NCI Cancer Center

2026 ANNUAL CANCER RESEARCH SYMPOSIUM

MARCH 13, 2026

OU Health | Stephenson Cancer Center

The UNIVERSITY of OKLAHOMA

The Stephenson Cancer Center wishes to recognize and thank the Oklahoma Tobacco Settlement Endowment Trust (TSET) for co-sponsoring the 2026 Stephenson Cancer Research Symposium.

In 2012 TSET awarded a five-year, $30.25 million grant to the Stephenson Cancer Center to establish the Oklahoma TSET Cancer Research Program. TSET's cumulative investment through its contract with the SCC and with the Health Promotion Research Center is $157 million.

The mission of the Oklahoma TSET Cancer Research Program is to decrease the burden of cancer in Oklahoma and nationally through promoting, coordinating and supporting innovative cancer research. It seeks to accomplish this mission through:

- Attracting cancer researchers with grant funding from the National Cancer Institute and other national sponsors to Oklahoma
- Developing trans-disciplinary, collaborative cancer research programs
- Promoting inter-institutional partnerships to leverage unique strengths at research institutions in Oklahoma
- Enhancing research infrastructure and shared resources to enable and support innovative and nationally-competitive cancer research
- Serving as a statewide resource for researchers and institutions that conduct cancer research

The Oklahoma TSET Cancer Research Program supports a wide range of programs, shared resources and initiatives designed to accomplish these goals.

Highlights

With support from the Oklahoma TSET Cancer Research Program the Stephenson Cancer Center accomplished the following:

- Increased cancer center membership from 56 to 350 members at ten academic institutions across Oklahoma
- Recruited over one hundred new cancer researchers to Oklahoma who account for over $300 million in new grants and contracts to Oklahoma
- Funded over fifty seed and directed-research grants to cancer investigators in Oklahoma
- Enhanced five Shared Resource facilities
- Hosted over 800 research seminar speakers
- Hosted annual statewide Cancer Research Symposium that bring together over 250 researchers from around the state
- Hosted over 100 undergraduate students from 35 different universities for summer cancer research experience
- Since the inception of the TSET grant, the SCC has enrolled more than 7,000 patients to interventional clinical trials

Health Promotion Research Center

OU Health Stephenson Cancer Center wishes to recognize and thank the TSET Health Promotion Research Center (HPRC) for co-sponsoring the 2026 Annual Cancer Research Symposium

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The TSET Health Promotion Research Center (HPRC) is a leading research program with a focus on the entire translational continuum – from the discovery of basic mechanisms of health behavior and behavior change, to the development and evaluation of novel interventions, to the dissemination and implementation of interventions, policies, and education throughout Oklahoma.

The **mission** of the HPRC is to reduce the burden of disease in Oklahoma by addressing modifiable health risk factors such as tobacco use, sedentary lifestyle, poor diet, and risky alcohol and other substance use through research, novel intervention development, and dissemination of research findings.

The HPRC contains four major resources that facilitate research: Mobile Health Shared Resource, Tobacco Treatment Research Program, Postdoctoral Fellowship Training Program, and Tobacco Regulatory Science Clinical Laboratory.

The center was established in 2007 with funding from the Oklahoma Tobacco Settlement Endowment Trust (TSET) as part of their efforts to support statewide and community-based cessation and intervention projects.

HPRC Directors
Michael Businelle, PhD (Co-Director)
Darla Kendzor, PhD (Co-Director)

TSET

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2026 Annual Cancer Research Symposium

7:30 – 8:00 am	**Poster Check-In & Registration**
8:00 – 8:30 am	**Breakfast & Networking**
8:30 – 8:45 am	**Welcome & Opening Comments** **Robert Mannel, MD** State of the Cancer Center
8:45 – 9:30 am	**ACS-IRG Highlights** *Moderator: Rajagopal Ramesh, PhD, DBA, FAIMBE*
8:45 – 9:00 am	**Geeta Rao, PhD** Targeting Anoikis Resistance in Ovarian Cancer
9:00 – 9:15 am	**Catherine Nagawa, PhD** Training Support Providers to Improve Smoking Cessation Outcomes among Adults with Mental Health Conditions: A 3-Month Pre–Post Study
9:15 – 9:30 am	**Soheil Hemmati, PhD & Raghavendiran Boopathy, PhD, DABR** Optimal Grid Placement and Fluence Map for Spatially Fractionated Radiation Therapy
9:35 – 10:35 am	**Cancer Biology Research Program** *Moderator: Xin Zhang, MD, PhD*
9:35 – 9:45 am	**Program Leaders Presentation** **Min Li, PhD** Introduction to the Program/Resources
9:50 – 10:05 am	**Senior Faculty Research Presentation** **Deepa Sathyaseelan, PhD** Hepatocyte MLKL Links Aging and Metabolic Stress to Hepatocellular Carcinoma
10:05 – 10:20 am	**Jr. Faculty Research Presentation** **Mojgan Padash Barmchi, PhD** A Cross-Species Drosophila Platform Reveals Specific Proteasome Subunit Dependencies In HPV-Driven Cancer

10:20 – 10:35 am **Trainee Flash Talks**

Zongkai Peng, PhD
Single-Cell Proteomic Profiling of Chemotherapy-Resistant Ovarian Cancer Cells

Ramasamy Selvarani, PhD
Mitochondrial Haplotype-Dependent Modulation of Liver Fibrosis In Novel OKC-HETB/W Rats During Aging and Western Diet Stress

Jose Juan Macias
Overexpression of Human MYC in Zebrafish Lymphoblasts Triggers the Development of Diverse Acute Lymphoblastic Leukemia Subtypes

10:35 – 11:35 am **Cancer Therapeutics Research Program**
Moderator: Raid Aljumaily, MD

10:35 – 10:45 am **Program Leaders Presentation**
Muhammad Furqan, MD
Introduction to the Program/Resources

10:50 – 11:05 am **Senior Faculty Research Presentation**
Muhammad Furqan, MD
Pharmacologic Ascorbate in NSCLC: From Redox Targeting to Immune Modulation

11:05 – 11:20 am **Jr. Faculty Research Presentation**
Mikail Abbasov, PhD
Reimagining Covalent Targeting of Lysines as an Emerging Modality for Cancer Therapeutics

11:20 – 11:35 am **Trainee Flash Talks**

Saurav Kumar, PhD
Store-operated calcium channels promote glioblastoma-associated vascular cell-induced microglia polarization towards an immunosuppressive phenotype

Falah Fayaz, MD
Antibody-Drug Conjugate Associated Pneumonitis (AAP) Across Novel First-in-Human Phase I Trials: A Pooled Single-Center Analysis

Lauren Falk, MD

	Feasibility of Treatment of Locally Advanced Cervical and Vaginal Cancer with INTERLACE Protocol in a Real-World Patient Population
11:45 – 12:45 pm	**Posters (Graduate Students & Medical Students)**
12:45 – 1:30 pm	**LUNCH**
1:30 – 2:30 pm	**Posters (Postdocs, Clinical Fellows, & Jr. Faculty)**
2:45 – 3:45 pm	**Cancer Prevention and Control Program** *Moderator: Darla Kendzor, PhD*
2:45 – 2:55 pm	**Program Leaders Presentation** **Timothy VanWagoner, PhD** Introduction to the Program/Resources
3:00 – 3:12 pm	**Senior Faculty Research Presentation** **Zsolt Nagykaldi, PhD, BTh** Implementing a Tribally-Engaged Lung Cancer Screening Program in Rural Oklahoma – The TEALS Trial
3:13 – 3:25 pm	**Jr. Faculty Research Presentation** **Tara Klinedinst, PhD, OTR/L** Feasibility of a Self-Determination and Occupational Therapy-Informed Program to Improve Physical Activity in Breast Cancer Survivors
3:25 – 3:45 pm	**Trainee Flash Talks**
	Brittany Hudson, PhD, MPH Beyond The App: A Qualitative Study Of Culture, Trust, And PSA Screening In A Randomized Digital Health Trial Among Black Men
	Adele Hammoudi, PhD Cannabis smoking induces immunosuppression and increases inflammation
	Gautham Chengizkhan, PhD Carcinogenic metal exposures from disposable e-cigarettes
3:45 – 4:30 pm	**Cancer Center Cores** *Moderator: Stevie Warner, MA, MHR*
3:45 – 4:00 pm	**Mark Doescher, MD, MSPH**

	Community Outreach and Engagement
4:00 – 4:15 pm	**Rajagopal Ramesh, Ph.D., DBA, FAIMBE** Cancer Research Training and Education Coordination
4:15 – 4:30 pm	**Sara Vesely, PhD** Biostatistics & Research Design Shared Resources
	Kar-Ming Fung, PhD Tissue Pathology & Biospecimen Shared Resources
	Michael Businelle, PhD Mobile Health Technology Shared Resources
	James Papin, PhD Molecular Biology and Cytometry Research Shared Resources
4:40 – 4:50 pm	**BREAK**
4:50 – 5:00 pm	**Awards/Closing Remarks – Early-Stage Investigator Award**

Cancer Center Leadership

Min Li, PhD
Program Leader, Cancer Biology

Mark Doescher, MD, MSPH
Associate Director, Community Outreach and Engagement

Kar-Ming Fung, MD, PhD
Director, Tissue Pathology & Biospecimen Shared Resource

Muhammad Furqan, MD

Associate Director for Clinical Research, Cancer Therapeutics

Rajagopal Ramesh, PhD
Associate Director, Education and Training

Michael Businelle, PhD
Program Leader, Cancer Prevention and Control
Director, Mobile Health

Timothy VanWagoner, PhD

Program Leader, Cancer Prevention & Control

Sara Vesely, PhD
Director, Biostatistics & Research Design Shared Resource

James Papin, PhD
Director, Molecular Biology & Cytometry Shared Resource

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State of the Cancer Center

Robert Mannel, MD

Director of OU Health Stephenson Cancer Center

Gynecologic oncologist Robert Mannel, M.D., is director of OU Health Stephenson Cancer Center at the University of Oklahoma Health Sciences. Additionally, he serves as associate vice provost for cancer programs at the University of Oklahoma Health Sciences and is a professor in the Department of Obstetrics and Gynecology at the OU College of Medicine. Dr. Mannel is a leader in the National Clinical Trials Network of the National Cancer Institute, and his clinical and research interests include laparoscopy for gynecologic malignancies, gynecologic oncology, and drug development for ovarian, endometrial, and cervical cancers. He has published more than 100 scientific articles dealing with the management of gynecologic malignancies. He completed medical school at the University of Texas Medical Branch at Galveston, his residency at Baylor Scott & White Medical Center, and a fellowship at the University of California, Irvine.

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ACS–IRG Highlights

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TARGETING ANOIKIS RESISTANCE IN OVARIAN CANCER

Geeta Rao

Background: High-grade serous ovarian carcinoma (HGSOC) is the most common and lethal subtype of ovarian cancer. Its high mortality is largely attributable to its remarkable metastatic potential. HGSOC tumor cells disseminates throughout the peritoneal cavity as multicellular spheroids that survive in the harsh ascites environment by resisting anoikis-a form of apoptosis triggered by loss of cell–matrix attachment. Although patients often respond to frontline therapy, recurrence is frequent and is driven by spheroid survival in the peritoneal microenvironment. Therefore, anoikis resistance (AR) is a critical driver of both metastatic dissemination and therapeutic failure. A deeper understanding of the molecular mechanisms underlying AR is therefore essential for the development of targeted interventions aimed at limiting metastasis and improving patient outcomes.

Hypothesis: Our previous studies and others have identified cystathionine β-synthase (CBS), a hydrogen sulfide (H_2S)–producing enzyme, as a promoter of ovarian cancer progression and therapy resistance. We hypothesize that CBS supports AR in ovarian cancer and that targeting CBS will suppress metastasis and cancer progression.

Methods and Results: We examined the role of CBS in AR using ovarian cancer cell lines, a tissue microarray (TMA), and *in vivo* models. Our findings demonstrate that CBS is a key determinant of spheroid viability and metastatic potential. Analysis of publicly available patient datasets and an in-house TMA showed that high CBS expression correlates with poor progression-free survival and clinically documented peritoneal/omental metastasis. Functional and proteomic studies revealed that CBS silencing induces apoptosis in 2D monolayers and, similarly, triggers apoptosis and disrupts spheroid architecture in 3D cultures. Mechanistically, loss of CBS resulted in downregulation of oncogenic stemness programs and epithelial–mesenchymal transition pathways.

Furthermore, proteomic and bioinformatic analyses identified ITGB1 as a central hub in ovarian cancer spheroidogenesis, and CBS knockdown abrogated ITGB1-mediated downstream signaling. Additionally, SP1 emerged as a key transcriptional regulator of CBS-driven spheroidal programs of stemness and invasiveness. *In vivo,* CBS loss impaired spheroid integrity via ITGB1 repression, leading to reduced metastatic seeding on the murine omental surface.

Conclusion:
These findings identify CBS as a central regulator of anoikis resistance and transcoelomic dissemination in ovarian cancer, highlighting CBS inhibition as a promising therapeutic strategy to block metastasis and enhance chemotherapy responsiveness.

FEASIBILITY OF TRAINING SUPPORT PROVIDERS TO IMPROVE SMOKING CESSATION OUTCOMES FOR ADULTS WITH MENTAL HEALTH CONDITIONS: A 3-MONTH PRE–POST STUDY

Catherine S. Nagawa[1,2], PhD; Sydney Newell Chesebro[1,2], BS; Frances K. Wen[3], PhD; Michelle R. vanDellen[1,2], PhD

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[2]Department of Health Promotion Sciences, University of Oklahoma Health Sciences, Oklahoma, USA

[3]Department of Family and Community Medicine, School of Community Medicine, The University of Oklahoma-Tulsa, Oklahoma, USA

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Funding
This work is supported by Institutional Research Grant (#IRG-23-1143225-04) from the American Cancer Society, the Oklahoma Tobacco Settlement Endowment Trust (TSET) contract (#00003615), and the OU Health Stephenson Cancer Center via an NCI Cancer Center Support Grant (P30CA225520). The funders had no role in the design, conduct, analysis, interpretation, writing, or the decision to submit this manuscript.

Introduction: Individuals with mental health conditions (MHC) continue to smoke at disproportionately high rates, contributing to persistent tobacco-related health disparities. Many adults with MHC who smoke express a desire to quit and actively seek social support during quit attempts. In observational research, social support is consistently positively associated with quitting. However, prior cessation support interventions have largely failed to improve the quality or effectiveness of support, limiting our ability to evaluate its role in quitting smoking.
One potential limitation of prior support interventions has been an inattention to theory-based techniques of support, including responsiveness. Responsiveness involves care, validation, and understanding, and is a key feature of social support that facilitates smoking cessation.
Moreover, support interventions have not incorporated pre-bunking strategies to address misbeliefs about the benefits of smoking cessation among higher-risk populations, including adults with MHC.

Methods: We conducted a three-month pre–post pilot study to assess the feasibility of a theory-based social support intervention for smoking cessation among adults with MHC. Grounded in perceived responsiveness theory, the crossover intervention targets an asymmetric dyadic mechanism by training a support provider to deliver responsive and validating cessation support to the individual attempting to quit smoking. Beginning in June 2025, we recruited adults with MHC who smoked and were ready to quit. Mental health was assessed using the Kessler-6 (K6), a validated measure of nonspecific psychological distress. Eligibility criteria included: age ≥18 years, K6 score ≥5, willing and able to use nicotine replacement therapy (NRT), and have identified a support partner willing to participate. Target

individuals received standard tobacco treatment care, including counseling and combination NRT, while support providers received structured, support-enhancing messages. Primary outcomes are changes in perceived social support, with a secondary outcome of 7-day point-prevalence smoking abstinence. Feasibility outcomes include recruitment, retention, and intervention engagement, assessed via tobacco treatment counseling attendance and support-provider message ratings. Recruitment is ongoing (74% complete) and will conclude in March 2026. All study methods received approval from the institutional review board (IRB #17894).

Results: To date, the study has enrolled 31 dyads (target sample: 50 dyads), yielding a recruitment rate of 39.2% (31/79). Of the 31 enrolled dyads, follow-up completion is 88.2% (n=15/17), target individuals attended a median of three tobacco treatment counseling sessions (IQR: 1–6), and support providers rated a mean of 11.2 support-enhancing text messages (SD=7.64). Of the 15 target individuals with currently available follow-up data, 33.3% (5/15) reported 7-day point-prevalence smoking abstinence. Participants who reported 7-day point-prevalence abstinence showed increases in responsive support from baseline to follow-up (mean change=0.24, SD=1.14), whereas those who continued smoking experienced declines (mean change=−0.90, SD=1.47). Full results will be reported in the final manuscript.

Expected Contribution: This study is expected to detail the feasibility and preliminary efficacy of a crossover responsiveness-based intervention to promote smoking cessation in adults with MHC through social support. Findings will inform the design of future randomized trials by identifying engagement benchmarks, refining outcome measures, and clarifying the potential role of support providers in cessation interventions targeting high-risk populations.

OPTIMAL GRID PLACEMENT AND FLUENCE MAP FOR SPATIALLY FRACTIONATED RADIATION THERAPY

Soheil Hemmati, PhD, Raghavendiran Boopathy, PhD, DABR

Spatially Fractionated Radiation Therapy (SFRT) is an emerging approach in radiation oncology that has gained interest in recent years as an effective method for the treatment of large and bulky tumors. Rather than prescribing a consistent, high dose of radiation to the entire tumor volume, SFRT prescribes delivery of high doses of radiation to discrete spheres within the tumor. While clinical guidelines exist regarding sphere size and separation, treatment planners rely on their own experience to determine sphere locations, aiming to maximize the number of spheres while satisfying clinical constraints. This step is typically followed by fluence map optimization, the primary task in radiation therapy planning, where the intensity of the radiation “beamlets” is computed. This manual sphere placement process introduces variation in both the number of spheres placed and the locations of these spheres. We propose a novel mathematical optimization model that computes the optimal SFRT treatment plan within fluence map optimization. Our model We conduct an experimental evaluation of our model using real imaging data provided by the National Cancer Institute through The Cancer Imaging Archive (TCIA). Our results demonstrate the effectiveness and flexibility of the proposed framework and its potential to assist clinicians in making more informed decisions that improve patient outcomes.

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Jose Juan Macias

Overexpression of Human MYC in Zebrafish Lymphoblasts Triggers the Development of Diverse Acute Lymphoblastic Leukemia Subtypes

HEPATOCYTE MLKL LINKS AGING AND METABOLIC STRESS TO HEPATOCELLULAR CARCINOMA

Phoebe Ohene-Marfo[1], Sabira Mohammed[1,2], Chao Jiang[1,2], Shylesh Bhaskaran[1,2], Constantin Georgescu[6], Chinthalapally V Rao[3,7], Willard M Freeman[6,7], Courtney Houchen[4,7], Jonathan D Wren[6], Deepa Sathyaseelan[1,2,5*]

[1]Department of Biochemistry & Physiology, [2]Stephenson Cancer Center, [3]Department of Medicine Hematology/Oncology, [4]Department of Medicine Gastroenterology, and [5]Oklahoma Center for Geroscience & Healthy Brain Aging, The University of Oklahoma Health Campus; [6]Genes and Human Disease Research Program, Oklahoma Medical Research Foundation. [7]The Oklahoma City Veterans Affairs Medical Center.

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Hepatocellular carcinoma (HCC) is a leading cause of cancer-related death worldwide and its incidence rises sharply with age and is further accelerated by obesity and diabetes. As global populations age and metabolic disease become increasingly prevalent, the burden of HCC in older adults is projected to grow disproportionately. Aging and cancer share common biological hallmarks, including chronic sterile inflammation and mitochondrial dysfunction. The geroscience hypothesis proposes that targeting fundamental aging mechanisms can delay or prevent multiple age-related diseases, including cancer, but specific aging pathways that drive HCC in the context of metabolic stress remain poorly defined. We identify the necroptosis effector Mixed lineage kinase domain-like protein (MLKL) as a novel, non-canonical regulator of hepatic inflammaging and obesity-driven HCC. MLKL expression increases in hepatocytes with age and Western/obesogenic diet exposure, independent of canonical necroptosis activation. Genetic loss of *Mlkl* reduces hepatic inflammation and improves mitochondrial function, whereas *Mlkl* overexpression promotes mitochondrial dysfunction and inflammatory signaling, suggesting that MLKL modulates two central hallmarks of both aging and cancer. Long-term Western diet feeding induced metabolic dysfunction-associated steatotic liver disease (MASLD)-associated HCC in mice by 17 months of age, corresponding to late middle age in humans, when HCC incidence begins to rise sharply. Strikingly, hepatocyte-specific *Mlkl* knockdown significantly reduced tumor number, tumor size, and stem cell marker expression in WD-fed mice. Reduced tumor burden was associated with improved mitochondrial function, dampened inflammatory signaling, and stabilization of the tumor suppressor mitofusin-2 (Mfn2), suggesting a mechanistic MLKL-Mfn2 axis linking mitochondrial dysfunction and inflammation to liver cancer progression. Together, these findings identify hepatocyte MLKL as a mechanistic mediator linking aging and metabolic stress to HCC and highlight the MLKL-Mfn2 axis as a potential therapeutic target in metabolic liver cancer in older adults.

Funding: R01AG059718 (NIA), R03 CA262044 (NCI), HHDC-SCC team science grant

A CROSS-SPECIES DROSOPHILA PLATFORM REVEALS SPECIFIC PROTEASOME SUBUNIT DEPENDENCIES IN HPV-DRIVEN CANCER

Rami Hassan[1], Amy L. Kennedy[1], Doris Benbrook[2], and Mojgan Padash Barmchi[1*]

[1]School of Biological Sciences, University of Oklahoma, Norman, OK, USA
[2] Department of Obstetrics and Gynecology, University of Oklahoma College of Medicine, Oklahoma City, OK, USA
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Cervical cancer, driven by persistent infection with high-risk human papillomaviruses (HPV), remains a major cause of cancer-related mortality among women worldwide. Alarmingly, cervical cancer incidence rate has risen by ~2% annually in women aged 30–44 years from 2012-2019, and Oklahoma has the second-highest age-adjusted cervical cancer incidence and mortality rates in the United States. Current treatments, including chemoradiation and surgery, are often limited by toxicity, long-term morbidity, and poor outcomes in advanced or recurrent disease. These challenges underscore an urgent need for targeted strategies that selectively eliminate HPV-positive cells while sparing normal tissue, and that can be applied not only for treatment but also for cancer prevention. Using a cross-species platform, which integrates a genetically engineered Drosophila model of HPV E6 oncogene expression with human cervical cell models, we identified two previously untargeted proteasome subunits that are required for HPV-associated cell survival. Using siRNA-mediated knockdown, we demonstrate that suppression of candidate proteasome subunits induces significant cytotoxicity in HPV-positive cervical cancer cells, while HPV-negative cervical cancer cells and non-cancerous cervical cells remain largely unaffected. In contrast, the FDA-approved proteasome inhibitor Bortezomib (the β5 subunit inhibitor) induces cytotoxicity in both HPV-positive and HPV-negative cervical cancer cells, highlighting the greater selectivity of our newly identified targets. Mechanistically, suppression of these candidate subunits triggers apoptotic cell death in HPV-positive cervical cancer cells, as evidenced by elevated levels of cleaved PARP, providing insight into how selective proteasome targeting eliminates HPV-positive cancer cells. To evaluate the therapeutic potential of our targets for chemoprevention, we modeled early transformation by exposing non-cancerous ectocervical ECT1/E6E7 cells to the tobacco-associated carcinogen NNK. siRNA-induced suppression of candidate proteasome subunits selectively eliminated these NNK-transformed, premalignant cells, while non-transformed cells remained largely unaffected. Together, these results identify HPV-selective proteasome subunit dependencies as actionable targets for both cervical cancer treatment and prevention, with minimal toxicity to normal cervical cells and strong potential for combination therapies to reduce resistance and recurrence.

SINGLE-CELL PROTEOMIC PROFILING OF CHEMOTHERAPY-RESISTANT OVARIAN CANCER CELLS

Zongkai Peng[1], Zhibo Yang[1]*

1 Department of Biochemistry and Physiology, University of Oklahoma Health Campus, Oklahoma City, OK, USA

Background

Mass spectrometry (MS)-based single-cell proteomics (SCP) enables quantitative profiling of protein expression at the level of individual cells across thousands of proteins, uncovering cellular heterogeneity and functional states that bulk analyses cannot resolve. SCP is poised to accelerate discoveries in complex biological processes, disease mechanisms, and precision oncology.

Objective

To identify protein biomarkers associated with chemoresistance, we profiled drug-resistant OVCAR8-CPR cells versus drug-sensitive OVCAR8-WT cells.

Methods

Label-free quantitative proteomics was performed using a Vanquish Neo UHPLC system coupled to an Orbitrap Exploris 480 mass spectrometer (Thermo Fisher Scientific). We analyzed single-cell samples and 25-cell pooled samples to assess proteome coverage and differential protein expression.

Results

We identified and quantified ~2,500 proteins per single cell and ~5,600 proteins in 25-cell samples. Comparative analysis revealed 375 proteins upregulated and 483 proteins downregulated in OVCAR8-CPR cells relative to OVCAR8-WT. Notably, S100A2, PLEC, and FLNB were upregulated, whereas SPANSC and ALDH1A3 were downregulated in the chemoresistant group.

