



The MD Anderson  
**Summer Experience**  
Explore Your Future in Cancer Research

THE UNIVERSITY OF TEXAS MD ANDERSON CANCER CENTER

# 2023 Summer Experience Program Abstracts

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# CPRIT-CURE Summer Undergraduate Program

Abstract Number: 1

## **Overlapping and distinct mechanisms of action by Immune Checkpoint Therapy and Neoantigen Cancer Vaccine in Mouse Melanoma Model**

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**Background:** CD4<sup>+</sup> and CD8<sup>+</sup> T cells play a pivotal role in cancer detection and elimination. However, high expression of negative immune checkpoint molecules, PD-1 and CTLA-4, on intratumoral T cells and their ligand by tumor cells allowing evasion of anti-tumor immunity. Immune checkpoint therapy (ICT) provides a promising approach to remove immunological breaks and improve anti-tumor immune responses. However, not all patients respond equally to treatment, as the efficiency may vary from patient to patient due to the various forms of cancers, suggesting that additional therapy is required. Neoantigen Cancer Vaccinations is a promising a personalized approach to mitigating the effects of cancer that could improve ICT.

**Methods:** We have generated Y1.7 melanoma cell line expressing MHC-I/II mutant neoantigens mLama4 and mltbg1. C57BL/6 mice were transplanted with  $0.5 \times 10^6$  Y1.7 melanoma cells on day 0 followed by treatment with immune checkpoint inhibitors (aCTLA-4 and /or aPD-1) on days 7, 10 and 13, and synthetic long peptide (SLP) vaccine on day 7 and 13. Tumor size were assessed through the course of the experiment. At the end of experiment, mice were euthanized, and tumors were assessed for infiltrated immune cells by Flow Cytometry and scRNAseq.

**Results:** Treatment with ICI or neoantigen vaccine showed promising but different grades efficacies. Mechanistically, while ICI increase the percentage of intratumorally CD4<sup>+</sup> and CD8<sup>+</sup> T cell, neoantigen vaccine induced percentage of antigen specific CD8<sup>+</sup> T cells. Additionally, upon both ICIs and Neoantigens vaccine treatments, M1 like macrophages were found predominant within the tumor. Thus, due to the shared and unique mechanism of ICT and neoantigen vaccination, their combination could lead to more efficient and long-lasting anti-tumor responses. In fact, the combination treatment with ICT plus neoantigen vaccine led to a more efficient tumor eradication of advanced tumors.

**Conclusion:** The research highlights the potential of both ICT and neoantigen cancer vaccines in reshaping the tumor microenvironment and enhancing T-cell responses. The combination of these approaches and their effects on myeloid cell populations offer insights into developing personalized cancer treatments.

**Keywords:** Immune checkpoint therapy (ICT), NeoVAX, T cells, M1 macrophages, YUMM1.7

**Program Affiliation:** CPRIT-CURE Summer Undergraduate Program

Abstract Number: 2

## **Preclinical model and treatment strategies for ICI-induced colitis**

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**Background:** Immune checkpoint inhibitors (ICIs) represent a groundbreaking therapeutic approach that revitalizes T cells to counter a diverse array of cancers by obstructing inhibitory signals such as CTLA-4 and PD-1. Nevertheless, their application can give rise to immune-related adverse events (irAEs), characterized by uncontrolled inflammation that can occur in any organ system. irAEs can prompt steroid use and the stop of ICI therapy, potentially raising cancer recurrence risk. Colitis in particular, is observed in approximately 9-14% of ICI-treated patients, severely impacting their quality of life. To gain insights into the underlying mechanisms of irAEs, it is imperative to employ preclinical models.

**Methods:** ICI-colitis was induced by treating C57BL/6 mice with DSS and anti-PD-1, anti-CTLA-4, or combination ICIs (anti-PD-1 and anti-CTLA-4). Daily weights were recorded, and upon experiment completion, serum, feces, and colons were collected for further analysis. In some experiments, ICI-colitis mice received therapeutic treatments. B16 melanoma cells were implanted into C57BL/6 mice followed by ICI treatment alone or in combination with ICI-colitis treatments.

**Results:** Mimicking what is seen in humans, combined ICI therapy led to heightened colitis severity in mice, marked by decreased body weight, shortened colon lengths, and deteriorated colon structure. Enrichment of CD8<sup>+</sup> T cells, CD4<sup>+</sup> T cells, particularly T helper (Th)1 and Th17 cell subsets were also observed. Different approaches targeting CD8<sup>+</sup> T cells and Th1/Th17 cytokines effectively mitigated ICI-colitis in this model. The best-performing treatments, when combined with ICIs, did not compromise the anti-tumor efficacy of ICIs in melanoma.

**Conclusion:** We created a preclinical murine model of ICI-colitis that only becomes apparent following the administration of ICIs. Blocking CD8 T cells and factors associated with Th1/Th17 cells emerges as an effective strategy for treating ICI-Colitis, underscoring their significant involvement in pathogenesis and providing relief to afflicted patients.

**Keywords:** Immune checkpoint inhibitors, immune adverse related events, ICI-colitis, Th1/Th17 cells, B16 melanoma

**Program Affiliation:** CPRIT-CURE Summer Undergraduate Program

Abstract Number: 3

## **Analysis and Prediction of Patient Survival After Radiotherapy For Liver Cancer Based On Volumetric Segmental Response and Clinically Relevant Factors**

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**Background:** Primary liver cancer is one of the leading causes of cancer fatalities globally, with over 830,000 deaths in 2020. The three major types of adult liver cancer are hepatocellular carcinoma (HCC), cholangiocarcinoma (CC), and colorectal metastasis (CRM). The liver's capability to regenerate functional tissue allows for recovery following cancer-associated damage. Namely, parenchymal tissue growth following external beam radiotherapy (RT) and contralateral hypertrophy after radioembolization have been documented. However, liver segment-specific hypertrophy due to RT and its relationship with liver cancer patient survival is not clearly known. Thus, my goals are to: 1. Analyze the relationship between post-RT liver segment hypertrophy in HCC, CC, and CRM patients and survival outcomes. 2. Build a binary risk prediction model to forecast 15-month survival for liver cancer patients, incorporating data on liver segmental response, radiation dosimetrics, and other relevant predictors.

**Methods:** From a dataset of 144 liver cancer patients, survival analysis including Multivariate Kaplan-Meier Curve Analysis, Cox Proportional Hazards Regression Analysis, and Log-Rank Tests were applied to analyze the relationships between post-RT liver segment hypertrophy as well as clinical factors and survival. Feature selection was completed leveraging Logistic Regression for numerical predictors and Chi-squared and Fisher Exact tests for categorical predictors. Different algorithms including Lasso Regression, Random Forest, Support Vector Machine, and XGBoost were tested and majority vote analysis conducted. The models were evaluated using metrics including accuracy, sensitivity, specificity, AUROC, and AUPRC.

**Results:** Patients in the overall cohort with hypertrophy in segments 2 and 3 had a 56.67% greater probability of surviving relative to those who did not at any given time point (log-rank:  $p=0.02$ ). Patients in all cohorts with portal vein thrombosis (PVT), with cirrhosis in the overall cohort, and with portal hypertension (PHT) in the HCC cohort, respectively ( $p<0.05$ ), were approximately 2 times as likely to die at any given time point [compared to the negative group]. All model accuracies, AUROC, and sensitivities were equal to or above 0.72, 0.79, and 0.90, respectively, demonstrating strong performance. Lasso Regression had the highest aforementioned metrics, proving to be the most robust model.

**Conclusion:** Liver hypertrophy in segments 2 and 3 significantly correlated with better survival. Clinical factors including PVT, PHT, and cirrhosis were significantly associated with greater mortality in certain liver cancer patient cohorts. Robust binary risk prediction models were developed to predict patient survival 15 months following the end of RT treatment.

**Keywords:** Liver hypertrophy, survival analysis, modeling

**Program Affiliation:** CPRIT-CURE Summer Undergraduate Program

Abstract Number: 4

## **High Fiber Dietary Intervention Induces Change in Role of *Faecalibacterium Prausnitzii* in Gut Microbiome Ecosystem**

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**Background:** A habitual high-fiber diet was associated with improved progression-free survival (PFS) in melanoma patients on immune checkpoint blockade (ICB) therapy, and gut microbial bacteria associated with response to ICB are fiber-responsive taxa. A high-fiber diet intervention (HFDI) was conducted in melanoma survivors to prospectively evaluate the effect of fiber on the microbiome. The relative abundance of fiber-responsive, pro-ICB response taxa (such as *Faecalibacterium prausnitzii*) did not change with a HFDI. However, increasing evidence supports that it is not the abundance of taxa that is important, rather the role they play in supporting the overall ecosystem. Prior studies have shown *F. prausnitzii* is a key producer of Short Chain Fatty Acids (SCFAs) which may be cross-fed to other intestinal microbiota, supporting a healthy microbial ecosystem. Network analysis of the gut microbiota throughout a HFDI allows the opportunity to examine how *F. prausnitzii* changes its microbial associations and role in the gut microbial ecosystem.

**Methods:** Ten melanoma survivors were enrolled to a 6-week HFDI, targeting 50 grams of fiber daily, derived from legumes, whole grains, vegetables, and fruit with all meals provided from MDACC Bionutrition Research Core. Metagenomic sequencing was conducted on DNA extracted from fecal samples and processed with MetaPhlan3 to create abundance profiles at each timepoint from screening (SCRN) to week 6 (W6) and 6 weeks after the end of the study (EOS). NetCoMi (Network Construction and Analysis for Microbiome Data) was used to construct microbial association networks.

**Results:** At SCRN, taxa are divided into a SCFA-Producing majority-Firmicutes cluster, a majority *Bacteroides* cluster, and other loosely associated commensal clusters, with *F. prausnitzii* embedded in the *Bacteroides* cluster. The SCFA-producing cluster predominates the microbiome and loosens associations within other clusters in response to the HFDI, and *F. prausnitzii* becomes tightly associated with the SCFA-Producing cluster. Removal from the HFDI by EOS causes reemergence of cluster divisions, and *F. prausnitzii* is no longer associated with the SCFA-Producing cluster.

**Conclusion:** Network analysis reveals dynamic shifts in microbial associations and a restructuring of the microbial ecosystem with a HFDI. The observed shifts in *F. prausnitzii* support its changing role in the ecosystem as it becomes tightly associated with SCFA-producing taxa. This suggests *F. prausnitzii* may be using products generated from fiber metabolism to cross-feed with taxa in the SCFA-producing cluster. When the HFDI is withdrawn, cluster divisions reemerge and *F. prausnitzii* dissociates from the SCFA-producing cluster. This may signify the end of cross-feeding with the SCFA-producing cluster.

Keywords: microbiome, fiber, networks, melanoma, immunotherapy

Program Affiliation: CPRIT-CURE Summer Undergraduate Program

Abstract Number: 5

## **Structural Disruptions of the 3D Genome Architecture in Human Brain Cancer**

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**Background:** Genomic rearrangements in human cancers can lead to significant alterations in the three-dimensional (3D) chromatin organization, impacting gene expression and cancer development. The formation of new chromatin loops, termed neoloops, has emerged as a key consequence of disrupted 3D genome architecture in tumors. However, the occurrence of neoloops in brain cancer and their association with tumor properties, such as IDH mutant status, tissue type, and subtype, remain poorly understood. Additionally, the altered expression of neoloop-associated genes may play a significant role in driving oncogenic characteristics within tumor samples. To address these gaps, the objective of this research is to conduct a comprehensive analysis of neoloop occurrence across 86 brain tumor samples, providing valuable insights into the impact of disrupted 3D genomic architecture in brain cancer.

**Methods:** For this study, we performed an extensive analysis of neoloop occurrence in brain tumor samples using Hi-C sequencing data. We integrated Whole Genome Sequencing (WGS) data with five structural variant detection tools to identify copy number alterations and detect neoloops. RNA sequencing and ATAC sequencing data were utilized for gene expression and epigenetic analysis.

**Results:** In this study, we analyzed a total of 86 patient samples, which represented various glioma types, including Glioblastoma, Astrocytoma, and Oligodendroglioma. Among the samples, IDH wild-type gliomas exhibited higher neoloop counts compared to IDH mutant gliomas, although not statistically significant ( $p = 0.0987$ ). Additionally, classical glioma subtype samples displayed a higher number of neoloops compared to other subtypes ( $t = 3.0305$ ,  $p = 0.0542$ ). 20 recurrent neoloop-associated genes were identified, with five of them (EGFR, IL21R, HOXC11, HOXC13, and RARA) showing significantly elevated expression when involved in neoloops. Notably, an enhancer hijacking event in genes HOXC11, HOXC13, and CDK4 within a glioblastoma multiforme sample resulted in significantly elevated gene expression, presumably concurrently influenced by alterations in gene copy number.

**Conclusion:** Our study highlights the substantial impact of disrupted 3D genomic architecture in human brain tumors, particularly through neoloop formation. The identification of neoloop-associated genes with altered expression suggests potential oncogenic roles and offers opportunities for further investigations in cancer biology. These findings provide crucial insights into cancer initiation and progression and may guide future therapeutic interventions.

**Keywords:** 3D genome architecture, structural variants, chromatin organization, neoloops, brain tumors.

**Program Affiliation:** CPRIT-CURE Summer Undergraduate Program



## CP RTP Summer Research Experience

Abstract Number: 6

### **Impact of Demographic and Clinical Factors on Remote Patient Monitoring Acceptance**

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**Background:** Remote patient monitoring (RPM) utilizes mobile technology and sensors to capture and transmit data about a patient's health away from the clinic setting, including biometrics (i.e., vital signs) and patient-reported outcomes (PROs). Systematic, remote, and electronic collection of PROs during chemotherapy, with provider intervention if symptoms worsen, has been associated with fewer symptoms, better quality of life (QOL), and improved survival. However, there are limited data on the efficacy of RPM that combines PROs and biometric data to support cancer patients during challenging treatment periods, particularly in medically underserved populations. I will investigate reasons why patients may or may not consent to integrate RPM in their outpatient cancer care, as well as the difference in implementation and efficacy of RPM platforms in primarily Spanish-speaking and English-speaking populations.

**Methods:** Adult patients with advanced solid tumor cancers at LBJ Hospital will be recruited for this study. Patients will be randomized into 2 arms: usual care, and daily RPM (including PROs and biometric data) + usual care. Validated QOL symptom and patient engagement measures will be administered at baseline, 4-weeks, 8-weeks, and 12 weeks (end of study).

**Results:** Because this study is longitudinal and due to the short timespan of the summer internship, data collected at baseline will be used to produce the results. REDCap (a database) will be used to analyze the quantitative data from patient questionnaires to understand patterns among refusers vs consenters. Likewise, correlations between primary language (Spanish vs English) and implementation of the RPM program will be identified.

**Conclusion:** This study will increase understanding of help visualize the impacts of the digital divide on un-insured (or under-insured) patients, as well as the sociocultural barriers preventing the integration of RPM into outpatient cancer care. On the other hand, an excess of data can cause information overload and potentially increase instances of worry and anxiety in patients (Xu & Yan, 2022). However, this study and the implementation of RPM in cancer care has the potential to reduce acute hospital visits and increase patients' quality of life.

**Keywords:** Behavioral Science, Telehealth, Technology Acceptance Model

**Program Affiliation:** CP RTP Summer Research Experience

Abstract Number: 7

## **Interventions Reducing Racial/Ethnic Disparities Across the Cancer Care Continuum: A Scoping Review**

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**Background:** Numerous studies have documented the persistence of racial and ethnic disparities in cancer mortality, stemming from suboptimal adoption of evidence-based practices (EBPs) along the cancer care continuum, from prevention to end-of-life. Evidence exists for implementations that increase the uptake of EBPs. There is a need to describe the current evidence base for interventions that reduce these disparities in an implementation science framework.

**Methods:** This scoping review utilized the checklist established by PRISMA-ScR and the scoping review framework established in the JBO Manual for Evidence Synthesis. A search strategy was formalized, and relevant articles from 2010 to August 2022 were pulled from Medline, Embase, Cochrane, and Scopus. Articles were included if they were an USA-based interventional study that aimed to reduce racial/ethnic disparity in the uptake of an EBP along key parts of the cancer care continuum: prevention (HPV prevention), screening/diagnosis, treatment, survivorship, and end-of-life care, regardless of cancer type, patient demographics, or methodology. We chose to limit the prevention continuum to HPV prevention, due to the existing reviews on tobacco cessation and physical activity/diet programs. Quantitative peer-reviewed journal articles that seek to will be included. Rayyan Systematic Review was utilized for the screening process. REDCap was used for the data collection, and RStudio was utilized for the data analysis.

**Results:** Our search strategy yielded 45,215 articles. After the screening process against previously defined inclusion/exclusion criteria, a total of 511 articles were selected for the data synthesis. We found robust research concerning prevention and screening (~75%), but a scarcity of studies addressing treatment, survivorship, and end-of-life (EOL) care. Our interim findings (n=28 articles) indicate diverse levels of intervention effectiveness in enhancing the adoption of evidence-based practices (EBP). Many studies targeted improving outcomes in breast, colorectal, or cervical cancer (~95%). We expect that common interventions, such as patient navigation programs, reminder tools, and mailed-screening kits, will show consensus in

improving uptake of EBPs. We hypothesize that majority of the outcomes assessed will be soft outcomes (e.g. screening knowledge, intention) rather than hard outcomes (e.g. screening rate). We have also observed limited research on implementation outcomes, especially regarding costs and sustainability, based on the available interim evidence.

Conclusion: Our findings highlight the gap of evidence for interventions that reduce disparities in treatment, survivorship, and end-of-life care. Future studies should focus on addressing areas of gap in the evidence-base, assessing implementation outcomes in successful interventions, and incorporating hard outcomes.

Keywords: implementation science, interventions, continuum, disparities

Program Affiliation: CPRTP Summer Research Experience

Abstract Number: 8

## **Patients' first line chemotherapy choice and treatment outcomes for HER2 positive breast cancer**

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**Background:** Overexpression of human epidermal growth factor receptor 2 (HER2) occurs in up to 20% of breast cancer cases, presenting poor prognosis and aggressive phenotype in patients. The administration of Trastuzumab, a human monoclonal antibody which inhibits cell growth by binding to the extracellular domain of the receptor, receptor's extracellular domain, with chemotherapy has improved survival in patients with HER2 positive early stage and metastatic breast cancer. The most common regimens for HER2 positive breast cancer are TH (paclitaxel and trastuzumab), H (trastuzumab), HP (pertuzumab, trastuzumab), TCH (docetaxel, carboplatin, and trastuzumab), TCHP (trastuzumab, pertuzumab, carboplatin, and docetaxel), AC-TH (doxorubicin plus cyclophosphamide followed by paclitaxel plus trastuzumab), AC-THP (doxorubicin and cyclophosphamide followed by paclitaxel, trastuzumab, and pertuzumab), THP (docetaxel, trastuzumab, and pertuzumab). This leads to the necessity of figuring out what which regimens among these are more efficient, since all of these are associated to different efficacies in reducing breast cancer recurrence and overall survival. Thus, we will develop an algorithm to identify HER2- positive based chemotherapy regimens with the better efficiency among the pool of currently used regimens.

**Methods:** We obtained data from Optum's de-identified Clinformatics Data Mart Database and selected a cohort of women 18 years and older, which were diagnosed with HER2 positive breast cancer and received trastuzumab based chemotherapy. Each patient had an index date that defined by the 1st chemotherapy claim date. The algorithm includes 3 steps to define regimen for cancer patients based on this index date. First, we identified patients who had trastuzumab on the index date. We identified all chemotherapy drugs that patient received on the index date. Based on the combination of drugs, we defined patients' regimen. Second, we selected patients who received trastuzumab after the index date but within 30 days of the index date and defined their regimen. Last, for patients who received trastuzumab after 30 days from the index date but within 1 year since index date, we identified all the unique chemotherapy drugs the patients received and define their regimen. The outcome variable of this study is regimen that patient received, and the covariate variables are patients' age, race, and year of breast cancer diagnosis.

**Results:** The reason for the constant shift in frequency usage of various chemotherapy regimens is greatly affected by the approval of new chemotherapy agents by the FDA. Also, patients' characteristics, drug toxicity, physician's characteristics, and drug cost may play a role in the choice of regimens in patients' treatment.

**Conclusion:** The algorithm can define patients' regimens based on chemotherapeutic agents received. The regimens defined were TH, H, HP, TCH, TCHP, AC-TH, AC-THP, and THP. Among these regimens the most used were TCH, TCHP, and ACTH. Finally, it was observed that regimen patterns were changed over time during the study period between 2007 to 2022.

**Keywords:** HER2 positive-breast cancer, Algorithm, Trastuzumab

**Program Affiliation:** CPRTP Summer Research Experience

Abstract Number: 9

**Psychosocial Concerns in Lung Cancer Patients and Family Caregivers: Identifying Behaviors of Focus to Improve Future Dyadic Behavioral Intervention Programs**

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**Background:** Over half of the concerns in a sample of lung cancer (LC) patients were found to be psychosocial in nature, indicating a greater need for attention in this area (V. Lidstone). Psychosocial concerns in LC patients and their caregivers thus need more research that identifies specific targets of intervention development for preventing future health issues.

**Methods:** This study presents secondary analyses of a parent trial where 33 dyads (LC patients and their primary family caregiver) were randomly assigned to the educational program group (control arm) and were asked to fill out a Concern Inventory. These data were used to run descriptive statistics to identify their most prominent concerns. Content analyses were run to identify nuances related to their concerns and developed and implemented a coding scheme to rate the qualitative data including codes for each participant and their partner's self-identified facilitators and barriers.

**Results:** Nineteen out of thirty-three (58%) dyads had at least one individual rate 'making a lifestyle change' a moderate to high concern. Of those nineteen dyads, ten (53%) dyads had both members with moderate to high concerns. Patients also had more facilitators (i.e., support) from their partner to make changes than from themselves (sig. 2 tailed = 0.025).

**Conclusion:** These findings highlight the need for dyadic level interventions in LC survivorship programs that leverage the support within the family to remove barriers and increase facilitators to implement action plans for behavioral changes that can improve their quality of life and survivorship.

**Keywords:** psychosocial concerns, lung cancer, dyad

**Program Affiliation:** CPRTP Summer Research Experience

Abstract Number: 10

## **Vulvar Cancer Outcomes in Women Living with HIV in the Age of Anti-Retroviral Therapy**

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**Background:** Vulvar cancer is relatively uncommon, making up about 0.3% of all new cancer cases in the United States. Women living with HIV (WLWH) experience a disproportionately higher rate of female genital tract cancers, including vulvar and cervical cancer, largely because they are more likely to have a persistent coinfection with HPV. Once diagnosed with forms of cancer, WLWH are known to have significantly worse survival and treatment adherence rates than women without HIV. The purpose of this study was to examine local recurrence-free and overall survival of HIV+ women who were diagnosed with pre-invasive and invasive vulvar cancer in the age of anti-retroviral therapy.

**Methods:** WLWH treated for vulvar cancer at Moffitt Cancer Center between 1997 and 2017 were queried for analysis and matched with HIV- patients when available. Patients were included if they had known HIV status, no other HPV-related cancer diagnoses, and were treated for pre-invasive or invasive vulvar cancer. Demographics and treatment variables were compared using Chi-square test, Fisher's Exact test, or Mann Whitney-U test. Kaplan-Meier survival analysis was performed to compare local recurrence-free survival in women with pre-invasive vulvar cancer (VIN) and overall survival in women with invasive vulvar cancer. All data transmitted from outside institutions included only limited patient identifiers and were in agreement with all institutions. The research protocol was IRB approved. SPSS Version 25.0 was used.

**Results:** WLWH treated for pre-invasive vulvar cancer were more likely to be Black ( $p=0.044$ ). For patients with invasive vulvar cancer, there was no significant difference in overall survival between WLWH and HIV- women ( $p=0.548$ ). For patients with pre-invasive vulvar cancer (VIN), there was no significant difference in local recurrence-free survival between WLWH and HIV- women ( $p=0.816$ ). Our small sample size limited our ability to definitively determine the difference between groups, but local recurrence appears to be common in vulvar cancer and VIN regardless of HIV status.

**Conclusion:** This was a small initial study, so the next steps would entail collecting more patient data from other institutions. In a larger study, we plan to assess markers of immunosuppression to evaluate if there is an effect on treatment outcomes. We aim to investigate treatment outcome and toxicity differences among WLWH who were adherent to their anti-retroviral therapy compared to those who were not. We also plan to include patients with other HPV-related cancers to evaluate relationship between such cancers and determine potential risk factors.

**Keywords:** vulvar cancer, gynecologic cancers, HPV, HIV, HPV-related cancers, women living with HIV

**Program Affiliation:** CPRTP Summer Research Experience

Abstract Number: 11

## **Environmental scan of Web-based Consumer Information on the Risk of HPV-Related Diseases in Patients with Systemic Lupus Erythematosus**

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**Background:** Patients with an autoimmune disease, like systemic lupus erythematosus typically receive intense immunosuppressant drugs such as steroids, chemotherapy or biological treatments which interferes with the body's ability to fight infections. This population is at a higher risk of developing human papilloma virus (HPV), and related diseases, specifically cervical cancer. Patients are relying on the internet to understand important health information. However, very little is known about the quality, type, and amount of information available for those who experience both Lupus and HPV. The purpose of this study is to assess the quantity and quality of education content about both HPV and autoimmune diseases

**Methods:** An environmental scan of currently available google websites providing education information for patients with both HPV and autoimmune diseases was performed. Independent investigators selected relevant uniform resource locators (URLs) and assessed source information. The sources primary source, type of webpage (organization, blog, social media, newspaper, business, forum, wiki, e-commerce), type of organization profit type of content (educational, news, post, FAQ, white paper, research & data), target audience (patients, physicians, general public), domain, agency developing the information, type of organization (publisher, governmental, national or international organization), language, year of last update and country of origin were evaluated.

**Results:** 100 websites were evaluated for the environmental scan. Only 17 websites were designed to be educational content for patients with lupus and HPV. 11 of the sources were for profit and 6 were nonprofit. Of the 17 sources, 12 had the domain ".com", 4 were ".org", 1 was ".edu" and, 1 was ".gov."

**Conclusion:** Conclusion: Based on the findings of the environmental scan, most of the relevant sources have a .com domain. Most of the relevant sources are for profit. Most of the sources available on google for both Lupus and HPV are not for patient educational purposes, therefore content needs to be created for this demographic. This information can be used to help future website creators and improve treatment, management and intervention practices for early detection of HPV-related diseases, like cervical cancer in patients with Systemic Lupus Erythematosus.

**Keywords:** Autoimmune Disease, Human Papillomavirus, Cervical Cancer, Environmental Scan, Cancer Prevention

**Program Affiliation:** CPRTP Summer Research Experience

Abstract Number: 12

### **Anti-inflammatory dietary patterns effect on cancer risk and mortality**

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**Background** The role of eating habits in shaping the gut microbiome, coupled with how host metabolism and metabolites interact with the gut microbiota and diet to shape gut health and immunity, hint that the fitness of this codependent relationship broadly affects cancer risk and outcomes. Observational and experimental studies have yielded important insights into the effect of diet and the gut microbiome on cancer risk and outcomes, as well as the underlying biological processes (i.e., immunity, inflammation, and metabolism) involved. However, new prospective cohorts with diet, PROs, and biospecimens longitudinally collected during the dynamic period of treatment and interventional studies across the cancer continuum are ultimately needed to examine causality. This project serves to understand how nutritional epidemiology can be applied in a clinical setting for cancer patient populations. Specifically, populations diagnosed with melanoma, patients initiating modern systemic therapies and high-risk patients on active surveillance.

**Methods/What will be learned** To study diet and nutrition related to the cancer patient's experience from patient-reported outcomes (e.g., appetite, fatigue, stress) to side effects/treatment tolerance to understand how to improve response to treatment and extend survival. To gain experience by applying information on diet and nutrition and epidemiologic methods and report on the information and experience gained on diet and nutrition related to cancer. Using a team-based approach, we analyze the most current data on dietary patterns and their role in cancer patient survival. We will use a hands-on approach to develop and deliver an evidence-based dietary intervention to cancer patients to improve health outcomes related to cancer.

**Results: Outcomes** Through the methods outlined above, we expect to confirm and progress the important and necessary role of dietary interventions in cancer treatment and prevention. The role of diet has an overwhelming number of positive results. However, it needs further investigation to determine which dietary pattern best serves the prevention and treatment of specific cancers and individuals, along with the interactions between various cancer treatments.

**Conclusion:** \*Same as results/outcomes\*

**Keywords:** Diet, cancer, anti-inflammatory

**Program Affiliation:** CPRTP Summer Research Experience



Abstract Number: 13

## Identifying and Characterizing Genetic Variants Associated with Colorectal Cancer

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**Background:** Colorectal cancer (CRC) is the third most common cancer diagnosed in both men and women in the United States<sup>1</sup>. Studies have identified several genes associated with CRC risk, but these genes only account for a small proportion of the disease heritability<sup>2</sup>.

Undiscovered rare, intermediate-risk variants may partly explain this missing heritability<sup>3</sup>. This study aims to identify novel CRC susceptibility genes potentially harboring rare pathogenic variants, produce refined risk estimates, and characterize variants of uncertain significance (VUS) in known CRC susceptibility genes.

**Methods:** This study utilized whole-exome and whole-genome sequencing of CRC cases and cancer-free controls from MD Anderson (2,161 cases, 4,097 controls), UK Biobank (3,690 cases, 75,850 controls), and the All of Us Research Program (4,448 cases, 223,870 controls). Exome-wide gene-based association tests were performed within each dataset using VAAST<sup>4</sup>, weighting all rare coding variants by their estimated degree of dysfunction, and a one degree of freedom CMC test of protein-truncating variants<sup>5</sup>. ACAT-combined p values for the VAAST and CMC results were generated for each dataset and meta-analyzed across the three datasets. For the topmost significant genes and nominally significant candidate genes in the meta-analysis, effect size estimates were generated for variants of different functional categories and used to calculate the percent of log familial relative risk explained.

**Results:** While no novel genes reached genome-wide significance in the meta-analysis ( $\alpha = 0.05$ /~20,000 genes =  $\sim 2.5 \times 10^{-6}$ ), six candidates reached nominal significance: BRCA1 ( $p = 5.9 \times 10^{-6}$ ), BRCA2 ( $p = 1.3 \times 10^{-5}$ ), ATM ( $p = 4.0 \times 10^{-3}$ ), SDHA ( $p = 0.028$ ), CDKN2A ( $p = 0.031$ ), and RAD51C ( $p = 0.022$ ). Notably, PMS2's truncating and pathogenic missense variants conferred moderate risk despite it being a Lynch Syndrome gene (OR= 1.74, 95% CI= 1.26, 2.40). For MSH2, both truncating variants (OR= 16.4, 95% CI= 8.08, 33.4) and pathogenic missense variants (OR= 2.90, 95% CI= 0.879, 9.59) conferred increased risk for CRC. APC pathogenic missense variants conferred non-significant risk, indicating potential variant misclassification. Overall, we estimate that rare coding variants from the genes highlighted in this study could explain approximately 3.1% of the familial relative risk of colorectal cancer. In comparison, GWAS-identified CRC variants account for ~12% of familial relative risk<sup>6</sup>.

**Conclusion:** By identifying new genes affecting CRC risk and improving existing risk estimates, this study will lead to more accurate CRC risk prediction models. Increasing the predictive accuracy of these models utilized in clinical settings can bolster CRC prevention and early detection efforts.

**Keywords:** colorectal cancer, rare genetic variants

**Program Affiliation:** CPRTP Summer Research Experience

Abstract Number: 14

**Developing Training and Mentoring Curriculum for Healthcare Providers to Reduce the Burden of Cervical Cancer in Medically Underserved Areas (MUAs) of Texas.**

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**Background:** Incidence rates of cervical cancer have currently leveled off and remain unacceptably high for a preventable disease. Data from the Texas Cancer Registry (TCR) predicts an estimated 1489 new cervical cancer cases and 464 related deaths in Texas for 2023. The 2015 – 2019 data shows an age-adjusted incidence rate of 9.4 cases per 100,000. Cervical cancer-related death in Texas is 2.8 per 100,000 women, 27% higher than comparable national rates. Many MUAs have a shortage of providers trained to diagnose and treat preinvasive cervical cancer. To our knowledge, there are currently no free courses for colposcopy in Texas and women are lost to follow-up in part because of a lack of available providers to perform diagnosis/treatment procedures.

**Methods:** This project strives to improve capacity and expertise in colposcopy, cervical biopsy, and preinvasive lesion identification through mentorship training tailored to Cancer Prevention and Research Institute of Texas (CPRIT) partners. The mentorship training is tailored for clinical providers (doctors and advanced practice providers) in MUAs of Texas. The mentorship program will include a self-paced review of required recorded lectures, two MD Anderson cervical cancer prevention courses including both components of didactics and hands-on training, four colposcopy image review sessions in collaboration with the MD Anderson team, identify a clinical mentor, attend a set number of Project ECHO (Extension for Community Healthcare Outcomes) Cervical Cancer Prevention sessions, present a set number of patient cases during project ECHO sessions, perform colposcopy, cervical biopsy including high-grade cases, endocervical curettage, and vulvar biopsy.

**Results:** We anticipate overall knowledge, confidence, and skills to improve among participating healthcare providers. We expect these capacity-building efforts to make cervical cancer preventive care more accessible to medically underserved communities by improving the expertise of healthcare providers in these resource-limited settings.

