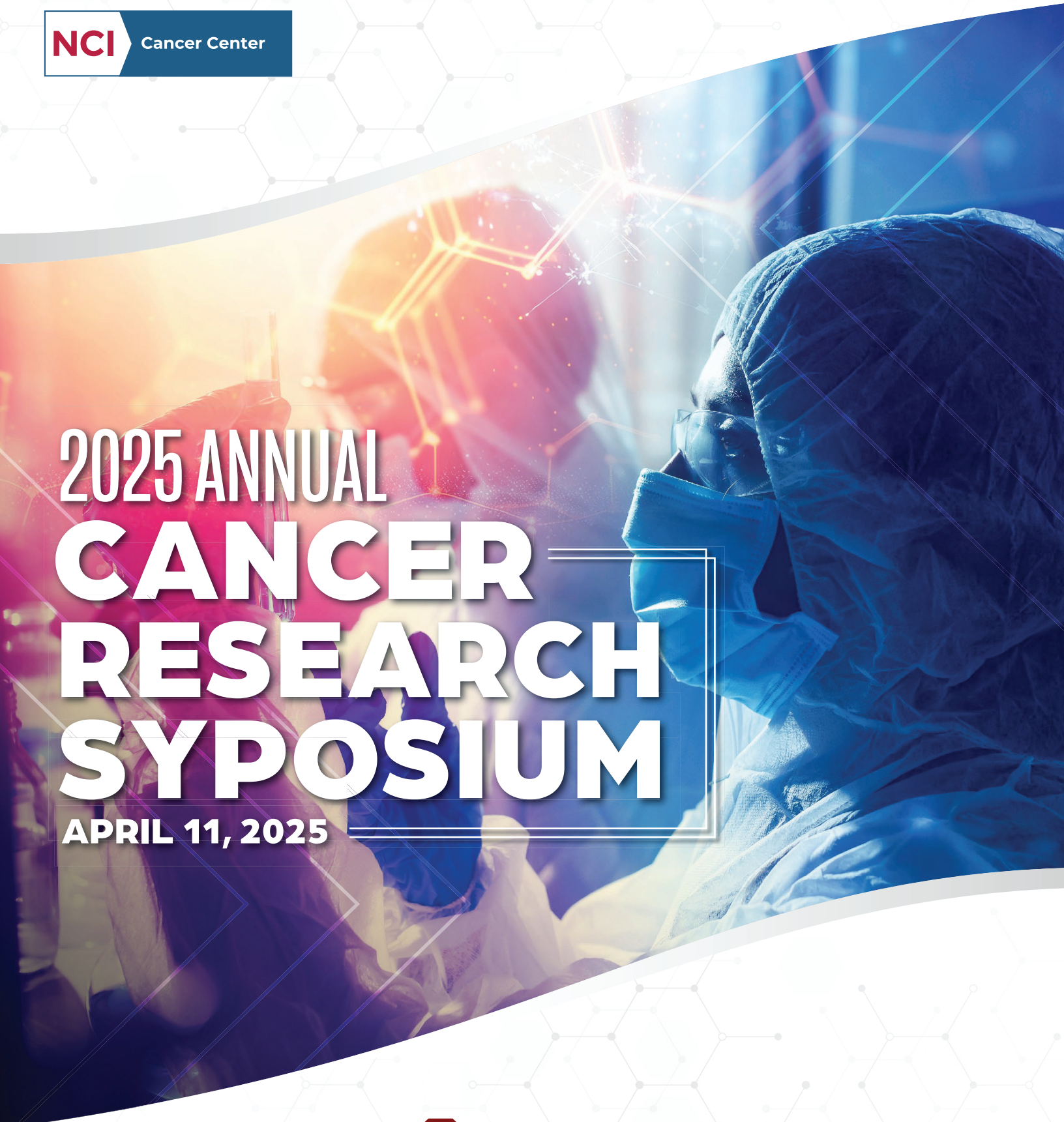
NCI Cancer Center



2025 ANNUAL CANCER RESEARCH SYPOSIUM

APRIL 11, 2025

OU Health | Stephenson Cancer Center

The UNIVERSITY *of* OKLAHOMA HEALTH SCIENCES

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The Stephenson Cancer Center wishes to recognize and thank the Oklahoma Tobacco Settlement Endowment Trust (TSET) for co-sponsoring the 2025 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. In 2017 TSET renewed this award for an additional five year period and in 2022 for an additional three year period.

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.

Ten Year Highlights

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

- Increased cancer center membership from 56 to 289 members at nine academic institutions across Oklahoma
- Recruited seventy one new cancer researchers to Oklahoma
- Funded over fifty seed and directed-research grants to cancer investigators in Oklahoma
- Enhanced five Shared Resource facilities
- Hosted over 330 research seminar speakers
- Hosted annual statewide Cancer Research Symposium that bring together over 250 researchers from around the state
- Hosted over 90 undergraduate students from 32 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 2025 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, Faculty
Michael Businelle, PhD (Co-Director)
Darla Kendzor, PhD (Co-Director)

TSET

OU Health | Stephenson Cancer Center
The UNIVERSITY of OKLAHOMA HEALTH SCIENCES

2025 Annual Cancer Research Symposium

7:30 – 7:50 am	**Poster Check-In** Nicholson Main Desk
8:00 – 9:45 am	**Poster Competition** Nicholson Rooms A, B, C, D, E (Posters)
9:30 – 10:00am	**Registration** Nicholson Main Desk
10:00 – 10:20 am	**Opening Comments** Nicholson Auditorium
10:20 – 11:20 am	**Keynote Speaker** Nicholson Auditorium
11:25 – 12:25 pm	Session I:
	Breakout Group – Translational Research Nicholson Auditorium
	Breakout Group – Cancer Prevention and Control Nicholson Conference Room A
12:30 – 2:00 pm	**Mentorship Lunch** Nicholson Conference Room B
2:00 – 3:00 pm	**Lecture** Nicholson Auditorium
3:05 – 4:05 pm	Session II:
	Breakout Group – Translational Research Nicholson Auditorium
	Breakout Group – Cancer Prevention and Control Nicholson Conference Room A
4:10 – 4:30 pm	**Break**
4:30 – 4:50 pm	**Awards/Closing Remarks – Early-Stage Investigator Award** Nicholson Auditorium
5:00 – 6:00 pm	**Reception – "Posters, Pinot & Pints"** Nicholson Auditorium & Rooms A, B, C, D, E

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10:00 – 10:20 am	**Opening Comments - Danny N. Dhanasekaran, Ph.D.,** Associate Director for Shared Resources Stephenson Cancer Center, OUHSC Nicholson Auditorium
10:20 – 11:20 am	**Keynote Speaker – David S. Ebert, Ph.D.** Interim Chief AI Officer, University of Oklahoma - Norman *The Potential of AI to Advance Cancer Research* Nicholson Auditorium
11:25 – 12:25 pm	Session I:

Breakout Group – Translational Research

- **Shriya Pandey** - *Development of a dual RET kinase inhibitor and protein degrader*
- **Sherwin Tavakol, MD, MPH** - *Longitudinal assessment of glioblastoma vascular remodeling and therapeutic response using functional ultrasound (fUS) imaging*
- **Hassan Abushukair, MD** - *Deciphering the Tumor Microenvironment of Alveolar Soft Part Sarcoma Using Single-Cell Spatial Transcriptomics*
- **Suryakant Niture, PhD** - *CD163+ Tumor-Associated Macrophage Evasion Contributes Radiation Resistance and Poor Prognosis in Estrogen Receptor-Negative Breast Cancer*

Nicholson Auditorium

Breakout Group – Cancer Prevention and Control

- **Gautham Chengizkhan, Ph.D. -** *Nicotine drives chemoresistance by enhancing drug efflux*
- **Vengatesh Ganapathy, Ph.D. -** *E-Cigarette Aerosols to Enhance NRF2-mediated Pathways and Cancer Stemness in Human Oral Cells*
- **Gaurav Kumar, Ph.D. -** *Socioeconomic Characteristics, Tobacco Use, and Service Utilization by County Poverty Status Among Oklahoma Tobacco Helpline Registrants*

- **Catherine Nagawa, Ph.D. –** *Effects of Alignment and Misalignment in Self- and Parter-Oriented Motivations to Quit on Individual and Joint Cessation Outcomes in Dual-Smoking Couples*

Nicholson Conference Room A
Moderators: Michelle vanDellen, Jason Oliver

12:30 – 2:00 pm **Mentorship Lunch**
Nicholson Conference Room B

2:00 – 3:00 pm **Lecture**

- **Doris Benbrook, BA, Ph.D. -** *Translating Discoveries to Clinical Trials in the Route 66 Endometrial Cancer SPORE and Stephenson Cancer Center*
- **Chinthalapally V. Rao, Ph.D. -** *Discovery and Development of Agents for Cancer Interception*

Nicholson Auditorium

3:05 – 4:05 pm Session II:

Breakout Group – Translational Research

- **Karl Thomas** - *Disruption of Cancer Survival Mechanisms via Omeprazole-Mediated Autophagy in Pancreatic Adenocarcinoma*
- **Ryan Bynum, MD** – *Improving the Dynamic Range of Multispectral Optoacoustic Imaging with a Novel PH Low Insertion Peptide in Pancreatic*
- **Clay Foster, Ph.D.** - *Understanding the tumorigenic effects of MYC on DNA replication and transcription in pediatric ALL*
- **Dhanamjai Penta, Ph.D.** - *Targeting Chemoresistant Ovarian Cancer with Mebendazole: A Promising Approach to Overcome Platinum Resistance*

Nicholson Auditorium

Breakout Group – Cancer Prevention and Control

- **Adele Hammoudi, Ph.D. -** *Does Cannabis Boost or Halt Your Inflammatory and Immune Responses?*
- **Michael Robertson, Ph.D., MPH** - *Digitally Mediated Occupational Therapy to Increase Physical Activity in Urban and Rural Breast Cancer Survivors Who Have Undergone Breast Surgery*
- **Jeremy Langford, Ph.D. -** *Comparison of the Temporal Characteristics of Participant Perceived Vs. Algorithm-Based Risk Factors for Smoking Lapse*
- **Darla Kendzor, Ph.D.** - *The impact of cannabis use on smoking among adults with low-income enrolled in a smoking cessation trial*

Nicholson Conference Room A
Moderators: Michelle vanDellen, Jason Oliver

4:10 – 4:30 pm **Break**

4:30 – 4:50 pm **Awards/Closing Remarks – Early-Stage Investigator Award**
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5:00 – 6:00 pm **Reception – "Posters, Pinot & Pints"**
Nicholson Auditorium & Rooms A, B, C, D, E

KEYNOTE ADDRESS

Dr. David S. Ebert

The Potential of AI to Advance Cancer Research

Dr. David Ebert is an Associate Vice President for Research and Partnerships, the interim Chief AI Officer, the Gallogly Chair Professor of electrical and computer engineering, and Director of the Data Institute for Societal Challenges (DISC) at the University of Oklahoma in Norman, OK. As Director of DISC, Dr. Ebert leads faculty and staff in creative innovations in data science, artificial intelligence (AI), machine learning (ML), and data-enabled research. His focus areas include foundational data science and data-enabled research related to aerospace, defense, and global security; community and societal transformation; the future of health; and environment, energy, and sustainability. Dr. Ebert also researches visual analytics, novel visualization techniques, interactive machine learning and explainable AI, human-computer teaming, and advanced predictive analytics. Dr. Ebert currently leads extensive research efforts applying AI/ML methods in predictive analytics for various funded projects to solve real world challenges.

TRANSLATIONAL SCIENCE TRACK

Translational – Session I

Nicholson Auditorium

11:25 am – 11:40 am	Development of a Dual RET Kinase Inhibitor and Protein Degrader **Shriya Pandey** Graduate Student Department of Pathology OU Health Sciences Center
11:40 am – 11:55 am	Longitudinal Assessment of Glioblastoma Vascular Remodeling and Therapeutic Response Using Functional Ultrasound (fUS) Imaging **Sherwin Tavakol, MD, MPH** Resident Department of Neurosurgery OU Health Sciences Center
11:55 am – 12:10 pm	Deciphering the Tumor Microenvironment of Alveolar Soft Part Sarcoma Using Single-Cell Spatial Transcriptomics **Hassan Abushukair, MD** Postdoctoral Fellow Department of Oncology Science and Medical Oncology OU Health Sciences Center
12:10 pm – 12:25 pm	CD163+ Tumor-Associated Macrophage Evasion Contributes Radiation Resistance and Poor Prognosis in Estrogen Receptor-Negative Breast Cancer **Suryakant Niture, Ph.D.** Staff Scientist Department of Radiation Oncology OU Health Sciences Center

Translational – Session II

Nicholson Auditorium

3:05 pm – 3:20 pm	Disruption of Cancer Survival Mechanisms via Omeprazole-Mediated Autophagy in Pancreatic Adenocarcinoma **Karl Thomas** Graduate Student Department of Pharmaceutical Sciences OU Health Sciences Center
3:20 pm – 3:35 pm	Improving The Dynamic Range Of Multispectral Optoacoustic Imaging With A Novel Ph Low Insertion Peptide In Pancreatic Cancer **Ryan Bynum, MD** Resident Department of Surgery OU Health Sciences Center
3:35 pm – 3:50 pm	Understanding the Tumorigenic Effects of MYC on DNA Replication and Transcription in Pediatric ALL **Clay Foster, Ph.D.** Postdoctoral Fellow Department of Pediatrics, Section Hematology/Oncology OU Health Sciences Center
3:50 pm – 4:05 pm	Targeting Chemoresistant Ovarian Cancer with Mebendazole: A Promising Approach to Overcome Platinum Resistance **Dhanamjai Penta, Ph.D.** Postdoctoral Fellow Department of Obstetrics and Gynecology OU Health Sciences Center

DEVELOPMENT OF A DUAL RET KINASE INHIBITOR AND PROTEIN DEGRADER

Shriya Pandey[1*], Yafeng Wang[2], Xueqing Hu[1], Ujjwol Khatri[1], Tao Shen[1], Jianfeng Cai[2], Jie Wu[1]

[1]Department of Pathology and Peggy and Charles Stephenson Cancer Center, University of Oklahoma Health Sciences Center, Oklahoma City, OK

[2]Department of Chemistry, University of Southern Florida, Tampa, FL

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Introduction: Rearranged during Transfection (RET) is a receptor tyrosine kinase that is a validated target for cancer therapy. Recently, two RET-selective protein tyrosine kinase inhibitors (TKIs), selpercatinib (LOXO-292) and pralsetinib (BLU-667), were granted FDA approval to treat RET oncogene-positive cancers. However, these RET TKIs induce feedback overexpression of the CCDC6-RET oncoprotein in cancer cells, reducing their efficacy. We developed a dual RET kinase inhibitor and protein degrader to overcome this feedback mechanism.

Methods: Using selpercatinib as the RET binder and lenalidomide/phenyl glutarimide (PG) as the cereblon ligand, we synthesized a panel of proteolysis targeting chimera (PROTACs) to inhibit RET kinase activity and degrade the protein simultaneously. PROTACs were screened for RET kinase inhibition and RET degradation using CCDC6-RET-positive thyroid carcinoma TPC-1 cells. Lead compounds were further evaluated in additional cell lines. Specificity was assessed using a cereblon-binding defective analog of the lead compound, performing a competition assay with lenalidomide, and conducting proteomic analysis. Proteasome-mediated CCDC6-RET degradation was verified using the proteasome inhibitor Bortezomib. After *in vivo* pharmacokinetics (PK) evaluation, a lead compound was evaluated for anti-tumor activity in a cell-derived xenografts (CDXs)mouse model.

Results: Three compounds were identified as potent dual RET kinase inhibitors and degraders. Only PG-based RET PROTAC YW-N-7 showed excellent *in vivo* PK properties. A cereblon-binding defective YW-N-7 analog retained RET inhibition activity but lost its degrader activity, indicating cereblon-dependent degradation. Lenalidomide and bortezomib also blocked the RET degrader activity of YW-N-7. Proteomic analysis showed that RET was the only protein significantly reduced by YW-N-7 in TPC1 cell lines. Furthermore, YW-N-7 potentiated the activity of selpercatinib in cell culture and significantly inhibited RET fusion oncogene-driven CDX tumor growth in animals.

Conclusion: YW-N-7 was identified as a highly effective RET-specific PROTAC that exhibits the dual action of inhibiting and degrading RET oncoprotein. YW-N-7 has excellent *in vivo* PK properties and displays anti-tumor activity in RET-driven CDXs in animal models. Our study exemplifies the potential of developing PROTACs as a novel therapeutic strategy for RET-altered cancers.

DEVELOPING AN IN-VIVO LONGITUDINAL FRAMEWORK FOR ASSESSING GLIOBLASTOMA VASCULAR REMODELING IN MICE USING FUNCTIONAL ULTRASOUND (fUS) IMAGING: IMPLICATIONS FOR THERAPEUTIC DISCOVERY

Sherwin A. Tavakol[1,2*], Sharon Negri[1,2], Zeke Reyff[1,2,3], Jennifer Ihuoma[1,2], Madison Milan[1,2], Eva Troyano Rodriguez[1,2,3], Rakesh Rudriboina[1,2], Farzaneh Amirmahani[3], Chandra Kumar Elechalawar[3], Deepthi Muthukrishnan[3], Priya Balasubramanian[1,2,3], James Battiste[1,3], Stefano Tarantini[1,2,3]

[1]Neuroscience and Neurosurgery Program, University of Oklahoma Health Science Center, OKC, OK
[2]Vascular Cognitive Impairment, Neurodegeneration and Healthy Brain Aging Program, Department of Neurosurgery, University of Oklahoma Health Sciences Center, OKC, OK
[3]The Peggy and Charles Stephenson Cancer Center, University of Oklahoma Health Science Center, OKC, OK
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Glioblastoma multiforme (GBM) is the most common primary malignant brain tumor, with an estimated incidence of 3.19 cases per 100,000 population in the United States. There is no cure for GBM, and the median survival for those undergoing treatment (surgery, chemotherapy, and radiation) is 12 to 18 months. The aggressiveness of this disease is owed, at least in part, to the invasiveness of the cancer cells even far past areas of contrast enhancement on conventional MRI and the hijacking of the surrounding blood flow through various neovascularization processes. However, in vivo rodent models that accurately capture the dynamic interplay between the tumor and both intrinsic and extrinsic cerebrovascular networks remain limited. A deeper understanding of GBM's progressive commandeering of blood flow, from tumor initiation to late-stage progression, could be pivotal for developing more effective anti-angiogenic therapies and blood-brain barrier (BBB)-penetrating chemotherapies. We aim to illustrate the feasibility of using in vivo functional ultrasound imaging to visualize GBM in a rodent model, and to monitor the impacts of tumor growth on the local cerebral vasculature.

As part of our methods, isocitrate dehydrogenase (IDH)-wt mouse GBM tumor cells (~5,000 cells/mouse) were stereotactically injected into the right frontal cortex of 8 immunocompetent C57/BL6 mice (aged: n=4; young: n=4) and a sham injection of the same volume of sterile water was injected into the contralateral frontal cortex to serve as an in-animal control. A chronic cranial window was implanted prior to the injection of the tumor cells to enable repeated, high-resolution fUS imaging of tumor-associated and healthy vasculature. Imaging parameters included vascular density, cerebral blood flow (CBF), and neurovascular coupling (NVC) at baseline and during tumor progression. Tumor engraftment and growth were trended with IVIS bioluminescent imaging and confirmed with 2-photon microscopy. Post-mortem histological analysis of brain parenchyma was also analyzed.

We anticipate that fUS imaging will reveal significant age-related differences in tumor vascularization, with aged mice exhibiting greater vascular heterogeneity, impaired perfusion, and reduced neurovascular coupling. We also expect that while the sham injection may induce a degree of gliosis and vascular remodeling, the impact of the tumor cells will have a more profound.

This study will establish fUS as a powerful tool for noninvasive, longitudinal assessment of GBM vascular dynamics and treatment response. By elucidating age-related differences in tumor vascular remodeling, our findings could inform the development of age-specific therapeutic strategies to improve GBM outcomes in older patients. The high-resolution vascular imaging data generated will provide a critical foundation for future NIH-funded research on cancer imaging and targeted interventions. Future directions will include the testing the impacts of anti-angiogenic therapy on tumor and healthy brain vascularization.

DECIPHERING THE TUMOR MICROENVIRONMENT OF ALVEOLAR SOFT PART SARCOMA USING SINGLE-CELL SPATIAL TRANSCRIPTOMICS

Hassan Abushukair[1,2]*, Woncheol Jung[1], Rameswari Velayutham[3], Samantha Ricketts[3], Kar-Ming Fung[3], Naoko Takebe[2], Doris Benbrook[4], Tae Gyu Oh[1#], Abdul Rafeh Naqash[2#]

[1]Division of Oncology Sciences; Stephenson Cancer Center, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA
[2]Medical Oncology, Stephenson Cancer Center, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA
[3]Department of Pathology, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA
[4]Department of Gynecologic Oncology, Stephenson Cancer Center, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA
*Presenting Author
[#]Corresponding Author, email: abdulrafeh-naqash@ouhsc.edu, taegyu-oh@ouhsc.edu

Background: Alveolar Soft Part Sarcoma (ASPS) is a rare soft tissue sarcoma (STS) driven by the *ASPSCR1::TFE3* oncogenic fusion. Contrary to most STSs, advanced ASPS is sensitive to immune checkpoint inhibitors (ICI) and has recently received FDA approval for Atezolizumab. There is limited data explaining ASPS selective ICI response. Our work utilizes single-cell spatial transcriptomics data to provide insights into ASPS's unique tumor microenvironment.

Methods: We analyzed tissue samples from patients with ASPS, stored as formalin-fixed paraffin-embedded blocks at the University of Oklahoma Department of Pathology using the 10x Genomics Xenium spatial transcriptomics platform. We used the Human Immuno-Oncology gene panel which includes 380 genes related to immune cells, pathways, and checkpoints in cancer as well as a 100-gene add-on oncogenic panel. A tissue microarray was used to prepare Xenium slides which consisted of two tumor cores and one adjacent normal tissue per sample. Generated data was processed and analyzed using multiple bioinformatics pipelines in R programming language.

Results: Ten ASPS samples were included in our analysis, which yielded 204,518 cells from ASPS regions and 58,493 cells from adjacent normal regions. Single-cell annotation using an STS-based reference showed high enrichment of myeloid cells (17.9%), primarily M2 macrophages (CD163, SPP1 +ve) and scarce lymphoid (2.7%) composition highlighted by exhausted CD8+ T cells (TIGIT, NKG7, GZMA/K +ve). Notably, malignant cell profiling revealed two distinct cellular phenotypes: fibroblast-like (VEGFA, NOTCH3, TGFB1 +ve) and epithelial-like (SDC1, MKI67, ERBB3/2 +ve). Cell communication analysis showed the most frequent and strongest signals were sent out by M2 macrophages and cancer-associated fibroblasts (CAFs), while exhausted CD8+ T cells were receiving the majority of these signals by way of the SPP1-CD44 and CXCL12-CXCR4 axes. Spatially, exhausted CD8+ T cells were isolated peripherally away from malignant cells as a result of CAF infiltration.