Conclusions

SCP provides robust proteome coverage at single-cell resolution and enables the discovery of candidate biomarkers linked to ovarian cancer chemoresistance. These findings lay the groundwork for validation and mechanistic studies and highlight the potential of SCP to inform patient-specific therapeutic strategies

MITOCHONDRIAL HAPLOTYPE-DEPENDENT MODULATION OF LIVER FIBROSIS IN NOVEL OKC-HET$^{B/W}$ RATS DURING AGING AND WESTERN DIET STRESS

Ramasamy Selvarani*, Hoang Van Michelle Nguyen[1], and Arlan Richardson[1,2]

[1]Department of Biochemistry and Physiology, University of Oklahoma, Oklahoma City, Oklahoma.

[2]VA Oklahoma Health Care System, Oklahoma City, Oklahoma.

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Fibrosis is a progressive pathological process marked by excessive extracellular matrix deposition that disrupts issue architecture and function, and it is a major contributor to aging-associated diseases and cancer. Mitochondria are central regulators of fibrotic remodeling through their roles in cellular metabolism, reactive oxygen species production, inflammatory signaling, and cell fate decisions. However, whether mitochondrial haplotype influences fibrotic susceptibility remains largely unexplored. To address this gap, we developed a novel genetically heterogenous rat model (OKC-HET) by crossbreeding four inbred strains (Brown Norway, Fischer 344, Lewis, and Wistar Kyoto), resulting in two mitochondrial haplotypes (OKC-HET^B and OKC-HET^W), which differ by 94 nucleotides. The impact of mt-haplotype on liver fibrosis was studied in male rats under two conditions: aging by comparing 9- and 24-month-old male OKC-HET^B and OKC-HET^W rats and feeding a western diet (WD: %Kcal-42% fat from lard, 29% carbohydrate from sucrose, and 0.203% cholesterol) for six months beginning at three months of age compared to chow-fed animals serving as controls.

Fibrosis was first measured by collagen deposition using picrosirius red staining, Masson's trichrome staining, and hydroxyproline content. These measures revealed an approximately twofold increase in fibrosis with age and WD exposure, with this increase being nearly twofold greater in W-haplotypes rats compared with B-haplotype rats. We next evaluated the severity of fibrosis using the Brunt pathological scoring system, based on the location and extent of fibrosis in liver that ranged from 0 (no fibrosis) to 4 (severe fibrosis). With aging, all W-haplotype rats exhibited more advanced fibrosis, with scores ranging from 2 to 3, whereas only 50% of B-haplotype rats showed fibrosis, limited to a maximum score of 2. Under WD exposure, 70% of W-haplotype rats developed significantly more severe fibrosis with a score of 3, compared with 33% of B-haplotype rats, which predominantly exhibited score of 2. Collectively, these findings demonstrate that mitochondrial haplotype modulates susceptibility to liver fibrosis across both aging and WD stress, with the W-haplotype exhibiting a heightened propensity for fibrotic progression. Because fibrosis is closely associated with increased hepatocellular carcinoma, these data highlight for the first time the potential of mitochondrial haplotype being a factor in the development of hepatocellular carcinoma.

OVEREXPRESSION OF HUMAN MYC IN ZEBRAFISH LYMPHOBLASTS TRIGGERS THE DEVELOPMENT OF DIVERSE ACUTE LYMPHOBLASTIC LEUKEMIA SUBTYPES

Jose Juan Macias[1], Clay Foster[1], & J. Kimble Frazer[1,2,3]
Departments of Microbiology & Immunology[1], Cell Biology[2], and Pediatrics, Section of Pediatric Hematology-Oncology[3], University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA.

Acute Lymphoblastic Leukemia (ALL), a malignancy of immature lymphocytes, is known for its heterogeneity, which has led to the identification of >40 distinct molecular subtypes. Many ALL subtypes have unique mutational landscapes and expression profiles; however, many subtypes share elevated MYC levels. Our lab, and others, have demonstrated transgenic MYC overexpression drives both T- and B-cell ALL at high penetrance. To study MYC's role in T-ALL and B-ALL, we built multi-transgenic zebrafish that overexpress human MYC *(hMYC*) in lymphoblasts with T- and B-lineage fluorescent reporters. Surprisingly, we discovered five fluorescent ALL populations, with several fish harboring multiple cancers simultaneously. We hypothesize that, as in human ALL, these populations arise from unique leukemogenic pathways at varying stages of lymphocyte development, and thus may each represent distinct ALL subtypes. If so, these may exhibit distinct gene expression profiles, cooperative mutations, and cells of origin, with phenotypic consequences, such as different engraftment potential. To investigate this, we are employing Next-Generation Sequencing (NGS), including RNA sequencing and Whole Exome Sequencing (WES), to define each ALL type's molecular profile and clonal heterogeneity. We are also allo-transplanting these different ALL into irradiated recipients to quantitatively assess engraftment efficiency, disease progression, and phenotypic plasticity. Preliminary results reveal that dually-fluorescent ALL have mixed T-/B-cell gene expression, and higher engraftment rates. Some fluorescent populations demonstrate the ability to switch subtype upon engraftment, while others exhibit more than one subtype after engrafting. We believe that characterizing these subtypes and their active leukemogenic pathways will allow us to recognize overlap with human ALL subtypes, enhancing their potential to investigate subtype-specific mechanisms and testing of therapeutic targets.

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Cancer Therapeutics

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10:50 – 11:05 am	**Senior Faculty Research Presentation** **Muhammad Furqan, MD** Pharmacologic Ascorbate in NSCLC: From Redox Targeting to Immune Modulation
11:05 – 11:20 am	**Jr. Faculty Research Presentation** **Mikail Abbasov, PhD** Reimagining Covalent Targeting of Lysines as an Emerging Modality for Cancer Therapeutics
11:20 – 11:35 am	**Trainee Flash Talks** **Saurav Kumar, PhD** Store-operated calcium channels promote glioblastoma-associated vascular cell-induced microglia polarization towards an immunosuppressive phenotype **Falah Fayaz, MD**

Antibody-Drug Conjugate Associated Pneumonitis (AAP) Across Novel First-in-Human Phase I Trials: A Pooled Single-Center Analysis

Lauren Falk, MD

Feasibility of Treatment of Locally Advanced Cervical and Vaginal Cancer with INTERLACE Protocol in a Real-World Patient Population

REIMAGINING COVALENT TARGETING OF LYSINES AS AN EMERGING MODALITY FOR CANCER THERAPEUTICS

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Targeted covalent therapeutics have transformed oncology, yet most discovery efforts remain cysteine-centric, leaving many cancer-relevant proteins and mechanisms pharmacologically inaccessible. Lysines provide an underexploited covalent handle: they are abundant, enriched at protein-protein and protein-nucleic acid interfaces, and are ubiquitous sites of regulatory post-translational modification. In this presentation, I highlight case studies drawn from our recent advances in synthetic chemistry, target-agnostic chemoproteomic technology, and functional biology that collectively reposition lysine targeting as a mechanistically distinct modality for cancer therapeutics.

First, proteome-scale lysine druggability mapping identified Lys351 in Ku70 as a tractable node in the DNA damage response. Covalent engagement of this interface lysine disrupts Ku70-Ku80 assembly in cells in a Lys351-dependent manner, providing a strategy to modulate non-homologous end-joining and probe vulnerabilities to genotoxic stress. Second, synthetic and mechanism-of-action studies of meroterpenoid natural products revealed allosteric control points in glycolysis. The enantiomer (+)-guadial B, but not (-)-guadial B, engages allosteric Lys688 in PFKP to produce Lys688-dependent, isoform-selective inhibition with metabolic consequences consistent with curbing glycolytic flux in the Warburg phenotype. Third, I describe a noncanonical mechanism of IDH2 inhibition in which the natural product jensenone engages Lys299 and Lys413 to induce IDH2 homodimerization that structurally clamps the NADP binding site shut. This allosteric dimerization obstructs oncogenic IDH2-R140Q-driven 2-hydroxyglutarate production, motivating lysine-directed mechanisms orthogonal to existing clinical inhibitors. Finally, activity-based acylome profiling technology extends lysine targeting beyond inhibition to in-cell proteoform engineering. Site-specific, paralog-selective acetylation of Lys150 in IFIT5 disrupts 5'-triphosphate RNA binding, illustrating how chemically written post-translational lysine acetylation states can reprogram RNA-protein interactions that intersect interferon signaling and metastatic programs in cancer.

Together, these case studies reposition lysine targeting from perceived promiscuous reactivity to a residue-defined, mechanism-driven modality that can control protein complexes, metabolic allostery, and regulatory interactions beyond classical pocket occupancy, expanding the actionable landscape for next-generation chemical tools and therapeutic modalities in cancer.

STORE-OPERATED CALCIUM CHANNELS PROMOTE GLIOBLASTOMA-ASSOCIATED VASCULAR CELL-INDUCED MICROGLIA POLARIZATION TOWARDS AN IMMUNOSUPPRESSIVE PHENOTYPE

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Glioblastoma (GBM) is characterized by extensive neovascularization and a profoundly immunosuppressive tumor microenvironment. GBM-associated microglia and macrophages (GAMs) constitute the predominant immune cell population within the tumor and play a central role in promoting tumor growth and immune evasion. Despite their importance, the mechanisms driving the acquisition of a pro-tumorigenic phenotype by GAMs remain incompletely understood. In this study, we demonstrate that GBM-associated vascular cells (GVCs) exhibit elevated expression of pro-tumorigenic and anti-inflammatory cytokines known to modulate macrophage function and polarization. Conditioned medium (CM) derived from GVCs was sufficient to drive microglial polarization toward an immunosuppressive phenotype. Transcriptomic profiling of GVC-reprogrammed microglia revealed significant enrichment of inflammatory gene signatures alongside increased expression of immunosuppressive markers and cytokines. Notably, differential gene expression analysis identified upregulation of the store-operated calcium channel ORAI3. Consistent with these findings, microglia cultured in GVC-CM displayed increased ORAI3 protein expression and elevated intracellular Ca^{2+} levels. Importantly, pharmacological inhibition of ORAI3 reversed the GVC-CM–induced immunosuppressive phenotype in microglia. Collectively, these results identify store-operated calcium channel signaling as a key mediator of GVC-driven microglial immunosuppression in GBM.

ANTIBODY-DRUG CONJUGATE ASSOCIATED PNEUMONITIS (AAP) ACROSS NOVEL FIRST-IN-HUMAN PHASE I TRIALS: A POOLED SINGLE-CENTER ANALYSIS

Falah Fayaz[1*], Ayesha Aijaz[1], Hassan Abu Shukair[1], Jafer Raza[1], Christina Caldwell[1], Debra Wright[1], Adanma Ayanambakkam[1], Raid Aljumaily[1], Susanna Ulahannan[1], Maida Hafiz[1], Debra Richardson[1], Kathleen Moore[1], Abdul Rafeh Naqash[1]

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BACKGROUND: Antibody-drug conjugates (ADCs) are increasingly used in cancer care. However, toxicities like Antibody-Drug Conjugate Associated Pneumonitis (AAP) have emerged as clinically significant and (&) potentially fatal adverse events. Data characterizing AAP across phase 1 trials is limited. METHODS: We retrospectively collected data on patients (pts) enrolled across Phase 1 ADC trials (2015-2025) at our center who were diagnosed (Dx) with AAP. Descriptive statistics were used for analysis. Time to AAP was analyzed using Kaplan–Meier (KM) method & cumulative incidence calculated as 1 – KM. RESULTS: Of 290 phase 1 trials, 25 trials used ADCs with 247 pts enrolled; 14.5% (n = 36/247) developed AAP. Median age at AAP Dx was 70 yrs (IQR = 64.7-74). Leading cancers were ovarian (55.6%, n = 20/36) & endometrial (30.6%, n = 11/36). Preexisting lung disease was present in 8.3% (n = 3/36; COPD: n = 2/3, asthma: n = 1/3); 16.7% (n = 6/36) had prior chest radiation. Median no. of prior therapies (Tx) was three. Prior to ADC start, 50% (n = 18/36) received checkpoint inhibitors. Baseline PFT was done in 36.1% (n = 13/36), with a median baseline DLCO of 58% (IQR 48–90). ADC monotherapy (75%, n = 27/36) was the commonly used Tx. Median duration of ADC Tx was 5.5 months (m). Top ADC targets were FOLR1 (33.3%, n = 12/36), TROP2 (30.6%, n = 11/36) & NaPi2b (19.4%, n = 7/36). Radiographic patterns of AAP are shown (Table). Median time from ADC start to AAP was 3.6 m. Estimated cumulative incidence of AAP was 41.7% (<3 m), 22.2% (3-6 m), & 22.2% (6-12 m). Grade (G) distribution was: G1 (63.9%; n = 23/36), G2 (22.2%; n = 8/36), G3/G4 (5.6%; n=1/36 each), G5 (8.3%; n=3/36). Steroids were given in 75% (n = 27/36) [oral<1 mg/kg (66.6%, n = 18/27); oral ≥1 mg/kg (25.9%, n = 7/27) & IV steroids (7.4%, n = 2/27)]. ADC Tx was permanently discontinued due to AAP in 55.6% (n = 20/36), with G1 AAP in 55% (n = 11/20). 13.9% (n = 5/36) were rechallenged (G1 AAP in 80%, n = 4/5), with 40% (n = 2/5) continuing on trial & 20% (n = 1/5) each discontinuing due to cancer progression, other toxicity, or AAP progression (G2 to G3). ADC therapy continued uninterrupted in 30.6% (n = 11/36), of which 72.7% (n = 8/11) had G1 AAP. CONCLUSION: To our knowledge, this is the largest dataset characterizing AAP across phase 1 ADC trials. The high cumulative incidence of AAP within the first 3m of Tx underscores the need for early recognition with important implications for safety monitoring in Phase 1 ADC drug development.

CT pattern distribution (not mutually exclusive)	**% [Pts with CT pattern/ Total pts (36)]**		
Patchy ground-glass opacities (GGO)	22.2 (8)		
Diffuse GGO	55.6 (20)		
Consolidation	25 (9)		
Nodules	25 (9)		
Fibronodular	16.7 (6)		
Reticular	2.8 (1)		
CT pattern distribution	**ADC Targets** % (CT pattern/Total pts with target)		
	FOLRα	TROP2	NaPi2b
Patchy GGO	8 (1/12)	55 (6/11)	14 (1/7)
Diffuse GGO	50 (6/12)	36 (4/11)	57 (4/7)
Consolidation	42 (5/12)	9 (1/11)	14 (1/7)
Nodules	0 (0)	0 (0)	43 (3/7)

TREATMENT OF LOCALLY ADVANCED CERVICAL AND VAGINAL CANCER WITH INTERLACE PROTOCOL IN A REAL-WORLD PATIENT POPULATION

Lauren Falk, MD[1,2*], Megan Marshalla, MD[1,2], Nicole Minalt, MD[1,2], Laura L Holman, MD, MS[1,2], Christina Washington, MD [1,2], Cassidy Blaiss, PharmD[2], Sarah Hayward, PharmD[2], Uyen-Minh Le, MS[3]

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Objective: To evaluate trends in treating locally advanced cervical and vaginal cancer with the INTERLACE Protocol, which consists of six cycles of induction chemotherapy followed by chemoradiation, in a real-world patient population with a high burden of medical comorbidities and social needs, and to identify patient- and treatment-related factors associated with difficulty completing therapy.

Methods: We conducted a retrospective cohort study of patients with locally advanced cervical or vaginal cancer who were treated with INTERLACE protocol at the Oklahoma University Stephenson Cancer Center, a large academic hospital system serving a high-need urban and rural population. INTERLACE protocol completion was defined as receipt of ≥5 cycles of induction carboplatin/paclitaxel, ≥4 cycles of concurrent cisplatin with 25 fractions of external beam radiation therapy, and vaginal brachytherapy. Completion rates were evaluated in relation to demographic, medical, and oncologic factors, as well as required interventions such as ED visits or admissions. Analyses were performed to identify statistically significant associations.

Results: Thirty-one patients were included (28 cervical, 3 vaginal cancers). Most patients, 77%, had stage II disease, with stage I and III also represented; 87% had squamous histology. Demographically, most patients were <65, had a BMI >30, and lived a median of 35 miles from the hospital [IQR 10-88 miles]. Most patients had at least one major comorbidity other than obesity. In all, 24/31 (77%) completed treatment with the INTERLACE protocol as defined. Notably, 54% of patients required more than 56 days to complete radiation treatment. In univariate analysis, incomplete treatment was associated with a higher median number of co-morbidities and the need for admission while being treated on protocol. Completion was not associated with age, baseline labs, distance to the hospital, or the number of clinic visits during treatment.

Conclusion: Although completion rates for the INTERLACE protocol in this highly comorbid population are similar to those reported in the initial trial data, the majority of patients did not complete chemoradiation within the recommended timeframe, indicating there may still be challenges to implementing this protocol in the real-world setting.

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Cancer Prevention & Control

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2026 Annual Cancer Research Symposium

2:45 – 3:45 pm **Cancer Prevention and Control Program**
Moderator: Darla Kendzor, PhD

2:45 – 2:55 pm **Program Leaders Presentation**
Timothy VanWagoner, PhD
Introduction to the Program/Resources

3:00 – 3:12 pm **Senior Faculty Research Presentation**
Zsolt Nagykaldi, PhD, BTh
Implementing a Tribally-Engaged Lung Cancer Screening Program in Rural Oklahoma – The TEALS Trial

3:13 – 3:25 pm **Jr. Faculty Research Presentation**
Tara Klinedinst, PhD, OTR/L
Feasibility of a Self-Determination and Occupational Therapy-Informed Program to Improve Physical Activity in Breast Cancer Survivors

3:25 – 3:45 pm **Trainee Flash Talks**

Brittany Hudson, PhD, MPH
Beyond The App: A Qualitative Study Of Culture, Trust, And PSA Screening In A Randomized Digital Health Trial Among Black Men

Adele Hammoudi, PhD

Cannabis smoking induces immunosuppression and increases inflammation

Gautham Chengizkhan, PhD
Carcinogenic metal exposures from disposable e-cigarettes

IMPLEMENTING A TRIBALLY-ENGAGED LUNG CANCER SCREENING PROGRAM IN RURAL OKLAHOMA – THE TEALS TRIAL

Zsolt Nagykaldi[1], PhD, BTh, Mark Doescher[1], MD, MSPH; Dorothy Rhoades[2], MD, MPH; Kathleen Dwyer[3], PhD, RN; Ann Chou[4], PhD, MPH; Michele Gibson[5], RN

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Introduction: Uptake of lung cancer screening (LCS) with low-dose computed tomography is very low nationwide (~10-15%). Native American (NA) populations generally have a high prevalence of smoking and lung cancer mortality but low rates of LCS. Awareness and perceptions of LCS among NA men and women have rarely been studied and community-wide LCS programs have rarely been implemented in tribal health systems.

Methods: Using a Community-Engaged Research (CEnR) approach, TEALS developed and tested a multi-level and multi-component LCS implementation program in partnership with Choctaw Nation Health Services in Oklahoma. Between 2021 and 2023, patients eligible for LCS from 6 tribal health clinics were cluster-randomized into early and late interventions groups (n=3 each) and completed a baseline survey before receiving LCS. Surveys included demographics, smoking history, use of cancer preventive services, beliefs regarding personal risk of lung cancer, and perceptions toward LCS. Patients were also followed for LCS uptake and follow-up services and some of them were interviewed about their experience. Practice and health system-level implementation outcomes were also measured.

Findings: Among 420 NA participants (56% women and 44% men), the mean age was 62 years, 49% reported annual household income below $25,000, and 43% reported high school or lower level of education. Seventy-two percent reported smoking currently and the calculated sample-wide pack-years was 51. Most (98%) had one or more primary care visits in the past 12 months and 55% received documented follow-up interventions. Documented LCS up-to-dateness increased from 44.7% at baseline to 68.5% post-intervention in the total sample (n=420; p=0.014). Over 6% of nodules were categorized as “suspicious” (Lung-RADS 4). Among LCS care and patient attitudes indicators, encouraging the patient to talk about health concerns (85% vs. 92%; p=0.04), offering clinical choices for patient care (79% vs. 83%; p=0.03), discussing care plans with the clinician (90% vs. 92% ; p=0.05), offering a CT scan to look for lung cancer (55% vs. 79%; p<0.01), and raising patient awareness about LCS (61% vs. 79%; p<0.01) significantly increased. Patient interviews indicated that strong clinician-initiated conversations and recommendations are critical for increasing LCS uptake. However, practices often lack the time, staff, and resources to provide patient education and shared decision-making. Additional training is also needed to address patient fears, misconceptions, stigma, and fatalism about LCS, as few existing interventions specifically target these barriers.

Conclusions: The TEALS trial significantly enhanced LCS uptake, patient–clinician interaction, shared decision-making, and screening navigation among a predominantly Native American, socioeconomically disadvantaged population. Our results demonstrate that well-designed, multi-level interventions can meaningfully improve LCS in underserved populations and offer a scalable model for increasing LCS uptake in similar community settings.

FEASIBILITY OF A SELF-DETERMINATION AND OCCUPATIONAL THERAPY-INFORMED PROGRAM TO IMPROVE PHYSICAL ACTIVITY IN BREAST CANCER SURVIVORS

K. Branstetter, OTS[1], N. Stanley, BA[2], M.C. Robertson, PhD, MPH[2], Z.C. Pope, PhD, ACSM-EP[2], and T.C. Klinedinst, PhD, OTR/L[1]

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Background: Breast cancer and its treatment commonly reduce aerobic physical activity (PA) and muscle-strengthening exercise (MSE), and many breast cancer survivors are unable to integrate these health-promoting behaviors into their daily lives after transitioning out of formal care settings. As a result, fewer than 20% of breast cancer survivors meet recommended PA guidelines. To address this gap, we developed a novel telehealth occupational therapy (OT) program that is guided by Self-Determination Theory (SDT) and promotes self-regulatory strategies to promote PA (e.g., self-monitoring via a wearable PA tracker). In this study, we aimed to assess intervention feasibility and implementation fidelity.

Methods: Participants engaged in an eight-week, Zoom-delivered OT program with a licensed and lymphedema-certified occupational therapist (*N*=20). Weekly sessions focused on improving knowledge and skills for (1) reducing functional limitations associated with cancer and its treatment and (2) developing behavioral skills for maintenance of aerobic PA and MSE. Participants were urban and rural breast cancer survivors within Oklahoma City and the surrounding area. We recruited participants via local survivorship organizations and the Stephenson Cancer Center Clinical Trials Office. Eligible participants were adults (≥18 years) with invasive breast carcinoma who completed primary treatment and/or surgery within 24 months of the enrollment date. We examined feasibility and reach via recruitment and retention rates, intervention dosage, urban vs. rural breakdown, and a program evaluation survey (*n*=17). We assessed fidelity by randomly selecting 20% of sessions and applying a predetermined fidelity checklist to evaluate the occupational therapist's adherence to the intervention protocol and program delivery competence.

Results: Recruitment rates averaged approximately two participants per month over the first 15 months, with five enrolled participants (25%) being rural-dwelling Oklahoma residents. The retention rate was 85% over this period. Participants completed 97.8% of expected OT sessions (133/136 total sessions; mean session duration: 40 minutes, *SD* = 12.38). Ninety-four percent of participants reported increased ability to be physically active. Observations indicated 98% adherence to the OT session protocol by the occupational therapist. Mean competence across sessions for the occupational therapist was 1.4 on a 0-2 scale (0 = inadequate, 1 = adequate, 2 = exceptional).

Discussion: Observations suggest that the remotely delivered, SDT-informed OT program is feasible among breast cancer survivors. Furthermore, results suggest that the program can be delivered with high-fidelity following the provision of basic training to the occupational therapist. Final study results will allow us to refine this program for fully powered efficacy testing and broader dissemination.

BEYOND THE APP: A QUALITATIVE STUDY OF CULTURE, TRUST, AND PSA SCREENING IN A RANDOMIZED DIGITAL HEALTH TRIAL AMONG BLACK MEN

Brittany L. Hudson, Pragya Dhar, Jordan Neil, Bingjing Mao, Ruosi Shao, Motolani E. Ogunsanya, Summer G. Frank-Pearce, Michael Businelle, Michael Cookson, Kelly Stratton, Mark Doescher, Stephanie Pharr, Valerie Moise, Brianna Fleshman, Jack Fronheiser, Kimberly Estrada, Iván Flores, David Bradley, Starla Johnson, Ashley Kendrick, Adam C. Alexander

Background: Prostate cancer is the most frequently diagnosed cancer and the second-leading cause of cancer-related death among Black men in the United States. Despite elevated risk, prostate-specific antigen (PSA) screening uptake remains low, shaped by cultural beliefs, structural barriers, and mistrust of the healthcare system. A pilot randomized controlled trial (RCT) evaluated the feasibility of a culturally tailored digital intervention, the Prostate Cancer Genius App (PCGA), compared with an existing U.S. Preventive Services Task Force (USPSTF) App, among Black men aged 55–69 in Oklahoma who were not up to date with PSA screening.

Objective: This qualitative study explored how Black men described shifts in perceptions of PSA screening after using each app, and how culture, masculinity, trust, and structural context shaped engagement, readiness, and follow-through.

Methods: Semi-structured interviews were conducted with 89 participants enrolled in the parent RCT (PCGA, n=46; USPSTF, n=43). Interim thematic analysis focused on 26 fully analyzed interviews (PCGA, n=16; USPSTF, n=10), examining app usability, engagement, screening experiences, and contextual influences on decision-making.