Conclusion: To eliminate cervical cancer as a public health problem, secondary prevention such as colposcopy and Loop Electrosurgical Excision Procedures (LEEP) training for providers in low-resource settings are essential. This comprehensive training is expected to support capacity-building efforts for cervical cancer prevention in Texas. It can also be used in other low-resource settings globally and be translated into other languages.

Keywords: Cervical Cancer mentorship training, cervical cancer prevention low resources setting, reduce burden of cervical cancer, cervical cancer in Texas, cervical cancer in underserved area

Program Affiliation: CPRTP Summer Research Experience

Abstract Number: 15

## **A Systematic Review of Clinical Practice Guidelines for Cancer Screening in Patients with Autoimmune Diseases**

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**Background:** Healthcare providers often make decisions about cancer screening based on clinical practice guidelines (CPGs), which are evidence-based recommendations developed by expert panels or organizations. CPGs provide cancer screening recommendations based on various factors, including cancer prevalence, cost-effectiveness, and risk factors. Although certain patients with autoimmune diseases are at a higher risk of cancer compared to the general population, the evidence for these patients is sparse and recommendations are limited. The objective of this study was to evaluate the CPGs and consensus recommendations regarding cancer screening in patients with autoimmune diseases.

**Methods:** We searched electronic databases (Medline [OVID], Embase [OVID], CINAHL) guideline registries, and relevant societies' websites from 2018 until May 2023 for cancer screening recommendations in patients with autoimmune diseases. The autoimmune diseases of interest were rheumatoid arthritis, systemic lupus erythematosus, and spondylarthritis. Cancers that were considered were cervical, colorectal, breast, lung, and skin cancer. These cancers were selected because they have screening recommendations for the general population and the potential association with the rheumatological conditions of interest. Two reviewers independently evaluated eligibility using the title and abstract of the CPGs and consensus statements. In the case of a conflict, reasons for exclusion were discussed by both reviewers. If there was no consensus, a third reviewer was consulted. Using the CPGs and consensus statements that passed this first screening step, the same reviewers reviewed the full text. CPGs and consensus statements about cancer screening or guidelines about rheumatoid arthritis, systemic lupus erythematosus, and spondylarthritis were included. Lastly, we plan to extract recommendation statements regarding cancer screening for patients with autoimmune conditions from these articles to appraise the quality of evidence and examine discrepancies, similarities, and gaps in recommendations. Reviewers examined the CPGs and consensus statements independently. They established inclusion and exclusion criteria before the screening began and were unable to access or view how a certain article was screened by the other reviewer. This prevented bias or influence in the screening process. By independently examining the CPGs and consensus statements, reviewers ensured their decision-making was solely based on the pre-established criteria. This minimized the risk of one reviewer influencing or being influenced by the screening outcomes of the other reviewer.

**Results:** Data extraction and analysis is currently ongoing. We began with 926 citations and found 62 that ultimately met our eligibility criteria. This is excluding the grey literature, which will be incorporated later.

Conclusion: Cancer screening plays a crucial role in early detection and reducing the risk of morbidity and mortality associated with certain types of cancer. Our analysis reflects the presence of differential screening recommendations for those with autoimmune conditions within general cancer screening guidelines. The limited evidence and recommendations for cancer screening in patients with autoimmune conditions must be addressed. This paper aims to address this gap through a systematic review of CPGs and consensus statements for cancer screening in adults with autoimmune conditions. This systematic review provides valuable insights into the existing evidence and recommendations for cancer screening in this unique patient population. It will help inform the decision-making of healthcare providers while informing future cancer screening recommendations.

Keywords: autoimmune disease, rheumatology, cancer screening, clinical practice guidelines

Program Affiliation: CPRTP Summer Research Experience

Abstract Number: 16

### **Cognitive Function in Older Breast Cancer Survivors after Chemotherapy**

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**Background:** In the United States, over 60% of breast cancer survivors are 65 years and older; however, little is known about patient-reported symptoms and the effect that cancer treatments could have on survivors years after their primary treatment and diagnosis. This study evaluated perceived cognitive function in older breast cancer survivors and whether prior chemotherapy was associated with cognitive outcomes.

**Methods:** Breast cancer patients aged 65 years and older, diagnosed 2012-2013, with local and regional stage disease, were identified through the linked Texas Cancer Registry-Medicare dataset (TCR). Survivors were mailed a survey to assess their cognitive function through the Functional Assessment of Cancer Therapy-Cognitive Function (FACT-Cog V3) instrument (section G of the survey). The survey also collected demographic and clinical data and was collected between April 2018 and October 2019. Utilizing the data from the self-administered questionnaires, TCR, and Medicare claims, the cognitive function and quality of life among elderly patients were evaluated to assess whether prior chemotherapy and/or endocrine therapy impacts long-term health.

**Results:** Of 4,448 eligible patients, 1,954 (43.9% response rate) responded to section G. Of these, 1,065 respondents completed all 4 sections, 37 questions. Eighty of those 1065 respondents self-reported disease recurrence which excluded them from the analyses in order to avoid biases, leaving a total of 985 cases for this study. Median time from diagnosis to survey completion was 68 months (IQR 62-73). The remaining data for this project has been collected but will be analyzed and presented at a later date.

**Conclusion:** The results of this study will help inform future doctors on whether chemotherapy should be utilized in older patients or not. The potential risk of decreased cognitive function highlights the importance of patient-centered discussions in order to make an informed decision on a patient's treatment plan to ensure the best quality of life for older breast cancer patients.

**Keywords:** Geriatric Oncology, Breast Cancer, Chemotherapy

**Program Affiliation:** CPRTP Summer Research Experience

Abstract Number: 17

## **Levonorgestrel Intrauterine Systems for Primary Prevention and Treatment of Endometrial Hyperplasia and Endometrial Cancer: A Systematic Review**

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**Background:** Endometrial cancer (EC), ranking fourth among women's cancers in the US, is showing an alarming increase in incidence among younger individuals. The standard of care for EC is a total hysterectomy, bilateral salpingectomy and/or bilateral oophorectomy. The levonorgestrel-releasing intrauterine system (LNG-IUS) is a popular and effective contraceptive method that continuously releases controlled amounts of levonorgestrel, a type of progesterone, into the uterus. Beyond contraception, researchers are studying its non-contraceptive benefits. Evidence indicates that progesterone plays a role in inhibiting uncontrolled estrogen-driven endometrium growth that can increase the risk of developing endometrial hyperplasia, a precursor to EC, and EC. There is growing interest in using LNG-IUS for hyperplasia and EC because the treatment effect concentrates in the uterus with minimal systematic side effects. This research provides the foundational infrastructure to build a decision analytic model and develop an educational tool for effective interventions, such as LNG-IUS, to prevent and/or control endometrial hyperplasia and EC by LNG-IUS.

**Methods:** A comprehensive systematic review was conducted using MEDLINE, Embase, and Cochrane, following responsible research practices and adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Two independent reviewers screened articles from these databases for eligibility based on predetermined criteria. Conflicts were resolved through discussion and consensus, with an arbitrator involved if needed. Inclusion criteria include US-based human studies on LNG-IUS EC prevention and/or control among randomized control trials (RCT), prospective and retrospective cohort studies, case-control studies, case series, and case reports. Non-English publications and animal/in vitro studies were excluded.

**Results:** Out of the 908 abstracts screened, we identified 471 articles for full-text screening. We expect to extract data from 65 articles on LNG-IUS and EC and/or hyperplasia. Among these, this includes 35 RCTs investigating its effects on EC and/or hyperplasia, 15 case-control studies examining its impact, 10 cohort studies providing long-term insights, and 5 case reports documenting specific cases. Preliminary analysis of study types suggests consistent evidence supporting the effectiveness of LNG-IUS against EC and hyperplasia.

Conclusion: Findings of this study will contribute to a comprehensive assessment of LNG-IUS on EC and hyperplasia. Rigorous methodology used will enhance the reliability of the findings, potentially influencing health policy and guidelines. These findings will inform clinical decision-making and aid in the development of decision models.

Keywords: Endometrial cancer, Endometrial hyperplasia, LNG-IUS

Program Affiliation: CPRTP Summer Research Experience



Abstract Number: 18

## **The Correlation Between Exercise and Sleep in Postmenopausal Women**

Rachel Sun, Health Disparities Research, Texas A&M University; Dr. Karen M. Basen-Engquist, Health Disparities Research, University of Texas MD Anderson Cancer Center

**Background:** Recent studies have shown that postmenopausal women have sleep disturbances, which could be caused by normal physiological changes associated with aging and postmenopausal related symptoms. Sleep deficiency can affect with work, driving, and social functioning. This could cause them to make less healthy lifestyle choices, which may increase the risk of cancer. Since exercise has been found to significantly improve sleep problems, we want to identify which aspects of sleep disturbances have the strongest relationship with exercise. Thus, our goal is to improve postmenopausal women's lifestyles and decrease their risk of cancer by implementing exercise interventions to improve sleep.

**Methods:** Postmenopausal women were recruited from MD Anderson Cancer Center employees and the general population. Participants completed the Godin Leisure Time Exercise Questionnaire and Pittsburgh Sleep Quality Index. The descriptive statistics of the PSQI data was used to determine which component most effects the participants. The PSQI Global score's statistics presented the sum of all the sleep components. The GLTEQ descriptive statistics were analyzed for what exercise participants do. The correlations between Godin total minutes of moderate and vigorous exercise and the PSQI components were analyzed to determine how exercise effects each sleep component.

**Results:** Each of the PSQI Components were rated from a range of 0 (no difficulty) to 3 (severe difficulty). PSQI Component 4 Sleep efficiency had the highest mean (1.64) and standard deviation (1.465). Component 5 Sleep disturbance has the next highest mean (1.23) and standard deviation (0.612). The PSQI Global score is from the range 0-21, higher scored worse sleep quality. The baseline data PSQI Global score was from the range of 1-12, mean 6.80, and standard deviation 2.966. The Godin Total number of strenuous exercise minutes mean (42.41) and range (0-225) were the lowest. The Godin Total number of moderate exercise minutes mean (90) and range (0-300) were the highest. The Godin Total number of mild exercise minutes (50.64) and range (0-300) were in the middle. In the study, Godin total min of moderate and vigorous exercise was used for the exercise component with the mean 132.41 and range 0-520. PSQI Component 1 Subjective Sleep quality had the largest negative Pearson Correlation of -0.397, sig. (2-tailed) 0.075. PSQI Component 4 Sleep efficiency (-0.341, sig. (2-tailed) 0.120), PSQI Component 7 Use of sleep medication (-0.323, sig. (2-tailed) 0.154), PSQI Component 3 Sleep duration (-0.246, sig. (2-tailed) 0.271), and PSQI Component 6 Use of sleep medication (-0.236, sig. (2-tailed) 0.302) all had a negative Pearson Correlation. PSQI Component 2 Sleep latency (0.065, sig. (2-tailed) 0.780) and PSQI Component 5 Sleep disturbance (0.110, sig. (2-tailed) 0.626) had positive correlations. PSQI Global score had the highest overall Pearson Correlation -.536, sig. (2-tailed) 0.015.

**Conclusion:** PSQI 4 Sleep efficiency effected the study participants the most. Overall based on the PSQI Global score, most did struggle with some of the sleep disturbances. From the GLTEQ, participants did moderate exercise the most and strenuous the least. The Godin Total minutes of moderate and vigorous exercise (110) was close to the recommend amount of 150

minutes. PSQI Component 1 Subjective Sleep quality and Component 4 Sleep efficiency had the largest negative Pearson Correlations of the sleep components with exercise. PSQI Global score had the largest overall negative Pearson Correlation that is significant at the 0.05 level (2-tailed). Based on these results, there isn't a strong correlation between the sleep disturbances and exercise, but there is a moderate correlation between the PSQI Global score and exercise.

Keywords: Subjective Sleep quality, Sleep efficiency, PSQI Global score, GLTEQ

Program Affiliation: CPRTP Summer Research Experience

Abstract Number: 19

### **Developing an immunocompetent mouse model of renal cell carcinoma bone metastasis**

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**Background:** Renal cell carcinoma bone metastases (RCCBM) lead to osteolytic lesions and impaired mobility in patients. An immunocompetent mouse model is needed to study any immune-related effects and relate it to the human body. Beta ig-h3 protein (BIGH3) was found to inhibit osteoblast differentiation and promote osteolytic lesions in RCCBM.

**Methods:** RT-qPCR analysis and DNA gel electrophoresis will be done to detect the relative gene expression of BIGH3 in K7 cells, a mouse RCC cell line. An ex vivo study will be done where K7 cells with and without a luciferase tomato (LT) gene will be seeded on C57BL6 mouse leg bone fragments. An in vivo study will also be done where SCID mice will be injected with K7 cells intracardially to get bone-derived cancer cells. The bone-derived K7 cells will be further selected using the intracardiac injection in SCID mice to get cells that specifically target bone. The specific bone-derived K7 cells will then be administered to immunocompetent C57BL6 mice as the new mouse model for RCCBM.

**Results:** We anticipate that the RT-qPCR results will show that K7 cells express BIGH3, similar to previous human renal cell carcinoma cell lines. In the ex vivo study, we anticipate that the K7 cells will attach to and grow on bone for up to fourteen days. In the in vivo study, we anticipate the live mice to experience the greatest tumor growth in the lungs, liver, and bone. It may take up to three cycles of selection to get bone-specific K7 cells.

**Conclusion:** If K7 cells express BIGH3 similar to previous human renal cell carcinoma cell lines, this supports using human anti-BIGH3 antibody as a potential avenue for treatment and prevention of bone metastasis in RCC. The future use of K7 cells in the RCCBM immunocompetent mouse model will depend on how rapidly the mice acquire aggressive metastatic cancer.

**Keywords:** renal cell carcinoma, bone metastasis, BIGH3, immunocompetent mouse model

**Program Affiliation:** CPRTP Summer Research Experience

Abstract Number: 20

### **The role of general vaccine hesitancy in HPV vaccine intention among young adults**

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**Background:** Human Papillomavirus (HPV) vaccination rates in the U.S. remain low despite the vaccine being a safe, effective means of preventing HPV-related cancers. HPV vaccination rates have declined since the COVID-19 pandemic, which may be due in part to increased vaccine hesitancy. Previous studies have examined the association between HPV-specific hesitancy and HPV vaccine intention, but not the association between general vaccine hesitancy and HPV vaccine intent in adults. The current study examined if general vaccine hesitancy was associated with HPV vaccine intention above and beyond established predictors from the Health Belief Model (HBM), including perceived disease severity, perceived susceptibility, perceived barriers, perceived benefit, and self-efficacy. Examining general vaccine hesitancy in addition to HPV-specific factors will reveal important insights for developing more efficacious HPV vaccine interventions.

**Methods:** Participants (N = 298) were racially diverse undergraduate students recruited at several Texas universities for the NO-HPV-4-ME study. Participants were 18-26 years old and unvaccinated against HPV. Participants completed a survey assessing attitudes, beliefs, and intentions regarding HPV and vaccines. Hierarchical regression was used to examine the association between general vaccine hesitancy and HPV vaccine intention. Block 1 contained relevant sociodemographic factors, Block 2 contained HBM variables, and Block 3 contained a measure of general vaccine hesitancy.

**Results:** Age, sexual activity, and health insurance were identified as covariates, accounting for 7% of variance in HPV vaccine intention ( $p = .002$ ). HBM variables accounted for 50.6% of variance ( $p < .001$ ) and the final model accounted for 53.2% of variance in HPV vaccine intention ( $p < .001$ ). General vaccine hesitancy was associated with HPV vaccine intention above and beyond sociodemographic and HBM variables accounting for 2.7% of additional variance. In the final model, self-efficacy had the strongest relationship to vaccine intention ( $\beta = .39$ ), followed by perceived benefits ( $\beta = .25$ ), perceived susceptibility (.20), general vaccine hesitancy (-.19), and perceived barriers ( $\beta = .15$ ).

**Conclusion:** General vaccine hesitancy plays an important role in HPV vaccine intention that is not captured by HBM factors specific to HPV and HPV vaccines. Targeting general vaccine hesitancy in addition to HPV-specific factors in vaccine interventions may improve vaccine uptake among young adults.

**Keywords:** HPV, vaccine, hesitancy

**Program Affiliation:** CPRTP Summer Research Experience

Abstract Number: 21

## **Phase 1 Results: Cultural Adaptation of a Mindfulness-Based Intervention for Latino Cancer Patients and Their Caregivers**

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**Background:** The exacerbation of cancer-related symptoms among patients due to increased stressors, such as psychosocial distress, has been documented. Approaches have been developed to address the impact that stressors may have on the overall quality of life of cancer patients and their caregivers. Examples include yoga, stress management, interpersonal counseling, and mindfulness sessions. However, not all interventions have been tailored and tested for their feasibility and acceptability across minority groups, including Hispanic/Latino (H/L) populations. The purpose of this study was to culturally tailor mindfulness-based intervention sessions for H/L advanced cancer patients and their family caregivers.

**Methods:** Phase 1 of the study involved in-depth, semi-structured interviews and brief mindfulness sessions with 20 H/L dyads recruited from a county hospital. Participants had to self-identify as H/L, be at least 18 years old, be able to speak either English or Spanish, and have internet access. Additional criteria for patients included having a stage III-IV tumor diagnosis and being in active treatment. Qualitative analysis was conducted using Atlas.ti. Findings from Phase 1 were combined with community-based feedback to inform adaptations for Phase 2, a pilot randomized controlled trial of the Mindful Purpose Training (MPT) intervention for H/L patient-caregiver dyads. All study procedures were conducted using HIPAA-compliant platforms.

**Results:** Seventy-five percent of patients (male: 55%; mean age: 51) and 70% of caregivers (male: 45%; mean age: 45) indicated that the mindfulness session was not difficult to follow. Overall, 95% of participants found it to be very helpful/helpful. Similarly, 95% of participants indicated that the language used was very easy/easy to understand. All participants indicated that the program could be useful for other families like them. Trained community members suggested that the language needed to include more common terms, that stigma regarding meditation among H/L should be addressed, and that family members should be further involved. Findings from Phase 1 are being used to inform the process of cultural adaptation for the MPT through intervention mapping for phase 2. Topics such as likes/dislikes, incorporation of cultural values, and barriers to participation were qualitatively assessed.

**Conclusion:** Mindfulness interventions may be a feasible and acceptable approach to manage mental and emotional burden within Latino families going through active cancer treatment. By evaluating interventions in minority groups, it is possible to tailor and culturally adapt these to the ongoing realities of these communities. Phase 2 of the parent study will test the feasibility of the culturally adapted MPT in H/L patient-caregiver dyads.

**Keywords:** dyadic intervention, cancer-related distress, caregivers, mindfulness, Hispanic/Latinos

**Program Affiliation:** CPRTP Summer Research Experience

Abstract Number: 22

## **Project Smoke Free**

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**Background:** Secondhand smoke exposure (SHSe) causes 42,000 deaths each year among nonsmokers.<sup>1</sup> According to the Centers for Disease Control and Prevention, secondhand smoke exposure occurs when people breathe in smoke breathed out by people who smoke or from burning products. Also contrary to beliefs, there is no safe level of SHSe even a short period of exposure can cause serious health problems and/or be deadly. In children, SHSe can cause the following: infant death syndrome, ear infections, and respiratory issues such as asthma attacks or localized infections.<sup>2</sup> SHSe-related deaths result in a loss of 600,000 years of potential life and \$6.6 billion in lost production (or \$158,000 per death), with African Americans suffering the greatest loss of output.<sup>1</sup> As a result of the higher smoking frequency among segregated populations and the air exchange that takes place in connected living spaces, residents of low-income housing are especially at an increased risk of SHSe.<sup>(3-6)</sup> In comparison to the general population, non-Hispanic black nonsmokers have greater risks of tobacco-related illness and death because nearly half of them are exposed to SHS (including 7 in 10 youngster).<sup>7</sup> Our ultimate goal is to lessen the disparities among SHSe that are present in African American public housing communities.

**Methods:** Potential participants will be recruited from four Houston public housing sites. Potential participants will be given a description of the study and provide consent to be screened. The study will enroll up to 392 participants. It's proposed to be single group, unblinded, non-randomized, multilevel intervention research in the four communities. These areas have more than 80% African American residents. Focus groups, in-depth interviews with PH residents and staff, property inspections for SFPH violations, and property observation will all be done at the baseline. We will provide residents and employees with specialized education and training as part of the intervention. Also, current smokers will be given need-based MAPS and NRT, and keep track of their 7-day self-reported abstinence status at 4, 12, and 24 hours.

**Results:** It's hypothesized that a culturally appropriate educational and smoking cessation intervention aimed at African American public housing communities residents as well as staff will result in appreciable drops in SHSe. Also, simultaneous attention to access and motivational variables is necessary to improve The U.S. Department of Housing and Urban Development smoke-free public housing rule compliance and smoking cessation.

**Conclusion:** Health disparities are an important issue to address and research similar to this one are essential to step by step overcome those disparities. A culturally appropriate educational and smoking cessation intervention can effectively reduce the secondhand smoke exposure amongst residents and staffs in Houston public housing sites. Please note these are unofficial results, the project is still at the early stages.

**Keywords:** Secondhand smoke exposure, nonsmokers, smoke

**Program Affiliation:** CPRTP Summer Research Experience

Abstract Number: 23

## **Pancreatic Cancer Early Detection through Hyperpolarized MRI**

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**Background:** Pancreatic ductal adenocarcinoma (PDAC) is an aggressive type of pancreatic cancer with a 5-year survival rate of 11%, however with early diagnosis the survival rate increases to 30%. Therefore, making early detection and prevention of PDAC very important and a high priority for the NCI. Due to pancreatic cancer's asymptomatic illustration in the earlier stages, it is hard to detect and diagnose in the early stages. Therefore, there is a high demand for non-invasive imaging markers that help identify the aggressive sub-type(s) in a pancreatic lesion early in the pancreatic cancer progression. Most commonly, the conversion of hyperpolarized pyruvate to lactate and alanine is used as imaging biomarkers, which has previously been shown in the Warburg effect as it kicks in and promotes the conversion to lactate. With the HP-MR the imaging power is increased 10X and allows for non-invasive metabolic detection.

**Methods:** Hyperpolarized 1-<sup>13</sup>C Pyruvate MRS was employed to study the metabolic processes in tamoxifen inducible genetically engineered mouse (GEM) models. These models include (P48CreERT2;LSL-KrasG12D (iKC)) with pre-invasive pancreatic intraepithelial neoplasia (PanIN) precursor lesions, invasive pancreatic cancer model (P48CreERT2;LSL-KrasG12D; LSL-p53R172H (iKPC)) and control animals (P48CreERT2 (iC)) without pancreatic lesions. The dissolution DNP (HyperSense, Oxford Instruments) operating at 3T was utilized to hyperpolarize 1-<sup>13</sup>C pyruvate. The <sup>13</sup>C magnetic resonance spectra of hyperpolarized 1-<sup>13</sup>C pyruvate were acquired at 7T Bruker MRI scanner.<sup>3</sup> These mice were imaged at different time points in their lifespan, before tamoxifen induction, 10-, 20-, and 30-weeks post induction.

**Results:** Preliminary results in the lab indicate that the alanine to lactate signal intensity ratio decreased as pancreatic cancer progressed from low-grade to high-grade PanINs. While the lactate-to-pyruvate ratio increased in the models with pancreatic cancer in comparison to the control models. These preliminary results show that there are significant differences in the alteration of the ALT and LDH in the early transformation of the PanINs lesions to the advanced stages. We will continue these studies to obtain more data for statistical significance.

**Conclusion:** The findings of this study and the HP-MR imaging techniques can be potentially used to clinically detect pancreatic lesions in high-risk patients and detect possible pancreatic cancer at earlier stages.

**Keywords:** Pancreatic Cancer, Hyperpolarized Magnetic Resonance Imaging, Cancer Diagnosis and Prevention

**Program Affiliation:** CPRTP Summer Research Experience

Abstract Number: 24

## **A Systematic Review Evaluating the New Media Landscape and its Effects on Skin Cancer Diagnostics, Prognostics, and Prevention**

Priscilla Haff, Dermatology, McGovern Medical School, The University of Texas Health Science Center at Houston; Alli Jacobson, Dermatology, Davidson College; Hayden Schandua, Dermatology, McGovern Medical School, The University of Texas Health Science Center at Houston; Madison Taylor, Dermatology, McGovern Medical School, The University of Texas Health Science Center at Houston; Dr. Hung Doan, Dermatology, University of Texas MD Anderson Cancer Center; Dr. Kelly Nelson, Dermatology, University of Texas MD Anderson Cancer Center

**Background:** The wide availability of online sources, including social media, has supported rapid wide-spread dissemination of health information. This dissemination can be an asset during public health emergencies but can also present challenges when the information is inaccurate or ill-informed. Many social media sources discuss cancer, specifically melanoma and keratinocyte cancers (basal/squamous cell).

**Methods:** We performed a systematic literature review to understand the new and evolving world of social media information and misinformation regarding the diagnostics, prognostics, and prevention of skin cancer.

**Results:** Following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) reporting guidelines, of the 1009 abstracts initially identified, 188 received full-text review and 112 met inclusion criteria. The included studies were divided into 7 separate groupings based on the publication's primary objective. Misinformation (35%), prevention campaigns (17%), engagement (15%), research (11%), education (10%), demographics (9%), and patient support (3%) were the most common identified themes.

**Conclusion:** Through this review, we gained a better understanding of the social media environment addressing skin cancer information.

**Keywords:** Skin, Skin Cancer, Social Media, Communication, Melanoma

**Program Affiliation:** CPRTP Summer Research Experience



Abstract Number: 25

## **Identifying the Prevalence of Vitamin C Deficiency and Examining the Associated Factors in Children, Adolescents, and Young Adults with Cancer**

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<sup>2</sup>Health Disparities Research, University of Texas MD Anderson Cancer Center

**Background:** Up to 70% of cancer patients were found to be vitamin C deficient. Patients with deficiency suffer lower quality of life and faster cancer progression. Cancer-related and treatment-related hormone and metabolic disturbances as well as decreased dietary intake of vitamin C contribute to the high-prevalence of vitamin C deficiency among cancer patients. However, research has mainly focused on adults. However, vitamin C deficiency could have unique and potentially more severe consequences in children due to their unique developmental needs. We aimed to determine the prevalence of vitamin C deficiency in children, adolescents, and young adults with cancer and ascertain the associated risk factors.

**Methods:** A prospective cohort study was performed. Patients were eligible if they were 6-39 years old, diagnosed with cancer, and followed at MD Anderson Division of Pediatrics for cancer care. Variables collected included demographic and clinical data from EPIC, activity data collected with a Fitbit Fitabase, and vitamin C serum levels drawn quarterly up to 4 times/year over 2 years. Descriptive analysis and multivariable logistic regression were employed

**Results:** There were 108 participants with available vitamin C laboratory data. The mean age was 17.74 ( $\pm 6.157$ ), range was 6-39 years old, and 40.7% were female. Additionally, at the time of data extraction, 73.1% were alive and 26.9% had expired. 45.9% of our participants were vitamin C deficient. Using only patients with complete data ( $n=71$ ), age at time of enrollment on study ( $p=0.038$ ), female sex ( $p=0.002$ ), surgery ( $p=0.041$ ), and higher number of hospitalizations ( $p=0.013$ ) all contributed significantly to the multiple regression model. For every one-unit increase in age, the odds of being deficient increased by 1.126; for every one-unit increase in the number of hospitalizations of participants, the odds of deficiency increased by 1.118. The odds of being deficient were 0.088 less for females as compared to males and 0.255 less for those who had cancer surgery as compared to those who did not have cancer surgery.

**Conclusion:** Similar to other published findings, we observed a high prevalence of vitamin C deficiency. Our data demonstrated that older age, male sex, no cancer surgery, and increased hospitalizations all raise the risk of vitamin C deficiency in children with cancer. Overall, these results demonstrate the importance of assessment for vitamin C deficiency at diagnosis and throughout treatment and further research is necessary to determine guidelines for the evaluation and management of vitamin C deficiency in this population.

**Keywords:** vitamin C, pediatric cancer, risk factors

**Program Affiliation:** CPRTP Summer Research Experience

Abstract Number: 26

**Project Self – Pilot Study testing the feasibility of implementing HPV self-collection kits among African American and Hispanic women**

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**Background:** Cervical cancer incidence and mortality rates have exposed an increasing trend in Texas especially among African American and Hispanic women. These disparities seem to be linked to the lack of access to cervical screening services. The standard screening service in the United States has been cervical cytology and is offered by the Texas Health and Human Services (TTHS). Even though these services are offered, large population of Hispanic and African American women are not screened due to lack of information, financial cost, and language barriers. New cervical screening through the detection of Human Papilloma Virus (HPV) by a self-collection kit which allow women to collect the test themselves and overcome the barriers they might face regarding the screening process.

**Methods:** This project will enroll 40 self-identify Hispanic or African American women from two public housing recruitment sites in Houston, TX. The participants will be given a criteria eligibility questionnaire. If eligible, a detailed informed consent document is provided, they will then be provided with a pre-health questionnaire which will be entered into REDCap (Research Electronic Data Capture). Participants will receive health education session, an HPV self-collection kit with instructions and timeline continued by a follow-up after one month.

**Results:** The study addresses the barriers that Hispanic and African American women face such as lack of health care access, high cost of cancer screening, immigration status, and language and cultural obstacles. In the study 13 African American women and 12 Hispanic women completed and mailed back the HPV self-collection kits, 12 African American women and 11 Hispanic women performed the test correctly (received a +/- response) as confirmed by EverlyWell, 13 African American women and 10 Hispanic women completed the study. Women experience lack of education regarding HPV vaccination which lead to higher incidence in cervical cancer. Based on age-adjusted cervical cancer incidence and mortality rates per 100,000 women in Texas, cervical cancer incidence in Hispanic women is higher while the mortality rate in cervical cancer is higher in African Americans.

**Conclusion:** New developments of HPV detection treatment such as self-collection kits for undeserved women in public housing living in Houston, TX would be key to cancer prevention. This innovative and scientific-based HPV screening method would target the disparities observed, provide education intervention related to cancer prevention and improve the cervical screening rates among African American and Hispanic women. Implementing this innovative and accessible form of HPV screening would reduce the cancer incidence rates and disparities observed among African American and Hispanic populations in Houston, Texas.

**Keywords:** HPV, Hispanic, African American

**Program Affiliation:** CPRTP Summer Research Experience

Abstract Number: 27

## **A Review of the Genomic Landscape of early cutaneous Squamous Cell Carcinoma**

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**Background:** Long-term sun exposure is a well-known inducer of actinic keratoses (AKs). While many AKs remain benign, a subset undergoes malignant transformation into cutaneous squamous cell carcinoma (cSCC), a potentially invasive and metastatic cancer. Understanding the genetic progression of healthy keratinocytes into chronically sun-exposed skin, AKs, and cSCC may identify targets for early diagnosis, prognosis, and effective treatment of cSCC, thus reducing the risk of metastasis.

**Methods:** We performed a systematic literature review investigating the large-scale genomic sequencing data in the early and precursor stages of UV-induced cSCC in immunocompetent patients. We selected studies available in English, written between January 2000 and June 2023, and indexed through MEDLINE, EMBASE, Cochrane Library, and PubMed which explored the early-stage oncogenesis of cutaneous squamous cell carcinoma. Following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) reporting guidelines, of the 4053 abstracts initially identified, 183 were assessed for full-text review, and 19 met the study's inclusion criteria.

**Results:** The included studies were then evaluated for significant dysregulation in driver genes related to cSCC and its precursor lesions to identify potential points of intervention. We identified target genes, methodologies, and significant findings of target genes in cSCC oncogenesis.

**Conclusion:** In this review, we provide an update on the genetic and epigenetic features of early cSCC and its precursor lesions, including candidate genes for future research as drivers of cSCC oncogenesis.

**Keywords:** actinic keratosis, squamous cell carcinoma, next-generation sequencing, mutation, skin

**Program Affiliation:** CPRTP Summer Research Experience

Abstract Number: 28

## **Effected Cancer Regions and Psychiatric Disorders in Smoking Cessation**

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**Background:** There is a known correlation between smoking cigarettes and cancer, especially lung cancer. Literature reflects a 30- 40% increase in survival likelihood for those who quit smoking when they are diagnosed. However, there is little reflected in literature regarding the correlation of differing cancer region diagnosis and smoking cessation, and the additional relationship of smoking cessation of those with psychiatric disorders. The literature suggests psychiatric disorders and Substance Use Disorder (SUD) share common risk factors, but their casual relationship remains unclear. Additionally, a cancer diagnosis exposes patients to the increased risk of psychiatric disorders. However, there is not information reflecting the interaction of primary affected cancer region and psychiatric disorders on smoking cessation.

**Methods:** We will examine if there is a correlation of primary affected cancer region and smoking cessation and if that correlation is impacted by the presence of psychiatric conditions. We aim to study the effect of four psychiatric disorders: Major Depressive Disorder, General Anxiety Disorder, Insomnia, and Panic Disorder. The data is extracted from the Tobacco Treatment Program (TTP) composed of 3245 patients, compiled from 2006-2014. The TTP uses initial questionnaires and follow up visits to assess psychiatric and smoking status, providing a free treatment plan conjoining the treatment of psychiatric disorders and substance abuse disorders. Then with the assistance of a department statistician, TTP data will be examined using regression models to determine if significant correlations exist.

**Results:** It has been found that cancer patients with psychiatric disorders take longer to quit and have a lower cessation rate compared to cancer patients without psychiatric disorders. Excluding the interaction of psychiatric disorders, those with cancers of the head and neck have a higher correlation with sustained tobacco abstinence, even compared to those with no cancer history. We will continue to use regression analysis to study the interaction of these two factors.