Conclusion: This is the first report of ASPS single-cell profiling and the largest across all STS. Our data show distinct myeloid dynamics in ASPS that dictate cytotoxic T cell functionality. We highlight the SPP1-CD44 and CXCL12-CXCR4 axes as key regulators of immune communication in ASPS. Our investigation is expected to have implications beyond ASPS, extending to other STS and fusion-driven cancers.

IMPROVING THE DYNAMIC RANGE OF MULTISPECTRAL OPTOACOUSTIC IMAGING WITH A NOVEL PH LOW INSERTION PEPTIDE IN PANCREATIC CANCER

Ryan C Bynum[1*], Happy Agarwal[1], Emma Sanderson[1], Ajay Jain[1], Barish Edil[1], Lacey R McNally[1]
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Introduction: The development of pancreatic cancer (PDAC) specific imaging is limited given the lack of PDAC specific biomarkers. The acidic microenvironment of PDAC has been successfully targeted using pH low insertion peptides (pHLIPs), but development of novel variants with improved dynamic range for use as part of an novel imaging paradigm using multispectral optoacoustic tomography (MSOT) would be beneficial. Informed by analysis of pHLIP variant higher order structure (HOS) using microfluidic modulation spectroscopy (MMS), we synthesized the novel pHLIP V7FS for imaging of PDAC with improvement in dynamic range.

Methods: KV7 and V7FS were synthesized using microwave chemistry with >90% purity and conjugated to HiLyte-750 dye and confirmed by spectroscopy. pH of human PDAC and uninvolved pancreas was measured intraoperatively using a microsensor. In vitro, KV7-750 and V7FS-750 signal was measured using near-infrared fluorescent imaging in S2VP10 and S2013 cells in pH specific media (6.6, 6.8, 7.4). Probes were imaged in tissue mimicking phantoms and an orthotopic murine model using MSOT. Higher order structure of the peptides was characterized using MMS. Statistical analysis was performed using parametric and nonparametric tests where appropriate.

Results: Human PDAC was more acidic vs uninvolved pancreas (pH 6.2-6.7 vs 7.2-7.3, $p<0.01$). MMS successfully identified improvements in favorable HOS for V7FS over existing pHLIPs. V7FS-750 was pH responsive with a preference for more acidic pH (pH 6.6, $p<0.001$) in vitro. In orthotopic murine models, V7FS-750 showed specificity for PDAC over the liver and kidneys ($p<0.001$), with up to a 122-fold tumor-specific change in signal.

Conclusions: Informed by HOS analysis using MMS, V7FS was shown to be a viable probe for pH targeted imaging of PDAC. V7FS was observed to have preference for more acidic pH in vitro and PDAC tumor specificity in orthotopic murine models. This novel pHLIP variant is a valuable step forward in the development of a target imaging modality with MSOT for PDAC.

Funding: R01CA281098, R01EB034731

UNDERSTANDING THE TUMORIGENIC EFFECTS OF *MYC* ON DNA REPLICATION AND TRANSCRIPTION IN PEDIATRIC ALL

Clay Foster[1], Hayley Harris[1], Katie Foster[1], Megan Malone-Perez[1], Pilar Andrade[1], Tyler Noble[2], Courtney Sansam[2], Christopher Sansam[2], Arpan Sinha[1], J. Kimble Frazer[1]

[1] Jimmy Everest Section of Pediatric Hematology-Oncology, Department of Pediatrics, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA
[2] Cell Cycle & Cancer Biology Research Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, USA

The proto-oncogene *MYC* is overexpressed in many human cancers, but the nature of its tumorigenic potential remains unclear. *MYC* plays a pivotal role in the development of acute lymphoblastic leukemia (ALL), a prevalent and deadly pediatric cancer that accounts for nearly 20% of childhood diagnoses and deaths. ALL, a hematological malignancy that affects immature B and/or T lymphocytes (called B- and T-ALL, respectively), exhibits considerably heterogeneity, encompassing over 40 known molecular subtypes, complicating both study and treatment. Many of these subtypes were first characterized using transcriptional profiling, an intuitive approach given MYC's role as a master transcription factor. However, MYC is also crucial to DNA replication, a process that has been largely underappreciated in the context of human cancers. Because of this, we believe that important leukemia-driving changes, and related therapeutic targets, have been overlooked. **We hypothesize that transcription, DNA replication, and MYC DNA-binding are complementary components of a unified leukemogenic process, and that integrating data from all three processes will provide novel insights into ALL development and progression.** To study *MYC*-driven ALL, we created a transgenic zebrafish model that overexpresses human *MYC* (*hMYC*) to drive the development of B- and/or T-ALL. Using RNA-Seq to profile transcription and WGS to assess DNA replication, we examined the consequences of *MYC* overexpression on these processes in relation to ALL. Our results reveal substantial global correlation between transcriptional activity and replication timing in both healthy and tumor cells, along with numerous localized regions exhibiting significant perturbations specific to ALL. To further explore these regions, we mapped the MYC regulome using CUT&RUN sequencing to pinpoint features directly regulated by MYC that exhibit differential transcription and replication. We now seek to validate these findings in human patients to identify promising therapeutic candidates that can be used to develop novel treatment strategies for pediatric ALL.

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CANCER PREVENTION & CONTROL TRACK

Session I – Cancer Prevention & Control

Nicholson Room A

11:25 am – 11:40 am	Nicotine Drives Chemoresistance by Enhancing Drug Efflux **Gautham Chengizkhan, Ph.D.** Postdoctoral Fellow Department of Otolaryngology - Head and Neck Surgery OU Health Sciences Center
11:40 am – 11:55 am	E-Cigarette Aerosols to Enhance NRF2-mediated Pathways and Cancer Stemness in Human Oral Cells **Vengatesh Ganapathy, Ph.D.** Faculty Department of Otolaryngology - Head and Neck Surgery OU Health Sciences Center
11:55 am – 12:10 pm	Deciphering the Tumor Microenvironment of Alveolar Soft Part Sarcoma Using Single-Cell Spatial Transcriptomics **Gaurav Kumar, Ph.D.** Postdoctoral Fellow Department of CMT Internal Medicine OU Health Sciences Center
12:10 pm – 12:25 pm	Effects of Alignment and Misalignment in Self- and Parter-Oriented Motivations to Quit on Individual and Joint Cessation Outcomes in Dual-Smoking Couples **Catherine Nagawa, Ph.D.** Assistant Professor Department of Health Promotion Sciences OU Health Sciences Center

Session II – Cancer Prevention & Control

Nicholson Room A

3:05 pm – 3:20 pm	Does Cannabis Boost or Halt Your Inflammatory and Immune Responses? **Adele Hammoudi** Postdoctoral Fellow Department of Otolaryngology OU Health Sciences Center
3:20 pm – 3:35 pm	Digitally Mediated Occupational Therapy to Increase Physical Activity in Urban and Rural Breast Cancer Survivors Who Have Undergone Breast Surgery **Michael Robertson, Ph.D., MPH** Assistant Professor Department of Family and Preventative Medicine TSET Health Promotion Research Center (HPRC) OU Health Sciences Center
3:35 pm – 3:50 pm	Comparison of the Temporal Characteristics of Participant Perceived Vs. Algorithm-Based Risk Factors for Smoking Lapse **Jeremy Langford, Ph.D.** Postdoctoral Fellow Department of Health Promotion Sciences OU Health Sciences Center
3:50 pm – 4:05 pm	Effects of Alignment and Misalignment in Self- and Parter-Oriented Motivations to Quit on Individual and Joint Cessation Outcomes in Dual-Smoking Couples **Darla Kendzor, Ph.D.** Faculty Department of Health Promotion Sciences OU Health Sciences Center

NICOTINE DRIVES CHEMORESISTANCE BY ENHANCING DRUG EFFLUX

Gautham Chengizkhan[1], Vengatesh Ganapathy[1], Mayilvanan Chinnaiyan[1], Lurdes Queimado[1,2]

[1]Department of Otolaryngology - Head and Neck Surgery, University of Oklahoma Health Sciences Center, Oklahoma City, OK

[2]Department of Cell Biology, TSET Health Promotion Research Center, University of Oklahoma Health Sciences Center, Oklahoma City, OK

Background: Cisplatin therapy remains the gold standard for treating oral cancer; however, intrinsic and acquired resistance limits its effectiveness. While nicotine is not classified as a carcinogen, evidence suggests it can influence cancer cell behavior. With nicotine replacement therapy (NRT) widely used for managing smoking addiction, it is crucial to determine if the low-dose nicotine contributes to the elusive mechanisms of chemotherapy resistance.

Methods: Head and neck cancer cell lines (SCC1, HN6, and HN30) were pre-exposed to nicotine (10, 20, or 40 ng/ml) for 48 hours, followed by cisplatin treatment (IC50 concentration) with or without nicotine for another 48 hours. Cell viability (MTT assay) and long-term proliferative potential (clonogenic assay) were assessed. Proliferation (Incucyte), ROS production (DCFDA assay), and apoptosis (Annexin V staining) were quantified. To confirm efflux-mediated chemoresistance, cells were pretreated with nicotine (20 ng/ml) for 48 hours, followed by cisplatin treatment for another 48 hours in the presence or absence of nicotine and verapamil, a P-glycoprotein (P-gp) inhibitor. Statistical significance was determined using Student's *t*-test and ANOVA.

Results: Nicotine exposure at all tested concentrations significantly impaired cisplatin efficacy, promoting cancer cell survival and enhancing clonogenic potential. Verapamil co-treatment restored cisplatin-induced cytotoxicity, indicating a nicotine-driven activation of drug efflux mechanisms. Mechanistically, nicotine increased proliferation, modulated oxidative stress, and disrupted apoptotic pathways, reinforcing its role in chemoresistance.

Conclusion: Our findings demonstrate that even low-dose nicotine promotes chemoresistance in oral cancer through P-gp-mediated drug efflux. Verapamil restores cisplatin sensitivity, confirming nicotine's role in activating efflux mechanisms that facilitate tumor survival. Given the widespread use of NRT, these results highlight the need to further investigate whether nicotine exposure at clinically relevant levels might influence treatment outcomes in oral cancer.

Grant support: NIH/NCI (R01CA242168, Queimado); TSET HPRC (Queimado).

SOCIOECONOMIC CHARACTERISTICS, TOBACCO USE, AND SERVICE UTILIZATION BY COUNTY POVERTY STATUS AMONG OKLAHOMA TOBACCO HELPLINE REGISTRANTS

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Background: Counties with persistent poverty have disproportionately high smoking rates and cancer mortality. The Oklahoma Tobacco Helpline (OTH) offers statewide cessation support, yet studies are lacking to describe differences in registrant characteristics and service utilization across counties with poverty status. Understanding these differences could inform targeted efforts to reduce tobacco use in disadvantaged areas.

Aims: This study examined differences in sociodemographic characteristics, tobacco use, and OTH utilization among its registrants from persistent poverty counties (PPCs), current poverty counties (CPCs), and non-poverty counties (NPCs).

Methods: We obtained data from 33,847 OTH registrants (July 1, 2023–June 30, 2024). We compared differences in registrant characteristics and service utilization by county poverty status using chi-square analyses and analyses of variance.

Results: Sociodemographic factors, including age, sex, race, education, income, and health insurance varied significantly by county poverty status (all *p*'s <0.05). Compared to NPC registrants, those from PPCs were more often female (65.1% vs. 59.5%) and American Indian/Alaska Native (16.0% vs. 9.1%). PPC/CPC registrants had lower educational levels (<high school; 17.3% and 17.9% vs. 14.1%), lower income (<$20,000: 53.4% and 53.2% vs. 44.5%), and were more likely to have Medicaid coverage (35.3% vs. 29.8%) than NPC registrants. PPC/CPC registrants reported higher nicotine dependence and heavier smoking than NPC registrants. OTH service utilization also varied, with CPC registrants showing patterns of lower intervention utilization.

Conclusion: PPC and CPC registrants shared similar sociodemographic, and tobacco use patterns, but those from PPCs more often differed from NPCs, indicating a continuum of disadvantage. Findings highlight the need for targeted efforts to address tobacco disparities.

DIGITALLY MEDIATED OCCUPATIONAL THERAPY TO INCREASE PHYSICAL ACTIVITY IN URBAN AND RURAL BREAST CANCER SURVIVORS WHO HAVE UNDERGONE BREAST SURGERY

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Background: The 5-year survival rate for breast cancer (BC) has increased in recent years. However, functional limitations associated with BC treatment (e.g., loss of strength, fatigue, lymphedema) often have far-reaching effects on survivors' physical and mental health. Aerobic physical activity (PA) and muscle strengthening exercise (MSE) can reduce functional limitations, and occupational therapy (OT) can support these health-promoting behaviors after treatment. Yet, barriers to access (e.g., time burden, distance to OT clinic) among BC survivors limit access to OT programming. This is particularly true in Oklahoma, where 33% of residents live in rural counties. Digital technologies (e.g., telehealth) can help rural and urban BC survivors circumvent these barriers. **Objectives:** We are investigating the feasibility of a novel OT program among rural and urban BC survivors that features eight once-weekly telehealth OT sessions targeting constructs grounded in Self-Determination Theory (SDT), and teaches self-regulatory strategies known to support aerobic PA and MSE in BC survivors, including self-monitoring via a wearable PA tracker, goal setting, and the provision of timely feedback. The study is focused on the transition from active treatment to the post-treatment period. **Methods:** This is a single arm feasibility trial. We are recruiting 38 BC survivors via local organizations, community-based advertising, and via referral from a collaborating oncologist. Participants include individuals who have undergone breast conserving surgery or mastectomy for BC in the last 12 months and who do not meet recommended PA levels at the time of enrollment. We are assessing self-reported program acceptability and feasibility via recruitment rates, study retention, and protocol adherence. Program safety is being assessed by tracking BC-related lymphedema events, musculoskeletal injuries, and other adverse events. Finally, we are assessing changes in aerobic PA and MSE participation during the program period using self-report and objective measurement tools. We hypothesize that the SDT-grounded OT program will be acceptable, feasible, and safe. We also expect pre- to post-program improvements in 1) SDT-informed determinants of PA; 2) levels of aerobic PA and MSE engagement; and 3) health-related quality of life. **Results:** We received funding in March 2024 and Institutional Review Board approval in September 2024. We began recruiting in November 2024 and currently have six active BC survivors in the study. We anticipate completing recruitment by June 2025 and data collection by November 2025.

Select study observations as of April 2025 will be presented. **Conclusions:** The novel OT program under investigation is designed to decrease barriers to engaging in aerobic PA and MSE among people who have undergone breast conserving surgery or mastectomy. The program combines tailored exercise instruction, guided by a qualified professional, with the benefits of telehealth delivery and health behavior change theory to integrate PA into the daily routines of people transitioning to life beyond cancer. If shown to be acceptable and feasible, this program will be amenable to scaling and widespread dissemination.

COMPARISON OF THE TEMPORAL CHARACTERISTICS OF PARTICIPANT PERCEIVED VS. ALGORITHM-BASED RISK FACTORS FOR SMOKING LAPSE

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Significance: Adults with lower socioeconomic status (SES) are more likely to smoke and less likely to quit compared with the general population. Detection of lapse risk factors prior to actual smoking lapse could be used to prompt intervention content to increase smoking cessation rates among adults with low SES.

Methods: This study used data from a randomized controlled trial that compared the efficacy of two smartphone-based smoking cessation interventions: Smart-T and QuitGuide. Participants were asked to complete daily ecological momentary assessments (EMAs) on their personal or study-provided smartphone for 27 weeks. In addition, participants were instructed to self-initiate EMAs both when they believed they were about to lapse and after a lapse. These self-initiated EMAs included questions about the timing of the lapse, number of hours of awareness of heightened lapse risk prior to the lapse, and coping skills that could have helped prevent the lapse. Further, a previously developed smoking lapse risk algorithm was used to identify moments that were high risk for smoking lapse. Descriptive statistics were used to summarize demographic information, temporal characteristics of smoking lapse risk, and coping skills; mixed models were fit to the data to test for group differences in pre-lapse warning signs and algorithm-detected risk.

Results: Overall, 182 participants (40% of the parent study sample) self-initiated an EMA to report a smoking lapse at least once during the 26-week, post-quit study period. Participants indicated that they detected warning signs prior to 70.1% of all lapses; however, warning signs were infrequently detected more than 4 hours in advance. Alternatively, the lapse risk algorithm detected elevated risk in 67% of lapses that were preceded by an EMA within 4 hours and 63% of lapses that were preceded by an EMA within 24 hours. After a lapse, participants most frequently endorsed coping with urges and coping with stress as skills they believed could have helped them avoid lapsing.

Conclusions: Broadening temporal windows in which heightened risk for smoking lapse can be detected and intervened upon is critical to improving the efficacy of smartphone-based smoking cessation interventions. EMA-informed algorithms show promise for detecting heightened smoking lapse risk before participants perceive warning signs.

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ROUTE 66 SPORE | CANCER INTERCEPTION

TRANSLATIONAL RESEARCH IN THE ROUTE 66 ENDOMETRIAL CANCER SPORE AND STEPHENSON CANCER CENTER

Doris Mangiaracina Benbrook, PhD,
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Associate Director of Translational Research Stephenson Cancer Center (SCC)

There are many variations of the translational research definition. A refined version for cancer research is: Progress of research through different disciplines with the goal of improving outcomes of patients with cancer and the general population. The translational pipeline can be subcategorized into T1-T4 Research. *T1 Research* moves discoveries from T0 Basic Science Research to early phase clinical trials. *T2 Research* progresses clinical research into later phase clinical trials and clinical research outcomes. *T3 Research* transitions the research from implications for clinical application to public health benefits. *T4 Research* involves population-level outcomes and public health policy to improve global health. One mechanism by which the **US National Cancer Institute (NCI) Translational Research Program (TRP)** fosters translational research is through supporting **the Specialized Programs of Research Excellence (SPOREs)** to translate novel scientific discoveries into clinical testing, including early-phase clinical trials.

In 2023, the **Stephenson Cancer Center (SCC)** was awarded the **Route 66 Endometrial Cancer SPORE**, which in collaboration with the Siteman and University of New Mexico Cancer Centers is bringing novel clinical trial opportunities to patients in our catchment area. *Project 1* is evaluating the mechanism, physiology-based pharmacokinetic modeling and biomarkers of patient sensitivity to a novel Heat Shock Protein 70 kDa-targeted drug, SHetA2, alone and in combination with paclitaxel or cyclin dependent kinase 4/6 inhibitors. *Project 2* is studying the molecular and metabolic mechanisms and biomarkers of patient sensitivity to an inhibitor of the Axl, Mer and c-Met receptor tyrosine kinases, zanzalintinib, alone and in combination with paclitaxel. Project 3 is evaluating the effect of weight loss controlled by exercise/counseling interventions or GLP-1 agonists., This SPORE has awarded multiple *career enhancement program and developmental research program grants* to SCC members, which are fostering the careers of individuals in endometrial cancer research and exploring novel ideas with high translational research potential.

The SCC is embarking on multiple tasks to develop infrastructure to foster the translation of SCC member discoveries through the translational research pipeline. Translational research opportunities and obstacles are being catalogued and prioritized through a survey and interviews. Resources at various OU colleges, contract research organizations and commercialization businesses are being catalogued with the goal of matching SCC member translational research needs with relevant resources. A translational research committee is developing a translational research grant funding mechanism that will soon be released. To increase awareness and motivation for translational research, a series of presentations, workshops, graduate level coursework and mentoring opportunities are being planned.

DISCOVERY AND DEVELOPMENT OF AGENTS FOR CANCER INTERCEPTION

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The overarching goal at the Center for Cancer Prevention and Drug Development (CCPDD), at Stephenson Cancer Center, is discovering and developing strategies to prevent or intercept the progression of preneoplastic lesions to malignant tumors and their further recurrence in higher-risk populations. We have established a collaborative research network to discover and develop molecularly or immunologically targeted agents designed to prevent or intercept the tumor progression on major organ-site cancers using the animal models, these include colorectal, lung, pancreas, prostate, breast, urinary bladder, ovarian, cervical, and endometrial. In this presentation, we will briefly discuss discovery and development of two interception agents, LFA-9, a selective mPGES-1/5-LOX inhibitor and ONC-201, a TRAIL inducing agent.

NSAIDs, like Aspirin, Naproxen and Celecoxib are useful to prevent the colonic polyp progression and reducing colorectal cancer (CRC) burden, however, continuous/chronic usage of these drugs are limited by GI toxicity and unwanted side effects. Thus, the rationale to establish safer anti-inflammatory agents for CRC prevention is important. Mechanistic studies suggest that sparing COX-1/2 and prostaglandin I_2 synthase and/or selectively targeting mPGES-1 and 5-LOX would reduce the cardiovascular side effects and may improve the interception of colon cancer. We used *in-silico* small molecular docking simulation approaches, and identified LFA-9 as a novel duel mPGES-1/5-LOX inhibitor among >35 analogs of Licofelone. In ex-vivo assays we have shown pharmacodynamic inhibitory effects of LFA-9 on mPGES-1 and 5-LOX and in a series of animal experiments, we established the dose-range of toxicity and optimal doses and potential efficacy against tumor progression of LFA-9 in various CRC models. We have completed IND-toxicology in rats and dogs and find it to be safe. Currently, NCI CP-NET program is considering human Phase I/Phase IIa studies.

Tumor necrosis factor-related apoptosis-inducing ligand (TRAIL), pathway is a critical effector mechanism in immune surveillance and is capable of selectively eliminating tumor cells via apoptosis without harming normal host cells. ONC201 is a first-in-class, orally active small molecule, TRAIL inducing agent, discovered by Dr. Wafik El-Deiry's lab and we further developed for the interception of colon and other cancers in collaborations with CCPDD, NCI PREVENT Cancer Program, and Chimerix. We have established optimal doses of ONC-201 in FAP-CRC models of mice and rats. *Apc*$^{min/+}$ mice treated with ONC201 showed >68% colon tumor multiplicity ($P<0.0001$) in male mice and by 75% ($p<0.0001$) in female mice. Furthermore, we evaluated ONC-201 for CRC interception in the PIRC rat model representing FAP cohort. Male and Female PIRC rats, after 26 weeks of ONC-201 treatment, lead to strong suppression of adenoma progression to adenocarcinomas as well as a significant decrease in the number of adenomas and ADCAs as compared to the placebo. Overall, these results led to approval of ONC-201 by NCI CP-NET program for Phase II clinical trials in FAP patients.