Data were analyzed using a hybrid inductive–deductive thematic analysis approach informed by a theoretical framework of acceptability. Deductive codes were derived from the framework and interview guide, while inductive coding captured emergent themes grounded in participants' narratives. Seven trained coders participated in the analysis, supported by structured onboarding, co-coding, and iterative codebook refinement. Weekly analytic meetings addressed reflexivity and positionality, resolved discrepancies, and supported methodological rigor. Dedoose software was used for data management and analysis.

Results: Across both study arms, PSA screening engagement was constrained by broader systemic factors. Economic strain, mental health burden, and limited systems literacy shaped screening readiness and follow-through, revealing gaps between increased awareness and sustained preventive action.

Among PCGA users, themes reflected cultural affirmation and trust-building, including validation through representation, reduced stigma via survivor narratives, reframing PSA screening as

responsible rather than threatening, and increased confidence rooted in culturally relevant messaging. Among USPSTF app users, themes reflected pragmatic acceptability and instrumental trust, characterized by knowledge as empowerment, convenience, privacy, and efficiency.

Across both groups, healthcare navigation burden emerged as a cross-cutting theme, including uncertainty about next steps, difficulty accessing providers, and persistent mistrust of healthcare systems.

Conclusion: Interim findings suggest that culturally tailored digital interventions may enhance relevance and confidence among Black men, but education alone is insufficient to overcome persistent structural and healthcare navigation barriers. Differences between culturally tailored and standard apps underscore the importance of representation and contextualized messaging, while shared challenges point to systemic constraints that extend beyond app design. These findings highlight the need for multilevel, culturally responsive strategies to support equitable prostate cancer screening.

CANNABIS SMOKING INDUCES IMMUNOSUPPRESSION AND INCREASES INFLAMMATION

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Introduction: Cannabis is the most used federally illegal drug in the United States with a percentage increased from 19.0% in 2021 to 22.3% in 2024 among people aged 12 or older. Smoking remains the most common mode of cannabis use, even among cancer patients. Despite the anti-inflammatory potential of certain cannabinoids, cannabis smoke contains numerous carcinogens and toxicants that can potentially disrupt immune homeostasis and heighten inflammation. Understanding these effects is crucial as inflammation and immune function shape cancer development, progression, and therapeutic response.

Objective: To characterize systemic inflammation and immune alterations associated with cannabis smoking.

Methods: Following IRB approval, 44 participants were recruited via Redcap, a secure online survey. Demographics, substance use data, and blood samples were collected for a total of 24 non-users (NU) and 20 exclusive cannabis users (CAN) who reported to smoke cannabis at least bi-weekly over the past month. Users of tobacco products, including blunts and e-cigarettes, were excluded. Product use status was biochemically verified using liquid chromatography tandem mass spectrometry (LC-MS) to quantify THC and its metabolite THC-COOH. Complete blood count (CBC) was obtained on each participant and (CBC)-derived inflammatory markers were calculated. A novel 13-antibody multiparametric flow cytometry panel was used to separate 21 immune cell subsets characterizing both myeloid and lymphoid cells. Data was analyzed using Welch's t-tests.

Results: Our CBC data shows significantly higher red blood cell distribution width-standard deviation (p=0.038) and lower absolute number of monocytes (p=0.038) in CAN users compared to NU. We also observed a significant increase in platelet-to-lymphocyte ratio in CAN users vs NU (p=0.028). Our myeloid immune cell phenotyping data show that cannabis smokers have significantly higher number of mature low-density neutrophils (LDNs) than NU (p=0.05) and lower number of dendritic cells (p=0.037) mainly plasmacytoid DCs ($CD11c^{inter/low}$ DCs) (p=0.010). These findings indicate that cannabis smoking induces systemic inflammation (higher PLR and LDNs) and suppresses immune responses (fewer DCs).

Conclusions: Our data demonstrate for the first time that cannabis smoking induces a pro-inflammatory and immunosuppressive state that may promote diverse human diseases, including cancer. We established the first comprehensive framework to evaluate the immunological effects of cannabis smoking. These findings reveal how cannabis use profoundly alters the immune system at both cellular and functional levels.

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CARCINOGENIC METAL EXPOSURES FROM DISPOSABLE E-CIGARETTES

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Significance: Conventional cigarette smoking has declined, while use of electronic cigarettes has increased, driven largely by disposable products such as Geek Bars that offer high nicotine delivery and ease of use. Although marketed as safer alternatives, their aerosol composition raises public health concerns. Understanding puffing behavior is critical for assessing exposure to carcinogenic and toxic metals that may increase cancer risk. This study examines how real-world puffing topography influences metal emissions from Geek Bar aerosols. **Methods:** Of 592 individuals screened via REDCap, 274 were eligible and 56 enrolled for an in-person visit. During an ad libitum 2-hour vaping session, continuous puff topography was recorded using an eTop device. A cluster was defined as ≥2 puffs occurring within 60 s of the previous puff; clusters were categorized as short (2-5), medium (6-10), or long (>10), while puffs >60 s apart were classified as single. Median puff duration, flow rate, and interpuff interval were obtained and used to program a puffing simulator under realistic use conditions. Aerosols were collected in ultrapure water (1 puff/mL) and analyzed for 19 metals by inductively coupled plasma mass spectrometry (ICP-MS). Two-way ANOVA with post-hoc pairwise testing was used for statistical analysis. **Results:** The study enrolled 22 disposable e-cigarette users (median age 28 years; 8 male, 14 female), contributing a total of 44 vaping sessions. Puff topography demonstrated substantial variability in vaping behavior, with distinct distributions of single and clustered patterns. Single puffs accounted for 62.1% of all bouts, followed by short clusters (2-5 puffs; 35.2%), medium clusters (6-10 puffs; 1.7%), and long clusters (>10 puffs; 1.0%). Puff duration, flow rate, and interpuff interval differed across cluster categories. Of the 19 metals analyzed, 5 are classified as known carcinogens, while the remaining metals are toxic or trace elements. In Geek Bar aerosols, elevated concentrations of carcinogenic metals (lead, chromium, arsenic, and cadmium) were observed even during single puffs. Notably, chromium release was sustained across all puff clusters, indicating continuous metal emission across vaping behaviors. **Conclusion:** This study demonstrates that carcinogenic metal exposure from Geek Bars is not limited to intensive puffing, as elevated emissions were detected even during single puffs and persisted across puffing patterns. These findings challenge assumptions of lower-risk use and provide evidence to

guide regulatory and public health efforts aimed at reducing metal exposure from disposable e-cigarettes.

Keywords: Disposable e-cigarettes, carcinogenic metals, puffing behavior, cancer risk

Funding sources: This work was supported in part by the National Cancer Institute (NCI) of the National Institutes of Health (R01CA242168, P30CA225520).

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2026 Annual Cancer Research Symposium

3:45 – 4:30 pm	**Cancer Center Cores** *Moderator: Stevie Warner, MA, MHR*
3:45 – 4:00 pm	**Mark Doescher, MD, MSPH** Community Outreach and Engagement
4:00 – 4:15 pm	**Rajagopal Ramesh, Ph.D., DBA, FAIMBE** Cancer Research Training and Education Coordination
4:15 – 4:30 pm	**Sara Vesely, PhD** Biostatistics & Research Design Shared Resources
	Kar-Ming Fung, PhD Tissue Pathology & Biospecimen Shared Resources
	Michael Businelle, PhD Mobile Health Technology Shared Resources
	James Papin, PhD Molecular Biology and Cytometry Research Shared Resources

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Poster Session

Poster Session

(Listed A-Z by Presenters First Name)

Poster #	First Name	Last Name	Appointment	SCC Research Program	Title of Abstract:
1	Ahmed A.	Adib	Graduate Student	Cancer Biology	MULTI-MODAL ANALYSES OF B CELLS IN FOLLICLES AND GERMINAL CENTERS DURING THYMIC INVOLUTION
2 OMITTED	Marjan	Ghanbariabdolmaleki	Graduate Student	Cancer Biology	SYSTEMATIC BENCHMARKING OF NUCLEI ISOLATION PROTOCOLS IN CELL LINES AND TISSUES
3 OMITTED	Md Shahadat	Hossain	Graduate Student	Cancer Biology	A CDK-CENTERED SWITHCH BALANCES ORIGIN USAGE AND FORK SPEED DURING GENOME DUPLICATION
4 OMITTED	Olajumoke	Oladapo	Graduate Student	Cancer Biology	ATLASCOLLECT: A SINGLE CELL DATA ATLAS PLATFORM AND UNIFIED PLATFORM FOR DATASETS COLLECTION AND INTEGRATION
5	Phoebe	Ohene-Marfo	Graduate Student	Cancer Biology	THE NON-NECROPTOTIC ROLE OF HEPATOCYTE MLKL IN THE PROGRESSION OF MASLD RELATED-HCC
6	Sagarika	Das	Graduate Student	Cancer Biology	SARS-COV2 GENES FUNCTIONALLY INTERACT WITH HUMAN PAPILLOMAVIRUS ONCOPROTEIN E6
7 OMITTED	Swati	Choudhary	Graduate Student	Cancer Biology	SMALL MOLECULE TARGETING OF OXYSTEROL-BINDING PROTEINS OVERCOMES CHEMORESISTANCE IN OVARIAN CANCER THROUGH REWIRING CELLULAR STRESS RESPONSES
8	Youla	Ali	Graduate Student	Cancer Biology	A CLUSTERING-BASED METRIC FOR ASSESSING BATCH EFFECT IN SINGLE-CELL RNA SEQUENCING DATA INTEGRATION
9	Arpan	Dey Bhowmik	Postdoctoral Fellow	Cancer Biology	REEXPRESSION OF miR-195 VIA AURO-LIPOSOME MEDIATED DELIVERY ENHANCES CHEMOSENSITIVITY AND SUPPRESS OVARIAN CANCER
10	Chao	Jiang	Postdoctoral Fellow	Cancer Biology	NECROPTOSIS-INDEPENDENT ROLE OF HEPATOCYTE MLKL IN LIVER INFLAMMATION AND METABOLIC DYSFUNCTION AS A POTENTIAL CONTRIBUTOR TO LIVER CANCER
11	Clay	Foster	Postdoctoral Fellow	Cancer Biology	A MULTI-OMIC DISSECTION OF MYC-DRIVEN LEUKEMIA REVEALS CONVERGENT TRANSCRIPTIONAL AND REPLICATIVE VULNERABILITIES
12	Megan	Marshalla	Clinical Fellow	Cancer Biology	POTENTIAL THERAPEUTIC TARGET: CHARACTERIZING DOUBLECORTIN LIKE KINASE 1 (DCLK1) EXPRESSION AND ROLE IN CHEMORESISTANT OVARIAN CANCER
13	Zoheb	Ahmed	Postdoctoral Fellow	Cancer Biology	DCLK1 MEDIATES HEPATOCYTE-MACROPHAGE DYSREGULATION TO DRIVE LIVER FIBROSIS AND HEPATOCARCINOGENESIS
14	Charles	Street	Undergraduate Student	Cancer Biology	COMPUTATIONAL TUMOR PROGRESSION ANALYSIS VIA SERIATION BASED TRAJECTORY INFERENCE

15	Iman	Owens	Research Trainee	Cancer Biology	TESTING LEUKEMIA-ESSENTIAL GENES VIA SOMATIC TRANSGENESIS AND SCALE ALLO-TRANSPLANTATION
16	Pearl	Daugaard	Research Assistant	Cancer Biology	CELLULAR AND MOLECULAR PROFILING OF THE INFERIOR COLLICULUS BRAIN REGION IN SINGLE NUCLEI RESOLUTION
17	Suryakant	Niture	Faculty	Cancer Biology	RADIATION-MEDIATED ELEVATED DUSP1 PROMOTES RADIORESISTANCE IN TRIPLE-NEGATIVE BREAST CANCER
18	Suryaveer	Kapoor	Graduate Student	Cancer Biology	WESTERN DIET AND PQQ DIFFERENTIALLY SHAPE LIVER (IMMUNE) CELL STATES REVEALED BY SINGLE-CELL RNA SEQUENCING.
19 OMITTED	Tuan	Nguyen	Graduate Student	Cancer Biology	CENTRAL GENES: A NOVEL CENTRALITY-BASED AB INITIO APPROACH FOR INFORMATIVE GENE SELECTION IN SINGLE CELL RNA-SEQ ANALYSIS
20	Anthonia	Oladokun	Graduate Student	Cancer Prevention and Control	PSYCHOLOGICAL AND SOCIAL CORRELATES OF CANCER INFORMATION-SEEKING: EVIDENCE FROM SINGAPORE
21	Esma	Sheikh	Graduate Student	Cancer Prevention and Control	SPATIOTEMPORAL ANALYSIS OF LUNG CANCER INCIDENCE AND MORTALITY TRENDS IN OKLAHOMA (2004-2022)
22	James	Nyamao	Graduate Student	Cancer Prevention and Control	A SYSTEMATIC REVIEW ON THE INFLUENCE OF CHRONIC HEALTH CONDITIONS ON COLORECTAL CANCER (CRC) SCREENING AMONG BLACK/AFRICAN AMERICAN ADULTS AGED 45 –75 YEARS
23	Joanna	George	Medical Student	Cancer Prevention and Control	ORAL CANCER RECURRENCE DECREASES 4-FOLD FOLLOWING SMOKING CESSATION AFTER DIAGNOSIS
24	Junyuan	Liu	Graduate Student	Cancer Prevention and Control	BASED ON STATIC-COMPRESSION OPTICAL COHERENCE ELASTOGRAPHY, QUANTITATIVE ELASTICITY ASSESSMENT METRICS ARE PROVIDED FOR BIOLOGICAL TISSUES
25 OMITTED	Kiana	Amani	Graduate Student	Cancer Prevention and Control	OPTIMAL ROUTING FOR MOBILE LUNG CANCER SCREENING VEHICLE UNDER UNCERTAIN SCREENING PARTICIPATION: A CASE STUDY IN OKLAHOMA
26	Kriti	Adhikari	Graduate Student	Cancer Prevention and Control	CO-DEVELOPING A MEDICATION MANAGEMENT APP TO SUPPORT TREATMENT PARTICIPATION AMONG ADOLESCENTS AND YOUNG ADULTS WITH HEMATOLOGY/ONCOLOGY CONDITIONS.
27	Madison	Hemenway	Graduate Student	Cancer Prevention and Control	DOUBLE UP OKLAHOMA DUO FOR HEALTH: LESSONS LEARNED AND FUTURE DIRECTIONS
28 OMITTED	Malika	Sekhri	Graduate Student	Cancer Prevention and Control	EXPLORING THE ROLE OF OBESITY-ASSOCIATED EXTRACELLULAR MATRIX IN LOCAL BREAST CANCER PROGRESSION
29	Mingwei	Huang	Graduate Student	Cancer Prevention and Control	POSTSURGICAL PERILESIONAL FUNCTIONAL CONNECTIVITY PREDICTS NEUROLOGICAL OUTCOME IN GLIOMA PATIENTS

30	Nubwa	St James	Graduate Student	Cancer Prevention and Control	FACTORS ASSOCIATED WITH WOMEN'S PREFERENCE FOR AT-HOME CERVICAL CANCER SELF-TESTING: A CROSS-SECTIONAL STUDY USING HINTS AND THE ANDERSEN BEHAVIORAL MODEL
31	Ronghao	Liu	Graduate Student	Cancer Prevention and Control	OPTICAL COHERENCE TOMOGRAPHY DETECTS BILIARY MICROSTRUCTURAL ALTERATIONS FOR EVALUATING BILE DUCT VIABILITY IN LIVER TRANSPLANTATION
32	Sophia	Darrow	Graduate Student	Cancer Prevention and Control	OKLAHOMA FOOD IS MEDICINE LANDSCAPE ANALYSIS: OPPORTUNITIES FOR CANCER PREVENTION, TREATMENT, AND RECOVERY
33	Bibi	Maryam	Resident	Cancer Prevention and Control	FINANCIAL HARDSHIP SCREENING IN NATIVE AMERICAN PATIENTS WITH CANCER: RESULTS FROM A QUALITY IMPROVEMENT PROGRAM AT AN NCI-DESIGNATED CANCER CENTER
34	Dorina	Nagy	Postdoctoral Fellow	Cancer Prevention and Control	CHEMO- AND RADIOTHERAPY PROMOTE CEREBROMICROVASCULAR PATHOLOGY IN A PRECLINICAL MODEL OF PEDIATRIC MEDULLOBLASTOMA
35	Jafer	Raza	Postdoctoral Fellow	Cancer Prevention and Control	CLINICAL CHARACTERISTICS AND TREATMENT PATTERNS OF RENAL CELL CARCINOMA AMONG NATIVE AMERICAN PATIENTS IN OKLAHOMA
36	Ravi	Gor	Postdoctoral Fellow	Cancer Prevention and Control	PASSIVE SMOKE EXPOSURE AT HUMAN-RELEVANT LEVELS ENHANCES STEM CELL-LIKE PROPERTIES IN HEAD AND NECK SQUAMOUS CELL CARCINOMA
37	Sulfath	Thottungal Parambil	Postdoctoral Fellow	Cancer Prevention and Control	DISTINCT ORAL MUCOSA TRANSCRIPTOMIC RESPONSES ASSOCIATED WITH VAPING AND SMOKING
38	Carl	Witten	HPRC Research Staff	Cancer Prevention and Control	USING DAILY SMARTPHONE-BASED SURVEYS TO UNDERSTAND HOW HEALTH BEHAVIORS IMPACT AFFECT
39	Carson	Freeman	Staff Research Assistant	Cancer Prevention and Control	CORRELATES OF EXPOSURE TO ANTI-TOBACCO CAMPAIGNS ON SOCIAL MEDIA AMONG YOUNG ADULTS WHO VAPE
40	Isaias	Salgado	Staff	Cancer Prevention and Control	USING EMA DATA TO EXPLORE RELATIONS BETWEEN DAILY ALCOHOL AND TOBACCO USE AND SLEEP
41 OMITTED	Jason	Oliver	Faculty	Cancer Prevention and Control	CHARACTERIZING AND EVALUATING THE IMPACT OF DAILY NON-SUBSTANCE REINFORCEMENT IN TOBACCO USE
42	Karly	Bradford	HPRC Research Staff	Cancer Prevention and Control	A LONGITUDINAL EXAMINATION OF RELATIONS BETWEEN OPTIMISM AND PSYCHOSOCIAL VARIABLES
43	Lacey	Caywood	Research Staff & Mentee	Cancer Prevention and Control	PILOT IMPLEMENTATION OF BEHAVIORAL NUDGES IN GROCERY STORES TO PROMOTE FRUIT AND VEGETABLE PURCHASING
44	Matthew	Masapollo	Assistant Professor	Cancer Prevention and Control	TRACKING LONGITUDINAL CHANGES IN SPEECH MOTOR CONTROL AFTER PARTIAL GLOSSECTOMY AND LINGUAL RADIATION

45	Na	Wang	Graduate Student	Cancer Prevention and Control	EFFECTS OF ALCOHOL-RELATED BREAST CANCER WARNINGS ON BEHAVIORAL INTENTIONS AMONG YOUNG ADULT FEMALES IN THE UNITED STATES WHO ARE CURRENT DRINKERS
46	Peter	Mukli	Faculty	Cancer Prevention and Control	CHEMOTHERAPY IMPAIRS NEUROVASCULAR COUPLING RESPONSES IN BREAST CANCER SURVIVORS: A PILOT STUDY
47	Sheryl	Buckner	Resident	Cancer Prevention and Control	EFFECTIVENESS OF CLINICAL TRIALS EDUCATION (CTE) FOR NATIVE AMERICAN (NA) PATIENTS WITH CANCER: A QUALITY IMPROVEMENT PROJECT
48	Angelina	Akomea	Graduate Student	Cancer Therapeutics	EXOSOME-GUIDED GENERATION OF TUMOR-TARGETING MONOCLONAL ANTIBODIES FOR PANCREATIC CANCER
49	Brian	Baharestani	Graduate Student	Cancer Therapeutics	THE IMMUNOMODULATORY EFFECTS OF GLYCATED CHITOSAN ON CYTOKINE REGULATION AND MACROPHAGE PHENOTYPE
50 OMITTED	Coline	Furrer	Graduate Student	Cancer Therapeutics	A MULTIFUNCTIONAL NANOMATERIAL PLATFORM FOR TUMOR ABLATION AND SUSTAINED ANTITUMOR IMMUNE PROTECTION
51	Federico Jesus	Flores Arce	Graduate Student	Cancer Therapeutics	TARGETED ANNEXIN A5–MERTANSINE CONJUGATE FOR LEUKEMIA THERAPY
52	Maryam	Firouzi	Graduate Student	Cancer Therapeutics	TUMOR-DERIVED EXOSOMES AS A PLATFORM FOR GENERATING TARGETED ANTIBODIES IN OVARIAN CANCER THERAPY
53	Mobina	Mohammadnejad	Graduate Student	Cancer Therapeutics	LABEL-FREE AND HIGH-THROUGHPUT QUANTIFICATION OF NANOPARTICLE-CELL INTERACTIONS AT THE SINGLE-CELL LEVEL WITH FLOW CYTOMETRY
54	Shriya	Pandey	Graduate Student	Cancer Therapeutics	CRITICAL ROLE OF STAT3 IN DRUG TOLERANCE TO RET-SELECTIVE PROTEIN TYROSINE KINASE INHIBITORS
55 OMITTED	Abhirami	Das	Resident	Cancer Therapeutics	CLINICOPATHOLOGIC FEATURES, TREATMENT PATTERNS, AND OUTCOMES OF AMERICAN INDIAN/ALASKA NATIVE MEN WITH PROSTATE CANCER IN OKLAHOMA: STEPHENSON CANCER CENTER EXPERIENCE COMPARED WITH SEER
56 OMITTED	Aleksandr	Shishkin	Postdoctoral Fellow	Cancer Therapeutics	NOVEL INTEGRATED CROSS-SPECIES PIPELINE FOR NEOEPITOPE PREDICTIONS.
57	Hassan	Abushukair	Postdoctoral Fellow	Cancer Therapeutics	MACHINE LEARNING (ML)–BASED PREDICTION OF FATAL IMMUNE CHECKPOINT INHIBITOR (ICI)–ASSOCIATED MYOCARDITIS (MC) WITH MULTI-COHORT VALIDATION
58	Kelsie	Guice	Resident	Cancer Therapeutics	ASSOCIATION OF PATIENT AND TUMOR CHARACTERISTICS WITH SURVIVAL IN UTERINE LEIOMYOSARCOMA PATIENTS
59 OMITTED	Lauren	Falk	Clinical Fellow	Cancer Therapeutics	FEASIBILITY OF TREATMENT OF LOCALLY ADVANCED CERVICAL AND VAGINAL CANCER WITH INTERLACE PROTOCOL IN A REAL-WORLD PATIENT POPULATION

60 OMITTED	Nisha	Thomas	Postdoctoral Fellow	Cancer Therapeutics	HEPARANASE AND SULF2 INHIBITION SENSITIZES TRIPLE-NEGATIVE BREAST CANCER TO CHEMOTHERAPY
61	Ryan	Kiser	Early Stage Investigator | Junior Faculty	Cancer Therapeutics	PREVALENCE OF THERAPY RELATED MICROVASCULAR LESIONS IN FIVE YEAR MEDULLOBLASTOMA SURVIVORS
62 OMITTED	Saurav	Kumar	Postdoctoral Fellow	Cancer Therapeutics	STORE-OPERATED CALCIUM CHANNELS PROMOTE GLIOBLASTOMA-ASSOCIATED VASCULAR CELL-INDUCED MICROGLIA POLARIZATION TOWARDS AN IMMUNOSUPPRESSIVE PHENOTYPE
63	Somasekhara	Derangula	Postdoctoral Fellow	Cancer Therapeutics	ATOVAQUONE ATTENUATES PANCREATIC CANCER–INDUCED CACHEXIA
64	Syed Saqib	Balkhi	Postdoctoral Fellow	Cancer Therapeutics	ECONOMIC AND TIME TOXICITY IMPACT OF PEMBROLIZUMAB DOSING SCHEDULE OPTIMIZATION IN ADJUVANT TREATMENT OF CLEAR CELL RENAL CELL CARCINOMA
65	Henley	Calhoun	Undergraduate Student	Cancer Therapeutics	TRACKING NANOPARTICLE SPATIOTEMPORAL DISTRIBUTIONS IN OVCAR8 OVARIAN CANCER SPHEROIDS USING EXPANSION MICROSCOPY
66	Isaac	Atkins	Undergraduate Student	Cancer Therapeutics	OPTICAL COHERENCE TOMOGRAPHY EVALUATION OF MEBENDAZOLE THERAPEUTIC EFFICACY IN OVARIAN CANCER XENOGRAFTS
67	Nicole	Minalt	Clinical Fellow	Cancer Therapeutics	CISPLATIN-INDUCED OTOTOXICITY IN GYNECOLOGIC MALIGNANCIES
68	Kaili	Liu	Faculty	Cancer Therapeutics	ANTI-TUMOR EFFECTS ON TUMOR-INFILTRATING NATURAL KILLER CELLS BY LOCALIZED ABLATIVE IMMUNOTHERAPY AND IMMUNE CHECKPOINT INHIBITORS: AN INTEGRATED AND COMPARATIVE STUDY USING SCRNASEQ ANALYSIS
69	Qinghao	Zhang	Graduate Student	Cancer Therapeutics	EVALUATING THE EFFICACY OF MEBENDAZOLE REPURPOSING FOR OVARIAN CANCER THERAPY USING OPTICAL COHERENCE TOMOGRAPHY
70	Sampurna	Chakraborti	Graduate Student	Cancer Therapeutics	ADVANCING TREATMENT FOR TRIPLE-NEGATIVE BREAST CANCER: INTEGRATING PHOTOTHERMAL THERAPY WITH IMMUNOMODULATION IN A PRECLINICAL MODEL

MULTI-MODAL ANALYSES OF B CELLS IN FOLLICLES AND GERMINAL CENTERS DURING THYMIC INVOLUTION

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Background: Thymic involution, which peaks during puberty, is the atrophy of thymic lymphocytes (i.e. thymocytes) due to reduced T cell production and adipose tissue replacement. Involution is the first major step of immunosenescence, or age-related immune function decline. In addition to diminished T cell output, thymic B cells are impacted by involution also. Intriguingly, pediatric thymic B and T cell cancers peak during thymic involution as well. How thymic involution occurs at a cellular level, and any possible relation to thymic cancers, are poorly understood.