**Conclusion:** A better understanding of the effect of affected regions and existence of psychiatric disorders would allow for more targeted cessation treatment, and understanding of the psychological impacts of differing cancer affected regions. Additionally, understanding the interaction of four dominant psychiatric disorders may point to differing treatment programs or allocation of resources according to psychiatric disorder, which could help treat and prevent smoking cessation, and in turn prevent cancer.

**Keywords:** smoking cessation, cancer, psychiatric disorder

**Program Affiliation:** CPRTP Summer Research Experience

Abstract Number: 29

## **What's keeping patients up at night? An examination of financial distress and sleep in patients with metastatic breast cancer and their caregivers**

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**Background:** As the cost of cancer increases and treatment periods are extended, patients with advanced cancer and their families are at risk for financial toxicity, which includes material (i.e. medical bills,), coping (i.e. treatment nonadherence), and psychological (i.e. stress) components. Many studies rightly focus on the material component; however, the subjective psychological experience of financial distress is observed to negatively impact both patients and their spousal caregivers. Anecdotally, both patients and their spouses share that their finances are “keeping them up at night” but the extent to which financial distress may be associated with sleep, a key health behavior for both patients and caregivers who are vulnerable to their own chronic health conditions, is yet to be fully explored.

**Methods:** As part of a larger study on couples coping with financial distress, patients diagnosed with Stage III or IV breast cancer in the past 12 months and their romantic partner (cohabitating >6mo) completed self-report assessments at a single time point to capture financial distress (COST, ENRiCH), workplace activity interference (WPAI), and sleep (ISI, PSQI for caregivers only). Cross-sectional analyses including Pearson correlations, linear regression models, and paired sample t-tests were utilized to evaluate associations among variables of interest.

**Results:** In the 100 dyad sample (n=200) (52% female, two same sex couples, mean age=50.16 years, 65.0% non-Hispanic white, 73.1% college educated, 72.6%≥\$75,001 income), 24% of patients reported moderate or severe symptoms of insomnia (ISI: M=10.0 (6.0) and overall tended to rate their sleep disturbance higher than their caregiver (ISI: t=1.36,p>.05, C: M=8.7 (6.2)). Greater financial stress (ENRiCH: P:M=3.6 (2.4), C:M=3.2 (2.2)) was associated with poorer sleep for both patients (ISI: r=.33, p<.01) and caregivers (ISI: r=.32, p<.01, PSQI<sub>tot</sub>: r=.38,p<.01). For caregivers, financial distress was associated with greater sleep disturbance and daytime dysfunction but not overall sleep latency (i.e. how long it takes to fall asleep). For both members of the couple, poorer sleep was associated with greater workplace activity interference.

**Conclusion:** For couples facing newly diagnosed metastatic breast cancer financial distress is not only associated with disturbed sleep for the patient, but it is also observed for their spousal caregiver. As interventions are developed with goals of reducing financial distress among patients with cancer, the present findings highlight potential value of incorporating aspects to target sleep. Future research extending across different samples and a longitudinal approach is needed.

**Keywords:** financial toxicity, insomnia, psychological well-being, quality of life

**Program Affiliation:** CPRTP Summer Research Experience

Abstract Number: 30

**Environmental Assessment of American Cancer-focused Institutions' Awareness, Practices, and Policies Regarding Alcohol as a Significant Preventable Cancer Risk Factor**

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**Background:** In 1998 [1], the International Agency for Research on Cancer (IARC) declared that the consumption of alcoholic beverages was carcinogenic to humans (i.e., Class I); the designation was reaffirmed in 2007 and 2010 [1, 2]. Although alcohol consumption is a highly preventable cancer risk factor, approximately 4% of new cancer cases worldwide in 2020 were attributable to alcohol intake [3]. Excessive alcohol use exponentially increases the risk of cancers of the upper aerodigestive tract- and linearly increases the risk of lower digestive tract cancers [4]. Despite the longstanding designation of alcohol as an established carcinogen, an increasing and consistent body of data noting alcohol as a leading contributor to the global cancer burden, and publication of policy statements by authoritative sources, it is unclear whether cancer-focused institutions are aware of these facts or acting on the data by implementing evidence-based policies and practices to limit alcohol-related cancer risks for their employees, guests, or the public. The purpose of this study is to survey leaders of major cancer institutions and societies in the United States to gain insight into the organizations' interpretation of current literature, existing policies, decision-making processes, inclination to act, and perceived responsibility to lead in areas of public education and policy implementation to mitigate alcohol-related cancer risks in the public's interest.

**Methods:** A structured questionnaire will be sent via REDCap to directors of cancer-focused institutions and professional societies, including the National Cancer Institute-designated cancer centers, National Comprehensive Cancer Network-affiliated centers, American Cancer Society, American Society of Preventive Oncology, American Society of Clinical Oncology, and American Association for Cancer Research, among others.

**Results:** Upon distribution of our survey to domestic cancer-focused institutions, we hope to achieve a 50% to 70% response rate. We anticipate a potential disconnect between institutional awareness and interpretation of the data versus their implementation of policies and practices providing an opportunity for possible future implementation of prioritized actions to curb the burden of alcohol-related cancers in the country.

**Conclusion:** Our data will demonstrate that alcohol-related cancers merit greater attention and action by those in various positions of cancer leadership within cancer-focused institutions and professional societies.

**Keywords:** alcohol-related cancer risks, policies, practices, public education, policy implementation

**Program Affiliation:** CPRTP Summer Research Experience

Abstract Number: 31

## **Enhancing Policy Effectiveness: Examining the Rollout of a Comprehensive Tobacco-Free Workplace Policy within Homeless-Serving Agencies and the Impact of Education Receipt**

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**Background:** Tobacco use has been causally linked to at least 12 different types of cancer and 30% of cancer deaths in the U.S. Despite declines in smoking among the domiciled adult population, commensurate reductions have not been achieved for individuals experiencing homelessness (current smoking prevalence = ~12% versus 80%). Tobacco-free workplace policies (TFWPs) that restrict or prohibit tobacco use onsite are recommended to address high rates of tobacco use in agencies that serve or shelter this group. However, TFWP effectiveness hinges on factors associated with its rollout (i.e., communication, awareness, enforcement, compliance); employee knowledge of the harms of smoking and benefits of quitting may affect these factors. Here, we examine these factors in 3 homeless-serving agencies that either implemented (N=2) or refreshed (N=1) a TFWP as part of participation in a comprehensive tobacco-free workplace intervention program.

**Methods:** Logistic regression analyses, controlling for agency, were used to investigate the effect of program implementation on TFWP communication (i.e., clear signage); client, contractor, and visitor TFWP awareness; fair and consistent TFWP enforcement; and TFWP compliance. Effects were examined overall and by changes in employee education (median split; larger versus smaller changes in agency-level educational exposure from pre- to post-implementation).

**Results:** Participating agencies served 3,265 clients annually across Zavala, Cameron, and Travis counties; employees provided data on TFWP factors at pre- (N=18) and post- (N=15) program implementation. Results indicated increases in reports of clear TFWP signage (from 61.11% to 80.00%;  $p=0.4220$ ); perceived client (55.56% to 93.33%,  $p=0.0514$ ), contractor (50.00% to 80.00%,  $p=0.1527$ ), and visitor (55.56% to 86.67%,  $p=0.1208$ ) TFWP awareness; consistent (66.67% to 80.00%,  $p=0.6626$ ) and fair (66.67% to 80.00%,  $p=0.6002$ ) TFWP enforcement, and TFWP compliance (72.22% to 86.67%;  $p=0.5491$ ). Employees' receipt of education increased (5.71% to 46.67%;  $p<0.01$ ); larger increases in education receipt were marginally associated with greater increases in client and visitor TFWP awareness over time ( $ps=0.0952$ ).

**Conclusion:** Factors related to successful TFWP rollout increased from pre- to post-program implementation within homeless-serving agencies; most factors were highly endorsed by

employees at post-implementation. Education receipt increased but reached only about half of employees. Employee turnover limits education penetration in this setting; cascade training within agencies can facilitate sustainable education exposure. Larger changes in exposure to education were accompanied by greater increases in client and visitor TFWP awareness. Novelty-of-information effects may have influenced employees to provide guidance about the TFWP to groups they commonly interacted with. Finally, small sample sizes limited the power to detect statistically significant results.

Keywords: Tobacco, Policy, Intervention, Implementation, Homeless

Program Affiliation: CPRTP Summer Research Experience



# Diagnostic Imaging Summer Training and Experiences Partnership

Abstract Number: 32

## **Colorectal Cancer: Association Between Changes in ctDNA and Post Ablation Metastases**

Sanaa McNeil<sup>1</sup>, Bruno Odisio<sup>1</sup>

<sup>1</sup>Interventional Radiology, University of Texas MD Anderson Cancer Center

**Background:** Colorectal cancer is the third most common cancer in the U.S. and second most common cause of cancer death. Detecting and treating colorectal cancer early before it has a chance to spread improves the chances of successful treatment and survival. Around 25–30% of patients diagnosed with colorectal cancer develop liver metastases during the course of their disease. These patients have an average survival of 5 to 20 months without treatment, and very low 2—5-year survival rates. While surgical resection is the preferred treatment method, only 20% of patients are eligible for surgery. Microwave ablation (MWA) is a minimally invasive alternative and destroys liver metastases using a probe that generates microwave energy, causing heat-induced death to the tumor cells. The objective was to evaluate if there is an association between changes in circulating tumor DNA (ctDNA) and disease progression following percutaneous microwave ablation of colorectal liver metastases.

**Methods:** Patient data was gathered from EHR, including blood samples for which levels of the following biomarkers were clinically evaluated: CEA, CA19-9, [ctDNA] TP53, APC, and KRAS. I analyzed the patient files and processed the data into redcap to ensure its quality and usability for analysis. From here we analyzed the data to generate graphs, charts, tests, and descriptive statistics, in rStudio, to identify any associations.

**Results:** The results were as shown: CEA (Wilcoxon test value of 0.14 and an AUC of 0.62), CA19-9 (not enough cases to determine strong analysis), TP53 (Wilcoxon test value of 0.46 and AUC of 0.60, APC (Wilcoxon test value of 0.17 and AUC of 0.71), and KRAS (Wilcoxon test value of 0.68 and AUC 0.62). Overall, the ctDNA biomarker for APC mutation showed the strongest association to disease progression, however, the results were only weakly associative, suggesting that additional studies in a larger sample size are needed to make a conclusive determination. KRAS was slightly better than the other biomarkers outside of APC. However, there were only 8 cases which is not enough to have statistical power.

**Conclusion:** The preliminary findings indicate ctDNA biomarkers for APC and KRAS mutation are potentially associated with disease progression and may show promise for further study. Their higher numbers on the ROC curve suggest they may be linked to post-ablation metastases. This study opens avenues for future research to explore if a change in these biomarkers directly relates to new metastases and help to identify when therapeutic intervention, such as MWA, is warranted.

**Keywords:** microwave ablation, liver metastases, ctDNA, biomarkers, colorectal cancer

**Program Affiliation:** Diagnostic Imaging Summer Training and Experiences Partnership

Abstract Number: 33

### **Using Magnetic Resonance Spectroscopy to Determine Brain Health in Smokers**

Brionna McZeal, Chemistry, Texas Southern University; Brian A. Taylor, Ph.D., Imaging Physics, University of Texas MD Anderson Cancer Center

**Background:** Tobacco use contributes to 6 million premature deaths per year worldwide and may contribute to the degradation of neuronal health. This may also be compounded by the addictive chemical, nicotine, used in tobacco. The neurological effects from nicotine and tobacco are not as well explored compared to its cancer-causing effects. Thus, we used magnetic resonance spectroscopy (MRS) to measure neurometabolite concentration levels towards exploring the effects of tobacco and nicotine use on neuronal health.

**Methods:** This study was approved by the Institutional Review Board. MRS was performed on 41 participants with a J-resolved Point-Resolved Spectroscopic Sequence (TE=80 ms, TR=2000 ms, 128 averages) in the dorsal anterior cingulate cortex (ACC). 5 participants in total were excluded due to poor quality spectra. PRESS data analysis was performed using LCModel with a simulated basis set with TE= 80 ms. Group differences of metabolite concentrations between smokers and non-smokers were tested using an unpaired, two-tailed Student's t-test.

**Results:** The metabolite concentration levels for smokers (S) and non-smokers (NS) of glutamate (S:  $5.8 \pm 0.5$  and NS:  $6.7 \pm 0.4$ ; p-value: 0.018), myo-inositol (S:  $5.9 \pm 0.9$  and NS:  $7.0 \pm 0.4$ ; p-value=0.048), n-acetylaspartate (S:  $7.4 \pm 0.5$  and NS:  $8.8 \pm 0.6$ ; p-value=0.002), and creatine with phosphocreatine (S:  $6.2 \pm 0.4$  and NS:  $7.0 \pm 0.3$ ; p-value=0.008) were all significantly lower in smokers than in non-smokers. No differences were noted in the concentrations of other metabolites examined between smokers and non-smokers. These metabolites included aspartate (ASP), glutamine (Gln), phosphocholine (PCh), glycerphosphocholine (GPC), and glutathione (GSH).

**Conclusion:** Metabolites glutamate, myo-inositol, n- acetylaspartate, and creatine with phosphocreatine were found to be significantly lower in smokers than in non-smokers and may be indicators of degradation of neuronal health in smokers. Future work to examine factors affecting these metabolite concentrations, such as age and amount of tobacco use, is underway.

**Keywords:** Magnetic resonance spectroscopy (MRS), smoking, tobacco use, addiction, metabolites, neuronal health

**Program Affiliation:** Diagnostic Imaging Summer Training and Experiences Partnership

## DISCOVER Program

Abstract Number: 34

### **Inflammatory Pseudotumors Induced by AdCre in Transgenic Oncopigs After In Situ Tumor Induction**

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**Background:** Comparable anatomy and physiology of pigs make them an ideal model for human diseases, and few large animal tumor models exist for use in interventional radiology. Hepatocellular carcinoma (HCC) is the second leading cause of cancer death worldwide. HCC, reportedly may be induced in transgenic oncopigs with hepatic injection of adenovirus encoding Cre-recombinase (AdCre). AdCre activates mutant KRASG12D and TP53R167H genes, inducing tumors local to the administration site. This study evaluated cellular composition of AdCre-induced oncopig liver lesions at three time points. The original goal was to produce a hepatocellular carcinoma model within 4 weeks post-injection. The objective of this study was to characterize these lesions using multiplex immunofluorescence assays.

**Methods:** Oncopigs (n=9) received hepatic AdCre injections. Pigs were sacrificed at 14 days (n=3), 21 days (n=3), and 28 days (n=3). Liver tissue was collected in 10% neutral buffered formalin, processed, and paraffin embedded. Tissue microarray (TMA) was created containing representative central and peripheral areas of liver lesions. 4µm thick sections were stained using a Leica Bond Rx autostainer and Akoya Biosciences Opal 7-color kit. Slides were imaged with Leica Versa 8 whole slide fluorescent scanner. Samples were evaluated using the nuclear stain DAPI with CD31 (endothelium), smooth muscle actin, CD45 (leukocytes), vimentin (mesenchymal cells), Ki-67 (proliferation), and pan-cytokeratin (epithelium) to determine total cell counts and relative abundances of each marker. Cell composition was evaluated and quantified using Halo v.3.6 and analyzed with GraphPad Prism v.9 for statistical significance.

**Results:** Vimentin, alpha smooth muscle actin, CD45+ leukocytes, and pan-cytokeratin+ expression increased significantly. By 4 weeks, lesions consisted predominantly of CD45+ leukocytes and vimentin. Ki-67+ co-localized with CD45+ cells consistent with immune cell proliferation. Vimentin and smooth muscle actin increased with statistical significance, with co-expression in some areas consistent with myofibroblasts. Increased myofibroblasts suggest wound healing after localized trauma caused by AdCre. A statistically significant uptick in CD45-expressing cells is strongly suggestive of a leukocyte-dominant inflammatory response. Finally, pan-cytokeratin inconsistently increased throughout the lesions in areas of reactive biliary

hyperplasia. Characteristics of increasing proliferating leukocytes, fibroblasts, and myofibroblasts share some features of a group of benign entities referred to as “inflammatory pseudotumors” (IPT) that resemble neoplasia clinically and on diagnostic imaging. IPT frequently presents as a single mass and consists of variable inflammatory, granulomatous, and myofibroblastic reactions.

Conclusion: Hepatic AdCre injection induces inflammatory pseudotumors in transgenic oncopigs resulting in targetable lesions for interventional radiology studies, although the biological significance of such models remains unclear.

Keywords: Hepatocellular Carcinoma, AdCre, OncoPig, Inflammatory Pseudotumor

Program Affiliation: DISCOVER Program

Abstract Number: 35

### **Tumor Stiffness is Associated with Reduced CD45+ Immune Cell Penetration of Tumors in a Buffalo Rat Hepatocellular Carcinoma Model**

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**Background:** Primary liver cancer is third in cancer death worldwide and the incidence has more than doubled in the past 40 years. Hepatocellular carcinoma (HCC) accounts for approximately 90% of all liver cancers. HCC progression is known to be modulated by the immune system. Tumor stromal heterogeneity has been shown to negatively impact immune surveillance in the tumor microenvironment. Few imaging techniques accurately predict stromal properties that correlate with prognostic and molecular features in liver cancer. Shear wave elastography (SWE) is a non-invasive technique that presents an avenue for analyzing tumor stromal elasticity/stiffness. This study aimed to determine how tumor stiffness correlates with immune cell infiltration across designated tumor zones and elucidate the molecular underpinnings associated with tumor stiffness in order to predict more aggressive tumor phenotypes using SWE.

**Methods:** Rat hepatoma cells McA-RH7777 expressing green fluorescent protein (GFP) were orthotopically implanted in the liver of Buffalo rats. Three weeks after tumor implantation, successful tumor engraftment was verified by B-mode ultrasound where shear wave elastography data was recorded in m/s. Tumors were collected, processed, and sectioned. Multiplex immunofluorescence (mIF) staining was performed using a Leica Bond Rx autostainer and Akoya Biosciences Opal 7-color kit. Two 7-color mIF panels were created to compare between soft and stiff tumors in tumor sections. Quantitative image analysis was performed using HALO v.3.6 software where tumors were partitioned into four separate zones (tumor-liver interface, peripheral, paracentral, and central). Quantitative data was analyzed and graphed using Graphpad Prism v.9. where P-values of <0.05 were considered significant for marker presence.

**Results:** SWE demonstrated variable tumor stiffness ranging from approximately 2.0 to 3.5 m/s with a mean of 2.7 m/s. Overall, vimentin+ mesenchymal cells and GFAP+ hepatic stellate cells were significantly increased in the tumor-liver interface (TLI) when compared to the tumor center. Analysis of the tumor zones also showed trends of reduced CD45+ leukocytes and IBA-1+ macrophages in more central and paracentral areas in comparison to the TLI. Increased CD45+ immune cells at the TLI positively correlated with tumor stiffness, suggesting that increased stiffness could be an indicator of poor immune infiltration into more central areas of the tumor.

Conclusion: Given our findings, shear wave elastography may be useful as a non-invasive technique for predicting tumor fibrosis and immune exclusion. Findings also suggest that increased mesenchymal (vimentin+) and hepatic stellate cells (GFAP+) at the TLI create a barrier resulting in poor CD45+ immune infiltration in central and paracentral areas of tumor

Keywords: Shear Wave Elastography, Tumor Stiffness, Immune Infiltration, Hepatocellular Carcinoma, Buffalo Rat, Tumor Microenvironment.

Program Affiliation: DISCOVER Program

Abstract Number: 36

### **Appendiceal Adenocarcinoma PDX Models Have Improved Tumor Growth in an Orthotopic Tumor Environment.**

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**Background:** Appendiceal adenocarcinoma (AA) is a rare cancer that most commonly metastasizes to the peritoneal cavity. Very few preclinical models of AA exist. Patient-derived xenograft (PDX) models have the advantage of maintaining molecular and histologic features of human tumors as well as inherent intratumoral heterogeneity. Most PDX models involve engraftment of tumors in the subcutis of immunodeficient mice. However, heterotopic tumor implantation may alter tumor growth and behavior. We hypothesized that orthotopic engraftment in the peritoneal cavity would more faithfully recapitulate the tumor microenvironment in metastatic AA and improve tumor growth. Improved preclinical modeling is critical for studying tumor biology of human cancers and accurately predicting patient responses to novel therapies.

**Methods:** Three AA PDX tumor models were used to compare tumor growth in the microenvironment of the peritoneal cavity compared to subcutis. Tumor size was measured over time and tumor growth rates were calculated and normalized. H&E and Immunohistochemical (IHC) staining were performed. Ki-67 staining was used to evaluate cell proliferation. Serial sections were also stained with human marker Ku80, GI epithelial marker CDX2, and mesenchymal marker vimentin. Slides were scanned with an Aperio AT2 whole slide digital scanner. Images were deconvoluted and merged using HALO v3.6 to evaluate persistence of human tumor cells and human stroma in PDX tumors.

**Results:** 2/3 of the tumor models evaluated showed a faster growth rate in the peritoneal cavity with increased Ki-67 proliferation rate and increased cellularity after engraftment. CDX2 and KU80 co-localized indicating that human appendiceal adenocarcinoma cells persisted in both environments; however, the stroma was predominantly murine in both subcutaneous and peritoneal engrafted tumors.

**Conclusion:** Our results showed that appendiceal adenocarcinoma PDX tumors implanted in the peritoneal cavity have a faster growth rate, increased cell proliferation, and increased cellularity compared to tumors grown subcutaneously in 2/3 models evaluated. We also found that PDX tumor cells persist in both environments but differences in murine stroma from different microenvironments may impact tumor growth of AA PDX tumors. This study highlights the

importance of tumor microenvironment in preclinical tumor modeling strategies and supports our hypothesis that the peritoneal cavity is a more preferred microenvironment for appendiceal adenocarcinoma to engraft, grow, and metastasize.

Keywords: Tumor microenvironment, Appendiceal Adenocarcinoma, Gastrointestinal Cancer, Veterinary Pathology, Patient-Derived Xenograft, PDX

Program Affiliation: DISCOVER Program



Abstract Number: 37

**Effects of Supplemental Calcium and Vitamin D on Circulating Biomarkers of Gut Barrier Function in Colorectal Adenoma Patients: A Randomized Controlled Trial**

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**Background:** Evidence from basic science experiments and human observational studies indicate a protective effect of calcium and vitamin D against colorectal cancer (CRC). The proposed mechanisms include calcium and vitamin D's effects on the cell cycle; calcium's ability to bind bile acids and fatty acids in the stool leading to less DNA damage to colorectal epithelium cells; and vitamin D's modulation of immune response, inflammation, growth factor signaling, androgen and estrogen receptor pathways, and angiogenesis. Inflammation, a potential factor contributing to the gut barrier disruption, plays a major part in colon carcinogenesis. On the other hand, a weakened gut barrier is more permeable to the foreign antigens causing endotoxemia and inflammation, which can promote CRC. Recent evidence suggests that calcium, vitamin D, and the vitamin D receptor (VDR) may be involved in maintaining the integrity of the intestinal mucosal barrier. However, human studies assessing the effects of supplemental vitamin D and calcium supplementation on circulating biomarkers of gut barrier function among individuals at high risk for colorectal cancer are scarce.

**Methods:** We conducted an "adjunct biomarker study" to a larger 11-center, randomized, placebo-controlled, partial 2x2 factorial chemoprevention clinical trial, the Vitamin D/Calcium Polyp Prevention Study (NCT00153816; referred to as "parent study"). Participants at two of the eleven study centers (South Carolina and Georgia) who were found eligible for the adjunct biomarker study were recruited and signed biomarker study consents. Participants were randomized into four different treatment groups: placebo, 1200 mg/day calcium supplementation, 1000 IU/day vitamin D supplementation, and 1calcium and vitamin D supplementation. Blood was collected at baseline and 1-year follow-up to measure two biomarkers (lypopolysaccharide-binding protein, or LBP and intestinal fatty-acid binding protein, or IFABP) significantly associated with chronic gut inflammation and gut barrier dysfunction. We will compare baseline characteristics of participants across treatment arms using the  $\chi^2$  test for categorical data and ANOVA or Student's T-test for continuous variables. Next, we will test the effects of treatment on biomarker concentrations in each treatment group relative to the placebo using a generalized linear model (PROC MIXED). Lastly, in a secondary analysis, we will test whether treatment effects may differ by important baseline factors chosen a priori using a stratified analysis.

**Results:** We hypothesize the calcium and/or vitamin D supplementation will strengthen the gut mucosal barrier, which will be accompanied by decreases in circulating concentrations of markers of colonic permeability (LBP and IFABP).

**Conclusion:** Vitamin D and calcium supplementation can be recommended to prevent colorectal neoplasms and the vulnerable population by their individual characteristics can be identified for further investigation.

**Keywords:** Colorectal Cancer, Gut Barrier, Vitamin D, Calcium

**Program Affiliation:** DISCOVER Program

# First Year Medical Student Program

Abstract Number: 38

## **The Effects of the Transcription Factor IRF-3 in Pam2/ODN Microbial Resistance**

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Michael Longmire, Department of Pulmonary Medicine, UT MD Anderson Cancer Center  
Scott Evans, Department of Pulmonary Medicine, UT MD Anderson Cancer Center

**Background:** Pneumonia is a common and dangerous clinical condition affecting many people worldwide. It is most lethal in immunosuppressed and immunocompromised patients; thus, major effort has been undertaken to discover novel preventative measures and treatments to ameliorate the effects from acquiring this condition. One treatment, the use of the TLR2 agonist Pam2CSK (Pam2) with the Class C oligonucleotide TLR9 agonist ODN M362 (ODN), has been shown to resist microbial infection. However, the complete mechanism of Pam2/ODN's action is not fully understood. Previous research has shown some activation of the transcription factor interferon regulatory factor 3 (IRF-3), but little is known of how IRF-3 contributes to Pam2/ODN's resistance to infections.

**Methods:** To determine how IRF-3 contributed to the infection resistance properties of Pam2/ODN, it was first important to prove that Pam2/ODN activates IRF-3. MLE-15 cells were cultured either alone or treated with Pam2/ODN to determine the level of IRF-3 activation, the cells were collected, and a western blot and quantitative PCR were completed to measure the phosphorylation of IRF-3 and the gene expression, respectively. Next MLE-15 cells were treated separately by two TBK1/IKKe inhibitors, Amlexanox and MRT67307, to prove that they could inhibit the phosphorylation of IRF-3 when compared to negative controls. Again, a western blot and q-PCR were run to establish levels of phosphorylated-IRF-3 activation. Finally, MLE-15 cells were treated with one of the inhibitors and Pam2/ODN then infected with influenza virus to measure viral burden when compared to negative controls.

**Results:** The western blots of the phosphorylated IRF-3 did not show any conclusive results and the results of the quantitative PCR were variable. The influenza infection experiment showed the effectiveness of Pam2/ODN in resisting viral infection, however, the drug worked so well it buried any observable response of IRF-3, however, when IRF-3 specific genes were tested from the infected cells it showed more IRF-3 activation with combination treatment than with inhibitor alone.

**Conclusion:** The results of the data collected did not conclusively answer the hypothesis, thus future experiments are necessary to answer this question. The same experiments should be repeated using alternate cell lines, such as HBEC3-KT and mTEC, which will give vital translational and foundational information for further experimentation.

**Keywords:** IRF-3, Pam2/ODN, Innate Immunity, Pneumonia

**Program Affiliation:** First Year Medical Student Program

Abstract Number: 39

## **Tumor Content Is Not Linked To Pembrolizumab Response In Rare Tumors**

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**Background:** Immune checkpoint inhibitors have shown promise in the treatment of several cancer subtypes. There are not, however, biomarkers that can be applied across tumor subtypes to predict response to immunotherapy treatment. This study utilized paired biopsies acquired from patients in a phase II pembrolizumab clinical trial to determine whether histological analysis of tumor content, necrosis, and proliferative fibrosis can be utilized to predict patient response to treatment.

**Methods:** A total of 232 biopsies (121 at baseline and 111 on-treatment) from 39 patients diagnosed with rare solid tumors and undergoing treatment in a phase II pembrolizumab clinical trial were included in this analysis. H&E-stained slides were scanned into Aperio Digital Scanner and annotated using ImageScope Digital Software. The percentage of tumor content (TC) and necrosis in each biopsy was determined and then classified as “high” or “low” according to a 10% cut-off. The percentage of proliferative fibrosis (PF) was also quantified and then classified as either “present” or “absent.” These classifications as well as the shift in TC from baseline to on-treatment were correlated with patient clinical response. Clinical response was defined in accordance with RECIST V.1.1.

**Results:** The patients in our cohort were diagnosed with 9 different types of rare tumors. No patients in this cohort had a complete response (CR) to treatment and only 4 patients had a partial response (PR) to treatment. At baseline, 3 patients had low TC while 6 had low TC on-treatment. A majority of the tumors displayed PF and necrosis. A high TC at baseline was associated with an increased time-to-progression (TTP;  $p=.025$ ). 10% ( $n=4$ ) of the patients had a decrease in TC from baseline. There is no association between a decrease in TC from baseline to on-treatment and objective response rate (ORR;  $p=.330$ ).

**Conclusion:** We cannot conclude that histological analyses of TC predict patient response to immunotherapy as a decrease in TC was not associated with an ORR. A previous study did show, however, that decreases in TC predict response to immunotherapy and increased progression-free survival. This incongruity can be explained by the power of this cohort, as the overall cohort was relatively small ( $n=39$ ) and there was only a small number of patients that had a low TC ( $n=3$  at baseline and  $n=6$  on-treatment). Therefore, it is reasonable to conduct similar analyses with larger cohorts in the future.

**Keywords:** Immunotherapy, Predictive Biomarkers, Tumor Content

**Program Affiliation:** First Year Medical Student Program

Abstract Number: 40

## **Evaluating The Efficacy Of ONC206 As A Treatment Strategy For Uveal Melanoma**

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<sup>2</sup>University of Minnesota Medical School, Minneapolis, MN

**Background:** Uveal Melanoma (UM) is a rare subtype of melanoma that originates in the uveal melanocytes of the eye. Although primary UM is highly treatable, about half of UM patients progress to metastatic disease. Metastatic tumors arise from the bi-allelic loss of BAP1 concurrent with the loss of a copy of chromosome 3.<sup>1</sup> Our previous studies have shown that metastatic UM have a metabolic vulnerability of high oxidative phosphorylation (OXPHOS), making it a target for therapies. Direct inhibition of OXPHOS is toxic in clinical studies. Imipridones can activate the mitochondrial protease ClpP, which targets mitochondrial OXPHOS effector proteins<sup>2</sup>. We hypothesized that the imipridone ONC206 would be able to effectively restrict UM cell growth, migration, and metabolism. In this study we aimed at determining whether ONC206 can effectively kill UM cells and inhibit cell migration.

**Methods:** MTT- based cell survival and Boyden chamber-based cell migration assays were used to assess cell survival and migration upon treatment with different concentrations of ONC206. Routine western blots were performed for molecular analysis of protein representing cell growth and metabolic stress. Statistical analysis of survival assays was performed using student t-test. P-values were calculated using untreated controls compared to various treatment doses and significance was determined as  $p \leq 0.05$ .

**Results:** Our experiments showed that ONC206 was successful in effectively reducing UM cell survival, with negative effects on cell viability upon treatment. The activity reached a plateau in multiple cells post 1uM dose of ONC206. Boyden chamber-based cell migration assays showed effective migration reduction in two UM cell lines. Western blots showed processing of PARP. Indicative of apoptosis induction. Western blots also showed decrease of SDHA and SDHB effector proteins of OXPHOS, indicating the drug is specific in its action.

**Conclusion:** ONC206 inhibits UM cell migration and survival. Protein markers analysis confirmed apoptotic pathways were being activated. While showing promise in our in vitro assays, ONC206 should be evaluated in the preclinical models of UM to move forward in the future. Sister imipridone compounds such as ONC201 and ONC212 are currently being evaluated for maximum efficacy and low toxicity outcomes.

**Keywords:** Uveal Melanoma, ONC206, oxidative phosphorylation, cell survival

**Program Affiliation:** First Year Medical Student Program

Abstract Number: 41

## **Serum nc886 expression predicts HPV16 status and survival in oropharyngeal squamous cell carcinoma patients**

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**Background:** The rising incidence of oropharyngeal squamous cell carcinoma (OPSCC) is attributed to an increase in HPV16 infections, as the other two major risk factors, alcohol, and tobacco consumption, have decreased globally. Interestingly, HPV16(+) OPSCC patients have better prognoses than HPV16(-) patients. Previous literature shows that a non-coding RNA, nc886, is hypermethylated in HPV16(+) OPSCC. The downstream effects of this hypermethylation play a role in tumor-sensing, a mechanism that may improve survivability. This study aims to elucidate nc886 expression, differential tumor HPV16 status, and related survival in patients with OPSCC.

**Methods:** A small cohort study of patients with histopathologically confirmed OPSCC who underwent radiation or radio-chemotherapy recruited from the University of Texas MD Anderson Cancer Center (MDACC) was performed. Patients completed an epidemiological questionnaire about demographics and risk factors; clinical and follow-up data were abstracted from their medical records. HPV16 status was determined by p16 IHC, in-situ hybridization, or specific RT-PCR. Serum nc886 levels were measured using RT-qPCR. Kaplan-Meier survival analysis, independent samples t-test, and Cox-proportions hazard model were performed in SAS.

