Dual-Drug-Loaded Targeted Polymeric Nanoparticle Therapy for BRCA-Mutated Ovarian Cancer: Advancing Precision Treatment and Health Equity

Vailoces Miller; Naga Nakka, Ph.D.; Debabrata (Dev) Mukhopadhyay, Ph.D.
Dept. of Biochemistry and Molecular Biology
Dept. of Cancer Biology
Mayo Clinic
4500 San Pablo Rd. S
Jacksonville, FL 32224

Ovarian cancer is a leading cause of cancer-related deaths in women, with survival rates remaining around 30- 40%, and it is disproportionately lethal for marginalized women due to systemic health inequities. In hereditary cases, about 65%-75% cases involve BRCA1/2 mutations, which impair DNA repair mechanisms and result in cancer cells relying on alternative methods of repairing DNA damage. These pathways create vulnerabilities that can be targeted with platinum-based drugs such as Cisplatin and PARP inhibitors such as Olaparib. While these agents can work synergistically, treatment challenges persist due to differences in how they behave in the body and harmful side effects.

This study evaluated a dual-drug laden targeted polymeric nanoparticle designed to co-deliver Cisplatin and Olaparib directly to ovarian cancer. Its performance was compared with free-drug combinations and single-drug nanoparticle formulations. The dual-drug nanoparticle treatment produced the strongest anticancer effects, resulting in the greatest reductions in cancer cell viability, migration, and colony formation. Importantly, it demonstrated enhanced activity in BRCA-mutated ovarian cancer cells compared with non-BRCA-mutated cells.

These findings suggest that dual-drug nanoparticle delivery can improve the effectiveness and specificity of ovarian cancer treatment while potentially reducing side effects. This approach may contribute to the development of more effective precision therapies and help address disparities in access to personalized cancer care.

Aaron Wang

Quantitative Spatial Profiling of the Glioblastoma Immune Microenvironment Using Self-Supervised Computational Pathology

Background: Glioblastoma (GBM) exhibits profound intratumoral heterogeneity and a complex immune microenvironment that may influence tumor behavior and therapeutic response. We investigated whether routine hematoxylin and eosin (H&E) histology could quantitatively characterize GBM tumor-immune spatial architecture and whether self-supervised computational pathology representations encode these biological phenotypes.

Methods: Diagnostic whole-slide images from TCGA-GBM underwent image quality control, tissue segmentation, and spatial sampling, yielding 377 evaluable tumors. HoVer-Net with PanNuke-derived cell classes was used to identify neoplastic and predicted inflammatory nuclei and other cellular populations. Sampling-convergence analysis established 200 spatially distributed regions per tumor, producing 75,400 regions and 3.53 million detected nuclei. We quantified inflammatory abundance, immune-depleted regions, tumor-inflammatory proximity, inflammatory clustering, spatial entropy, intratumoral heterogeneity, and immune-rich niches. A DINO-style Vision Transformer was self-supervised on H&E regions from 262 training patients. Frozen representations were evaluated on held-out patients and compared with generic DINO and pathology foundation models UNI and CONCH.

Results: GBM demonstrated marked interpatient and intratumoral immune heterogeneity. Among 375 tumors evaluable for cellular composition, the median predicted inflammatory fraction was 12.3% (IQR, 3.7% - 23.1%; range, 0.3% - 58.1%), while the median tumor contained 21% of sampled regions without predicted inflammatory nuclei. Unsupervised analysis revealed structured variation in tumor-immune architecture, with the first two principal components explaining 81.2% of spatial-feature variance. In held-out tumors, the GBM-adapted representation strongly predicted immune-depleted region frequency (Spearman $\rho = 0.956$), tumor-inflammatory proximity ($\rho = 0.926$), spatial entropy ($\rho = 0.918$), and inflammatory abundance ($\rho = 0.866$). Spatial information remained after adjustment for overall inflammatory abundance, including immune-depleted regions ($\rho = 0.858$) and tumor-inflammatory proximity ($\rho = 0.806$). Generic DINO, UNI, and CONCH also strongly encoded these phenotypes, supporting representation-independent biological signal. However, 86.5% of the analytic cohort was White, highlighting limited demographic representation for subgroup validation.

Conclusions: Routine H&E histology contains quantifiable information describing GBM tumor-immune organization. Computational pathology revealed substantial variation in immune burden, spatial heterogeneity, and tumor-immune proximity and captured these phenotypes across multiple self-supervised and pathology-pretrained representations. These findings support scalable H&E-based profiling of the GBM immune microenvironment while emphasizing the need for more representative cohorts to ensure equitable validation of computational cancer biomarkers.

Aashrith Sai Thoutham

Title: Rural and Socioeconomic Disparities in Drive-Time Access to Phase 3 Lung Cancer Clinical Trials Across US Counties

Background: Geographic access to a participating site is a prerequisite for clinical trial enrollment. Prior national studies have demonstrated that many US counties, particularly those outside metropolitan areas, lack access to cancer clinical trials, but have largely characterized access as present or absent. As a result, it remains unknown how many trial sites are available to counties that do have access, and whether gaps in access concentrate in socioeconomically deprived counties. The objective of this national analysis was to evaluate the availability and depth of drive-time access to phase 3 lung cancer clinical trials across US counties by rurality and area deprivation.

Methods: Interventional, recruiting, phase 3 trials evaluating an anticancer drug or biologic for the treatment of lung cancer were identified from ClinicalTrials.gov (cohort frozen July 30, 2026). Drive times from population-weighted county centers to each recruiting trial site were estimated using a road-network routing model built on an August 2026 OpenStreetMap extract. Access was defined as at least 1 recruiting trial site within 60 minutes, and access depth was defined as the number of distinct physical sites reachable (0, 1, or ≥2). Counties were classified as metropolitan, larger nonmetropolitan, or rural or small town using the 2023 US Department of Agriculture Rural-Urban Continuum Codes, and socioeconomic deprivation was assessed using Area Deprivation Index quintiles. Annual county lung cancer deaths (2018-2022) were obtained from county mortality data, and suppressed counts were retained as bounds rather than imputed.

Results: A total of 57 trials with 951 unique site locations were included. Of the 3,109 counties analyzed, 1,406 (45.2% [95% CI: 43.5-47.0%]) had no recruiting phase 3 lung cancer trial site within 60 minutes. Rural or small-town counties were more likely than metropolitan counties to lack access (67.8% vs. 14.5%; RR: 4.68 [95% CI: 4.06-5.39]). Access was also less redundant in rural areas: only 10.8% of rural or small-town counties could reach 2 or more sites, compared to 60.5% of metropolitan counties, and 354 of 533 (66.4%) rural or small-town counties with access relied on a single site. The proportion of counties without access increased with area deprivation, from 24.4% in the least deprived quintile to 70.0% in the most deprived quintile, while the proportion with 2 or more sites decreased from 57.4% to 8.6%. This gradient was observed among metropolitan counties (9.6% vs. 35.5% without access), whereas rural or small-town counties had low access at every level of deprivation (58.7%-75.2% without access). Counties without access were home to 10.7% of the US population but accounted for 14.3%-16.2% of annual lung cancer deaths.

Conclusions: In this national analysis, nearly half of US counties had no recruiting phase 3 lung cancer trial site within a 60-minute drive, and access was least common and least redundant in rural and socioeconomically deprived counties. Counties without access carried a disproportionate share of lung cancer deaths. These results suggest that efforts to expand lung cancer trial networks should prioritize rural and deprived counties, where most counties with access depend on a single site.

Development and Evaluation of MICRA: A Computational Pipeline for Quantitative Cancer Microscopy Image Analysis

Ahmed Khan

Microscopy image analysis often requires multiple processing and measurement steps, which can make analysis time-consuming and difficult to standardize. This project developed MICRA, a Python-based computational pipeline that integrates established image-processing and segmentation methods into a standardized workflow for quantitative analysis of cancer microscopy images. The pipeline performs image preprocessing, background correction, segmentation, quality control, and feature extraction, producing quantitative measurements of staining intensity, cellular morphology, and spatial characteristics alongside annotated visual outputs. Microscopy images provided by a research laboratory were used to evaluate the pipeline. Pipeline performance was assessed based on segmentation and measurement outputs, quality-control results, and visual inspection of generated overlays. Rather than introducing new image-processing algorithms, this project evaluates the effectiveness of integrating established computational methods into a single reproducible workflow. The results demonstrate the pipeline's ability to process microscopy images and generate structured quantitative outputs while identifying images or regions requiring additional review. MICRA provides a standardized framework for quantitative microscopy analysis that can be further evaluated across different imaging conditions, staining methods, and biological datasets.

Akshara Guddeti

Novel Design of a Population-Optimized Neoantigen Panel to Increase Accessibility to mRNA-Based Immunotherapy Vaccines for Triple Negative Breast Cancer

The majority of mRNA-based immunotherapy vaccines require the need for personalized tumor sequencing and epitope discovery, resulting in high costs, limiting accessibility of this promising therapy to underserved communities. This study aimed to design a population-optimized panel of engineered neoantigens for the treatment of triple negative breast cancer (TNBC) using computational methods, which are applicable to the broader population reducing the need for individualized epitope discovery. A merged TCGA/METABRIC dataset of whole exome somatic mutation data was used to find recurrent missense hotspot mutations, which were then ranked according to the frequency of occurrence in patients. For top hotspot mutations, 9-11mer peptide windows on the mutation site were designed, with conservative anchor residue optimization achieved by allowing optimization at predicted MHC class I anchor residue positions, while maintaining the mutation site and TCR-facing residues. Candidate peptides were also screened using MHC binding affinity prediction, including differences in binding affinities between the mutated and wild-type peptides, as well as human proteome similarity screening to reduce the risk of autoimmune affects. Finally, a population coverage maximization algorithm was used to iteratively choose the designed peptides that maximize HLA population coverage while minimizing repetitiveness. The final output was the design of a panel of 11 engineered neoantigens, with computational modeling suggesting this panel provides 90% HLA coverage and mutation representation across TNBC. This panel supports the future development of standardized, broad-coverage mRNA-based immunotherapies that can reduce costs and increase accessibility compared to fully personalized approaches

Balancing Clinical and Social Determinants of Health in Cancer Clinical Trials: A Proposed Continuous-Covariate Minimization Framework

Alexander Healy
Pearland High School

Background: Minimization is commonly used in cancer clinical trials to improve treatment group balance on important prognostic factors, particularly in studies with limited sample sizes. However, traditional minimization approaches typically require continuous variables to be categorized before randomization. This practice may reduce prognostic information and obscure meaningful variation in both clinical characteristics and social determinants of health. As cancer trials increasingly seek to improve representation and advance health equity, methods that better balance continuous clinical and social risk factors are needed.
Objective: To propose a continuous-covariate minimization framework that directly incorporates clinical and social determinants of health into treatment allocation decisions without requiring categorization.
Methods: The proposed framework will calculate treatment assignment probabilities using a global imbalance score derived from continuous participant-level measures. Candidate variables include age, symptom burden, biomarker levels, neighborhood deprivation, financial hardship, and healthcare access indicators. Unlike conventional minimization methods that rely on predefined cut points, the proposed approach preserves the full range of information available in continuous measures. Planned simulation studies will compare the proposed framework with simple randomization and traditional categorized minimization under scenarios reflective of small cancer clinical trials. Outcomes will include balance of clinical and social risk factors, treatment allocation predictability, statistical power, precision of treatment effect estimates, and validity of subgroup analyses.
Expected Impact: By preserving continuous information and balancing both clinical and social determinants of health, this framework may support more equitable treatment allocation, improve statistical efficiency, and strengthen disparities-related findings in cancer clinical trials.
Conclusions: This proposed methodology addresses an important gap in covariate-adaptive randomization and may provide a practical approach for advancing both methodological rigor and health equity in cancer research.

