired with a 400 MHz NMR to visualize the exchangeable protons. Dynamic light scattering was used to measure the nanoparticles' size, distribution, and zeta potential. CEST was observed using Bruker BioSpec 7T MRI.

Results: The ^{1}H NMR reveals exchangeable amide proton peaks that were visible in DMSO-d_6/ $CDCl_3$ and disappeared upon the addition of methanol-d_4. The CEST peaks for the exchangeable amide protons at 3.0 and 4.5 ppm offsets were used to acquire MRI and visualize the 166 nm liposomal solution and compared to iopromide.

Discussion and Conclusion: We have developed a lipoCEST agent with brain tumor targeting to produce intense localized CEST during MRI acquisition. Adding maltobionic acid to the polar head of amphiphilic lipid will provide the GLUT1 targeting alongside Warburg effect for better tumor targeting. In future work will compare with other agents to determine its class. This amphiphilic lipid is expected to have lower toxicity to viable cells and pharmacokinetics similar to natural/semisynthetic lipids.

Acknowledgement: This work was supported by the University of California Davis Comprehensive Cancer Center with funds from the NCI's Paul Calabresi K12 program 5K12CA138464-12

<<ET-01>> UC DAVIS COMPREHENSIVE CANCER CENTER SHARED RESOURCES

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