**Results:** We recruited 83 OPSCC patients including 63 HPV16(+) and 20 HPV16(-) OPSCC patients. These patients underwent radiation or radio-chemotherapy at MDACC. HPV16(+) patients expressed significantly less nc886 than HPV16(-) patients ( $p=0.008$ ). Low nc886 expression predicted better overall survival than high nc886 expression among all OPSCC patients ( $p=0.036$ ). This effort was particularly evident within the HPV16(+) OPSCC cohort ( $p=0.026$ ). After adjusting for age, sex, race, smoking/alcohol status, pack-years of smoking, stage, treatment, and comorbidities, the Cox-proportions hazard model revealed that low nc886 expression confers a 91% (95% CI: 44-99%) reduced risk of overall death in HPV16(+) OPSCC patients compared those with high nc886 expression in the same cohort.

**Conclusion:** HPV16(+) OPSCC constitutes a unique subgroup characterized by divergent etiology, treatment responsiveness, and survival. HPV16 status serves as a crucial prognostic factor in OPSCC. Furthermore, nc886 expression might exert a functional influence on tumor HPV16(+) status, etiology, and treatment response of OPSCC. Nc886 may serve as a crucial prognostic predictor in OPSCC, particularly in HPV16(+) OPSCC, despite the substantial heterogeneity observed in the outcomes of HPV16(+) cases. Although our study is limited by a small sample size at MDACC, our findings demonstrate that nc886 may play a role in the development of more severe OPSCC, involve molecular pathways that incite different sensitivity to radiation or radio-chemotherapy, and serve as a future therapeutic target.

**Keywords:** HPV, Non-coding RNA, nc886, oropharyngeal cancer, OPSCC survival

**Program Affiliation:** First Year Medical Student Program

Abstract Number: 42

**Primary Hurthle cell thyroid carcinoma treated with surgery: A single institution experience of 92 patients**

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**Background:** Oncocytic carcinoma of the thyroid (OCA), previously known as Hurthle cell thyroid carcinoma (HCTC) accounts for 3-5% of all thyroid cancers. Surgery is considered the primary treatment and is often followed by radioactive iodine (RAI). OCA has often had a more aggressive course and poorer prognosis compared to other differentiated thyroid cancers. Given the rarity of OCA, there are relatively few series which describe the disease presentation, diagnosis methods, treatment, and follow up. Herein we report 92 patients with OCA treated with primary surgery at MD Anderson Cancer Center in order to characterize patterns of disease recurrence and survival.

**Methods:** Retrospective chart review of 92 patients who had surgery for newly diagnosed Hurthle cell thyroid carcinoma (HCTC)/ oncocytic carcinoma (OCA) at a single institution from 1996-2023. We included patients with a new diagnosis of HCTC/OCA that underwent primary thyroid surgery at MD Anderson Cancer Center and excluded patients with previous thyroid surgery treatment at an outside facility as well as patients who presented as a recurrence. Kaplan Meier method was used to analyze survival.

**Results:** 63% were female, 84% caucasian, and median age at diagnosis was 58 years. All patients had primary surgery (71% total/completion thyroidectomy, 29% lobectomy) 28% had neck dissection. 41% received radioactive iodine, 3% received chemotherapy, 9% received radiation therapy to the neck, 4% received targeted therapy. 6 (7%) patients developed locoregional recurrence. 17% of patients either presented with distant metastasis or ultimately developed them with their primary disease or recurrent disease. Median recurrence free survival estimate is 158.7 months and the median overall survival estimate is 181.8 months.

**Conclusion:** In one of the largest single institution experiences describing surgical treatment and outcomes of primary hurthle cell/ oncocytic thyroid carcinoma (OCA) patients, locoregional recurrences are rare (<7%), while a significant number of patients either present with distant metastases, ultimately develop them, or have recurrence with distant metastases (17%). Nevertheless, 10-year overall survival for newly diagnosed OCA patients undergoing surgery is approximately 70%.

**Keywords:** Hurthle cell carcinoma, oncocytic thyroid carcinoma, retrospective review, primary surgery

**Program Affiliation:** First Year Medical Student Program

Abstract Number: 43

## **Culturing Human Bronchial Epithelial Cells to Dissect Mechanisms of Airway Mucin Secretion**

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**Background:** Mucus plays a vital role in shielding the lungs against harmful inhaled substances such as particles, pathogens, and chemicals. The mucus layer captures these harmful elements and expels them out of the airways through ciliary beating. However, mucus hypersecretion contributes to respiratory diseases including asthma, cystic fibrosis, COPD, and interstitial lung diseases. Similar to secretion from other cell types, mucin secretion is mediated by a four-helix SNARE complex regulated by Munc and Synaptotagmin proteins. Remarkably, however, distinct molecular machines mediate baseline and stimulated mucin secretion. While all of the core components of the stimulated secretion machine have been identified, two components of the baseline secretion machine remain unknown – the Syntaxin and the Synaptotagmin isoforms. Both the Syntaxin and the Synaptotagmin families contain 16 members, so to identify candidates mediating mucin secretion, it would be helpful to know their expression in airway secretory cells. To perform quantitative expression analyses, secretory cells must be separated from the other major airway epithelial cell types – ciliated and basal cells. The most straightforward way to do this would be by fluorescence-activated cell sorting (FACS) of well-differentiated human airway epithelial cells (HAEC).

**Methods:** HAEC cells obtained from Lonza were expanded and then cultured at an Air-Liquid Interface (ALI) for 28 days. Cells in ALI culture were treated with IL-13 to stimulate the differentiation of secretory cells and their production of high levels of mucins, similar to normal human physiology. FACS was performed using acridine orange that concentrates in acidic organelles, including mucin granules.

**Results:** Two different lots of HAEC containing 500,000 cells per vial were expanded in cell culture. Expansion of the first lot yielded 36 vials with 500,000 cells per vial and the second lot yielded 28 vials with 500,000 cells per vial for the creation of a HAEC archive for experimental use. Microscopic analysis after 28 days in culture showed beating cilia and both secretory and ciliated cells by histochemical staining. Secretory cell enrichment by FACS using lysosomatropic agents such as acridine orange is ongoing, as is the analysis of compound exocytosis using styryl dyes and fluorescent-labeled dextran.

**Conclusion:** The expansion of two lots of HAEC and validation of their differentiation by ALI culture and IL-13 stimulation provides a crucial tool for further studies of human airway mucus secretion.

**Keywords:** Human airway epithelial cells, Mucus, Mucin, Syntaxin

**Program Affiliation:** First Year Medical Student Program

Abstract Number: 44

## **Associations between Sociodemographics and Pediatric Osteosarcoma Characteristics**

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**Background:** Osteosarcoma is the most common primary malignancy of bone, and the eighth leading cause of childhood cancer. Few studies have examined how the presentation, treatment and outcomes of osteosarcoma vary across specific sociodemographic groups in the pediatric, adolescent, and young adult populations.

**Methods:** We downloaded case-level data from the Surveillance, Epidemiology, and End Results (SEER) database. Cases included patients ages 0-24 who were diagnosed with Osteosarcoma between 2004-2020. We used multivariate logistic regression to evaluate the associations between patient demographics and dichotomous variables related to tumor characteristics and treatment. Variables related to patient characteristics included sex, race/ethnicity, age, county income, and county rurality. Outcome variables included presence of metastases, tumor size, primary site, administration of amputation, administration of chemotherapy, and time from diagnosis to treatment. We used multivariate Cox regression to evaluate the relationship between patient characteristics and disease-specific survival. We controlled for factors related to cancer severity when evaluating variables related to treatments and survival.

**Results:** We extracted 2391 osteosarcoma cases for our analysis. We found that osteosarcoma patients living in rural counties were significantly more likely to present with axial tumors (OR=1.60, p=0.04). When examining differences across race and ethnicity, we compared Hispanic patients, non-Hispanic Asian patients, and non-Hispanic Black patients to non-Hispanic White patients. We found that Hispanic patients were significantly more likely to present with metastases (OR=1.54, p<0.01), have tumors >8cm (OR=1.38, p<0.01) and undergo amputation (OR=1.56, p<0.01). Non-Hispanic Asian patients were significantly less likely to present with non-extremity tumors (OR=0.52, p=0.02), but more likely to have tumors >8cm (OR=1.89, p<0.01) and to undergo chemotherapy (OR=4.91, p<0.01). Non-Hispanic Black patients were significantly more likely to have ≥1 month pass between diagnosis and treatment (OR=1.33, p=0.03). However, we found no differences in disease-specific survival in osteosarcoma between racial/ethnic groups when accounting for stage.

**Conclusion:** There are numerous disparities in the presentation, treatment and outcomes of osteosarcoma and Ewing sarcoma in the pediatric population, especially across racial/ethnic groups. These differences likely have multifactorial causes. Further work is needed to address these disparities and ensure equitable treatment of pediatric bone cancer patients.

**Keywords:** osteosarcoma, pediatric, epidemiology, surgical oncology

**Program Affiliation:** First Year Medical Student Program



# ITERT Undergraduate Summer Research Training Program

Abstract Number: 45

## **Spatial Point Processes - A novel**

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**Background:** Among renal cell carcinomas (RCCs), clear cell RCCs (ccRCCs) are the most prevalent, accounting for 70-80% of all RCCs, with a 5 year survival rate of 50-69% percent. Owing to the increased use of imaging studies, the detection and incidence of ccRCC have risen steadily over the past few decades. However, there are several weaknesses to traditional pathological examination. Primary diagnostic tumors often do not encapsulate the total extent of the cancer and ISUP/Furhman Grading, a gold-standard metric of tumor severity in diagnostic tumors, suffers from low pathologist agreement, an inability to stratify patient prognoses in intermediate grades (II/III), and a lack of G1/IV patients, so pathologists often resort to costly and time-consuming clinical markers. Precise, quantifiable metrics of ccRCC outcomes that are not burdened by the limitations of existing diagnostic tools and can be used on a primary diagnostic tissue alone are imperative. A promising area of focus involves using measures that reflect patterns in the Tumor Microenvironment (TME). Metastasis, an outcome linked to survival involves dynamic cell mobilization, so an analysis of spatial patterns beyond a pathologist's naked eye could additional avenues for stratifying prognoses in complicated cases.

**Methods:** In our study, 35 Metastatic and 41 Non-metastatic ccRCC H&E diagnostic slides were queried from TCGA. Each slide was loaded into QuPath, where 3 annotations 750 um x 750 um were randomly. One annotation was randomly selected, artifacts, blood vessels, and blood cells and object classification to remove non-tumor cells. The resulting region was extracted, and treating tumor cells as points, a Pair Correlation Function was applied to each annotation, the values of which were used as features to try and stratify outcomes of 1) Metastasis found at diagnosis 2) The stage of the tumor 3) ISUP/Fuhrman Grade. Our analysis revealed the formation of 2 distinct spatial signatures from our tumor samples.

**Results:** These clusters fell under 2 characteristics, a high severity cluster, with patients having increased stage and high incidence of metastasis, had tumor cells that are roughly following a pattern of completely spatial randomness and a low severity cluster showing more clustering and attractiveness.

**Conclusion:** We demonstrated that mathematical point models can stratify advanced clinical outcomes given only a diagnostic slide of a primary ccRCC tumor. The use of spatial metrics can potentially affect clinical disease management pathways such as directing more intense screening for metastasis versus a definitive resection. More analysis needs to be done to reveal the biological basis for these patterns, such as in contact inhibition and cell-cell adhesion genes.

**Keywords:** Spatial, RCC, Computational, Mathematics

**Program Affiliation:** ITERT Undergraduate Summer Research Training Program

Abstract Number: 46

## **Antibody Validation and Dual IHC Staining of Glioblastoma Multiforme to Isolate Microglia Cells in Glial Cell Population for Biomarker Identification**

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**Background:** Glioblastoma Multiforme (GBM) is a malignant grade IV brain tumor and is the deadliest form of brain cancer. GBM arises from glial cells in the central nervous system, where it grows rapidly and destroys healthy tissue. Early signs of GBM are nonspecific and vary from case to case, making a diagnosis nearly impossible. Current treatment methods for GBM are complex and unsuccessful. There are no effective immune biomarkers for GBM, and the development of an accurate tumor microenvironment (TME) immune profile is crucial. Microglia are important in the glioblastoma TME as the resident myeloid cells of the brain, making them potential target biomarkers in immunotherapy.

**Methods:** Four antibodies in microglia and glia cells were validated: IBA.1, Olig-2, PU.1, and GFAP and dual staining was performed for isolation of microglia from glial cells. Tissue sections of tonsil and GBM were stained in a Leica Bond Max Biosystem. Sections were deparaffinized and rehydrated. Antigen retrieval was performed with Bond Epitope Retrieval Solution 1/2 (ER1 pH 6.0/ER2 pH 9.0) at 100 °C for 5 or 20 minutes. The diluted antibody was employed for 15 or 30 minutes at room temperature. Primary antibody was detected using diaminobenzidine (DAB) as chromogen. Slides were counterstained with hematoxylin, dehydrated, and cover slipped. Antigen retrieval solution and time and antibody dilution and incubation time were determined using antibody data sheets as baselines and adjusting values for each trial as needed. For dual staining, antibody 1 was detected with DAB chromogen and antibody 2 with Red chromogen. Pretreatment and primary antibody optimal conditions from single staining were applied.

**Results:** Following multiple assays, optimal conditions were GFAP (1:7000 ER1), IBA.1 (1:100 ER1), PU.1 (1:100 ER2), and Olig-2 (1:50 ER2) for single staining and PU.1 (1:25 ER2 DAB) + GFAP (1:15000 ER2 Red), Olig-2 (1:10 ER2 DAB) + IBA.1 (1:200 ER2 Red), and IBA.1 (1:100 ER1 DAB) + GFAP (1:7000 ER1 Red) for dual staining. All four antibodies were successfully validated with optimal conditions. Dual staining was effective, providing a detailed GBM profile with successful separation of microglia from other glial cells.

**Conclusion:** Microglia isolation allows for future projects to study solely microglia and its relation to tumoral cells through digital image analysis. This opens the door for activation of microglia as potential biomarkers for immunotherapy due to the large role microglia plays in the TME of GBM.

**Keywords:** glioblastoma, PU.1, IBA.1 GFAP, Olig-2

**Program Affiliation:** ITERT Undergraduate Summer Research Training Program

## King Foundation

Abstract Number: 47

### **Optimizing Of The High-Throughput DNA Repair Assay For Immunotherapy**

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**Background:** Homologous recombination repair (HR) is made up of a number of interconnected pathways that are involved in the repair of interstrand crosslinks (ICL) and double-stranded breaks in DNA. Additionally, recombination contributes to DNA damage tolerance by helping DNA replication recover from stopped or broken replication forks. Following the creation of I-Sce1 induced double stranded breaks, green fluorescent protein (GFP) assay is used to evaluate HR by flow cytometry. The goal of our project is to optimize this HR assay for high-throughput chemical screening to identify small compound agents that can inhibit HR repair and trigger DNA damage dependent immune response.

**Methods:** We did 2 experiments for HR assay using standard ThermoFisher Lipofectamine 3000 Reagent transfection protocol. The I-sce1, green fluorescent protein (GFP), and red fluorescent protein (RFP) were isolated using standard protocol. All samples contain a total of 3 micrograms of plasmid DNA. The first experiment was used with a 6-well plate with a negative control with no plasmid and the other 5 wells contain I-sce1, I-sce1+RFP, RFP, GFP, and RFP+GFP respectively. Eight 60-mm dishes were for the second experiment. One of the dishes contains no plasmid, and three of the dishes were used to measure the RFP efficiency using 2:1, 1:1 and 1:2 ratios of I-sce1+RFP plasmid combination. The other 4 dishes were samples of I-sce1, RFP, GFP, and RFP+GFP combined respectively. The transfected cells were analyzed using flow cytometry 48 hours after transfection.

**Results:** Our results showed that the I-sce1+RFP 1:2 ratio in a 60-mm experiment showed the most effective plasmid concentration with 12.6% RFP cells. Additionally, there was more GFP transfection efficiency in the 6-well plate with 36.8% GFP cells than the 60-mm dish with 17.9% GFP cells.

**Conclusion:** Collectively our experiments optimized transfection conditions to achieve the best efficiency of HR repair assay in a high-throughput format. Changing the calculated cell concentration, plasmid concentration, and produced GFP intensity, we can achieve better GFP signaling to measure HR repair efficiency. Future tests of the efficacy of an HR inhibitor drug can be done by estimating how much the GFP intensity is reduced. We expect the new HR inhibitors have a potential to modulate immune responses through regulating DNA damage accumulation for immunotherapy.

**Keywords:** Homologous recombination repair, GFP, Interstrand Crosslinks, HR inhibitor

**Program Affiliation:** King Foundation

Abstract Number: 48

## Evaluation of Structural Flexibility and Cross-Reactivity of the T-Cell Receptor

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**Background:** T-cells have become of interest for cancer therapies due to their ability to recognize and engage with tumor antigens. On a molecular level, a T-cell receptor (TCR) interacts with a peptide-major histocompatibility complex (pMHC) to trigger an immune response. TCR complexes contain  $\alpha$  and  $\beta$  chains each with variable and constant domains. Each variable domain contains three complementarity-determining regions (CDRs): CDR1, CDR2, and CDR3. While CDR1 and CDR2 primarily interact with MHC helices, CDR3 loops are the most structurally diverse and interact with peptides to a great extent. Evaluation of structural flexibility and cross-reactivity of TCR will help to reach a greater understanding and advance therapeutic interventions. Our project presents two aims: (1) explore the structural flexibility of TCR when bound to pMHC and (2) evaluate the role of TCR structural flexibility in cross reactivity.

**Methods:** For Aim One (structural flexibility), we gathered 38 pairs of bound and unbound TCR complexes from the RCSB PDB website, truncated all PDBs to only include the CDR loop regions, and performed root-mean-square deviation (RMSD), template modeling score (TM-score), and Local Distance Difference Test (IDDT) tests, which provide a quantitative assessment of similarity between two structures (pairs of bound and unbound CDR loops, in this case). For Aim Two (cross-reactivity), we evaluated 31 pairs of cross-reactive (CR) TCR complexes and 8 pairs of non-cross-reactive (NCR) TCR complexes using the same three methods. P-values were calculated by T-test.

**Results:** Greater RMSD, lower TM-score, and lower IDDT values all correspond with greater differences between two structures and greater loop flexibility. In all three methods, most values were significantly different from each other ( $p < 0.05$ ). CDR3 $\alpha$  (RMSD: 0.18-2.36 Å; TM-score: 0.23508-0.892; IDDT: 0.5452-0.9769) and CDR3 $\beta$  (RMSD: 0.17-2.28 Å; TM-score: 0.31443-0.90425; IDDT: 0.6044-1) presented the greatest RMSD and lowest TM-score/IDDT among all  $\alpha$  and  $\beta$  loops, respectively, indicating that CDR3 has the greatest degree of flexibility among all CDR loops. In contrast, none of the values were significantly different between the CR and NCR groups for all loops ( $p > 0.05$ ), suggesting that each CDR loop within a paired CR and NCR group have similar degrees of structural flexibility.

**Conclusion:** CDR3 $\alpha/\beta$  loops display a greater degree of structural flexibility than other CDR loops. CDR3 $\alpha/\beta$  loop-mediated structural flexibility is found in CR groups. Future studies will incorporate more TCR complexes, implement more structural difference methods, and evaluate the role of MHC flexibility in cross-reactivity.

**Keywords:** TCR-pMHC complex, complementarity-determining region, structural flexibility, cross-reactivity

**Program Affiliation:** King Foundation

Abstract Number: 49

## **Comparative Effects of Combustible Cigarette versus Electronic Cigarette Exposures on K-ras Mutant Lung Cancer Promotion**

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**Background:** Combustible cigarette smoking (CCS) is linked to approximately 90% of all lung cancer cases by inducing a multitude of tumor-initiating effects, including inflammation. Inflammation has been shown to persist even after smoking cessation. The use of non-combustible smoking vectors, such as electronic cigarette vapors (ECV), has recently seen increasing popularity among younger generations. Despite this alarming trend, the long-term health effects of ECV are yet poorly understood. Our lab aimed to compare the effects of CCS and ECV on lung immune response and tumor growth using a specific mouse model of lung adenocarcinoma with a K-ras mutation in the airway epithelium (CC-LR).

**Methods:** Three cohorts of CC-LR mice were exposed to either room air, CCS, or ECV for 2 hours each day, five days per week for 8 weeks between 6-14 weeks of age. For CCS exposure, we used 3R4F research cigarettes. For ECV exposure, we used a 72 mg/ml liquid nicotine solution diluted in 50% propylene glycol/vegetable glycerin.

**Results:** We found that CCS, but not ECV, promotes tumor growth demonstrated by increased surface tumor counts, and percent tumor area in hematoxylin and eosin-stained tissue sections, along with increased tumor cell proliferation (Ki67 positivity) and angiogenesis (ERG positivity). However, both CCS and ECV cohorts had significantly increased immune cell infiltrates within the bronchoalveolar lavage fluid (BALF). Flow cytometry analysis of the whole lung showed that CCS and ECV differentially modulate myeloid cell populations, while both similarly reduced CD8<sup>+</sup> IFN $\gamma$ <sup>+</sup> and CD8<sup>+</sup> GZMB<sup>+</sup> cytotoxic T cells and increased CD4<sup>+</sup> FOXP3<sup>+</sup> regulatory T cells. Furthermore, via qPCR and ELISA we found that there was a significant decrease in expression levels of Nos2, IFN $\gamma$ , and Arginase 1 and secretion of TNF $\alpha$  and GZMB in both groups. A significant increase in IL-10 expression was also observed. These findings collectively show induction of an immunosuppressive phenotype in CCS and ECV exposed mice.

**Conclusion:** Although both CCS and ECV promoted lung inflammation, with CCS inducing a more immunosuppressive phenotype than ECV, only CCS significantly promoted tumorigenesis in lung. Future studies probing the cell-to-cell crosstalk within CCS and ECV-exposed CC-LR mice are needed for the development of a precise therapeutic strategy targeting K-ras mutant lung cancer.

**Keywords:** K-ras, Lung Cancer, Cigarette Smoking, Vaping

**Program Affiliation:** King Foundation

## Medical Student Program Radiation Oncology Summer

Abstract Number: 50

### **Characterization of Proton Radiation-Induced Necroptosis in Cerebral Organoid Model**

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**Background:** Radiation therapy (RT) has proven to be an effective treatment modality for aggressive brain tumors as its high local tumor control exceeds that of systemic therapies. However, less is known about the effect of proton therapy on healthy tissue. Necroptosis is an important cell death pathway tumor cells utilize and is stimulated by radiation to induce tumor cell death. Evidence suggests brain tissue and neurons in the surrounding tumor microenvironment undergo necroptosis and this is linked to cognitive decline, a major concern for pediatric patients. The purpose of this study is to gain insight into the necroptosis pathway, assess the effectiveness of a RIPK1 inhibitor to reduce necroptosis in pre-established human induced pluripotent stem cell (hiPSC) derived cerebral organoid models, and verify the use of these 3D models for such aims.

**Methods:** 48 hiPSC derived organoids were collected, assayed, and analyzed for necroptosis at three timepoints. In Experiment 1, 18 organoids were collected, and half were incubated with a RIPK1 inhibitor 45 minutes before proton radiation. Organoid proteins were isolated by western blot 6 days post RT. In Experiment 2, 30 organoids were incubated with the inhibitor 1.5 hours prior to RT and protein isolation occurred 2 hours and 48 hours post RT. Organoids in both experiments received either 0Gy or no radiation, 10Gy, or 20Gy radiation and two-way ANOVA was used to determine significance between groups.

**Results:** 6-day timepoint protein isolation yielded increased levels of necroptosis markers tRIPK1, tMLKL, and pRIPK3 (not significant) with radiation dose compared to non-radiated controls. Protein levels in radiated conditions decreased in the presence of the RIPK1 inhibitor compared to the non-inhibitor group (not significant). 2-hour and 48-hour timepoint isolations yielded no consistent changes in pRIPK1, pMLKL, or tRIPK1 with radiation dose or in the presence of inhibitor. pRIPK1/tRIPK1 ratio was significantly reduced by the inhibitor at the 48-hour timepoint in the 20Gy radiated group only.

**Conclusion:** Small sample size, high organoid variability, and the inability to verify inhibitor penetration were the challenges of this study. Additionally, repeating the experiment in mature neurons and neural stem cells separately would be more informative as the organoids are heterogeneous mixtures of both mature and immature cell types. This study highlights the need to use an improved organoid model with vasculature and non-neuronal cell types like endothelial cells and microglia to better recapitulate the human brain.

**Keywords:** Proton therapy, necroptosis, cerebral organoid, RIPK1 inhibitor

**Program Affiliation:** Medical Student Program Radiation Oncology Summer

Abstract Number: 51

### **Understanding the effect of NKTR-255 on circulating lymphocyte levels post-radiotherapy**

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**Background:** The ability of radiation therapy to damage the DNA inside a cancer cell has led it to become one of the keystone options for treating cancer; however, it has also been shown to lead to a state of immunosuppression by also destroying the patient's lymphocytes. An alternative that has emerged to address this concern is NKTR-255, a polymer-conjugated IL-15 that, in mice, has been observed to increase the activation and proliferation of NK and CD8+ T cells, while not influencing the levels of regulatory T cells. The purpose of this experiment is to determine whether this effect can be safely replicated in non-small cell lung cancer (NSCLC) patients that have undergone radiotherapy. We predict that patients that receive NKTR-255 will achieve an absolute lymphocyte count (ALC)  $> 1$  by 8 weeks post-radiotherapy, having much higher lymphocyte levels and quicker recovery rates than patients that do not receive NKTR-255.

**Methods:** This investigation is part of the RESCUE trial, a single-arm phase II trial testing standard of care treatment for cancer together with NKTR-255. The control individuals retrospectively analyzed as part of this experiment were all NSCLC patients who received standard 30 fractions of radiation therapy with concurrent chemotherapy, alone or with durvalumab, between 2016 and 2023. The trial group are patients that underwent the treatment regimen described above, but also elected to receive NKTR-255. Demographic and complete blood count data, particularly the ALC, was extracted from the charts of individuals belonging to the two groups to determine what factors account for lymphocyte values before, during and after radiotherapy. An ALC equal to or greater than 1 was selected as the threshold for recovery as anything below 1 is considered toxic.

**Results:** Control patients, independently of whether they are given durvalumab, do not tend to recover to normal lymphocyte levels after radiation. On the other hand, patients injected with NKTR-255 have much quicker recovery times, with 3 of them achieving an ALC $>1$  one week following radiation and the other 2 reaching the same mark by the 4th week. Patients from both groups have no significant differences in ALC throughout radiation treatment; however, NKTR-255 injection results in trial patients having significantly greater circulating lymphocyte levels by 8 weeks post-radiotherapy.

**Conclusion:** Our findings indicate that NKTR-255 could be a solution to radiation-induced lymphopenia, with patients that received this drug having greater post-treatment lymphocyte levels and quicker lymphocyte recovery rates.

**Keywords:** NKTR-255, Absolute Lymphocyte Count (ALC), Radiation Therapy, Radiation-Induced Lymphopenia

**Program Affiliation:** Medical Student Program Radiation Oncology Summer

Abstract Number: 52

## **LINAC-Based Stereotactic Body Radiation Therapy for Benign Tumors of the Skull Base**

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Catherine Wang, Ph.D., Radiation Oncology, University of Texas MD Anderson Cancer Center;  
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**Background:** Linear accelerator (LINAC)-based stereotactic body radiation therapy (SBRT) combines high definition multileaf collimators based linear accelerators with image guidance to precisely deliver ablative radiation dose to localized tumors while sparing surrounding healthy tissues. SBRT can be used to treat benign, slow-growing tumors including paragangliomas, schwannomas, and myxoid tumors. These tumors can be found at the base of the skull, a location adjacent to several critical structures. The surrounding structures necessitate therapy that limits damage to untargeted areas.

**Methods:** This is a retrospective analysis of outcomes of patients presenting with a benign tumor of the skull base treated with LINAC-based SBRT. Patients enrolled in the prospective skull base registry and treated between 2017 and 2023 were included in the study. All patients were evaluated for surgery and the risk of potential cranial nerve injury was the primary reason for consideration of radiation therapy. Variables that were used to measure outcome included local control (LC), overall survival (OS), state of pre-treatment symptoms, and toxicity. LC is defined as radiographic evidence of lack of progression. Follow up interval is defined as the end of SBRT to last follow up date.

**Results:** Thirty-one patients formed the cohort. The median age was 51 years. Twenty-three cases were paragangliomas, 7 cases were schwannomas, and 1 case was a myxoid tumor. Twenty-six cases were in the jugular foramen/jugulotympanicum, 3 in the carotid space, 1 in the hypoglossal canal, and 1 in the petrous apex. Thirty patients had gross disease at the time of SBRT. One case was treated after resection. Six patients were treated prior to SBRT among those with gross disease: five surgically and one had prior fractionated radiation. Indications for treatment were growth or symptomatic progression. Hearing loss and tinnitus were the most common reported pre-treatment symptoms. Seventeen patients (55%) reported an improvement in symptoms and 14 patients (45%) reported no worsening symptoms. The treated tumors were radiographically stable in all patients treated for gross disease, and the patient treated adjuvantly remained disease free. There was 1 grade 1 tinnitus, 1 grade 2 facial nerve palsy and 1 grade 2 nausea but no grade 3 or higher toxicities.

**Conclusion:** In this largest series to date, SBRT for benign skull base tumors resulted in excellent local control, minimal toxicity, and overall improvement in presenting symptoms. SBRT is a favorable treatment option for those who would otherwise have potentially significant cranial nerve injury following surgical resection.

**Keywords:** SBRT, benign tumors, schwannoma, paraganglioma

**Program Affiliation:** Medical Student Program Radiation Oncology Summer



Abstract Number: 53

## **Pseudoprogession After Proton Therapy of Pediatric Spinal Pilocytic Astrocytoma and Myxopapillary Ependymoma**

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**Background:** Pseudoprogession (PsP) is a post-radiation increase in tumor size with subsequent decrease in size without additional tumor-directed therapy. PsP can be clinically symptomatic and difficult to differentiate from true progession. The rate of pseudoprogession after proton therapy of pediatric spinal tumors is unknown.

**Methods:** Records of pediatric patients with spinal pilocytic astrocytoma (sPA; n = 11) or myxopapillary ependymoma (MPE; n = 10) with gross disease treated with proton therapy with at least 6 months of follow up from completion of proton therapy were retrospectively reviewed for demographics, treatment characteristics, and occurrence of pseudoprogession. Statistical comparison was performed with Fisher's exact test to obtain a two-tailed p-value.

**Results:** Twenty-one patients were analyzed. PsP was identified in 7/21 patients (33%): 6/11 sPA patients (55%) and 1/10 MPE patients (10%). PsP occurred at a median of 3.15 months (range, 2.76 – 5.44 months, standard deviation, 1.15 months) after proton therapy. Median dose for the cohort was 50.4 GyRBE (range, 39.6 – 54 GyRBE), 45 GyRBE (range, 39.6 – 50.4 GyRBE) for sPA patients and 50.4 GyRBE (range, 45 – 54 GyRBE) for MPE patients. Minimum RT dose for PsP was 41.4 GyRBE. Of patients receiving at least 41.4 GyRBE, PsP was more common in patients with sPA (6/9 = 67%) than MPE (1/10 = 10%; p < 0.02). Median age at RT for the cohort was 10.1y (range, 5.9 – 16.8y), 10.1y (range, 5.9 – 16.2y) for sPA patients and 10.65y (range, 7.2 – 16.8y) for MPE patients. Median follow up after proton therapy was 44 months (range, 9 – 99 months). Three sPA patients with pseudoprogession were symptomatic and improved with medical therapy.

**Conclusions:** Preliminary analysis suggests that PsP occurs frequently within 6 months after proton therapy for sPA and infrequently after proton therapy for MPE. Pseudoprogession rates increased above doses of 39.6 GyRBE.

**Keywords:** Proton therapy, pseudoprogession, pediatric spinal tumors, pilocytic astrocytoma, myxopapillary ependymoma

Program Affiliation: Medical Student Program Radiation Oncology Summer

## Non-Affiliated Summer Students

Abstract Number: 54

### **An Integrated Liquid Biopsy Analysis for Comprehensive Investigation of Uveal Melanoma**

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**Background:** Uveal melanoma (UM) is the most common primary intraocular tumor in adults, accounting for <5% of all melanomas. Studies reveal that approximately 50% of patients with early-stage UM will develop metastatic disease. Liquid biopsies offer a non-invasive and inexpensive method to monitor tumor-related genetic changes by examining cellular and molecular components in the peripheral circulation. Currently, there are no blood biomarkers, such as circulating tumor cells (CTCs) and cell-free DNA (cfDNA), that identify patients with UM who are at higher risk of disease relapse. The purpose of this study is to determine if the presence of CTCs and cfDNA could prognosticate an increased risk of relapse.

**Methods:** We reviewed patients presenting with UM at MDACC between December 1, 2014, and July 26, 2023, who were enrolled in IRB Protocol LAB11-0314. CTCs were identified using CellSearch™ Circulating Melanoma Cell Assay®. cfDNA was isolated from patient plasma using MagMax™ cell-free DNA Isolation Kit and quantified using the Qubit™ dsDNA HS Kit (Invitrogen™). Circulating tumor DNA (ctDNA) was sequenced using OncoPrint™ Pan-Cancer Cell-Free Assay (Thermo Fisher Scientific) and Ion Torrent™ Technology. Blood biomarkers and clinicopathological factors were examined using univariable and multivariable Cox regression modeling.