POSTERS

Poster Session Nicholson Rooms A, B, C, D, E

(Listed A–Z by Presenters First Name)

Poster Number	First Name:	Last Name:	Academic Appointment: - Selected Choice	SCC Research Program Affiliation	Title of Abstract:
2	AHMED AHSAN	ADIB	GRADUATE STUDENT	CANCER BIOLOGY	DISCOVERY OF THYMIC B CELL FOLLICLES AND GERMINAL CENTERS COINCIDENT WITH THYMIC INVOLUTION
29	AMBER	VU	STAFF SCIENTIST	CANCER BIOLOGY	PHARMACOLOGICAL INHIBITION OF HUMAN ANTIGEN R (HUR) INDUCES ENDOPLASMIC RETICULUM STRESS AND ACTIVATES THE UNFOLDED PROTEIN RESPONSE
12	AMEERA	HASAN	POSTDOCTORAL FELLOW	CANCER BIOLOGY	UNRAVELING THE COMPLEX DYNAMICS OF IMMUNE MICROENVIRONMENT AND RISK OF OVARIAN CANCER WITH AGING USING GENETICALLY ENGINEERED MOUSE MODEL
63	AMEERA	NOON	GRADUATE STUDENT	CANCER THERAPEUTICS	AN IN-VITRO STUDY OF ANTINEOPLASTIC EFFECTS OF DANDELION ON HUMAN DERMAL FIBROBLASTS AND CERVICAL CANCER CELLS
13	ANDREW	HOJJAT	MEDICAL STUDENT	CANCER BIOLOGY	SURVIVAL OUTCOMES OF PRIMARY GENITOURINARY LYMPHOMAS COMPARED TO NODAL
10	ANNA	GIERLIKOWSKA	RESEARCH TECHNICIAN	CANCER BIOLOGY	EXPLORING MPS1-DEPENDENT PATHWAYS FOR TARGETED CANCER THERAPIES

28	ANNA	SZULTA	TRAINEE/RESEARCH TECHNICIAN	CANCER BIOLOGY	THE ROLE OF LRPPRC IN OVARIAN CANCER METABOLISM AND PROGRESSION
23	ANTHONY	PHAN	HIGH SCHOOL STUDENT	CANCER BIOLOGY	SECONDHAND SMOKE EXPOSURE DRIVES STEMNESS AND THERAPEUTIC RESISTANCE IN HEAD AND NECK CANCER
9	ARPAN	DEY BHOWMIK	POSTDOCTORAL FELLOW	CANCER BIOLOGY	MICRORNA-195 INHIBITS OVARIAN CANCER PROGRESSION BY MODULATING WNT/Î²-CATENIN SIGNALING AND ENHANCES DRUG-SENSITIVITY
24	ASLI	SADLI	POSTDOCTORAL FELLOW	CANCER BIOLOGY	USE OF ADVANCED IMAGING AND GENOME-WIDE CRISPR/CAS9 SCREENING METHODS TO IDENTIFY THE GENES IMPORTANT FOR MICRONUCLEUS FORMATION
51	AYESHA	AIJAZ	POSTDOCTORAL FELLOW	CANCER THERAPEUTICS	INCIDENCE OF AKI AND KIDNEY REPLACEMENT THERAPY (RRT) AFTER OUTPATIENT CHIMERIC ANTIGEN RECEPTOR T (CAR-T) CELL THERAPY IN PATIENTS WITH HEMATOLOGICAL MALIGNANCIES
19	BARBARA	MENSAH SANKOFI	GRADUATE STUDENT	CANCER BIOLOGY	FGF1 REGULATES BREAST CANCER GROWTH AND METABOLIC REPROGRAMMING THROUGH ETV4
36	BARISH	EDIL JR.	UNDERGRADUATE STUDENT	CANCER PREVENTION AND CONTROL	DEVELOPMENT OF CD147-TARGETED S100A9-750 FLUORESCENT PROBE FOR ENHANCED IMAGING OF PANCREATIC DUCTAL ADENOCARCINOMA.
56	BENJAMIN	BLITTSCHAU	GRADUATE STUDENT	CANCER THERAPEUTICS	PSMA PET-CT AND MRI TO IDENTIFY LYMPH NODE

					METASTASES IN ADVANCED PROSTATE CANCER
43	BIBI	MARYAM	RESIDENT	CANCER PREVENTION AND CONTROL	USE OF IMMUNE CHECKPOINT INHIBITORS AS FIRST LINE THERAPY FOR UNTREATED, UNRESECTABLE PLEURAL MESOTHELIOMA: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS.
40	CAMERON	JERNIGAN	GRADUATE STUDENT	CANCER PREVENTION AND CONTROL	USING PARTNER REFERRAL TO INCREASE HPV VACCINE UPTAKE IN HIDDEN POPULATIONS
16	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
49	CHEN	WANG	POSTDOCTORAL FELLOW	CANCER PREVENTION AND CONTROL	A NOVEL IMAGING PROBE FOR RENAL CARCINOMA BIOPSY NAVIGATION
61	CHRISTINA	HENSON	FACULTY	CANCER THERAPEUTICS	ENHANCING DIVERSITY AND INCLUSIVITY IN HEAD AND NECK CANCER CLINICAL TRIALS: STRATEGIES FOR EFFECTIVE PARTICIPANT ENGAGEMENT AND RETENTION
6	CONNOR	BAROODY	RESEARCH ASSISTANT	CANCER BIOLOGY	VISUALIZING NANOPARTICLE SPATIOTEMPORAL DISTRIBUTIONS IN ENTIRE TUMOR SPHEROIDS USING EXPANSION MICROSCOPY
25	COURTNEY	SANSAM	STAFF SCIENTIST	CANCER BIOLOGY	THE REPLICATION INITIATION FACTOR MTBP COORDINATES WITH MUVB TO ENSURE PROPER TRANSITION TO MITOSIS.

59	ELIZABETH	DOLAN	GRADUATE STUDENT	CANCER THERAPEUTICS	ENHANCED VISUALIZATION OF GAS VESICLES BY EXPRESSING REPORTER GENES USING GAS VESICLE PROTEIN C
65	EMMA	SANDERSON	UNDERGRADUATE STUDENT	CANCER THERAPEUTICS	DEVELOPMENT AND ASSESSMENT OF PH-RESPONSIVE V3 VARIANT PEPTIDES FOR IDENTIFICATION OF PANCREATIC CANCER
54	ENKHBOLOR	BATTUMUR	GRADUATE STUDENT	CANCER THERAPEUTICS	IMMUNOGENIC CELL DEATH AND DAMPS SIGNALING AS IMMUNE MODULATORS: PEPTIDE AGGREGATION VIA THE CO-ASSEMBLY OF OPPOSITELY CHARGED PEPTIDE-BASED STRATEGIES
4	FARZANEH	AMIRMAHANI	POSTDOCTORAL FELLOW	CANCER BIOLOGY	KAT5 MEDIATES THERAPY-INDUCED PLASTICITY IN GLIOBLASTOMA
35	GRACE	DUININCK	CLINICAL FELLOW	CANCER PREVENTION AND CONTROL	CERVICAL DYSPLASIA AND FOLLOW UP PATTERNS AMONG THE INCARCERATED WOMEN IN OKLAHOMA
55	GRANT	BENSON	GRADUATE STUDENT	CANCER THERAPEUTICS	OPTIMAL GRID PLACEMENT IN SPATIALLY FRACTIONATED RADIATION THERAPY USING DISCRETE MATHEMATICAL OPTIMIZATION MODELS
15	HANLIN	JIANG	GRADUATE STUDENT	CANCER BIOLOGY	ROLE OF JMJD4 IN BREAST AND PANCREATIC CANCER
3	HAPPY	AGARWAL	POSTDOCTORAL FELLOW	CANCER BIOLOGY	ACIDIC MICROENVIRONMENT TARGETED LIPOSOMES IDENTIFY PANCREATIC ADENOCARCINOMA IN VIVO
22	IMAN	OWENS	RESEARCH TRAINEE WITH CRTEC STRONG PROGRAM	CANCER BIOLOGY	TESTING LEUKEMIA-ESSENTIAL GENES VIA SOMATIC TRANSGENESIS AND SCALE TRANSPLANTATION

8	JACQUELINE	BOHN	CLINICAL FELLOW	CANCER BIOLOGY	DIFFERENTIAL INSULIN-LIKE GROWTH FACTOR 2 AND IMMUNE MICROENVIRONMENTS IN ASCITES FROM PATIENTS WITH NEWLY-DIAGNOSED COMPARED TO RECURRENT OVARIAN CANCER
18	JOSE JUAN	MACIAS	GRADUATE STUDENT	CANCER BIOLOGY	EXPLORING LYMPHOBLASTIC MALIGNANCIES USING ZEBRAFISH: INSIGHTS FROM A TRIPLE-TRANSGENIC MODEL REVEALS NOVEL MECHANISMS AND ENGRAFTMENT DYNAMICS IN ACUTE LYMPHOBLASTIC LEUKEMIA
37	KAMRYN	FORD	GRADUATE STUDENT	CANCER PREVENTION AND CONTROL	RISK OF LATE EFFECTS AND ACUTE CARE UTILIZATION AMONG CHILDHOOD, ADOLESCENT, AND YOUNG ADULT CANCER SURVIVORS.
39	KELSIE	GUICE	RESIDENT	CANCER PREVENTION AND CONTROL	NUTRITION RISK STRATIFICATION USING THE PATIENT GENERATED SUBJECTIVE GLOBAL ASSESSMENT IN PATIENTS WITH GYNECOLOGIC MALIGNANCIES IN THE OUTPATIENT SETTING
52	KIANA	AMANI	GRADUATE STUDENT	CANCER THERAPEUTICS	THE IMPACT OF OPTIMIZED ROUTING FOR MOBILE LUNG CANCER SCREENING
62	LAURA	MORTAN	GRADUATE STUDENT	CANCER THERAPEUTICS	BIOMARKERS OF OVARIAN CANCER SENSITIVITY TO SHETA2
33	MAHALAXMI	DAS	GRADUATE STUDENT	CANCER PREVENTION AND CONTROL	DISTINCT MOTIVES FOR TOBACCO USE AMONG RURAL- VERSUS URBAN-RESIDING SEXUAL MINORITY YOUNG ADULTS IN OKLAHOMA AND SURROUNDING STATES

47	MALIKA	SEKHRI	GRADUATE STUDENT	CANCER PREVENTION AND CONTROL	EXPLORING THE ROLE OF OBESITY-ASSOCIATED EXTRACELLULAR MATRIX IN LOCAL BREAST CANCER PROGRESSION
50	MARY	WILLIAMS	GRADUATE STUDENT	CANCER PREVENTION AND CONTROL	RACIAL DISPARITIES IN INVASIVE SECOND BREAST CANCERS AMONG WOMEN WITH PRIMARY DUCTAL CARCINOMA IN SITU IN OKLAHOMA
60	MARYAM	FIROUZI	GRADUATE STUDENT	CANCER THERAPEUTICS	LEVERAGING CANCER-DERIVED SMALL EXTRACELLULAR VESICLES FOR ANTIBODY-DRIVEN TARGETING IN OVARIAN CANCER
31	MAYILVANAN	CHINNAIYAN	STAFF-RESEARCH PROJECT MANAGER	CANCER PREVENTION AND CONTROL	ORAL INFLAMMATION AND IMMUNE REGULATION IN CANNABIS AND TOBACCO SMOKERS
45	MCKENNA	NHEM	POST-BACC RESEACH ASSISTANT	CANCER PREVENTION AND CONTROL	ASSOCIATIONS OF DISCRIMINATION, MENTAL HEALTH SYMPTOMS, AND SUBSTANCE USE AMONG SEXUAL MINORITY YOUNG ADULTS: DIFFERENCES BY TYPE AND SOURCE OF SOCIAL SUPPORT
14	MD SHAHADAT	HOSSAIN	GRADUATE STUDENT	CANCER BIOLOGY	UNDERSTANDING THE MECHANISMS OF DORMANT ORIGIN FIRING DURING DNA REPLICATION
46	MICHAEL	ROBERTSON	FACULTY	CANCER PREVENTION AND CONTROL	DEVELOPING AND EVALUATING AN MHEALTH INTERVENTION TO PROMOTE ACTIVE LIVING AMONG PEOPLE WITH METASTATIC BREAST CANCER
11	MOHAN SHANKAR	GOPINATHA PILLAI	POSTDOCTORAL FELLOW	CANCER BIOLOGY	EVALUATING THE ROLE OF EXTRACELLULAR VESICLES IN PROGRESSION OF UTERINE CARCINOSARCOMA

44	NICOLE	MINALT	CLINICAL FELLOW	CANCER PREVENTION AND CONTROL	DOES ORDER MATTER? SINGLE INSTITUTION RETROSPECTIVE REVIEW OF PATIENTS WITH PLATINUM RESISTANT OVARIAN CANCER WHO RECEIVED WEEKLY PACLITAXEL BEFORE OR AFTER MIRVETUXIMAB SORAVTANSINE
66	NISHA	THOMAS	POSTDOCTORAL FELLOW	CANCER THERAPEUTICS	TAMOXIFEN EFFECTS ON ADIPOCYTE PROGENITORS LINK BREAST CANCER THERAPY TO DIABETES RISK
26	PALLAB	SHAW	POSTDOCTORAL FELLOW	CANCER BIOLOGY	EXPLORING THE ROLE OF CYSTATHIONINE-Î²-SYNTHASE IN ANOIKIS RESISTANCE AND METASTASIS OF EPITHELIAL OVARIAN CARCINOMA
21	PHOEBE	OHENE-MARFO	GRADUATE STUDENT	CANCER BIOLOGY	HEPATOCYTE-SPECIFIC MLKL REGULATES CELL CYCLE AND TUMOR DEVELOPMENT IN DIET-INDUCED MASLD
38	RAVI	GOR	POSTDOCTORAL FELLOW	CANCER PREVENTION AND CONTROL	N-NITROSONORNICOTINE EXPOSURE ENHANCES CANCER STEMNESS MARKERS IN HEAD AND NECK SQUAMOUS CELL CARCINOMA
57	RICHARD	BUI	GRADUATE STUDENT	CANCER THERAPEUTICS	INHIBITION OF OVARIAN CANCER PROLIFERATION: TARGETING OXYSTEROL-BINDING PROTEINS AND INTRACELLULAR LIPID TRANSPORT
1	RIKKI	ADAMS	GRADUATE STUDENT	CANCER BIOLOGY	HERITABLE VARIATION IN GENOME ORGANIZATION IN CANCER
27	ROHIT	SINGH	POSTDOCTORAL FELLOW	CANCER BIOLOGY	DEVELOPMENT OF AN ANGIOTENSIN TARGETED PROBE DETECTS ORTHOTOPIC PDAC
67	SAGAL	PANNU	POSTDOCTORAL FELLOW	CANCER THERAPEUTICS	LEVERAGING HIGH VARIANT ALLELE FREQUENCIES (VAF)

					OF DNA DAMAGE REPAIR (DDR) MUTATIONS (MUTS) IN LIQUID BIOPSY (LBX) AS A SURROGATE FOR GERMLINE TESTING AND IMPLICATIONS FOR PRECISION MEDICINE
34	SAGARIKA	DAS	GRADUATE STUDENT	CANCER PREVENTION AND CONTROL	A DROSOPHILA STUDY IDENTIFIES IPLA2-VIA AS POTENTIAL NOVEL CHEMOPREVENTION TARGET FOR HPV-INDUCED CANCER
58	SAMPURNA	CHAKRABORTY	GRADUATE STUDENT	CANCER THERAPEUTICS	ADVANCING TREATMENT FOR TRIPLE-NEGATIVE BREAST CANCER: INTEGRATING PHOTOTHERMAL THERAPY WITH IMMUNOMODULATION IN A PRECLINICAL MODEL
32	SARAH	CORCORAN	GRADUATE STUDENT	CANCER PREVENTION AND CONTROL	INDIVIDUAL LEVEL BARRIERS TO AND FACILITATORS OF LOWERING ULTRA-PROCESSED FOOD INTAKE
17	SAURAV	KUMAR	POSTDOCTORAL FELLOW	CANCER BIOLOGY	GLIOBLASTOMA-ASSOCIATED VASCULAR CELLS REWIRE MICROGLIA TOWARDS AN IMMUNOSUPPRESSIVE AND PRO-TUMORIGENIC STATE VIA NFATC1 SIGNALING
64	SEONGHYUN	RYU	GRADUATE STUDENT	CANCER THERAPEUTICS	A NOVEL WAY TO TARGET NON-SMALL CELL LUNG CANCER(NSCLC) TUMOR USING SMALL EXTRACELLULAR VESICLES (SEVS) BASED MONOCLONAL ANTIBODY.
7	SHYLESH	BHASKARAN	STAFF SCIENTIST	CANCER BIOLOGY	HEPATOCYTE MLKL LINKS AGING- AND OBESITY-ASSOCIATED INFLAMMATION TO HCC DEVELOPMENT
48	SULFATH	THOTTUNGAL PARAMBIL	POSTDOCTORAL FELLOW	CANCER PREVENTION AND CONTROL	CHRONIC EXPOSURE TO E-CIGARETTE AEROSOLS IMPAIRS IMMUNE

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DISCOVERY OF THYMIC B CELL FOLLICLES AND GERMINAL CENTERS COINCIDENT WITH THYMIC INVOLUTION

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Background: In the thymus, T-cells are created and selected to recognize peptides of foreign, but not self, proteins. This continues throughout our lifetime, but markedly slows during puberty as the thymus undergoes 'involution.' During involution, thymic lymphocyte (i.e., thymocyte) numbers fall, being replaced by adipose tissue. Consequently, the generation of new T-cells declines drastically. The thymus is typically considered a T cell organ, but another thymocyte type is also impacted by involution, thymic B cells. Compared to T cells, the function(s) of thymic B cells are poorly understood, but they have roles in thymic T-cell self-tolerance and are linked to several autoimmune diseases.

Objective: To define changes in thymic B cells during thymic involution.

Design & Methods: We collected 35 thymic specimens from patients aged 1 month-19 years [infant (birth-1 year, n=9), toddler (1-6 years, n=5), pre-pubertal (6-10 years, n=9), and peri-pubertal (≥10 years, n=12). We performed H&E and IHC staining for B cells (CD19), Follicular Dendritic Cells (CD21), and Germinal Centers (BCL6) on multiple sections. Here, the H&E sections were used to observe the level of thymocytes replaced by adipose tissue. We also conducted multiplex protein identification via Imaging Mass Cytometry (IMC) on 13 representative sections for each age group, analyzing 4 regions of interest (ROI) for each (total = 52).

Results: Unexpectedly, we discovered B cell follicles (CD19/21^{+} foci) in pre-pubertal thymi; these occur exclusively in medulla. However, during involution (i.e., peri-pubertal thymi), we detected Germinal Centers (GC; CD19/CD21/BCL6^{+} foci). These changes in thymic morphology were highly statistically significant. IMC analyses showed the presence of 19 cell types, with follicles and GC comprising unique cellular neighborhoods, unlike cortical B cells.

Conclusion: We have discovered that thymic B cell follicles develop as puberty approaches, with germinal centers forming coincident with puberty and thymic involution. Thymic follicles and GC are described in several autoimmune diseases (myasthenia gravis, SLE, IDDM, and others), but not during normal thymic physiology. We hypothesize these structures may play roles in the involution process. Our future studies will employ spatial transcriptomic approaches and IMC to compare B cell microenvironments in different age groups, and between follicles and GC of thymi vs. tonsils.

PHARMACOLOGICAL INHIBITION OF HUMAN ANTIGEN R (HUR) INDUCES ENDOPLASMIC RETICULUM STRESS AND ACTIVATES THE UNFOLDED PROTEIN RESPONSE

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Introduction: The mRNA-binding protein, human antigen R (HuR), is increased in many cancer types and regulates the expression of oncogenes related to tumor growth, metastasis, angiogenesis, and chemoresistance. Its expression is increased in many cancer types which often correlates with increased tumor size, invasiveness, and poor prognosis. Inhibition of HuR function via small-molecule inhibitor(CMLD-2) or its expression, through siRNA methods, results in tumor-cell specific cytotoxicity *in vitro* and *in vivo*. This mechanism includes increased ROS production, increased DNA damage, and cell cycle arrest. However, the role of HuR on proteostasis remains unclear. In this study, we analyzed the effect of chemical inhibition of HuR on endoplasmic reticulum (ER) stress and activation of the unfolded protein response (UPR) pathway in lung (H1299) and breast (MDA-MB-231) cancer cell lines.

Methods: H1299 and MDA-MB-231 cells were treated with vehicle control (DMSO) or CMLD-2 (10 µM, 20 µM or 30 µM). Protein and mRNA-levels of gene representatives in the UPR pathway were measured. mRNA was measured at 6 hr and 24 hr post-treatment, while protein levels were analyzed 24 hr and 48 hr post-treatment

Results: CMLD-2 treatment led to an increase in expression (both mRNA and protein levels) of several key ER stress response molecules of the Protein Kinase RNA-like Endoplasmic Reticulum Kinase (PERK) pathway in both H1299 and MDA-MB-231 cells. This includes BiP, PERK, and CHOP. Additionally, CMLD-2 treatment elevated the protein levels of key PERK pathway components such as phosphorylated PERK, phosphorylated EIF2a, and ATF4 in both cell lines tested. Additionally in H1299 cells, cleavage of Activating Transcription Factor 6 (ATF6) was detected following CMLD-2 treatment, suggesting activation of the ATF6-dependent UPR pathway

Conclusions: Inhibiting HuR function with CMLD-2 triggers ER stress, leading to the activation of both the PERK- and ATF6-dependent UPR pathways. These findings highlight the novel roles of HuR in protein stability regulation.

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UNRAVELING THE COMPLEX DYNAMICS OF IMMUNE MICROENVIRONMENT AND RISK OF OVARIAN CANCER WITH AGING USING GENETICALLY ENGINEERED MOUSE MODEL

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Ovarian cancer, a challenging malignancy with late-stage diagnoses and limited therapeutic options, has increasingly become a subject of intense investigation to unravel the complex interactions between age related changes in the ovarian immune system and cancer incidence. Aging ovaries undergo considerable changes in tissue composition such as depletion of primordial follicle reserve and increased in fibrosis and inflammation, which create a favorable microenvironment for the cancer growth. Macrophages are the most abundant immune cells in the ovary and play a pivotal role in ovarian homeostasis and optimal fertility. Interestingly, the number of macrophages increases in the ovaries with age, shifting towards more pro-cancerous M2-like phenotype. Studies have shown that M2-like polarization of macrophages occurs due to the upregulation of the mTOR signaling pathway in various tissues. mTOR hyperactivity is also a key factor in ovarian aging and is present in up to 80% of ovarian tumors. Our own preliminary data showed that 12 months old (premenopausal) mouse group have significantly higher incidence of ovarian cancer than younger mice (2 and 6 months old). The 12 month old mice ovaries also exhibit increase infiltration of macrophages and mTOR hyperactivity. Based on these results we hypothesize that age-related changes in ovarian microenvironment create a more favorable niche for ovarian cancer development, in particular macrophages play a critical role in tumor initiation and progression through mTOR signaling pathway. We are testing this hypothesis by using genetically engineered mouse model: Col1a1-CreERT2-TSC1fl/fl. Upon tamoxifen treatment, these mice undergo rapid follicular exhaustion due to enhanced mTORC1 kinase activity as early as 6 months of age, which is similar to the phenotype of human menopause. We are utilizing this mouse model to investigate age-related changes in ovarian immune cells and their contribution to ovarian cancer risk. Specifically, we aim to assess the impact of ovarian macrophage depletion using clodronate liposomes and mTOR signaling inhibition with rapamycin. The findings of this study will be presented at the conference.