ImmunoEP: Improving Neoantigen Immunogenicity Prediction through Evolutionary Context and Physicochemical Properties

Angad Hayer

Abstract:
Cancer immunotherapy has transformed oncology in recent years. Tumor specific peptides that are derived from somatic mutations and present by MHC class I molecules are critical components in personalized cancer vaccine candidates. Current pipelines, such as pVAC-Seq, give rankings to candidates solely based on binding affinity. Binding is necessary, but not efficient as many high affinity binders fail to trigger T-cell responses, while some moderate ones may provoke robust ones. To combat this we developed ImmunoEP which is a random forest classifier that in addition to binding affinity, utilizes evolutionary context (self similarity to human proteome, and viral mimicry to Epstein-Barr Virus, Influenza A, and cytomegalovirus) and physicochemical to determine peptide immunogenicity (Kyle-Doolittle hydrophobicity, molecular charge). The similarity features were created from UniProt reference proteomes, and to avoid leakage, 10,357 HLA-A*02:01 examples were drawn from IEDB, excluding TESLA peptides from training. The independent TESLA benchmark (N=208), ImmunoEP had a lower AUC than the affinity baseline (0.53 vs. 0.76). However, it outperformed the baseline and DeepImmuno in the early enrichment zone (ROC 0-0.1) achieving superior if not equal precision-at-top for N=1-19. Feature importance determined hydrophobicity as a major determinant (~41%), with affinity (~50%), suggesting that a peptide's ability to bind to the MHC groove is as important as its fit for the groove is. This top-of-list behavior provides a clinically relevant regime. Precision amongst the highest rank determines whether the candidate may be used as a viable target, which is especially important considering that peptide synthesis and experiment validation are highly rationed. Extending coverage beyond HLA-A*02:01 remains a prerequisite for generalizing these gains across a wide variety of genetic populations.

Anticancer Potential of Resveratrol Against A549 Lung Cancer Cells via PI3K/AKT/mTOR Pathway Regulation.

Ashley Gupta, Manya Singh, Briana Kinnel, Rajakumar Thangarasu, Krishna Chinchili, and Rajesh Singh

Department of Microbiology, Biochemistry and Immunology, Cancer Health Equity Institute, Morehouse School of Medicine, Atlanta, GA

Introduction: Lung cancer remains one of the leading causes of cancer-related mortality worldwide and is characterized by aggressive tumor progression, metastasis, and therapeutic resistance. Dysregulation of the phosphoinositide 3-kinase/protein kinase B/mammalian target of rapamycin (PI3K/AKT/mTOR) signaling pathway plays a crucial role in promoting cancer cell proliferation, survival, and disease progression, making it an important target for anticancer therapy. Resveratrol, a naturally occurring polyphenolic compound found in grapes and various plant sources, has gained considerable attention due to its antioxidant, anti-inflammatory, and anticancer properties.

Methods: The present study evaluated the anticancer potential of resveratrol against non-small cell lung cancer (NSCLC) using A549 cells through experimental and computational approaches. Cell viability following resveratrol treatment was determined using the MTT assay to assess dose-dependent cytotoxicity. A live/dead cell assay was performed to examine cell survival and membrane integrity by distinguishing viable and non-viable cell populations. Additionally, molecular modeling and docking studies were conducted to investigate the interaction of resveratrol with key proteins associated with the PI3K/AKT/mTOR signaling pathway.

Results: Resveratrol treatment induced a concentration-dependent (0–300 μM) reduction in A549 cell viability, as demonstrated by the MTT assay. The calculated IC50 values were 187 μM, 103 μM, and 92 μM at 24, 48, and 72 hours, respectively, indicating enhanced cytotoxicity with prolonged exposure. Live/dead cell analysis further confirmed increased cell death following treatment with 187 μM resveratrol at 24 hours, suggesting significant apoptotic and cytotoxic effects. Molecular docking studies demonstrated favorable binding interactions between resveratrol and PI3K/AKT/mTOR pathway-associated proteins, indicating its potential to inhibit signaling activity and disrupt mechanisms involved in cancer cell survival.

Conclusion: The findings demonstrate that resveratrol exhibits significant anticancer activity against A549 lung cancer cells through modulation of the PI3K/AKT/mTOR signaling pathway. The combined in vitro and computational evidence highlights the therapeutic potential of resveratrol as a promising candidate for targeted lung cancer treatment and supports further investigation through preclinical and clinical studies.

Acknowledgements: ***SPARC – DICRIDG-21-072-01-DICRIDG (American Cancer Society)***

Targeting Cell Cycle-Arrested Hypoxic Glioblastoma

Caroline Moon[1], Vafa Ismayilova[2,3], Waaqo Daddacha[2,3]

1. ***Davidson Fine Arts School, Augusta, GA, USA***
2. ***Georgia Cancer Center, Augusta University, Augusta, GA, USA***
3. ***Biochemistry and Molecular Biology, Augusta University, Augusta, GA, USA***

Abstract

Glioblastoma is an aggressive brain cancer in which hypoxia contributes to treatment resistance by promoting cell-cycle arrest. This study investigated whether increasing deoxyribonucleoside triphosphate (dNTP) availability could promote cell-cycle re-entry and enhance radiation sensitivity. Hypoxic LN229 GBM cells treated with deoxynucleosides (dNs) bypassed G1 arrest and resumed cell-cycle progression. Combining dN supplementation with ionizing radiation significantly increased apoptosis compared with radiation alone. Additionally, CRISPR-Cas9 successfully knocked out an undisclosed protein (Nuclease1). These findings demonstrate that manipulating dNTP metabolism may sensitize hypoxic GBM cells to radiation and offer a potential strategy to overcome treatment resistance and recurrence.

Background

Glioblastoma (GBM) is the most aggressive and common brain cancer and is characterized by frequent recurrence, therapy resistance, and poor prognosis for survival. Tumor recurrence is largely driven by treatment-resistant cell populations that survive within the hypoxic tumor microenvironment (TME). This highlights the need to understand and target molecular mechanisms that promote DNA damage repair and therapeutic resistance in hypoxic TME.

Cell Cycle and dNTP

Accurate DNA replication and repair require tightly regulated intracellular pools of deoxyribonucleoside triphosphates (dNTPs), the building blocks of DNA. During the S phase of the cell cycle, dNTP synthesis is upregulated to support genome replication, while balanced dNTP concentrations are maintained throughout the cell cycle to preserve genomic stability. Supplementation with exogenous deoxyribonucleosides (dNs) increases intracellular dNTP pools via the nucleoside salvage pathway, in which cellular kinases sequentially phosphorylate dNs to dNMPs, dNDPs, and ultimately dNTPs.

Hypoxia

Linked with cell-cycle arrest in G1 in dividing cells and mediating the effects of chemotherapy, radiotherapy, and immunotherapy, hypoxia, (low-oxygen conditions) is closely associated with poor prognosis and recurrence in various cancer patients.[2]

Together, these findings support investigating dNTP regulation and Nuclease1 as potential mechanisms underlying the survival and treatment resistance of hypoxic GBM cells.

Study Aim and Hypothesis

Given its role in promoting active cell cycle, dNTP represents a promising therapeutic target to make hypoxic cancer cells behave similarly to normoxic cancer cells. Through treatment with dN and dN+IR, potential therapies for tumors in hypoxia can be investigated to prevent tumor recurrence. By using CRISPR-mediated Nuclease1 knockout (KO), potential therapies for GBM under hypoxic conditions can be investigated.

Methods

A pCMV-Cas9-GFP all-in-one CRISPR plasmid was used to generate Nuclease1 knockout (KO) in a glioblastoma (GBM) cell line. The all-in-one system contained both the Cas9 nuclease and guide RNA (gRNA) in a single construct. Cas9 expression was driven by the cytomegalovirus (CMV) promoter, and a green fluorescent protein (GFP) reporter was included to monitor transfection efficiency. A gRNA targeting the coding region of Nuclease1 was selected to minimize predicted off-target effects and cloned into the pCMV-Cas9-GFP vector.

Bacterial cultures containing the CRISPR plasmid were grown overnight in selective medium and harvested by centrifugation. The cells were lysed, plasmid DNA was purified, and GBM cells were transfected with the purified

CRISPR all-in-one plasmid. Transfection efficiency was monitored using GFP expression, and successful Nuclease1 knockout was verified by Western blot.

Cell-cycle distribution was analyzed under normoxic and hypoxic conditions at 24 and 48 hours. The proportions of cells in the G0/G1, S, and G2/M phases were determined using flow cytometry.

Results

Under severe hypoxic conditions (0.1% O_2), non-treated (NT) GBM cells remained predominantly arrested in the G1 phase after 24 hours. In contrast, cells supplemented with exogenous deoxynucleosides (+dN) showed a shift in cell-cycle distribution, indicating that dN supplementation enabled hypoxic GBM cells to bypass the G1-phase block and resume cell-cycle progression.

Apoptosis was then evaluated under hypoxia across four treatment groups: no treatment (NT), dN supplementation alone, ionizing radiation (IR) alone, and combined dN plus radiation (dN+IR). dN treatment alone increased the apoptotic cell population compared with NT, but this difference was not statistically significant (ns). In contrast, the dN+IR combination produced a statistically significant increase in apoptosis compared with IR alone, demonstrating that dN supplementation enhanced radiation-induced cell death under hypoxic conditions.

CRISPR-Cas9-mediated Nuclease1 knockout was confirmed by Western blot analysis. Nuclease1 protein was detected in parental LN229 cells but absent in Nuclease1-knockout LNUTR cells. GAPDH expression was present in both samples and served as the loading control. These results confirmed successful targeted knockout of Nuclease1 and established the knockout model for further investigation of Nuclease1-mediated dNTP regulation in hypoxic GBM cells.

Discussion and Implications

Our findings demonstrate that manipulating dNTP availability can overcome a key mechanism of treatment resistance in hypoxic GBM cells. Increasing dNTP availability through dN supplementation allowed hypoxic cells to escape G1 arrest, and combining this cell-cycle re-entry strategy with radiation significantly increased apoptotic cell death. These results support an approach in which resistant tumor cells are first forced out of their protective, non-dividing state and then targeted with radiation.

The successful generation of Nuclease1-knockout GBM cells provides a model to determine whether directly targeting Nuclease1can recapitulate the effects observed with dN supplementation. Importantly, the current study confirmed Nuclease1 knockout but did not yet establish that it increased radiation sensitivity; therefore, this remains a direction for further investigation.

This study identifies dNTP metabolism and Nuclease1 as promising areas for understanding and potentially overcoming hypoxia-associated treatment resistance in GBM. By targeting the hypoxic tumor cells that can survive initial therapy and contribute to recurrence, this strategy may ultimately help improve the effectiveness of existing treatments for glioblastoma and provide a foundation for continued investigation of metabolism-based approaches to cancer therapy.

Acknowledgements

The author sincerely thanks Drs. Lisa Middleton, Kenza Mamouni, Darryl Nettles, and Yeun-Keng Ng for their mentorship, guidance, and encouragement throughout this research, and the Georgia Cancer Center Summer Research Experience Team for providing the opportunity and support that helped make this work possible.