Objective: To define changes in thymic B cells during involution, including changes in these populations as evidenced by their protein and gene expression profiles.

Methods: We collected 35 thymic specimens from patients 1 month-19 years [infant (birth-1y, n=9), toddler (1-6y, n=5), pre-pubertal (6-10y, n=9), and peri-pubertal (≥10y, n=12). H&E and IHC staining for CD19 (B cells), CD21 (follicular dendritic cells), and BCL6 (germinal centers, GC) were performed to identify follicles and GC. To analyze protein expression, Imaging Mass Cytometry (IMC) was conducted on 13 sections representing all age groups, testing 4 regions of interest (ROI) in each (n = 52). To profile gene expression, Xenium™ Spatial Transcriptomic (ST) analysis of 5000 genes was conducted on 32 ROI across 4 age groups. Tonsil sections served as controls for IMC and ST.

Results: Unexpectedly, we identified B cell follicles (CD19/21$^+$ foci) in pre-pubertal thymi, found exclusively in medulla. However, during involution (i.e., peri-pubertal thymi), we detected GC (CD19/CD21/BCL6$^+$ foci). IMC corroborated these patterns, revealing medullary follicles and GC comprising unique cellular neighborhoods. Our findings were further validated by ST, which showed cell clusters with different gene expression in and surrounding follicles and GC. Moreover, tonsillar vs thymic GC comparisons demonstrated distinct transcriptional signatures.

Conclusions: We have established thymic B cell follicles develop as puberty approaches, and GC form coincident with puberty and involution. We also demonstrated these structures reside in distinct medullary cellular neighborhoods. We hypothesize follicle and GC formation may play a

role in involution, and that involution perturbations may spawn thymic lymphoid malignancies. Future work will investigate the antigenic targets that trigger the genesis of thymic follicles and GC, and genetic pathways underlying their formation.

EXOSOME-GUIDED GENERATION OF TUMOR-TARGETING MONOCLONAL ANTIBODIES FOR PANCREATIC CANCER

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Introduction: Pancreatic ductal adenocarcinoma (PDAC) remains highly lethal because of late diagnosis, rapid progression and resistance to standard therapies. We propose an exosome-guided antibody discovery strategy in which small extracellular vesicles (sEVs) from pancreatic cancer cells are used as immunogens to generate monoclonal antibodies (mAbs) that retain high affinity for antigens displayed on the surface of the parent tumor cells.

Method: In this study, the size and concentration of exosomes isolated from Panc-1 human cell line were characterized by nanoparticle tracking analysis (NTA). The affinity tests were accomplished through immunochemistry technology. Mice were then immunized by three intraperitoneal (IP) injection of Panc-1 exosomes (5 $x10^9$ particles/dose with complete and incomplete adjuvants) at 2-week intervals. Following administration, antibody production in mice serum were visualized by immunocytochemistry against Panc-1 cells. Hybridoma cells were then generated by fusing the splenic B-cells from the immunized mice with myeloma cells. Antibody screening was conducted by testing the supernatants from multiple hybridomas for binding affinities to Panc-1 cells. Single-cell cloning was subsequently used to isolate hybridomas capable of producing monoclonal antibodies for selective targeting of pancreatic cancer cells.

Results/Conclusions: The size and concentration of exosomes were an average size of ~100 nm and concentration of $1.6x10^{11}$ particles/ml respectively. The serum from vaccinated mice showed the parent pancreatic cancer cell affinity, proving the production of antibody within the body. After successful establishment of hybridoma cells, the antibody showing the highest affinity to the parent pancreatic cancer cell was screened. Our results shows that Panc-1 derived exosomes can be used to generate specific monoclonal antibodies that bind strongly to these pancreatic cancer cells. These antibodies will enable ligand discovery for future development of targeted therapeutics for PDAC. Future studies will focus on optimizing exosome formulations by using oxaliplatin-loaded $CD8^+$ T-cell derived in Panc-1 tumor bearing mice.

PSYCHOLOGICAL AND SOCIAL CORRELATES OF CANCER INFORMATION-SEEKING: EVIDENCE FROM SINGAPORE

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Background: Breast cancer remains the most commonly diagnosed cancer and the leading cause of cancer-related death among women. Despite national screening programs, Singapore reports the highest breast cancer incidence in Southeast Asia. Although prior research has identified barriers to screening, less is known about how cancer-related beliefs, perceived susceptibility, and social influences shape active cancer information-seeking behaviors in multi-ethnic Asian contexts. Guided by the Health Belief Model (HBM), this study aimed to identify key psychological and social factors associated with cancer information-seeking among older women in Singapore.

Methods: We conducted a cross-sectional survey of 326 Singaporean women aged 50–69 years recruited from the Singapore Cancer Society's screening database. Cancer information-seeking was assessed as a composite outcome aggregating traditional media, print materials, interpersonal sources, online sources, and health professionals. Seventeen Health Belief Model–based variables reflecting perceived severity, susceptibility, benefits, and barriers related to breast cancer and screening were included as correlates. Demographic characteristics were included to account for potential confounding effects.

Results: Using a forward selection regression approach (entry criterion $p < .10$), five HBM-based variables were retained in the final model, explaining 11.7% of the variance in cancer information-seeking. Higher cancer-related worry was positively associated with greater information-seeking ($\beta = 0.185$, $p < .001$), as was family encouragement for mammography screening ($\beta = 0.072$, $p = .029$). In contrast, higher perceived personal susceptibility to breast cancer was negatively associated with information-seeking ($\beta = -0.133$, $p = .017$). Two additional barrier-related factors showed borderline negative associations with the outcome.

Conclusion: These findings suggest that cancer communication interventions should move beyond susceptibility-focused messaging and instead engage affective responses, such as cancer-related worry, while leveraging family encouragement as a key interpersonal cue. Interventions that distinguish between cognitive and affective dimensions of risk perception and actively involve family members may be more effective in promoting cancer information-seeking among older women.

Keywords: cancer information-seeking, breast cancer, health beliefs, risk perceptions, Singapore

REEXPRESSION OF miR-195 VIA AURO-LIPOSOME MEDIATED DELIVERY ENHANCES CHEMOSENSITIVITY AND SUPPRESS OVARIAN CANCER

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Background:
Ovarian cancer (OvCa) remains the most lethal gynecologic malignancy, largely due to late-stage detection, early metastasis, drug-resistance. Cancer stem-like cells (CSCs) drive tumor recurrence and drug-resistance by sustaining cancer growth. WNT7A is highly overexpressed in OvCa and plays a critical role in maintaining CSC phenotypes and epithelial–mesenchymal transition (EMT) and drug-resistance whereas miR-195 is frequently downregulated. Here, we investigated whether re-expression of miR-195 could suppress cancer progression and enhance drug-sensitivity and developed a novel Auro-Liposome (AuLPs) delivery system for miR-195.

Methods:
Drug resistant cells were prepared by exposing them from lower to higher concentration of drugs gradually. miR-195 expression was assessed by qRT-PCR, functional assays were performed to observe the role of miR-195 on CSC markers, EMT. An *in vivo* omental homing assay was performed to check miR-195's anti-metastatic potential.

Results:
Spheroid-derived CSCs showed enhanced expression of cancer stem cell markers. Interestingly in this spheroid, miR-195 expression was significantly decreased. Reexpression of miR-195 reduced stemness markers, impaired spheroid growth, and enhanced drug-sensitivity. miR-195 directly targeted WNT7A and inhibited WNT7A/β-catenin signaling, EMT pathway. Furthermore, *in vivo* homing assay demonstrated that stable miR-195 re-expression significantly reduced CP20 adhesion to the mice omentum, underscoring its potential to inhibit metastatic colonization. Novel Auro-Liposome (AuLPs) system conferred superior intracellular delivery of miR-195 compared to commercial agents and inhibition of oncogenic WNT7A/β-catenin pathway.

Conclusions:
miR-195 as a key suppressor of OvCa progression and enhancer of cisplatin-sensitivity via directly modulating WNT7A/β-catenin pathway.

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FINANCIAL HARDSHIP SCREENING IN NATIVE AMERICAN PATIENTS WITH CANCER: RESULTS FROM A QUALITY IMPROVEMENT PROGRAM AT AN NCI-DESIGNATED CANCER CENTER

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Background:
Many Native American (NA) patients with cancer are at risk of substantial financial hardship related to their illness. However, financial hardship screening (FHS) has rarely been implemented in this population. Funded by a grant from the American Cancer Society, we instituted FHS for NA patients in the NA Navigation (NAN) program at the Stephenson Cancer Center (SCC) in Oklahoma City.

Methods:
SCC's NAN program coordinates oncology referrals for adult patients from Indian Health Service, Tribal Health, or Urban Indian Health (I/T/U) programs across the state of Oklahoma. NAN patients with cancer who were seen at SCC between July 1, 2023, and February 28, 2025, received FHS using the Comprehensive Score for Financial Toxicity (COST) tool. Patients first answered the single question, "My illness has been a financial hardship to my family and me." Patients who responded "Not at all" or "a little bit" did not receive further screening. Patients who reported "Somewhat," "Quite a bit," or "Very much," were asked to complete the remaining 11-item COST survey. COST scores (0–44) were grouped into: no/mild (≥26), moderate (14–25), or severe (0–13) financial hardship. Descriptive statistics and item-level response patterns were analyzed.

Results:
Among 128 total patients screened, 113 patients answered the initial screening question indicating more than a little financial hardship. After completing the full COST Tool, 33 of the 113 (29.2%) screened positive, indicating at least some financial hardship. Of these, the mean COST score was 14.97 ± 8.08; median 13.00 (IQR: 9.00–19.50), indicating severe financial distress. Most of these patients (88%) reported "not at all" to having enough money in savings or assets to cover treatment. Approximately three-quarters of patients (72%) who screened positive were highly concerned about future financial problems. Over half felt they had no choice over how much to spend on their cancer care (66%) and were frustrated by their inability to work or contribute financially (56%). Furthermore, nearly half of these patients reported not feeling in control of their financial situation (47%) and only one-third (34%) reported being able to meet monthly expenses. Screening positivity rose from 22.9% (Jul–Dec 2023) to 41.2% (Jul–Dec 2024).

Conclusions:
One-quarter (24.5%) of the 113 patients with cancer reported experiencing significant financial hardship associated with their illness, with scores suggesting severe hardship. Lack of savings, employment strain, and high stress were often reported. The COST tool was acceptable and useful in identifying unmet needs. These findings support expanding structured, culturally competent FHS and financial navigation within NAN programs.

THE IMMUNOMODULATORY EFFECTS OF GLYCATED CHITOSAN ON CYTOKINE REGULATION AND MACROPHAGE PHENOTYPE

Brian Baharestani

Immunostimulants are a class of therapeutics focusing on enhancing or modulating the immune system to defend against various viruses and diseases. In the past two decades, immunostimulants have gained traction, specifically in cancer immunotherapy. Glycated Chitosan (GC) is a novel immunostimulant with the potential to modulate the Tumor Microenvironment (TME). Tumor-Associated Macrophages (TAMs) play a crucial role in shaping the TME, often promoting immunosuppression and resistance to cancer therapies. This is largely due to the abundance of M2-polarized TAMs that fuel tumor growth and treatment resistance. Previous literature has identified that GC can influence the TME, but its direct effects on macrophages have been largely unexplored.

Here, we investigate the effects of GC on murine Bone Marrow Derived Macrophages (BMDM) polarization and inflammatory signals using *in vitro* murine models. Using fluorescent imaging, ELISAs, and flow cytometry, we characterized macrophage populations to assess changes in inflammatory signaling pathways and polarization post-GC treatment.

Following GC stimulation of BMDMs, M0 macrophages expressed a significant increase of pro-inflammatory cytokines such as IL-1β and TNF-α. Independently, these same M0 macrophages also expressed a decrease in anti-inflammatory cytokines such as IL-6 and IL-10. This suggested that GC could shift macrophage phenotype from M0 towards M1, and away from M2. This was confirmed with flow cytometry, where GC-treated BMDMs had a greater percentage of CD86 (a pro-inflammatory macrophage marker) and a lower percentage of CD206 (an anti-inflammatory macrophage marker).

Together, these findings show that GC can promote macrophage polarization towards an M1-like profile/phenotype. This immunomodulatory effect provides mechanistic insights into how GC can remodel the TME and support its use in cancer immunotherapy and antiviral strategies.

USING DAILY SMARTPHONE-BASED SURVEYS TO UNDERSTAND HOW HEALTH BEHAVIORS IMPACT AFFECT

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Introduction: In 2022, 18% of adults experienced recent symptoms of anxiety and 21% experienced symptoms of depression. Studies have shown that some health behaviors are linked with levels of anxiety and depression. For example, multiple studies have indicated that daily exercise is associated with lower stress and negative affect and increased positive affect. However, most of the published work examining associations between health behaviors and measures of affect has relied on retrospective recall. Smartphone-based ecological momentary assessment (EMA) enables researchers to collect ecologically valid information in a minimally intrusive fashion.

Methods: Data for the current secondary data analyses were collected during a randomized controlled trial that tested a smartphone-based intervention with racially/ethnically diverse adults with anxiety and/or depression. All participants were asked to complete smartphone-based EMAs twice daily for 6 months. Daily EMAs asked about health behaviors (i.e., fast-food consumption, quality of sleep, sleep hours, physical activity, alcohol use) and current affect and stress (e.g., stress, depression, anxiety, happiness, calmness, relaxation, sadness, boredom, worry, loneliness). Multilevel models with random effects were used to assess associations between health behaviors and next day affect and stress. For each time-varying predictor, within-person and between-person components were separated using person-mean centering. Model covariates included biological sex, age, race/ethnicity, education, and treatment group.

Results: The study sample (N=801) was 65% female and 38.5 years old on average. Due to the study design, nearly identical numbers of White, Black, American Indian, and Hispanic/Latino individuals were enrolled into the study. On average, participants completed EMAs on approximately 69% of days. Between-effects models showed significant associations between quality of sleep and amount of sleep with all 10 affect variables ($p < .05$). Consuming fast-food was associated with next-day feelings of anxiety, stress and worry, and greater physical activity was associated with next-day feelings of happiness ($p < .05$). Within-effects models showed that quality of sleep was associated with next-day feelings of anxiety, calm, depression, happiness, relaxation, sadness, stress, and worry ($p < .05$). Getting more hours of sleep was associated with next-day feelings of anxiety, happiness, loneliness, sadness, and worry ($p < .05$). Greater physical activity showed a relationship with next-day feelings of calm, depression, happiness, loneliness, relaxation, and worry ($p < .05$). Consuming more alcohol than average was related to next-day feelings of anxiety, depression, and loneliness, and fast-food consumption was associated with next day feelings of happiness ($p < .05$). No other examined relationships showed statistical significance.

Discussion: Results indicated that daily healthy and unhealthy behaviors were related to many discrete emotions the next day in adults with anxiety and/or depression. Future research should further examine daily relations between health behaviors and affect and intervene in real-time to reduce unhealthy behaviors and improve affective outcomes.

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CORRELATES OF EXPOSURE TO ANTI-TOBACCO CAMPAIGNS ON SOCIAL MEDIA AMONG YOUNG ADULTS WHO VAPE

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Background: Social media has become an efficient and vital medium for the spread of public health information, especially to young people. Indeed, anti-tobacco campaigns distributed on social media have been successful in reducing the intensity of smoking in youth and increasing anti-smoking attitudes. Research suggests that factors such as socioeconomic disparities, mental health symptoms, and unhealthy social media use may place certain youth at elevated risk for nicotine and tobacco use. Thus, it is important to investigate *who* is being exposed to anti-tobacco campaigns on social media platforms, to evaluate whether campaigns are effectively targeting those who need them. This study examines the sociodemographic, mental health, and social media use correlates of exposure to anti-tobacco campaigns on social media.

Methods: Participants were 206 (134 female) US young adults aged 18-25 (M = 21.79, SD=1.97) who reported daily social media use and current non-daily nicotine vaping. Participants reported whether and where they had seen each of 7 widely-distributed anti-tobacco campaigns (no; yes, on social media; yes, from another source; yes, from social media and another source). Participants were coded as having exposure to the campaign if they answered "yes, on social media" or "yes, from social media and another source." We computed an anti-tobacco social media campaign exposure score by summing the number of campaigns (0-7). Participants completed self-report measures of depressive symptoms (Center for Epidemiologic Studies Depression Scale), anxiety symptoms (Generalized Anxiety Disorder-7), stress (Perceived Stress Scale), nicotine dependence (Hooked on Nicotine Checklist), attitudes toward nicotine vaping, problematic (i.e., addiction-like) social media use, social comparison on social media, frequency of social media use activities (i.e., focusing on friends' content, engaging with strangers' content, browsing profiles, posting content). Self-reported sociodemographic characteristics were age, race, ethnicity, sex, gender, sexual identity, or education. Bivariate Pearson's correlations and one-way ANOVAs tested associations of anti-tobacco social media campaign exposure with participant characteristics. All analyses were completed using SPSS version 30.

Results: On average, participants reported exposure to 2.31 (SD=1.66) of the 7 anti-tobacco social media campaigns. Greater exposure to anti-tobacco campaigns was significantly correlated with higher anxiety (r = .29, p < .001), depression (r = .19, p = .006), stress (r = .16, p = .02) problematic social media use (r = .27, p < .001), nicotine dependence (r = .22, p = .002), positive attitudes toward nicotine vaping (r = .15, p = .038), social comparison on social media (r = .21, p = .002), posting frequency (r = .18, p = .011), frequency of browsing others' profiles (r = .23, p = .001), and frequency of engaging more with strangers' content (r = .36, p < .001). Exposure to anti-tobacco campaigns did not significantly differ among sociodemographic groups (p-values > .05). Finally, the only social media variable that was not associated with more exposure to campaigns was focusing on friends' content (p=.091).

Conclusions: Anti-tobacco social media campaigns may be successfully targeting young adults at greatest risk for escalation in nicotine vaping, including those with higher nicotine dependence, more positive attitudes toward vaping, worse mental health symptoms, and less healthy social media habits. While higher scores on social media measures were broadly associated with more exposure to campaigns, those who reported focusing on friends (typically a healthy social media use behavior) did not have elevated exposure to anti-tobacco campaigns, perhaps because they mostly see content posted by friends. Young adults whose friends use nicotine/tobacco may encounter harmful social media content that could be tempered with paid anti-tobacco campaigns. Future research should continue to investigate how campaigns are distributed among young adults to target campaign resources to those most in need.

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NECROPTOSIS-INDEPENDENT ROLE OF HEPATOCYTE MLKL IN LIVER INFLAMMATION AND METABOLIC DYSFUNCTION AS A POTENTIAL CONTRIBUTOR TO LIVER CANCER

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Mixed lineage kinase domain-like (MLKL) is the terminal effector of necroptosis, a form of programmed cell death that induces inflammation through the release of damage-associated molecular patterns (DAMPs). However, MLKL also exerts non-necroptotic functions independent of necroptosis. Emerging evidence suggests that MLKL plays a role in metabolic dysfunction-associated steatotic liver disease (MASLD) and its progression to metabolic dysfunction-associated hepatocellular carcinoma (HCC), particularly in the context of obesity. We found that MLKL protein expression is significantly increased in hepatocytes in obesity, suggesting a role in obesity-driven liver pathology. In this study, we investigated the impact of hepatocyte-specific MLKL overexpression using a conditional transgenic mouse model ($MLKL^{HepOE}$). Our findings revealed that five months after hepatocyte MLKL overexpression, liver inflammation, extracellular vesicle (EV) release, and cellular senescence were significantly increased, without activation of necroptosis or apoptosis. $MLKL^{HepOE}$mice exhibited enhanced hepatic macrophage infiltration, upregulation of proinflammatory cytokines and chemokines, and increased EV secretion enriched with HMGB1, a key DAMP implicated in liver inflammation and tumorigenesis. Over time (13 months post-overexpression), $MLKL^{HepOE}$mice developed increased hepatic triglyceride accumulation, a hallmark of MASLD, which may contribute to metabolic stress and promote HCC development. However, even at 18 months of age, $MLKL^{HepOE}$mice did not develop liver cancer, suggesting that additional external stressors, such as lipotoxicity, are required for tumorigenesis. Given that MLKL expression is elevated in hepatocytes in obesity and in both MASLD and HCC, our findings highlight a potential mechanism by which hepatocyte MLKL drives chronic inflammation, metabolic dysfunction, and liver cancer risk. Mechanistically, our data suggest that MLKL-driven inflammation and metabolic alterations occur independently of necroptosis, providing a rationale for targeting MLKL as a therapeutic strategy in obesity-associated MASLD and HCC.

COMPUTATIONAL TUMOR PROGRESSION ANALYSIS VIA SERIATION BASED TRAJECTORY INFERENCE

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Precise lineage or evolution path determination play a crucial role in discerning the dynamic developmental or temporal progression patterns observed in single cell RNA-Seq data. In this work, we present a novel computational approach for progression pattern inference of normal or tumor cell populations that are actively progressing along a dynamic pathway in single cell resolution. This is achieved via ordering the cellular transcriptional profiles identifying the progression of cell populations along differentiation, signaling, or tumor evolution paths. Here, we developed a seriation-based progression pattern inference method using optimally reordered hierarchies and provide advanced principal-curves-based visualization of the inferred paths in three-dimensional latent space representation of scRNA-Seq data. Additionally, we present novel metrics for evaluating the reconstructed order and identified pathways and evaluate our approach using real single cell transcriptomics datasets.

A MULTI-OMIC DISSECTION OF MYC-DRIVEN LEUKEMIA REVEALS CONVERGENT TRANSCRIPTIONAL AND REPLICATIVE VULNERABILITIES

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The proto-oncogene *MYC* is overexpressed in many cancers, yet the mechanisms underlying its tumorigenic potential remain poorly defined. *MYC* plays a central role in acute lymphoblastic leukemia (ALL), which accounts for ~20% of childhood cancer diagnoses and deaths. Although the MYC protein's function as a master transcription factor has been extensively studied, its essential role in DNA replication has been largely underappreciated in the context of human cancers. We therefore hypothesized that key leukemia-inducing changes, and associated therapeutic vulnerabilities, have been overlooked.

To address this gap, we performed an integrated multi-omics analysis of *MYC*-driven ALL using a transgenic zebrafish model that faithfully recapitulates human B- and T-lineage ALL. We profiled transcription (RNA-Seq), DNA replication timing (WGS), and MYC chromatin binding (CUT&RUN) across three disease states: healthy lymphocytes, pre-leukemic *MYC*-overexpressing lymphocytes, and leukemic cells. This approach revealed hundreds of dysregulated genes, including a core subset exhibiting coordinated alterations at all three levels (transcription, replication, and chromatin binding). Notably, several of these genes showed strong prognostic associations in pediatric ALL, despite having no prior links to the disease.

We are now functionally validating these candidates *in vivo* using somatic transgenesis to evaluate their roles in disease progression and therapy resistance in our transgenic zebrafish system, with plans to test existing small-molecule inhibitors targeting the most promising candidates. In parallel, we are assessing the relevance of these genes to human ALL pathogenesis using independent patient-derived datasets. Together, this work demonstrates how integrating data across distinct biological processes can more precisely identify leukemogenic drivers and uncover previously unrecognized therapeutic opportunities in *MYC*-driven ALL.