Survival Outcomes of Primary Genitourinary Lymphomas Compared to Nodal Lymphomas: The Impact of Primary Site and Stage

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Introduction: Primary genitourinary lymphoma (PGUL) is a rare and heterogeneous subtype of extranodal lymphoma that arises in the kidneys, prostate, bladder, testis, and other genitourinary structures. Despite its clinical significance, PGUL remains underrepresented in research. This study compares survival outcomes of PGUL and nodal lymphomas, using data from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database.

Methods: SEER data from 2010–2015 was analyzed for PGUL, primary nodal follicular lymphoma (FL), and primary nodal diffuse large B-cell lymphoma (DLBCL). Kaplan-Meier analysis assessed median overall survival (OS) and 5-year OS probabilities. Stage-stratified analysis was conducted, with significance defined by a 95% CI and p-value <0.0001.

Results: A total of 25,674 cases were analyzed, with primary nodal lymphoma (PNL) comprising 96.92% (24,858 cases) and PGUL 3.08% (816 cases). Median age at diagnosis was 71 for PGUL and 66 for PNL. The cohort was predominantly male (55.7%) and non-Hispanic white (72.1%). Late-stage disease accounted for 64.28% of cases. Survival analysis indicated that Nodal FL had the most favorable prognosis, with median (OS) not reached (Figure 1). PGUL and Nodal DLBCL had similar median OS times of 81 months (CI: 71-97) and 76 months (CI: 73-79), respectively (Figure 1). Five-year OS probabilities were comparable between Nodal DLBCL (53.48%, CI: 52.8%-54.2%), and PGUL (57.15%, CI: 53.9%-60.7%), while Nodal FL (80.75%, CI: 79.8%-81.7%) was highest. Stage impacts survival in PGUL and nodal lymphomas. Early-stage PGUL (100 months, CI: 90–113) and nodal DLBCL (129 months, CI: 120–135) had longer median OS than late-stage PGUL (31 months, CI: 19–57) and nodal DLBCL (51 months, CI: 47–54). Median OS for nodal FL was not reached for either stage (Figure 2). For 5-year early-stage OS, PGUL (63.21%, CI: 59.36%–67.30%) and nodal DLBCL (64.87%, CI: 63.7%–66.1%) showed similar survival, while nodal FL was highest (82.5%, CI: 81.05%–83.97%). In late-stage disease, PGUL (43.2%, CI: 37.4%–49.9%) and nodal DLBCL (47.82%, CI: 46.96%–48.7%) had comparable outcomes, but nodal FL remained superior (79.6%, CI: 78.4%–80.9%).

Conclusion: Analysis revealed notable similarities in the 5-year (OS) probabilities and median OS months between PGUL and Nodal DLBCL, which may indicate comparable disease prognoses for these groups. These similarities persisted even when stratifying by stage, although late-stage appears to have poorer prognosis than early-stage disease for each respective group. The Nodal FL group exhibited significantly superior survival outcomes than PGUL and Nodal DLBCL on all measures.

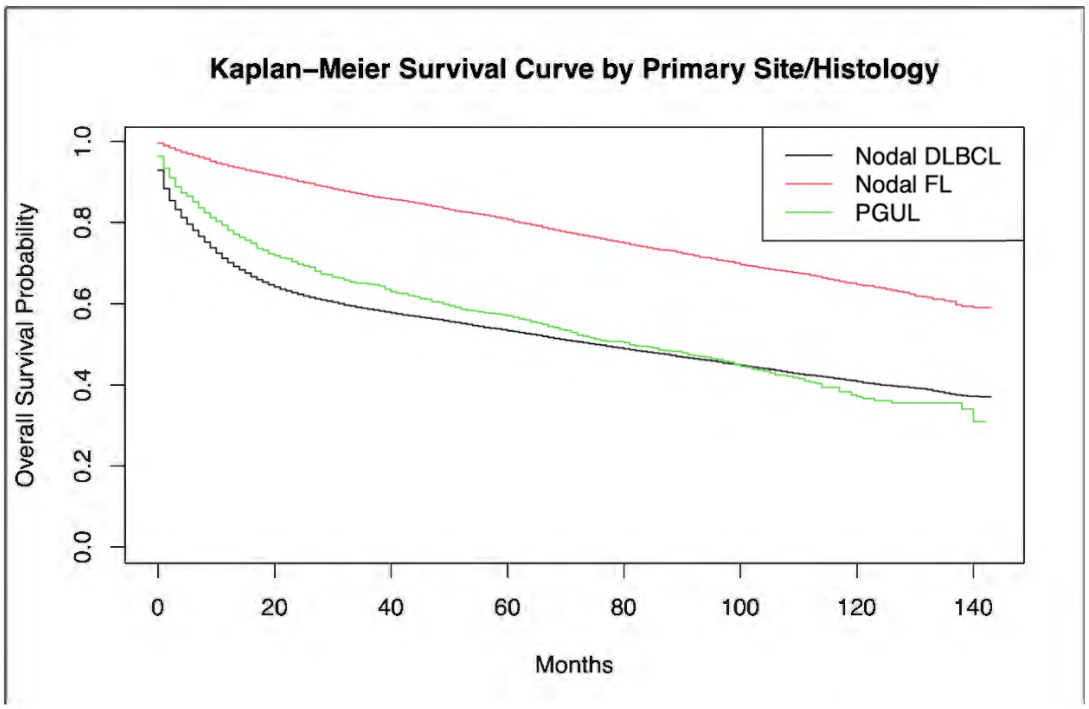

Figure 1. Overall survival probability by primary site/histology

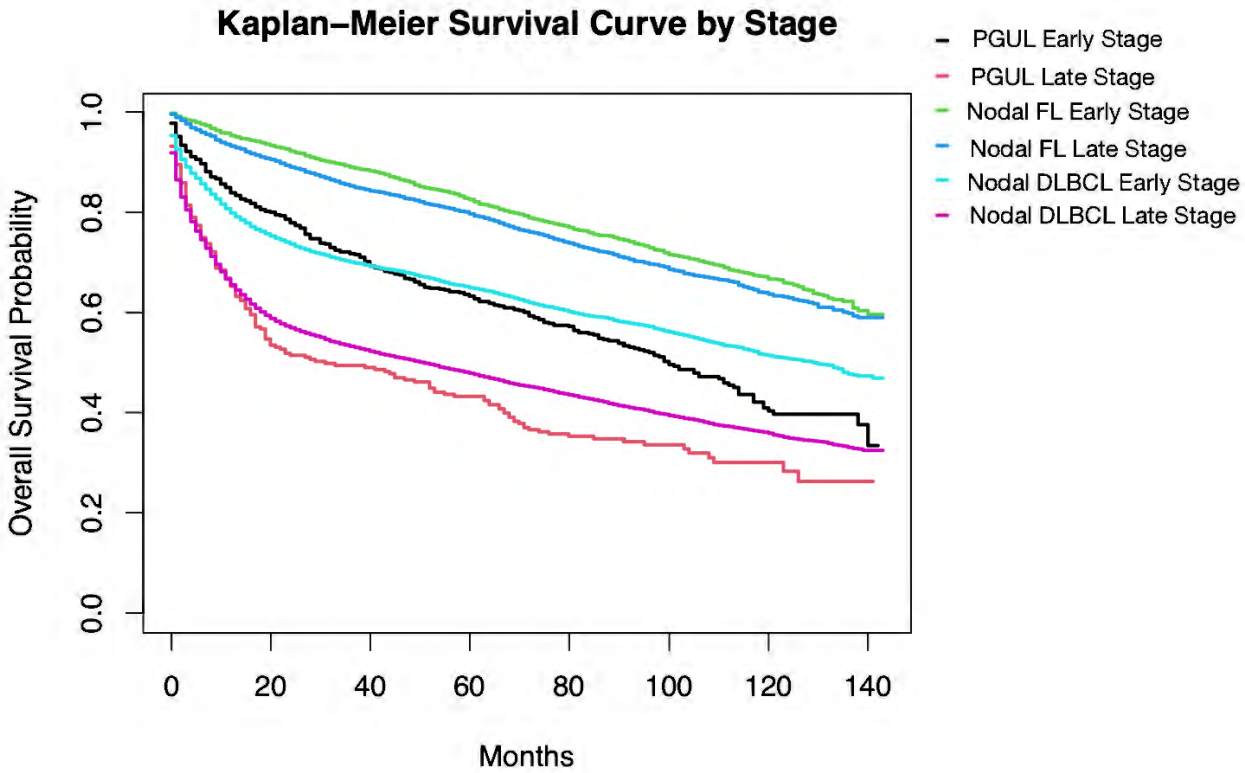

Figure 2. Overall Survival probability by primary site/histology and stage

EXPLORING MPS1-DEPENDENT PATWAYS FOR TARGETED CANCER THERAPIES

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MPS1 is a kinase essential for proper chromosome segregation during cell division and tissue regeneration. Many tumor cells, especially those with aberrantly high numbers of chromosomes (aneuploidy) exhibit MPS1-addiction, relying on high MPS1 activity for survival. While MPS1 inhibitors show promise as cancer therapies, they broadly disrupt MPS1 functions, including tissue regeneration, which may impact recovery. A more selective approach would target only the MPS1-dependent pathways crucial for tumor proliferation, but these pathways remain unknown.

THE ROLE OF LRPPRC IN OVARIAN CANCER METABOLISM AND PROGRESSION

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Ovarian cancer remains the most lethal of gynecologic malignancies, primarily due to the limited availability of effective treatment options and chemotherapy resistance. A key factor influencing the survival of ovarian cancer cells under treatment is their remarkable ability to adapt their metabolism to environmental conditions, a phenomenon that significantly impacts their response to chemotherapy. Thus, a more thorough understanding of the mechanisms that regulate ovarian tumor metabolism could be pivotal in identifying novel and effective therapeutic strategies. Our research identified leucine-rich pentatricopeptide repeat-containing (LRPPRC) protein as a potential oncogene that plays a critical role in the dysregulation of cancer metabolism. LRPPRC is indispensable for maintaining proper mitochondrial function, stabilizing RNA, and directly influencing the levels of electron transport chain (ETC) proteins at both the transcriptional and translational levels. This regulation enhances cellular energy production and supports metabolic adaptations that allow cancer cells to survive and proliferate in hostile environments. Using molecular cloning techniques, we generated human and murine cell lines with knockdown of LRPPRC, enabling us to investigate the metabolic consequences of its loss. Our findings demonstrated that the depletion of LRPPRC leads to a marked decrease in ETC protein levels, which impairs mitochondrial ATP production and forces the cell to rely on alternative metabolic pathways, such as glycolysis. This shift is accompanied by an increase in reactive oxygen species (ROS), which contributes to cellular dysfunction, metabolic imbalance, and, in extreme cases, cell death. A deeper understanding of the precise mechanisms underlying LRPPRC's regulation of mitochondrial metabolism and it signaling pathways could open avenues for the development of targeted therapies, offering much-needed solutions for precise targeting of ovarian cancer cells and improving patient outcomes.

IMPACT OF SECONDHAND SMOKE EXPOSURE ON CANCER STEMNESS IN HEAD AND NECK SQUAMOUS CELL CARCINOMA

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Background: Secondhand smoke (SHS) contains numerous carcinogens, is associated with various cancer risks, and has been shown to independently predict cancer recurrence in patients with head and neck squamous cell carcinoma (HNSCC). Cancer stem cells (CSCs) play a critical role in tumor initiation, progression, and recurrence; however, the impact of SHS on CSC regulation remains poorly understood. This study investigates the effects of SHS exposure on CSC markers and SHS enrichment in HNSCC.

Methods: Human HNSCC cell lines (UM-SCC-1, WSU-HN6, and WSU-HN30) were treated with sidestream smoke (SS, the main component of SHS) extract at various dilutions (1:100, 1:500, and 1:1000) for 48 hours, while control groups received HEPES buffer. CSC enrichment was assessed using spheroid formation assays, cell proliferation was evaluated via Ki-67 immunofluorescence, and the expression of CSC markers (CD44, OCT4, and Nanog) was quantified through Western blot analysis. Statistical significance was determined using one-way ANOVA.

Results: SS smoke exposure led to a significant increase in spheroid formation in UM-SCC-1 cells ($p<0.03$) following SS exposure, indicating enhanced CSC enrichment. While Ki-67 staining in UM-SCC-1 cells suggested an increase in cell proliferation, the difference was not statistically significant. Western blot analysis demonstrated a consistent upregulation of CSC markers CD44 and OCT4 across all cell lines, suggesting increased stemness properties. However, Nanog expression was decreased in WSU-HN6 and UM-SCC-1 but remained unchanged in WSU-HN30.

Conclusion: Overall, our findings suggest that SHS exposure contributes to CSC enrichment and the development of stem-like characteristics in HNSCC, potentially leading to therapeutic resistance and tumor recurrence. Further research is necessary to clarify the molecular mechanisms underlying SHS-induced CSC maintenance and to develop targeted interventions aimed at reducing SHS impact on HNSCC progression.

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MICRORNA-195 INHIBITS OVARIAN CANCER PROGRESSION BY MODULATING WNT/B-CATENIN SIGNALING AND ENHANCES DRUG-SENSITIVITY

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Background: Ovarian cancer (OC) confers highest mortality rates among the gynaecological malignancies. Diagnosis at advanced stages, drug-resistance and reoccurrence are the main reasons of high mortality. Studies suggest 'Cancer Stem Cells' (CSCs) has the capacity to regrow the cancer after treatment and making the cancer more aggressive by causing drug-resistance. Our previous study revealed decreased expression of miR-195 in OC cell lines and ectopic expression inhibited clonal growth and invasion. The miR-195 re-expressing group had significantly lower tumor volumes and greater tumor doubling time over control.

Hypothesis: We hypothesized that miR-195 may regulate ovarian cancer progression by modulating stem cell population and sensitizes cancer cells against anti-cancer drugs.

Methods: The functional enrichment of the ovarian cancer stem cell population was done by growing them as an anchorage-independent spheroid. To confirm the enrichment of cancer stem cell population, immunoblotting of cancer stem cell markers were performed. To correlate the expression of miR-195 in a cancer stem cell-enriched population, RT-QPCR was carried out. To further confirm the role of miR-195 in the ovarian cancer stemness/cancer progression, EMT and WNT/β-catenin signaling pathways were checked and drug-sensitivity was also evaluated after miR transfection.

Results: OC spheroid were enriched in stem cell population which was confirmed by the enhanced expression of cancer stem cell markers NANOG, OCT4, cMYC, SOX2, ALDH1A, KLF4. In this spheroid, miR-195 expression was significantly decreased as compared to cells grown as monolayers. To confirm the regulation of stemness is mediated through miR-195, we measured the NANOG expression in OC cells transfected with either miR-CTL, miR-195, or anti-miR-195, and observed decreased NANOG expression with miR-195 over-expression, while increased NANOG levels with the anti-miR-195 transfection compared to the miR-CTL suggesting, expression of miR-195 is associated with OC stemness and subsequently, we found that miR-195 decreases the cancer spheroid volume. To gain a thorough understanding of miR-195-mediated signaling in OC, mass spectrometry was carried out. Importantly, the over-expression of miR-195 effectively inhibits pathways associated with malignant solid tumors, as well as colony formation, which serves as a measure of stemness. Further, studies revealed miR-195 targets WNT7A which was found to be over-expressed in ovarian cancer and ultimately, inhibited WNT/β-catenin signaling, the EMT pathway and enhanced drug-sensitivity.

Conclusions: Although a large proportion of the tumor mass may be eradicated through conventional therapies but therapy-resistant CSCs remain and over time they can grow into tumors with more aggressive phenotype than the primary malignancy. In this context, miR-195 has shown potential to combat this scenario and cumulatively, our results support that miR-195 is a potent therapeutic target in ovarian cancer.

USE OF ADVANCED IMAGING AND GENOME-WIDE CRISPR/CAS9 SCREENING METHODS TO IDENTIFY THE GENES IMPORTANT FOR MICRONUCLEUS FORMATION

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Micronuclei are small, membrane-bound structures that contain chromosomes or chromosome fragments. Micronuclei arise when chromosomes fail to become packaged in the nucleus because of segregation errors in mitosis. Micronuclei can be detected in various cell types and are often considered as a sign of genomic instability which is a hallmark of cancer. The exact molecular mechanisms that cause micronucleus formation are not very well understood. One significant challenge had been the difficulty in conducting large-scale genetic screens for genes involved in micronucleus formation due to the challenge of acquiring large numbers of cells with micronuclei. To identify the genes and cellular pathways that prevent micronucleus formation, we are doing a CRISPR/Cas9 screen in HCT116 carcinoma cell lines to knockout human genes using sgRNA libraries. We will employ an automated cell imaging system to mark and collect the cells that form micronuclei upon depletion of the target genes. The identified sgRNAs in the collected cells will be the candidate genes that normally prevent micronucleus formation. The results of the screen will enhance our understanding of the molecular mechanisms behind micronuclei formation offering novel potential strategies for cancer treatment by targeting either to these structures or their causes.

FGF1 REGULATES BREAST CANCER GROWTH AND METABOLIC REPROGRAMMING THROUGH ETV4

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Breast cancer is the most frequently diagnosed cancer in women worldwide. Obesity increases resistance to breast cancer therapies and patient mortality, particularly for estrogen receptor-positive (ER+) tumors that represent 70% of all cases. Adult weight gain in women with obesity, characterized by adipose tissue expansion, is an independent prognostic factor for breast cancer. In a preclinical model, we found that weight gain promoted ER+ tumor growth after endocrine therapy through adipose-derived fibroblast growth factor 1 (FGF1). To determine the underlying mechanisms, we used cultured ER+ breast cancer cells (MCF7, tamoxifen-resistant MCF7 cells, and UCD12 cells) treated with FGF1, combined with gene expression profiling and metabolic analysis. ETS variant 4 (ETV4), which regulates ER activity and cancer cell glycolysis, was the top gene induced by FGF1 in multiple ER+ lines. ETV4 was shown by others to regulate breast cancer metabolism and stemness, contributing to disease progression. We hypothesized that ETV4 mediates the FGF1-dependent effects on breast cancer glycolytic reprogramming in obesity-associated breast tumors. ETV4 was upregulated in human PDX tumors grown in obese versus lean mice. In invasive human breast cancer specimens, high versus low ETV4 expression predicted a shorter recurrence-free survival for patients with ER+ tumors. ETV4 knockdown in cultured endocrine-resistant breast cancer cells prevented the proliferation and induction of glycolytic genes with FGF1 treatment. Conversely, overexpression of ETV4 was sufficient to increase glycolytic gene expression and enzyme activity, as well as cell proliferation. Taken together, our data suggest a mechanism by which FGF1 supports breast cancer endocrine therapy resistance in the context of obesity through ETV4 induction and glycolytic metabolic reprogramming. Understanding this process may aid in designing effective treatments, especially for patients resistant to current ER-targeted therapies. Furthermore, ETV4 may be a biomarker to identify breast tumors with excess FGF signaling and patients at high risk for progression.

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DEVELOPMENT OF CD147-TARGETED S100A9-750 FLUORESCENT PROBE FOR ENHANCED IMAGING OF PANCREATIC DUCTAL ADENOCARCINOMA.

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Background: Pancreatic ductal adenocarcinoma, PDAC, remains one of the most resistant cancers in which surgery is the only potentially curable treatment. Only 15-20% of patients are candidates for surgical resection, and up to 70% of these patients have positive margins. Extracellular matrix metalloproteinase inducer, EMMPRIN, also designated CD147, is a membrane-bound glycoprotein. CD147 is highly expressed on most cancer cells but has limited expression in normal cells. Using an S100A9 ligand, a CD147 targeted fluorescent probe was created to visualize pancreatic tumor cells via NIR fluorescent and multispectral optoacoustic tomographic imaging.

Methods: Pancreatic adenocarcinoma cancer cell lines, MiaPaca2, Panc1, Suit2, S2VP10 and S2013 were assessed for CD147 levels using western blot. S100A9 (100 amino acids) was synthesized using microwave chemistry and lyophilized. Hilyte 750 succinimidyl ester and Hilyte 750 amine reactive dyes were independently conjugated to the S100A9 peptide to determine the optimal orientation of the dye. The result was S100A9 N-Terminus through the succinimidyl ester reactive 750 dye and C-terminus through the amine reactive 750 dye. Spectroscopy confirmed successful conjugation. Binding of 750-S100A9 (N-terminal) and S100A9-750 (C-terminal) probes to S2VP10 cells were determined using NIR imaging and tissue mimicking phantoms via MSOT.

Results: The western blot demonstrated that MiaPaca2, Panc1 and S2013 were highly positive for CD147 while Suit2 and S2VP10 were less positive. C-terminal conjugation of the 750 dye to S100A9 resulted in higher signals of 279,600 a.u. at 500 nM vs. 4,055 a.u. of N-terminal 750-S100A9 in S2VP10 cells. Panc1 cells also showed high signals at C-terminal conjugation averaging 100,420 at 500 nM. The tissue mimicking phantoms displayed an increased signal of S100A9-750 in S2VP10 at 22.4 a.u. Shrinking S100A9 peptide to 89 amino acids demonstrates the highest signal in the cancer cells versus the full-length peptide.

Conclusion: CD147/EMMPRIN is a suitable target for PDAC using an S100A9 ligand conjugated near infrared fluorescent dye. The findings suggest that S100A9 could facilitate active targeting of dyes or potentially for nanoparticles to improve detection and treatment of pancreatic cancer.

PSMA PET-CT AND MRI TO IDENTIFY LYMPH NODE METASTASES IN ADVANCED PROSTATE CANCER

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BACKGROUND: Between 5-12% of patients with organ confined prostate cancer will develop regional lymph node metastasis.1 Ga 68 PSMA-11 targeted PET-CT imaging was approved for men with recurrent prostate cancer or suspected prostate cancer metastasis by the FDA in 2020.2 Therefore, we plan to evaluate the predictive value of PSMA PET-CT in defining regional lymph node metastasis vs. the standard 3T Pelvic MRI imaging in men with advanced prostate cancer.