References

1. Meng, B., Zhao, N., Mlcochova, P., Ferreira, I. A. T. M., Ortmann, B. M., Davis, T., Wit, N., Rehwinkel, J., Cook, S., Maxwell, P. H., Nathan, J. A., & Gupta, R. K. (2024). Hypoxia drives HIF2-dependent reversible macrophage cell cycle entry. *Cell reports, 43*(7), 114471. https://doi.org/10.1016/j.celrep.2024.114471
2. Chen, Z., Han, F., Du, Y., Shi, H., & Zhou, W. (2023). Hypoxic microenvironment in cancer: molecular mechanisms and therapeutic interventions. *Signal transduction and targeted therapy, 8*(1), 70. https://doi.org/10.1038/s41392-023-01332-8

Evaluating the effects on Vitamin D3 and Serrapeptase

Mina J.S Banks

As the number of people diagnosed with Multiple Sclerosis, and autoimmune diseases increases, The amount of research being done on it is relatively low. Scientific research may not have come up with an affordable and concrete cure. Though in the older days herbs and animal-created ingredients were today's miracle cures. Most of the research done has used mechanical cures and injections, but there are a small few that talk about the natural cures. This scientific review is talking about cures for Autoimmune diseases using nature.

There are multiple studies explaining what could possibly be affected in these patients who have an autoimmune disease compared to those without. *Can at al. (2020),* determined that diagnosed patients had lower levels of Creatinine than those without an autoimmune disease. This could help decide if adding more of this chemical into a diagnosed person could potentially reverse certain effects from autoimmune diseases. This could be a potential bases for testing out the research question. Other research has shown that more natural resources can be used to support cell regeneration.

One study found that a special enzyme in silkworms could regenerate damaged cells. The enzyme is called Serrapeptase. It is known for its miracle healing properties and could be another potential basis for the research project. Another article by *Epstein. (2010),* talks about the many healing properties of different animal derived products, amung them were multiple different kinds of animal products that could repair cell damage. Since Multiple sclerosis is an autoimmune disease that targets healthy cells, natural remedies like this could be revolutionary for many peoples lives.

Based on the reviewed studies, this research will focus on the natural non-surgical; methods of healing the damaged cells. These pieces of literature support the research topic of finding natural remedies that can reverse or slow the effects of multiple sclerosis. The Super D vitamins and the silkworm enzymes are known ro have regeneratuve properties. Which may possibly solve the research question of whether Autoimmune disease can be healed using natural remedies.

Evaluating the Neuroprotective Effects of Antioxidant Compounds and Their Combinations Under Oxidative Stress

Savannah Browne

Oxidative stress, caused by an imbalance between reactive oxygen species (ROS) and the cell's ability to neutralize them, can damage cellular structures and contribute to neurological dysfunction. This study will investigate whether selected antioxidant compounds can protect neuronal cells from oxidative stress and whether combining compounds produces greater protection than using individual compounds alone. The compounds examined will be CoQ10, turmeric, grapefruit extract, Dry E-400, taurine, and L-ascorbic acid. Neuronal cells will serve as the primary experimental model and will be exposed to controlled oxidative stress before receiving individual antioxidant treatments or selected combinations. Cellular responses will be evaluated using appropriate laboratory methods to measure cell viability, oxidative stress, and observable changes in neuronal morphology and growth. Measurements from experimental groups will be compared with appropriate control groups across repeated trials to determine how each treatment affects neuronal survival and oxidative stress. An additional earthworm model will be used to examine whether antioxidant treatments produce measurable protective effects beyond cultured neuronal cells. Results will be compared across individual and combination treatments to identify compounds and combinations with the greatest potential for reducing oxidative stress-related cellular damage. This study may provide insight into how different antioxidant compounds interact and whether combining compounds can enhance protection of neuronal cells under oxidative stress.

Flavonoid Efficacy in UV & Cancer Research

Ashley Chen & JoJo Zheng

Chronic exposure to ultraviolet (UV) radiation accelerates the accumulation of reactive oxygen species (ROS) in epidermal tissue, triggering oxidative stress, DNA damage, and chronic inflammation. These molecular changes serve as primary drivers for cutaneous malignancies, commonly known as skin cancer, and tumor proliferation. Flavonoids, natural plant polyphenols with known antioxidant and anti-inflammatory properties, offers a promising therapeutic strategy against UV-induced oxidative damages. This study investigated the protective and therapeutic efficacy of plant derived flavonoids apigenin and luteolin against UV-induced damage and oxidative stress both in vivo using, zebrafish embryos and in vitro, using skin cancer cell lines. Flavonoids apigenin and luteolin were extracted with crushed and dried celery and parsley leaves, using deep eutectic solvents of HBA Choline Chloride and HBD Glycerol. After this process, antisolvent precipitation was completed to rid the DES mixture and drop out the hydrophobic flavonoids. Using Self-Nano Emulsifying Drug Delivery System (SNEDDS), the insoluble flavonoids were dissolved. Zebrafish embryos were treated with varying concentrations of apigenin and luteolin following UV exposure while skin cancer cells were directly treated without any UV exposure. ROS accumulation, cell viability, and markers of oxidative stress and inflammation were noted using MTT assay and consistent check ups on zebrafish embryos as they grow, observing any anatomy changes. Both apigenin and luteolin significantly reduced ROS levels and improved cell survival under UV exposure compared to untreated controls. Overall, these findings demonstrate the photoprotective and anti-oncogenic potential of apigenin and luteolin, showing their potential application as important therapeutic agents or protective treatments against UV-induced skin damage and carcinogenesis.

The Novel Delivery of Diosmin to Melanoma Skin Cells Via Sonoporation and Poly-D Lysine Nanocarriers

Aniyah Cox

Rationale

Melanoma is generally considered the most dangerous skin cancer as it grows quickly and can spread to any organ. Melanoma occurs when melanocytes—the cells that gives skin its color—change and reproduce aggressively. As of 2019, the number of cases of melanoma have been increasing faster than any other cancer (Melanoma – Harvard Health, 2019). Diosmin has been found to possess anti-cancer properties by inducing apoptosis (programmed cell death) in various types of cancer cells, including skin cancer cells. Poly-D Lysine (PDL) has a polycationic nature, making it an excellent option for non-viral gene and drug delivery and sonoporation—the formation of small pores in cell membranes using ultrasound—open cavitations bubbles that induce plasma membrane perforation. This assists in the delivery of drugs and genes to living cells

This project aims to explore cheaper and more efficient options for cancer treatment. The common issue with orally taken drugs is their varying absorption. Furthermore, cancer medication in general is often expensive. However, the use of novel delivery techniques has become a talking point in science communities as they can improve of efficiency of drugs delivery. Both poly-d lysine and sonoporation are relatively new techniques for novel delivery, but both have great potential. In this project, sonoporation and poly-d lysine are explored as techniques for the novel delivery of diosmin to both melanoma skin cells and normal skin cells.

Lidocaine and Tetraethylammonium Effects On Neuronal Cell Viability During Glutamate Excitotoxicity

Kaleb Dove

Rockdale Magnet School for Science and Technology

As the years go on, the quantity of elderly people expected to get Alzheimer's increases. An estimated 7.2 million Americans age 65 and older live with Alzheimer's dementia today. With 7.2 million Americans 65 and older estimated of having dementia today, with the number expected to increase to 13.8 million by 2060 (Alzheimer's Association, 2025, Section Abstract).

Alzheimer's itself is a neurodegenerative disease that slowly destroys memory recall, thinking skills, and carrying out simple daily tasks. While also being a neurodegenerative disease it is also one of the most commons form of dementia. Dementia being a general term for conditions that disturb someone is mental ability enough to interfere with their daily life or thinking. While there have been efforts to find a solution for dementia but to no avail.

Glutamate ties deeply into the subject of this due to its connection to memory as a neurotransmitter that is related to synaptic plasticity. Synaptic plasticity is the brain's way of learning/remembering new information, with stronger connections lasting longer than shorter connections. These connections can be thought of as memory. When a normal amount of glutamate is released, it causes an appropriate amount of calcium to be released triggering synaptic plasticity. When an excessive amount of glutamate is released, it causes excessive amounts of calcium to also be released, causing excitotoxicity.

By investigating how varying levels of glutamate can induce excitotoxicity in mouse neurons, their desired results are to see how lidocaine and tetraethylammonium can influence the damage on the cells.

Spencer Fortson

Abstract

Morphine is a commonly used opioid analgesic for the treatment of moderate to severe pain, but its administration can produce histamine-mediated reactions that may be incorrectly documented as true allergies (pseudoallergies). These pseudoallergic reactions can complicate clinical decision-making and potentially restrict access to effective pain management. This project investigates whether antihistamines can mitigate physiological responses associated with elevated histamine levels using *Drosophila melanogaster* and mice embryonic fibroblast models. Because morphine and other opioids will not be administered, histamine dihydrochloride will be used to model the histamine-mediated component of an opioid-associated pseudoallergic response. *Drosophila melanogaster* will be exposed to controlled concentrations of histamine dihydrochloride, followed by a treatment of diphenhydramine hydrochloride (active agent in Benadryl), Cetirizine (active agent in Zyrtec), and Loratadine (active agent in Claritin). Physiological outcomes, including survivability, developmental progression, and reproductive outcomes, will be compared between untreated control, the histamine-exposed control, and antihistamine-treated groups. The mice embryonic fibroblasts model will be used to examine cellular responses to histamine exposure and determine whether selected antihistamines produce measurable changes in histamine-associated cellular activity. The study hypothesizes that antihistamine treatment will reduce histamine-induced physiological and cellular responses. By examining responses across an invertebrate organism and mammalian cells, this research may provide preliminary evidence for distinguishing histamine-mediated pseudoallergic responses from other adverse drug reactions and contribute to future approaches for improving the recognition and management of opioid-associated reactions.

Audrey Fovie

How Antibiotics Affect Melanoma Cells

Abstract/Rationale

Melanoma is a form of skin cancer known for its ability to resist treatment. Immune checkpoint inhibitors have become the leading treatment for advanced melanoma, offering improved survival by enhancing anti-tumor immune responses (Liang et al., 2025). Patients with melanoma often take antibiotics during treatment to manage or prevent concurrent infections. Research on melanoma patients receiving immunotherapy has shown that antibiotics can affect treatment effectiveness. Many studies attribute this to gut microbiome disruption, highlighting the importance of understanding their direct impact on cancer cells (Aminzadeh-Gohari et al., 2020). While antibiotics are primarily designed to target bacterial infections, research shows that some antibiotics classes directly alter human cell proliferation, metabolic survival pathways, and responses (Zhang & Xu, 2023). Because antibiotics are not primary treatments for cancer, melanoma cells don't defend themselves against antibiotics the way bacteria do (Lu & Tong, 2024).

There is a need for research on the effects of antibiotics without the influence from the systemic microbiome. It is known that antibiotics can affect cell mitochondria, so they might unintentionally damage or help cancer cells (Mohiuddin et al., 2021). Antibiotics play supporting and sometimes indirect roles in oncology. Although antibiotics are commonly used in medicine, there is still limited evidence on whether they have a positive or negative effect on melanoma cells. This gap in knowledge creates a need to investigate this topic in a controlled environment.

Influence of Plant-Based Compounds on Molecular Pathways in the Cell Cycle of Prostate Cancer.

London McAlister

Rationale:

Cancer continues to be an ongoing issue as it is one of the leading causes of death worldwide. Including Prostate cancer. Prostate Cancer is the second most diagnosed cancer and the fifth cause of cancer death amongst men worldwide. Furthermore, many patients do not respond well to traditional treatments like chemotherapy and radiation. Because of this, scientists are attempting to search for ways to eliminate cancer without causing harm to the patient. Research shows that many plant-based compounds, also known as phytochemicals, may slow cancer cell growth, reduce inflammation, and even cause cancer cells to die.

Studies show that although some patients are initially responsive to chemotherapy, resistance typically occurs 1-2 years afterwards. This creates a serious problem for doctors because once cancer becomes resistant to treatment, it becomes much harder to control. Many phytochemicals isolated from plants have shown to be cytotoxic tumors. These natural substances are found in many plants and have been shown in laboratory studies to slow the growth of cancer cells and reduce inflammation. Because of these properties, phytochemicals could play a vital role in improving future cancer treatments.