CHEMO- AND RADIOTHERAPY PROMOTE CEREBROMICROVASCULAR PATHOLOGY IN A PRECLINICAL MODEL OF PEDIATRIC MEDULLOBLASTOMA

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Pediatric medulloblastoma survivors treated with cranial radiotherapy and combination chemotherapy frequently develop late-onset cerebrovascular complications, including cerebral microhemorrhages, white-matter injury and elevated risk of stroke. However, why these cerebrovascular pathologies arise only years after cancer therapy remain poorly understood. Growing evidence suggests that the key driver might be the chronic, gradual accumulation of senescent cells within the cerebral microvasculature. We hypothesized that combined radio- and chemotherapy (CRT+CCT) synergistically promote endothelial senescence, leading to heightened vascular fragility and delayed-onset cerebrovascular dysfunction (e.g., blood-brain-barrier (BBB) breakdown, increased cerebral microhemorrhage (CMH) burden). Transgenic p16-3MR mice, which express red fluorescent protein to enable identification of senescent cells, received clinically relevant fractionated CRT (5 Gy, twice weekly for 2.5 weeks) and CCT (cisplatin, vincristine, cyclophosphamide) treatment. Endothelial senescence in the brain was quantified by flow cytometry. BBB permeability was assessed via intravital two-photon imaging following the injection of 40 kDa, 3 kDa, and 0.3 kDa fluorescent dextrans. CMHs were induced via a hypertension-based vascular stress model using angiotensin II delivered by osmotic minipumps and L-NAME administered in drinking water. Motor performance was evaluated with the CatWalk XT® gait analysis system. CMH number and area were quantified histologically using diaminobenzidine and hematoxylin staining. Flow cytometry results confirmed that CRT+CCT induced endothelial senescence in the brain. BBB assessment showed sustained, therapy-induced increases in permeability. CRT+CCT also accelerated the onset of neurological signs associated with CMHs, and caused detectable impairments in motor coordination (e.g., reduced regularity index). Moreover, both the number and total area of CMHs were significantly elevated in treated mice compared with controls. Our findings demonstrate that CRT+CCT-induced endothelial senescence contributes to increased cerebrovascular fragility, characterized by BBB disruption and higher CMH burden. These CRT+CCT therapy-induced changes may underlie the delayed cerebrovascular impairments observed in pediatric medulloblastoma survivors. Targeting senescent cells may therefore offer a promising therapeutic strategy to mitigate cancer therapy–induced vascular injury and support long-term brain health.
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SPATIOTEMPORAL ANALYSIS OF LUNG CANCER INCIDENCE AND MORTALITY TRENDS IN OKLAHOMA (2004-2022)

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Introduction: Lung cancer is the leading cause of cancer death and the second most frequently diagnosed cancer in both men and women in the United States (US). Nationally, Oklahoma (OK) ranks 10th worst in lung cancer age-adjusted cancer incidence rate, and 8th worst for age-adjusted lung cancer mortality rate from 2018-2022.[1] Although smoking rates in the US have decreased over the past two decades, a large portion of current and former smokers remain at risk for lung cancer. Understanding the geographic distribution of both incidence and mortality is critical for targeting public health interventions. This study aimed to identify spatial clusters of lung cancer to determine if the disease is randomly distributed or significantly aggregated across the state's 77 counties.

Methods: We analyzed age-adjusted lung cancer incidence and mortality rates across Oklahoma's 77 counties from 2004 – 2022. Too address missing and suppressed data in the rural areas, estimating 10.53% of lung cancer incidence and 4.94% of the mortality dataset, K-nearest spatial neighbors' approach (K=8) was utilized. Data was structured using Space-Time cube consisting of 10, two-year time steps, January 1st being the start date. Spatiotemporal trend was evaluated using the Mann-Kendall test. Finally, Emerging Hotspot Analysis (EHSA) was employed to identify cold spots, using fixed distance neighborhood to determine localized clustering.

Results: Both lung cancer incidence and mortality demonstrated a statistically significant state-wide decreasing trend over the time period (Mann-Kendall statistics (Trend Statistic: -3.0411, p = 0.0024). While the incidence dataset required more estimation due to rural data suppression, the overall downward trend remained robustly synchronized. EHSA identified significant clustering of declining trends across the state. For lung cancer incidence, 15 or 77 counties (19%) were identified as significant cold spots. In contrast, the mortality analysis identified nearly twice as many significant locations, with 28 of 77 counties (36%) classified as cold spots. This indicates a sustained and expanding reduction in lung cancer deaths. No hot spots were identified. Both analyses utilized a consistent neighborhood distance, ensuring the results are directly comparable.

Discussion: The disparity between the number of incidence cold spots (15) and mortality cold spots (28) is a key finding for this study. The findings indicate that while lung cancer incidence has become more spatially clustered over time, mortality is more heavily aggregated than incidence. This disparity suggests that geographic variations may be driven not only by smoking prevalence but also by localized disparities in healthcare access, screening uptake, and stage at diagnosis. While prevention efforts (like smoking cessation) may be driving the incidence trends

in cities, improvements in treatment, earlier detection, and healthcare access may be successfully reducing mortality even in areas where the number of new cases has not yet significantly dropped. Lung cancer screening (LCS) remains significantly underutilized state-wide, and the observed declines underscore the critical need for continued and expanded access. The success in these areas provides a strong argument for the continued scaling of Stephenson Cancer Center initiatives, such as the mobile lung cancer screening units, to reach rural populations where mortality clusters remain more stagnant.

Conclusion: The synchronization of state-wide decreasing trends (Trend Statistic: -3.0411, p = 0.0024) combined with the widespread emergence of mortality cold spots provides strong evidence of improving lung cancer outcomes in Oklahoma. These findings suggest that public health strategies are effectively reaching beyond urban centers to reduce the mortality burden in a significant portion of the state.

Summary

	Incidence EHSA	**Mortality EHSA**
Total Significant Locations	15 of 77	28 of 77
New Cold Spots	5	8
Consecutive Cold Spots	6	13
Sporadic Cold Spots	3	4
Oscillating Cold Spots	1	3
Neighborhood Distance	68,924.98m	68,924.98m

Reference:

1. Sheikh E, Campbell JE, Sambo AB, and Doescher MP. Cancer in Oklahoma Data Brief Series: Lung Cancer in Oklahoma – Update 2025. Community Outreach and Engagement, Stephenson Cancer Center, OU Health. Update 2025.

TARGETED ANNEXIN A5–MERTANSINE CONJUGATE FOR LEUKEMIA THERAPY

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Abstract: Leukemia remains a global health burden, with over 460,000 new cases and 310,000 deaths annually. Acute Myeloid Leukemia (AML) predominates in adults, while Acute Lymphoblastic Leukemia (ALL) is most frequent in children. In the United States, AML causes 22,000 new diagnoses and 11,000 deaths yearly, whereas ALL accounts for 6,100 new cases. Despite progress in chemotherapy, relapse and resistance remain common due to non-specific cytotoxicity and poor tumor targeting.

Mertansine (DM1), a maytansinoid microtubule inhibitor, induces mitotic arrest and apoptosis at sub-nanomolar concentrations but suffers from hydrophobicity, rapid plasma clearance, and severe off-target toxicity. To address these limitations, annexin A5 (ANXA5) was conjugated to DM1 via a non-cleavable sulfo-SMCC linker to generate a targeted cytotoxic conjugate (ANXA5–DM1). ANXA5 binds phosphatidylserine(PS) a phospholipid abnormally externalized on malignant and apoptotic cells—with sub-nanomolar affinity in a calcium-dependent manner, enabling selective delivery of DM1 to leukemia cells.

Binding and cytotoxicity assays were performed on three murine leukemia cell lines: C1498 (myeloid AML), P388D1 (monocytic/lymphoid), and L1210 (lymphoid ALL). Specific binding was confirmed for all lines with dissociation constants (Kd) of 0.37 nM for C1498, 0.93 nM for P388D1, and 0.32 nM for L1210, consistent with strong PS-mediated targeting. Cytotoxicity, evaluated by Alamar Blue after 72 h exposure (100 µM–1 pM), revealed potent dose-dependent inhibition: IC_{50} = 1.03 nM (C1498), 1.20 nM (P388), and 0.26 nM (L1210). Compared to free DM1 (IC_{50} ≈ 4.5 nM for C1498; 264 nM for P388; 93 nM for L1210), the conjugate achieved a 4- to 350-fold increase in efficacy, validating its targeting advantage. Ongoing studies are assessing binding and cytotoxicity on normal PBMCs to confirm selectivity.

These results suggest that the ANXA5–DM1 conjugate represents a promising next-generation therapy for AML and ALL, combining high specificity, strong cytotoxicity, and reduced systemic toxicity, potentially improving patient outcomes beyond current chemotherapy standards.

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MACHINE LEARNING (ML)–BASED PREDICTION OF FATAL IMMUNE CHECKPOINT INHIBITOR (ICI)–ASSOCIATED MYOCARDITIS (MC) WITH MULTI-COHORT VALIDATION

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Background: ICI-induced MC is a rare but highly fatal immune-related adverse event (irAE). Identifying clinical predictors of MC-specific fatality remains an unmet need, specifically across heterogeneous real-world cohorts. Herein, we develop and externally validate an ML model to predict ICI-MC fatality using clinical and laboratory features.

Methods: The WHO Vigibase database was queried through December 22, 2024, to identify cases of ICI-MC with complete clinical data, including age, sex, cancer and ICI type, co-occurring irAEs, overlap status with myositis (MS) and/or myasthenia gravis (MG), MC timing from ICI start, and MC-specific fatality. Multivariable logistic regression was used to assess correlates of MC-specific fatality. An XGBoost ML model using all collected clinical data was trained to predict MC-specific fatality using an 80/20 split of data for training and testing. We augmented our clinical ML model with troponin (T or I) values at the time of ICI-MC diagnosis from two institutions (n = 37: OU n = 13, MGH n = 24), normalized to institutional upper limits of normal (ULN). Two additional external cohorts (n = 68: VUMC n = 18, MDACC n = 50) were used to validate our final clinical and augmented models.

Results: We identified 822 cases from VigiBase with ICI-MC, with a median age of 69 years (IQR: 60-76), 59.1% (n = 486) were males, and patients with lung cancer had the highest proportion of cases (23.7%, n = 195). Most patients received ICI monotherapy (59%, n = 485), and median time to MC onset was 30.4 days (IQR: 21-91.3). MC occurred alone in 588 cases (71.5%) and with MS and/or MG in the remainder. MC-specific fatality occurred in 147 cases (17.9%). After multivariable adjustments, MC onset within the first month of ICI start was associated with higher MC-fatality odds compared with later onset (vs 1-3 months: OR = 0.38 [0.21-0.67], vs 3-12 months: OR = 0.5 [0.25-0.95]). Co-occurring non-MC major cardiac adverse events (OR: 0.27 [0.17 - 0.44]) and pneumobronchitis (OR: 0.29 [0.11 - 0.78]) were also associated with increased MC-specific fatality. The optimized MC-fatality clinical ML model achieved AUCs of 0.76 (training) and 0.73 (testing), with early MC onset as the highest contributing feature to MC-fatality. External validation (n = 37) of our clinical model yielded an AUC of 0.74. Augmenting our clinical ML model with baseline troponin (n = 37) significantly improved performance (AUC: 0.79, likelihood-ratio test p = 0.046), with an external validation (n = 68) AUC of our augmented ML model of 0.67. Our

ML model is available online for use through: https://ohbiolab.shinyapps.io/ici-mc_fatality_predictor/.

Predicted outcome probabilities were used to categorize patients into low, intermediate, and high risk groups. Probabilities ≤ 0.172 identified low-risk patients with a negative predictive value of 91.7%, while probabilities ≥ 0.807 identified high-risk patients with a positive predictive value of 66.7%.

Conclusion: ICI-MC timing and co-occurring reactions are key determinants of MC-specific fatality While this approach still requires further validation and training data on an expanded scale, our data supports the potential for early risk stratification and intensified monitoring using a combination of clinical and readily available baseline troponin values.

TRACKING NANOPARTICLE SPACIOTEMPORAL DISTRIBUTIONS IN OVCAR8 OVARIAN CANCER SPHEROIDS USING EXPANSION MICROSCOPY

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In the United States, an estimated 21,010 women are to be diagnosed, and 12,450 women are to die from ovarian cancer in 2026, so there is a need to explore safer and more effective treatments. In this study, we focus on gold nanoparticles as a model system for ovarian cancer nanomedicines. Using 3D super-resolution microscopy, we track the spatiotemporal distribution of these nanoparticles in multicellular OVCAR8 ovarian cancer spheroids. The spheroids were exposed to nanoparticles in cell culture for up to seven days. After fixation, the spheroids were infused and polymerized with swellable hydrogels. Next, the spheroid-hydrogel hybrids were stained with fluorescent NHS-dyes to label the proteome of the spheroids. Upon submerging the stained hybrids in deionized water, we achieved expansion factors of up to 10 times via hydrogel swelling. This expansion process enables the 3D super-resolution microscopy of entire OVCAR8 spheroids with lateral resolutions approaching ~20 nm using conventional confocal laser scanning microscopy systems. Using this workflow, we track the time-dependent accumulation of gold nanoparticles in OVCAR8 spheroids with 3D intracellular context. We hypothesize that most of the internalized gold nanoparticles will actively interact with ovarian cancer cells instead of passively distributing across the extracellular matrix. Additionally, we hypothesize that gold nanoparticles are more likely to reach the spheroid center when incubated for longer. Our research shows the importance of using 3D cancer model systems with in vitro tumor environments that more closely mimic those found in humans, and combining these cancer models with 3D super-resolution microscopy. Our approach may serve as a workflow for evaluating nanoparticle-tumor interactions across various malignancies, with the goal of developing next-generation cancer nanomedicines that are safer and more effective.

Acknowledgments

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TESTING LEUKEMIA-ESSENTIAL GENES VIA SOMATIC TRANSGENESIS AND SCALE ALLO-TRANSPLANTATION

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Leukemia is a hematologic cancer and the most common childhood malignancy. Zebrafish and humans share similar adaptive immune systems and key immunologic and oncologic pathways, making zebrafish useful to study ALL (Acute Lymphoblastic Leukemia) biology. Our lab uses zebrafish with transgenic human MYC (*hMYC*) controlled by a lymphoblast-specific promoter (*rag2*) to drive ALL. We pair this with lineage-specific markers (e.g., *lck*:*mCherry*, *cd79a*:*GFP*) in multi-transgenic fish, creating fish with color-coded B- and T-lineage ALL. MYC drives oncogenesis, but cannot cause ALL in isolation; other genes also contribute, making them potential therapeutic targets. To test candidate genes putatively essential to ALL initiation and progression *in vivo*, we sought a method to rapidly enhance or ablate genes in only ALL cells. We selected TEAZ (Transgene Electroporation in Adult Zebrafish), a somatic transgenesis system. TEAZ introduces DNA into some—but not all—cells, creating competing populations of modified vs. unmodified ALL cells. TEAZ can introduce transgenes that enhance, or CRISPR components to ablate, gene function. Traditionally, TEAZ directly injects plasmids into tissues of living fish, but to 'scale up' TEAZ, we are piloting a new method: We harvest ALL-infiltrated scales from a donor fish, perform TEAZ on scales *ex vivo*, and then implant TEAZ'd scales into immunosuppressed recipients. One donor fish provides dozens-to-hundreds of ALL-infiltrated scales, so we can test many genes in parallel simultaneously, comparing otherwise-identical ALL cells to find those crucial to ALL survival and growth. Scale abundance also allows transplants with large cohorts to achieve statistically-significant results quickly. Thus, scale transplants permit functional target testing to ascertain which genes merit development of novel ALL therapeutics. We will present an overview of our project's schema and current progress.

OPTICAL COHERENCE TOMOGRAPHY EVALUATION OF MEBENDAZOLE THERAPEUTIC EFFICACY IN OVARIAN CANCER XENOGRAFTS

Isaac Atkins

Ovarian cancer remains the most lethal gynecological malignancy, largely due to late-stage diagnosis and the emergence of chemoresistance to standard treatments like cisplatin. This study evaluates the therapeutic potential of Mebendazole (MBZ) as a repurposed treatment for cisplatin-resistant ovarian cancer. An orthotopic xenograft mouse model with luciferase-tagged cisplatin-resistant human ovarian cancer cells was used to monitor tumor progression and treatment response over 30 days. Spectral Domain Optical Coherence Tomography (SD-OCT) was employed to monitor tumor dynamics and quantitatively assess the treatment efficacy though advanced texture analysis and machine learning.

The study demonstrates that the combination of MBZ and cisplatin produces the most pronounced suppression of tumor progression. From SD-OCT imaging, 2562 special and superficial texture features were extracted, which revealed that different treatment regimens produce unique, quantifiable morphological changes in the tumor structure. An optimized subset of 60 features showed that drug-induced alterations can be distinguished, with the Support Vector Machine (SVM) achieving a classification accuracy of 72.7% and a AUC of 0.79.

These results underscore the clinical potential of MBZ in overcoming chemoresistance in ovarian cancer and validate the OCT-based texture analysis as a sensitive, non-invasive tool for evaluating in vivo treatment efficacy. Integrating advanced imaging with machine learning provides a robust framework for real-time monitoring of internal tumor architecture and drug-induced structural changes.

USING EMA DATA TO EXPLORE RELATIONS BETWEEN DAILY ALCOHOL AND TOBACCO USE AND SLEEP

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Introduction: Sleep plays an important role in regulating a variety of biological processes. Insufficient sleep has been linked with numerous negative health outcomes, which may be worsened by the use of substances. To date, few studies have used ecological momentary assessments (EMAs) to study within-person associations between substance use and sleep. The present study aims to address this gap.

Methods: Study data were collected as part of a nationwide randomized controlled trial designed to compare the efficacy of two smartphone-based interventions for depression and anxiety. All participants were asked to complete EMAs twice daily for 6 months. EMAs assessed the prior day's sleep quality, sleep duration, alcohol consumption, and cigarette smoking. Mixed-effects regression was used to examine daily associations between alcohol and cigarette use (a binary measure of use days vs. no use days, a continuous measure of the number of drinks/cigarettes per day) and sleep duration and quality.

Results: Participants (*N*=770) were mostly women (65.6%), 25.2% White (*n*=194), 24.9% Black (*n*=192), 24.4% American Indian (*n*=188), 25.5% Hispanic (*n*=196), and 38.4 (*SD*=12.8) years old on average. Averaged across the study period, the proportion of alcohol use days and average drinks per day were not significantly associated with sleep hours or quality. However, drinking on a given day (95% CI [-0.18, -0.04]) and drinking more than one's personal average on a given day (95% CI [-0.05, -0.01]) were significantly associated with a decrease in sleep hours. Similarly, averaged across the study period, the proportion of cigarette use days and average cigarettes per day were not significantly associated with sleep hours or quality. However, smoking on a given day (95% CI [-0.47, -0.12]) and smoking more cigarettes than one's personal average on a given day (95% CI [-0.05, -0.01]) were significantly associated with a decrease in sleep hours, on average. Additionally, smoking more than a person's average on a given day was significantly associated with a decrease in sleep quality (95% CI [-0.02, -0.002]).

Discussion: Findings showed that day-level differences in both alcohol and cigarette use were associated with a reduction in sleep duration and higher than usual cigarette use was associated with a decrease in sleep quality. Thus, minimizing alcohol and cigarette use may improve sleep duration and quality in adults with anxiety and/or depression.

Funding Statement: Funding to support this study was provided by the National Institute on Mental Health (NIMH; R01MH126586), the Oklahoma Tobacco Settlement Endowment Trust (TSET; STCST00400_FY25), and used the OU Health Stephenson Cancer Center mHealth Shared Resource which is partially funded by an NCI Cancer Center Support Grant (P30CA225520).

RENAL CELL CARCINOMA AMONG NATIVE AMERICAN PATIENTS IN OKLAHOMA: A SINGLE-INSTITUTION EXPERIENCE FROM AN NCI-DESIGNATED CANCER CENTER

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Background:

Native American (NA) patients in Oklahoma experience disproportionately higher mortality from renal cell carcinoma (RCC), with state registry data showing more than twice the incidence of kidney and renal pelvis cancers compared with Non-Hispanic White (NHW) populations. However, population-based datasets lack patient-level clinical detail, limiting understanding of outcomes both overall and at academic cancer centers. We characterized age, stage, and overall survival (OS) among NA patients with RCC treated at Stephenson Cancer Center (SCC) and contextualized outcomes using SEER and Oklahoma registry data.

Methods:

We conducted a retrospective cohort study of NA patients with RCC treated at SCC between 2003 and 2024. Patient-level demographic and staging data were obtained via electronic medical record review. Population-level comparison data for NA and NHW patients were obtained from SEER, and statewide incidence and stage data were obtained from the Oklahoma Central Cancer Registry (OK2Cancer). Stage at diagnosis was categorized using American Joint Committee on Cancer (AJCC) staging. OS was analyzed using Kaplan–Meier methods with log-rank testing.

Results:

A total of 159 NA RCC cases were included. Median age at diagnosis was 60 years (29-83), with a male preponderance (62.3%, 99), and predominantly clear cell histology (n=142, 94.0%). Compared with SEER-reported NA patients, SCC patients were diagnosed at a significantly younger age (60 vs 65 years, $p<0.0001$). At diagnosis, 58.4% had Stage I–II disease, 32.9% had Stage III disease, and 8.7% had Stage IV disease; stage was unknown in 6.3%. Relative to SEER benchmarks, SCC cohort had a significantly lower proportion of Stage IV (metastatic) disease (8.7% vs 28.4%, $p<0.0001$) and a higher proportion of Stage III disease (30.8% vs 9.9% among SEER NA and 9.2% among SEER NHW patients). Nephrectomy was performed in 91.8% of patients, primarily among those with localized or locally advanced disease, and 10.1% received radiation therapy. OS was significantly improved compared with SEER-reported NA populations (log-rank

p<0.0001). One-, three-, and five-year OS rates were 99.4%, 95.3%, and 93.9%, respectively, with overall survival significantly improved compared with SEER-reported NA populations (log-rank *p*<0.0001).

Conclusion:

Despite a high burden of locally advanced disease at diagnosis, NA patients with RCC treated at SCC, an NCI-designated tertiary cancer center, demonstrated significantly improved OS compared with population-based benchmarks. In the context of persistent statewide disparities in RCC incidence and mortality among NA populations, these findings suggest that access to specialized, multi-disciplinary oncologic care supported by community-engaged outreach may meaningfully improve outcomes and mitigate RCC disparities.

THE INFLUENCE OF CHRONIC HEALTH CONDITIONS ON COLORECTAL CANCER SCREENING AMONG BLACK/AFRICAN AMERICAN ADULTS AGED 45-75 YEARS: A SYSTEMATIC REVIEW

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Abstract

Background: Black/African American adults experience disproportionately higher colorectal cancer (CRC) incidence and mortality, partly due to lower screening rates and later-stage diagnosis. Highly prevalent chronic health conditions may further widen screening inequities by competing with preventive care priorities and interacting with structural barriers, including medical mistrust, limited culturally responsive care, and socioeconomic stressors. **Objectives:** This systematic review examined (1) how chronic health conditions influence CRC screening uptake and adherence among Black/African American adults aged 45–75 years in the United States and (2) which screening modalities are most commonly utilized among guideline-eligible individuals with chronic conditions. **Methods:** Following PRISMA 2020 guidelines, we searched Scopus, Embase, MEDLINE, and CINAHL for U.S.-based, English-language studies published between 2000 and 2025 that reported CRC screening uptake or adherence among Black/African American adults with at least one chronic condition. The protocol was registered in PROSPERO (CRD420251207870). Three reviewers independently screened records in Covidence. Of 2,262 identified records, 914 duplicates and 1,270 citations were excluded during title and abstract screening. Sixteen articles were not retrieved, and 45 full-text articles were excluded, resulting in 17 observational studies that met inclusion eligibility. Due to heterogeneity in chronic condition definitions, screening measures, and effect estimates, findings were synthesized narratively. Risk of bias was assessed using Cochrane RoB-2 and ROBINS-I, and certainty of evidence was evaluated using GRADE. **Results:** Associations between chronic conditions and CRC screening were heterogeneous. Approximately half of observational studies reported higher screening uptake among individuals with at least one chronic condition, often reflecting regular healthcare engagement. However, multimorbidity was associated with lower colonoscopy uptake in several studies, with some shift toward noninvasive tests. Frequently examined conditions included diabetes, cardiovascular disease, hypertension, obesity, chronic kidney disease, COPD, and depression. Diabetes was consistently associated with higher screening, particularly stool-based testing, whereas cardiovascular disease and obesity showed mixed associations. Hypertension demonstrated generally neutral to modestly positive effects. Preliminary GRADE assessment indicates low to moderate certainty due to inconsistency and indirectness. Full quantitative synthesis will be presented at the conference. **Implications:** Chronic disease management may both facilitate and hinder CRC screening. Integrating screening into chronic care visits and addressing structural and provider barriers may improve equitable uptake.

ORAL CANCER RECURRENCE DECREASES 4-FOLD FOLLOWING SMOKING CESSATION AFTER DIAGNOSIS

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Oral cancer is the sixth most common cancer in the world and has a well-established link to tobacco use. While it is known that quitting tobacco use lowers the risk of oral cancer, little is understood regarding the impact of tobacco cessation at diagnosis and its impact on oral cancer recurrence. This study looks at the impact of quitting smoking after diagnosis on recurrence and overall survival after oral cancer diagnosis.

We performed a retrospective chart review and identified 119 patients newly diagnosed with oral cavity cancer between 2002 and 2023 who were current smokers and treated with intent to cure. Demographic and clinical data of these patients were retrospectively collected. Patients were further separated in two groups based on whether they quit smoking prior to treatment initiation (quitters) or not (active smokers) Recurrence-free survival and overall survival were calculated. Chi-square tests, logistic regression, Kaplan Meier curves and Cox-proportional hazards survival analyses were done to understand the impact of smoking on recurrence. Analyses were adjusted for sex, race, alcohol use, primary site, tumor stage, and treatment group.

Our study population (n=119) was 65% male, 86% white, and 48% were alcohol users. The mean age of our population was 60 years (SD ±10 years). Eighty-six percent had early-stage cancer. Most patients received surgery plus radiation (41%, n=49) or surgery, chemotherapy, and radiation (26%, n=31). Of the 119 patients who smoked at time of diagnosis, 52 (44%) quit smoking before initiating first-line therapy. There was no significant difference between sex, race, and stage between those who quit and those who did not. There was also no significant difference in treatment response, as assessed via complementary imaging, between quitters and active smokers. However, quitters had only a 7% recurrence rate compared to active smokers at 27% (p=0.016), showing about a 4-fold decrease in recurrence rates in quitters. On multivariable analysis, the odds of recurrence were significantly lower among quitters than active smokers (p=0.003).

Our data documents that there is greater risk of recurrence for patients who continue to smoke through treatment compared to those who quit after diagnosis. Thus, smoking cessation is essential to mitigate oral cancer recurrence. Counseling patients regarding cessation even at time of cancer diagnosis is vital in improving their life after cancer treatment and in lowering their chances of recurrence.