METHODS: We retrospectively reviewed patients who received a PSMA PET-CT scan between January 2022 and July 2024. Out of these 789 patients, we identified a cohort of 190 who had a concurrent pelvic MRI scan. For the purpose of this study, concurrent is defined as no more than 120 days between the two scans. On each scan, we recorded whether or not lymph node metastases were seen, as well as the size of any malignant lymph nodes. The sensitivity, specificity, positive predictive value, and the negative predictive value of MRI versus PSMA PET-CT in identifying lymph node metastases were calculated. In addition, the mean size of the lymph nodes in each positive category as identified by PSMA were calculated. The difference in these means was tested using a one tailed T-Test.

RESULTS: The 190 patients were grouped as positive or negative for both their MRI and PSMA PET-CT scans, as shown in Figure 1. MRI achieved a sensitivity, specificity, positive predictive value, and negative predictive value of 58.5% (CI: 43.4, 72.2), 96.0% (CI: 91.5, 98.1), 80% (CI: 62.7, 90.5), and 89.4% (CI: 83.6, 93.3), respectively. The mean size of lymph nodes positive in both scans was 1.8cm while the mean size positive only in the PSMA scan was 0.91cm. The lymph nodes positive in both scans were significantly larger than the nodes only positive in the PSMA scan (P=0.0155).

CONCLUSIONS: Overall, PSMA PET-CT was more sensitive in identifying lymph node metastases in prostate cancer than MRI imaging. This is especially true for small sized lymph node metastases. Since identifying lymph nodal involvement is crucial in determining a patient's stage, and therefore treatment, PSMA PET-CT is an important instrument for accurate workup of patients with advanced prostate cancer. Further study with larger sample sizes is needed to reinforce these findings.

		PSMA PET-CT	
		+	-
MRI	+	24	6
	-	17	143

Figure 1: Results of PSMA-PET and MRI scans

1. Datta K, Muders M, Zhang H, Tindall DJ. Mechanism of lymph node metastasis in prostate cancer. Future Oncol. 2010 May;6(5):823-36. doi: 10.2217/fon.10.33. PMID: 20465393; PMCID: PMC2892838.

2. FDA. (n.d.-a). FDA approves first PSMA-targeted pet imaging drug for men with prostate cancer.

U.S. Food and Drug Administration.

https://www.fda.gov/news-events/press-announcements/fda-approves-first-psma-targeted-pet-imaging-drug-men-prostate-cancer

TITLE: USE OF IMMUNE CHECKPOINT INHIBITORS AS FIRST LINE THERAPY FOR UNTREATED, UNRESECTABLE PLEURAL MESOTHELIOMA: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS.

Bibi Maryam, Adolfo Jose Diaz Barba, Mohammad Jamil, Muhammad Asif, Bilqees Khanam, Abdul Manaf, Ryan Nipp, Raid Aljumaily

Background: Malignant pleural mesothelioma represents an uncommon malignancy, typically found in adults with prior exposure to asbestos. Despite the benefits of surgical resection in the early stages of disease, the survival rate for patients with advanced, unresectable disease remains low with median survival of 11 months in stage IV disease. Immune checkpoint inhibitors (ICIs) are included in current guidelines as first line therapy, but data on the overall effect of (ICIs) as group remains limited. We sought to conduct a systematic review and meta-analysis of phase 3 randomized controlled trials (RCTs) regarding use of ICI as part of first-line therapy for advanced, unresectable pleural mesothelioma.

Methods: We performed a systematic search in Medline and Embase, following PRISMA guidelines. We included phase 3 RCTs describing the use of ICIs as first-line therapy for advanced, unresectable pleural mesothelioma (either as monotherapy or in combination with chemotherapy), reporting at least one outcome of interest. Studies describing the use of ICI in previously treated, resected or potentially resectable mesothelioma. Data was collected for the outcomes of interest (primary endpoint included median overall survival, and secondary endpoints were median progression free survival, median overall survival for epithelioid mesothelioma, and rate of adverse events). A meta-analysis for the outcomes of interest was performed in R studio version R 4.4.2, using Hazard Ratios (HR) and relative risk (RR) to report results. A common effects model was used considering low heterogeneity, due to exclusive inclusion of RCTs.

Results: We screened 950 studies, and 3 studies met inclusion for final analysis (CheckMate 743, KEYNOTE 483, and BEAT-Meso), with a total of 725 patients in the intervention group and 720 patients in the control group. After performance of meta-analysis, median overall survival (mOS) demonstrated a HR of 0.78 (95%CI 0.69-0.89), favoring the intervention group. For the secondary endpoints, median progression free survival (mPFS) showed a HR of 0.84 (95%CI 0.75-0.94), with statistically significant benefit for intervention group; mOS in patients with epithelioid histology demonstrated a HR of 0.91 (95%CI 0.79-1.04), which was not statistically significant. RR for grade 3-4 adverse events was 1.17 (95%CI 1.01-1.35), with a statistically significant increase in the intervention group.

Conclusions: Use of immune checkpoint inhibitors as part of first-line therapy for advanced, unresectable mesothelioma demonstrated statistically significant benefits in survival outcomes

(OS and PFS), but also a higher risk of grade 3-4 adverse events. Notably, benefits in mOS were not statistically significant for subgroup analysis of patients with epithelioid histology, and additional research is needed to better understand the benefits of ICI across various subgroups.

Figure 1. Pooled analysis of median overall survival.

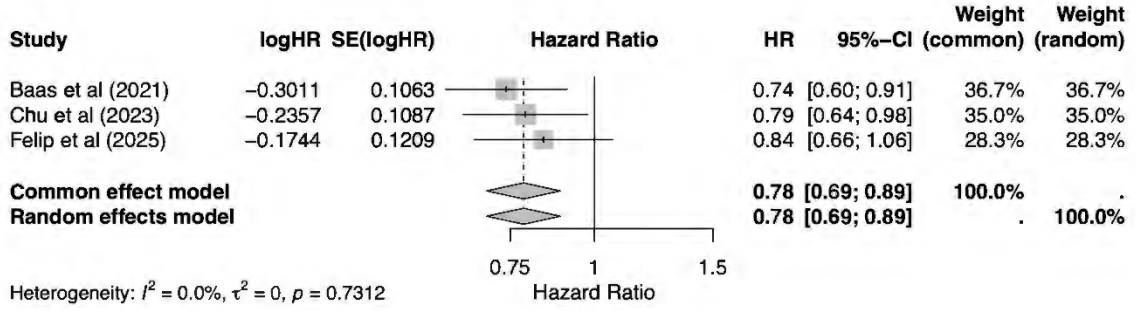


Figure 2. Pooled analysis of median progression free survival.

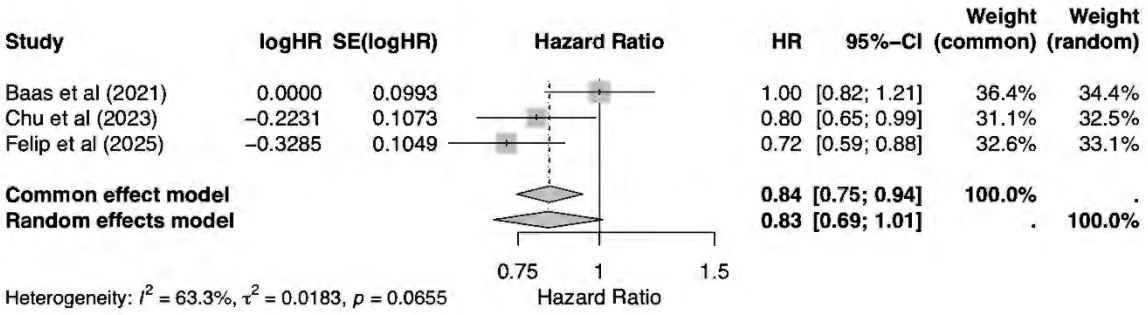
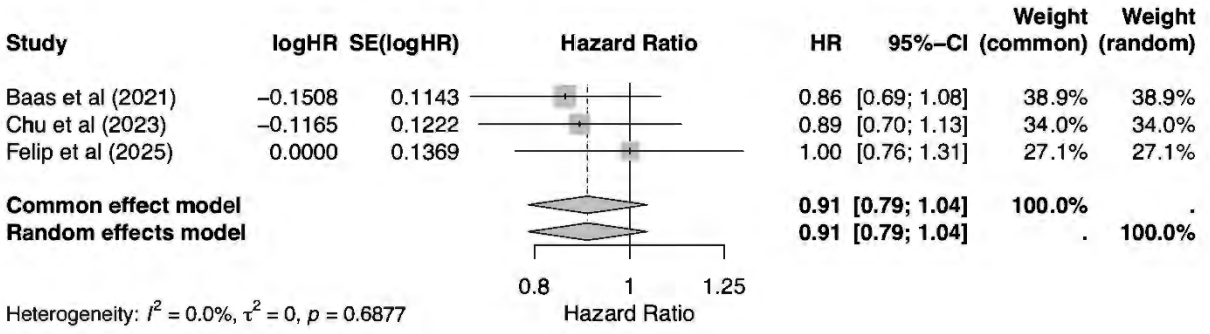


Figure 3. Pooled analysis of mOS for epithelioid type MPM.



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.

ENHANCING DIVERSITY AND INCLUSIVITY IN HEAD AND NECK CANCER CLINICAL TRIALS: STRATEGIES FOR EFFECTIVE PARTICIPANT ENGAGEMENT AND RETENTION

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This literature review critically examines the state of diversity and inclusivity in head and neck cancer (HNC) clinical trials. While recent years have seen incremental improvements, the current representation of women and racial minorities remains inadequate, underscoring the persistent gap between ideal representation and reality. We delve into a comprehensive array of strategies aimed at bridging this disparity, encompassing community engagement, participant-centric trial design, strategic site selection, innovative enrollment techniques, retention methodologies, and effective monitoring and dissemination protocols. Our analysis further reveals the pivotal roles of flexible trial architectures, targeted outreach initiatives, and collaborative partnerships with advocacy groups in fostering greater inclusivity. Additionally, we underscore the importance of transparent demographic reporting, trust-building within historically underserved communities, and regulatory frameworks incentivizing diversity. Recognizing the intersectionality of race, gender, socioeconomic status, and geography is vital in dismantling systemic barriers. Sustained, multifaceted efforts are paramount to ensuring that clinical trial outcomes genuinely reflect the heterogeneous patient population and contribute meaningfully to advancing equity in healthcare research.

VISUALIZING NANOPARTICLE SPATIOTEMPORAL DISTRIBUTIONS IN ENTIRE TUMOR SPHEROIDS USING EXPANSION MICROSCOPY

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Understanding the nanoparticle spatiotemporal distributions across the tumor microenvironment is crucial for designing safer and more effective cancer nanomedicines. However, current imaging techniques present challenges in visualizing nanoparticle distribution at high resolution and large volumes. For example, transmission electron microscopy (TEM) provides nanoscale resolution. Still, it is constrained by small sample sections. In contrast, alternative electron microscopy methods, such as focused ion beam scanning electron microscopy (FIB-SEM) and serial block-face electron microscopy (SBEM), offer greater volumetric imaging but require extensive time and processing. To address these limitations, we propose using expansion microscopy (ExM), which works by physically expanding biological samples within a hydrogel matrix, enhancing resolution while preserving the relative molecular and structural integrity. By integrating ExM with conventional confocal laser scanning microscopy (CLSM) and axially swept light-sheet microscopy (ASLM), we achieve detailed 3D visualization of nanoparticle distributions throughout entire cancer spheroids. Our proof-of-concept study demonstrates the integration of ExM with light-scattering-based imaging techniques, providing an innovative framework for visualizing nanoparticle spatiotemporal distributions and distribution mechanisms in large tissue volumes. Ultimately, this approach will enable the design of safer and more effective cancer nanomedicines that can reach cells within the tumor microenvironment more efficiently.

THE REPLICATION INITIATION FACTOR MTBP COORDINATES WITH MUVB TO ENSURE PROPER TRANSITION TO MITOSIS.

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DNA replication occurs at tens-of-thousands of individual sites or “origins”, along DNA strands and are initiated throughout the S-phase of the cell cycle. DNA replication initiation must be coordinated with other cellular processes to avoid genomic instability and to ensure that the entirety of the genome is copied faithfully prior to mitosis. While genetic screens in yeast have been invaluable for the identification of proteins involved in DNA replication origin firing and DNA fork elongation, mammalian cells have a larger genome, a more complex chromatin landscape, and are governed by additional regulatory mechanisms. To identify novel regulators of DNA replication initiation, we performed a genome-wide CRISPR/Cas9 sgRNA knockout screen in human HCT116 cells in which both alleles of a crucial replication initiation factor, MTBP, were fused to an auxin-induced degron. This cell line displays weakened DNA replication and impaired proliferative capacity following exposure to Auxin and the cells enter mitosis with under-replicated DNA. We used the BrunelloV2 sgRNA library, targeting 19,114 human genes, to identify those gene whose loss either suppressed or enhanced the phenotypes in these cells, both with and without Auxin treatment. From this screen, we identified a genetic interaction between MTBP and the MuvB transcriptional complex. The MuvB complex is a multi-protein core complex that interacts with transcription factors p130/E2F4, B-Myb, and FoxM1 sequentially at distinct times during the cell cycle to either activate or repress gene expression. Inactivation of the MuVB rescues the premature mitotic entry phenotype following loss of MTBP. Results from our screens suggest a broader network of genes may function to coordinate DNA replication with mitosis in human cells.

Funding provided by Presbyterian Health Foundation

DEVELOPMENT AND ASSESSMENT OF PH-RESPONSIVE V3 VARIANT PEPTIDES FOR IDENTIFICATION OF PANCREATIC CANCER

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Introduction: Pancreatic cancer poses challenges for targeted treatment and imaging because the heterogeneity of the tumors complicates the ability to identify overexpressed cell receptors. However, pancreatic cancer cells are acidic relative to the rest of the body's cells, and targeting this acidity with pH-responsive peptides, such as the V3 peptide, offers a solution to the poor treatment response and inoperability that pancreatic cancer patients suffer. Two new pH-responsive peptides—V3-Pro and V3-ProFS—were synthesized in the laboratory based on the V3 peptide structure and analyzed with fluorescence to evaluate their ability to identify pancreatic cancer as compared to the preexisting V3 peptide.

Methods: Modifications to the V3 peptide sequence were designed to make the V3-Pro and V3-ProFS sequences, and then these variants were synthesized using microwave technology. The peptides were conjugated to a 750 C2 maleimide dye to make the V3-750, V3-Pro-750, and V3-ProFS-750 fluorescence probes. S2VP10 pancreatic cancer cells were plated and then acclimated to 7.4, 6.8, and 6.6 pH, then treated with the imaging probes at 1 μM. Cells were washed with pH-specific PBS, and then plates were imaged using near-infrared fluorescence.

Results: The V3-750 probe had the highest fluorescence at 6.8 pH, while the V3-Pro-750 and V3-ProFS-750 probes had the highest fluorescence at 6.6 pH. After statistical analysis, cells treated with the V3-Pro-750 and V3-ProFS-750 probes featured comparable fluorescence signals for 6.6 pH, with a large contrast between 6.6 and 7.4 pH, when compared to cells treated with the V3-750 treated cells.

Conclusion: Fluorescence signal values for cells treated with the V3-Pro-750 and V3-ProFS-750 imaging probes suggest that the modified sequences target 6.6 pH, while the original V3-750 probe targets 6.8 pH.

CERVICAL DYSPLASIA AND FOLLOW UP PATTERNS AMONG THE INCARCERATED WOMEN IN OKLAHOMA

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As of 2023, the United States (US) has 1.9 million incarcerated people, of which 172,700 are women. Cancer has surpassed heart disease as the leading cause of death in state prisons, and the most common cancers in this population have effective screening tools. Barriers to access to preventative healthcare include lack of insurance, homelessness, mental illness and substance use, which are common among incarcerated women. Incarcerated women have higher rates of high grade cervical dysplasia and more likely to be lost to follow-up than non-incarcerated women. The aim of this study is to characterize the population of incarcerated women seeking care at our institution for an abnormal pap smear, describe the care received, and determine the rate of follow-up after their initial treatment. After IRB approval, a retrospective chart review between January 2021- June 2024 of incarcerated patients with cervical dysplasia was performed. Demographics, clinical and pathological characteristics, and treatment data were collected and analyzed. Descriptive statistics were utilized to summarize data. In total, 188 patients met inclusion criteria. The average age was 36 years and 44% were Caucasian. Regarding medical history, 46% had a mental health disorder, 17% had a history of sexually transmitted infections, and 73% reported tobacco use prior to incarceration. Only 4% of patients reported vaccination against HPV prior to their visit, however the HPV vaccination series was initiated in 66% of patients. ASCUS was identified in 36% of pap smears, with HSIL in 24%, and 91% of all patients were HPV+. Of the 89% who underwent colposcopy, 42% had HSIL, 33% were benign. An excisional procedure was performed on 44% of patients. 78% of patients who had an excisional procedure had HSIL histology, 1% had AIS and 1% had carcinoma. The average time between pap smear and colposcopy was 3.4 months, and the average time between pap smear and excisional procedure was 5.4 months. In all, 68% of patients did not have the recommended follow up in clinic within 18 months of their last appointment. Of those released, 66% were lost to follow up. Women who are incarcerated are of lower socioeconomic status than the general population, lack health insurance, are less likely to undergo screening, and less likely to be educated on the importance of HPV vaccination. After counseling in clinic, 66% of eligible patients were amenable to initiation of the HPV vaccine series, demonstrating the importance of education. Although the prison system often allows incarcerated women access to medical care, barriers to care remain that delay treatment, as evidenced by the length of time between pap smear, colposcopy, and excisional procedure. Our research highlights the many opportunities for improvement in the care of incarcerated women with cervical dysplasia, and further research is warranted.

OPTOACOUSTIC IMAGING IMPROVES PANCREATIC TUMOR DETECTION USING ACIDIC MICROENVIRONMENT TARGETED LIPOSOMES

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Background: Pancreatic ductal adenocarcinoma (PDAC) management is limited due to insufficient early diagnosis and complete tumor resection challenges during surgery. Fluorescent dyes assisted image-guided surgery for resection surgeries are restricted by penetration depth of up to 8 mm, highlighting the necessity of developing novel contrast agents. Multispectral optoacoustic tomography (MSOT), an advanced imaging modality shows promise for real-time tracking of contrast agents *in vivo* to assist in image guided surgery. Nanocontrast agents can be actively targeted towards the highly acidic tumor microenvironment of PDAC to facilitate the detection, diagnosis, and monitoring of the treatment response. The proposed research explores acidosis as a potential tumor target for active targeting of IR-780 contrast agent-loaded liposomes (Lipo-780). Liposomes decorated with pH-low insertion peptide variant 7 (V7) were used to access tumor-specific accumulation in orthotopically implanted pancreatic tumors.

Methods: Lipo-780 was prepared using thin film hydration technique and active targeting of liposomes (V7-liposomes) was performed by conjugating pH-responsive V7 peptide using SMCC linker. Size, polydispersity and zeta potential of liposomes were characterized using a Malvern Zetasizer ZS^{TM} (Malvern Instruments Ltd., Malvern, UK). pH-dependent tumor-specific uptake of liposomes were validated in an in vitro PDAC model (S2VP10, S2013 cells) through NIR fluorescence imaging, and cell internalization assay. Liposomes administered intravenously in athymic nude mice with orthotopically implanted PDAC tumors were evaluated for their tumor-specific uptake using MSOT.

Results: Enhanced tumor-specific uptake of actively-targeted V7-lipo-780 compared to passively targeted Lipo-780 at acidic pH 6.6 was observed (S2VP10- $p \leq 0.001$; S2013- $p \leq 0.05$). MSOT indicated enhanced tumor uptake of V7-lipo-780 post 6 h of IV injection *in vivo* ($p < 0.001$).

Conclusion: Actively targeted liposomes can specifically target PDAC with minimal off-target binding effects in vivo. V7-lipo-780 delivers contrast agent for imaging tumor margins and expands the potential of MSOT for clinical applications.

TESTING LEUKEMIA-ESSENTIAL GENES VIA SOMATIC TRANSGENESIS AND SCALE TRANSPLANTATION

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Leukemia is a bone marrow cancer and the most common malignancy in the pediatric age group. Zebrafish and humans share an adaptive immune system and key immunologic and oncologic pathways, making them an ideal model 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*, *cd79b*:*GFP*) in multi-transgenic fish, creating zebrafish with color-coded B- and T-lineage ALL. MYC is the oncogenic driver in our system, but it cannot initiate and sustain ALL in isolation, other genes are necessary, making them potential therapeutic targets. To test candidate genes that are essential for ALL causation and progression *in vivo*, we sought a means to rapidly enhance or ablate genes that was also rapid. We are using a somatic transgenesis system, TEAZ (Transgene Electroporation in Adult Zebrafish), for this. TEAZ introduces genetic material into some—but not all—cells, creating competing populations of modified vs. unmodified ALL cells. TEAZ can introduce transgenes to enhance, or CRISPR components to reduce, gene function. Traditional TEAZ injects plasmid DNA directly into tissues of a live animal, but to 'scale up' this technique, we are piloting a new method: We remove ALL-infiltrated scales from a donor fish, perform TEAZ *ex vivo*, and then implant TEAZ'd scales into immunosuppressed recipient fish. A single donor zebrafish provides dozens-to-hundreds of ALL-infiltrated scales, so we can test many genes in parallel simultaneously, comparing otherwise-identical ALL cells to determine which genes are essential to ALL survival and growth. Scale abundance also facilitates transplant into large cohorts to achieve statistically significant results. Thus, scale transplants can functionally test targets to ascertain which merit development of novel ALL therapeutics. We will present an overview of our project's schema and current progress.

DIFFERENTIAL INSULIN-LIKE GROWTH FACTOR 2 AND IMMUNE MICROENVIRONMENTS IN ASCITES FROM PATIENTS WITH NEWLY-DIAGNOSED COMPARED TO RECURRENT OVARIAN CANCER

Jacqueline A. Bohn, Laura Mortan, Brooke A. Meelheim, Zitha Redempta Isingizwe, Doris M. Benbrook

Ovarian cancer is most often detected at later stages where ascites represents a microenvironment for promotion of cancer recurrence. The objective of this study was to identify factors in ascites specimens that could be targeted for detection and prevention of recurrence. Ascites specimens were collected from patients with ovarian cancer and compared between newly diagnosed and recurrent disease by RNA sequencing, ELISA and survival analysis. The immunosuppressive insulin-like growth factor 2 (IGF2) was the most differentially expressed gene between the two specimen types. IGF2 RNA and protein were present at significantly higher levels (t-test; $p<0.05$) in the recurrent compared to newly diagnosed specimens. Multiple immunoglobulin genes were expressed at significantly lower levels in the recurrent ascites in association with reduced memory and plasma B cells. In conclusion, IGF2 and factors that suppress B cells were identified as candidate biomarkers and drug targets for prevention of ovarian cancer recurrence.