This research focuses on how phytochemicals may interfere with molecular pathways involved in prostate cancer and cell control. Phytochemicals as anti-cancer delegates in the treatment of prostate cancer can have remarkable impacts on the future of the healthcare system. More research aims to better understand how phytochemicals relation with cancer cells could lead to new alternatives for preventing or treating prostate cancer in the future.

Smart Delivery: Using A pH-Responsive Chitosan-STPP Nanocarrier for Targeted Delivery of BIM BH3 to Melanoma Cells

Rickie E. Reed., Courtney O. Powell Jr.

930 Rowland Rd, Conyers GA 30012

Rockdale Magnet School for Science and Technology

September 19, 2026

Abstract

By 2040 there will be a 50% increase in skin cancer incidents (Carr, Q. L., 2025) which will also lead to a 68% increase in skin cancer mortalities worldwide (Sweazy, A., 2025) but new developments in cancer nullifying and targeting have caused a 25.2% decrease in mortality from skin cancer (Connor, C.,2025). Micro polymorphs (Lythgoe, M. P., 2022) and other carriers can help deploy certain treatments more accurately (Hollister E. B., 2019). Research Question: If BIM BH3 and Tumor Necrosis Factors are used to clear out melanoma cells, will it be able to accurately target cancer cells without harming large amounts of healthy skin cells.

The independent variables of the research will be both healthy and melanoma cells because they will be subjected to the same treatments. These cells will be testers that we will observe to see whether the pH-sensitive polymer + BIM BH3 is actively able to target the cancer cells. This will be important for helping decrease mortality rates.

The dependent variable in this research would be the mortality of the cells due to activity of the BIM BH3. Study on BIM BH3 has shown that it can have both positive and negative effects on cancer cells by targeting cancer cells while also wiping out healthy cells. This is the purpose of the polymer that would be created which would help to find out if we could eliminate the negative effects of the BIM BH3 by targeting cancer cells.

Project Title: Do curcumin and ginger extract modulate inflammatory-induced barrier dysfunction in intestinal epithelial cells?

Student Name: Caitlyn Rivera

Rationale: Inflammatory bowel diseases (IBD) are chronic inflammatory disorders affecting more than 1.6 million people in the United States and millions worldwide (Ng et al., 2017). Continuous inflammation damages intestinal epithelial cells and disrupts the intestinal barrier, which protects gut health by preventing dangerous bacteria, toxins, and pathogens from entering the bloodstream. When inflammation and oxidative stress degrade this barrier, intestinal permeability increases, creating a cycle that accelerates disease development and causes additional health problems (Turner, 2009).

Intestinal barrier dysfunction occurs mainly because oxidative stress damages the barrier system. During inflammation, cells produce reactive oxygen species (ROS), including hydrogen peroxide (H_2O_2), which can damage proteins, lipids, and DNA. This weakens epithelial cell junctions and cell survival, damaging the intestinal lining (Rezaie, Parker, & Abdollahi, 2007). Researchers need compounds that can protect intestinal epithelial cells (CRL-1592) from inflammation-related damage.

Turmeric (Curcuma longa) contains curcumin, a component studied for its anti-inflammatory and antioxidant properties. Previous research suggests curcumin can reduce inflammation by inhibiting inflammatory signaling pathways and scavenging ROS (Aggarwal & Harikumar, 2009). It has also been studied as a treatment for gastrointestinal disorders, including IBD, because it can decrease oxidative stress while preserving cellular function (Hewlings & Kalman, 2017). However, its immediate effects on gut epithelial cells during active inflammatory stress remain unclear.

This project will determine whether curcumin protects CRL-1592 intestinal epithelial cells from H_2O_2-induced oxidative stress by testing different curcumin doses and their effects on cell survival and physical structure. Findings may support future dietary and medical treatments for patients.

Title: Investigating Antioxidants as Modulators of Scorpion Venom Cytotoxicity

Researchers: Devin Swims and Jackie Pimentel-Martinez

Abstract:

How do antioxidant treatments interact to modulate the cytotoxicity of scorpion venom in cancerous and non-cancerous cells? Scientists have long researched natural combatants of cancer, and scorpion venom has shown potential as an anticancer agent; scorpion venom contains complex mixtures of enzymes, peptides, and small organic compounds known for their ability to interact with receptors and cellular signaling pathways. Due to side effects and resistance of tumors for current cancer treatments such as surgeries and radiation, there is a persistent need for new, more effective, and efficient methods of treatment. This project investigates the effects of scorpion venom on cancer cells as a natural method of cancer treatment and examines the extent to which venom exposure reduces cancer cell viability. This study builds on previous findings and seeks to evaluate the potential of scorpion venom with and without additives on cancer and non-cancerous cells, which remains relatively unexplored. Vitamin C and quercetin are examples of antioxidants and have proven to be useful in cancer remediation through their ability to stop the production of free radicals, which cause mutations in the DNA of cells. This project seeks to evaluate the extent to which antioxidants and scorpion venom interact, and thus can be used to aid in the advancement of cancer research. This study will investigate how antioxidants influence the cytotoxic effects on cancerous cells versus non-cancerous cells, which may help identify selective toxicity toward cancer cells while minimizing damage to healthy cells.

Title: Effects of mitochondrial stress on Skin vs Melanoma cells

Name: Diana Tapia-Ramos

Mitochondria are essential parts of cells because they produce energy and help control whether a cell survives or dies. When mitochondria become stressed or damaged, they may stop producing energy properly and trigger cell death pathways such as apoptosis (Abate et al., 2019). Understanding mitochondrial function is important because it explains how cells respond to stress and maintain balance (Alberts et al., 2015).

This is especially important when studying cancer. Cancer cells can behave differently from normal cells, particularly in how they produce energy and respond to stress. Research shows that mitochondria in cancer cells can adapt to stressful conditions, allowing them to survive environments that would normally be harmful (Huang et al., 2021). Cancer cells also often have higher levels of oxidative stress, which may make them more vulnerable if stress increases further. Since cancer affects millions of people worldwide, understanding how cancer cells respond to stress could help improve future treatments (American Cancer Society, 2023).

Studying mitochondrial stress in normal and cancer cells can show how cells respond to damage. By increasing mitochondrial stress using hydrogen peroxide, differences in cell survival can be observed. Cell survival can be measured using the Trypan Blue exclusion test, which distinguishes living cells from dead cells (Strober, 2015). This project compares normal skin cells and melanoma cells under the same conditions to determine whether cancer cells respond differently to mitochondrial stress. The results may improve understanding of how cancer cells survive stress and how they could be targeted in future treatments.

Makayla Varnado, Alicia Henry

Title: Investigating the Combined Effects of Paclitaxel and Resveratrol on Prostate Cancer Cell Viability

Prostate cancer is one of the most common cancers affecting men worldwide and remains a leading cause of cancer-related deaths. While chemotherapy can be effective, it can cause severe side effects that damage healthy cells. Resveratrol has strong antioxidant and anti-inflammatory properties, so combining it with paclitaxel, a chemotherapeutic drug that has shown positive results on its own, may enhance and prolong inhibition of prostate cancer cells. Results from this study could be used to further explore new and affordable treatments. The tested hypothesis is this: If resveratrol is combined with Paclitaxel and applied to prostate cancer cells, then cell viability will decrease more than with either treatment alone, as measured by an MTT assay. The experiment will be conducted over the course of three days: on the first day, plate the cells; on the second day, apply treatments; on the third day, collect data. There are two treatments to be used: Resveratrol and Paclitaxel.

AI-Guided Evaluation of Metal-Organic Framework Nanocarriers for Receptor-Mediated Transcytosis Across the Blood–Brain Barrier in Glioblastoma

Diya Rajkumar, Obra D. Tompkins High School, Katy, TX
Mentor: Gaurav Sharma, Eigen Sciences, Apex, NC

Abstract

Glioblastoma Multiforme (GBM) is an aggressive primary brain tumor whose treatment is strongly limited by the blood-brain barrier (BBB), which restricts the penetration of many therapeutic compounds. Metal-organic frameworks (MOFs) are highly porous crystalline materials with tunable cavities that may function as nanocarriers for targeted drug delivery. This study evaluated MOFs for receptor-mediated delivery of therapeutic compounds across the BBB. Three-dimensional MOF structures, including MOF-505 (NOTT-100), MIL-88B, NU-1301, and PCN-160-$CoCl_2$, were obtained from crystallographic databases, and their pore and cavity characteristics were evaluated using CageCavityCalc. A BBB-associated receptor structure was modeled using AlphaFold. Candidate neurological and anticancer compounds were obtained from PubChem, and molecular docking was performed using HDOCK to evaluate predicted interactions. Among the initially screened compounds, temozolomide demonstrated the strongest mean HDOCK docking score (-220.67 ± 6.98), followed by risperidone (-85.54 ± 17.74), whereas sertraline exhibited the weakest predicted interaction (-18.15 ± 3.44). Based on the strong performance of temozolomide, ten structurally related compounds, including mitozolomide, 9-methylguanine, 7-methylguanine, and temozolomide-related imidazole derivatives, were further evaluated against multiple MOF structures. Comparative docking demonstrated substantial variation among MOF–compound combinations, indicating that MOF architecture and ligand structure influence predicted molecular association. These results identify promising MOF–drug combinations for further investigation as nanocarrier systems. Future molecular dynamics, drug-loading, release, permeability, cytotoxicity, and experimental BBB studies will be required to validate whether these computationally prioritized systems can improve therapeutic delivery to glioblastoma.

Phosphomimetic Substitution in the Inhibition of Mutant p53 Aggregation

Elyse Khieu
Gwinnett School of Mathematics, Science, and Technology

In 2025, there were over 2 million cancer cases with over 600,000 resulting in death. By 2050, there is projected to be 30.5 million cancer cases and 18.6 million deaths caused by cancer. The p53 protein plays a significant role in the regulation of the cell cycle, which is critical to tumor suppression. p53 mutations–with R175H being the most common among cancer patients–lead to loss of wild-type function and gain-of-function when mutant p53 aggregates with itself or other proteins and transcription factors. The gain-of-function caused by mutant p53 leads to higher resistance to anticancer treatments. This research evaluates the research question: *To what extent does a T55D phosphomimetic substitution on p53-R175H inhibit the protein's aggregation propensity?* The T55D mutation mimics phosphorylation at the site hypothesized to inhibit protein aggregation. The hypothesis is p53 with the T55D substitution and the R175H mutation (p53-R175H,T55D) will exhibit less aggregation than p53 with only the R175H mutation (p53-R175H).

Computational models of the protein variants were created with AlphaFold and analyzed for their relative levels of exposed hydrophobic surface area–with high levels correlating with higher aggregation propensity. The FoldX software removed steric clashes and optimized the structure of the p53 sequence to bring it closer to *in vivo* working conformations before performing mutagenesis. Energy decomposition analysis (EDA), a novel approach to quantifying the chemical phenomena affecting intermolecular interactions, divides intermolecular interaction energy into components such as electrostatics, polarization, and charge transfer, providing data behind the available free energy of the protein. Using the Aggrescan3D software, the same procedure for FoldX was performed, yielding an Aggrescan3D score, a structure-based metric that predicts protein aggregation propensity by analyzing the three-dimensional structure of a protein. A comparative analysis was done between the results obtained from each software to confirm consistent *in silico* results.