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BASED ON STATIC-COMPRESSION OPTICAL COHERENCE ELASTOGRAPHY, QUANTITATIVE ELASTICITY ASSESSMENT METRICS ARE PROVIDED FOR BIOLOGICAL TISSUES

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Abstract: Optical coherence elastography (OCE)- as an extension of optical coherence tomography (OCT)-enables quantitative characterization of the mechanical properties of biological tissues. Within OCE, static (quasi-static) compression OCE (SCOCE) is a comparatively simple approach that requires no external excitation; it characterizes tissue mechanics by computing phase changes in the OCT signal between pre- and post-compression states. The elastic modulus of the specimen is then quantified by comparison with reference phantoms of known mechanical properties, measured under identical loading and imaging conditions. We have already achieved promising results in tumor margin detection, quantitative assessment of tissue elasticity, and tissue classification.

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ANTI-TUMOR EFFECTS ON TUMOR-INFILTRATING NATURAL KILLER CELLS BY LOCALIZED ABLATIVE IMMUNOTHERAPY AND IMMUNE CHECKPOINT INHIBITORS: AN INTEGRATED AND COMPARATIVE STUDY USING SCRNASEQ ANALYSIS

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Localized ablative immunotherapy (LAIT), a combination of photothermal therapy (PTT) and the immunostimulant glycated chitosan (GC), has demonstrated therapeutic efficacy in cancer treatment. However, its impact on the tumor microenvironment (TME), particularly on tumor-infiltrating natural killer (TINK) cells, remains to be fully elucidated. Using single-cell RNA sequencing (scRNAseq), we analyzed the transcriptional and functional modulations of TINK cells by LAIT in a mouse breast cancer model. Additionally, we investigated immune checkpoint inhibitor (ICI)-induced changes in NK cells across multiple cancer types and evaluated the clinical relevance of these transcriptional changes using The Cancer Genome Atlas (TCGA) database. ScRNAseq revealed five NK cell subtypes, with LAIT increasing the proportion of interferon-enriched NK cells and enhancing NK cell differentiation and cytotoxicity. Functional analyses demonstrated that LAIT upregulated activation, cytotoxic, and interferon pathway genes while downregulating immune-suppressive genes, effects largely driven by GC. Comparative analysis showed significant transcriptional overlap between ICI and LAIT, highlighting shared pathways in NK cell-mediated cytotoxicity and chemokine signaling. Prognostic models constructed from ICI- and LAIT-induced gene signatures effectively stratified breast cancer patients by survival risk, with LAIT-induced genes showing the highest predictive performance. Furthermore, higher NK cell proportions and the expression of key prognostic genes, such as PSME2, IGKC, and KLRB1, were associated with improved overall survival. LAIT and ICIs enhance NK cell-mediated antitumor responses via distinct yet complementary mechanisms, emphasizing their potential for synergistic use. These findings provide novel insights into NK cell modulation within the TME and support the development of combinatorial immunotherapy strategies.

Keywords:

Single-cell RNA sequencing, natural killer cell, localized ablative immunotherapy, immune checkpoint inhibitor, N-dihydrogalactochitosan

A LONGITUDINAL EXAMINATION OF RELATIONS BETWEEN OPTIMISM AND PSYCHOSOCIAL VARIABLES

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Introduction:
Optimism has been shown to be associated with positive health behaviors, such as sleep and physical activity, and lower pain perception in cross-sectional studies. However, few studies have examined how associations between optimism and affect, pain, and health-related behaviors change over time. Ecological momentary assessment (EMA), a methodology that involves repeatedly collecting data in naturalistic environments, is commonly used to examine time-varying associations. The purpose of the present study was to longitudinally examine bidirectional associations between optimism and a range of psychosocial variables and health-related behaviors.

Methods:
This secondary analysis used data from a 2x2x2x2x2 factorial randomized controlled trial designed to determine best practices in EMA studies. All participants completed a baseline assessment, up to 2 or 4 EMAs every day over the 28-day study period, and a follow-up assessment via smartphone. EMAs assessed optimism weekly and measures of positive and negative affect, health behaviors, and substance use daily. Associations between optimism, affect, and health-related behaviors were examined with linear mixed-effects regression adjusting for demographic characteristics and separating within- and between-participant effects.

Results:
Participants (*N*=236) were mostly female (74.6%), White (75%), and were 49.9 years old (*SD*= 12.0) on average. Averaged across the study period, greater optimism was significantly associated with an increase in positive affect measures (95% CIs for: calm [10.7, 15.5]; energetic [8.9, 16.1]; happy [15.0, 19.2]), a decrease in negative affect measures (95% CIs for: anxious [-17.6, -7.4]; depressed [-21.5, -14.8]), better quality sleep (95% CI [6.5, 11.1]), and less pain (95% CI [-14.9, -7.7]). Week-to-week differences in within-person optimism were not found to be related to affect, sleep, or pain. Additionally, neither between- nor within-person differences in optimism were significantly associated with alcohol or cigarette use.

Discussion:
These findings indicate that optimism is related to affect (positive and negative), sleep, and pain. Future longer duration studies should examine whether smartphone-based interventions can be used to increase optimism and subsequently effect affect, pain, and sleep.

Funding Statement: The current study was funded by the University of Oklahoma Health Sciences Center. Programming and technological support was provided through the mobile health shared resource of the Stephenson Cancer Center via an NCI Cancer Center Support Grant (P30CA225520). Data analysis and manuscript preparation were additionally support through R00DA046564, and through the Oklahoma Tobacco Settlement Endowment Trust.

ASSOCIATION OF PATIENT AND TUMOR CHARACTERISTICS WITH SURVIVAL IN UTERINE LEIOMYOSARCOMA PATIENTS

Kelsie Guice

Background

Uterine leiomyosarcoma (uLMS) is a rare tumor with a high risk of recurrence and poor prognosis. Despite this, some patients experience no disease recurrence and longer overall survival compared to other patients with the same diagnosis. There have been few studies evaluating the association of patient and tumor characteristics with clinical outcomes and overall survival. Additionally, studies are scarce that evaluate the molecular composition of uterine leiomyosarcomas and potential associations between somatic mutations and clinical outcomes. The objective of this study is to determine the relationship between patient and tumor characteristics, including somatic mutations, clinical courses, and survival in patients diagnosed with uLMS.

Methods

An IRB-approved retrospective chart review of patients diagnosed with uLMS at any stage from January 2006 to September 2024 at a single institution was performed. Patient demographics, tumor characteristics, clinical characteristics, and treatments received were analyzed. Overall survival (OS) was evaluated using the Kaplan Meier method. Log-rank tests were used to determine the presence of statistically significant differences between the survival of groups. Descriptive statistics of the demographics, oncologic characteristics, and treatments were used to summarize data. Next generation sequencing (NGS) data was obtained from two databases, Foundation Medicine and Caris Life Sciences.

Results

56 patients met inclusion criteria for this study. The median age of the patient population at diagnosis was 54 years (48-61 yrs). Of these patients, 66.1% were Caucasian. 12.5% were African American. 3.6% were Hispanic. 17.9% were of another race. 24 patients (42.9%) were Stage I at diagnosis. 20 patients (35.7%) were Stage IV at diagnosis. Median OS of the patient population was 68 months (35.1-124). Patients were divided into cohorts of short-term survivors and long-term survivors. Short-term survival was defined as survival < 1 year. Long-term survival was defined as survival > 1 year. 16 patients (28.6%) were short-term survivors. 40 patients (71.4%) were long-term survivors. Median overall survival (OS) in the short-term survivor population was 8.51 months, while median overall survival in the long-term survivor population was 86 months.

19 patients (33.9%) of the total patient population had foundation testing performed on tumor specimens. TP53 was the most common mutation present, followed by ATRX and RB1. None of the mutations identified were associated with short- or long-term survival.

Short-term survivors and long-term survivors were analyzed to determine factors associated with survival. Stage at diagnosis was significantly associated with survival with 62.5% of short-term survivors being stage IV at diagnosis compared to just 25% of long-term survivors (p-value <0.001). Having undergone more than 1 line of therapy was associated with improved survival (p-value 0.019) as was having surgery at time of diagnosis (p-value 0.020). Residual disease after surgery, defined as > 1 cm, was associated with worse survival (p-value 0.007). ER/PR receptor status, patient race, and tobacco use did not correlate with overall survival.

Conclusions

Uterine leiomyosarcoma is a devastating cancer that has not seen an overall improved survival rate despite years of study. One possible barrier to this is the overall rarity of this malignancy. However, the overall poor prognosis of uterine leiomyosarcoma highlights the importance of studying patient and tumor characteristics to determine if any associations exist between these and overall survival. The prognostic factors associated with improved survival in our study suggest that upfront surgery with no residual disease left improves overall survival. Additionally, gynecologic cancer treatment has evolved to include many targeted therapies based on tumor genetics. However, treatment of uterine leiomyosarcomas has not followed this trend. The somatic mutations found in our study are similar to what has been previously reported about uterine leiomyosarcomas. While out study did not find an association of any of these mutations with disease progression or disease recurrence, future studies are needed with larger sample sizes to further assess if there is a relationship of certain tumor characteristics with overall survival and if certain therapies could target tumor mutations to decrease disease progression.

CO-DEVELOPING A MEDICATION MANAGEMENT APP TO SUPPORT TREATMENT PARTICIPATION AMONG ADOLESCENTS AND YOUNG ADULTS WITH HEMATOLOGY/ONCOLOGY CONDITIONS

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Introduction: Adolescents and young adults (AYAs) with certain hematology/oncology conditions (HOC) often require long term oral medication regimens. AYAs represent a clinically important population affected by serious and often life-threatening diseases, including acute lymphoblastic leukemia (ALL), central nervous system (CNS) malignant and benign tumors, and sickle cell disease (SCD). Treatment participation (i.e., adherence) can be challenging due to complex schedules, side effects, medication burden, and completing school and work demands. Mobile health (mHealth) tools can support medication management through reminders and tracking. Co-development with patients will help ensure these tools are engaging and aligned with AYA needs and preferences. Our goal is to co-develop an mHealth app called TEACH (Treatment Engagement in Adolescents with Hematology/Oncology Conditions).

Methods: This study was approved by the University of Oklahoma Institutional Review Board and informed consent was obtained from all participants. Semi-structured interviews were conducted with 13 AYAs receiving treatment for HOC both virtually and in-person depending upon the participants preference and lasted approximately 20 minutes. Interviews were conducted regarding oral medication dose and schedules, medication management support, barriers to treatment participation, and preferences for using an mHealth app. In addition, five of these participants attended an mHealth app development meeting to provide feedback on design concepts for a cozy space that participants can decorate (e.g., bedroom with furniture) and avatar options. Data collection, including provider interviews, is ongoing, thus we are presenting preliminary results of research in progress.

Results: Medication management varied among participants, including use of pill organizers, automated dispensers, phone alarms, and routines linked with daily activities. Dosing frequencies ranging from 1 to 4 times daily with changes to medications occurring after monthly clinic visits for some patients. Family support was common, though some participants managed medications independently. Key barriers included forgetting doses, complex timing of doses, side effects and unpleasant taste, high number of pills, competing school or work demands, and limited understanding of treatment at initiation. Patients expressed interest in mHealth app features to support medication management, such as reminders, simple medication tracking and clear information about medication and side effects. During the app development meeting, participants provided feedback on art for the cozy space. Participants responded positively to the overall concept of room decorations, but suggested having more mature options (e.g., regular furniture instead of dinosaur themed). Participants emphasized the importance of interactive

elements in the app. Avatar customization was well received, with interest in customizable clothing and accessories.

Discussion: Initial results from patient interviews demonstrated the need for reminders, medication tracking, and clear education. Feedback from the mHealth app development meeting emphasized strong interest in customizable cozy spaces for a range of age groups, interactive features, and avatar personalization. These findings are informing the co-development of a patient centered mHealth medication management app designed to support engagement, usability, and treatment participation among AYAs.

PILOT IMPLEMENTATION OF BEHAVIORAL NUDGES IN GROCERY STORES TO PROMOTE FRUIT AND VEGETABLE PURCHASING

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The American Institute for Cancer Research endorses fruits and vegetables as the foundation for building a cancer preventive dietary pattern, yet Oklahoma ranks 49th nationally in fruit and vegetable consumption. Food marketing is typically used to incentivize unhealthy, ultra processed foods, but these principles can be applied to promote purchases of healthy foods. A form of food marketing, behavioral nudges involve intentional environmental, choice architecture changes at or near the point of sale. Few studies have examined the effect of behavioral nudges on fruits and vegetable sales in grocery settings, and no studies have examined the influence of behavioral nudges as a complementary strategy to boost fruit and vegetable sales when delivered alongside nutrition incentive programs for Supplemental Nutrition Assistance Program (SNAP) consumers. This pilot study describes the early implementation of behavioral nudges designed to boost fruit and vegetable sales in select grocery stores participating in the Double Up Oklahoma (DUO) nutrition incentive program, including initial feasibility and implementation processes through site visit–based process evaluation.

We conducted a literature review to identify behavioral nudge strategies for healthy food purchasing that resulted in the selection of cognitive fatigue, feedback and planning, scarcity/loss aversion, descriptive social norms, and product placement/priming as key strategies. These concepts were applied to develop cling signage on freezer doors, shelf blade signage, shopping cart signs, pharmacy medication bags, pharmacy medication handouts, staff buttons, in-store posters, and social media posts. The primary messages on marketing signs were designed to apply to all shoppers with a secondary message at the bottom of signs being tailored specifically to SNAP consumers.

Materials were finalized collaboratively with the study team, retail grocery partner, and Hunger Free Oklahoma (HFO), the organization implementing DUO. Structured site visits collected process evaluation measures including direct observation of produce stocking and quality,

signage placement and quality, and informal discussions with store managers and staff regarding operational capacity, trends in sales, and perceived acceptability of proposed nudges. The first pilot store was launched in October 2025, with another group (n=5) launched in January 2026, and the remaining (n=4) launching in February 2026 for a total of 10 pilot stores. Site visits documented an average of 9 nudge signs displayed at each site. While cling signage on freezer doors were present without quality issues, the planned freezer blades did not fit well so new fixtures were ordered by the grocery stores. DUO-eligible frozen fruits and vegetables were found to be fully stocked at only 39% of site visits, which may indicate greater demand for advertised products. Store staff were generally positive about the nudge signage and requested larger, bolder signage. Sales data analyses to estimate the impact of signage on produce purchasing relative to control stores are underway. Preliminary findings from this process evaluation suggest that behavioral nudges to promote fruit and vegetable consumption in grocery store settings is feasible. Pre-implementation planning that involved collaboration between study teams and implementing agencies supported initial execution of the project. In addition to ongoing site visit evaluations, future evaluation will analyze the impact of nudges on fruit and vegetable sales and on DUO redemption across multiple stores compared to control stores.

Double Up Oklahoma is a program of Hunger Free Oklahoma. This work is supported by the Gus Schumacher Nutrition Incentive Program, project award no. 2022-70415-41628, from the U.S. Department of Agriculture's National Institute of Food and Agriculture, as well as support from the Oklahoma Department of Human Services (OKDHS), the Tobacco Settlement Endowment Trust (TSET), Ascension St. John, and other matching funders. Hunger Free Oklahoma is an equal opportunity provider.

DOUBLE UP OKLAHOMA DUO FOR HEALTH: LESSONS LEARNED AND FUTURE DIRECTIONS

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Fruit and vegetable consumption is an essential part of chronic disease prevention and management, including many cancers. Yet many patients, particularly those participating in the Supplemental Nutrition Assistance Program (SNAP), face financial and knowledge barriers to accessing and consuming fruits and vegetables. Double Up Oklahoma (DUO) is a nutrition incentive program that provides SNAP participants with a dollar-for-dollar match on SNAP purchases through vouchers that can be used on fresh produce in select grocery stores and farmers markets across Oklahoma. DUO provides financial incentives for fruit and vegetable purchases; however, participation remains limited among eligible populations. Additionally, healthy behavior change materials have been shown to be more impactful and more likely to initiate behavior change when presented to patients by their healthcare providers. Launched in 2022, DUO for Health connects healthcare providers to brief trainings about the DUO program and provides free patient facing nutrition and DUO educational materials to be used in routine healthcare encounters. This poster summarizes lessons learned over the full project period and highlights future directions for program expansion.

To be a DUO For Health provider, individuals must provide healthcare to adults with diabetes or hypertension and must practice in a community that has DUO-eligible grocery stores. DUO For Health providers complete enrollment and quarterly follow up surveys. Provider surveys capture provider type, patient type, clinical food insecurity screening and nutrition referral processes, nutrition counseling frequency, perceived impact of fruit and vegetable consumption on patient health, and the provider's own fruit and vegetable consumption. Quarterly surveys include questions about the use of DUO for Health materials, nutrition counseling frequency, perceived patient interest in DUO For Health materials, and open-ended feedback and patient impact questions. Descriptive analyses were conducted to summarize provider engagement and survey responses over time.

Since the program start in May 2022, 95 healthcare providers enrolled in the DUO for Health program, including physicians, physician assistants, nurses, care coordinators, dietitians, health educators, and pharmacists from 40 unique clinics. DUO for Health providers are active in 19 rural and urban communities in Oklahoma, 63% of the communities with current DUO eligible grocery

stores. The vast majority reported they were very or extremely satisfied (86%) with the DUO for Health materials.

Key implementation lessons include the importance of easy-to-use materials, ongoing communication with clinical sites, and flexibility to meet the needs of clinics and providers. DUO for Health demonstrates the benefit of embedding nutrition incentive education within healthcare settings and highlights the value of provider guidance in promoting fruit and vegetable consumption. Lessons learned have informed planned program expansions, including promoting provider engagement through regular DUO for Health updates, implementation into retail pharmacy settings, and the development of provider cooking classes to further reinforce nutrition education beyond the clinic visit. Future directions may include developing versions of materials for pediatric patient populations and exploring scalable partnerships within organizations that serve high-risk populations, like food banks, to broaden reach and sustainability.

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TUMOR-DERIVED EXOSOMES AS A PLATFORM FOR GENERATING TARGETED ANTIBODIES IN OVARIAN CANCER THERAPY

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Targeted cancer therapy remains constrained by the limited availability of tumor-specific ligands and the heterogeneity of tumor antigens, resulting in inefficient drug delivery and off-target toxicity. To address this challenge, we developed a novel strategy that exploits cancer-derived small extracellular vesicles (sEVs; also referred to as exosomes) as immunogens for the generation of tumor-targeting monoclonal antibodies. Since exosomes recapitulate the membrane features of their parent cancer cells, antibodies generated against these vesicles possess inherent tumor specificity.

sEVs isolated from ovarian cancer cells (OVCAR-8) were used to immunize mice, followed by hybridoma generation and monoclonal antibody screening. Two lead antibodies were identified: AB1, selected based on maximal cytotoxic activity against OVCAR-8 cells, and AB2, selected for superior tumor-cell targeting specificity relative to non-cancerous HOSE cells. Both antibodies were conjugated to paclitaxel-loaded $CD8^+$ T cell–derived exosomes to generate targeted delivery systems (AB1-TSEV/P and AB2-TSEV/P).

In vitro, both paclitaxel-loaded exosomes and antibody-decorated exosomes produced significantly greater cytotoxicity than free paclitaxel, confirming the delivery advantage of exosomal formulations. In vivo studies using an OVCAR-8 xenograft model revealed that both AB1-TSEV/P and AB2-TSEV/P induced marked tumor regression over an 80-day study period ($p<0.0001$) without affecting body weight, demonstrating strong efficacy and tolerability. Biodistribution analyses using IVIS imaging showed significantly enhanced tumor accumulation of antibody-decorated exosomes ($p<0.0001$). Mechanistic studies with bulk RNA sequencing and spatial transcriptomics demonstrated downregulation of proliferative drivers such as MYC and LIF, along with enrichment of apoptotic, immune, T-cell receptor–related, and antigen receptor–related pathways.

Together, these findings establish cancer-derived sEVs as a platform for generating tumor-targeting antibodies and show that antibody-decorated exosomes deliver chemotherapy with enhanced precision, efficacy, and mechanistic impact, while providing a foundation for future personalized cancer therapy.

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TRACKING LONGITUDINAL CHANGES IN SPEECH MOTOR CONTROL AFTER PARTIAL GLOSSECTOMY AND LINGUAL RADIATION

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Background: Oropharyngeal cancers (OC) and their treatments frequently disrupt speech motor function by damaging key articulatory structures, particularly the tongue. Surgery and radiotherapy (RT) can alter efferent motor commands, afferent sensory feedback, and tissue elasticity, resulting in persistent motor speech impairments. However, the mechanisms linking treatment-related structural changes to functional speech deficits remain poorly understood, and prospective longitudinal kinematic studies are lacking.

Purpose: This project investigates how surgical and RT-induced changes in lingual sensorimotor processing affect speech motor control in patients treated for tongue tumors.

Methods: This ongoing longitudinal study uses electromagnetic articulography and ultrasound to quantify real-time tongue and jaw kinematics in OC patients before treatment and up to three years post-treatment, alongside matched healthy controls. Radiation dosimetry and CT imaging are integrated to assess dose–response effects within functional tongue subregions.

Hypotheses: We hypothesize that structural and sensory disruptions degrade movement precision and inter-articulator coordination, and that speech motor impairment is proportional to radiation dose delivered to critical tongue regions.

Conclusions: By defining mechanisms underlying treatment-related speech deficits, this work aims to inform surgical planning, radiation targeting, and personalized rehabilitation to improve long-term functional outcomes and quality of life.

POTENTIAL THERAPEUTIC TARGET: CHARACTERIZING DOUBLECORTIN LIKE KINASE 1 (DCLK1) EXPRESSION AND ROLE IN CHEMORESISTANT OVARIAN CANCER

Megan Marshalla, Bethany Werner, Samrita Dogra, Cole Hladik, Bethany Hannafon

Background. Poly (ADP-ribose) polymerase inhibitors (PARPi) have improved outcomes for homologous recombination (HR)–deficient ovarian cancer (OC), yet acquired resistance emerges in ~40-70% of patients, limiting durable benefit. Established resistance mechanisms, including HR restoration and BRCA reverse mutations, highlight the need for additional, targetable dependencies that sustain PARPi-refractory disease. Doublecortin-like kinase 1 (DCLK1), a serine/threonine kinase linked to stem-like programs, epithelial-mesenchymal plasticity, and therapy resistance, is associated with significantly worse progression-free (p=0.0035) and overall survival (p=0.0026) in OC. Loss of DCLK1 can resensitize chemoresistant cells to platinum. This study therefore aimed to define DCLK1-mediated regulation of cell-cycle checkpoint and DNA repair pathways in chemoresistant OC and to map intracellular versus cell-surface DCLK1 expression as a potential therapeutic vulnerability to enhance PAPPI response in resistant disease.

Methods. DCLK1 expression was profiled across a panel of human ovarian cancer cell lines including OVCAR8, OVCAR8 cisplatin-resistant (CPR), IGROV-1, UWB1.289, UWB1.289 olaparib-resistant (Olres), PEO1, and PEO1 Olres. Cell surface (extracellular) DCLK1 abundance was quantified by flow cytometry in HR-deficient models and their matched Olres derivatives. UWB1.289 cells and corresponding Olres derivatives were then treated in vitro with olaparib, the selective DCLK1 inhibitor (DCLK1-IN-1), or the combination. At 72-hours, metabolic activity was measured as a surrogate for cell viability, and drug interaction effects were evaluated to determine potential synergy between DCLK1-IN-1 and PARPi. In parallel, cell-cycle distributions were assessed by flow cytometry, and treatment-associated modulation of DNA repair pathway proteins were measured. Finally, gene expression changes were characterized in a xenograft mouse model using OVCAR8 CPR spheroids.

Results. DCLK1 exhibited a nonredundant role in homologous recombination–associated signaling and cell-cycle checkpoint control, supported by pharmacologic inhibition coupled with downstream proteomics, RNA sequencing, and immunoblot validation. Co-treatment with cisplatin and the DCLK1 kinase inhibitor DCLK1-IN-1 increased G1-phase arrest relative to either agent alone. Consistent with cross-resistance, platinum-resistant ovarian cancer models displayed reduced sensitivity to PARPi, with higher Olaparib IC50 values than parental counterparts. Across PARPi-resistant derivatives, DCLK1 isoforms were broadly upregulated, and cell-surface DCLK1 was significantly enriched in PARPi-resistant lines compared with PARPi-sensitive parental cells under both 2D and 3D culture conditions, with maximal expression observed in resistant spheroids. Functionally, combined olaparib and DCLK1-IN-1 treatment produced significant synergy in both platinum- and PARPi-resistant settings. Finally, in a xenograft model, combination therapy significantly suppressed tumor growth compared with either monotherapy, supporting DCLK1 as a therapeutically actionable liability in PARPi-refractory disease.

Conclusions. DCLK1 has emerged as a mechanistically distinct regulator of HR–associated programs and cell-cycle checkpoint control in OC. DCLK1 abundance tracked with altered olaparib sensitivity, with increased expression observed in Olres derivatives. Therapeutically, co-targeting DCLK1 and PARP produced a significant antitumor effect in vivo, reducing primary tumor growth and metastatic burden relative to single-agent treatment. Collectively, these findings support DCLK1 targeting as a rational combinatorial strategy to overcome PARPi resistance in OC.