**Results:** Of the 157 patients studied, 111 had early-stage UM and 46 had metastatic UM. Based on data from relapse and non-relapse patients, a positive CTC cutoff was defined as any non-zero value and a positive cfDNA result was >3.9 ng cfDNA/mL plasma. Using an unpaired t-test to examine associations between blood biomarkers at first blood draw and disease monitoring, significant relationships were found between CTCs and relapse at both time points ( $p=0.0147$ ,  $0.009$  respectively), as well as cfDNA and relapse at both time points ( $p=0.0132$ ,  $0.0229$  respectively). However, upon combining the two biomarkers, the strongest correlation during follow-up was observed between CTCs, cfDNA, and relapse ( $p=0.0059$ ). No significant association was discovered for clinicopathological features using Cox regression modeling.

**Conclusion:** Patients with UM who tested positive on liquid biopsy (non-zero CTC count and >3.9 ng/mL cfDNA) during surveillance were more likely to experience relapse ( $p<0.01$ ). Ultimately, a comprehensive liquid biopsy approach has the potential to offer clinicians information about prognosis, treatment response, and risk stratification, opening an avenue for tailored treatment strategies and improved patient outcomes.

**Keywords:** Uveal melanoma, liquid biopsy, circulating tumor cells (CTCs), cell-free DNA (cfDNA), relapse

**Program Affiliation:** Non-Affiliated Summer Students

Abstract Number: 55

## Elucidating the Mechanistic Role of IL-1R in Late-Stage K-ras Mutant Lung Cancer: Uncovering Therapeutic Potential

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**Introduction:** K-ras mutant lung adenocarcinoma (KM-LUAD) is associated with enhanced pro-tumor inflammation mediated by the activation of the nuclear factor- $\kappa$ B (NF- $\kappa$ B) pathway and elevated expression of various cytokines including IL-1 $\beta$ . While IL-1 $\beta$  is a product of NF- $\kappa$ B, it is also its potent activator, amplifying cytokine production via a positive feedback mechanism. Thus, a deeper understanding of underlying pro-inflammatory molecular mechanisms is necessary to develop effective targeted therapies. We have shown that IL-1 $\beta$  blockade elicits an anti-tumor immune response in a mouse model of KM-LUAD driven by lung epithelial cell-specific expression of Kras<sup>G12D</sup> (CCSP<sup>Cre</sup>/LSL-Kras<sup>G12D</sup>, CC-LR). Additionally, conditionally knocking-out the interleukin-1 receptor (IL-1R), which IL-1 $\beta$  binds to, in the tumor epithelium of CC-LR mice (LR/IL-1R <sup>$\Delta/\Delta$</sup> ) at 14 weeks (early-stage KM-LUAD) showed significantly reduced tumor burden and increased inflammation. However, the precise mechanistic role of IL-1R from early- to late-stage KM-LUAD within the tumor epithelium still remains poorly understood. To address this, we investigated the impact of targeting the IL-1R receptor on tumor epithelial cells in 18-week-old mice in comparison to age-matched CC-LR counterparts.

**Methods:** Surface tumor number was counted upon dissection. To visualize microanatomy and measure tumor area, H&E staining was used. Ki-67 and ERG markers via immunohistochemical (IHC) staining allowed for the quantification of tumor cell proliferation and angiogenesis respectively. Immune cell populations in broncho alveolar lavage fluid (BALF) were measured to discern immunoinflammatory response. qPCR analysis was used to quantify gene expression for respective inflammatory pathways and immune cell subsets.

**Results:** The LR/IL-1R <sup>$\Delta/\Delta$</sup>  group showed a significant reduction in tumor area with a shift in tumor phenotype from adenocarcinoma to atypical adenomatous hyperplasia. This was supported by an increase in tumor cell proliferation and angiogenesis. BALF analysis indicated a significant decrease in neutrophils, suggesting that the immunosuppressive phenotype of the tumor epithelium was being combatted. This was reinforced by a decreased trend in *Cxcl1*, *IL-17*, and *IL-6*, known neutrophil chemo-attractants, as well as a significant decrease in *Arg1* and other myeloid cell specific immunosuppressive markers. These results support the potential mechanistic involvement of IL-1R in regulating tumor burden within the tumor microenvironment, specifically in late-stage KM-LUAD.

**Conclusion:** Our data indicates a shift in immunoinflammatory response upon late-stage knockout of IL-1R. This potentially supports targeting IL-1R for immuno-preventative therapy at the early rather than late-stage timepoint. Going forward, we would like to run a comparative study to confirm our findings.

**Keywords:** K-ras, IL-1R, IL-1 $\beta$ , NF- $\kappa$ B, immunotherapy

**Funding support:** R01 grant from NIH/NCI (R01CA225977); Lung Cancer Discovery Award from the American Lung Association (LCD821433)

Abstract Number: 56

## **Effect of Expansion and Tumor Challenge on Chemokine Receptor Expression in Cord Blood-Derived CAR-NK Cells**

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**Background:** Natural killer (NK) cells are innate lymphoid cells that have an essential function in tumor surveillance. Chimeric antigen receptor (CAR) NK-cell therapy has emerged as a promising immunotherapy for cancer. A persistent challenge, however, involves insufficient trafficking to tumor sites which is governed by chemokine and adhesion receptors/ligands expression on NK cells. The chemokine receptor profile of NK cells can be influenced by a variety of factors including expansion techniques and cytokine exposure. In this project, we analyzed the effect of expansion, cytokine exposure, and tumor interactions on the expression on CXCR3, CXCR4, and CD62L which have been shown to be very relevant to NK cell trafficking and infiltration.

**Methods:** Methods: Cord blood NK cells were either normally expanded (NE) with universal antigen presenting cells (uAPCs) or were first pre-stimulated with IL-12/IL-15/IL-18 and subsequently expanded (PE) with uAPCs. CAR-NK cells were generated by NK cell transduction using a retroviral construct encoding a CAR targeting CD70 (CAR.70) and IL-15 (CAR.70/IL-15). As controls, we used non-transduced (NT) NK cells, NK cells transduced to secrete IL-15 without a CAR (IL-15 NK) or to express a CAR.70 without IL-15 (CAR.70 NK). NK cells were cocultured with CD70+ UMRC3 kidney cancer cells. Receptor and ligand analysis were performed using flow cytometry after isolation (Day 0), transduction (Day 8), and secondary expansion (Day 15).

**Results:** Results: CXCR3 expression increased in the NE NT ( $p < 0.05$ ), PE NT ( $p < 0.001$ ), NE CAR.70/IL-15 ( $p < 0.05$ ), and PE CAR.70/IL-15 ( $p < 0.001$ ) NK cell conditions from Day 0 to 8 followed by a trend towards a decrease in expression ( $p < 0.05$  in the NE CAR.70/IL-15 condition). CD62L increased from Day 0 to 8 across all conditions - with statistical significance in the NE NT, NE IL-15, and NE CAR.70 conditions (all  $p < 0.05$ ). Interestingly, CD62L decreased back to baseline levels on Day 15. Changes in CXCR4 expression did not reach statistical significance across groups. In the tumor coculture assay, CXCR3 expression was lower in the cocultured samples while CD62L and CXCR4 did not have a discernable trend.

**Conclusion:** Conclusion: The expression of CXCR3, CXCR4 and CD62L are dynamically regulated by conditions such as expansion and coculture conditions. No differences between expansion conditions (NE and PE) were observed at the time points analyzed. We acknowledge that our study is limited by the number of biological replicates used and donor-to-donor

variability. We aim to expand the panel of chemokine receptors profiled and include more biological replicates in future experiments.

Keywords: CAR, NK cells, chemokine receptors, and adhesion ligands.

Program Affiliation: Non-Affiliated Summer Students

## Partnership for Careers in Cancer Science and Medicine Summer Program

**Abstract Number: 57**

### **Effects of AS-1763 in Combination with other Targeted Agents for Chronic Lymphocytic Leukemia**

Lizbeth Loza, McGovern Medical School, University of Texas Health Science Center at Houston; Natalia Timofeeva, Department of Experimental Therapeutics, University of Texas MD Anderson Cancer Center; Shady Tantawy, Department of Experimental Therapeutics, University of Texas MD Anderson Cancer Centers; Varsha Gandhi, Department of Experimental Therapeutics, University of Texas MD Anderson Cancer Center

**Background:** Bruton's tyrosine kinase (BTK) is an integral receptor in white blood cell signaling. BTK inhibitors disrupt the signaling promoting cancerous lymphocyte survival. Despite the effectiveness of BTK inhibitors, there is resistance with C481S mutant BTKs. AS-1763, a novel non-covalent BTK inhibitor, shows potential in targeting wild-type and mutant BTKs. We conducted experiments using AS-1763 in combination with other treatments to assess synergism and biological effects.

**Methods:** Peripheral blood mononuclear cells from 11 untreated chronic lymphocytic leukemia (CLL) patients were isolated using Ficoll-Hypaque method. Cells were treated with AS-1763, Venetoclax (BCL-2 inhibitor), AZD5991 (MCL-1 inhibitor), APR-246 (glutathione modulator), and NVP-AUY922 (HSP90 inhibitor). Cell Titer Glo 2.0 cell viability assay for the drugs alone and with AS-1763 was performed after 72 hours. Apoptosis assay using Annexin V/Propidium Iodide staining flow cytometry was done at 24 hours and 72 hours. Cellular reactive oxygen species (ROS) and mitochondrial superoxide (MitoSOX) were measured at 4 and 24 hours, respectively. GSH-Glo luminescent assay was used to measure reduced glutathione for cells treated with AS-1763, APR-246, and in combination. Western blot was performed to detect PARP, HSP90, c-MYC, BTK, p-BTK AKT, MCL-1, Caspase-3, BCL-2, BCL-XL, catalase, SOD1, thioredoxin. Vinculin, B-actin, and SM actin were loading controls. Synergy was measured using CompuSyn and Synergy Finder (ZIP, Loewe, HSA, Bliss) software.

**Results:** AS-1763 demonstrated mild cytotoxicity (IC<sub>50</sub> of 29  $\mu$ M) in Cell Titer Glo 2.0 assay and increased apoptosis in Annexin V/PI flow cytometry. CompuSyn software indicated AS-1763 had mostly synergistic effects with Venetoclax and additive effects with APR-246. Synergy Finder showed potentiation of AS-1763 (0.5-30  $\mu$ M) with low doses of Venetoclax and APR-246. AS-1763 with AZD5991 and NVP-AUY922 increased apoptosis in Annexin V/PI flow cytometry 24 hours. QVD (pan-caspase inhibitor) rescued toxicity. AS-1763 with Venetoclax and AZD5991 had mean apoptotic increases of 22.33% and 28.66%, respectively, compared to individual treatments in Annexin V/PI flow cytometry 72 hours. AS-1763 induced ROS at 1  $\mu$ M. There was a trend decrease in SOD1 protein with AS-1763 and in MCL-1 protein with AS1763 10  $\mu$ M – Venetoclax 10nM.

**Conclusion:** AS-1763 displays moderate toxicity and potentiates low doses of Venetoclax and APR-246. It increases apoptosis with AZD5991 and NVP-AUY922; QVD rescues these cells, suggesting caspase activation in the apoptosis mechanism of these treatments. AS-1763

elevates ROS and MitoSOX at 1  $\mu$ M, implying oxidative stress influence. Glutathione remained unaffected, indicating other antioxidants (SOD1) might be involved. AS-1763's decrease of SOD1 requires further investigation.

Keywords: CLL, BTK, synergism, ROS, AS-1763

Program Affiliation: Partnership for Careers in Cancer Science and Medicine Summer Program

Abstract Number: 58

### **Estimating the Burden of T-Cell Lymphoma among Hispanic and Rural Patients**

Maria Cristina Maldonado Barreno, Lymphoma & Myeloma, University of Texas MD Anderson Cancer Center; Veronica Leautaud, Lymphoma & Myeloma, University of Texas MD Anderson Cancer Center; Luis Malpica, Lymphoma & Myeloma, University of Texas MD Anderson Cancer Center

**Background:** T-Cell lymphoma is a rare cancer that arises from T-lymphocytes, a type of white blood cell essential for immune system function. Due to its infrequency, research on T-Cell lymphoma has been limited. In areas where HTLV-1 is endemic, the retrovirus HTLV-1 has been linked to specific forms of T-cell lymphomas, like Adult T- cell Leukemia/Lymphoma.

**Methods:** To investigate the frequency of T-Cell Lymphoma in the United States, we utilized data from SEER Research Plus Limited-Field Data, specifically SEER Research Plus Limited-Field Data, 22 Registries, Nov 2022 Sub (2000-2020). For the analysis, we used SEER\*Stat software, from the National Cancer Institute, which allowed us to process and examine the relevant data. We included all cases of Non-Hodgkin T-cell lymphoma in the year 2020, excluding Cutaneous T-cell lymphomas. To calculate incidence, we used SEER # cases reported for year 2020, and data from the 2020 Census results to estimate the population in the USA during the same period.

**Results:** Lymphoma affects all races/ethnicities. A lower number of cases among Hispanic patients over the last 20 years, was associated with a lower incidence rate for all T-cell lymphomas. In contrast, the incidence for ATLL appeared to be the higher for Hispanic patients when compared to non-Hispanic patients. Regardless of whether Texas counties are categorized as rural or metropolitan, our data supports a clear relationship between the number of diagnosed T-Cell Lymphoma cases and total county population. While the incidence of T-Cell Lymphoma does not appear to increase in rural regions, there is a significant number of cases among people living in rural counties (like Val Verde, Reeves, Pecos, or La Salle) This data suggests that T-Cell Lymphoma affects individuals from diverse geographic backgrounds, emphasizing the importance of considering both rural and metropolitan populations in healthcare strategies and interventions.

**Conclusion:** These findings highlight the importance of thorough cancer surveillance and research to better understand the underlying variables that contribute to T-Cell Lymphoma development. We can better understand this rare cancer and improve preventive, diagnosis, and treatment efforts by investigating potential risk factors and demographic variations. Moving forward, it is critical to continue monitoring T-Cell Lymphoma trends across different geographies and population densities in order to create focused and effective measures to combating this illness.

**Keywords:** T-Cell Lymphoma, Hispanic population, Population density, SEER

**Program Affiliation:** Partnership for Careers in Cancer Science and Medicine Summer Program



Abstract Number: 59

**CRISPR/Cas9-Mediated Genome Editing of Y705 Residue of STAT3 for Genetic Validation of Small Molecule Inhibitors In Breast Cancer Cells**

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Background: Signal transducer and activator of transcription 3 (STAT3) is involved in the regulation of cell proliferation, differentiation, and cell survival. When dysregulated, STAT3 is responsible for causing a multitude of inflammatory diseases and cancer. Constitutively activated STAT3 is present in 70% of primary tumors in humans. Studies have shown that many drugs undergoing clinical trials in oncology do not modulate their putative target and a common mechanism of action of these drugs is due to off-target toxicity. STAT3 inhibitors competitively inhibit STAT3 activation by directly targeting the pY-peptide binding site within STAT3's SH2 domain, thus blocking phosphorylation of the Y705 residue required for dimerization.

In this work we used CRISPR/Cas9 HDR method to mutate STAT3 Y705 to F705 in MDA-MB-468 breast cancer cell lines. These cell lines will be useful as genetic tools for the validation of the mechanism of action of STAT3 inhibitors including TTI-101. F705 knock-in was confirmed by sanger sequencing. Analysis by western blot and RT-PCR shows lack of STAT3 phosphorylation and transcriptional activation in Y705F mutants in response to Interleukin-6 (IL6) stimulation, respectively.

Results: CRISPR/Cas9 strategy generated stable and complete edits of tyrosine (Y) to phenylalanine (F) at position 705 of STAT3 in MDA-MB-468 cell lines, showing the inhibition of STAT3 phosphorylation and the expression of STAT3 activated genes.

Conclusion: Future work aims to design RNA-Seq experiments to compare Y705F mutants and TTI-101 treated cells, confirm its effect on proliferation, and compare this effect with C188-9/TTI101 treated cells.

Keywords: STAT3, CRISPR, IL-6, Cancer, TTI-101

Program Affiliation: Partnership for Careers in Cancer Science and Medicine Summer Program

Abstract Number: 60

### **Preclinical Testing of Metabolic Inhibitors with Erlotinib in Renal Medullary Carcinoma**

Daisha Lewis<sup>1</sup>, Dalia Karimi<sup>1</sup>, Pedro Pesquera<sup>1</sup>, Tapati Maity<sup>1</sup>, Manuel Ozambela<sup>1</sup>, Pavlos Msaouel<sup>1</sup>, Niki M. Zacharias<sup>1</sup>

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**Background:** Renal medullary carcinoma (RMC) is a rare and severe form of kidney cancer that primarily affects young Black people with sickle cell trait. RMC is frequently detected at stage IV, and the prognosis is poor, with a 13-month survival rate. RMC is currently treated using platinum-based chemotherapy, such as cisplatin. Despite this, many patients remain resistant to treatment. Recently, our lab successfully created patient-derived xenograft (PDX) models of RMC. In these models, we detected tumor growth inhibition after treatment with erlotinib, an epidermal growth factor (EGF) signaling inhibitor. We hypothesize that adding a metabolic inhibitor will improve erlotinib's efficacy in treating RMC.

**Methods:** Using patient-derived UOK360 RMC cells, we tested the individual and combined effects of EGFR inhibitor erlotinib and metabolic inhibitors AZD3965 and telaglenastat. We completed multiple drug assays on black 96-well plates. CellTiter-Glo was used to quantify ATP and indicate number of metabolically active cells following 48-hour drug assay.

**Results:** We observed a reduction in cell proliferation in RMC cells treated with erlotinib and telaglenastat individually. Significant reduction was not observed with the use of AZD3965. As well, we observed a statistically significant reduction in cell proliferation when 500 nM erlotinib was combined with 750 nM telaglenastat ( $P < 0.02$ ) compared to the single agents.

**Conclusion:** These results demonstrate that metabolic inhibitor compound, telaglenastat, as well as EGFR inhibitor, erlotinib, are effective agents for cell proliferation reduction in RMC. As well, their effect is enhanced when combined; however, more research is needed.

**Keywords:** RMC, Drug Assay, Erlotinib, Telaglenastat

**Program Affiliation:** Partnership for Careers in Cancer Science and Medicine Summer Program

Abstract Number: 61

### **Beta-Catenin Transcription is essential for Müllerian Duct Regression**

Evelyn Carrion, Genetics, University of Saint Thomas; Rachel Mullen, Genetics, University of Texas MD Anderson Cancer Center; Richard Behringer, Genetics, University of Texas MD Anderson Cancer Center

**Background:** This study investigates the role of beta-catenin in Müllerian duct regression during male differentiation. Beta-catenin has two distinct activities: cell adhesion and transcription. In the presence of Wnt glycoproteins, beta-catenin can translocate from the cytoplasm to the nucleus where it can bind with BCL9 and other co-activators to regulate the transcription of specific target genes. For its adhesion function, beta-catenin binds to alpha-catenin that interacts with the actin cytoskeleton. Beta-catenin also binds to E-cadherin through its armadillo repeats. Cadherins span the plasma membrane and are part of the adherens junctions that mediate adhesion between cells. In a previous study, beta-catenin was deleted in the Müllerian ducts of male mouse fetuses, resulting in a block to Müllerian duct regression and the development of a uterus (Kobayashi et al., 2011). In the current study, I analyzed male mice who have a beta-catenin double mutation (DM) that results in the loss of transcriptional activity but retention of adhesion function.

**Methods:** Using morphological, histological, and immunofluorescence analyses

**Results:** I found that these male DM mutants do not regress the Müllerian ducts, resulting in the formation of a uterus.

**Conclusion:** These studies suggest that the transcriptional activity of beta-catenin is required for Müllerian duct regression during male development.

**Keywords:** Müllerian duct, Beta-catenin, Wnt glycoproteins, BCL9, and alpha-catenin

**Program Affiliation:** Partnership for Careers in Cancer Science and Medicine Summer Program

Abstract Number: 62

## **Hypoxia inducible factor 1a in kidney cancer**

Dalia Karimi<sup>1</sup>, Daisha Lewis<sup>1</sup>, Niki Zacharias Millward<sup>1</sup>, Pedro Pasquera<sup>1</sup>, Tapati Maity<sup>1</sup>, Nasir Uddin<sup>2</sup>, Pavlos Masaouel<sup>1</sup>, Steve Millward<sup>2</sup>

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**Background:** Renal cell carcinoma (RCC), which accounts for approximately 90 percent of kidney cancers, encompasses more than 10 different cancer subtypes. Hypoxia and hypoxia inducible factor (HIF) signaling are dominant drivers in clear cell RCC (ccRCC) and renal medullary carcinoma (RMC). Approximately 90% of ccRCC tumors bear inactivating mutations in the von Hippel-Lindau (VHL) gene, which codes for the VHL protein. In ccRCC, inactivating mutations in VHL lead to accumulation of HIF1 $\alpha$  and HIF2 $\alpha$ . My project is to monitor HIF1 $\alpha$  signaling in ccRCC and RMC and determine if HIF1 $\alpha$  inhibition will lead to reduction in cell proliferation in ccRCC and RMC cell lines.

**Methods:** Experiment 1: Bioluminescence of kidney cancer cells transfected with HIF1 $\alpha$  signaling vector Luciferin dissolved in phosphate buffer was added to 6-well plates (25  $\mu$ l per well) and incubated for 10 minutes prior to imaging. Bioluminescence was imaged used an IVIS Imager. Experiment 2: Validating HIF signaling We tested 4 siRNAs against HIF1 $\alpha$  in RCC4 – VHL cells. We labeled the siRNAs A, B, C, and D. We also ran a Western blot illustrating the reduction of HIF1 $\alpha$  expression with siRNAs against HIF1 $\alpha$ . Experiment 3: Soft agar colony assay We made three 6 well plates (plate 1: DMSO and media, media only. Plate 2: cells treated with PT2399. Plate 3: cells treated with PX-478). Mixed 8 ml of 2x media with 2 ml of FBS (20%), and 5 ml of 3% agarose solution to get 1% agarose solution. Added 2 ml per well. Then added 6.5 ml of normal DMEM media with glutamine and 400,000 cells and put 1 ml in each well. Lastly Added 1.5 ml of media with drug and changed twice a week. After 18 days, removed media and added iodonitrotetrazolium chloride (0.1%), waited 48 hours and took the image.

**Results:** We observed 60% reduction in bioluminescence 48 hours after siRNA D is added to the media compared to the transfection reagent alone. Unfortunately, we were not able to visualize a large number of colonies even on control plates (media and DMSO).

**Conclusion:** We were able to generate transfected cell lines that express luciferase and GFP when HIF1 $\alpha$  is expressed and illustrate that luciferase activity was dependent on HIF1 $\alpha$  expression using siRNA D knockdown. We are still in the process of determining if HIF1 $\alpha$  inhibition reduces cell proliferation in soft agar colony assay and optimizing the number of cells to use in the assay.

**Keywords:** HIF1 $\alpha$ , siRNA, Luciferase, Soft agar colony

**Program Affiliation:** Partnership for Careers in Cancer Science and Medicine Summer Program

Abstract Number: 63

**Prospective Study Evaluating Management of Hypertension Induced by anti-VEGF Therapy in Patients with Active Cancer: VEGFHTN Trial**

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**Background:** Anti-neoplastic agents that target vascular endothelial growth factor (VEGF) signaling are used to treat many cancers, but they are known to have cardiovascular toxicities, primarily hypertension. A novel blood pressure (BP) scoring system that incorporates both antihypertensive medication usage and blood pressure values has been shown to correlate with cancer progression. We describe changes in the novel BP scoring method in patients with an antihypertensive algorithmic approach to managing anti-VEGF therapy-induced hypertension.

**Methods:** A single-center prospective cohort of patients with cancer starting anti-VEGF therapy was used. Interval blood pressure data was collected, and antihypertensive medications were started per a standardized anti-VEGF therapy hypertension treatment algorithm. The novel BP scoring system was calculated for all patients and a subgroup analysis of patients with 4-month BP follow-up was performed. Survival analysis with Kaplan-Meier curves and log-rank tests were used to compare overall mortality.

**Results:** There were 153 patients included in the study with the average age being  $61.2 \pm 11.6$  years and majority male (52%). A majority of patients had pre-existing hypertension (65%) and the most common malignancies were renal cell carcinoma (21%) and hepatocellular carcinoma (18%). A majority of patients developed hypertension after anti-VEGF therapy (89%) and 88 patients had a 4-month BP follow up visit. No statistically significant changes were observed in systolic or diastolic BP between follow up timepoints. However, in the 4 month follow up cohort the novel BP score increased from  $1.84 \pm 1.60$  to  $3.35 \pm 1.63$  ( $p < 0.0001$ ). Additionally, overall survival was improved for patients with increases of 1 or 2 in the novel BP compared to those who had increases  $\geq 3$  or those without increases ( $p = 0.0271$ ).

**Conclusion:** A considerable proportion of patients receiving anti-VEGF therapy will develop hypertension. Although there was no statistically significant difference for systolic or diastolic blood pressures after starting anti-VEGF therapy, there was an increase in the novel BP score driven by rapid initiation and uptitration of antihypertensive medication. Patients in the 1- or 2-point increase in novel BP score were found to have improved overall survival.

**Keywords:** Prospective, Anti-VEGF therapies, Hypertension

**Program Affiliation:** Partnership for Careers in Cancer Science and Medicine Summer Program

Abstract Number: 64

**Modulation of de novo lipogenesis to sensitize castration-resistant prostate cancer cells to next-generation antiandrogens via ferroptosis.**

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**Background:** Despite next-generation antiandrogens, drug resistance in castration-resistant prostate cancer (CRPC) inevitably develops. To fulfill a need for increased fatty acids required in proliferation, cancer cells can either increase their uptake of circulating lipids, transfer Fatty Acids (FAs) from adipocytes to prostate cancer cells, or simply increase de novo synthesis of FAs. Androgen Receptor (AR) activates the sterol regulatory element binding proteins (SREBP) to regulate key lipid metabolic genes that endogenously synthesize lipids and control lipid transport. De novo lipogenesis generates monounsaturated fatty acids (MUFAs) that are poor substrates for lipid peroxidation and as such can suppress ferroptosis by reducing the amount of lipid peroxides available for ferroptosis. Ferroptosis is a form of cell death that results from the overwhelming iron-dependent accumulation of lethal amounts of ROS.

**Methods:** CRISPR/Cas9 was used to create ATGL KO cells that would be treated with the SREBP inhibitor Fatostatin, FASN inhibitors C75 Trans and TVB3166, and GPX4 inhibitor RSL3. Resazurin assay was used to measure cell viability following various treatment conditions. The quantity of resorufin produced is proportional to the number of viable cells.

**Results:** ATGL KO cells exhibited a synergistic effect when treated with AR inhibitor Enzalutamide and ferroptosis inducer RSL3. ATGL KO cells exhibited higher cell death with AR inhibition. Wildtype ATGL reverses the sensitivity to Enza and RSL3, and S47A+ATGL KO cells did not die as much as ATGL KO cells. No statistically significant response was observed against the control. ATGL KO and control cells were treated with SREBP inhibitor Fatostatin, and FASN inhibitor C75 Trans. There was no statistically significant response observed when ATGL KO and control cells were treated with a combination of SREBP inhibitor, FASN inhibitor TVB3166, FASN inhibitor C75 Trans, and ferroptosis inducer RSL3.

**Conclusion:** My data do not support the hypothesis that inhibiting SREBP or FASN increases cells' sensitivity to ferroptosis. However, ATGL KO appears to sensitize prostate cancer cells to TVB-3166, albeit in an RSL3-independent manner. It is possible that we did not use enough RSL3 concentration to induce ferroptosis. Other regulators of de novo lipogenesis such as SCD1 and ACC should be investigated.

**Keywords:** De-novo lipogenesis, prostate cancer

**Program Affiliation:** Partnership for Careers in Cancer Science and Medicine Summer Program

Abstract Number: 65

## **Examining the Benefits of Distributing HPV Self-Collection Kits in Hispanic and African American Communities**

Habibatou Diallo, Department of Health Disparities Research, The University of Texas- MD Anderson Cancer Center; Surendranath Shastri, Department of Health Disparities Research, The University of Texas MD Anderson Cancer Center; Alicia Palao, Department of Health Disparities Research, The University of Texas- MD Anderson Cancer Center

**Background:** Human papillomavirus (HPV) is a common sexually transmitted infection that usually appears on the human body as warts and is known to cause several cancers. HPV leads to development of cancer by infecting cells and causing miscommunication between them, eventually resulting in uncontrolled cell growth. Of the cancers HPV can cause, the most prominent is cervical cancer, as 9/10 cases are caused by HPV, making the prevention of HPV through the HPV vaccine of much importance to cervical cancer research. Starting at age 21, women are recommended to go in for routine pap smears, during which cells are removed from the surface of the cervix and observed for signs of abnormality. In Texas, Hispanic and African American women have the highest cervical cancer incidence and mortality rates. Despite this, there are still large numbers of women in both of these populations that do not go in for routine cervical cancer screenings due to lack of access to reliable transportation, lack of knowledge on the importance of screening, and various language and cultural barriers. Considering the benefits of screenings in regards to cervical cancer prevention, there has been interest in exploring alternative options to traditional screening methods, such as HPV self-collection kits.

**Methods:** African American and Hispanic women who fit the necessary requirements were recruited from two public housing developments in Houston. Participants were provided instruction on how to use the self-collection kits before being given a kit at the end of their visit. Two follow-up calls were made to ensure that participants were completing the self-collection and mailing the completed kits back. Four weeks after recruitment, participants were required to attend a follow-up visit in person during which participants with a positive result will be referred to a diagnostic facility. All data is entered and analyzed through RedCap, a web-based data collection tool.

**Results:** Of the 68 African American women and 47 Hispanic women contacted, 40 were deemed eligible and given the self-collection kit. As of July 31, 25 women have completed and mailed the test back with 23 women performing the test correctly. 13 African American women and 10 Hispanic women have completed the study.

**Conclusion:** Process of recruitment, carrying out self-collection, and returning for follow-up is well understood by the majority of participants, proving feasibility of normalizing the use of HPV self-collection kits.

**Keywords:** HPV, Cervical Cancer, HPV self-collection kit, Project Self

**Program Affiliation:** Partnership for Careers in Cancer Science and Medicine Summer Program

Abstract Number: 66

## **Investigating the Function of Arginine Methylation at Two Mutated Sites of CBP by CARM1**

Nicole Dawson, Epigenetics and Molecular Carcinogenesis, Carleton College; Jee Won Hwang, Epigenetics and Molecular Carcinogenesis, University of Texas MD Anderson Cancer Center; Margarida Albuquerque Almeida Santos, Epigenetics and Molecular Carcinogenesis, University of Texas MD Anderson Cancer Center

**Background:** CARM1 is a Co-activator Associated Arginine Methyltransferase 1 (CARM1). Arginine Methyltransferase are proteins that transfer a methyl group (CH<sub>3</sub>) onto an Arginine amino acid and is an important mechanism for turning “on” or “off” a gene for transcription processes across cell divisions. CARM1 was found to regulate transcription in CBP. CBP is the CREB Binding Protein, a long protein encoded in the CREBBP gene. This is a co-activator necessary for activation of transcription and is associated with many proteins. Specifically, we have noticed that mutations in the genes that code for these proteins are more frequent in DLBCLs or Diffuse Large B Cell Lymphoma; are mutually exclusive. CARM1 methylates arginine residues in CBP in 2 of 5 domains of the gene, IBiD and KIX. In this study we will be investigating the function of arginine methylation at two mutated sites of the IBiD domain of the CBP gene by CARM1 (RKA and RKB). This is crucial for understanding DLBCLs since genetic mutations in these genes are its characteristic.

**Methods:** We first proceeded with a standard cell culture procedure on U2OS, Osteosarcoma, cell lines. We did Transfection with U2OS, Co-Immunoprecipitation (Co-IP) and lastly performed a standard western Blot multiple times showing interactions between CARM1, NFIBme2a (known to be methylated by CARM1) and the generated mutations. We did site-directed mutagenesis to synthesize a Double RK (2RK) mutants and did E. Coli transformation with a competent cell. To make sure our plasmid integrated with DNA, we cloned for lentiviral plasmid, generating two hybrid plasmids. We then used comp. cell to do transformation, spread well on agar plates of Ampicillin and waited for colonies to emerge.

**Results:** First Co-IP Western Blot showed inconclusive evidence between CARM1 and RKA mutation. We repeated after the successful 2RK mutagenesis. We have contradictory results showing CARM1 interaction was weak within mutations but the Co-IP Western Blot with NFIBme2a was strong. Lastly, after checking the lentiviral plasmid colonies, we were not able to proceed with the Mini-prep to obtain DNA because there was an issue with the ampicillin powder used in the agar plate.

**Conclusion:** There seems to be active methylation by CARM1 at the two mutant sites in the CBP-IBiD domain. We will do more experiments in the future to check for interactions and protein stability, as well as repeating the lentiviral plasmid cloning. This could lead to more knowledge about mutations and their consequences in DLBCLs.

**Keywords:** DLBCLs, Mutations, CARM1, CBP

**Program Affiliation:** Partnership for Careers in Cancer Science and Medicine Summer Program



Abstract Number: 67

## **Allostatic Load Markers as Predictors of Melanoma Outcomes**

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**Background:** Melanoma, an aggressive form of skin cancer, presents varied outcomes contingent on multiple factors. One such factor, allostatic load, represents the physiological burden on the body stemming from chronic stress. Accumulating evidence suggests allostatic load, gauged through various physiological parameters, may have implications for cancer progression and outcomes. This study explores allostatic load and outcomes for advanced disease melanoma patients who received immunotherapy.