EXPLORING LYMPHOBLASTIC MALIGNANCIES USING ZEBRAFISH: INSIGHTS FROM A TRIPLE-TRANSGENIC MODEL REVEALS NOVEL MECHANISMS AND ENGRAFTMENT DYNAMICS IN ACUTE LYMPHOBLASTIC LEUKEMIA

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Abstract: Zebrafish are a powerful model to elucidate mechanisms of hematopoiesis, including those of hematologic malignancies like Acute Lymphoblastic Leukemia (ALL). ALL is a rapidly-progressing blood cancer characterized by aggressive proliferation of immature lymphocytes. We generated color-coded triple-transgenic zebrafish where T cells fluoresce red (mCherry), B cells are green (eGFP), and human MYC (hMYC) induces both B-ALL and T-ALL. Surprisingly, our lineage-specific reporters revealed a unique population that is both GFP+ (B-lineage) and mCherry+ (T-lineage). In normal fish (i.e., lacking transgenic hMYC), such 'dual-lineage' cells are abundant in thymus and also present in marrow. We conducted RNAseq on T- (mCherry-only), B- (eGFP-only), and mixed- (mCherry/eGFP double-positive) lineage lymphocytes from these animals. We hypothesized that different stages of T cell maturation might explain these phenotypic variations, and analyses of RNAseq results suggest this to be the case. Investigations of these novel mixed-lineage lymphocytes in wild-type (WT) fish are ongoing. In view of these findings in WT animals, we next investigated if such cells were present in ALL samples. Using triple-transgenic fish (both fluorophore reporters, plus lymphoblast-specific hMYC), we analyzed T- and B-ALL. By fluorescent microscopy, we found examples of red-only (T-lineage), green-only (B-lineage), and mixed (red + green) ALL, and we confirmed this by flow cytometry. In these analyses, we often see that red-only ALL (by microscopy) also contain small numbers of red + green cells (by flow cytometry). So, even ALL that appear to be of one lineage include dual-lineage lymphoblasts. To examine whether these populations have different cellular behaviors, we have begun ALL allo-transplantation experiments to determine if single- vs. dual-lineage ALL cells differ in their engraftment potential. Preliminary results indicate dual-lineage ALL cells engraft better than red-only T-ALL from the same donor ALL. Further, red-only T-ALL can generate red + green dual-lineage ALL upon engrafting. Together, our preliminary results suggest dual-lineage ALL cells may contain more Leukemia Stem Cells (i.e., their engraftment potential is greater) and that single- and dual-lineage ALL cells exhibit plasticity, with an ability to inter-convert between phenotypes.

RISK OF LATE EFFECTS AND ACUTE CARE UTILIZATION AMONG CHILDHOOD, ADOLESCENT, AND YOUNG ADULT CANCER SURVIVORS.

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Introduction: Remarkable progress in the survival of childhood cancer comes at a significant cost with late therapy-associated toxicities. Late effects of treatment include chronic health conditions and subsequent malignant neoplasms, which vary by original cancer diagnosis and treatment received. While factors impacting long-term survivorship health outcomes have been identified, there remains a gap in understanding healthcare utilization within the first few years after cancer diagnosis.

Methods: We conducted a retrospective cohort study to assess the relationship between risk stratification for late effects of cancer and both emergency department visits and hospitalizations, occurring 3-10 years after the cancer diagnosis. We identified cancer survivors from the University of Oklahoma (OU) Health cancer registry and linked with claims data from the Oklahoma Health Care Authority (OHCA), which maintains data for the state's Medicaid program. We included survivors diagnosed with cancer between 2010 and 2017 who were aged 0-29 years at the time of diagnosis. We used modified Poisson regression to estimate risk ratios (RR) and 95% confidence intervals (CI) to account for confounding factors.

Results: We identified 494 survivors that linked with an OHCA claims record. Approximately half of survivors were female (51%) and a child at diagnosis (49% compared to adolescent [16%] or young adult [35%]). Nearly half of survivors were at intermediate risk of late effects (49%), followed by low risk (35%), and high risk (13%). In our multivariable models, we found no association between risk stratification and hospitalizations (High risk RR: 0.73, 95% CI: 0.33, 1.60; Intermediate risk RR: 0.93, 95% CI: 0.53, 1.63 compared to low risk) or emergency department visits (High risk RR: 0.87, 95% CI: 0.60-1.24; Intermediate risk RR: 0.89, 95% CI: 0.67-1.17, compared to low risk).

Discussion: We observed no significant differences in acute healthcare utilization among cancer survivors within 3-10 years after their cancer diagnosis. However, we were unable to measure healthcare utilization during periods when survivors were not covered by Medicaid, which may be particularly challenging for survivors transitioning into adulthood as eligibility for Medicaid requires lower income than during childhood.

NUTRITION RISK STRATIFICATION USING THE PATIENT GENERATED SUBJECTIVE GLOBAL ASSESSMENT IN PATIENTS WITH GYNECOLOGIC MALIGNANCIES IN THE OUTPATIENT SETTING

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Objective: Patients with cancer are often found to be malnourished at time of diagnosis and as a result of cancer directed therapies. Malnutrition accounts for about 20% of cancer related deaths. The purpose of this study is to evaluate if the validated nutritional assessment, patient generated subjective global assessment (PG-SGA) short form, is an appropriate screening tool to identify patients at risk for malnutrition or nutrition deficits upon initial consultation for a gynecologic malignancy. The assessment includes questions pertaining to weight, food intake, symptoms, and functional status. The tool provides a score ranging from 0-36, with a higher score indicating a higher risk for malnutrition. A score ≥9 indicates critical need for symptom management and intervention. The aim of this study is to show the risk of malnutrition of those with gynecologic malignancies at our institution, asses if scores affect perioperative outcomes, and identify areas for intervention to improve nutritional deficits.

Methods: The PG-SGA short form was routinely completed by all patients during the initial consultation in the outpatient setting at our institution with both gynecologic and breast oncology. Surveys completed were used to perform a retrospective cohort study from January 2023 to September 2024. Patients with a gynecologic malignancy who underwent surgery as part of the initial treatment were included in the final analysis of perioperative outcomes. Demographics and clinical data were abstracted. Descriptive analyses were created for both continuous and categorical variables. Independent samples t-tests and Chi-Square analysis were used to measure associations with outcomes.

Results: A total of 677 patients completed a PG-SGA short form at their initial consultation. Of the 677 patient-completed forms, 259 (38.3%) had a diagnosis of a gynecologic malignancy, 237 (35.0%) had a benign gynecologic concern, 177 (26.1%) had a non-gynecologic malignancy, and 4 (0.6%) were not classified. A total of n=220 patients with a gynecologic malignancy who completed a PG-SGA form were included in the analysis. Forty-six patients (20.9%) had a score 0-1, 37 (16.8%) scored 2-3, 67 (30.5%) scored 4-8, and 70 (31.8%) scored ≥9. Of the 220 patients, 114 (51.8%) underwent primary surgical intervention for treatment. A total of 16 patients had a postoperative complication, and 4 of those patients scored ≥9 on the PG-SGA which was not a significant association. For patients with scores ≥9, only 3 out of 25 patients were recognized by a provider as being at risk for malnutrition (p=0.0354) with inadequate intervention.

Conclusion: The PG-SGA short form is a validated screening tool to identify patients at risk for malnutrition. We found that our population is at risk for malnutrition and providers underdiagnose this condition and underutilize available resources within our system to meet patient needs. This tool can be

implemented in the outpatient setting for providers to determine who might benefit from dietitian intervention to improve cancer-directed therapy outcomes.

BIOMARKERS OF OVARIAN CANCER SENSITIVITY TO SHETA2

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Despite the introduction of new therapies, 80% of patients with ovarian will recur within three years with resistant and more aggressive forms highlighting the need for improved and personalized treatments. SHetA2 (Ess-Het-Aye-Too) is an investigational new drug in a Phase 1 clinical trial for patients with advanced or recurrent solid tumors (clinicaltrials.gov: NCT04928508) at the Stephenson Cancer Center.

The objective of this study was to identify biomarkers of SHetA2 sensitivity that could be used to identify patients with ovarian cancer most likely to benefit from treatment with this drug in planned Phase 2 clinical trials. For our research platform, we utilized an ovarian cancer hallmark, the spread of the cancer throughout the peritoneal space to form metastatic lesions and cancer recurrence after primary therapy. A buildup of ascites fluid containing heterogeneous mixtures of cancer, immune and other cells, cytokines and other soluble factors in the peritoneum of patients with advanced ovarian cancer fosters this cancer dissemination and recurrence.

In this study, ascites specimens were collected from patients with ovarian cancer consented under IRB protocol #15770. Sensitivities of the ascites cultures to SHetA2 were compared by measuring their metabolic viability with a tetrazolium dye assay after treatment with a range of SHetA2 concentrations. Specimens were categorized as being sensitive (potency <10 μM) or resistant (potency ≥10 μM) and then probed for proteins identified to be differentially expressed in solid tumors compared to ascites specimens of an animal model. Of the 21 probed proteins evaluated, four, aldehyde dehydrogenase 1 family member A3, nucleoside diphosphate kinase 1, triosephosphate isomerase 1, and tropomyosin 1 (ALDH1A3, NME1, TPI1, TPM1, respectively) were expressed at significantly different levels between the two groups, with higher expression in the sensitive compared to the resistant group. To determine if these proteins play functional roles in the SHetA2 mechanism, we evaluated the effect of modulating their expression on drug sensitivity in a high grade serous ovarian cancer cell line. There were no significant changes in SHetA2 potency or efficacy caused by the overexpression of these proteins. However, the siRNA knockdown of TPM caused increased drug resistance (decreased potency) compared to the siRNA scrambled control cells. The knockdown of the other candidate biomarkers did not affect SHetA2 sensitivity of the high grade serous ovarian cancer cell line.

In conclusion, ALDH1A3, NME1, TPI1, and TPM1 were identified as candidate biomarkers of SHetA2 sensitivity that could be screened in ascites of patients with ovarian cancer to identify those most likely to benefit from SHetA2 treatment. The validity of TPM as a biomarker of SHetA2 sensitivity and down-stream mechanistic actor are supported by knockdown studies. Further studies are planned to verify these findings and translate their use in planned future clinical studies and trials.

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DISTINCT MOTIVES FOR TOBACCO USE AMONG RURAL- VERSUS URBAN-RESIDING SEXUAL MINORITY YOUNG ADULTS IN OKLAHOMA AND SURROUNDING STATES

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Background: Sexual minority-identifying young adults (SMYAs) report higher tobacco use rates and more frequent use relative to their heterosexual-identifying peers. Prior work suggests that SMYAs residing in rural (vs. urban) areas are at even greater risk for tobacco use. However, less is known regarding reasons for tobacco use disparities among rural- vs. urban-residing SMYAs. The current study examined distinct tobacco use motives, including social reasons, boredom relief, coping, and self-enhancement as mechanisms contributing to geographic disparities in tobacco use outcomes for SMYAs.

Methods: We analyzed data from 366 female (M_{age}=21.56 [SD=2.15], 40.7% racial/ethnic minority, 52.7% gender minority, 36.9% rural) and 177 male (M_{age}=22.14 [SD=1.98], 53.1% racial/ethnic minority, 28.8% gender minority, 24.3% rural) SMYAs residing in Oklahoma and surrounding states. Participants completed 2 online surveys 6 months apart, from Fall 2023 to Spring 2024. The baseline survey assessed sociodemographics and 4 tobacco use motives (social, boredom relief, coping, self-enhancement). Motives were assessed by asking participants to indicate why they currently use (if reporting current use) or would use tobacco (if reporting nonuse). The follow-up survey assessed 4 tobacco use outcomes: (1) past-month cigarette use frequency and (2) past-month e-cigarette use frequency (among all participants) and (3) polytobacco use (vs. single product use) and (4) nicotine dependence severity (among current users). We conducted 4 sets of multivariable regressions examining: 1) associations of rural vs. urban residence with tobacco use motives; and 2) associations of rural vs. urban residence and tobacco use motives with each tobacco use outcome. Regressions controlled for age, race and ethnicity, gender identity, and education and were conducted among female and male SMYAs, separately.

Results: Among female SYMAs, rural (vs. urban) residence predicted greater boredom and coping tobacco use motives, cigarette use frequency, and nicotine dependence severity. Boredom motives were in turn, associated with greater cigarette use frequency and nicotine dependence severity, while coping motives were associated with greater cigarette use frequency only. Among male SMYAs, rural (vs. urban) residence predicted lower social and self-enhancement motives, as well as a greater nicotine dependence severity. Only coping motives were associated with greater nicotine dependence severity.

Conclusions: Findings highlight boredom relief and coping tobacco use motives as potential mechanisms contributing to greater cigarette use and nicotine dependence severity among female SMYAs in rural (vs. urban) areas. Although tobacco use motives did not appear to contribute to geographic disparities in nicotine dependence among male SMYAs, coping motives were associated with nicotine dependence among male SMYAs, broadly. Findings highlight the need for interventions that support healthier coping strategies alongside community-level interventions promoting SM acceptance. Creating healthy leisure activities and spaces for SYMAs in rural areas may also offset geographic disparities in tobacco use.

RACIAL DISPARITIES IN INVASIVE SECOND BREAST CANCERS AMONG WOMEN WITH PRIMARY DUCTAL CARCINOMA IN SITU IN OKLAHOMA

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Introduction: Breast cancer is the leading cause of cancer-related death among women in the United States and Oklahoma. Outcomes from ductal carcinoma in situ (DCIS) are generally favorable, however, up to 50% of patients will develop a second breast cancer (SBC) after DCIS, with approximately 30% diagnosed as invasive SBC. Our research objective was to evaluate whether the risk of developing an SBC among women initially diagnosed with DCIS differs by race, ethnicity, and socioeconomic groups in Oklahoma accounting for laterality and age at the primary DCIS diagnosis.

Methods: We conducted a retrospective cohort study comparing the rate of developing an SBC in women with a previous DCIS residing in Oklahoma at the time of initial DCIS diagnosis by demographic factors. We obtained data from the Oklahoma Central Cancer Registry (OCCR) and included women diagnosed with DCIS from 1997-2021. An SBC includes invasive ipsilateral SBC (iiSBC), invasive contralateral SBC (icSBC), ipsilateral secondary DCIS, and contralateral secondary DCIS that occurred at least six months after the initial DCIS. We evaluated demographic and cancer-related characteristics among women diagnosed with DCIS as their initial cancer by calculating percentages and 95% confidence intervals. We also evaluated the rate of an SBC after diagnosis of a DCIS by demographics using the Cox proportional hazards models.

Results: We identified 7,903 women with DCIS as their initial cancer. Of these women, 491 (6.2%) were subsequently diagnosed with an SBC. Of the women with a primary DCIS, 80% were over 50 years of age at diagnosis and the majority were non-Hispanic white women (85%). Of those with a SBC,35.6% had iiSBC, 40.7% had icSBC, 8.2% had ipsilateral secondary DCIS, and 15.5% had contralateral secondary DCIS. NH American Indian women had the highest rate of developing an icSBC, with a hazard ratio of 1.9 (95% CI 0.8, 4.4) though the estimate was imprecise. NH Black women had the highest rate of developing any invasive SBC (ipsilateral or contralateral), with a hazard ratio of 1.6 (95% CI 1.04, 2.4).

Discussion: As a next step, we will further evaluate the rate of SBC among women in the OCCR accounting for demographic and cancer-related covariates such as hormone receptor status and evaluate overall survival among women who develop an SBC. We also plan to evaluate factors related to SBC nationally using the National Cancer Database.

ASSOCIATIONS OF DISCRIMINATION, MENTAL HEALTH SYMPTOMS, AND SUBSTANCE USE AMONG SEXUAL MINORITY YOUNG ADULTS: DIFFERENCES BY TYPE AND SOURCE OF SOCIAL SUPPORT

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Background: Sexual minority young adults (SYMAs) are at elevated risk for mental health problems and substance use, particularly tobacco use. These disparities are driven, in part, by unique stressors related to their marginalized identity, including discrimination. In accordance with the stress-buffering hypothesis, social support may mitigate the negative effects of minority stress on health and well-being. Research is needed to clarify the specific types and sources of social support that may serve as protective factors for SMYAs facing discrimination based on their sexual orientation.

Methods: We analyzed data from 549 SMYAs residing in Oklahoma and surrounding states (M_{age}=21.75 [SD=2.11]; 44.6% racial and/or ethnic minority, 45.5% gender minority, 67.4% female, 32.6% rural residing). Participants completed 2 online surveys 6 months apart from Fall 2023 to Spring 2024 assessing sociodemographics, sexual identity-related discrimination, and different types of social support at baseline (i.e., parent support of sexual identity, general parent support, peer support of sexual identity, general peer support, community acceptance, SM community connectedness) and health outcomes (i.e., mental health symptoms, past-month tobacco use, cannabis use, alcohol use) at follow-up. We conducted 4 sets of multivariable logistic regressions examining main effects of discrimination and each type of social support on each health outcome, as well as interactions between discrimination and each type of social support in relation to each health outcome controlling for participant age, race/ethnicity, gender identity, sex at birth, education level, and geographic residence.

Results: Discrimination predicted higher odds of mental health symptoms, tobacco use, and cannabis use, but not alcohol use. Furthermore, associations of discrimination and mental health symptoms were moderated by parent SM support, such that discrimination was more strongly associated with mental health symptoms for those with lower (vs. higher) levels of parent SM support. Additionally, peer SM support moderated the association between discrimination and tobacco use, such that discrimination was associated with tobacco use for those with lower, but not higher levels of peer support. General community support moderated the association between discrimination and alcohol use, such that discrimination was associated with higher odds of alcohol use for those with lower, but not higher levels of community acceptance. Social support did not moderate the relationship between discrimination and cannabis use.

Conclusions: The present findings highlight the protective role of social support on SMYAs' likelihood of reporting mental health symptoms, tobacco use, and alcohol use in response to discrimination. SM-specific support from parents and peers may be particularly beneficial for preventing mental health symptoms and tobacco use, respectively, in response to discrimination, whereas living in an area with greater acceptance of SM individuals may be beneficial for preventing alcohol use among SMYAs experiencing discrimination. These findings underscore the need for interventions that strengthen affirming family, peer, and community support networks and social connectedness to foster resilience among SMYAs, which may be key in reducing mental health and substance use disparities in this population.

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DEVELOPING AND EVALUATING AN mHEALTH INTERVENTION TO PROMOTE ACTIVE LIVING AMONG PEOPLE WITH METASTATIC BREAST CANCER

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Background: People with metastatic breast cancer (MBC) now commonly live many years after diagnosis. This population commonly experiences pronounced fatigue, loss of physical function, and psychological distress. Symptom burden can negatively affect health-related quality of life and cancer treatment options. Physical activity (PA) is generally safe in this population and can reduce cancer- and cancer treatment-related symptom burden. Motivation is critical for sustained PA; the motives that tend to be most compelling to people with advanced cancer, however, may be unique. Unfortunately, people with MBC are often excluded from active living research. Novel PA interventions that are tailored to the needs and motivations of this population are needed.

Objective: Our objective is to equip people with MBC with potent tools of behavioral medicine to help manage distressing symptoms and preserve functional independence. We hypothesize that PA programming oriented toward higher order processes of mental, social, and spiritual well-being will be especially effective among people with MBC.

Methods: We will recruit people diagnosed with MBC who are either undergoing active treatment or receiving supportive care. We will recruit participants via the SCC Clinical Trials Office, obtaining permission to approach potential participants from their oncologist. For **Aim 1**, we will engage in a user-centered development process (N=12) to create an 8-week mobile health (mHealth) PA intervention. The intervention will include a mobile application (app) and target various aspects of well-being with physical (e.g., mindful walking, yoga classes, ability to opt in to receive tailored muscle strengthening programming), mental (e.g., mindfulness/relaxation practices), and social components (e.g., an asynchronous game designed to evoke playful experiences and self-persuasion for active living). We will ground app development in an mHealth-specific dissemination and implementation model and employ Team Science best practices to capitalize on insights from complementary patient and scientific advisory panels (*disciplines involved: breast medical oncology, radiation oncology, psycho-oncology, pain psychology, exercise physiology, yoga, occupational therapy, and translational cancer communication*). For **Aim 2**, we will use quantitative and qualitative methods to evaluate the acceptability, feasibility, and potential efficacy of the intervention developed in Aim 1 (N=33). This project will contribute a nuanced

understanding of potent and scalable techniques for promoting active living and improving health-related quality of life among people with MBC.

Results: The *Moving Moments* intervention has been developed and is presently under review by our scientific advisory panel. Recruitment will launch in March 2025. We will present preliminary study observations as of April 2025.

Conclusions: The novel PA program being developed and tested in the present study is designed to provide meaningful supportive care to people with advanced breast cancer. It combines behavior change tools and techniques known to support active living, tailored muscle strengthening exercise programming, acceptance- and mindfulness-based supportive care, and elements of game design to support PA and well-being among people with MBC. This study will help fill knowledge gaps regarding how to meaningfully engage and support people with MBC in active living research.

EVALUATING THE ROLE OF EXTRACELLULAR VESICLES IN PROGRESSION OF UTERINE CARCINOSARCOMA

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Background: Uterine carcinosarcoma (UCS) is a rare, aggressive malignancy, constituting under 5% of uterine cancers but causing 16.4% of uterine cancer-related mortality. UCS is histologically unique, comprising both carcinoma and sarcoma components, with the sarcoma arising through redifferentiation of the carcinoma. Tumors with heterologous sarcoma is associated with lower progression-free survival (PFS) than those with a homologous sarcoma when paired with carcinoma of similar grade, suggesting the tumor supporting of the sarcoma. Interestingly, UCS metastasis is majorly driven by the carcinoma component, suggesting a complex interplay between the two, wherein the sarcoma component could enhance the progression of the carcinoma.

Hypothesis: Extracellular vesicles (EVs) are known to play a role in every aspect of tumor progression. We hypothesize that EVs secreted by the sarcoma component of UCS influence the carcinoma component, enhancing its tumorigenic potential and contributing to overall disease progression.