POSTSURGICAL PERILESIONAL FUNCTIONAL CONNECTIVITY PREDICTS NEUROLOGICAL OUTCOME IN GLIOMA PATIENTS

Mingwei Huang

The study investigated glioma patients after surgical resection of tumor tissue using postoperative functional magnetic resonance imaging (fMRI) for the purpose of assessing cavity-adjacent (perilesional) functional connectivity as a predictor of overall survival and functional recovery. We developed an analytic method to quantify the postoperative whole-brain functional connectivity. Resting-state whole-brain fMRI scans acquired from twelve glioma patients following surgical resection were then analyzed as a proof-of-concept study. In particular, connectivity of the perilesional area was compared to that of corresponding contralateral homologue region, and the difference between perilesional and contralateral connectivity was calculated. In order to test whether the functional connectivity metric could predict the recovery of neurological outcomes, we compared patients' connectivity metric from postoperative scans with the changes in Karnofsky Performance Status (KPS) score between preoperative assessment and six months follow-up. Additionally, we examined whether the connectivity metric could predict the overall survival, by separating the patients into subgroups according to their median survival time and comparing the difference of the connectivity metric. Our analysis showed altered functional connectivity between perilesional and contralateral regions following surgical resection of glioma. The connectivity metric from postoperative scans was found to be significantly correlated with the recovery of neurological outcomes as KPS changes across the preoperative to six months postoperative period ($rho = 0.97$, $p < 0.001$). Moreover, individuals with survival time greater than 15 months showed significant higher connectivity than those with shorter survival time ($p = 0.0016$ and Cohen's $d = 2.74$ in all subjects, $p = 0.02$ and Cohen's $d = 1.90$ in the subset of subjects with Grade IV gliomas). Furthermore, we developed machine learning models based on the functional connectivity features and the models were able to predict the survival time with the accuracy of 92% and predict the KPS changes with absolute error of 5.84 ± 6.08. Overall, our study showed that resting state fMRI from patients after glioma resection is relevant to their long-term neurological outcome. The reported analytics on post-surgical fMRI scans in combination with the machine learning model could provide important prognostic information in the management of postsurgical recovery.

LABEL-FREE AND HIGH-THROUGHPUT QUANTIFICATION OF NANOPARTICLE-CELL INTERACTIONS AT THE SINGLE-CELL LEVEL WITH FLOW CYTOMETRY

Mobina Mohmmadnejad

Investigating the interactions between nanoparticles and cells at the single-cell level is vital for advancing the design and development of next-generation nanomedicines. To address this need, we explored using flow cytometry as a quantitative, label-free single-cell analytical technique. Specifically, we demonstrated that conventional side-scatter signals in flow cytometry can accurately quantify interactions between nanoparticles and individual cells. Our findings were validated through optical super-resolution microscopy and elemental mass spectrometry. By analyzing >1,000 cells per minute, this high-throughput approach enabled the evaluation of how various physicochemical properties of nanoparticles, such as size, composition, and surface properties, influence their cellular interactions. This information provides the foundation for the rational engineering of nanoparticle drug delivery systems that are safer and more effective, including next-generation cancer nanomedicines.

EFFECTS OF ALCOHOL-RELATED BREAST CANCER WARNINGS ON BEHAVIORAL INTENTIONS AMONG YOUNG ADULT FEMALES IN THE UNITED STATES WHO ARE CURRENT DRINKERS

Wang, N., Massey, Z. B., Anbari, A. B., Adediran, A., Martinez, P., & McCarthy, D.

Background. Awareness of alcohol consumption as a breast cancer risk remains limited among young adult women in the United States.
Methods. In an online experiment, young adult women ages 18–29 who reported alcohol use in the past 30 days (N=1,038) were randomized to view one of three alcohol–breast cancer health warnings (mortality, mastectomy, or hair loss) or a non-alcohol control warning. Participants reported baseline binge drinking frequency and post-exposure negative affect, perceived threat of alcohol harms, and alcohol-related behavioral intentions. Manipulation checks indicated no differences across the three alcohol-warning themes. Therefore, the health warnings were combined into a single treatment condition (exposure to any alcohol–breast cancer warning) versus the control condition for analyses. Structural equation modeling (SEM) assessed direct and indirect effects of warning exposure and binge drinking frequency on behavioral intention outcomes via negative affect and perceived threat of alcohol harms.
Results. The SEM demonstrated acceptable global fit, $\chi^2(11)=76.81$, $p<.001$, RMSEA=.076 (90% CI [.060, .092]), CFI=.98, TLI=.93, SRMR=.036. Health warning exposure increased negative affect ($\beta=.12$, $p<.001$), which was associated with greater perceived threat of alcohol harms ($\beta=.35$, $p<.001$). Higher binge drinking frequency was associated with greater negative affect ($\beta=.21$, $p<.001$) and perceived threat ($\beta=.13$, $p<.001$). Greater perceived threat was associated with stronger intentions to reduce drinking ($\beta=.24$, $p<.001$), stop drinking ($\beta=.17$, $p<.001$), seek information ($\beta=.34$, $p<.001$), discuss alcohol harms with friends and medical professionals ($\beta=.31$, $p<.001$), and support alcohol warning policies ($\beta=.15$, $p<.001$).
Conclusions. Findings inform mechanisms underlying the effectiveness of alcohol-related health warnings, suggesting that negative affect and perceived threat mediate alcohol-related behavioral intentions among young adult women. Higher binge drinking frequency was associated with greater negative affect and perceived threat, indicating that heavier drinkers may be especially responsive to warnings that make alcohol harms feel personally relevant. Future research should consider people's drinking patterns such as binge drinking when designing and test warning features that stimulate affective and threat responses to strengthen risk-reduction behavioral intentions.
Keywords: binge drinking; alcohol; breast cancer; health warning messages;

CISPLATIN-INDUCED OTOTOXICITY IN GYNECOLOGIC MALIGNANCIES

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Objective

Cisplatin is a key chemotherapy for gynecologic malignancies, but its ototoxicity impacts patient quality of life. Guidelines for ototoxicity monitoring exist but are not standard practice. This study aims to determine compliance with ototoxicity monitoring at our institution, assess audiologic changes occurring during cisplatin therapy in patients with gynecologic malignancies, and evaluate the preventative/ototoxicity management measures taken based on audiology monitoring.

Methods

We conducted a retrospective cohort study of patients with gynecologic malignancies treated with cisplatin from May 2023 to September 2024 at a single institution. Data on demographics, clinical factors, and audiology were abstracted via chart review. Descriptive analyses, logistic regression, and Wilcoxon rank-sum tests were performed.

Results

Among 153 patients included in the final analysis, 71.9% were non-Hispanic white, with a mean age of 54.9; 24.2% had baseline otologic complaints. Cervical cancer was the most common diagnosis (56.3%), and 70.2% had stage III/IV disease. Cisplatin was used primarily for initial treatment (79.7%), with an average of 5.32 ± 2.67 cycles. Despite 81.7% being referred to audiology, only 55.6% had baseline audiograms and 16.3% had end-of-treatment (EOT) audiograms, with 95.8% of EOT audiograms being abnormal. However, only 12.9% had treatment holds and 4.4% had discontinuations due to ototoxicity.
After adjusting for baseline age, race, starting dose, and cancer stage, an increased number of cisplatin cycles correlated with worsening otologic complaints (OR = 1.23; 95% CI = 1.05 - 1.49; p = 0.0146). Self-reported tinnitus and dizziness significantly worsened from baseline to EOT (p = 0.0002 and p = 0.0045, respectively). Tinnitus prevalence rose from 13.7% to 26.8%, while dizziness increased from 0.7% to 7.2% during treatment.

Conclusions

Despite routine audiology referrals for patients treated with cisplatin, baseline audiograms were conducted in only half of patients, with even fewer at EOT. Greater integration of audiologists during cisplatin treatment may enhance the quality of life of patients through measures such as provider education, noise conservation, hearing aids, and treatment modifications.

FACTORS ASSOCIATED WITH WOMEN'S PREFERENCE FOR CERVICAL CANCER AT-HOME SELF-TESTING: A CROSS-SECTIONAL ANALYSIS USING HINTS AND THE ANDERSEN BEHAVIORAL MODEL

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INTRODUCTION: Despite expanded access to screening, cervical cancer remains a significant public health concern in the United States, with most cases occurring among women who are never or inadequately screened. Human Papillomavirus (HPV) self-tests offer a patient-centered alternative that may help reduce barriers to screening. This study examines predisposing, enabling, and need factors, as defined by the Andersen Behavioral Model, associated with U.S. women's preference for at-home HPV self-testing.

METHODS: Data from HINTS 7 were analyzed for women aged 21 -65 years. The outcome was preference for at-home self-testing versus provider-administered screening. Independent variables included participants' predisposing (age, marital status, education status, race/ethnicity, cancer fatalism), enabling (family income, employment status, quality of healthcare received, healthcare discrimination, trust in health system, transport barriers, and difficulty paying medical bills), and need factors (health status and health limitations). Descriptive statistics and logistic regression estimated odds ratios with 95% confidence intervals.

RESULTS: Overall, 24.8% of women preferred at-home cervical cancer self-testing. In the final adjusted analyses, women aged 50-65 years (OR [95% CI] = 2.55 [1.26-5.15]) and those who reported healthcare discrimination and transportation barriers had higher odds of preferring at-home self-testing. Non-Hispanic Black/African American, Hispanic women, and women with health limitations (OR [95% CI] = 0.43 [0.23-0.78]) had lower odds of preference.

CONCLUSION: Preference for at-home cervical cancer self-testing is influenced by structural, demographic, and health-related factors. Targeted education and awareness efforts, along with accessible implementation strategies, are essential to support equitable adoption of at-home self-testing, particularly among underserved and underscreened women.

CELLULAR AND MOLECULAR PROFILING OF THE INFERIOR COLLICULUS BRAIN REGION IN SINGLE NUCLEI RESOLUTION

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The inferior colliculus (IC) is an integrative structure in the central auditory system that combines input from downstream pathways to localize and map sound in the organism's environment. The IC is implicated in auditory pathologies like hearing loss, tinnitus, and various auditory processing disorders; studying the mechanisms of brain regions like the IC is vital for understanding hearing disabilities and determining therapeutic targets. Despite receiving significant focus in research, much of the IC's local circuitry and cellular composition is incompletely understood. While prior research has aimed to describe IC cell types by morphology, neurotransmitter expression, or intrinsic membrane properties, only a few studies have consolidated multiple aspects of classification and identified specific molecular markers for IC neuronal subtypes.

Here, we performed 10X Genomics single-nucleus RNA-sequencing on the adult mouse IC with and without sound exposure to establish a complete cellular profile of the IC. We obtained gene expression profiles of 72,081 nuclei and used advanced computational approaches to identify 16 high level cell clusters and multiple subpopulations with various transcriptomic profiles, including several groups of excitatory (i.e. glutamatergic) and two major groups of inhibitory (GABAergic) neurons. We also identified various non-neuronal cell types such as microglia, oligodendrocytes and oligodendrocyte precursor cells, astrocytes and endothelial cells. Using these data, we further examined the transcriptomic profiles of the IC cell types and compared gene expression disparities in CBA/CaJ mice of both sexes between sound-exposed and control mice. After sound exposure, we found upregulated expression in programmed cell death and apoptotic process genes, particularly in GABAergic neurons. These findings further characterize how molecular changes in the IC may represent deterioration in key inhibitory processes, contribute to sound-induced hearing loss and tinnitus generation.

CHEMOTHERAPY IMPAIRS NEUROVASCULAR COUPLING RESPONSES IN BREAST CANCER SURVIVORS: A PILOT STUDY

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Background: Chemotherapy-related cognitive impairment (CRCI), is a condition that has been reported in up to 75% of breast cancer survivors. Normal brain function requires moment-to-moment adjustments of cerebral blood flow to match the needs of active brain regions, a phenomenon known as neurovascular coupling (NVC). Memory processes also depend on functional connectivity (FC) between task-associated brain regions. It is not fully understood whether impaired NVC contributes to CRCI and if it is compensated by increased FC. **Objectives:** To evaluate the effect of chemotherapy on NVC responses, FC and cognitive performance in breast cancer survivors. **Methods:** We recruited 11 female breast cancer survivors (BCS) who had completed chemotherapy at least 12 months prior (cases), and 11 age-matched controls. We also assessed NVC responses in the brain cortex during a working memory (n-back) and a motor paradigm (finger tapping) using functional near-infrared spectroscopy. A proxy of NVC was assessed by dynamic retinal vessel analysis during flickering light stimulation. Cognitive performance was measured using the Cambridge Neuropsychological Test Automated Battery and a working memory paradigm. **Results:** BCS group demonstrated longer reaction time during 1-back task compared to controls ($p<0.05$). Between-group comparison revealed significantly impaired NVC responses in frontal cortical areas ($q<0.05$) which was accompanied by increased FC ($p<0.05$) and attenuated retinal arteriolar reactivity in the BCS cases ($p<0.05$). **Conclusion:** Our pilot data suggest long-lasting impairment of NVC responses in female breast cancer survivors compensated by recruitment of more functionally connected brain regions, which may indicate greater risk of CRCI.

THE NON-NECROPTOTIC ROLE OF HEPATOCYTE MLKL IN THE PROGRESSION OF MASLD RELATED-HCC

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Mixed Lineage Kinase Domain-Like (MLKL), the executioner of necroptosis, is upregulated in metabolic-associated steatotic liver disease (MASLD) and hepatocellular carcinoma (HCC). While systemic MLKL manipulation showed complex, dose-dependent effects in diet-induced obesity models, the hepatocyte-specific role of MLKL in driving MASLD progression to HCC remains poorly defined, particularly under chronic Western diet (WD) stress. We employed hepatocyte-specific MLKL knockout mice (*Mlkl*^{HepKO}) fed a long-term WD to model MASLD-driven HCC progression. We analyzed MASH pathology, tumor burden, cell proliferation, cancer stemness, and mitochondrial respiration. Findings were validated in human HCC cell lines using genetic knockdown and the human MLKL inhibitor, necrosulfonamide (NSA). WD feeding robustly increased hepatic MLKL, yet canonical necroptosis markers (RIPK3, P-MLKL oligomers) were absent. Strikingly, *Mlkl*^{HepKO} mice exhibited reduced hepatocarcinogenesis, showing fewer and smaller tumors, decreased proliferation (Ki67), and suppressed cancer stem markers (DCLK1, OCT4). This anti-tumor effect occurred independently of obesity, liver inflammation, fibrosis, or liver injury, suggesting a dissociation between steatohepatitis severity and tumor progression. Mechanistically, MLKL loss protected against mitochondrial dysfunction and induced remodeling of mitochondrial dynamics, resulting in improved basal and maximal cellular respiration. Clinically, high MLKL expression in human HCC correlated with poor patient survival, and NSA phenocopied genetic MLKL knockdown in HepG2 cells, suppressing proliferation and improving respiration. Our data reveal a novel hepatocyte-intrinsic, non-necroptotic role for MLKL as a tumor progression factor in MASLD-driven HCC. MLKL promotes tumorigenesis by coupling altered mitochondrial dynamics and cellular respiration to cancer cell survival and stemness. Our studies reveal MLKL as a druggable biomarker and therapeutic target for metabolic liver cancer.

EVALUATING THE EFFICACY OF MEBENDAZOLE REPURPOSING FOR OVARIAN CANCER THERAPY USING OPTICAL COHERENCE TOMOGRAPHY

Qinghao Zhang

Ovarian cancer (OvCa) remains the leading cause of gynecological cancer mortality, with most patients developing chemoresistance. Drug repurposing offers promising alternatives, with mebendazole (MBZ) showing anticancer activity. This study evaluates MBZ efficacy using Spectral Domain Optical Coherence Tomography (SD-OCT). We conducted longitudinal imaging of 40 wild-type (WT) and cisplatin-resistant (CPR) OVCAR8 multicellular tumor spheroids over 11 days. Four analyses were performed: volume analysis, optical attenuation analysis, uniformity analysis, and texture feature analysis. Volume analysis showed MBZ reduced spheroid growth in both groups, with greater effects in CPR-MCTs. Optical attenuation analysis revealed increased necrotic tissue ratios in treated spheroids. Uniformity analysis demonstrated MBZ targets heterogeneous tissues effectively. Texture analysis identified significant structural changes, with 866 altered features in CPR spheroids versus 124 in WT spheroids. Cell viability assays confirmed MBZ's effectiveness against standard and chemo-resistant OVCAR8 tumors. This study demonstrates SD-OCT's utility for non-invasive therapy monitoring in 3D cancer models.

PASSIVE SMOKE EXPOSURE AT HUMAN-RELEVANT LEVELS ENHANCES STEM CELL-LIKE PROPERTIES IN HEAD AND NECK SQUAMOUS CELL CARCINOMA

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Background: Secondhand cigarette smoke (SHS) contains over 70 known carcinogens and is linked to various cancer risks. In 2023, approximately 56 million Americans, including 16% of whom are nonsmoking cancer survivors, were involuntarily exposed to SHS. A retrospective clinical study reported that SHS is an independent predictor of recurrence and survival after head and neck cancer treatment. Our earlier study found that SHS exposure increases cisplatin resistance in head and neck squamous cell carcinoma (HNSCC). However, the impact of SHS exposure on cancer stem cells (CSC), a major contributor to tumor recurrence, remains unknown. **Methods:** Sidestream smoke (SS), the main component of SHS, was extracted as previously described. To simulate the SHS exposure levels reported in the saliva of passive smokers, three human HNSCC cell lines (UM-SCC1, WSU-HN6, and WSU-HN30) were exposed to SS extract at various dilutions (1:100, 1:500, and 1:1000) for 48 hours. The 1:100 dilution corresponds to the nicotine concentration observed in a passive smoker's saliva (~ 48 ng/ml of nicotine). Vehicle control (VC) cells were exposed to HEPES alone. The effect of SS extract on cell viability and proliferation were assessed using MTT and Ki-67 immunofluorescence, respectively. CSC growth was determined by the CSC enrichment assay, and CSC markers (CD44, OCT4, and NANOG) expressions were quantified by western blot assay. Data were analyzed using a one-way ANOVA test. **Results:** The HNSCC cells exposed to SS extract had no significant impact on cell viability, or cell proliferation in all three dilutions tested compared to VC. However, CSC enrichment assays showed SS extract exposure significantly increased the number of spheroid formations ($p<0.05$) compared to VC. Western blot analysis revealed that SS extract exposure significantly increased CD44 protein expression ($p<0.05$), while OCT4 and NANOG expression were not altered compared to the VC. **Conclusion:** Our findings revealed for the first time that human-relevant SHS exposure increases CSC enrichment and properties in HNSCC, which may contribute to a new tumor microenvironment and chemoresistance/cancer recurrence. Further research elucidating the impact of SHS on CSC maintenance and strategies to overcome chemoresistance/recurrence is warranted.

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OPTICAL COHERENCE TOMOGRAPHY DETECTS BILIARY MICROSTRUCTURAL ALTERATIONS FOR EVALUATING BILE DUCT VIABILITY IN LIVER TRANSPLANTATION

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Purpose:

Biliary complications remain a major cause of graft dysfunction and post-transplant morbidity. Peribiliary glands (PBGs) serve as regenerative progenitor niches; thus, early detection of PBG injury and stromal remodeling may improve donor duct viability assessment. This study evaluates whether optical coherence tomography (OCT) can non-invasively identify microstructural alterations in bile ducts prior to transplantation.

Methods:

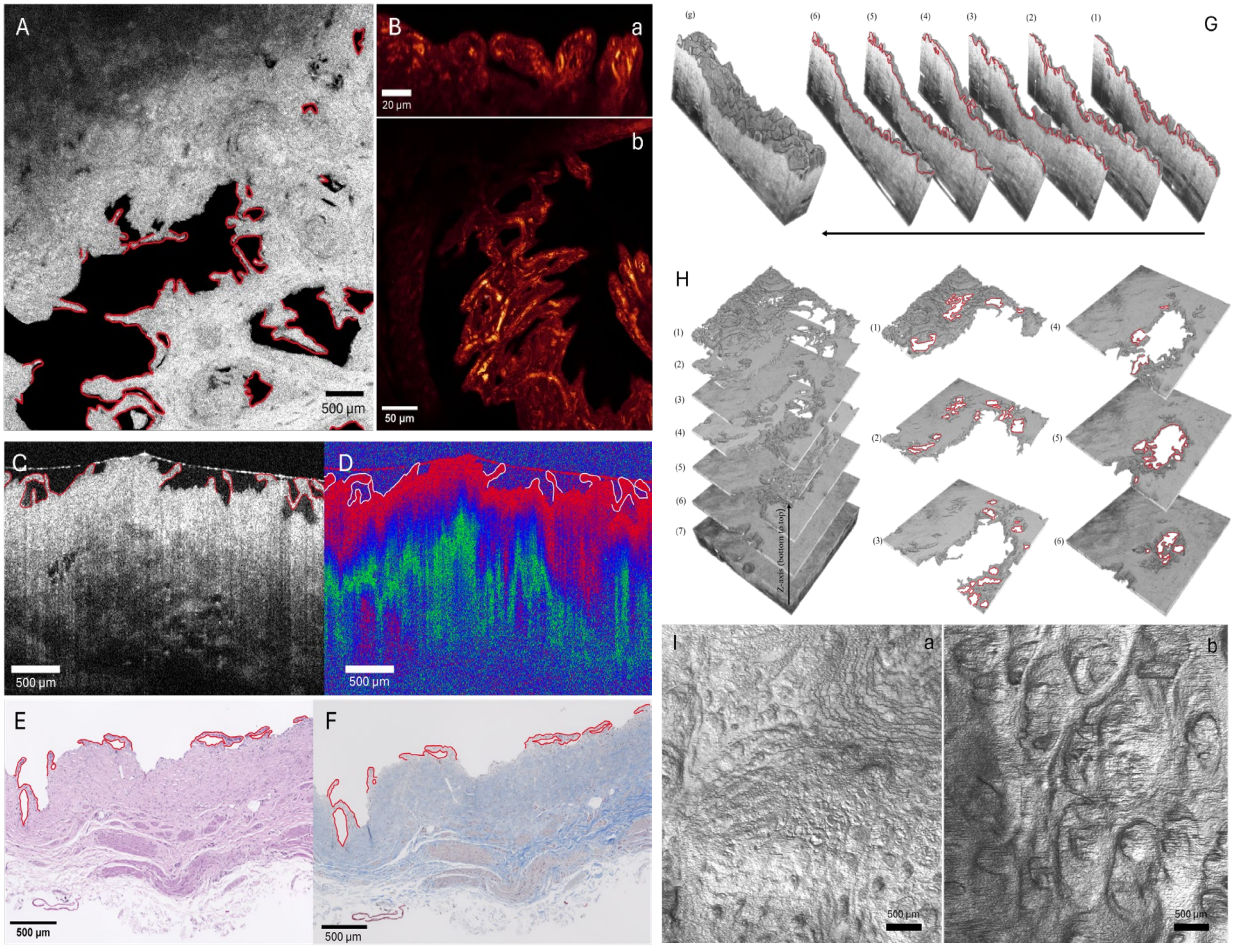
Twenty human extrahepatic bile ducts from donor livers were imaged ex vivo with polarization-sensitive OCT to visualize epithelial integrity, PBG morphology, subepithelial edema, and ductal wall thickness. Corresponding regions were validated using confocal microscopy and histology (H&E and Masson's trichrome). Quantitative wall thickness heatmaps were generated to evaluate early stricture patterns.

Results:

Healthy bile ducts displayed continuous epithelium and organized PBG architecture. In contrast, pathological ducts demonstrated (1) periglandular injury, (2) cystic dilation of PBGs, (3) subepithelial edema, and (4) localized wall thickening suggestive of early stricture formation. OCT accurately distinguished these features in real time and correlated strongly with histology. Thickness mapping further identified focal regions of abnormal narrowing not detectable by gross evaluation. Representative images of cystic dilation in PBGs were shown to illustrate the correlation between OCT and histology.

Conclusions:

OCT provides depth-resolved, real-time visualization of epithelial and subepithelial pathology in donor bile ducts. By detecting early PBG injury and stromal remodeling, OCT may improve donor graft selection and reduce post-transplant ischemic cholangiopathy. Future integration with endoscopic devices may enable in vivo assessment.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PREVALENCE OF THERAPY-RELATED MICROVASCULAR LESIONS IN FIVE-YEAR MEDULLOBLASTOMA SURVIVORS

Ryan Kiser

Background:

Medulloblastoma treatment typically includes radiation therapy (RT) and chemotherapy (CT), achieving an overall survival rate of ≥80%. However, survivors suffer significant long-term morbidities, including progressive cognitive decline. Increasing evidence links therapy-related cognitive decline to delayed microvascular injury resembling accelerated cerebral small-vessel disease. Both CT and RT can cause senescence in cerebromicrovascular endothelial cells, contributing to vascular fragility, blood–brain barrier disruption, neuroinflammation, and white-matter injury. Cerebral microhemorrhages (CMH), detectable on diffusion-weighted imaging (DWI) or apparent diffusion coefficient (ADC) MRI sequences, serve as a marker of such vascular damage.

Objective:

To explore the prevalence of CMH on 5-year follow-up MRI in medulloblastoma survivors. Secondary aim - compare the prevalence in survivors treated with RT plus CT versus CT alone.

Methods:

Using the electronic medical record, we identified patients diagnosed with medulloblastoma in 2000-2020 who remained relapse-free for at least 5 years after diagnosis. Clinical and treatment data, including RT dose and CT regimen, were reviewed. 5-year follow-up MRIs were evaluated for number of CMH in a double-blinded manner by two independent physicians. Cases with discrepancies of ≥2 lesions were adjudicated by a third reviewer. CMH counts were compared between patients treated with RT plus CT and those treated with CT alone.