**Methods:** Using Epic healthcare software, we analyzed data from 141 melanoma patients who underwent wide local excision. Patients were categorized into early adjuvant treatment (67 patients) and late adjuvant-palliative immunotherapy (74 patients). Data accuracy was ensured by cross-verifying MRNs and birth dates, leading to the exclusion of 10 patients for various discrepancies. Our analysis focused on 66 MRNs from the late immunotherapy group due to the unavailability of recurrence data for the early group. Allostatic load was assessed using physiological parameters and lab markers, with each factor assigned a binary code (1 or 0). The Allostatic Load Score (ALS) was calculated for each MRN, categorizing patients into "High" or "Low" allostatic load groups. Kaplan-Meier curves for time-to-progression and overall survival were generated based on these categorizations.

**Results:** In our study, the low allostatic load group (score: 0-2) had an average age of 62.14, with a gender distribution of 29 males and 14 females, and a mean BMI of 25.56. Contrastingly, the high allostatic load group (score: 3-5) registered an average age of 69.94, with 14 males, 8 females, and an average BMI of 26.38. Regarding progression-free survival, the low group reported 79.8%, 61.2%, and 45.3% at 1, 3, and 5 years, while the high group exhibited 67.4%, 56.1%, and 56.1%. Overall survival for the low group was 90.9%, 72.7%, and 0.0% respectively, whereas the high group marked 86.1%, 69.6%, and 69.6% across the same intervals.

**Conclusion:** Upon analyzing the Kaplan-Meier curves for progression-free survival and overall survival, we identified no significant association between allostatic load score and survival outcomes. Importantly, our analysis was based on 66 patients from the original cohort of 141, exclusively from the late immunotherapy group. This was due to challenges in procuring recurrence data for the early immunotherapy group (67 individuals) and accurate immunotherapy commencement dates for three patients from the late group. This limitation in sample size may have influenced the study's findings.

**Keywords:** Allostatic load, melanoma

**Program Affiliation:** Partnership for Careers in Cancer Science and Medicine Summer Program

Abstract Number: 68

## **Investigating Copy Number Alterations and Mutational Signatures in Ultra Rare CNS Tumors**

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**Background:** Mutational signatures provide invaluable insights into the intricate genetic alterations driving distinct cancer types, shedding light on the interplay between intrinsic and extrinsic factors that govern disease evolution. Copy number alterations, involving changes in genomic copy numbers relative to the normal diploid state, play a pivotal role in this context. By examining copy number signatures, we gain a deeper comprehension of the underlying processes, potential preventive strategies, and the identification of clinical biomarkers. While previous research has predominantly focused on mutational signatures in prevalent cancers like breast and lung cancer, investigating mutational signatures in exceedingly rare brain tumors presents captivating inquiries. Exploring mutational signatures in ultra-rare central nervous system (CNS) tumors holds the key to unearthing vital insights that could pave the way for targeted clinical treatments tailored to these unique tumor types. By unlocking new therapeutic avenues, this research carries profound implications for the clinical management of rare brain tumors.

**Methods:** Mutect2 was used to first identify somatic mutations in each tumor type: chordoma, skull base chondrosarcoma, ganglioglioma, and metastatic hemangiopericytoma. These files were used as the input to identify mutational signatures using two different algorithms: SigProfilerAssignment and Signal. Signal was able to identify single base substitutions (SBS) signatures for each tumor type. SigProfilerAssignment is more diverse and identifies single-base substitutions, double-base substitutions, indels, and copy number mutational signatures. To analyze copy number alterations in each of the tumors, PURPLE files were analyzed, and we identified gene drivers that have copy number changes that deviate from the normal.

**Results:** In general, many driver genes are involved in copy number changes in all the tumor types in this investigation. For example, MDM2 is a driver gene with a driver likelihood of over 0.99 and showed a copy number gain in comparison with the rest of the gene location. Copy number signatures showed how chromothripsis and focal loss of heterozygosity are potential processes that can explain copy number alterations in these tumors. The mutational signatures identified by both algorithms exhibited partial discrepancies and did not align completely.

**Conclusion:** Our study revealed that there is limited applicability of SigProfiler and Signal for identifying mutational signatures in rare tumor cases since they are more often used in more common cancers. Further explorations involving multiple samples of the same tumor type would facilitate a more comprehensive comprehension of the mutational signatures inherent in these rare tumors.

**Keywords:** Copy number alterations, Mutational signatures, Rare tumors

**Program Affiliation:** Partnership for Careers in Cancer Science and Medicine Summer Program

Abstract Number: 69

### **Upregulation of the oncometabolic IDO/AhR pathway during viroimmunotherapy**

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**Background:** Glioblastoma is an aggressive brain cancer that carries a poor prognosis, with a median overall survival of 15 months. For the past 20 years, standard treatment involving surgery, radiotherapy, and temozolomide, has failed to eradicate these tumors. Oncolytic viroimmunotherapy offers an innovative approach by selectively killing tumor cells and eliciting an anti-tumor response. Our laboratory has developed and translated into the clinic an oncolytic adenovirus, Delta-24-RGD, with encouraging results. In clinical trials in adult and pediatric malignant gliomas, prolonged survival was observed in 20% of patients. Our laboratory is currently investigating mechanisms of resistance to virotherapy to improve the response of patients with gliomas to this type of therapy. One of the pathways involved in promoting an immunosuppressive microenvironment is the tryptophan pathway. Specifically, AhR is activated through the kynurenine (Kyn) pathway, where an enzyme indoleamine 2,3-dioxygenase 1 (IDO1) catalyzes the breakdown of tryptophan (Trp) into Kyn. In this study, we aim to further analyze the role of this metabolic pathway in the resistance to viroimmunotherapy.

**Methods:** We have analyzed changes in the tumoral transcriptomes using bulk RNAseq of murine glioma tumors infected with Delta-24-RGDOX. Subcellular localization of AhR after viral infection was assessed by immunofluorescence. The AhR transcriptional activity was analyzed using AhR reporter cells expressing a luciferase reporter gene functionally linked to an AhR-responsive promoter. This was corroborated by performing Q-PCR to quantify the levels of expression of AhR targets, such as CYP1A1, CYP1B1, and AhRR, in glioma and immune cells.

**Results:** Bulk RNAseq of murine glioma tumors showed that treatment with Delta-24-RGDOX induced increased levels of the IDO/AhR pathway. We aim to confirm the activity of this pathway by studying the downstream player, AhR. Of interest, immunofluorescence staining of AhR showed that after viral infection, AhR localized into the nucleus. These data were further confirmed by the detection of increased levels of several targets of AhR, such as CYP1A1, CYP1B1, AHRR, after viral infection.

**Conclusion:** Our data demonstrates that the infection of glioma cells and immune cells with Delta-24-RGDOX results in the activation of the tryptophan metabolic pathway, which is involved in promoting tumoral immunosuppression. These results suggest that the combination of oncolytic adenoviruses with AhR inhibitors might result in better outcomes for patients with brain tumors.

**Keywords:** oncolytic virus, immunotherapy, IDO, AhR, kynurenine

**Program Affiliation:** Partnership for Careers in Cancer Science and Medicine Summer Program

Abstract Number: 70

### **Utilizing CD24 as an indicator for tumor aggressiveness and metastasis**

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**Background:** CD24 is a multifaceted membrane protein that plays crucial roles in cell adhesion, migration, and various biological processes, including B-cell development and neurogenesis. In the context of cancer, heightened CD24 expression has been associated with oncogenic signaling and immune system evasion, making it a subject of great interest in cancer research. Notably, CD24's role in breast cancer has been highlighted, specifically in facilitating cell movement within the bloodstream, resulting in increased invasiveness to distant sites. However, intriguingly, high CD24 expression does not uniformly promote metastasis and tumor progression across different tumor histology, emphasizing the complexity of CD24's effects on tumors.

**Methods:** We collected data on human breast primary cancer sites that had metastasized to the brain using Immunofluorescence at 30x magnification. Polyclonal CD24 antibodies were used to stain the CD24 protein on the cell membrane. Additionally, we employed flow cytometry on four cell lines and Western blotting to analyze CD24 protein expression. Moreover, we differentiated monocytes to produce BMDM and conducted a phagocytosis assay by co-culturing macrophages with 4T1 and CT2A cancer cells. These techniques allowed us to gain comprehensive insights into the molecular characteristics and interactions of metastatic breast cancer cells within the brain microenvironment and the potential role of CD24 in the metastatic process.

**Results:** In this study, we investigated CD24 expression in paired human breast primary tumors and brain metastatic tumors. Immunofluorescence imaging revealed a distinct pattern of heightened CD24 expression on cell membranes in both types of tumors, suggesting a potential role of CD24 in the metastatic process. Additionally, we examined several murine breast cancer cell lines, with the aggressive 4T1 and 4T1 BR4 lines exhibiting the highest CD24 expression levels. Furthermore, we demonstrated that these cell lines were more susceptible to phagocytosis when treated with an anti-CD24 antibody, indicating the potential for immune recognition and clearance of CD24-expressing cancer cells.

**Conclusion:** In conclusion, our study uncovers the enigmatic nature of CD24's effects on tumors, particularly in breast cancer metastasis, and presents CD24 as a potential immunotherapeutic target. The findings provide a foundation for further investigation into the molecular mechanisms underlying CD24's role in cancer progression and the development of targeted therapies to combat metastatic breast cancer.

**Keywords:** CD24, Phagocytosis, Metastasis, Breast Cancer

**Program Affiliation:** Partnership for Careers in Cancer Science and Medicine Summer Program

Abstract Number: 71

## **Cancer immunotherapy based on MUSIC platform and STING activation in brain cancer cells**

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**Background:** To develop a new effective cancer immunotherapy that was developed by the MD Anderson Cancer Center researchers of Dr. Kim and Dr. Jiang's lab. They have pioneered the MUSIC strategy that targets efficient immune activation and maximizes antitumour effects. This platform uses nanocomplex-conjugated microbubbles that specifically target antigen-presenting cells (APCs) to effectively deliver cGAMP into their cytosol, facilitated by ultrasound which then activates the STING pathway. This innovative use of immunotherapy allows STING activation with cGAMP which then efficiently primes the antigen-specific T cells in primary tumors. While the MUSIC platform has been successful in breast cancer, there is an interest in demonstrating the versatility of the MUSIC platform with other cancer types, specifically brain cancer.

**Methods:** IVIS images: To monitor the progression of the tumor in the mice, we used IVIS imaging and luciferin. The IVIS images of the mice's heads were used to detect luminescence signals in the brain. MUSIC treatment: Four different groups of mice were treated: 1) cGAS (cGAMP only), 2) Empty microbubbles with ultrasound, 3) MUSIC (cGAMP filled microbubbles with ultrasound), 4) no treatment (only injected tumour). Five mice in each group which were a) anesthetized with isoflurane, b) then injected with 5  $\mu$ L of treatment near the bolt, and one group was treated with ultrasound. Lastly, the incisions made onto the mice are closed.

**Immunofluorescence staining:** We stained four sets of slides that were controlled, treated with cGAMP and MUSIC. We baked slides in 60°C incubator for 30 mins, then deparaffinized with xylene, washed with ethanol, and blocked with 10%-goat serum+90%-TBST+2%-BSA+0.3%-Triton x100. After adding the blocking buffer, incubate for 2 hours. Primary antibody solutions PSTING and PIRF3 (1-200  $\mu$ L dilution) were added to incubate overnight in the dark at 4°C. After washing the primary solution, secondary antibody Alexa Fluor 546 (1-2000  $\mu$ L dilution) was added then incubated in room temp for 1 hour. After adding DAPI stain (1-1000  $\mu$ L dilution), incubate for 8 mins at room temp. After adding autoquench solution (1-20  $\mu$ L dilution), incubate for 2 mins. We used these two antibodies and DAPI to image signals of either PSTING or PIRF3 being activated.

**Results:** Confocal fluorescence microscopy images of four total (2 in each) control and MUSIC groups in PSTING and PIRF3.

**Conclusion:** Based on the results, the cGAMP MUSIC treatment was effective. In the confocal images, we can see higher fluorescence intensity and activation in PSTING and PIRF3. We hypothesize the MUSIC treatment is effective in brain cancer since MUSIC can effectively enhance STING activation in APCs, leading to improved priming of T cell responses.

**Keywords:** cGAMP, nanocomplex-conjugated microbubbles (ncMBs), microbubble-assisted ultrasound-guided immunotherapy of cancer (MUSIC), Stimulator of Interferon Genes (STING), PIRF3 (phospho-IRF3)

**Program Affiliation:** Partnership for Careers in Cancer Science and Medicine Summer Program

Abstract Number: 72

## **Exploring the Effect of Cabozantinib on Osteolysis in Renal Cell Carcinoma Bone Metastasis**

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**Background:** Renal Cell Carcinoma (RCC) affects 85% of kidney cancer patients, with up to 40% developing bone metastases that are usually osteolytic. Bones undergo constant remodeling, a balanced process involving bone formation by osteoblasts and bone resorption by osteoclasts. In RCC, this process becomes dysregulated, leading to osteolysis, which is very painful and leads to impaired mobility. Cabozantinib, a tyrosine kinase inhibitor, has shown effectiveness in reducing bone metastasis progression in RCC by targeting tumor angiogenesis. However, its specific effects on osteolysis are unknown. Our project is aimed at modeling and analyzing osteolysis in RCC and exploring the effect of cabozantinib on osteolysis.

**Methods:** Eight-week old BALB/c mice were intratibially injected with renal adenocarcinoma cells (RENCA) lacking the von Hippel Lindau (VHL) gene and expressing both green fluorescence protein (GFP) and luciferase (LUC). Seven days later they were randomized into two groups: vehicle (control) and cabozantinib (treated; 40 mg/kg of cabozantinib oral gavage daily). After 12 days, tibias were extracted and fixed in 4% paraformaldehyde (PFA) overnight then microcomputed tomography ( $\mu$ CT) was used for 3D imaging. Tibias were decalcified, sliced to 300  $\mu$ m, stained for four markers (DAPI, endomucin, alkaline phosphatase, and tartrate-resistant acid phosphatase (TRAP)) and imaged using confocal microscopy. In the second model, eight-week-old severe combined immunodeficiency (SCID) mice were injected with GFP and LUC-expressing 786-O cells following the identical protocol. Tibia slices were stained for TRAP activity using the TAKARA staining kit and visualized using EVOS microscope.

**Results:** Cabozantinib treatment significantly reduced tumor growth, stabilizing bioluminescence signaling (an indicator of lesion growth) for ten days, while lack of treatment increased tumor growth and bioluminescence signaling. Cabozantinib treatment showed increased osteoclast number compared to the control. Slices without the tumor displayed red staining, indicative of TRAP activity, around the trabecular bone. The untreated group had the highest TRAP activity, with red staining lining a channel created by the tumor. Cabozantinib-treatment led to the lowest TRAP activity, with little-to-no red staining around the trabecular bone. Preliminary  $\mu$ CT analysis showed a trend with the control having less trabecular bone and lower bone volume fraction compared to cabozantinib-treated bones. We are increasing sample sizes for the bones for future experiments.

**Conclusion:** Cabozantinib appears to reduce osteoclast activity and osteolysis in RCC bone metastasis, evidenced by decreased TRAP activation and bone degradation, combined with increased trabecular thickness, cortical thickness, and bone surface area.

**Keywords:** Renal Cell Carcinoma, Bone metastasis, Osteolysis, Cabozantinib, TRAP

**Program Affiliation:** Partnership for Careers in Cancer Science and Medicine Summer Program

Abstract Number: 73

## **Purification and Biochemical Characterization of DNA Mismatch Repair (MMR) Proteins WRN and RPA**

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**Background:** DNA mismatch repair (MMR) is a DNA repair pathway that maintains genomic stability during DNA replication. When MMR is deficient, DNA damage can alter the length of microsatellite repeats which results in microsatellite instability (MSI). Colorectal, endometrial, and gastric cancers often exhibit the MSI-high (MSI-H) phenotype and become resistant to therapy. Thus, it is important to find new targets, or new therapies to overcome these challenges. Werner helicase (WRN) is an ATP-dependent helicase plays a role in DNA repair, replication, and telomere maintenance. Studies have shown a synthetic lethal interaction of WRN in MSI-H cell lines, so evaluating this protein as a possible target in MSI-H cancer is of interest. WRN is involved in DNA metabolism processes like stabilization of stalled replication forks. This stabilization allows DNA replication to proceed and cell proliferation to occur. In MSI-H cells, the dMMR system is impaired making cells dependent upon WRN. Inhibiting WRN leads to replication fork destabilization causing increased double stranded breaks, cell cycle arrest, and apoptosis. WRN's helicase activity is enhanced in the presence of RPA, a heterotrimeric single-stranded DNA binding protein also involved in genome stability processes. We expressed recombinant human WRN and RPA, purified these proteins and investigated their enzymatic activity. The goal was to express WRN and RPA to make a complex and study the enzymatic activity of these proteins. If the proteins are active, they can be use in other assays to investigate potential new treatments.

**Methods:** Transformation: a plasmid with the recombinant protein was introduced into competent cells. Growth: The cells were cultured in nutrient-rich media and once the optimal cell density was reached, it was induced to express the protein. The cells were lysed, sonicated, and centrifuged to remove cellular debris. Purification: WRN and RPA were purified with affinity, size exclusion, and ion exchange

**Results:** Human WRN is difficult to express in E. coli, but insect cells were found to be the optimal expression system. RPA purification from E. coli cells was successful. Full length WRN and RPA showed good enzymatic activity, and WRN had higher activity in the presence of RPA.

**Conclusion:** Although human WRN is a protein difficult to express and purify, the enzymatic results indicate that we can produce both recombinant WRN and RPA in insect cells and E. coli, thereby enabling structural biology and assay development for new therapies.

**Keywords:** WRN, RPA, recombinant protein, expression

**Program Affiliation:** Partnership for Careers in Cancer Science and Medicine Summer Program

Abstract Number: 74

## **Evaluating the Effects of a Tobacco-Free Workplace Program on Provider Beliefs about Guest/Client Tobacco Use and Self-Efficacy to Intervene at Texas Homeless-Serving Agencies during COVID-19**

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**Background:** Cigarette smoking, a known cause of cancers, is elevated among people experiencing homelessness, with a prevalence of ~78%. There is considerable interest in quitting smoking in this group; however, agencies that serve them rarely provide evidence-based tobacco screening and intervention. Barriers to care provision include inaccurate provider beliefs that their clients are not concerned about quitting smoking, and lack of knowledge on how to address tobacco dependence. Consequently, it is critical to implement comprehensive tobacco-free workplace programs (TFWPs) that include provider training in settings where people experiencing homelessness receive services. One such TFWP has been implemented in homeless-serving agencies pre-COVID-19, yielding significant increases in providers' capacity to address tobacco use. Here, we extended the TFWP to new agencies, examining its effects on providers' beliefs about their guests'/clients' smoking and knowledge about evidence-based cessation interventions during COVID-19.

**Methods:** From 2021-2023, the TFWP was implemented in 3 homeless-serving agencies serving 1,355 adults annually across 3 Texas counties. Providers at each agency completed anonymous surveys at pre- (N=9) and post-implementation (N=6) where they rated their agreement with 5 items (e.g., "My guests/clients are concerned about smoking"; "I have the required skills to help my guests/clients quit smoking"; etc.) on a 5-point Likert scale ranging from 1=strongly disagree to 5=strongly agree. Logistic regression analyses were used to measure changes in key variables over time, controlling for agency.

**Results:** Analyses demonstrated increases in providers' beliefs about guest/client concerns about smoking (11.11% to 50.00%), beliefs guests/clients who smoke want to quit smoking (0.00% to 50.00%), and beliefs they have the skills to help guests/clients quit smoking (33.33% to 66.67%); however, increases were not statistically significant (ps range=0.9084-0.9480). Variables related to whether guests/clients follow provider advice (55.56% to 33.33%) and referral knowledge for guests/clients to receive cessation care (55.56% to 50.00%) decreased, but not significantly (ps range=0.4203-0.9914).

**Conclusion:** In this expansion study, TFWP implementation led to some desirable changes in provider beliefs about smoking among their guests/clients; the lack of significant findings may be due to small sample sizes, low statistical power, and observed COVID-19 challenges to agency capacity-building. Results may reflect the need for enhanced agency engagement in provider training (i.e., Motivational Interviewing, tobacco treatment specialist) to increase skills addressing tobacco dependence; only 1 agency participated in these opportunities. Future studies should include more agencies/providers, considering program adaptations to



accommodate competing priorities that may arise (e.g., COVID-19) that can disrupt TFWP investment and participation.

Keywords: Tobacco, Homeless, Smoking, Policy, Implementation

Program Affiliation: Partnership for Careers in Cancer Science and Medicine Summer Program

Abstract Number: 75

### **Understanding Virally Induced NK Cell Memory: HLAs as a Potential Mechanism**

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**Background:** Glioblastoma brain tumors and pancreatic tumors have a dismal prognosis, with life expectancies of less than a year. Despite constant innovation, current treatment options can only delay the effects of these aggressive cancers. Natural Killer (NK) cells are effective at killing these solid tumors in the innate immune system. However, they are deficient at breaking into the tumor microenvironment. So, oncolytic viruses (OVs) such as the Delta-24-RGD adenovirus are genetically engineered to penetrate this microenvironment and help kill tumors. Combination immunotherapy of NK cells and OVs presents a promising treatment option against solid tumors. Preliminary data shows that when NK cells are trained using tumors infected with OVs, they gain a “memory-like effect” increasing the NK cells’ ability to kill tumors. My research aims to understand the mechanism behind this memory. We hypothesize that the viral infection increases the interaction between Human Leukocyte Antigens (HLAs), immune regulating cell surface proteins expressed on the tumor cells, and Killer Immunoglobulin Receptors (KIRs), which activate/inhibit NK cell activity. HLAs-A/B/C bind to inhibiting receptors on NK cells, while HLA-F has been shown to bind to the activating receptor KIR3DS1 on NK cells.

**Methods:** Perform flow cytometry on virally infected glioblastoma and pancreatic cancer and control (non-infected) cells using fluorescent HLA antibodies to understand how viral infection regulates HLA expression. Train NK cells using tumor cells that have HLA-F/ABC knocked out and rechallenge the NK cells to kill fresh tumor cells to understand whether HLAs F/ABC are crucial in NK cell memory.

**Results:** Flow cytometry data shows that from the control to the infected PATC148 (pancreatic tumor cells) and GSC8-11 (glioblastoma stem cell), infected tumors had a significantly lower MFI (mean fluorescence index) for HLA-ABC and significantly higher MFI for HLA-F compared to the control tumor cells.

**Conclusion:** Viral infection of tumor cells upregulates HLA-F and downregulates HLAs-ABC. This aligns with our expectations, as HLA-F may activate NK memory, while HLAs-ABC may inhibit NK memory. The NK training/rechallenge experiment for HLA KO cancer cells is ongoing. Results showing a difference in killing ability between NK cells trained in virally infected HLA-F/ABC KO tumor cells and NK cells trained in non-KO virally infected tumor cells (control) would indicate HLAs as being crucial in NK-induced cell memory.

**Keywords:** Natural Killer Cell, Oncolytic Virus, Human Leukocyte Antigen, Glioblastoma, Pancreatic tumor

**Program Affiliation:** Partnership for Careers in Cancer Science and Medicine Summer Program

Abstract Number: 76

## **The Role of SGK1-NDRG1 Axis in Inflammatory Breast Cancer Stem Cells**

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**Background:** Inflammatory breast cancer (IBC) is a rare form of breast cancer, accounting for only 2%-4% of cases but contributing to a disproportionately high percentage (10%) of breast cancer-related deaths. IBC has one of the lowest 5-year survival rates of all breast cancers, therefore, more specific and more effective treatments are desperately needed for these patients. Our recent studies demonstrated the correlation of N-myc downstream regulated gene 1 (NDRG1) with poor outcome in IBC patients. Additionally, we demonstrated that NDRG1 promotes cancer stem cells, tumor progression, and brain metastasis in preclinical models of IBC. Discovering which molecules regulate NDRG1 is important because it has the potential to reveal new modalities of treatments. We hypothesize that targeting the Serum and Glucocorticoid-Regulated Kinase 1 (SGK1), a direct upstream activator of NDRG1, effectively inhibits the expression of NDRG1 and phospho-NDRG1 and reduces IBC aggressiveness via inhibition of cancer stem cells.

**Methods:** We treated the IBC cell line SUM149 using varying concentrations (ranging from 0.00025 nM to 25  $\mu$ M) of the SGK1 inhibitor, GSK650394, over 72h to determine the dose necessary to reduce cell viability by 50% (IC50). Based on the IC50, we examined the effects of the inhibitor on NDRG1 and phospho-NDRG1 inhibition in SUM149 cells by using doses ranging from 125 nM to 30  $\mu$ M for 1h. Western blot analysis was conducted to examine the most effective dose in reducing SGK1 and its downstream target, phospho-NDRG1 and total NDRG1 expression. Subsequently, cells were treated with the identified most effective doses for 1 hour followed by flow cytometry to examine the breast cancer stem cell population using the CD44+/CD24- cell surface markers.

**Results:** The IC50 for GSK650394 in SUM149 cells was 1.02  $\mu$ M. Concentrations of 10  $\mu$ M and 30  $\mu$ M of GSK650394 inhibited SGK1, phosphorylation of NDRG1, and total NDRG1. However, treatment of SUM149 cells with GSK650394 for 1h did not significantly reduce the percentage of CD44+/CD24- cancer stem cell population.

**Conclusion:** Treatment with GSK650394 resulted in a reduction of NDRG1 phosphorylation, indicating its impact on SGK1's downstream target. However, the inhibitor did not significantly reduce cancer stem cells. Further investigation is warranted to determine the specific effects of GSK650394 on cancer stem cells, including identifying the optimal dose and duration of treatment in IBC cells.

**Keywords:** Inflammatory breast cancer, NDRG1, Cancer stem cell, SGK1

**Program Affiliation:** Partnership for Careers in Cancer Science and Medicine Summer Program

## Summer Imaging Research Program

Abstract Number: 77

### **Maximum NI-RADS Primary Score as Predictor of Pathologic Recurrence in Oropharyngeal Squamous Cell Carcinoma Treated with Definitive Radiation Therapy**

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**Background:** The Head and Neck Imaging Reporting and Data System (NI-RADS) surveillance template for head and neck cancer includes a numeric assessment of suspicion for recurrence (1– 4) for the primary site. Category 1 indicates no evidence of recurrence; category 2, low suspicion of recurrence; category 3, high suspicion of recurrence; and category 4, known recurrence. Our purpose was to evaluate the population performance of the NI-RADS scoring system to predict pathologic disease recurrence.

**Methods:** This study was classified as a quality-improvement project by the institutional review board. A retrospective database search yielded 629 OPSCC cases treated with definitive radiation interpreted using the NI-RADS template. Cases without non-squamous cell carcinoma primary tumors and primary squamous cell carcinoma outside the head and neck were excluded. The electronic medical record was reviewed to determine the subsequent development of pathology proven recurrence. Patients without NIRAD scored reports had reports scored via trained NLP algorithm.

**Results:** A total of 5652 scans in 629 targets met the inclusion criteria. Among the 629 patients, 71% were max NI-RADS 1; 7% were max NI-RADS 2; and 22% were max NI-RADS 3+. 96 patients had pathologically proven recurrence. The rates of recurrence were 11.5%, 18.2%, and 26.7% for each NI-RADS category, respectively. Max NIRADS score demonstrated a strong association between the score and ultimate disease recurrence, with  $P = .005$ .

**Conclusion:** The population performance of NI-RADS was good, demonstrating significant discrimination among the categories 1–3 for predicting disease. This methodology could be useful in comparative population analysis.

**Keywords:** NI-RADS, oropharyngeal squamous cell carcinoma, surveillance, pathological recurrence

**Program Affiliation:** Summer Imaging Research Program

Abstract Number: 78

## **Comparison of 18 and 20-Gauge Ultrasound-Guided Fine-Needle Aspiration in Detecting Persistent Nodal Disease after Chemoradiation**

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**Background:** Viable malignant disease is uncommon in patients with persistent adenopathy after chemoradiotherapy (CRT) for head & neck squamous cell carcinoma (HNSCC). Preoperative ultrasound-guided fine needle aspiration (USFNA) can prevent unnecessary salvage neck dissection. Post-radiation fibrosis can complicate the approach, resulting in an inadequate aspirate volume when using standard 20 or 22-gauge needles. We assessed the comparative 18 and 20-gauge diagnostic accuracy of USFNA in detecting persistent viable nodal malignancy in patients with HNSCC with nodal metastasis treated with CRT.

**Methods:** We identified a 209-patient cohort (193 male, 60.4±9.8 y) presenting between 2002-2023 with HNSCC and biopsy-proven cervical nodal metastases, all treated with CRT. After CRT, a suspicious nodal remnant underwent biopsy with an 18 or 20-gauge needle: 71 patients received biopsy with a 20-gauge; 138 received a biopsy with a 18-gauge. Biopsy results were compared to post-biopsy surgical (sx) pathology results or at least 3 months of CT or PET follow-up (f/u).

**Results:** FNA in 167/209 (79.9%) cases showed no viable metastatic disease on cytology evaluation. 20-gauge cases were performed with 1.36±0.51 passes. 18-gauge cases were performed with 1.08±0.27 passes (p=0.03). Neck dissection was performed within 90 days in 38 patients. Between FNA and sx pathology, 18/24 cases were positive concordant (PC) and 14/14 cases were negative concordant (NC), with the overall concordance being 32/38 (84.2%). Between FNA and imaging f/u, 152/153 cases without surgery were NC and 17/18 cases without surgery were PC, with the overall concordance being 169/171 (98.8%). Overall FNA showed PC of 35/42, NC of 166/167, sensitivity of 97.2%, specificity of 95.9%, accuracy of 96.2%, PPV of 83.3%, and NPV of 99.4%. 20-gauge FNA showed PC of 21/23, NC of 46/48, sensitivity of 91.3%, specificity of 95.83%, accuracy of 94.4%, PPV of 91.3%, and NPV of 95.8%. 18-gauge FNA showed PC of 14/19, NC of 118/119, sensitivity of 93.3%, specificity of 95.9%, accuracy of 95.7%, PPV of 73.7%, and NPV of 99.2%.

**Conclusion:** Residual cervical lymph node FNA after CRT is an accurate procedure with small performance differences between 18 and 20-gauge needles. Although the PPV was lower for 18-gauge needles, the biopsies were performed with a lower number of passes for satisfactory cytopathological acceptance.

**Keywords:** head & neck squamous cell carcinoma (HNSCC), ultrasound-guided fine needle aspiration (USFNA), 18-gauge needle, 20-gauge needle

**Program Affiliation:** Summer Imaging Research Program

Abstract Number: 79

## **Deep Learning for Automatic Detection and Segmentation from CT Angiography of Deep Inferior Epigastric Vascular Structures for Preoperative Planning of TRAM Flap Surgeries**

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**Background:** Breast reconstruction helps to improve self-appearance and quality of life for breast cancer patients after mastectomy. Reconstruction can be either implant-based or autologous tissue-based, with the latter approach offering several advantages, including a more natural appearance and lifetime durability. Among the different types of tissue-based reconstruction, the free TRAM flap offers the best final cosmesis. However, careful preoperative mapping of the relevant vascular structures is needed because this type of reconstruction is accountable for approximately 30% of vascular complications [1]. The objective of this study was to develop and validate a deep learning method that can automatically detect and segment the vascular structures (focusing on the deep inferior epigastric arteries (DIEA) and dominant subcutaneous branches or perforators) to potentially aid preoperative planning of TRAM flap surgeries.

**Methods:** From the institutional radiology database, patients who had CT angiography (CTA) TRAM exam at MD Anderson Cancer Center between 01/01/2005 through to 07/31/2018 were identified. The CTA images were transferred to a MIM workstation (Maestro 7.2.5, MIM Software Inc., Cleveland, OH). For 100 consecutive CTA exams, the DIEA and dominant perforator vessels were manually segmented. 68/100 contoured CTA images were used to train nnU-Net, a self-configuring deep-learning segmentation method, 17/100 contoured CTA images were used for validation, and the remaining 15/100 contoured CTA images were reserved for independent testing with nnU-Net generated images. nnU-Net produced 5 configurations: 2D U-Net, 3D low resolution U-Net, 3D full resolution U-Net, 3D cascade, and ensemble [2]. The performance of the trained model was assessed by comparing Dice similarity coefficients between manual contours, which were considered the ground truth, and nnU-Net generated configurations with 15 independent testing sets of CTA images.

**Results:** The mean and standard deviation of Dice are 70.33%±8.63% for 2D U-Net, 37.88%±7.72% for 3D low resolution U-Net, 71.96%±8.16% for 3D full resolution U-Net, 72.31%±8.28% for 3D cascade, and 72.28%±8.20% for ensemble. A statistical analysis demonstrated similar performances between 2D, 3D full resolution, 3D cascade, and ensemble ( $p < .0001$ ). 3D low resolution performed significantly worse than the other four methods.

**Conclusion:** In this pilot project, our preliminary results suggest that the model can accurately identify and segment the DIEA vessels. Additional work with a larger sample size is needed to verify that this algorithm can reliably automate the detection of the vessels of interest and their associated perforators as well as the mapping of the location of these vessels.