Methodology: To model the sarcoma component, we utilized UCS cell lines- CS99 and JHUCS1, both of which exhibit mesenchymal characteristics. EVs were isolated by ultracentrifugation of serum-free media conditioned by fully confluent UCS cells for 24h. Nanoparticle tracking analysis (NTA) was done to determine EV size and concentration, while transmission electron microscopy (TEM) was used to visualize their morphology. The enrichment and purity of the EV samples were assessed by western blot for EV specific markers. Ishikawa, which harbor mutations in *TP53, PIK3R1, and PTEN*—mutations frequently observed in UCS, was used as a surrogate for the carcinoma component. The effect of UCS-derived EVs on carcinoma progression was assessed by proliferation, invasion, and expression of epithelial-mesenchymal transition (EMT)-related genes. Cellular uptake of EVs was examined using WGA-FITC-labeled EVs.

Observation: Western blot and immunofluorescence showed high mesenchymal signature as assessed by expression of EMT-related proteins in UCS cells, validating the utility of this model for our study. Western blot of EV-protein showed a high abundance of EV markers- CD9, CD81, Flotillin and absence of GM130, a negative EV marker, indicating sample purity. TEM imaging further confirmed the presence of membrane-bound, cup shaped vesicles characteristic of EVs. Treatment of Ishikawa cells with UCS-derived EVs resulted in increased proliferation, enhanced invasive potential, and upregulation of EMT-related genes suggesting that sarcoma-derived EVs facilitate carcinoma progression. EV uptake studies demonstrated a time-dependent increase in the internalization of labeled EVs, with uptake being majorly dependent on clathrin and caveolin-mediated endocytosis.

Conclusion: Our findings indicate that EVs secreted by the sarcoma component of UCS enhance the tumorigenic properties of the carcinoma component, thereby contributing to disease progression. This suggests that sarcoma-derived EVs act as critical mediators of UCS aggressiveness and may represent potential therapeutic targets for disrupting sarcoma-carcinoma interplay in UCS.

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DOES ORDER MATTER? SINGLE INSTITUTION RETROSPECTIVE REVIEW OF PATIENTS WITH PLATINUM RESISTANT OVARIAN CANCER WHO RECEIVED WEEKLY PACLITAXEL BEFORE OR AFTER MIRVETUXIMAB SORAVTANSINE

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Objectives:

Mirvetuximab soravtansine-gynx (MIRV) and weekly paclitaxel are two mainstay treatments for the management of platinum-resistant ovarian cancer. MIRV, a folate receptor alpha (FOLR1) antibody-drug conjugate (ADC), demonstrated an objective response rate (ORR) of 42.3% in phase III confirmatory trial MIRASOL and weekly paclitaxel has been shown to have an ORR of 30-50%. This study aimed to determine if the sequencing of the treatments impacts progression-free survival (PFS) and overall survival (OS).

Methods:

We conducted a retrospective chart review identifying patients treated with both MIRV and weekly paclitaxel at a single institution between 2012 and 2024. Demographics and clinical data were abstracted. Survival outcomes were calculated using Kaplan-Meier and log rank statistics.

Results:

At our institution, between 2012 and 2024, we have treated 120 patients with MIRV in a variety of contexts. Thirty-four patients who received both MIRV and weekly paclitaxel in the recurrent setting were identified. Seventeen patients (50%) received MIRV before weekly paclitaxel and the remaining 17 patients (50%) received weekly paclitaxel before MIRV. The median ages were 58.1 and 60.1, respectively and the majority of patients were white (94.1%) with serous histology (97.1%). Patients who received MIRV prior to weekly paclitaxel received fewer lines of prior therapy (3.1 vs 5.8, P = 0.0005). Progression-free survival on MIRV was significantly longer in those who received MIRV before weekly paclitaxel (7.8 months vs 5.1 months, P = 0.006). Comparatively, there was no significant difference in PFS when weekly paclitaxel was given prior to MIRV (6.68 vs 2.93 months, P = 0.090). There was a trend towards an improvement in OS in patients who received MIRV prior to weekly paclitaxel, although this was not statistically significant (31.9 months vs 27.8 months, P = 0.241).

Conclusions:

The study findings reveal an association between earlier treatment with MIRV and improvement in progression-free survival. Utilizing ADCs, such as MIRV, highlights the importance of

early implementation of targeted therapies and the future of oncologic care. It is imperative to understand how these treatments impact tumor biology and disease response to traditional cytotoxic chemotherapies. Ongoing evaluation of other anticancer drugs and the importance of sequence will be presented.

TITLE: EXPLORING THE ROLE OF CYSTATHIONINE-B-SYNTHASE IN ANOIKIS RESISTANCE AND METASTASIS OF EPITHELIAL OVARIAN CARCINOMA

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Background: Ovarian cancer is the most lethal gynecological malignancy, with 90% of cases originating from epithelial tissue. A critical early step in epithelial ovarian carcinoma (EOC) metastasis is the detachment of cancer cells from the primary tumor into the peritoneal cavity, where they form multicellular aggregates (MCAs). These aggregates consist of cells that evade anoikis, a form of programmed cell death triggered by loss of attachment, allowing them to survive and propagate in suspension. Targeting anoikis resistance (AR) could therefore be a potential strategy to hinder EOC metastasis.

Cystathionine-β-synthase (CBS), a key enzyme in the transsulfuration pathway responsible for hydrogen sulfide (H_2S) production, is highly expressed in EOC and is associated with increased tumor aggressiveness by promoting cell survival and invasiveness. In this study, we investigate the role of CBS in the anoikis resistance of EOC cells.

Methods: We utilized the COV318, A2780-CP20, and OVCAR8 cell lines, which exhibit high CBS expression and represent ascites-derived, drug-resistant, and high-grade serous ovarian cancer model, respectively. CBS was transiently silenced using siRNA in both monolayer (2D) and spheroid (3D) cultures, with the latter serving as a model for MCAs. After 96 hours post-transfection, we assessed cell viability using phalloidin staining for 2D cultures and Calcein-AM/ethidium homodimer staining for 3D cultures, followed by fluorescence imaging. Western blot analysis was conducted on cell lysates from both culture conditions to examine markers of cell death, stemness, and epithelial-mesenchymal transition (EMT).

Results: Phalloidin staining of 2D cultures revealed disrupted cytoskeletal organization and increased cell death in CBS-depleted cells. This was confirmed through immunoblotting of PARP1 which showed cleavage upon CBS knockdown. In 3D cultures, CBS knockdown significantly impaired spheroid formation, as indicated by reduced spheroid size and increased cell death, as detected by Calcein-AM/ethidium homodimer staining. These findings correlated with the upregulation of cell death markers and the downregulation of stemness and EMT markers.

Conclusion: The loss of cell viability in spheroids upon CBS depletion underscores the role of CBS in promoting anchorage independent survival in ovarian carcinoma cell lines. Furthermore, the observed changes in stemness and EMT markers suggest that CBS contributes to key pathways involved in cancer progression, highlighting its potential as a therapeutic target in EOC.

"INHIBITION OF OVARIAN CANCER PROLIFERATION: TARGETING OXYSTEROL-BINDING PROTEINS AND INTRACELLULAR LIPID TRANSPORT"

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"Ovarian cancer's late-stage diagnosis and resistance to standard-of-care (SOC) therapies pose significant challenges. We investigate the role of cholesterol and oxysterol-binding proteins (OSBP and ORP4) in the context of ovarian cancer spheroids, which often metastasize in nutrient-poor peritoneal environments.

Prior evidence reveals that serum cholesterol and LDL levels correlate with disease aggressiveness, highlighting the potential significance of cholesterol access in ovarian cancer spheroids. We demonstrate that a compound targeting OSBP/ORP4 exhibits nanomolar anticancer activity against in vitro ovarian cancer spheroids and clinical ovarian cancer patient ascites, surpassing the efficacy of SOC drugs like paclitaxel, cisplatin, and carboplatin.

OSBP regulates intracellular cholesterol movement and is hypothesized to act as an overall lipid sensor, while ORP4's function remains elusive but is highly expressed in ovarian cancer. We propose that targeting OSBP and ORP4, as well disrupting cholesterol transport and usage, may exploit the sensitivity of ovarian cancer spheroids, as evidenced by lipid depletion and statin-cholesterol biosynthesis blocking, enhancing the anticancer activity of OSBP/ORP4 targeting natural compound OSW-1, but not SOC drugs.

Our findings support the potential development of OSBP-specific and ORP4-specific compounds, offering insights into these intriguing targets. This research opens doors to precision cancer treatments and a deeper understanding of cholesterol-related mechanisms in ovarian cancer."

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HERITABLE VARIATION IN GENOME ORGANIZATION IN CANCER

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The human genome is spatially organized within the nucleus, and heterochromatin is kept separate from euchromatin. Genome organization plays a role in cell function and is disrupted in cancer cells. Previous research has shown that low levels of linker histone H1, which is associated with heterochromatin, are highly correlated with cancer cell proliferation and cancer stem cell fate, linking heterochromatin specification to intra-tumor heterogeneity. I seek to understand the role of genome organization in intra-tumor heterogeneity. I use HCT-116 human colorectal carcinoma cells to investigate the variability of genome organization in cancer cells to determine whether genome organization is a variable and heritable trait in cancer cells. I sparsely plated the cell line to obtain colonies from single cells to investigate heritability. I performed DNA fluorescence in situ hybridization, (FISH), and measured heterogeneity by comparing distance distributions between colonies and calculating the coefficients of variation in the pooled population. As expected, facultative heterochromatin marked by trimethylation of lysine 27 on histone 3 exhibited more variability in cancer cells than in normal immortalized cells (IMR90). Furthermore, I identified specific probe pairs in cancer cells that exhibit heritable variation, which was not observed in normal cells. While heterochromatin organization appeared heritable after 10 days of colony growth, subcloning revealed that heterochromatin organization was not heritable after a month of continuous culture. We conclude that heterochromatin organization is transiently heritable in HCT116 colorectal carcinoma cells. Future experiments will test the duration of this heritability and its generalizability across different cancer cell lines.

DEVELOPMENT OF AN ANGIOTENSIN TARGETED PROBE DETECTS ORTHOTOPIC PDAC

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Background

Angiotensin receptor role in progression and development of pancreatic ductal adenocarcinoma (PDAC) is well established. We explored these receptors for the non-invasive detection of PDAC in-vivo setting. We developed and tested an Angio-1 750 NIR probe for detection using multispectral optoacoustic imaging in orthotopic mice model.

Methods

Angio-1 750 NIR probe was developed using Angiotensin-1 peptide conjugated to HiLyte Fluor C2 maleimide 750 NIR dye to detect the overexpressed receptor on pancreatic cancer cells. To confirm the differential binding of Angio-1 probe with pancreatic cancer cells (S2VP10 and PANC-1) in comparison to the Hep3B cells, flow cytometric analysis was performed using Angio-1 555 probe which was developed by conjugation of Angio 1 peptide with C2 maleimide 555 dye. Hep3B cells served as a negative control due to less expression of membranous ATR-1 receptor. Further Angio-1 NIR probe treated cells were imaged using NIR based odyssey imaging to confirm binding and detection. Athymic nude mice implanted with S2VP10 L cells were allowed to grow tumor for 5 days. Tumor-specific uptake of Angio-1 750 probe injected intra venously was evaluated using multispectral optoacoustic imaging (MSOT) at 3 and 24 hours post injection. Control mice were injected with the Indocyanine green (ICG) which serves as an untargeted control for the in vivo experiment.

Results

The Angiotensin-1 peptide conjugation with 750 and 555 dye was confirmed using UV-Visible spectrophotometric analysis. Flow cytometry confirmed Angio-1 probe had increased binding in S2VP10 cells with higher expression of angiotensin1-R vs low angiotensin-1R expressing Hep3B cells with mean fluorescence intensity values demonstrated 48 % positive S2VP10 cell population compared with 28% positive Hep3B cell population ($P<0.05$). In vitro cellular uptake analysis revealed 2-folds higher uptake of Angio-1 750 NIR probe in S2VP10 cells than the Hep3B cells ($P<0.05$). MSOT analysis indicated pancreatic tumor uptake of Angio-1 750 NIR probe in S2VP10 orthotopic tumors after 3 and 24 hours of intravenous administration. ICG injected mice did not show any signal at 3- and 24-hours post injection.

Conclusion - Our findings indicated tumor-specific uptake abilities of angio-1 750 NIR probe due to binding with overexpressed angiotensin receptor in PDAC tumor tissue in vitro and in vivo settings.

LEVERAGING HIGH VARIANT ALLELE FREQUENCIES (VAF) OF DNA DAMAGE REPAIR (DDR) MUTATIONS (MUTS) IN LIQUID BIOPSY (LBX) AS A SURROGATE FOR GERMLINE TESTING AND IMPLICATIONS FOR PRECISION MEDICINE

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BACKGROUND

LBx based next-generation sequencing (NGS) provides a minimally invasive means to detect true DDR muts as well as DDR muts that represent clonal hematopoiesis of indeterminate potential (CHIP), and in certain cases identifying high VAF DDR muts of suspected germline origin. Herein, we aim to address the knowledge gap in interpreting these findings to guide germline testing.

METHODS

We retrospectively collected data on patients (pts) with cancer who underwent LBx with *FoundationOne Liquid CDx* (311 gene panel) from 2022-2024 and tissue biopsy (TBx) based NGS using either Caris Life Sciences or FoundationOne CDx. A panel of 22 muts directly involved in the DDR pathway were designated as DDR muts. Findings from LBx and TBx were reported using descriptive statistics. Best objective clinical responses were evaluated using RECIST v1.1.

RESULTS

The study cohort consisted of 637 pts tested using LBx, with the majority being male (62.6%; n=399) and white (81%; n=517). Lung (24.2%; n=154), prostate (16.7%; n=106), and colorectal cancer (14.9%; n=95) were the top 3 cancer types.

On LBx, 203 pts (31.8%; n=203/637) were identified to have one or more DDR muts. Paired testing with LBx and Tbx was available for 221 pts of which 28 (12.6%) pts had ‘true CHIP’ (identified on LBx but not on TBx), all contributed by ATM and CHEK2 (50% each; n=14/28). Of pts who had paired LBx and TBx (n=221), 24 pts (10.8%) had the same DDR mut on both, suggesting likely somatic origin (True DDRs), the most common being ATM (25%; n=6/24), PALB2 (12.5%; n=3/24) and CDK12 (12.5%; n=3/24). Using a linear mixed-effects model to

account for patient- and gene-level variability in VAF, true DDR muts had a significantly ($p < 0.001$) higher VAF (median: 46.8, IQR: 49.6, n = 26) compared to true CHIP DDRs (median: 0.24, IQR: 0.29, n = 31).

LBx revealed potential germline implications based on high VAF in 7.9% pts (n=50/637) of which 45 pts had DDR muts. Genetic referrals were initiated in 48% (n=24/50) with subsequent confirmatory germline testing done for 66.6% (n=16/24), all confirming germline muts(table 1). Notably, for the 52% (n=26/50) without genetic referrals, 73% (n=19/26) lacked documentation of a referral discussion. Out of the 50 pts with muts likely of germline origin, 19 were enrolled in phase-1 clinical trials, with 6 receiving matched therapies targeting DDR muts (PARP and ATR inhibitors). Of these, 1 had a partial response (CHEK2) and 3 had stable disease (1-MUTYH, 2-PALB2).

CONCLUSION

LBx can be used as a potential surrogate indicator of likely germline muts as evidenced by high VAFs. Our findings underscore the need for improved interpretation of LBx reports to guide timely genetic referrals and confirmatory germline testing.

Table 1

Gene	**Median VAF (IQR)**
BAP1 (n=1)	52.4% (52.4-52.4)
MUTYH (n=2)	51.3% (50.7–51.9)
CHEK2 (n=2)	51.0% (50–52)
ATM (n=2)	50.2% (49.8–50.6)
BRCA2 (n=4)	50.0% (48.5–52.2)
PALB2 (n=2)	48.4% (46.7–50.2)
MSH6 (n=1)	46.6% (46.6-46.6)

A DROSOPHILA STUDY IDENTIFIES IPLA2-VIA AS POTENTIAL NOVEL CHEMOPREVENTION TARGET FOR HPV-INDUCED CANCER

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High-risk human papillomaviruses (HR-HPVs) are responsible for almost all cervical malignancies as well as considerable proportion of vaginal, vulvar, penile, and oropharyngeal cancers worldwide. Current treatments for cervical cancer are limited to radiotherapy and chemotherapy and besides an immunotherapy-based therapeutic for advanced stages of cancer, there is no molecularly targeted therapeutic as standard-of care for cervical cancer treatment or prevention. Therefore, there is a critical need for development of novel molecularly targeted interventions. HR-HPVs function by persistent expression and action of two viral oncogenes E6 and E7. E6 with the assistance of human E3 ubiquitin ligase (hUBE3A) targets several cellular proteins including tumor suppressor protein, p53 and select members of PDZ domain containing proteins for proteasomal-mediated degradation. For development of novel molecularly targeted therapies, understanding the actions and mechanisms of E6 and E7 is crucial. Using a *Drosophila* model of HPVE6 plus hUBE3A and performing a large-scale deficiency screening we identified the calcium-independent phospholipase A2 VIA (iPLA2-VIA), as a gene whose single deleted copy suppresses morphological defects caused by co-expression of E6 and hUBE3A. These results were confirmed using two null alleles of iPLA2-VIA. We show that reduction of iPLA2-VIA suppresses E6+hUBE3A-induced perturbed ommatidial organization and proteasomal degradation of PDZ domain protein Magi. We further demonstrate that E6+hUBE3A expression alters the level of iPLA2-VIA in the mitochondria and leads to mitochondrial deficiencies and ROS release. Further analysis revealed that E6 alters the level and localization of both protein isoforms of iPLA2-VIA, PA and PB. We find that the PA isoform that is predominantly cytoplasmic translocate to mitochondria and the PB isoform which is predominantly mitochondrial is present as cytoplasmic aggregates and punctuated. These results suggest that iPLA2-VIA is likely to play a role in E6-induced mitochondrial deficiencies. To gain insight into the role of iPLA2-VIA in E6-associated cellular perturbation, we are currently conducting immunoprecipitation experiments to identify the interactors of PA and PB protein isoforms in E6+hUBE3A-expressing cells. Furthermore, given the role of iPLA2-VIA in lipid metabolism and membrane homeostasis we have performed lipidomic and are currently in the process of data analysis. Given that the human homolog of iPLA2-VIA, PLA2G6, can functionally replace its *Drosophila* counterpart, suggests a conserved mechanism of action. Hence, the *Drosophila* studies are combined with mammalian cell line studies for validation of *Drosophila* findings and to further demonstrate the potential of iPLA2-VIA as novel chemoprevention target for cervical cancer.

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

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Triple-negative breast cancer (TNBC) is an aggressive subtype with limited treatment options and poor prognosis, necessitating innovative therapeutic strategies. Our study explores the potential of combining photothermal therapy (PTT) with immunomodulation to enhance tumor regression and improve survival outcomes in a preclinical TNBC model. By integrating targeted thermal ablation with immune stimulation, we aim to develop a more effective and synergistic treatment approach.

We utilized single-walled carbon nanotubes (SWCNTs) conjugated with annexin A5 as a targeted agent for photothermal therapy (PTT) at 45°C and 55°C. Before administering the conjugate *in vivo* in the 4T1 TNBC mouse model, we conducted an *in vitro* imaging study to evaluate its specificity using EMT6 breast cancer cells and HUVEC endothelial cells. Confocal laser scanning microscopy (Leica SP8, 63x oil objective) confirmed that SWCNT-annexin A5 conjugated to Alexa Fluor™ 488 selectively bound to EMT6 cells, while exhibiting minimal binding to HUVEC cells. Fluorescence intensity analysis showed significantly higher signals in EMT6 cells compared to their intrinsic autofluorescence, validating the conjugate's tumor-targeting capability.

We conducted an *in vivo* study using EMT6 tumor-bearing mice, where a combination of photothermal therapy and immunomodulation (IMQ and anti-PD-1) resulted in an 80% survival rate for up to 100 days. Encouraged by these promising findings, we extended our study to the aggressive 4T1 TNBC mouse model. In this model, mice bearing 4T1 tumors were treated with photothermal therapy in combination with immunomodulatory agents, including Imiquimod (IMQ) and anti-PD-1 checkpoint blockade, followed by surgical tumor resection. Preliminary results demonstrated significant tumor regression and extended survival in treated mice. Further immune analysis through cytokine profiling by ELISA and flow cytometry revealed enhanced immune activation in response to the combination therapy, highlighting its potential as an effective treatment strategy for TNBC.

As a next step, we aim to refine our approach by implementing local photothermal therapy, wherein an optical fiber will be inserted directly into the tumor for precise heat delivery. Unlike surface irradiation, this technique ensures deeper and more uniform thermal distribution within the tumor mass, reducing potential heat dissipation and improving therapeutic efficacy. Given TNBC's high metastatic potential

and resistance to conventional therapies, optimizing PTT with precise tumor targeting may offer a more effective strategy for eliminating cancer cells and preventing recurrence.

Our findings underscore the potential of combining photothermal therapy with immunomodulation as a promising therapeutic avenue for TNBC. This presentation provides an overview of our research and outlines future directions aimed at optimizing treatment strategies to improve patient outcomes.

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INDIVIDUAL LEVEL BARRIERS TO AND FACILITATORS OF LOWERING ULTRA-PROCESSED FOOD INTAKE

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Introduction: Excessive ultra-processed food (UPF) intake is associated with increased risk of obesity and cancer. Despite documented risks, UPF intake comprises nearly 60% of calories in diets of US adults. Relatively little is known regarding precise reasons for excessive UPF intake, nor how individuals respond to decreases in UPF intake in free-living contexts. The objective of this study was to characterize individual responses to attempting to lower UPF intake in free-living adults.

Methods: Semi-structured interviews (SSIs) were conducted with participants following a randomized controlled trial during which they were educated on UPF and asked to abstain from consuming them for a period of six months. SSIs were delivered according to the participants' level of success in lowering their UPF intake over six-month intervention period. Questions were designed to capture general perceptions as well as barriers to and facilitators of lowering UPF per the Health Belief Model. Inductive coding was utilized by two members of the research team to code themes and subthemes under barriers and facilitators.

Results: Interviews are underway with a total of n=60 participants. Qualitative analysis is ongoing, though a preliminary examination of barriers indicates the following themes: Insufficient Knowledge, Food-related Misperceptions, Execution Difficulty, Interpersonal Challenges, UPF Appeal, Sociocultural Backgrounds, and Practical Logistics. Facilitators identified include Daily Patterns, Health Concerns, Increased Motivation, Objective Effects, Improved Knowledge, Interpersonal Support, and Sociocultural Background. Illustrative quotes include "…It's just a nostalgia feeling. It's something that just brings back like a happy memory or something." (Barrier: UPF Appeal (theme), Preference for Familiarity (subtheme)) and "the non-ultra processed foods…have made me feel better. Just within my like my own body." (Facilitator: Objective Effects (theme), Objective health benefits (subtheme)).