The total change in free energy between p53-R175H and p53-R175H,T55D was 1.33456 kcal/mol–a value greater than the biophysics standard for biological significance of 1 kcal/mol. At every residue from 51 to 57, the Aggrescan3D score of p53-R175H was larger than that of its corresponding residue in p53-R175H,T55D. At residues other than 51-57, there is no difference in Aggrescan3D score between the two proteins. The results indicate that the T55D substitution creates a biologically significant change in the energetics of the mutant p53, which results in lower aggregation propensity around the site, residues 51 to 57. The insight gained from this study effectively fills the gap of knowledge in the efficacy of phosphomimetic substitution utilization for mutant p53 aggregation inhibition. Furthermore, the results of this study have implications for improving anticancer treatment effectiveness as well as for neurodegenerative pathology treatment, which involves aggregation-prone proteins.

Isabella Nguyen

Structure-guided Design of Novel Antibody Targeting CTHRC1 in Glioblastoma Multiforme (GBM)

Glioblastoma Multiforme (GBM) is an aggressive form of brain cancer with uncontrolled growth of glial cells. Collagen triple helix repeat containing 1 (CTHRC1) is a secreted glycoprotein and is linked to tissue repair, bone formation, and vascular remodeling. CTHRC1 is overexpressed in GBM tissues, promoting tumor growth, migration, and cell invasion, and may be a potential target for GBM treatment. This research aimed to computationally design novel antibodies that could bind the protein's predicted binding site and block its activity. We used the UniProt amino acid sequence and AlphaFold 3 to model CTHRC1's 3D structure. We validated the designed CTHRC1 structure using a Ramachandran plot. We used ANARCI to screen antibody sequences and selected ten based on complementarity-determining region (CDR) variability. We also designed five de novo antibody candidates using Boltzgen for further analysis. We performed molecular docking simulations between CTHRC1 and the antibodies using the HDOCK 2.0 web server. Based on binding free energy (−11.4 kcal/mol, $K_d = 4.4 \times 10^{-9}$ M at 25 °C) and the number of interactions [hydrogen bonds = 12 (bond distance range from 2.82 Å- 3.86 Å), hydrophobic interactions = 6 (~2.01 Å- 3.87 Å), π-cation interactions = 1 (4.80 Å)], we selected antibody PDB ID: 2VXS as an appropriate candidate. We then evaluated antibody humanization using BioPhi to assess stability for further drug development. In addition, antibody 2VXS had the highest thermal stability (59.0 °C) and the lowest predicted T cell activation among all antibodies, further validating its selection. Finally, we further validated CTHRC1-2VXS complex stability by performing molecular dynamics simulations, which showed a stable Root mean square deviation (RMSD) of ~2 nm. Moreover, cluster analysis showed that 2VXS remained bound to the CTHRC1 protein throughout the MD simulation. This study represents a computational workflow to identify potential CTHRC1-targeted antibodies. These findings provide a foundation for further experimental validation and analysis toward developing targeted therapy for aggressive GBM.

Calibration Thresholds for a Transcriptomic Glioma Risk Tool Do Not Transfer Between US and Chinese Cohorts

Ivy Datta

Marvin Ridge High School, Waxhaw, North Carolina

Background

Transcriptomic prognostic tools for glioma are developed almost entirely in The Cancer Genome Atlas (TCGA), a predominantly US cohort. Whether risk thresholds derived from such a reference apply to patients in other populations is rarely tested, because most tools report discrimination in a single cohort and never attempt transfer. This work builds a risk stratification tool for IDH-mutant lower-grade glioma and tests its transfer to two independent Chinese cohorts.

Methods

The tool computes the Transcriptomic Ambiguity Index (TAMI), the Shannon entropy of a regularized logistic classifier's posterior probability over low- and high-grade reference states, from a 200-gene RNA-sequencing panel. It was developed on TCGA (n=528 lower-grade glioma samples; IDH status assigned from histologic subtype rather than genotype) and evaluated on two Chinese Glioma Genome Atlas cohorts, CGGA-693 and CGGA-325, in which IDH status was genotyped and neither of which contributed training data. Analyses were restricted to WHO Grade III tumors and adjusted for age. MGMT methylation status and histologic grade were assessed in a separate joint model. Proportional-hazards assumptions were verified using scaled Schoenfeld residuals, and multiplicity was controlled by the Benjamini-Hochberg procedure at a false discovery rate of 0.05.

Results

TAMI stratified overall survival in all three cohorts (hazard ratio per 1-SD increase 1.26, p=0.005 in TCGA, n=270; 1.48, p<0.001 in CGGA-693, n=166; 1.93, p=0.001 in CGGA-325, n=42), with no association in Grade II tumors in any cohort (p=0.22, 0.40, and 0.51). TAMI retained significance alongside existing markers in a joint model containing MGMT status, grade, and age (HR 1.16 per 1-SD, p=0.02), for a modest gain in model concordance (0.799 to 0.803). Transfer of the calibrated tool failed completely: absolute band thresholds derived from TCGA assigned every CGGA sample to the highest risk band. Recalibrating cutpoints against each target cohort's own score distribution restored stratification (log-rank p=0.0001 in CGGA-693; p=0.0028 in CGGA-325).

Conclusions

The cohorts differ in both sequencing platform and patient population, so this transfer failure cannot be attributed to ancestry. It does establish that a risk tool calibrated on a US reference cohort misclassified an entire non-US cohort, and that per-cohort recalibration is a deployment requirement rather than an optional refinement. Tools validated only for discrimination may conceal calibration failures of this magnitude.

Characterization of Human Colorectal Cancer Cell Lines for In Vitro Research Applications

Upparchinta, Lasya P.; Muralidharan, Janani; Bhatt, Ankit, PhD; Singh, Shailesh, PhD; Mir, Hina, PhD

Department of Microbiology, Biochemistry, and Immunology; Cancer Health Equity Institute, Morehouse School of Medicine, Atlanta, Georgia

Introduction: Colorectal cancer is one of the leading causes of cancer-related deaths worldwide. Established colorectal cancer cell lines are widely used as *in vitro* models to investigate colorectal cancer biology and evaluate responses to treatments. The objective of this project was to establish, maintain, and characterize three commonly used colorectal cancer cell lines (Caco-2, DLD-1, and HCT116) while developing fundamental mammalian cell culture skills that support future studies.

Methods: Caco-2, DLD-1, and HCT116 colorectal cancer cell lines were cultured. Cryopreserved cells were recovered from liquid nitrogen storage and grown in complete culture media under standard culture conditions. Cell morphology, attachment, and confluence were monitored daily using an inverted microscope, and the culture medium was replaced as needed to maintain healthy cell growth. Once the cells reached approximately 70–80% confluence, they were passaged using trypsin-EDTA and transferred to new flasks containing fresh medium. Morphological features and growth characteristics of each cell line were documented and compared throughout routine culture.

Findings: The three colorectal cancer cell lines showed distinct morphology, attachment characteristics, and growth rates, demonstrating the importance of selecting appropriate *in vitro* models for colorectal cancer studies.

Implications/Future Directions: Developing proficiency in aseptic technique, sterile cell culture practices, and routine mammalian cell culture is an essential component of biomedical research training. Established colorectal cancer cell lines provide a foundation for future investigations of cancer biology and therapeutic response. Future studies will utilize these cell lines to evaluate chemotherapy-induced changes in cell viability using MTT assays and treatment-associated alterations in protein expression through Western blot analysis.

Evaluating Boundary Disagreement in U-Net Skin Lesion Segmentation

[1]Levend Eski; [2]Hakan Celepcikay; [3]Sinan Kockara

[1]Harmony School of Innovation Sugar Land, Sugar Land, Texas, United States

[2]Harmony School of Innovation Sugar Land, Sugar Land, Texas, United States

[3]Rice University, Houston, Texas, United States

leski209@gmail.com; hakanctx@gmail.com; sk212@rice.edu

Abstract

Area-overlap scores summarize skin-lesion segmentation performance but do not directly describe the distribution of contour errors. This exploratory study examines boundary disagreement alongside Dice and intersection over union (IoU) in U-Net segmentation, and assesses how a composite boundary score relates to its mean-distance component. We used 900 dermoscopic images and corresponding expert masks from the ISIC 2016 Part 1 training dataset. Image-mask pairs were resized to 256 × 256 pixels and randomly divided into 765 development images and 135 held-out test images. Five-fold cross-validation was performed within the development set, followed by final model training on that set. Training included data augmentation, and predicted probabilities were thresholded at 0.5. Original model predictions were evaluated without component cleanup. For each evaluable boundary pair, Euclidean nearest-boundary distances were pooled across both directions. Their mean provided a boundary-point-weighted average symmetric surface distance (ASSD). An exploratory boundary disagreement score added half the pooled standard deviation to this mean; the weight was heuristic. Division by the expert mask's equivalent circular radius produced a dimensionless normalized score. On the test set, mean Dice was 0.824 and mean IoU was 0.722. Across evaluable boundaries, mean boundary distance was 11.51 pixels, mean composite score was 16.07 pixels, and mean normalized score was 0.291. The composite score closely tracked mean boundary distance (Spearman $\rho = 0.983$), while the normalized score was strongly inversely associated with Dice ($\rho = -0.909$). A retrospectively selected illustrative pair had similar Dice values of 0.848 and 0.849 but normalized boundary scores of 1.201 and 0.194, respectively, demonstrating that similar overlap can accompany different contour disagreement. For the higher-score case, diagnostic component removal using the expert mask eliminated 62 false-positive pixels and reduced the normalized score to 0.208, while Dice increased to 0.857. These findings support reporting boundary measurements alongside overlap metrics, but do not establish added value from the standard-deviation term. The score measures prediction-to-annotation disagreement rather than clinical border ambiguity or model uncertainty. This single-dataset analysis, based on one held-out split without external validation, provides preliminary descriptive evidence. Establishing a distinct contribution requires comparison against established boundary metrics, sensitivity analysis of the variability weight, and independent validation.

Keywords: skin lesion segmentation; boundary disagreement; U-Net

Targeting Cancer Stem Cell Genes Pou5f1 and Sema3C: A Systematic Review and Meta-Analysis of Stemness-Related Outcomes

Lucas Pan

Background: Cancer stem cells (CSCs) are widely recognized as key drivers of tumor initiation, metastasis, therapeutic resistance, and recurrence — yet the role of stemness-related genes in these processes remains critically underexplored. Pou5f1, which encodes the transcription factor Oct4, plays a central role in maintaining stemness in both embryonic and cancer stem cells, and its expression is frequently associated with chemoresistance, poor prognosis, and tumor relapse. Similarly, Sema3C, a member of the semaphorin family, has been implicated in promoting CSC survival, tumorigenicity, invasion, and peritoneal dissemination across multiple cancer types. This systematic review and meta-analysis aimed to evaluate the effect of gene knockdown of Pou5f1 and Sema3C on stemness-related outcomes in preclinical cancer models.

Methods and Results: PubMed and Cochrane Library databases were systematically searched for preclinical studies reporting stemness-related outcomes following knockdown of the targeted genes. Effect sizes were calculated using Hedges' G, with all statistical analyses performed in JASP.

Sixteen studies met inclusion criteria. Compared to controls, gene knockdown was associated with significant reductions in cell proliferation ($z = -4.44$, $p < 0.001$, 95% CI -8.588 to -3.328), cell invasion ($z = -3.90$, $p < 0.001$, 95% CI -8.402 to -2.786), colony formation ($z = -4.91$, $p < 0.01$, 95% CI -9.204 to -3.953), cell motility ($z = -4.93$, $p < 0.01$, 95% CI -9.246 to -3.988), sphere formation ($z = -5.33$, $p < 0.01$, 95% CI -8.931 to -4.128), CD44 expression ($z = -3.43$, $p < 0.01$, 95% CI -7.584 to -2.066), Wnt protein expression ($z = -3.06$, $p < 0.02$, 95% CI -11.375 to -2.487), Sox2 expression ($z = -8.485$, $p < 0.04$, 95% CI -11.927 to -5.044), NANOG expression ($z = -4.59$, $p < 0.001$, 95% CI -10.844 to -4.355), and chemoresistance ($z = -7.59$, $p < 0.001$, 95% CI -6.593 to -3.885).