**Keywords:** TRAM flap surgery, deep learning, breast reconstruction, vasculature, nnU-Net

**Program Affiliation:** Summer Imaging Research Program

## Summer Program in Cancer Research

Abstract Number: 80

### **Investigating the Effect of Wwox Deletion on Canonical NF-kB Pathway using Mouse Embryonic Fibroblasts**

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**Background:** The WWOX gene was originally discovered as a putative tumor suppressor associated with progression, therapy resistance, and poor disease outcomes in multiple cancer types. In more recent studies, WWOX has been recognized for its role in a much wider array of human pathologies including metabolic conditions and central nervous system (CNS) related disorders. Evidence from studies in cancer and various inflammatory pathologies strongly suggest that WWOX regulates inflammation and direct associations between WWOX and the NF-kB and IL-6/JAK2/STAT3 inflammation signaling pathways have been demonstrated. WWOX has been shown to physically bind ERK and IκBa complex and prevents IκBa from proteasomal degradation, which is necessary for canonical NF-kB pathway activation. We hypothesize that Wwox deficiency may lead to IκBa proteasomal degradation and subsequent NF-kB pathway activation triggering an inflammatory response.

**Methods:** We generated mouse embryonic fibroblasts (MEFs) from Wwox-WT (n=2) and Wwox-KO mice (n=2). MEFs were treated with 100 ng/ml Lipopolysaccharide (LPS). Activation and degradation of different components of NF-kB pathway was measured by western blot analysis along with activation of target inflammatory cytokines and enzymes by qRT-PCR.

**Results:** Both WT and KO cell lines showed an initial immune response to LPS with increased pNF-kB protein at 15 min, however, in the KO cells pNF-kB protein levels remained high at 60 and 120 min, in comparison to WTs where the levels decreased over time. Consequently, Wwox deletion in KO cells lead to increased expression of proinflammatory cytokines (Il-1b, Tnf-a, Il-6) and enzymes (iNos and Cox2).

**Conclusion:** WWOX deficiency appears to play a role in modulating NF-kB pathway activation and lead to a notable increase in pro-inflammatory cytokines and enzymes. Our findings provide a potential mechanism by which WWOX loss of function leads to inflammatory response in diseased conditions.

**Keywords:** WWOX, NF-kB pathway, inflammation, pro-inflammatory cytokines

**Program Affiliation:** Summer Program in Cancer Research

Abstract Number: 81

### **Mammalian Surface Antigens Display (mSAD): To Test the Efficiency of Surface Binding Recombinant Monoclonal Antibodies**

Ariq Rabee<sup>1</sup>, Somnath Paul<sup>1</sup>, Joshua B Plummer<sup>1</sup>, Alexandra L Hebertson<sup>1</sup>, Kevin McBride<sup>1</sup>

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**Background:** B-Cells are a type of white blood cell that produces antibodies against unique biomolecules called antigens. Antigens can be pathogen- or host-derived, ranging from proteins like cancer-associated antigens to bacterial metabolites. The recombinant antibody production core (RAPC) can harvest antibody sequences from the host immune response, fabricate and purify these antibodies, and test their functionality. Functional screening of these specific antibodies can help determine their potential for providing a protective response against diseases as seen in the case of immunotherapeutic drugs. My project involved developing a tool to screen surface-binding antibodies that can help to enhance immunotherapies in cancer patients and a pipeline with surface-associated antigens that can determine the utility and/or potency of tumor-derived antibodies.

**Methods:** For establishing the pipeline, we worked with two known antigens (FLAG & GFP) genetically engineered into plasmids having either the transmembrane protein domain of CD138 or a truncated form of the transferrin receptor (TrTfR) such that the antigens are expressed and presented on the surface of host cells (HEK293). Using flow cytometry, microscopy, and immunoblotting we determined the expression and co-localization of the antigens.

**Results:** The expression of transfected plasmids was determined using an intracellular GFP signal. Flow cytometry analysis showed almost equal signal intensity for FLAG and GFP, using their respective antibodies. Further analysis of the cells using fluorescence microscopy revealed the colocalization of the GFP and FLAG antigens on the surface of the cells. Additionally, we performed immunoblotting to assess the protein expression using total lysates of the transfected cells.

**Conclusion:** We found that with the use of transmembrane epitopes, desired antigens can be placed on the surface and tracked using antibodies. Because GFP lost its tertiary structure extracellularly, it was detected using an anti-GFP antibody. For establishing the pipeline, GFP was used to demonstrate the targeting of foreign antigens, while FLAG was used as a reporter for expression. This pipeline will accelerate the assessment of antigen: antibody reactivity in the future, specifically for surface-binding antibodies such as human therapeutic candidates.

**Keywords:** Surface antigen, Surface-binding antibodies, Research and innovation, Recombinant antibodies

**Program Affiliation:** Summer Program in Cancer Research



Abstract Number: 82

## **Identifying Candidate Genes for Verification of the scPASU Pipeline**

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**Background:** Polyadenylation (poly(A)) is the addition of adenine to mRNA after transcription. Alternative cleavage and polyadenylation (APA) is the usage of different poly(A) sites to generate different mRNA and protein isoforms. This is regulated by DNA methylation and the recruitment of mRNA and DNA binding proteins. Current APA analysis is very general and is not cell specific, generating a need for single-cell analysis of poly(A) sites. Thus, the single cell poly(A) site usage (scPASU) pipeline was created to repurpose scRNA-seq data to observe poly(A) site usage. To validate the pipeline's findings experimentally, filters need to be generated for APA candidates to be tested by RNA FISH.

**Methods:** In this workflow, filters were created to find candidate genes that met three criteria. This was repeated for each differential gene comparison produced by the scPASU pipeline to develop a table of gene candidates.

**Results:** A list of candidate genes for each group of cell-to-cell comparisons was generated for FISH visualization.

**Conclusion:** Generating probes for RNA FISH requires specific parameters for the probes to fluoresce desired targets correctly. By filtering out genes from differential gene comparisons, the candidate genes we identified for each cell-to-cell comparison can be used in developing probes for experimental verification of the scPASU pipeline.

**Keywords:** APA, polyadenylation, DNA methylation

**Program Affiliation:** Summer Program in Cancer Research

# Summer Undergraduate Research Program

Abstract Number: 83

## **Synthesis of Prodrug Moieties for Inhibition of Tumor Glycolysis in ENO1-Deleted Hepatocellular Carcinoma**

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**Background:** Inhibition of tumor glycolysis is considered one of the most promising new techniques in stopping the spread of cancer because of its ability to cut off cancer cells' pathways of providing energy for growth and metastasis. The penultimate step of the aerobic glycolytic pathway involves the enolase enzyme, which is encoded for on the 1p36 tumor suppressor locus by two genes: ENO1 and ENO2. In certain glioblastomas, specifically in liver cancer, it has been shown that there are homozygous deletions of ENO1, making these tumor cells extremely vulnerable to inhibition of the ENO2 gene. The prodrug HEX, a phosphoramidite derivative, has been previously synthesized and shown to inhibit glycolysis as a substrate-competitive enolase inhibitor. However, due to the anionic nature of HEX at physiological pH, it faces considerable difficulty with membrane permeability. The focus of this work is to explore different synthetic routes of attaching prodrug moieties to the active sites of HEX to create a stable, membrane-permeable prodrug that can have its prodrug moieties cleaved in the presence of carboxylesterases concentrated in the liver.

**Methods:** Large non-polar chain moieties with nucleophilic terminal regions were synthesized to be used in coupling reactions using Mitsunobu conditions or the formation of phosphoramidite acid chloride to attach these moieties in high yield with minimal byproduct. All reactions to attach the prodrug moieties were conducted under argon (dry conditions) to avoid hydrolysis cleavage of the intermediates. Final products were purified using a combination of organic-aqueous separations, high performance liquid chromatography (HPLC), and automated flash chromatography, before subsequent characterization using Liquid Chromatography Mass Spectroscopy (LCMS) and <sup>1</sup>H or <sup>31</sup>P Nuclear Magnetic Resonance (NMR).

**Results:** The prodrug moieties could be synthesized in high yield, and in this experiment the attachment of a thioester alcohol and an amine group were investigated as possible candidates for improved membrane permeability. Attachment of the amine was possible in high yield, however with the previously defined conditions there was no evidence that suggests successful attachment of the thioester alcohol to the phosphoramidite derivative of HEX.

**Conclusion:** This work contributes to the current body of knowledge surrounding phosphoramidite chemistry and provides an outline for the synthesis of prodrug moieties and their subsequent attachment to active sites on prodrugs. There is still more to be known about why these nucleophilic terminal regions of the thioester alcohol and amide were unable to successfully attach to the phosphoramidite region of HEX and efforts in the future should be devoted to investigating this phenomenon.

**Keywords:** Phosphoramidite, prodrug, moiety, LCMS, HPLC

**Program Affiliation:** Summer Undergraduate Research Program

Abstract Number: 84

## **A First in Class Study to Determine if Melanoma Organoid Can Replace its in vivo Tumor Model for Evaluating Targeted Therapies**

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**Background:** Melanoma is a skin cancer with a low incidence yet high mortality rate. Despite progress with targeted therapies, the need to identify drugs that can treat melanoma and overcome resistance is still imperative. To work towards this goal, the development of new, inexpensive, and accurate models to test drug efficacy is necessary. This study evaluates the ability of melanoma tumor organoids to replace animal studies for testing drug responses and molecular features.

**Methods:** To understand the usefulness of tumor organoids as surrogates for animal studies, their growth over time and alterations in key protein markers were used to evaluate their response to targeted therapies in two 2D cell cultures (grown in RPMI media or PDXo differentiation media), 3D organoids (grown in PDXo media), and patient derived xenografts (grown in mice). The growth studies were conducted using a standard CellTiterBlue assay for 2D cultures, a novel AI optimized imaging analysis for 3D organoids, and standard tumor measurements for PDXs respectively. In all four growth conditions, the efficacy of three treatments was evaluated: the standard of care Dabrafenib+Trametenib, and two experimental therapies for melanoma, Pelcitoclax (BCL2 inhibitor), and Talazoparib (PARP inhibitor). The molecular differences between the different growth conditions and their drug treatments were evaluated by western blotting.

**Results:** Organoids had similar drug induced growth response as in vivo tumors for the standard of care Dab+Tram and the experimental Pelcitoclax. However, organoids were not representative of in vivo response to Talazoparib. Examination of Phospho- $\beta$ -Catenin and Phospho-MAPK proteins in pre-treatment control samples showed a decrease in organoid and tumor samples compared to 2D cultures suggesting an increase in WNT differentiation signaling and decrease in MAPK proliferation signaling. PARylation was detected only in the in vivo growth conditions suggesting elevated PARP activity, which may explain the significant difference in response to Talazoparib by in vivo tumors only. Examination of post-treatment protein levels showed a decrease of Phospho- $\beta$ -Catenin in 2D epithelial growth conditions (RPMI) compared to 2D mesenchymal growth conditions (PDXo), organoid and in vivo tumors, for all drug treatments. P-MAPK levels decrease with Dab+Tram treatment for all groups, most potently in the 2D cultures. P-MAPK alteration did not follow a specific trend with Pelcitoclax and Talazoparib treatments.

**Conclusion:** Melanoma organoid models are effective surrogates of in vivo tumors for evaluating Dab+Tram, did not reach significance for Pelcitoclax, and are not effective for Talazoparib.

**Keywords:** Tumor organoids, Melanoma, targeted therapy, surrogate model

**Program Affiliation:** Summer Undergraduate Research Program

Abstract Number: 85

## **Electrospun Bioresorbable Polymer Blends as Vascular Grafts**

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**Background:** Vascular bypass procedures typically employ autologous tissue from healthy vessels. However, many patients lack viable tissue for this procedure. Polymeric prosthetic grafts (i.e., Dacron) may be utilized in large-caliber vessels but can still induce stenosis and thrombosis. We hypothesize that including alternative biocompatible and hydrophilic polymers in polymer grafts can increase patency and recruitment of vascular endothelial cells.

**Methods:** Selected polymer blends—PCL (polycaprolactone), PCL:PEG (polyethylene glycol), PCL:PLGA (poly lactic-co-glycolic acid), and PCL:PLA (polylactic acid)—were dissolved in 3:1 ratios and electrospun at 15 kV to yield polymeric grafts. Graft-incubated media was used to test hemolysis and cytotoxicity against RF24 or MOVAS cells. The proliferation of RF24 or MOVAS cells on the scaffolds were also determined at 4, 24, 48, and 96 hours. Samples were also placed in an in vitro pump system to simulate the in vivo degradation of the grafts under constant pulsatile flow. At 2-week intervals, maximum stress and modulus of elasticity were measured using an MTest Quattro machine (ADMET, Shirley, NY). For the in vivo assay, a scaffold of each type was grafted onto the abdominal aorta of Sprague-Dawley rats. A 5th control rat had their abdominal aorta cut and sutured back together. After 4 weeks, rats were sacrificed, and the scaffolds were removed and imaged for analysis.

**Results:** All polymer combinations were shown to be non-hemolytic and non-cytotoxic. Additionally, PCL, PCL-PEG, and PCL-PLA all showed comparable values of porosity, while PCL-PLGA showed a significantly lowered porosity value. We also found that while PCL-PEG had one of the lowest maximum stresses, it was on par with PCL-PLGA with having a lower modulus of elasticity. In our cell proliferation assay, PCL-PEG demonstrated the greatest amount of proliferation at the end of the 96 hours for both RF24 cells and MOVAS cells. Finally, after analysis of our in vivo samples, we found both PCL and PCL-PLGA scaffolds induced significant stenosis of the vessel. PCL-PEG demonstrated proper cell layers and an inner endothelial monolayer and PCL-PLA also had a developing vessel with appropriate cell layers, but it had some interruptions in its endothelial monolayer with a little narrowing of the vessel.

**Conclusion:** PCL-PEG is the most ideal polymer combination to continue testing against for vascular graft synthesis and the inclusion of a biocompatible hydrophilic polymer enhanced polymer grafts' ability recruit cells for vascular reconstruction with a decreased incidence of stenosis and thrombosis.

**Keywords:** Polymer, Vascular graft, Electrospin

**Program Affiliation:** Summer Undergraduate Research Program

Abstract Number: 86

**Generation of MLE-15 IRF9 knockdown cells for studying the antimicrobial role of TLRs agonist-induced lung epithelium's reactive oxygen species**

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Background: Viral and bacterial pneumonias remain prominent global health threats. The Evans Laboratory previously showed that immunomodulation via inhalation of synergistic agents Pam2CSK4 ("Pam2," a TLR2/6 ligand) and ODN M362 ("ODN," a TLR9 ligand), together "Pam2ODN," broadly protects mice against lower respiratory tract infections by lung epithelial reactive oxygen species (ROS)-mediated pathogen killing. Current efforts focus on understanding the mechanism underlying this Pam2ODN-induced ROS. The Interferon-Stimulated Gene Factor 3 (ISGF3) transcription factor complex—composed of STAT1, STAT2, and IRF9—drives a DUOX2-induced ROS antiviral immune response through its non-canonical STAT2/IRF9-dependent pathway. Previous microarray data reported the upregulation of IRF9 by Pam2ODN and highlighted the requirement of Pam2ODN-induced Duox2 and ROS to protect mice against infection. Our examination of IRF9, STAT1, and STAT2 gene regulation using small interfering RNA (siRNA) showed a significant decrease in Duox2 expression with the siRNA IRF9 and STAT2, but saw normal Duox2 with siRNA STAT1, alluding to the hypothesis that IRF9 and STAT2 are likely required for DUOX2 expression and ROS production.

Methods: To evaluate the relationship between IRF9 and Duox2, we apply molecular biology techniques to generate a stable IRF9 knockdown MLE-15 cell line for study. Bacterial transformation using competent *E. coli* cells was used to clone IRF9 and insert the DNA sequence into a vector backbone. Extracted DNA was used in lentiviral transfection with 293T cells; viral media was collected and used to infect MLE-15 cells to complete IRF9 knockdown. Green fluorescent protein (GFP) expression was measured to confirm the knockdown of IRF9 in the MLE-15 line.

Results: GFP-positive MLE-15 cells were sorted and expanded following viral infection. The expression of GFP in MLE-15 cells alludes to successful IRF9 lentiviral infection and creation of an IRF9 knockdown.

Conclusion: The IRF9 knockdown is critical for evaluating the relationship between IRF9 and Duox2, as well as other ISGF3-induced genes, as the line offers RNA stability not provided by the siRNA IRF9. Use of the knockdown will be used in further molecular biology and immunology experiments including qPCR, blotting, and microarrays to explore the driving relationship between IRF9 and DUOX2 expression.

Keywords: pneumonia, IRF9, DUOX2

Program Affiliation: Summer Undergraduate Research Program

Abstract Number: 87

## **Fucosylation Enhances Activity of Chimeric Antigen Receptor T-cells Against Lung Cancer**

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**Background:** One of the major hurdles of adoptive chimeric antigen receptor (CAR)-T cell therapy is the scant infiltration of CAR-T cells and adoptively transferred T cells into tumors. Without the homing of T-cells to tissue, the immune system is unable to fully elicit an immune response and combat the growth of cancerous tissue. This is a major deterrent to cancer adoptive cellular therapy (ACT). However, through fucosylation, a process whereby fucosyltransferases (FTs) add fucose groups to cell surface glycoproteins, this challenge may be overcome, particularly in the context of non-small cell lung cancer (NSCLC). Fucosylated (CAR)-T cells were shown to preferentially home to inflamed tissues. Here we show a novel approach to enhance homing to NSCLC tumors.

**Methods:** Using the enzyme FT-VII, we fucosylated CAR-T cells that target epidermal growth factor receptor (EGFR), which is highly expressed in NSCLC. We performed in vitro homing and migration assays, as well as cytotoxicity assays to study the effects of fucosylation on EGFR-CAR-T cell homing and target killing. We used in vivo mouse models to demonstrate the effects of ex vivo fucosylation on EGFR-CAR-T cell anti-tumor activities against NSCLC.

**Results:** Our data show that fucosylation increases in vitro migration, homing and cytotoxicity of antigen specific CAR-T cells. Furthermore, fucosylation enhances in vivo CAR-T homing to lung cancer tissue in NOD/SCID gamma (NSG) and immunocompetent mice, ultimately boosting the anti-tumor activity of the antigen-specific CAR-T cells.

**Conclusion:** Together, our data establish ex vivo fucosylation of EGFR-CAR-T cells as a novel approach to improving the efficacy of ACT, which may be of great value for the future of ACT for cancer.

**Keywords:** Immunotherapy, T cells, Lung Cancer, Fucosylation

**Program Affiliation:** Summer Undergraduate Research Program

Abstract Number: 88

### **Characterization of Mouse MS4a4a and MS4a6a Antibodies**

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**Background:** Single nucleotide polymorphisms (SNPs) within the membrane-spanning 4-domains subfamily A (MS4A) gene locus are linked with protection from Alzheimer's Disease (AD) risk, delayed age-at-onset, and reduced expression of MS4A4A and MS4A6A in myeloid cells. MS4A4A and MS4A6A are exclusively expressed by microglia, myeloid cells in the brain. Microglia have been shown to play a critical role in AD pathogenesis, with several AD-associated risk genes being microglial. In addition to the MS4A proteins, triggering receptor expressed on myeloid cells 2 (TREM2) is a genetically validated AD target and there have been associations between MS4A4A and TREM2. Tools to investigate the pathophysiological role of MS4A4A and MS4A6A in AD are lacking, and targeting these proteins with small-molecule drugs has proven difficult. Our overarching goal is to develop functional antibodies targeting MS4A4A and MS4A6A to induce a protective microglial phenotype in humans. The aim of this study is to develop mouse-specific antibodies, which can then be used to obtain in vivo data before progressing the human therapeutics into the clinic.

**Methods:** Monoclonal antibodies were developed using hybridoma technology. Hybridoma supernatants were screened for cell surface binding by flow cytometry using cell lines overexpressing either Ms4a4a or Ms4a6d. Clones recognizing the native protein were selected for antibody production. BMDMs (bone marrow-derived macrophages) were treated with purified antibodies. Soluble TREM2 (sTREM2) levels and ATP content were measured by ELISA and CTG assay, respectively. 6-month-old non-transgenic (nTg) and transgenic (Tg) 5xFAD microglia were stained with mouse antibodies to measure levels of Ms4a4a and Ms4a6d by flow cytometry. Wild-type mice were dosed once a week (4x) with either Ms4a4a or Ms4a6d antibody. Mouse plasma sTREM2 levels were measured by ELISA.

**Results:** Purified antibodies from Ms4a4a hybridoma clones showed binding to Ms4a4a-GFP-positive cells. Purified antibodies from Ms4a6d hybridoma clones showed binding to Ms4a6d-mCherry-positive cells. BMDMs treated with these promising antibody clones showed increased sTREM2 levels and improved cellular health. Ms4a4a and Ms4a6d expression increased in microglia of transgenic mice. Plasma sTREM2 levels increased in mice dosed with Ms4a4a or Ms4a6d antibodies.

**Conclusion:** Antibodies targeting Ms4a4a and Ms4a6d specifically bind the proteins of interest and show functional effects in vitro. Further in vivo characterization is required, including increasing concentrations of antibodies to ensure sufficient brain exposure.

**Keywords:** Alzheimer's Disease, MS4A, TREM2

**Program Affiliation:** Summer Undergraduate Research Program

Abstract Number: 89

### **Establishing a Novel Murine Model for Dysphagia**

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**Background:** Oropharyngeal squamous cell carcinoma (OPSCC) is one of the most common types of head and neck cancer. Treatment for OPSCC includes surgery, radiotherapy, chemotherapy or a combination of therapies. Despite the advancement of treatment, functional impairment is still a major burden in patients with OPSCC.

**Methods:** Neuronal modulation: antibody conjugated with saporin. Implanted OPSCC tumor cells. Radiation treatment: 24 Gy in 3 consecutive doses. Behavioral analysis: using Lickometer. Data analysis: using JMP pro15 and p value of < 0.05 considered statistically significant. Three experimental groups were included, and animals were randomly allocated. The ages range between 4–6-weeks and the c57BL/6J strain was used.

**Results:** Cholinergic (Chat) and nociceptive neurons (CGRP) play a significant role in swallowing outcomes. Post radiation swallowing dysfunctions could be minimized by the ablation of chat and CGRP in the tumor microenvironment (TME) of OPSCC. Radiation treatment impairs swallowing functions suggesting that there are other components of the TME, besides chat and CGRP, that may play a crucial role in swallowing outcomes in OPSCC.

**Conclusion:** The enrichment of Chat and CGRP in the OPSCC TME could possibly lead to long-term swallowing impairment. Despite the effects of CGRP ablation on improving swallowing function, Chat ablation improves posttreatment swallowing outcomes in OPSCC treated with radiation more significantly. Targeting Chat and CGRP in the TME of OPSCC could be a novel strategy for patients with post-treatment swallowing dysfunction. This study establishes a novel murine OPSCC model that merits further investigation in order to explore the roles of nerves in posttreatment swallowing impairment.

**Keywords:** OPSCC, Dysphagia, Neuromodulation, Cholinergic, Nociceptive

**Program Affiliation:** Summer Undergraduate Research Program



Abstract Number: 90

## **Enhancing the Design and Consistency of an $\alpha$ -particle Irradiator for In Vitro Experiments**

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**Background:** Radiation therapy utilizes different forms of radiation with varying effects on DNA within cells, depending on their linear energy transfer (LET). High-LET  $\alpha$ -particles (70-200 keV/ $\mu$ m) are effective in inducing clustered DNA lesions, resulting in higher cell kill and immunostimulatory effects. However, delivering  $\alpha$ -particles to the entire solid tumor volume through conventional brachytherapy is challenging due to their limited range (<90  $\mu$ m in water). Diffusing  $\alpha$ -Emitters Radiation Therapy (DaRT) overcomes this challenge by using interstitial cylindrical seeds coated with radium-224 (Ra-224), which extends  $\alpha$ -particles' range by utilizing a unique decay chain, including radon-220. This allows  $\alpha$ -particles to deposit doses over 2-3 mm from the seed.

**Methods:** In 2D cultures, achieving consistent dosimetry with DaRT is difficult due to the geometry of the seeds, causing a rapid dose rate decline. To address this issue, a specialized  $\alpha$ -particle irradiator was designed, utilizing an Americium-241 (Am-241) source to provide controlled and predictable exposure. To achieve controlled shutter movement, a high-performance solenoid was employed and activated using an Arduino Uno micro-controller. The Arduino IDE Code was used to define pins and interface with the motor driver and motor, allowing for precise motor control operations.

**Results:** The implementation of the shutter system using the solenoid and Arduino Uno demonstrated the feasibility of achieving controlled and precise shutter movements. By combining the BTS7960 power motor with the Arduino Uno, full voltage delivery to the solenoid was achieved, leading to robust and consistent performance of the shutter system. This improved dosimetric accuracy during radiation exposure, eliminating potential errors associated with manual interventions.

**Conclusion:** The study successfully improved the accuracy of dosimetry delivery through the implementation of a reliable shutter system. The combination of the high-performance solenoid and Arduino Uno micro-controller facilitated seamless interfacing and precise control of the shutter. Although some aspects, such as power consumption and heating issues, need attention and further improvement, the work laid a solid foundation for enhanced radiation delivery systems for in vitro experimentation using  $\alpha$  irradiators. The dedication and ingenuity showcased in this study pave the way for ongoing advancements in this field, including the potential incorporation of a collimator to enhance dosimetry precision for more sophisticated in vitro experiments.

**Keywords:**  $\alpha$ -particles, irradiator, solenoid, shutter

**Program Affiliation:** Summer Undergraduate Research Program

## University Outreach - Bryn Mawr College

Abstract Number: 91

### **PLK4 as a Novel Therapeutic Target in TP53-mutant Acute Myeloid Leukemia**

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**Background:** Resistance to current therapies is one of the major challenges for the cure of TP53-mutant (mut) acute myeloid leukemia (AML). Polo-like kinases (PLK1-PLK5) play a critical role in the cell cycle (Lee S.Y., et al., *Dev Reprod.* 2014). PLK4, which is responsible for centriole duplication, has been found to be overexpressed in lung cancer and TP53-mut AML (Kawakami M., et al., *Proc Nat Acad Sci USA.* 2018; Boettcher S., et al., *Science.* 2019). Thus, PLK4 has emerged as a promising therapeutic target for TP53-mut in AML. We hypothesize that the inhibition of PLK4 may exhibit anti-leukemia activity in TP53-mut AML, and potentially improve the efficacy of current AML therapeutic agents.

**Methods:** Human MOLM-13 AML cells with TP53 wild-type (WT), TP53-knockout (KO), or various TP53-mut were treated with PLK4 inhibitor CFI-400945 and/or Bcl-2 inhibitor venetoclax at various doses for 24 and 48 hours. Cell cycle and polyploidy were measured using an Edu Click-it Kit and FXCycle, respectively. Apoptosis was measured using FACS-flow cytometry after cells were stained with cleaved (Civ)-PARP antibody or AnnexinV/7 aminoactinomycin D (7AAD). Protein levels were measured by western blot.

**Results:** PLK4 inhibition induces polyploidy and apoptosis in TP53-mut AMLs. CFI-400945 decreases viability in blasts of a patient with TP53-mut AML. CFI-400945 induces apoptosis and enhances venetoclax efficacy in MOLM-13 cells with TP53-Y220C mutation. CFI-400945 and venetoclax combination induces more polyploidy and apoptosis in MOLM-13 TP53-mut compared to TP53-WT isogenic cells.

**Conclusion:** TP53-mut or TP53-KO AML cells express higher levels of PLK4 than the isogenic TP53-WT cells. Inhibition of PLK4 induces polyploidy and cell death in TP53-mut cells. PLK4 inhibition enhances the therapeutic efficacy of venetoclax in TP53-mut AML cells.

**Keywords:** AML, TP53, PLK4, Polyploidy, Apoptosis

**Program Affiliation:** University Outreach - Bryn Mawr College

Abstract Number: 92

## **Enhancer activation by CRISPR/Cas9-based acetyltransferase rescues loss of function in CREBBP point mutant**

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**Background:** Follicular Lymphoma (FL) is caused by frequent gene mutations, specifically in the regulatory protein CREB-binding protein (CREBBP). CREBBP is a Lysine Acetyltransferase (KAT), regulating gene expression by coordinating transcriptional processes. Together with E1A-binding protein P300 (EP300), the CREBBP/EP300 complex regulates the acetylation of histone and non-histone proteins, thus managing gene expression. However, mutations in the protein can lead to the development of lymphoma. The Green Lab previously performed molecular characterization using isogenic CRISPR/Cas9-modified lymphoma cells and identified H3K27Ac loss at enhancers associated with MHC II. The loss of H3K27Ac affects the enhancer regions of a gene and the loci that are involved in the Antigen presentation pathway, including HLA-DR, a major histocompatibility complex II cell surface receptor, and CD74, a protein-coding gene. Loss of antigen function results in a decrease in the adaptive immune response to cancer.

**Methods:** To investigate the potential enhancement of KAT, a dCas9-P300 complex was formed to serve as a source for gene activation. Cloning was used to change the structure of the dCas9-P300 complex from its original and universal promoter, Elongation Factor 1 Alpha (EF1 $\alpha$ ), to a B-cell-specific promoter, Spleen Focus-Forming Virus (SFFV). In comparison to the promoter, the enhancer of the structure was significantly larger, therefore requiring the use of two guide RNA structures (gRNA): GFP-labelled and mCherry-labelled. Both gRNAs serve as fluorescent protein markers that aid in monitoring gene activity, expression, and localization. The dCas9-P300 structure and the respective genetic markers were used to guide the P300 complex to the loci of the DNA where there was a significant k27Ac loss. Fluorescent markers were analyzed using flow cytometry.

**Results:** Flow cytometry showed the highly transduced efficiency in B-cell lymphoma with over 85% double positive population in both CD74 and MHC II guides transduction. The expression of CD74 and HLA-DR (direct target of CIITA) increased dramatically in a dose dependent manner.

**Conclusion:** The data obtained indicated that the use of two gRNA constructs resulted in the activation of a gene's enhancer region via increasing the acetylation of their locus and promoting the transcription, which partially rescues the loss of function in CREBBP point mutant.

**Keywords:** B-cell Malignancies, gRNA, CREBBP, dCas9-P300, Lymphoma

**Program Affiliation:** University Outreach - Bryn Mawr College

## University Outreach - High School Summer Program

Abstract Number: 93

### **Improving The Efficiency of Prostate MRI Segmentation workflow through computerized provider order entry (OneConnect)**

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**Background:** Manual orders can be error-prone and time consuming. Since urologists are unaware that segmented images of the prostate are available, the MRI-Ultrasound fusion biopsy is delayed. Patient diagnosis and treatment are subsequently hindered which raises patient anxiety and may result in delays in initiating appropriate therapies.

**Methods:** Several strategies were used in the study of the efficacy of prostate MRI segmentation. To begin, visual flowcharts for both current and future state processes were created using process mapping. Second, a GEMBA walk was done to watch and follow staff directly, gaining significant insights into the actual workflow. Third, cycle time analysis was used to estimate overall efficiency by measuring the total time taken from the beginning to the finish of the segmentation process. A fishbone diagram was also utilized to examine the various aspects influencing the implementation of CPOE for prostate MRI orders. Furthermore, a Failure Modes and Effects Analysis (FMEA) was carried out systematically to assess potential process failures and their consequences. Finally, control charts were used to monitor important process indicators throughout the investigation.

**Results:** Prostate MRI segmentation orders done by CPOE in OneConnect grew from 0% to an average of 91.6% (6 months running average) between June 2019 and June 2021. This well exceeded the intended target of 50%.

**Conclusion:** Based on revenue results, CPOE and the radiologist notification strategy have proven effective. Revenue increased considerably when these approaches were applied. The workflow changes enhanced revenue profits and resource utilization, thereby minimizing delays in MRI data interpretation.

**Keywords:** MR (MAGNETIC RESONANCE) Prostate Segmentation, biopsy

**Program Affiliation:** University Outreach - High School Summer Program

Abstract Number: 94

## **Aerobic Exercise Impacts the Tumor Microenvironment by Altering CAF Abundance and CAF-Activating Cytokines in Pancreatic Cancer**

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**Background:** Pancreatic Ductal Adenocarcinoma (PDAC) is one of the deadliest types of cancer, with an overall 5-year survival of 12% due to the high resistance to anti-cancer therapies and a complex tumor microenvironment. Excessive deposition of extracellular matrix (desmoplasia) and the high density of CAFs (cancer-associated fibroblasts) contribute to this resistance and to tumor progression. Desmoplasia causes a physical barrier to chemotherapy delivery and promotes cancer cell proliferation and metastasis. CAFs, beyond being responsible for ECM deposition, play a central role in tumorigenesis as regulatory cells able to promote tumor growth and anti-cancer therapy resistance via secretion of numerous growth factors. We investigated the effect of two different exercise intensities on CAF abundance and desmoplasia in mice bearing Hy 15549 and on the levels of CAF-promoting cytokines in mice bearing KPC 4662 cells.

**In Vivo:** Pancreatic cancer cell Hy15549 or KPC 4662 were injected into the thickest portion of the pancreas in C57BL/6J mice. When tumors reached around 30mm<sup>3</sup>, mice were randomized and divided into three groups: sedentary and mice that performed treadmill exercise at 8 m/min or 16 m/min for 45 minutes daily, 5 days per week for 3 weeks. **In Vitro:** Tumor desmoplasia was analyzed by Masson's trichrome. CAFs abundance was assessed by immunofluorescence with antibodies against PDNP,  $\alpha$ SMA, Desmin, NG2. Tumor vascular density was analyzed by immunofluorescence using CD31 antibody. The levels of CAF-promoting cytokines (TNF- $\alpha$ , IL-1b, and TGF- $\beta$ ) were measured by western blot.

**Results:** In Hy 15549-bearing, exercise at 8 m/min reduces the abundance of intratumoral  $\alpha$ SMA+ CAFs whereas both 8 and 16 m/min reduce NG2+ CAFs. This result was associated with a reduction of collagen deposition induced by both exercise intensities. Exercise does not impact the levels of CAF-promoting cytokines in PDAC KPC 4662 mice.