Conclusion: This study is providing critical insights into how individuals perceive lowering their UPF intake in free-living contexts, including barriers and facilitators. These data will be instrumental in designing future individual-level interventions, including in specific high-risk groups.

HEPATOCYTE MLKL LINKS AGING- AND OBESITY-ASSOCIATED INFLAMMATION TO HCC DEVELOPMENT

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Hepatocellular carcinoma (HCC), the primary tumor of the liver, represents the second leading cause of cancer related mortality with a five-year survival of about 18%. Among the various etiological factors implicated in the development of HCC, metabolic dysfunction-associated steatotic liver disease (MASLD) has recently surfaced as a prominent contributor. Mechanistically, non-resolving chronic inflammation is proposed to be a major contributor in the development and progression of HCC. Necroptosis is a programmed cell death pathway that plays a major role in inflammation and MLKL (Mixed lineage kinase domain-like protein) is the key effector molecule of the pathway. We reported that MLKL protein expression is increased in the liver of a mouse model of diet induced Metabolic dysfunction-associated steatohepatitis (MASH)-related HCC and blocking MLKL (*Mlkl*$^{-/-}$ mice) reduced inflammation, tumor multiplicity and tumor volume. Based on our finding that hepatocytes are the primary liver cell type that express MLKL, we hypothesized that hepatocyte MLKL is a key mediator in the pathogenesis of MASLD driven HCC. To test our hypothesis, we developed and characterized hepatocyte specific MLKL knockout (MLKL^{HepKO}) mice by injecting AAV8-TBG-iCre (MLKL^{HepKO}) or AAV8-TBG-Null (Control) virus. The mice were fed a normal chow diet (CD) or MASLD-inducing western diet (WD) diet for 15 months, starting at 2 months of age. In the WD diet fed MLKL^{HepKO} mice, the body weight and liver weight remained comparable between the corresponding study groups. Strikingly, WD diet feeding in control mice resulted in 70% tumor incidence when compared to 37.5% in the MLKL^{HepKO} group fed the same diet. Remarkably, the control group when fed with WD exhibited greater tumor multiplicity and tumor volume, while MLKL^{HepKO} had reduced tumor multiplicity and volume. *In vitro* studies using a human liver cancer cell line, HepG2, showed that blocking MLKL reduced cell proliferation and sphere formation compared to corresponding controls, as confirmed through genetic (siRNA) and pharmacological (necrosulfonamide) inhibition. In conclusion, our data highlights a critical role of MLKL in liver cancer with prospective roles in tumor initiation and progression. It also points towards the possible role of MLKL in exerting non-necroptotic functions in promoting cancer cell survival and proliferation. Our findings identify hepatocyte MLKL as a key mediator linking aging to HCC, highlighting its potential as a therapeutic target in the emerging field of gero-oncology to mitigate liver cancer risk in aging and obesity.

TRANSURETHRAL ULTRASOUND ABLATION OF THE PROSTATE (TULSA-PRO) REDUCES PSA LEVELS AND FUNCTIONAL SIDE EFFECTS COMPARED TO HIGH-INTENSITY FOCUSED ULTRASOUND ABLATION (HIFU)

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Introduction: MRI-guided Transurethral Ultrasound Ablation of the Prostate (TULSA-PRO) and High-Intensity Focused Ultrasound Ablation (HIFU) are ablative treatments for localized prostate cancer (PCa). Both procedures aim to provide effective oncological treatment while minimizing adverse effects. However, since TULSA is an emerging technology, the relative benefits compared to HIFU are unknown. This retrospective study compares quantitative and functional outcomes of TULSA and primary HIFU to evaluate their effectiveness in treatment.

Methods: We retrospectively reviewed our institutional database to identify patients with prostate cancer undergoing primary treatment who received TULSA (n=9) or HIFU (n=16). Pre-treatment clinical measures included but were not limited to prostate-specific antigen (PSA), PSA density, and Prostate Imaging-Reporting And Data System (PI-RADS) score. Primary post-treatment clinical measures included 6-month PSA, 6-month PSA density, and 6-month prostate volume. Clinician-derived functional outcomes such as erectile dysfunction (ED) and lower urinary tract symptoms (LUTS) were also measured. Basic statistical analysis was performed using a Two-Sample t-test assuming equal variances.

Results: The mean PSA at 6 months post-TULSA was 1.1 ± 0.6 ng/mL and the mean PSA at 6 months post-primary HIFU was 2.5 ± 1.8 ng/mL. The PSA level with TULSA was significantly lower compared to primary HIFU 6 months post-treatment ($p < 0.05$). At 6 months post-treatment, the mean PSA density for TULSA patients was 0.03 ± 0.01 ng/mL/cm3, significantly lower than the 0.10 ± 0.08 ng/mL/cm3 observed in primary HIFU patients ($p < 0.05$). In the 12-month follow-up period, one patient from each group developed new-onset ED. In addition, 55% of patients who received TULSA treatment and 37.5% of patients who received primary HIFU reported improved LUTS.

Conclusions: In this early adoption study, our findings demonstrate a significantly lower post-treatment PSA level in patients treated with TULSA compared to HIFU. Postoperative patient-reported quality of life assessments suggest a trend towards better functional outcomes in TULSA than with HIFU. While further research is required to elucidate differences between TULSA and HIFU, both treatments are safe and acceptable for treating localized PCa.

TARGETING PANCREATIC CANCER: OPTIMIZING PH-LOW INSERTION PEPTIDES WITH SERINE, ASPARTIC ACID, AND PHENYLALANINE MODIFICATIONS

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Purpose: Pancreatic cancer has one of the lowest relative survival rates of only 12.8%, with just 20% of patients being eligible for surgical resection. Achieving R0 resection is imperative, as it forms the most definite curative treatment strategy. pH low insertion peptides (pHLIPs), a novel class of targeted imaging agents, are being developed for use with multispectral optoacoustic imaging (MSOT) for potential clinical or intraoperative applications. However, existing pHLIPs have limitations in dynamic range and solubility. To address these issues, 3 new pHLIP variants, V7Ser, V7Asp, and V7Phe, were designed to enhance both solubility and dynamic range for identifying the acidic tumor microenvironment in pancreatic cancer.

Methods: V7, KV7, V7Ser, V7Asp, and V7Phe peptides were synthesized using microwave chemistry, then removed from resin, lyophilized, and rehydrated. The peptides were conjugated with HiLyte 750 dye via maleimide chemistry and confirmed through spectroscopy. Pancreatic cancer cell lines S2VP10 and S2013 were treated with each probe at pH 7.4, pH 6.8, and pH 6.6. Probe uptake was assessed using near-infrared fluorescence imaging.

Results: V7Phe demonstrated a significantly higher signal in vitro than V7 at both pH 7.4 and pH 6.6 ($p<0.01$). V7Phe-750 also exhibited greater signal in more acidic conditions ($p<0.01$). Additionally, the V7Ser and V7Asp showed increased signal in more acidic conditions ($p<0.01$), and an enhanced dynamic range compared to the commercial KV7 in both cell lines. Although solubility was moderately improved, V7Phe-750 did not show an enhanced dynamic range compared to V7-750, with the ratio of signal at pH 6.6 to 7.4 being 1.19 for V7Phe-750 versus 1.39 for V7-750 ($p=0.21$) across both cell lines.

Conclusion: V7Ser, V7Asp, and V7Phe effectively target acidic tumor microenvironments, demonstrating improvements in peptide solubility through serine, aspartic acid, and phenylalanine substitution respectively. Enhancement in dynamic range was observed for V7Ser and V7Asp, but not for V7Phe.

MECHANISMS DETERMINING WHERE DNA REPLICATION INITIATES IN THE HUMAN GENOME

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The selection of replication origins is a defining characteristic of DNA replication in higher eukaryotes, yet its mechanism in humans has not been well-defined. In yeast, origin selection involves replication initiation factor (Sld3-Sld7) recruitment to origins during G1. In this study, we use Cut&Run to examine genomic binding locations for TICRR and MTBP, the Sld3 and Sld7 orthologs. We have constructed two HCT116 human colorectal cancer cell lines in which the endogenous TICRR or MTBP loci were tagged at their carboxy-termini with mClover. Using these cell lines, we have shown that TICRR and MTBP genomic binding sites can be mapped using Cut&Run with anti-GFP antibody. We mapped TICRR and MTBP binding throughout the cell cycle by performing experiments in asynchronous, G1, or G2-arrested cells. Peaks of TICRR and MTBP binding frequently overlap at Ini-seq replication origins. Interestingly, our data show that TICRR and MTBP binding patterns are less defined in asynchronous cells than G1, possibly due to cell cycle phase-specific recruitment of TICRR-MTBP to replication origins in human cells. Further, we asked if TICRR-MTBP binding was dependent on the presence of licensed origins. Using dox-inducible non-degradable Geminin cell lines to prevent loading of MCMs, we performed Cut&Run for TICRR and MTBP. The results showed binding for TICRR and MTBP in the absence of licensed origins was comparable to controls. This data in human cells provides a model that diverges from mechanisms that have been shown in yeast.

METABOLIC-EPIGENETIC REGULATION OF NEUTROPHILS IN PANCREATIC CANCER

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Pancreatic ductal adenocarcinoma (PDAC) remains one of the most lethal malignancies, with a 5-year survival rate of under 12%. PDAC is characterized by a highly immunosuppressive tumor microenvironment (TME), where metabolic reprogramming leads to excessive lactate production. Lactate is a byproduct of tumor glycolysis that can be converted to lactyl-CoA and added into histones as a novel epigenetic modification known as histone lactylation. Recent studies showed histone lactylation role in reprogramming some immune cells. However, its contribution to shaping neutrophil phenotypes in PDAC is less understood. Tumor-associated neutrophils (TANs) are a myeloid component of the TME, but their role can range from anti-tumor (N1) to pro-tumor (N2) phenotypes. We performed a comprehensive bioinformatic analysis to determine how lactate-driven histone lactylation might influence neutrophil infiltration and polarization in PDAC.

We used The Cancer Genome Atlas (TCGA) PAAD cohort (n=177) to perform single-sample Gene Set Enrichment Analysis to stratify samples into high vs. low histone lactylation groups based on expression of histone lactylation-related genes. We then applied CIBERSORT to estimate the proportions of different immune cell types, including neutrophils, within tumor tissues. We compared differentially expressed genes (DEGs) between high vs. low lactylation groups to identify potential functional pathways and neutrophil-related gene signatures.

Our findings show a positive correlation between predicted histone lactylation status and neutrophil infiltration. We observed the high histone lactylation group showed a higher predicted proportion of neutrophils. Also, neutrophil-specific markers (CD177 and CEACAM8) were upregulated in this group which shows a potential increase in TANs in the PDAC TME. Moreover, neutrophils in the high histone lactylation group showed upregulation of genes such as OLR1, RETN and NCF2, which are often linked to immunosuppressive or tumor-promoting functions (N2). In contrast, fewer neutrophils were shown in the low histone lactylation group and these cells had higher expression of genes like LTF, CTSG and PADI4, which are likely to suggest more classical antimicrobial or cytotoxic roles (N1).

In conclusion, our results suggest that a high-lactate environment in PDAC can increase neutrophil infiltration as well as their shifting toward a pro-tumor phenotype, potentially through histone lactylation. We observed a strong link between lactate metabolism, histone modifications and neutrophil plasticity. However, it is still unclear whether lactate itself or the epigenetic changes caused by histone lactylation are driving these effects. We hypothesize that immune-related gene promoters might be particularly affected by histone lactylation which can help neutrophils polarize to a more pro-tumor role. Since our analysis is based on bioinformatics, we need further experiments to confirm these connections. But overall, these results highlight lactate metabolism and its impact on neutrophil function as potential targets for future therapies in pancreatic cancer.

CASE REPORT: EPITHELIOID HEMANGIOENDOTHELIOMA AT THE JUNCTION OF THE INTERNAL JUGULAR AND SUBCLAVIAN VEIN

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Background: Epithelioid hemangioendothelioma (EHE) is an exceptionally rare vascular tumor, accounting for less than 1% of vascular neoplasms, with an estimated incidence of less than 1 per million people per year. Due to its rarity, much remains unknown about its etiology and clinical presentation. This case report highlights a unique presentation of EHE at the confluence of the left subclavian and internal jugular veins, presenting distinct diagnostic and therapeutic challenges.

Case presentation: A 65-year-old female presented to the clinic with progressive left-sided neck swelling and dysphagia for the past 6 months. Fine needle aspiration (FNA) of the left supraclavicular mass was suspicious for malignancy with inconclusive flow cytometry results. Subsequent core needle biopsy confirmed epithelioid hemangioendothelioma. The patient underwent direct laryngoscopy, left selective neck dissection (levels 2–4), left internal jugular vein sacrifice, and reconstruction of the left subclavian and innominate veins using a saphenous vein graft. Due to positive surgical margins, the patient is scheduled to receive adjuvant radiation therapy.

Discussion: This case discusses the challenges of diagnosing and managing EHE in a complex vascular region. Treatment is complicated by the tumor's proximity to critical vascular structures, requiring a multidisciplinary team approach to achieve optimal outcomes.

Conclusion: Early recognition of EHE in complex anatomical locations is essential for optimal conditions. A multidisciplinary approach with otolaryngologists, vascular surgeons, radiologists, pathologists, and oncologists is essential for accurate diagnosis and effective treatment. Further research is needed to enhance understanding and establish standardized management protocols for EHE in the head and neck region

OMITTED ABSTRACTS

Abstracts Omitted per Presenters' Request

Translational Oral

CD163+ TUMOR-ASSOCIATED MACROPHAGE EVASION CONTRIBUTES RADIATION RESISTANCE AND POOR PROGNOSIS IN ESTROGEN RECEPTOR-NEGATIVE BREAST CANCER

Suryakant Niture, Subhajit Ghosh, Jerry Jaboin, and Danushka Seneviratne

DISRUPTION OF CANCER SURVIVAL MECHANISMS VIA OMEPRAZOLE-MEDIATED AUTOPHAGY IN PANCREATIC ADENOCARCINOMA

Karl N. Thomas[1], Rohit Singh[2], Lacey McNally[2]

TARGETING CHEMORESISTANT OVARIAN CANCER WITH MEBENDAZOLE: A PROMISING APPROACH TO OVERCOME PLATINUM RESISTANCE

Penta Dhanamjai[1], Dey Debasish K[1], Benbrook Doris M[1], Wang Lin[2], Bieniasz Magdalena[2], Chandra Vishal[1], Dockery LE[1], Rai Rajani[1#]

Cancer Prevention and Control Oral

E-CIGARETTE AEROSOLS TO ENHANCE NRF2-MEDIATED PATHWAYS AND CANCER STEMNESS IN HUMAN ORAL CELLS.

Vengatesh Ganapathy[1], Jimmy Manyanga[1], Gautham Chengizkhan[1], Mayilvanan Chinnaiyan[1], Balaji Sadhasivam[1,2], Ilangovan Ramachandran[5], David A. Rubenstein[6] and Lurdes Queimado[1,3,4].

EFFECTS OF ALIGNMENT AND MISALIGNMENT IN SELF- AND PARTNER-ORIENTED MOTIVATIONS TO QUIT ON INDIVIDUAL AND JOINT CESSATION OUTCOMES IN DUAL-SMOKING COUPLES

Catherine S. Nagawa, PhD; Fangzhi Luo, MS; Ye Shen, PhD; James M. MacKillop, PhD, Steven R. H. Beach, & Michelle vanDellen, PhD

DOES CANNABIS BOOST OR HALT YOUR INFLAMMATORY AND IMMUNE RESPONSES?

Adele Hammoudi[1], Mayilvanan Chinnaiyan[1], Daniel Brobst[1], Geraldine Chissoe[1], Balaji Sadhasivam[1,2], Vengatesh Ganapathy[1], Lurdes Queimado[1,3,4*]

THE IMPACT OF CANNABIS USE ON SMOKING AMONG ADULTS WITH LOW-INCOME ENROLLED IN A SMOKING CESSATION TRIAL

Darla E. Kendzor, Ph.D., Amy M. Cohn, Summer G. Frank-Pearce, Laili Kharazi Boozary, Yunyu Tsai, Michael S. Businelle, Roma Thakur, Morgan Davie, and Shannon Gwin

Cancer Biology Poster

KAT5 MEDIATES THERAPY-INDUCED PLASTICITY IN GLOBLASTOMA

Farzaneh Amirmahani, Saurav Kumar, Ashley Mathew, Sree Deepthi Muthukrishnan

UNDERSTANDING THE MECHANISMS OF DORMANT ORIGIN FIRING DURING DNA REPLICATION

Md Shahadat Hossain, Tyler D Noble, Kimberlie A Wittig, Courtney G Sansam, Christopher L Sansam

ROLE OF JMJD4 IN BREAST AND PANCREATIC CANCER

Hanlin Jiang, Sangphil Oh, Shin Sook, Ruicai Gu, Ralf Janknecht

GLIOBLASTOMA-ASSOCIATED VASCULAR CELLS REWIRE MICROGLIA TOWARDS AN IMMUNOSUPPRESSIVE AND PRO-TUMORIGENIC STATE VIA NFATC1 SIGNALING

Saurav Kumar, Farzaneh Amirmahani, Sree Deepthi Muthukrishnan

HEPATOCYTE-SPECIFIC MLKL REGULATES CELL CYCLE AND TUMOR DEVELOPMENT IN DIET-INDUCED MASLD

Phoebe Ohene-Marfo, Sabira Mohammed, Chao Jiang, Albert L Tran, Shylesh Bhaskaran, Georgescu Constantin, Jonathan Wren, and Deepa Sathyaseelan

Cancer Prevention & Control Poster

IMPLEMENTATION OF ARTICLES 11, 13, AND 16 OF WORLD HEALTH ORGANIZATION FRAMEWORK CONVENTION ON TOBACCO CONTROL IN THE ASEAN REGION – A SCOPING REVIEW

Thanh Cong Bui, MD, DrPH, Shweta Kulkarni, Bijay Rimal, Shari Clifton, Laura A. Beebe

ORAL INFLAMMATION AND IMMUNE REGULATION IN CANNABIS AND TOBACCO SMOKERS

Mayilvanan Chinnaiyan, Gautham Chengizkhan, Daniel Brobst, Adele Hammoudi, Geraldine Chissoe, Balaji Sadhasivam, Vengatesh Ganapathy, Lurdes Queimado

N-NITROSONORNICOTINE EXPOSURE ENHANCES CANCER STEMNESS MARKERS IN HEAD AND NECK SQUAMOUS CELL CARCINOMA

Ravi Gor, Christine Vo, Anthony Phan, Vengatesh Ganapathy, Lurdes Queimado, Balaji Sadhasivam

USING PARTNER REFERRAL TO INCREASE HUMAN PAPILLOMAVIRUS VACCINE UPTAKE WITHIN HIDDEN POPULATIONS

Jernigan Cameron, Tina N. Le, Khue-Tu Doan, Summer G. Frank-Pearce, Darla E. Kendzor, Jasmin Kurien, Douglas A. Drevets, Patrick McGough, Cate Moriasi, and Thanh Cong Bui

EXPLORING THE ROLE OF OBESITY-ASSOCIATED EXTRACELLULAR MATRIX IN LOCAL BREAST CANCER PROGRESSION

Malika Sekhri, Stevi Johnson-Murguia, Alexander Filatenkov, Queen M. Pierre, Michael Kinter, Rebecca L. Scalzo, Bethany N. Hannafon, and Elizabeth A. Wellberg

CHRONIC EXPOSURE TO E-CIGARETTE AEROSOLS IMPAIRS IMMUNE RESPONSES THROUGH TLR-MEDIATED INTERFERON SIGNALING

Sulfath Thottungal Parambil, Vengatesh Ganapathy, Constantin Georgescu, Dan Brobst, Jimmy Manyanga, Jonathan Wren, David A. Rubenstein, and Lurdes Queimado

A NOVEL IMAGING PLATFORM FOR RENAL CARCINOMA BIOPSY NAVIGATION

Chen Wang, Haoyang Cui, Qinghao Zhang, Paul Calle, Feng Yan, Kar-Ming Fung, Zhongxin Yu, Ajay Jain, Sean Duguay, William Vanlandingham, Nathan A. Bradley, Sanjay G. Patel, Chongle Pan, Qinggong Tang

Cancer Therapeutics Poster

INCIDENCE OF AKI AND KIDNEY REPLACEMENT THERAPY (RRT) AFTER OUTPATIENT CHIMERIC ANTIGEN RECEPTOR T (CAR-T) CELL THERAPY IN PATIENTS WITH HEMATOLOGICAL MALIGNANCIES

Ayesha Aijaz, Adolfo Jose Diaz-Barba, Bibi Maryam, Noha Soror, Nivedita Popuri, Satya Sai Venkata Lakshmi Arepalli, Aminah Tayyab, Silas Day, Michael Machiorlatti, Taha Al-Juhaishi

THE IMPACT OF OPTIMIZED ROUTING FOR MOBILE LUNG CANCER SCREENING

Kiana Amani, Soheil Hemmati

IMMUNOGENIC CELL DEATH AND DAMPS SIGNALING AS IMMUNE MODULATORS: PEPTIDE AGGREGATION VIA THE CO-ASSEMBLY OF OPPOSITELY CHARGED PEPTIDE-BASED STRATEGIES

Enkhbolor Battumur, Beyza Sultan Aydin, Afan Hasić, and Handan Acar

OPTIMAL GRID PLACEMENT IN SPATIALLY FRACTIONATED RADIATION THERAPY USING DISCRETE MATHEMATICAL OPTIMIZATION MODELS

Grant Benson

ENHANCED VISUALIZATION OF GAS VESICLES BY EXPRESSING REPORTER GENE USING GAS VESICLE PROTEIN C

Elizabeth Dolan, Musarrat Amin, Sangpil Yoon, PhD

AN IN-VITRO STUDY OF ANTINEOPLASTIC EFFECTS OF DANDELION ON HUMAN DERMAL FIBROBLASTS AND CERVICAL CANCER CELLS

Ameera Noon, Kayley McBride, Melville B. Vaughan, Hari Kotturi, and Christina

A NOVEL WAY TO TARGET NON-SMALL CELL LUNG CANCER (NSCLC) TUMOR USING SMALL EXTRACELLULAR VESICLES (SEVS) BASED MONOCLONAL ANTIBODY

Seonghyun Ryu, Dongin Kim

TAMOXIFEN EFFECTS ON ADIPOCYTE PROGENITORS LINK BREAST CANCER THERAPY TO DIABETES RISK

Nisha S Thomas, Rebecca L. Scalzo, Elizabeth A Wellberg

LEVERAGING CANCER-DERIVED SMALL EXTRACELLULAR VESICLES FOR ANTIBODY-DRIVEN TARGETING IN OVARIAN CANCER

Maryam Firouzi, Changsun Kang, Xiaouyu Ren, Dongin Kim

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