Conclusion: This meta-analysis provides preliminary evidence that knockdown of Pou5f1 and Sema3C is associated with significant reductions in multiple stemness-related outcomes, suggesting these genes may become potential therapeutic targets for cancer stem cell-driven tumor progression and recurrence. However, the statistical power of these findings is largely limited by the small sample sizes characteristic of preclinical research (predominantly $n = 3$), and significant heterogeneity in effect sizes raises concerns about reliability and potential bias, even after Hedges' G correction. These findings suggest the need for more rigorously designed preclinical studies with larger sample sizes, standardized methodologies, and reduced risk of bias, which would strengthen the foundation for future translational research targeting stemness pathways in cancer therapy.

Population-Associated Variability and Reproducibility of Circulating miRNA Biomarkers for Non-Small Cell Lung Cancer Detection

Melody Farahani
Student
San Dieguito Academy High School
Encinitas, CA, USA
Orcid.org/0009-0007-0687-3178

Prof. Christian Agatemor
Department of Chemistry
Bucknell University
Lewisburg, PA, USA
Orcid.org/0000-0001-6485-2382

Abstract

Circulating miRNA biomarkers are promising for noninvasive detection of non-small cell lung cancer (NSCLC). Ensuring that cancer biomarkers perform consistently across diverse populations is important for their equitable clinical implementation. This original research evaluated the reproducibility of circulating miRNA biomarkers across datasets representing populations from Russia, China, and the United States. Overlapping candidate biomarkers were identified across multiple publicly available miRNA expression datasets obtained from GEO and EMBL-EBI BioStudies/ArrayExpress. Area under the curve (AUC) similarity ($|\Delta AUC| < 0.05$), overlap of 95% confidence intervals, and statistical significance in both datasets ($p < 0.05$) were considered when evaluating descriptive reproducibility. Across 68 qualifying biomarker comparisons performed in this research, only 2 (2.9%) met all the descriptive reproducibility criteria, 24 (35.3%) supported limited reproducibility, and 42 (61.8%) showed mixed evidence. miR-130b-3p, for instance, met all descriptive reproducibility criteria in a Russian and a U.S. dataset. It demonstrated strong discrimination in a U.S. dataset (AUC = 0.906) and a Russian dataset (AUC = 0.881), with $|\Delta AUC| = 0.025$, overlapping confidence intervals, and statistical significance in both. In contrast, miR-324-5p demonstrated strong discrimination in one Russian dataset (AUC = 0.902) but weak discrimination in another Russian dataset (AUC = 0.532), with non-overlapping confidence intervals, indicating poor reproducibility even between two Russian datasets. Biomarker performance differences between datasets collected in the same country suggest that factors such as sample size, assay method, smoking status, health history, environmental factors, and sample processing methods may also contribute to these differences. These findings demonstrate the importance of validating biomarkers across diverse populations to reduce the risk of diagnostic bias and healthcare disparities in underrepresented populations.

Theoretical Application of CRISPR technology for Pancreatic Cancer for Lower Income Communities

Mohnish Chintalapudi, Shriyans Nomula, Nived Syam

Pancreatic cancer is one of the deadliest cancers, with an estimated 53,000 deaths among the 68,000 individuals expected to be diagnosed in the United States in 2026. Current methods for identifying pancreatic cancer often require extensive and expensive imaging techniques, such as computed tomography (CT) and magnetic resonance imaging (MRI), which typically do not detect the disease until a tumor has formed. By the time the majority of cases are identified, treatment options are often limited. However, the majority of pancreatic cancers are pancreatic ductal adenocarcinomas (PDACs), which predominantly carry mutations in the KRAS gene. These mutations can appear early during pancreatic intraepithelial neoplasia (PanIN), a precursor to pancreatic adenocarcinoma. Theoretically, current applications of CRISPR technology could be used to develop a simple and inexpensive diagnostic test capable of identifying KRAS biomarkers, potentially allowing pancreatic cancer to be detected before the formation of a tumor.

Structure-Based Virtual Screening and Molecular Dynamics Identification of Fibrinogen Inhibitors for Targeted Pancreatic Cancer Therapy

Natasha Vora, Seaforth High School, Pittsboro, NC
Mentor: Gaurav Sharma, Eigen Sciences, Apex, NC

Abstract:

Pancreatic cancer is an aggressive malignancy characterized by late diagnosis, limited treatment options, and poor survival. Fibrinogen, a blood-clotting protein involved in fibrin formation, may promote pancreatic cancer progression and metastasis by supporting tumor-associated coagulation and remodeling of the tumor microenvironment. This study aimed to identify potential small-molecule fibrinogen inhibitors using a structure-based computational drug-discovery workflow. The three-dimensional structure of fibrinogen was prepared using AlphaFold 3, and potential ligand-binding pockets were identified using P2Rank/PrankWeb. We subjected candidate compounds from the ZINC20 database to virtual screening with AutoDock Vina. We selected the highest-ranked ligands (based on the docking score) through fibronectin-ligand interaction analysis, drug-likeness assessment, ADMET prediction, and molecular dynamics simulations. Six compounds L566, L623, L632, L633, L634, and L890, showed promising predicted binding affinities and formed hydrogen-bond and hydrophobic interactions with the target protein. Compound L623 showed the most hydrophobic contacts, while the selected compounds displayed varying pharmacokinetic and toxicity profiles. Molecular dynamics analysis provided additional evidence regarding the stability of the fibronectin-L623 complex. Overall, these findings identify promising fibrinogen-binding compounds that may serve as preliminary lead candidates for pancreatic cancer therapy. Experimental in vitro and in vivo studies are required to confirm their binding, biological activity, safety, and therapeutic effectiveness.

Keywords: Pancreatic Cancer, Structure-Based Virtual Screening, Molecular Dynamics, Fibrinogen

InterVUS: An Interface-Aware Framework for Reclassifying Variants of Uncertain Significance in Hereditary Breast Cancer Genes

Nathan Zhao

Over 98% of missense mutations are classified as variants of uncertain significance (VUS) in important hereditary breast cancer genes like BARD1. VUS are most common in Asian, Black, and Hispanic patients, largely because databases for classifying variants are predominantly built of people with European ancestry. Many variants also lack experimental validation, and current methods of structural prediction often address this issue through testing whether a substitution destabilizes a protein. However, these methods fail to consider variants that retain stable folding in an isolated state, but prove pathogenic when binding in protein-protein interfaces. To determine whether variants may be misclassified by current methods like AlphaMissense and if interface-aware prediction could improve classification in underrepresented groups, the study compared predicted classifications against 38,000 experimentally validated variants from Saturation Genome Editing (SGE) on MaveDB, and utilizes recent structural predictive models (AlphaFold3) to predict complexes of BRCA1, BRCA2, and BARD1, important hereditary breast cancer genes. Missense variants were mapped onto experimental and AlphaFold-predicted complexes, then each residue was classified based on solvent accessible surface area, and changes in folding and binding free energy are calculated with FoldX. These structural features were measured to develop Interface-aware prediction, which was applied to unresolved variants in breast cancer genes BRCA1, BRCA2, PALB2, BARD1, and RAD51D. For every variant the framework classifies, it reports a calibrated confidence score on how likely harmful the variant is and its specific structural mechanism: destabilization or by blocking partner interaction, providing doctors with results that can help tell whether a variant raises cancer risk. Then, for each resolved variant from our framework, we compared how often it appears in different ancestry groups in the gnomAD population database, where our framework was able to resolve more variants carried by underrepresented groups.

Pranav Kolluri

Title: The Impact of Cumulative Social Vulnerability and Cancer-Related Acute Stress on Emergency Department Utilization

Background: Cancer care depends on rides, food, housing, and symptom control at home. When that support slips, patients end up in the emergency department (ED). US adults with cancer made 35.5 million ED visits from 2012 to 2019. Visits rose 67% while new cancer cases rose 7.5%, and 51.6% of visits were potentially preventable. I asked how neighborhood vulnerability, unmet social needs, and psychological stress relate to ED use in adults with cancer, and whether screening at triage could help.

Methods: I reviewed 29 published sources and public data: PubMed and PMC studies, the 2022 CDC Social Vulnerability Index (SVI), NCI State Cancer Profiles for Georgia, and national ED data as published. For each study I recorded sample size, exposure, outcome, and effect size with its 95% confidence interval. The studies were too different to pool, so I compared direction and size of effects. This is a targeted review, not a formal systematic review, and it uses no new patient data.

Results: All 7 odds ratios for ED use were above 1.0, from 1.34 to 2.67. The largest was the SVI housing and transportation theme (aOR 2.67) in a claims analysis of 26.7 million patients. Severe distress went with 1.83 times the odds of ER use in colorectal cancer survivors and 2.57 times in prostate cancer survivors. Among 5,236 oncology patients, unmet needs went with more ED visits within a year (24.7% vs 14.2%). Food-insecure survivors were about 3 times as likely to skip follow-up care, and food insecurity ranged from 10.3% among US cancer survivors to 83.6% in FQHC pantry programs. In randomized trials, including PRO-TECT, symptom monitoring and navigation paired with symptom checks reduced ED or unplanned care. Social-needs help alone gave mixed results, in non-cancer groups.

Conclusions: Neighborhood vulnerability and personal stress both track with ED use, and missed outpatient care is the likely link. Help works best when paired with symptom care. No study I found measured SVI, distress, and ED use together, so a "cumulative" effect is a hypothesis, not a result. I propose linking tract-level SVI to ED encounters, adding a distress screen and three social-needs questions at triage, and piloting a navigator call for positive screens.

Do Ewing sarcoma cells depend on RNF216 more than other cancer cells do?

Ramcharan Nagisetty

The fusion protein EWS FLI1 is the primary cause of Ewing sarcoma, a bone cancer that mostly affects children and teens. Since there isn't already a medication that specifically targets it, it's critical to identify further cancer weak points. Do Ewing sarcoma cells rely more on RNF216 than other cancer cells? was the study topic. Using publicly available CRISPR data from the Cancer Dependency Map, over 1,000 cancer cell lines had their genes switched off one at a time to determine which genes the cells needed to live. Two separate screens from the Sanger Institute and the Broad Institute were used to verify the outcome. In order to ensure that the precise cell lines were not responsible for the outcome, Sanger Ewing cell lines that Broad had never studied were also examined. One Ewing cell line was eliminated at a time to ensure that it wasn't the cause of the whole outcome. Ewing sarcoma was also compared to other children cancers rather than simply all malignancies together. The research also revealed known Ewing genes such as FLI1, EWSR1, and TRIM8. 19 Ewing sarcoma cell lines were much more dependent on RNF216 than other cancer cell lines in the Broad data. With a p value of 2.5 x 10^{-2}, the average gene impact was minus 0.43 in Ewing as opposed to minus 0.09 in the other malignancies. The Sanger data with 11 Ewing cell lines revealed the same trend, with a p value of 4.3×10^{-2}. RNF216 remained significant with a p value of 0.022 in eight Sanger Ewing cell lines that Broad never analyzed. RNF216 was rated second out of 17,348 genes in the Sanger data and fifth out of 17,786 genes in the Broad data. Additionally, RNF216 behaved much like TRIM8, which is linked to EWS FLI1 and is previously known to be significant in Ewing sarcoma. Although there aren't many Ewing sarcoma cell lines accessible and this was still relied on public CRISPR data, the findings indicate that RNF216 may be another weak place in Ewing sarcoma. To find out what RNF216 is really doing and if inhibiting it truly damages Ewing sarcoma cells, laboratory testing would be necessary.