Results:

Twenty-eight non-relapsed medulloblastoma survivors met inclusion criteria: 4 treated with CT alone and 24 with RT plus CT. The RT+CT group demonstrated an average of 2.5 CMH per patient, compared with 0.5 CMH per patient in the CT-only group.

Conclusion:

Survivors treated with RT plus CT exhibited a greater burden of late-developing microhemorrhages than those treated with CT alone, suggesting more pronounced long-term microvascular injury. These findings indicate neurovascular compromise may contribute to

premature vascular aging and cognitive decline and underscore the importance of understanding therapy-related vascular changes to guide future treatment strategies.

Authors in order?

Kiser, Balsara, Ba, Barkyoumb, Csiszar, McNall

SARS-COV2 GENES FUNCTIONALLY INTERACT WITH HUMAN PAPILLOMAVIRUS ONCOPROTEIN E6

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High-risk human papillomaviruses (HR-HPVs), particularly types of HPV 16 and 18, drive nearly all cervical cancers, and a significant number of vaginal, vulvar, penile, and oropharyngeal cancers through the persistent expression of HPV viral oncogenes E6 and E7. Although HPV vaccines are available, due to the long latency period, low vaccination rate, and the lack of molecularly targeted drugs for early treatment, the incidence of HPV-associated cancers continues to rise. Therefore, understanding the mechanisms of HPV-induced tumorigenesis is critical for developing new and effective strategies to prevent and treat the disease. Recently, synergistic activities between HPV and Sars-CoV2 have been reported, and it is shown that cervical intraepithelial neoplasia and the epithelial cells of oral mucosa have the factors necessary for Sars-CoV2 infection. However, no study to date has investigated the functional interaction between the two viruses and its impact on disease progression. Understanding these interactions is crucial for identification of actionable drug targets to eliminate coinfected cells. In this study, we investigated functional interaction between HPV and Sars-CoV2 genes using transgenic *Drosophila* (the fruit fly) expressing HPV and Sars-Cov2 genes. Using a Gal4-UAS binary expression system to direct gene expression in desired tissue, we performed a functional genetic screen to identify Sars-CoV2 genes whose expression modified E6 oncogene-induced defects. We found that from all Sars-CoV2 genes examined, only nsp3, nsp6, ORF6, and ORF3a were able to modify E6-induced defects, suggesting a functional interaction. Further examination revealed that Sars-CoV2 genes, nsp3 and ORF3a, were both proapoptotic and when expressed in conjunction with E6, disrupted the pro-survival function of E6, promoting apoptotic cell death. Conversely, nsp6 and ORF6 were not proapoptotic when expressed alone, however, similar to nsp6 and ORF6, they interfered with the anti-apoptotic function of E6. These results suggest that Sars-CoV2 and HPV functionally interact and promote cellular and morphological abnormalities that are distinct from those induced by each of these viruses individually. We are currently investigating the mechanism that underlie these interactions to identify druggable targets that can be exploited for development of targeted therapies to eliminate HPV/Sars-CoV2 coinfected cells.

ADVANCING TREATMENT FOR TRIPLE-NEGATIVE BREAST CANCER: INTEGRATING PHOTOTHERMAL THERAPY WITH IMMUNOMODULATION IN A PRECLINICAL MODEL

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Abstract: Triple-negative breast cancer (TNBC) is an aggressive disease with few options and high metastatic risk. Using an orthotopic 4T1 BALB/c model, we evaluated a multimodal regimen combining anti-PD-1, intratumoral imiquimod (IMQ) hydrogel, and near-infrared photothermal therapy (PTT), with or without surgery. 4T1 cells (1×10^5) were implanted in the fourth mammary fat pad. When tumors reached ~3 mm, mice received anti-PD-1 (days 0,3, 7), IMQ (day 0), and intratumoral SWCNT–annexin A5 (day 3) followed by PTT delivered either as 45 °C for 5 min or immediate shut-off at 55 °C using a 980-nm laser; temperatures were monitored by thermal imaging. Surgery was performed on day 5 in designated groups. Tumor growth, survival (Kaplan–Meier), serum cytokines (day 7), splenic immune profiling (day 15), and toxicity (weights, organ ratios, H&E) were assessed. The combination of anti-PD-1 + IMQ + 45 °C/5-min PTT + surgery produced the strongest benefit: marked tumor regression and prolonged survival versus controls and other arms. Cytokine profiling showed elevated IFN-γ, TNF-α, IL-6, and IL-12, consistent with immune activation. Flow cytometry revealed increased $CD4^+$ and $CD8^+$ T cells and reduced MDSCs. Toxicity evaluations found no significant adverse effects. Notably, animals receiving anti-PD-1 + IMQ + PTT without resection later developed firm abdominal masses, suggesting residual tumor or fibrosis and underscoring the value of removing thermally primed lesions. Motivated by these results, we will expand the regimen with additional immune priming. Specifically, we plan to (i) add an agonistic anti-CD137 (4-1BB) antibody to enhance T-cell activation and durability, and/or (ii) extract the whole tumor, devitalize the cells ex vivo, and re-inject autologous tumor antigens with adjuvant support. These arms will be tested alongside surface 45 °C PTT (~5 min) to evaluate survival, systemic immunity ($CD4^+$/$CD8^+$, MDSCs, cytokines), and safety. Our goal is to develop a clinically translatable treatment regimen suitable for human pilot studies.

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EFFECTIVENESS OF CLINICAL TRIALS EDUCATION (CTE) FOR NATIVE AMERICAN (NA) PATIENTS WITH CANCER: A QUALITY IMPROVEMENT PROJECT

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Introduction
Native American (NA) populations are underrepresented in cancer clinical trials. We sought to address this disparity through clinical trials education (CTE) for NA patients with cancer.
Methods
The American Indian Navigation program at the Stephenson Cancer Center in Oklahoma developed a model incorporating CTE at initial navigation visits, based on input from an Indigenous community advisory board. From September 2023 to December 2024, NA patients completed a 6-item survey assessing attitudes and perceptions toward clinical trials including importance of minority participation, likelihood of seeking out information, searching for clinical trials, discussing trials with clinicians, talking with family and friends, and joining a trial. Patients responded using a five-point scale; high score (5) indicated strong agreement and low score (1) strong disagreement. The navigator presented an 11-slide CTE presentation on clinical trial types, ethical treatment, informed consent, participation risks/benefits, and clinical research. Pre- and post-presentation identical surveys were assessed by change in agreement scores, and by performed group comparisons.
Results
106 patients completed pre/post-CTE surveys. Over 25 different cancers were reported, with prostate cancer the most common (11%). Average age was 57 years (SD +/-13) and 56.5% were female. An increase in pre/post-CTE scores occurred for importance of minority participation (3.93 to 4.21, $p < 0.001$). Post-CTE scores showed higher agreement with likelihood of seeking out information (2.60 to 2.92, $p = 0.005$), discussing with clinicians (4.13 to 4.31, $p = 0.005$), and with family/friends (4.10 to 4.30, $p = 0.005$). No changes occurred in likelihood of actively searching for trials (3.69 to 3.67, $p = 0.82$) or of joining a trial (3.71 to 3.69; $p = 0.76$).

Conclusion
In-person CTE increased understanding and attitudes towards clinical trials among NA patients with cancer, particularly regarding the importance of diversity and engaging in discussions with clinicians and family. Additional efforts are needed to assess whether improved awareness translates into increased participation in clinical trials.
Source of funding:
Supported by a patient navigation capacity-building grant from the American Cancer Society.

CRITICAL ROLE OF STAT3 IN DRUG TOLERANCE TO RET-SELECTIVE PROTEIN TYROSINE KINASE INHIBITORS

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Introduction: Rearranged during Transfection (RET) protein tyrosine kinase is a validated target for cancer therapy. Two RET-selective protein tyrosine kinase inhibitors (TKIs), selpercatinib (LOXO-292) and pralsetinib (BLU-667), are currently used to treat RET-altered cancers. However, fewer than 10% of selpercatinib- or pralsetinib-treated patients had a complete response. The drug-tolerant residual tumors eventually evolve to RET TKI-resistance, resulting in disease progression. Understanding and targeting the mechanisms of tolerance to RET TKIs are critical for increasing the depth of response to these inhibitors for eliminating residual tumors to achieve a cure.

Methods and Results: While selpercatinib or pralsetinib inhibited CCDC6-RET and ERK1/2 kinases in the RET fusion-positive human cancer cells, they increased STAT3 tyrosine phosphorylation and nuclear localization. In transcript footprint analysis of selpercatinib-treated TPC1 cells, selpercatinib increased the JAK-STAT pathway activity. Selpercatinib and pralsetinib could not completely inhibit CCDC6-RET fusion-positive human thyroid cancer and non-small cell cancer cells at concentrations that maximally inhibit RET kinase activity. Significantly, combination of the clinical-stage STAT3 inhibitor TTI-101 with selpercatinib or pralsetinib eliminate these RET TKI-tolerated cells.

Conclusion: Inhibition of CCDC6-RET oncogenic kinase by selpercatinib or pralsetinib in human cancer cells activates STAT3, which confers RET TKI tolerance. A STAT3 inhibitor can be used in combination with selpercatinib or pralsetinib to overcome the RET TKI tolerance.

ATOVAQUONE ATTENUATES PANCREATIC CANCER–INDUCED CACHEXIA

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Abstract

Cancer-associated cachexia is a multifactorial metabolic syndrome characterized by systemic inflammation, progressive skeletal muscle wasting, and poor therapeutic outcomes. Pancreatic cancer is among the malignancies most frequently associated with cachexia, contributing significantly to patient mortality. Given the lack of FDA-approved therapies to counteract cachexia, drug repurposing offers a promising alternative strategy. Atovaquone, an FDA-approved antimalarial compound with potent anti-inflammatory properties, has previously been shown to inhibit STAT3 activation—a key driver of cancer-induced wasting.

In this study, we evaluated the anti-cachectic potential of atovaquone in pancreatic cancer–induced cachexia using both in vitro and in vivo models. Treatment of myotubes with S2013 pancreatic cancer cell–conditioned media (CM) induced classical cachectic responses, including upregulation of *atrogin-1* and *MuRF1* and downregulation of myosin heavy chain. Co-treatment with atovaquone reversed these effects, as confirmed by real-time PCR and Western blot analysis, indicating attenuation of muscle degradation. Mechanistically, atovaquone inhibited mitochondrial oxidative phosphorylation, leading to a reduced oxygen consumption rate (OCR) and activation of a compensatory glycolytic shift. This was evidenced by an increase in extracellular acidification rate (ECAR), glucose uptake, and lactate production. Enhanced glycolysis restored cellular energy balance and suppressed catabolic signaling, thereby protecting against CM-induced myotube atrophy. Inhibition of glycolysis with 2-deoxy-D-glucose (2-DG) abrogated the protective effects of atovaquone, underscoring the importance of glycolytic compensation in its mechanism of action.

Collectively, our findings demonstrate that atovaquone mitigates cancer-induced muscle wasting by reprogramming myotube metabolism from oxidative phosphorylation to glycolysis, thus preserving muscle mass and function. These results highlight atovaquone as a promising metabolic intervention for managing pancreatic cancer–associated cachexia.

Keywords: Atovaquone • Cancer cachexia • Mitochondrial oxidative phosphorylation • Glycolytic shift • Muscle wasting

Acknowledgment of Funding:

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OKLAHOMA FOOD IS MEDICINE LANDSCAPE ANALYSIS: OPPORTUNITIES FOR CANCER PREVENTION, TREATMENT, AND RECOVERY

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Abstract

Background: Nutrition plays an integral role in the prevention, successful treatment, and remission of many cancers. Oklahoma's food insecurity rates exceed the national average, and cancer patients and survivors are far more likely to experience food insecurity. Food is Medicine (FIM) initiatives are gaining momentum nationwide as an emerging strategy for addressing the fundamental links between food insecurity, personalized nutrition, and health. Amid growing interest in these models among providers, payers, and policymakers, little is known about current FIM program activities and reach within the state. **Methods:** We conducted a landscape analysis to identify past, existing, and in-development FIM programs throughout the state. Using a mixed-methods approach, we administered quantitative surveys to identified programs to capture and summarize their characteristics. We then conducted key informant interviews with FIM program respondents who agreed to further participate. **Results**: We identified 7 produce prescription, 4 medically-tailored grocery, and 2 medically-tailored meal programs that were concentrated heavily in northeastern Oklahoma. Most programs focused on enrolling patients with cardiovascular disease, diabetes, and hypertension. No programs were identified for cancer prevention, treatment, or recovery. **Discussion**: Findings reveal a growing network of FIM programs, yet none have an emphasis on cancer-related care. The passage of SB806, the Food is Medicine Act, directs the Oklahoma Healthcare Authority to pursue a federal funding pathway for FIM coverage among Medicaid members. Cancer stakeholders should actively engage with FIM program planners to co-develop, implement, and evaluate FIM interventions that reflect their unique needs.

DISTINCT ORAL MUCOSA TRANSCRIPTOMIC RESPONSES ASSOCIATED WITH VAPING AND SMOKING

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Introduction: Electronic cigarettes (e-cigs) have become epidemic and are one of the most popular recreational products in the United States. According to the CDC, e-cig use has significantly increased from 4.5% in 2019 to 6.5% in 2023. Amid the evolving generations of e-cig devices, "pod"-type devices are the most celebrated in the US population. These are lightweight and ultraportable designs engineered for convenient use. However, identifying the health risk associated with them is yet to be fully uncovered.

Methods: To evaluate the chronic impact of e-cigs and tobacco cigarettes on oral mucosal transcriptome, self-declared healthy participants, 18 to 45 years old, volunteered for the study through REDCap, a protected online survey. 64 were enrolled for this study: 10 tobacco smokers (S), 20 e-cig POD device users (POD), 14 dual users (S+POD), and 20 non-users of tobacco products (NU). User status was documented via exhaled carbon monoxide and cotinine quantification. Oral swabs were collected, immediately cryopreserved, and later subjected to RNA isolation and RNAseq analysis. Differentially expressed genes (DEGs) in S, POD, and S+POD groups were identified by comparison to NU using DESeq2 R package, with q-value < 0.05. Gene set enrichment analysis (GSEA) was performed, followed by Ingenuity Pathway Analysis (IPA) (-log(p-value) >1.3 and activation Z-score ±2).

Results: GSEA identified 270 and 257 DEGs in the S and POD groups, respectively, relative to NU, while 465 genes were dysregulated in the S+POD group. Sixty genes were commonly dysregulated in POD and S+POD groups, revealing a unique POD-associated signature. A total of 109 DEGs were shared between S and S+POD users, and 23 transcripts were commonly dysregulated across all three groups. IPA showed that smokers have significant upregulation in the pathways associated with cell communication and protein trafficking, while receptor-mediated signaling, especially RXR activation, was significantly downregulated. In POD and S+POD users several pathways involved in the immune response exhibited significant upregulation. Smokers showed overrepresented functions associated with decreased cancer cell death and increased tumor cell proliferation, movement, and viability. Exclusive POD users and S+POD users also showed downregulation of tumor cell apoptosis and increased propensity for cell viability and clonogenicity.

Conclusion: Our data show that vaping induces a distinct transcriptomic signature that persists in dual POD and combustible cigarette users. POD use, irrespective of concurrent smoking, was associated with dysregulation of pathways favoring cancer cell hallmarks, with the strongest effects observed in dual users. All three groups commonly displayed dysregulation of immune response and inflammatory profile. Together, our data suggest that e-cig use may disturb immune homeostasis and promote a tumorigenic environment in the oral mucosa.

RADIATION-MEDIATED ELEVATED DUSP1 PROMOTES RADIORESISTANCE IN TRIPLE-NEGATIVE BREAST CANCER

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Abstract

Dual-specificity protein phosphatase 1 (DUSP1/MKP1) dephosphorylates threonine and tyrosine residues on MAPKs (ERK, JNK, and p38). By regulating MAPK activity, DUSP1 modulates context-dependent and tumor-specific cell survival, proliferation, differentiation, epithelial-mesenchymal transition (EMT), and drug and radiation resistance. The effect of radiation therapy and DUSP1 regulation in hormone receptor-positive (HR+) and triple-negative (HR-) breast cancer (BC) is not clearly defined. Our IHC data revealed a higher expression of DUSP1 in HR positive and TNBC tumors compared to normal breast samples. We obtained tumor tissues from a phase II trial involving preoperative delivery of 25 Gy in 5 fractions to the whole breast. We performed nano-string targeted RNA sequencing approach to examine the RT impact on BC gene expression. RT induced DUSP1 expression in HR-positive and TNBC tumors as well as in patient serum after post-RT. Radiation-mediated induction of DUSP1 reduced cleaved-PARP expression, apoptosis, and proliferation in TNBC cells, predominantly by increasing ERK phosphorylation. Overexpression of DUSP1 increased c-PARP expression, and knockdown/inactivation of DUSP1, followed by radiation exposure, reduced c-PARP expression/apoptosis and acquired radioresistance in TNBC cells. DUSP1 regulates EMT biomarkers E-Cad and N-Cad expression, and chronic irradiation increased DUSP1 activity, pERK, and cancer stem cell markers expression in TNBC cells. Collectively, our data suggest that DUSP1 may serve as a prognostic biomarker in BC and DUSP1 activity regulates radioresistance in TNBC.

WESTERN DIET AND PQQ DIFFERENTIALLY SHAPE LIVER (IMMUNE) CELL STATES REVEALED BY SINGLE-CELL RNA SEQUENCING

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Obesity is a chronic condition associated with increased risk of metabolic-associated steatotic liver disease (MASLD), type 2 diabetes, cardiovascular disease, and cancer. Western diet (WD) feeding is commonly used to model obesity in vivo and promotes MASLD risk in mice. In contrast, pyrroloquinoline quinone (PQQ), a redox cofactor with antioxidant properties, has shown promise in reducing visceral fat accumulation and modulating obesity-associated inflammation. In this study, we compared WD, WD+PQQ, and chow diets in male mice to define diet-associated immune responses in the liver at single-cell resolution. We annotated immune cell types and states within liver tissue and assessed diet-associated programs using differential expression, pathway enrichment, and cell–cell communication analyses.

Single-cell RNA-seq analysis demonstrated phenotypes associated with inflammation , stress-response, and tissue remodeling across liver immune populations. PQQ supplementation, however, showed transcriptional signatures enriched in immune regulatory and stress-mitigation pathways. Cell–cell communication analysis revealed increased interaction strength signaling under Western diet, whereas PQQ showed intercellular networks biased toward more balanced immune communication patterns.

Together, these results indicate that PQQ may alter Western diet–induced immune dysregulation by restoring coordinated immune-related cellular phenotypes and signaling in mouse liver.

ECONOMIC AND TIME TOXICITY IMPACT OF PEMBROLIZUMAB DOSING SCHEDULE OPTIMIZATION IN ADJUVANT TREATMENT OF CLEAR CELL RENAL CELL CARCINOMA

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BACKGROUND

Immune checkpoint inhibition with pembrolizumab has transformed the treatment landscape across multiple malignancies, resulting in a substantial and growing population of patients receiving prolonged therapy. Pembrolizumab is approved in multiple dosing regimens, including intravenous (IV) 200 mg every 3 weeks (Q3W) and IV 400 mg every 6 weeks (Q6W), as well as two subcutaneous (SC) regimens, 395 mg Q3W or 790 mg Q6W, administered with beta-hyaluronidase alfa. Each dosing strategy offers distinct advantages related to infusion frequency, health care resource utilization, and treatment-related **time toxicity**, defined as time spent in contact with the health care system for therapy administration. However, the comparative economic and time toxicity impact of these dosing options in the adjuvant setting remains poorly defined. We used adjuvant clear cell renal cell carcinoma (ccRCC) as a representative model to evaluate the potential cost and time toxicity savings associated with pembrolizumab dosing schedule optimization.

METHODS:

A pharmacoeconomic model simulated patients with high-risk ccRCC receiving one year of adjuvant pembrolizumab, informed by treatment duration and disease-free survival data from KEYNOTE-564. Analyses were conducted from a U.S. payer perspective using Medicare reimbursement and 2026 pricing assumptions. Four dosing strategies were evaluated: IV pembrolizumab 200 mg Q3W, IV pembrolizumab 400 mg Q6W, SC pembrolizumab 395 mg Q3W, and SC pembrolizumab 790 mg Q6W. Total costs included drug acquisition and administration. Treatment-related time toxicity was estimated based on the number of treatment visits and expected administration duration for IV versus SC therapy. Sensitivity analyses evaluated variations in imaging frequency and administration assumptions.

Results

Drug acquisition costs were comparable across all dosing strategies, reflecting fixed-duration

therapy and low early recurrence rates in the adjuvant setting. Compared with IV Q3W dosing, IV Q6W dosing resulted in modest overall cost savings of about $1321 per year, according to our calculations, driven by reduced infusion administration frequency. SC pembrolizumab further reduced administration-related costs and was associated with the lowest estimated time toxicity due to fewer treatment visits and shorter administration time. Across sensitivity analyses, both IV Q6W and SC dosing strategies remained cost-neutral or cost-saving relative to IV Q3W dosing, with consistent reductions in health care resource utilization and time toxicity.

Conclusions and Relevance

Optimization of pembrolizumab dosing schedules in the adjuvant ccRCC setting, including extended-interval IV dosing and SC administration, can achieve comparable drug costs while reducing infusion-related resource utilization and treatment-related time toxicity. In a disease context characterized by fixed treatment duration and low early progression rates, alternative pembrolizumab dosing strategies represent economically favorable and patient-centered approaches. These findings support broader consideration of dosing schedule optimization as pembrolizumab use continues to expand across oncology.

A CLUSTERING-BASED METRIC FOR ASSESSING BATCH EFFECT IN SINGLE-CELL RNA SEQUENCING DATA INTEGRATION

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Gallogly college of Engineering / Data Science and Analytics institute
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While integrating multiple single-cell RNA sequencing (scRNA-seq) datasets is essential for building large-scale cell atlases, it also introduces batch technical variations arising from differences in sequencing platforms, reagents, or experimental conditions (Büttner et al., 2019). Metrics such as kBET, LISI, and ASW work at the local neighborhood level and have shown variable sensitivity and dataset-dependent performance (Lütge et al., 2021).

To address these limitations, we developed a clustering-based metric to assess cell populations relative to their originating datasets and to quantify the average weighted similarity across integrated clusters. We applied hierarchical clustering, and we calculated pairwise cosine similarities across all contributing datasets. We weighted similarity scores within each cluster by cell counts to generate per-cluster integration scores, which we averaged to compute an overall similarity score for the integrated dataset.

We first tested the metric using two subsampled PBMC datasets and their merged dataset, which yielded a similarity score of 0.85. We then tested the metric across five integration scenarios that increased biological and technical variance. Integration of four lung datasets yielded a mean score of 0.78, indicating high consistency in their contributions to the merged cluster. Introducing a single liver dataset reduced the score to 0.60. Replacing one lung dataset with a second liver or adding a spleen dataset produced similar scores of 0.56 and 0.57, respectively.

The most pronounced decrease occurred when integrating a COVID-19 scRNA-seq dataset with three lung samples, yielding a score of 0.31. This reduction corresponded to clusters composed mostly of a single dataset in the composition analysis and to near-zero cross-dataset cosine similarities in the heatmaps, demonstrating that the metric effectively distinguishes between batch-driven and biologically driven differences in cluster structure. We implemented the method in R, and it is compatible with standard scRNA-seq analysis pipelines.

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DCLK1 ORCHESTRATES HEPATOCYTE-MACROPHAGE DYSREGULATION TO DRIVE LIVER FIBROSIS AND HEPATOCARCINOGENESIS

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Hepatocellular carcinoma (HCC) is the most common primary liver cancer and the third leading cause of cancer-related deaths worldwide. It typically develops in the setting of chronic liver injury, inflammation, and cirrhosis. Despite substantial progress made in the treatment of HCC, most patients are unresponsive and ultimately succumb to their disease, underscoring the urgent need for new treatment strategies. Lineage-tracing models have established hepatocytes as the cell of origin for HCC. We previously demonstrated that the cancer stem cell marker doublecortin-like kinase 1 (DCLK1) is highly induced in chronic liver disease but absent in normal liver. Here, we show that hepatocyte DCLK1 is essential for polarizing Kupffer cells and peripheral blood monocytes into a previously undefined M2-like hybrid macrophages with inflammatory and immunosuppressive characteristics, co-expressing CD206, S100A9, PD-L1, and DCLK1. Using a hepatocyte-specific Dclk1 knockout murine model (HSD1-KO), we demonstrated that hepatocyte Dclk1 drives profibrotic and carcinogenic responses including macrophages polarization into hybrid phenotype subsets. Pharmacological inhibition of DCLK1 suppressed both proinflammatory (TNF-α, IL-1β, IFN-α/β/γ) and immunosuppressive (IL-10) cytokines in cocultures, revealing DCLK1's central role in immune dysregulation. Mechanistically, DCLK1 activates a distinct DCLK1/β-catenin(p48)/cyclin D1 oncogenic signaling axis that differs from the canonical Wnt/β-catenin(p92) pathway, which is required for normal liver regeneration. Quantitative proteomics of HSD1-KO versus control livers identified DCLK1-dependent regulation of toxicity, inflammation, immune signaling, and cell cycle progression. Collectively, these findings uncover a novel DCLK1-regulated hepatocyte-macrophage partnership as a key driver of liver carcinogenesis and establish DCLK1 as a promising therapeutic target for the prevention and treatment of HCC.

Feedback Survey