TGF-β pathway inhibition via combination treatment of polyphenols

Lauren Gabrielle D Ramos

TGF-β (transforming growth factor beta) signaling is a crucial pathway in the regulation of tumor heterogeneity, a phenomenon in cancers characterized by the wide and varied genetic makeup of cells within a tumor, decreasing the efficacy of cancer therapies due to treatment resistance. Therefore, inhibition of the TGF-β pathway and upstream pathways, such as SIRT1, has the potential to decrease therapeutic resistance. Current research suggests that breast cancer tumors display some of the highest levels of heterogeneity due to the high variety of cells that make up the mammary epithelium. Thus, treatments targeting tumor heterogeneity may improve outcomes for breast cancer patients in more advanced stages.

Natural compounds that have demonstrated suppressive effects on the TGF-β pathway include emodin, naringin, and its derivative, naringenin. A limitation in the efficacy of these compounds is their low bioavailability; as only small concentrations are able to reach the intended active sites, their scope of use in drug development is limited. However, these compounds have exhibited synergistic effects in similar cellular pathways, opening up the possibility of a combination treatment, a common strategy in overcoming bioavailability issues.

An in silico analysis was performed in order to visualize the interactions between the targeted receptors and drugs. Before binding affinity analysis could be performed, the receptors and ligands were imported into PyMOL, a software designed to visualize the structure of molecules and prepare models for docking. Existing 3D conformer models of emodin, naringin, and naringenin were sourced from PubChem's database, and the receptor models (TGFβR1 and SIRT1) were retrieved using the "fetch" command in PyMOL. The binding affinity of each drug and receptor was calculated in silico by utilizing the models to generate the optimal position of the ligands to bind within receptors. DockingPie was selected as a way to calculate the binding affinities between the different proteins and ligands directly within PyMOL, as it allowed for simultaneous visualization of docking positions and affinity data. Each molecule was imported into the DockingPie window and was run through an ALLVSALL simulation.

The average binding affinity of each compound as well as each combination, against both receptors was calculated as follows: emodin (-8.5), naringin (-6.7) naringenin (-8.15), emodin-naringenin (-8.325), emodin-naringin (-7.6), naringin-naringenin (-7.425). The results of this experiment demonstrate that the combination of emodin and naringenin had the best score out of all the proposed combination treatments. However, the study found that emodin treatment alone displays slightly stronger docking scores at both receptors, suggesting that the proposed combination treatments did not significantly demonstrate stronger docking affinity than existing single-compound treatments when modeled in silica, thus implying limited clinical potential. Further in vitro studies are necessary to strengthen these results

Structure-Guided Computational Discovery of Molecular Glue Degraders Targeting PP2ACα Reactivation for Therapeutic Intervention in Non-Small Cell Lung Cancer

Rohan Sengupta, Centennial High School, Ellicott City, MD

Abstract

NSCLC, or non-small cell lung cancer, is the most common form of lung cancer and remains a leading cause of cancer-related death worldwide. PP2ACa is a protein that removes phosphate groups from other proteins to regulate their activity and also controls cell growth and programmed cell death, keeping cells from growing out of control. Molecular glues are small molecules that enable protein interactions, allowing for cell targeting or the destruction of cancerous proteins. The aim was to computationally design and evaluate molecular glue compounds that can restore the tumor-suppressing activity of the PP2ACα protein in non-small cell lung cancer. We hypothesize that if molecular glue compounds can effectively bind PP2ACα and recruit an E3 ligase, then they can restore its tumor-suppressor function and inhibit the progression of non-small cell lung cancer. We obtained the amino acid sequence of PPC2a from UniProt and predicted its three-dimensional structure using AlphaFold. We used P2Rank to identify potential binding sites and docked candidate molecular glue compounds with HDOCK. We studied protein-ligand interactions using PLIP and PRODIGY, and assessed drug-likeness using SwissADME. Based on the above findings, molecule M4 formed the strongest interaction with the proteins. In addition, compounds M5, M6, M7, M8, and M10 demonstrated favorable drug-like and pharmacokinetic properties. This research will help with tumor suppression, targeted therapy, and overcoming drug resistance, and can also be extended to other cancers involving disrupted protein-regulation pathways.

Health Disparities in Endometrial Cancer Among Black Women: A Systematic Review

Authors: Arulthasan, Y., Bilal, A., Lai, J., Liang, A., Pandian, A., Parmar, S., Patel, S., Rajeshkumar, S., Foto, N.
Affiliation: EnvisionSTEM

Abstract

Endometrial cancer (EC) presents a paradox that current interventions have failed to resolve: Black women are diagnosed with EC less often than White women, yet die from it at nearly twice the rate, a gap that has widened, not narrowed, over 26 years of dedicated research. This systematic review synthesizes evidence from 2013 to 2025 across the United States and United Kingdom to identify why. We find that structural equity alone cannot explain the gap — Black women face higher EC mortality even within healthcare systems offering equal access — but neither can biology alone, since molecular subtype differences remain understudied due to small sample sizes in existing research. More urgently, we identify a compounding risk in the field's current trajectory: Black patients are significantly more likely to carry aggressive, treatment-relevant molecular subtypes (copy-number-variant-high, or CNV-high; “mitotic”; and cluster 4) that newer targeted therapies are designed to address, yet Black women remain severely underrepresented in the clinical trials validating those same therapies — in one major metastatic EC trial, just 3.7% of participants were Black. As EC treatment shifts toward molecularly targeted care, this gap in trial representation risks widening, not closing, the mortality disparity it is meant to help solve. We further find that standard diagnostic tools, including transvaginal ultrasound thresholds for postmenopausal bleeding, have recently been shown to miss roughly five times more cases in Black women, suggesting part of the diagnostic delay reflects tool miscalibration rather than access or behavior alone. We argue that closing this gap requires simultaneous investment in structural reform, prospective diagnostic validation in Black patient populations, and deliberate representation in the clinical trial pipeline driving the next generation of EC treatment.

Ancestry-Specific Inflammasome Activation: Do APOL1 Risk Variants Promote Oxidative DNA Damage in Renal Epithelial Cells?

Stefania Liu

Abstract: African ancestry populations experience disproportionately high rates of renal cell carcinoma, but the molecular mechanisms driving this disparity remain unclear. The APOL1 G1 and G2 variants, common in West African ancestry, cause kidney disease and are emerging as renal cancer risk factors. APOL1 forms membrane pores that trigger NLRP3 inflammasome activation and reactive oxygen species production, yet whether this pathway causes oxidative DNA damage is unknown. This project investigates whether APOL1 risk variants increase inflammasome activation, reactive oxygen species, and oxidative DNA damage in renal epithelial cells compared to wild-type APOL1. HK-2 renal epithelial cells will be transfected with APOL1-G0, APOL1-G1, APOL1-G2, or empty vector and cultured with or without inflammatory stimulation using lipopolysaccharide and interferon gamma. Inflammasome activation will be measured by caspase-1 activity assay and interleukin-1 beta enzyme-linked immunosorbent assay. Reactive oxygen species will be quantified by DCFDA flow cytometry, and oxidative DNA damage by 8-hydroxydeoxyguanosine enzyme-linked immunosorbent assay. The NLRP3 inhibitor MCC950 will test pathway dependence. Cells expressing APOL1-G1 or G2 are expected to show higher caspase-1 activity, interleukin-1 beta secretion, reactive oxygen species, and oxidative DNA damage than G0 cells, with effects amplified by inflammatory stimulation and reversed by MCC950. If confirmed, this work would define an inflammasome-driven oxidative DNA damage axis linking an ancestry-specific variant to cancer risk, providing a biochemical mechanism for renal cancer disparities and a rationale for evaluating NLRP3 inhibitors in high-risk populations.

Targeting TDG as a Potential Therapeutic Strategy in BAP1-Deficient Uveal Melanoma Cells

Tanmayi Chennapragada
Fox Chase Cancer Center, Philadelphia, Pennsylvania
Leander High School, Leander, Texas

Abstract

Uveal melanoma (UM) is an aggressive ocular cancer with limited therapeutic options, especially after metastasis, creating a need to identify new molecular vulnerabilities. This study investigates thymine DNA glycosylase (TDG), a DNA repair enzyme involved in base-excision repair and epigenetic regulation, as a potential therapeutic target in UM. We hypothesized that reducing TDG activity would impair UM cell survival and that BAP1-deficient cells may show increased sensitivity to TDG loss. TDG was targeted through genetic depletion using shRNA and pharmacologic inhibition with a small-molecule TDG inhibitor. CellTiter-Glo assays measured viability after 3- and 7-day treatments across multiple UM cell lines, while clonogenic assays, Incucyte live-cell imaging, and microscopy were used to evaluate long-term survival, proliferation, and treatment-associated morphology. Across several UM cell lines, TDG inhibition reduced measured viability. In 94.2 and 92.1 cells, viability at 15–30 μM was lower after 7 days than after 3 days of treatment. In OMM2.3 cells, 7-day viability was lower than 3-day viability at every tested nonzero concentration, while OMM2.5 cells showed reduced viability relative to untreated controls at higher concentrations at both time points. These findings indicate that TDG inhibition can reduce viability in UM cells, although the magnitude and time dependence of the response vary among cell lines. Further comparison of pharmacologic inhibition with genetic TDG depletion and BAP1 status will be necessary to determine whether BAP1 loss creates a specific dependency on TDG. Overall, these results support continued investigation of TDG as a potential therapeutic vulnerability in uveal melanoma. Generative AI was used solely for drafting and language refinement and was not used to conduct experiments, analyze experimental data, or create or interpret graphs. All scientific content, results, and conclusions were reviewed and verified by the authors.

Engineering the Tumor Surface: Synthetic Nutrient Mimicry Peptides as Stable Extracellular Anchors for Precision Cancer Therapy

Tejas Bachu

Abstract

We developed a new way to investigate how Synthetic Nutrient Mimetic Peptides (SNMPs) might be used as 'extracellular membrane anchors' in targeted cancer therapy. SNMPs are short peptides that have undergone modifications to add synthetic lipid tails, allowing them to bind to the membranes of tumor cells. Our investigation identified the initial membrane anchoring step as the main factor affecting the targeting specificity and the stability at the membrane anchor. Using CHARMM-GUI Membrane Builder, we built a tumor mimic lipid bilayer that was enriched in both cholesterol and negatively charged phospholipids. We compared three dual-palmitoylated SNMP designs to a non-lipidated control using a series of static membrane packing predictions to determine the positions of the lipid tails within the membrane, the orientations of the peptides within membranes, and the solvent accessibility of the peptide backbones. Peptides were considered 'anchored' when the lipid tails of the peptides had reached the membrane interface, while the peptide backbones remained accessible to the surrounding environment. Overall, our study demonstrated that lipidation is an essential requirement for the binding of SNMPs to membranes. However, it does not ensure that the bound peptides are effectively anchored to the membrane. Peptides with compact geometries consistently led to interfacial insertion of the peptide into the membrane, whereas peptides with extended geometries led to less efficient membrane interaction, even when both types of peptides were equally lipidated. Therefore, we conclude that peptide geometry is one of the most significant design characteristics that determine SNMP anchoring properties.



Viraj Maini
10th Grade
South Forsyth High School
Healthcare Teacher: Mr. Daniel Spence

Generative AI vs. Hospital Websites in Diagnosing Medical Symptoms

A Survey of High School and College Students

Prepared for the 2026 The Science of Cancer Health Disparities Conference

How do young adults search for health information, and what do they trust?

South Forsyth High School
Grade: 10

Introduction

With the rise of generative AI and online medical resources, many young adults now turn to the internet for health information. This study explores how students and peers use and trust generative AI and hospital websites when experiencing medical symptoms, and how these tools may influence care-seeking decisions. These questions are relevant to health disparities because access to clear, trusted health information can shape when people seek professional care.

Research Question

How do young adults use and trust generative AI and hospital websites for medical symptoms, and what factors influence whether they rely on online tools or seek care from a real doctor?

Methods

Survey Design
Online Qualtrics survey with 15 questions

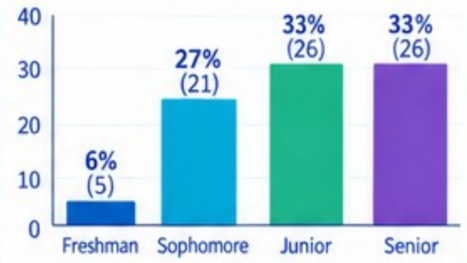
Participants
84 students and peers surveyed; most analyses use 78 valid responses

Data Collection
Anonymous convenience sample

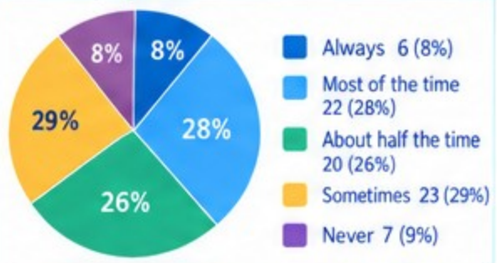
Analysis
Descriptive statistics: counts, percentages, and mean ratings

Results

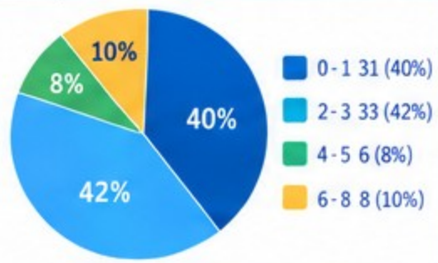
1. Year of Study (n = 78)



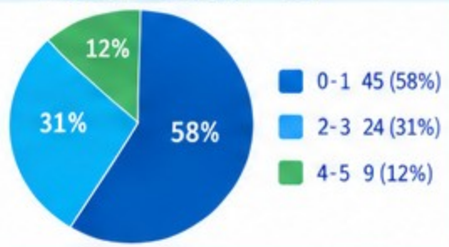
2. How Often Do You Search Online for Symptoms? (n = 78)



3. Use of Generative AI for Symptoms (in past 4 months) (n = 78)



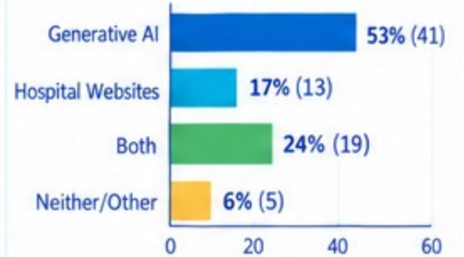
4. Use of Hospital Websites for Symptoms (in past 4 months) (n = 78)



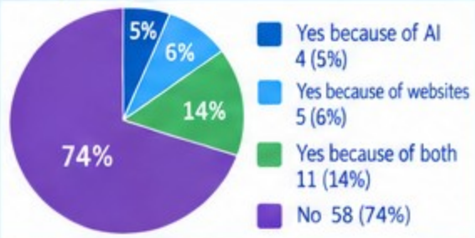
5. Trust in Medical Information (1 = low, 5 = high) (n = 78)



6. Which Tool Is Easier & Faster? (n = 78)



7. Changed Mind About Seeing a Doctor? (n = 78)



8. Likelihood of Using Online Tools Instead of a Doctor Because of Cost (1 = low, 5 = high) (n = 78)



9. Future Preference for Mild-Severe Symptoms (n = 78)



Key Findings

Higher trust in hospital websites
Students trusted hospital websites more (4.28/5) than generative AI (2.51/5).

AI is faster and easier
53% found generative AI easier and faster compared with 17% for hospital websites.

Cost influences behavior somewhat
Hospital websites (2.58/5) were seen as slightly more likely than AI (1.97/5) to be used instead of a doctor because of cost.

Most still do not change doctor decisions
74% said online information did not change their decision to see a doctor.

Doctors remain the top future choice
69% would still prefer to see a doctor for mild to severe symptoms.

Discussion

- Students frequently use online tools, especially generative AI, to look up symptoms.
- Generative AI is viewed as quicker and easier to use, but hospital websites are trusted more.
- Most respondents did not let online information replace professional medical care.
- Doctors remain the most preferred source for future care decisions.
- These findings suggest that digital health education may help reduce information gaps and support more equitable healthcare decision-making.

Limitations

- Small, non-random convenience sample
- Mostly students and peers
- Self-reported responses may be affected by recall or response bias
- Study is not cancer-specific and does not directly measure outcomes
- Some survey items had missing responses

Conclusion

Generative AI and hospital websites are widely used for symptom information, but trust remains much higher for hospital websites and future care remains centered on real doctors. Improving digital health literacy and access to reliable information may support better decisions and may be relevant to reducing health disparities, including in areas such as cancer awareness and early help-seeking.

Better Information. Healthier Decisions. A More Equitable Future.

Comparing MicroRNA- and IsomiR-level Quantification in the Study of Primary Brain Tumor Biomarkers

Y. Yang[1,*], R. Magee[2]

[1]Granville High School, Granville, USA
yinglingyang1024@gmail.com

[2]Mass General Brigham, Boston, USA
rogan.magee@pennmedicine.upenn.edu

[*]**Corresponding author:** Yingling Yang, yinglingyang1024@gmail.com

PURPOSE

We compared differential expression across two datasets using microRNA-level and isomiR-level quantification to assess whether isomiR analysis increases the yield of reproducible biomarker candidates differentiating glioblastomas and astrocytomas.

METHODS

We analyzed isomiR-level data from bulk small RNA sequencing of primary brain tumor tissue samples. Samples were collected from two separate projects of The Cancer Genome Atlas (TCGA): TCGA-GBM (glioblastoma) and TCGA-LGG (low-grade glioma).

Samples were stratified by IDH1 status, with mutant samples designated as astrocytoma and wild-type samples as glioblastoma, reflecting the IDH-associated molecular distinctions of the 2021 WHO classification. TCGA-GBM included 233 wild-type and 21 mutant samples, while TCGA-LGG included 41 wild-type and 130 mutant samples. We retained 18-26nt sequences from mature microRNAs (miRNAs) and summed isomiRs by source mature miRNA for miRNA-level quantification. Each project included 1,531 miRNA and 15,810 isomiR sequences.

Differential expression was performed using DESeq2 for both isomiR and miRNA data. Sequences with false discovery rate (FDR) < 0.05 were considered differentially expressed (DE). miRBase was used as the reference for canonical miRNA sequences. All analyses were run in R version 4.3.1.

RESULTS

In TCGA-GBM, 103 miRNAs were significantly upregulated in astrocytoma versus glioblastoma samples, 47 downregulated, and 1,381 not significantly DE. Among isomiR sequences, 950 were upregulated, 87 downregulated, and 14,773 not significantly DE.

In TCGA-LGG, 90 miRNAs were significantly upregulated, 90 downregulated, and 1,351 not significantly DE. 522 isomiRs were upregulated, 517 downregulated, and 14,771 not significantly DE.

Across both projects, 12 isomiRs and 2 miRNAs were significantly upregulated, while 1 miRNA was downregulated. Of the 12 consistently upregulated isomiRs, 11 differed from the canonical miRBase sequence.

CONCLUSIONS

Because 11 of the 12 upregulated isomiRs differed from their canonical miRNA sequences, analyzing reference miRNAs alone risks overlooking potentially useful biomarker signals. Across both projects, isomiR-level analysis yielded more upregulated sequences than conventional miRNA quantification, providing a larger pool of biomarker candidates for tumor classification. Furthermore, because differential expression varied among isomiR variants from the same miRNA locus, aggregating them would mask or dilute isomiR-specific signals, potentially reducing the ability to identify useful and reproducible biomarkers.

These results suggest that preserving isomiR-level resolution may facilitate identification of reproducible biomarker candidates across datasets. Compared to conventional miRNA-level quantification, this approach could better retain variant-specific expression patterns during bioinformatic processing and differential expression analysis.

Abstract

InterVUS: An Interface-Aware Framework for Reclassifying Variants of Uncertain Significance in Hereditary Breast Cancer Genes

Nathan Zhao

Over 98% of missense mutations are classified as variants of uncertain significance (VUS) in important hereditary breast cancer genes like BARD1. VUS are most common in Asian, Black, and Hispanic patients, largely because databases for classifying variants are predominantly built of people with European ancestry. Many variants also lack experimental validation, and current methods of structural prediction often address this issue through testing whether a substitution destabilizes a protein. However, these methods fail to consider variants that retain stable folding in an isolated state, but prove pathogenic when binding in protein-protein interfaces. To determine whether variants may be misclassified by current methods like AlphaMissense and if interface-aware prediction could improve classification in underrepresented groups, the study compared predicted classifications against 38,000 experimentally validated variants from Saturation Genome Editing (SGE) on MaveDB, and utilizes recent structural predictive models (AlphaFold3) to predict complexes of BRCA1, BRCA2, and BARD1, important hereditary breast cancer genes. Missense variants were mapped onto experimental and AlphaFold-predicted complexes, then each residue was classified based on solvent accessible surface area, and changes in folding and binding free energy are calculated with FoldX. These structural features were measured to develop Interface-aware prediction, which was applied to unresolved variants in breast cancer genes BRCA1, BRCA2, PALB2, BARD1, and RAD51D. For every variant the framework classifies, it reports a calibrated confidence score on how likely harmful the variant is and its specific structural mechanism: destabilization or by blocking partner interaction, providing doctors with results that can help tell whether a variant raises cancer risk. Then, for each resolved variant from our framework, we compared how often it appears in different ancestry groups in the gnomAD population database, where our framework was able to resolve more variants carried by underrepresented groups.

Beyond Survival: Geographic and Racial Disparities in Eye Preservation Among Children With Retinoblastoma in the United States, 2015–2023

Author: Zoe Kaushik

Research Category: Pediatric Oncology, Cancer Epidemiology, and Health Disparities

Study Design: Proposed Retrospective Population-Based Study

Abstract

Background: Retinoblastoma is a rare pediatric malignancy in which treatment decisions can determine whether a child retains an affected eye. Advances in chemotherapy and localized therapies have expanded opportunities for ocular preservation. However, previous research has identified racial, socioeconomic, and geographic disparities in enucleation, the surgical removal of an eye. Whether these disparities have narrowed during the modern treatment era remains an important question.

Objective: To investigate temporal trends in enucleation among children diagnosed with retinoblastoma in the United States between 2015 and 2023, with particular emphasis on geographic and racial or ethnic disparities in ocular preservation.

Methods: This proposed retrospective study will utilize population-based data from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program. Pediatric patients diagnosed with retinoblastoma between 2015 and 2023 will be identified using cancer registry records. Enucleation will serve as the primary outcome. Demographic, geographic, and available clinical characteristics will be evaluated using descriptive statistics and multivariable logistic regression. Interaction analyses will investigate whether geographic and racial or ethnic differences in enucleation have changed across treatment periods. Available clinical characteristics will be incorporated to account for potential differences in disease presentation.

Expected Contribution: This study aims to characterize changes in pediatric retinoblastoma treatment and investigate whether disparities in ocular preservation have narrowed over time. By examining the intersection of geographic residence, race, ethnicity, and treatment era, this research seeks to identify potential inequities warranting further investigation and inform future efforts to improve equitable access to specialized pediatric oncology care.

Keywords: Retinoblastoma; Pediatric Oncology; Cancer Health Disparities; Enucleation; Ocular Preservation; SEER; Healthcare Equity.