**Conclusion:** Exercise may be an effective tool for increasing anti-cancer therapy efficacy and reducing metastasis by reducing tumor CAF abundance and desmoplasia. Exercise-induced these effects may not rely on the reduction of CAF-promoting cytokines within the tumor. Further investigations are needed to understand the molecular mechanism driving the exercise-induced remodeling of the tumor microenvironment.

**Keywords:** Exercise, CAFs (cancer-associated fibroblasts), Desmoplasia, CAF-promoting cytokines, Collagen

**Program Affiliation:** University Outreach - High School Summer Program

Abstract Number: 95

## **Chimeras- Greek Mythology or Scientific Reality? Identification of Actionable Chimeric RNAs for Personalized Prevention of Breast Cancer.**

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<sup>2</sup>Department of Biochemistry, University of Houston

**Background:** For those at-risk for breast cancer, the only available prevention option is anti-estrogen-based drugs. This approach does not account for the specific subtype of breast cancer that the patient may be at risk for or the unique alterations in their mammary tissue.

Personalized therapies based on individual molecular characteristics of patient tumors are desperately needed to improve breast cancer prevention. Fusions, including the ones that are created by joining at the RNA level, can form during cancer development and thus present an attractive possibility to target with a vaccine. The objective of the current project is to identify novel actionable RNA fusions for the personalized prevention of breast cancer.

**Methods:** A list of RNA fusions was previously obtained by mining the RNA sequencing data from breast cancer samples. RNA fusion candidates from this list were processed through a multistep pipeline framework to evaluate their actionability. The workflow of the project included the following steps: 1) cBioPortal/Survival analysis to predict the association of individual gene partners with breast cancer patient survival and prognosis, 2) cBioPortal/Co-Expression analysis to study if the gene partners are expressed together or have common gene partners, 3) Determining fusion junction and Open Reading Frame (ORF) Finder to identify if the fusion is predicted to be translated and makes a unique product, and lastly 4) qPCR to validate the fusion RNA expression in breast cancer cell lines.

**Results:** RNA fusions PACSIN2-ARFGAP3, F8-CLIC2, and NSF-LRRC37A2 were investigated and fusion junctions were successfully mapped. Although these fusions have been reported before, their fusion junctions have not been mapped. Positive correlations were noted between gene partners of these 3 gene fusion pairs. TCGA mining showed that deletion mutations or single nucleotide mutations in these genes are prevalent in less than 0.5% patients and thus no conclusive association between gene mutations and overall survival or disease-free survival in breast cancer patients was noted. Interestingly, each chimeric RNA (PACSIN2-ARFGAP3, F8-CLIC2, and NSF-LRRC37A2) did generate a unique ORF, suggesting that these fusions are predicted to be translated. Lastly, the mRNA expression of NSF-LRRC37A2 fusion was tested in twelve breast cancer cell lines by real-time PCR. It was confirmed to be present in three of out of the twelve samples, suggesting that NSF-LRRC37A2 is likely to be expressed in patient breast tumors as well.

**Conclusion:** Chimeric RNAs appear to be relatively abundant in breast cancer and therefore may provide an attractive target for vaccine development. Additional preclinical testing of a neo-antigen peptide vaccine generated from these fusions will be needed to determine if such vaccines targeting fusions are effective at breast cancer prevention.

**Keywords:** breast cancer, RNA fusions, prevention, TCGA data mining

**Program Affiliation:** University Outreach - High School Summer Program

Abstract Number: 96

### **Fabrication of radiopaque, drug loaded resorbable inferior vena cava filters**

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<sup>1</sup>Interventional Radiology, The University of Texas MD Anderson Cancer Center

**Background:** Pulmonary embolism (PE) affects about 10 million individuals annually in the world [1]. The most conventional way to prevent PE is to use metallic inferior vena cava filters (IVCFs) to catch these clots. However, only 35% of metal filters are eventually retrieved [2]. Therefore, the objective of our study is to infuse imaging enhancers made up of nanoparticles and drugs onto the absorbable polymers to facilitate its imaging over time and to prevent thrombosis, which is the most common adverse reaction when implanting medical devices.

**Methods:** IVCFs were fabricated by modifying a cork with nails and braiding the poly-p-dioxanone (PPDO) sutures around the cork. Simultaneously, gadolinium nanoparticles (GdNPs) were synthesized through the thermal decomposition method where its size and morphology were characterized using a transmission electron microscope (TEM). After braiding, these IVCFs were infused with GdNP and/or dipyridamole (DPA) using the wet dipping method. Characterization was done using scanning electron microscopy (SEM), micro-computed tomography (mCT), and mechanical strength Hemolysis assay and in vitro cell toxicity was done against RF24 and MOVAS cells lines.

**Results:** Synthesis of GdNP yielded plate like structures with average diameters of  $35.76 \pm 3.71$  nm as shown in TEM. SEM showed rougher surface with infusion of GdNP and/or DPA as compared to control. SEM-EDX showed the presence of Gd on Gd and Gd+DPA infused PPDO sutures. Physicochemical characterization showed no significant difference among the groups in terms of melting temperature ( $103.32$ - $105.90$  °C) and load-at-break ( $4.39$ - $5.38$  kg). Micro- CT imaging showed that the stents containing the Gd had an average radiopacity of  $2713 \pm 105$  HU for Gd alone and  $1516 \pm 281$  HU for Gd+DPA, which is significantly more than the average radiopacity of the control ( $-130 \pm 38$  HU) and DPA alone ( $-135 \pm 172$ ). There was also a decrease in radiopacity in the stents containing gadolinium over a period of 6 weeks. The hemolysis with the suture treated media did not show a significant lysis in cells. In vitro viability assay against RF24 and MOVAS cell lines did not show any toxicity among all groups.

**Conclusion:** A novel radiopaque, resorbable IVCF made up of PPDO infused with GdNP and DPA was successfully fabricated. By incorporating GdNP into the PPDO material, such as Gd nanoparticle, into the degradable polymer, routine imaging of these implantable medical devices would be possible. Furthermore, addition of drugs could help prevent the formation of neointimal hyperplasia.

**Keywords:** inferior vena cava filters, gadolinium nanoparticles, dipyridamole, polydioxanone, computed tomography

**Program Affiliation:** University Outreach - High School Summer Program

Abstract Number: 97

### **Pre-operative portal vein ligation and MSC injection in a rat model**

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**Background:** Hepatic resection is commonly used to treat liver cancer by removing diseased sections of the liver. Pre-operative portal vein embolization or ligation (PVL) can be used prior to the resection to redirect portal flow to the future liver remnant (FLR) to induce hypertrophy in the healthy portion of the liver, allowing the liver to continue essential functions, and reducing the chance for complications after the surgery. The use of mesenchymal stem cells (MSCs) as an adjunct can expedite liver growth rates, further minimizing the risk of liver-related complications. Therefore, this study aims to assess whether the use of MSCs, in conjunction with pre-operative PVL, positively affects FLR in a rat model.

**Methods:** Three rats were randomly allocated into the following groups: 1) Control, 2) PVL, and 3) PVL+MSC. Red fluorescent protein (RFP)-labeled Sprague-Dawley rat bone-marrow-derived MSCs were obtained from Creative Bioarray (Shirley, NY). In the PVL or PVL+MSC rats, the portal vein branches for the left and middle lobes were ligated. MSCs were then injected into the non-occluded portal vein branches of the PVL+MSC rat. CT imaging of the whole liver was performed at weeks 0 and 2 with the injection of 350  $\mu$ L of iodixanol (320 mg/mL). The liver volumes were quantified using MIM7.1.4 software. After 2 weeks, the rats were sacrificed, and liver samples were collected, weighed, and stained for RFP.

**Results:** All the rats survived for 2 weeks with no complications noted. The liver volume estimations from CT imaging showed an increase in the non-ligated liver of 70.2% in the PVL+MSC group (1.54 to 3.08 mL) compared to the PVL group, which had a 41.4% increase in liver volume (1.19 to 1.91 mL) and control which showed a decrease in liver volumes (2.99 to 1.35 mL). Necropsy revealed that PVL+MSC had the highest FLR/Total weight ratio. Histological evaluation confirmed the presence of MSCs only in the PVL+MSC group but not in PVL nor control.

**Conclusion:** Our study showed that MSCs can improve the effectiveness of PVL in inducing liver hypertrophy. Further research, such as improving MSC retention, would allow the use of MSCs in conjunction with PVL to become a more common option when approaching treatment for liver cancer and other liver diseases that would require a resection.

**Keywords:** Computed tomography, Liver hypertrophy, Mesenchymal stem cells, Portal vein ligation

**Program Affiliation:** University Outreach - High School Summer Program



Abstract Number: 98

## **The Effects of a Glutamine-Free Diet on Tumor Progression and the Immune Landscape of the Ovarian Tumor Microenvironment**

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**Background:** Epithelial ovarian cancer, the most common type of ovarian cancer, is a leading cause of cancer deaths in women. Additional research on the tumor microenvironment (TME) is needed to develop more effective therapies and can provide insights into the behavior of ovarian cancer as it includes fibroblasts, endothelial cells, lymphocytic infiltrates, and extracellular matrix proteins, which can directly affect cancer cell initiation, growth, migration, and differentiation. Ovarian cancer cells (OVCA) and cancer-associated fibroblasts (CAFs) have an upregulated glutamine metabolism due to increased energy needs for cell division. Increased CAF-derived glutamine can also affect the activity of immune cells, modulating OVCA growth. We therefore hypothesize that lowering glutamine levels by adopting a glutamine-free diet can suppress ovarian cancer growth by suppressing the malignant phenotype of ovarian cancer.

**Methods:** The effects of a glutamine-free diet on tumor growth were determined using a novel mouse model in which syngeneic fallopian epithelial cell-derived cancer cells were injected into C57BL/6 mice two weeks after feeding mice with either a normal diet or a glutamine-free diet. Imaging mass cytometry (IMC) was used to identify spatially resolved key immune cell types in their states and explore EMT-related proteins. Tissue microarrays (TMAs) were developed with collected tumors and stained with a panel of 22 metal-conjugated antibodies followed by IMC data acquisition by a Helios CyTOF instrument equipped with a Hyperion System laser ablation module. Image analysis including tissue detection, tissue segmentation, AI-driven nuclei and cell detection, phenotyping, and neighborhood analysis were performed using Visiopharm software. Cell densities in the stromal and epithelial compartments and expression levels of various biomarkers were quantified.

**Results:** Data analysis revealed a greater cell density of B cells in the stroma of mice fed with glutamine-free diet and greater cell density of EPCAM+ ECAD+ cells in the tumor of mice fed with glutamine-free diet. Moreover, cell density of FN+ Vim+ cells, EPCAM+ CD44+ cells, and FN+ Ki67+ cells was higher in the stroma of mice fed with control diet compared to glutamine-free.

**Conclusion:** Mice fed with a glutamine-free diet have significantly lower ovarian cancer burden, reduced stemness and EMT, and greater B-cell-related immune responses in the TME compared to control diet mice that have more activated CAFs, leading to increased stiffness of the ECM that may enhance the malignant phenotype of OVCA. We will further classify the subtypes of immune cells as well as their spatial relationships by performing IMC staining with more functional markers.

**Keywords:** Ovarian Cancer, glutamine, IMC, cancer-associated fibroblasts (CAFs)

Abstract Number: 99

## **Summer Experience Activities and Student Career Trajectories: Exploring their Relation**

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**Background:** The Cancer Prevention Research Training Program (CPRTP) is a federally funded initiative by the National Cancer Institute since 1992. CPRTP provides mentorship as well as activities such as career conversations and informational interviews which are tailored to trainees' interests and inquiries about cancer prevention. By emphasizing students' active engagement, CPRTP works towards increasing exposure and understanding of the various careers in cancer prevention research. However, more analysis and exploration of each component of this short-term research experience program (10 weeks) is needed to better design and tailor these elements to help students in the process of career-planning and decisions. The current study examines key factors that influence student self-efficacy in career exploration.

**Methods:** The halfway and final essay reports from 70 CPRTP summer experience students between 2015-2017 were de-identified and anonymized. Student reports were qualitatively analyzed to identify themes and patterns relating to the students' summer experiences and their subsequent career paths. Team members were assigned to one of the three year's reports. After coding themes within each year, we combined our results to form major themes or agents of change. In addition, current career status was documented.

**Results:** From our diverse trainee group (27 undergraduate college students, 31 graduate students, 2 pharmacy students, and 10 medical students), the following agents of change emerged from their narratives: activity-based learning, people, and hands-on experiences. Trainees mentioned how the CPRTP activities gave them abundant networking opportunities, emphasized the effect of peers and mentors, and described maturity and responsibility that came with conducting lab work and manuscript writing. Furthermore, they mentioned how these factors contributed to higher self-efficacy in conducting research, further professional skill development, and a better understanding of different research fields. Upon this mapping, we decided to utilize the Social Cognitive Career Theory as our main framework. Labeling our three agents of change as the "catalysts" for career development, we identified changes in self-efficacy, career expectations, and career interests. Currently, 31 of the 70 students are in training, 10 are not doing research or have not clarified their status, 18 are doing research, and 11 are working in clinical fields.

**Conclusion:** The CPRTP summer experience has fulfilled its aim of helping them better understand cancer prevention and aiding in their personal and career goals. Reviewing student narratives has contributed to a deeper understanding of the program's role in shaping their career interests and has provided valuable insights for further program development.

**Keywords:** Summer experience, cancer research, Social Cognitive Career Theory, qualitative analysis

Abstract Number: 100

**Excess TGF- $\beta$  Induces MMP-9 and SPP-1 Expression in the Skeletal Muscle of Cancer Patients with Bone Metastases: Association with Muscle Dysfunction**

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**Background:** Patients with bone metastases experience muscle weakness which can lead to a severe loss of muscle mass and function known as cachexia, a paraneoplastic syndrome for which there is no treatment. Bone metastases causes pathologic fractures and further increase mortality rate by 32%. Tumors in the bone lead to excessive bone resorption, releasing growth factors including TGF- $\beta$  from the bone matrix. MMP-9 and SPP-1 are secreted proteins downstream in the TGF- $\beta$  signaling pathway and promote the expression and activation of TGF- $\beta$ . MMP-9 and SPP-1 further promote osteoclast activity and bone resorption. As muscle is one of the organ systems responsive to bone-derived signals, recent evidence suggests that pathologic, accelerated bone resorption causes muscle weakness. Muscle weakness promotes immobilization of patients, which further increases bone loss and increases fracture risk. Understanding the mechanisms involved in bone-muscle cross talk due to osteolytic bone metastases has implications for treatment.

**Methods:** We analyzed muscle biopsies and blood samples from lung, breast and renal patients with bone metastases and validated our findings on Camurati-Engelmann Disease (CED) mice with excessive TGF- $\beta$  release and extreme bone turnover.

**Results:** Muscle biopsies from patients with bone metastases displayed a 26.08% reduction in myofiber cross-sectional area, suggesting reduction of muscle mass, and an accumulation of phospho-Smad2/3 protein in the myonuclei, showing increased TGF- $\beta$  activation. We found that platelet-free plasma TGF- $\beta$  concentrations in these patients were significantly higher ( $P < 0.001$ ) than non-tumor controls, indicating that bone metastases-related muscle loss is associated with TGF- $\beta$ /Smad signaling activation. RNA sequencing identified MMP-9 and SPP-1 gene upregulation in the muscle biopsies of patients with bone metastases. We also found that in CED mice and humans with abnormal bone resorption as a result of CED or bone metastases respectively, the gene encoding MMP-9 and SPP-1 are expressed at higher than normal levels in skeletal muscle. The secreted proteins are also upregulated in skeletal muscle and plasma obtained from CED mice and humans with bone metastases. Both MMP-9 and SPP-1 can be induced by TGF- $\beta$  while the secreted proteins are additionally capable of promoting TGF- $\beta$  and osteoclast activation. Our results indicate that cancer-related bone loss is a central mediator of muscle tissue breakdown, via increased TGF- $\beta$  activity and muscle production of MMP-9 and SPP1.

**Conclusion:** Bone-derived TGF- $\beta$  and muscle secretion of MMP-9 and SPP-1 may fuel a feed-forward vicious cycle of muscle weakness and bone destruction.

**Keywords:** Bone Metastases, TGF- $\beta$ , MMP-9, SPP1, muscle dysfunction

**Program Affiliation:** University Outreach - High School Summer Program

## University Outreach– Augustana College

Abstract Number: 101

### **The Impact of COVID-19 on Smoking Cessation Motivation and Lung Cancer Screening in Quitline Clients**

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**Background:** There were 38% fewer lung cancer cases diagnosed during the pandemic compared to before, but cases diagnosed during the pandemic were at a more advanced stage (Mojsak et al., 2023). Smoking is the leading cause of lung cancer, accounting for 90% of all cases in men and 70-80% in women (Walser et al., 2008). Previous research has found that both people who smoke or have a smoking history and lung cancer patients have an increased risk of COVID and worse outcomes if infected (Bungaro, 2022; Koczkodal et al., 2022; Reddy et al., 2021). This study aims to identify the best ways to assist the quitline client population following the COVID-19 pandemic and help the scientific community aim research focus and allocate resources.

**Methods:** A chi-square analysis was run from online survey results completed by quitline clients who expressed interest in lung cancer screening and are ages 55-80 with a 30-pack year smoking history.

**Results:** 116 quitline clients completed the survey and had an average of 51.81 pack-years smoking history (SD=19.39). Results showed that there is a significant association between interest in lung cancer screening and motivation to quit smoking, but there was no overall change in smoking cessation motivation or interest in lung cancer screening during the pandemic.

**Conclusion:** These findings suggest that the pandemic did not have an overall large effect on interest in lung cancer screening and smoking cessation motivation and progress made before the pandemic was not lost, so time and money can be spent on improving access and awareness to lung cancer prevention resources.

**Keywords:** smoking cessation, lung cancer screening, COVID-19, quitline clients

**Program Affiliation:** University Outreach– Augustana College

Abstract Number: 102

### **Exploring the relationship between stomal supply usage and communication participation in tracheoesophageal speakers following total laryngectomy**

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<sup>1</sup>Head and Neck Surgery, The University of Texas MD Anderson Cancer Center

**Background:** Tracheoesophageal (TE) speech is considered the gold standard of alaryngeal voice restoration following total laryngectomy (TL). To improve pulmonary and communication outcomes, patients are recommended stomal supplies including heat and moisture exchangers (HMEs), adhesives, and intraluminal devices. Currently, the relationship between the use of specific stomal supplies and patient-perceived communication is not well-understood. This study's purpose is to determine the effect of stomal supply usage and self-rated communication participation in patients who use TE speech.

**Methods:** This is a secondary analysis of the prospective PATH Registry (NCT05036330) including 73 patients having undergone TL and tracheoesophageal puncture (TEP). Differences in Communication Participation Inventory Brief (CPIB) scores and stomal supply usage questionnaire responses were stratified by demographic factors and surgical data retrieved from patient chart review.

**Results:** The mean age of participants was 66.98 (SD: 10.23) years old with 82.19% being male. The average time since tracheoesophageal puncture (TEP) was 5.18 (SD: 4.80) years. The Median CPIB score was 17 which translates to a mild reduction in communication participation. 21% of patients' scores were considered normal participation, 32% had mildly reduced participation, 35% had moderately reduced participation, and 12.5% experienced severely reduced communication participation. The demographic factors associated with lower CPIB scores were being Hispanic or Latino and experiencing anxiety and/or depression. Surgical factors associated with lower CPIB scores were undergoing pharyngectomy with reconstruction, displaced orientation of TEP relative to stoma, and undergoing a salvage or functional salvage TL procedure. All patients reported using HME devices and having a functional stoma seal when occluding. Patients who used more than one attachment housing for HMEs demonstrated a lower CPIB score than those who used only one primary attachment device. No other stoma supply factors demonstrated differences in median CPIB score.

**Conclusion:** Based on this analysis, TE speakers experience mildly reduced communication participation. Stoma supplies had a negligible effect on communication participation, with only the use of more than one HME attachment negatively impacting CPIB scores. The drivers of communication participation in TE speakers are multifactorial and appear inclusive primarily of psychosocial and physiologic drivers. Future directions for this work include analyzing data to identify any significant associations between CPIB and surgical, demographic, and stomal supply factors and expanding upon these covariates to include psychosocial factors.

**Keywords:** Total laryngectomy, Tracheo-esophageal speech, Stoma supplies, Communication

**Program Affiliation:** University Outreach– Augustana College

Abstract Number: 103

### **Exploring the Feasibility, Validity, and Reliability of DIGEST after Maxillectomy**

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**Background:** Dynamic Imaging Grade of Swallowing Toxicity (DIGEST) is a validated tool to grade results of modified barium swallow studies (MBS) in head and neck cancers. DIGEST was initially validated to assess the pharyngeal stage of swallowing, which excluded cancers beyond the pharyngeal region. While DIGEST is utilized in clinical practice amongst oral cavity cancers at MD Anderson Cancer Center (MDACC), it has yet to be validated or assessed for this population, such as patients with maxillary cancer treated with a maxillectomy. The objective of this study was to assess the feasibility, validity, and reliability of DIGEST in patients with maxillary cancer.

**Methods:** This was a retrospective cohort study analyzing patients who underwent a maxillectomy with a post-operative MBS at MDACC from 2016-2021. Measurements of criterion validity including the Modified Barium Swallowing Impairment Profile (MBSImP) oral and pharyngeal totals, MD Anderson Dysphagia Inventory (MDADI) composite and physical scores, and Performance Status Scale for Head and Neck Cancer Patients (PSS-HN) diet were assessed relative to DIGEST. DIGEST was chart abstracted from electronic health records and double-blind rated for reliability.

**Results:** 114 patients with a median age of 63 were analyzed post-maxillectomy. The cohort was predominantly male (57%) and white (83.3%). Squamous cell carcinoma was the leading histology (59.7%), with the maxillary sinus being the most common tumor site (27.2%). 66 patients underwent an infrastructure maxillectomy and free flap transfers were the favored reconstruction method (85.1%). Radiation was administered to 100 (87.7%) patients. A “rule-out leak” MBS was indicated in 80 (70.2%) patients to assess radiographically for healing before oral intake. Higher MBSImP oral and pharyngeal impairment scores were seen as DIGEST increased ( $r = 0.43$ ,  $p = 0.00$ ;  $r = 0.82$ ,  $p = 0.00$ ), however, DIGEST did not correlate with postoperative quality of life or oral diet, as measured by the MDADI physical ( $r = -0.14$ ,  $p = 0.31$ ) and composite ( $r = -0.08$ ,  $p = 0.54$ ) and PSS-HN diet scores ( $r = -0.14$ ,  $p = 0.13$ ). Inter-rater reliability was substantial to almost perfect ( $k = 0.75-0.87$ ) with blind laboratory ratings achieving >80% exact agreement.

**Conclusion:** DIGEST is a feasible and reliable tool for measuring pharyngeal dysphagia as a component of swallowing assessment after maxillectomy. DIGEST maintains validity with comparable performance to the original validation in non-oral HNC on MBS-criterion measures but not on non-MBS measures (e.g. MDADI and PSS-HN scores). Further research is needed to assess the usage of DIGEST among other populations.

**Keywords:** maxillectomy, dysphagia, modified barium swallow, oral cavity cancer

**Program Affiliation:** University Outreach– Augustana College

## University Outreach– Baylor University

Abstract Number: 104

### **CAF-derived MFAP5 is a novel transcription regulator for immune checkpoint CD47 in ovarian cancer**

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**Background:** High-grade serous ovarian cancer (HGSC) is the most widespread type of epithelial ovarian cancer, accounting for approximately 75% of all epithelial ovarian cancers. The tumor microenvironment (TME), composed primarily by fibroblasts, endothelial cells, lymphocytic infiltrates and extracellular matrix proteins, directly affects cancer cell growth, migration, and differentiation. Cancer associated fibroblasts (CAFs) are responsible for producing the structural components of the TME and secrete factors such as cytokines and growth factors that maintain normal tissue homeostasis but have been shown to play a key role in modulating the malignant phenotypes of HGSC. Microfibrillar-associated protein 5 (MFAP5) has recently been shown by Dr. Mok and others to be upregulated in CAFs of several tumor types and is associated with poor prognosis in ovarian cancer when overexpressed. MFAP5 has an RGD binding motif that binds  $\alpha\beta3$  integrin to enhance angiogenesis and metastatic potential of HGSC cells through the activation of calcium-dependent FAK/ERK/LPP and FAK/CREB/TNNC1 pathways. Silencing MFAP5 in CAFs using MFAP5 specific siRNAs suppressed HGSC growth, metastasis, and angiogenesis in vitro and in vivo. Since our preliminary data showed exogenous MFAP5 increased CD47 mRNA expression in ovarian cancer cells, we hypothesize that CAF-derived MFAP5 can transcriptionally up-regulate CD47.

**Methods:** To identify the molecular mechanisms by which MFAP5 regulates CD47 expression, we analyzed the promoter sequence of CD47. A transcriptome analysis of MFAP5-treated ovarian cancer cell OVCA 432 was used to identify differentially expressed immune-related genes induced by MFAP5.

**Results:** qRT-PCR analysis and flow cytometry staining showed a significant increase in mRNA and protein expression of CD47 after 48h treatment with MFAP5 compared to control cells. Computational analysis of CD47 promoter revealed CREB and NF-kB consensus binding sequence in ovarian cancer cells. Three cell lines from qRT-PCR analysis that showed highest fold increase in CD47 expression were chosen for transduction with a luciferase reporter vector

cloned with WT and mutated CREB binding sites. The luciferase assay from these cells showed a decreased binding activity signal in cells transduced with CREB or NF- $\kappa$ B mutated plasmids compared to cells transduced with the WT plasmid.

Conclusion: MFAP5 mRNA expression in microdissected CAFs and CD47 mRNA expression in ovarian cancer cells show that CAF-derived MFAP5 may play a role in CD47 expression regulation in ovarian cancer cells. Moreover, MFAP5 responsive elements on the CD47 promoter consist of a CREB and a NF- $\kappa$ B binding sites. Future study to delineate the signaling network involved in transcriptionally up-regulation of CD47 by MFAP5 is warranted.

Keywords: CD47, MFAP5, CD8+ T cells, High-grade serous carcinoma (HGSC)

Program Affiliation: University Outreach– Baylor University



Abstract Number: 105

## **T cell receptor engineering targeting FOXM1 for the treatment of lung cancer**

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**Background:** Despite its success, checkpoint blockade immunotherapy has proven challenging in selected lung cancer patient populations. This is in part due to the extensive intratumor heterogeneity at play and infiltration of bystander T cells which recognize non-tumor antigens. Recent clinical trials have demonstrated some efficacy for adoptive cell therapy using bulk unenriched tumor-infiltrating lymphocytes, but success remained limited. Accordingly, novel tumor antigens are needed to further improve upon this success of cellular immunotherapy in lung cancer. Forkhead Box M1 (FOXM1) is a transcription factor expressed in 90% of lung cancers and lacks expression in brain tissue, making it an appealing target for T cell receptor (TCR) engineering. Interestingly, up-regulation of FOXM1 is associated with drug resistance to tyrosine-kinase inhibitors (TKIs), highlighting another potential therapeutic application for this target. Here, we assessed the immunogenicity of FOXM1 and its potential as a cellular therapy target in non-small cell lung cancer.

**Methods:** Antigen-specific T cells were isolated and then expanded by peptide stimulation of HLA-matched healthy donor PBMCs. Antigen-specific T cells were then isolated by tetramer sorting and underwent single-cell TCR sequencing to identify full length alpha and beta chains of the TCR. TCRs were retrovirally-engineered into healthy donor PBMCs and function was assessed via chromium-51 release (cytotoxicity), ELISpot (IFN-gamma secretion) and ELISA (MIP-1beta secretion).

**Results:** An epitope of FOXM1 (YLVPIQFPV) was immunogenic when presented on HLA-A\*02:01 (42% of United States population). This epitope was confirmed to be naturally-processed and presented using H1975 cells. Assessment of cytotoxicity revealed that 51% of H1975 cells were lysed by TCR-engineered PBMCs, compared to only 10% for H1975 parental cells devoid of FOXM1 expression ( $p < 0.0001$ ). Cytokine assessment via ELISpot demonstrated a significant increase in IFN-gamma spots ( $p < 0.05$ ) and MIP-1beta secretion by ELISA ( $p < 0.05$ ).

**Conclusion:** Our findings confirm the immunogenicity of FOXM1 when presented on the most prevalent HLA allele in the United States and support the feasibility of TCR-engineered targeting FOXM1 for the treatment of lung cancer.

**Keywords:** T cell receptor, FOXM1, immunotherapy, T cell engineering

**Program Affiliation:** University Outreach– Baylor University

Abstract Number: 106

## **Characterizing the Importance of Microglial Qki in the Progression of Alzheimer's Disease**

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**Background:** Alzheimer's Disease (AD) is one of the most prevalent neurodegenerative diseases worldwide, leading to cognitive and motor deficits in patients. Amyloid plaque, a major hallmark of AD, forms when there are mutations in the genes regulating the processing of amyloid protein, leading to formation of aggregates and disruption of neuronal signaling. These plaques are phagocytosed by resident immune cells of the brain called microglia. One of the major regulators of microglial phagocytosis is Quaking (Qki), a master regulator gene of RNA processing. Despite its increased expression in AD patients, Qki's role in AD remains unknown. Given Qki's role in microglial phagocytosis and its upregulation in AD patients, we hypothesize Qki promotes microglial phagocytosis to attenuate AD progression.

**Methods:** To characterize changes in microglial Qki expression in AD, brain tissue samples from AD patients were categorized as early-stage and late-stage. Immunofluorescent (IF) staining was performed on these samples to assess Quaking expression in microglia. Various plaque regions were analyzed to establish potential correlations with amyloid plaque burden. To understand the contribution of microglial Qki in AD progression, we conditionally deleted Quaking in microglia by utilizing the Cx3Cr1 Cre-Lox system in 5xFAD mice. 5xFAD is a mouse model that exhibits key features of AD pathology. IF staining was performed to evaluate the impact of Quaking deficiency in microglia on amyloid plaque accumulation. Additionally, tests such as the Barnes Maze and Open field were used to evaluate spatial memory and locomotor activity, respectively.

**Results:** We found in regions of high plaque burden, there was significantly lower expression of Qki in microglia compared to sparse plaque regions for AD patients. This may suggest that microglia in high plaque regions adopt a dysfunctional state where their Qki expression is downregulated, leading to increased progression of AD. Additionally, loss of microglial Qki in AD mice resulted in increased amyloid plaque burden, motor deficits, and cognitive deficits, suggesting microglial Qki play an important role in attenuating the progression of AD.

**Conclusion:** Our findings provide novel insights into the role of Qki in the pathogenesis of AD, specifically highlighting its importance in microglial phagocytosis and subsequent cognitive and motor function. Future research will focus on characterizing changes in microglial states with Qki loss and identifying Qki-regulated microglial pathways in AD. Ultimately, therapeutic strategies to slow AD progression can be explored through readily available agonists that alleviate Qki deficiency.

**Keywords:** Alzheimer's Disease, Quaking, Microglia

**Program Affiliation:** University Outreach– Baylor University

Abstract Number: 107

## **Integrating Cervical Cancer Prevention Services to Improve Healthcare Access in the Texas Rio Grande Valley**

Alaina Le, Gynecologic Oncology and Reproductive Medicine, University of Texas MD Anderson Cancer Center

**Background:** Cervical cancer incidence and mortality rates in Public Health Region 11 are both approximately 35% higher than the state. The Rio Grande Valley (RGV) in the Texas-Mexico border is part of this region. It is known that 90% of cervical cancers are caused by persistent human papillomavirus (HPV) infection. Screening and the HPV vaccine can effectively prevent cervical cancer but are offered in separate clinical settings to different age groups, which challenges RGV patients who struggle with scheduling, transportation, financial cost, and low health literacy, among other barriers to care. A pilot study combining cervical cancer prevention services and education on one date, in a clinical setting, was proposed to address these challenges.

**Methods:** Five Saturday health fairs were held October 2021 to June 2023, offering combined cervical cancer screening, HPV vaccination, and cancer prevention education. Most women scheduled did not have a previous screening history, and most children were past-due for second HPV vaccine doses. MD Anderson's team supported planning and provided educational materials (English/Spanish) on cervical, breast, and colorectal cancer screening. Surveys (English/Spanish) were developed to assess patients' awareness of and satisfaction with the combination of services. Survey data was collected and managed through the Research Electronic Data Capture (REDCap) tool approved by MD Anderson.

**Results:** The events hosted 630 participants. There were 330 visitors educated, 116 patients screened, and 132 patients HPV-vaccinated. 123 survey participants indicated receiving a cervical cancer prevention service. Of these, 45% preferred communicating in Spanish and 66% indicated that they scheduled a follow-up appointment. 43% of those who were asked about their prior awareness of the events indicated they were unaware. Among those who indicated awareness (57%), telephone reminders were most frequently cited as their reason for awareness.

**Conclusion:** Integrating cervical cancer prevention services and education into one clinic may be an effective cervical cancer prevention strategy. More specifically, this approach may effectively reach women who were not previously screened or who were overdue per screening guidelines, and patients who were not previously vaccinated or who needed a follow-up dose. RGV health fairs should continue to provide adequate Spanish resources to accommodate the nearly even proportion of Spanish-speakers to English-speakers. Better event planning and advertising is suggested to increase patients' awareness and participation in the services offered. Telephone reminders and other advertisement forms (e.g. flyers and social media) could be explored and improved upon.

**Keywords:** Cervical Cancer, HPV Vaccination, Cancer Prevention Education, Combination of Clinical Services, Health Fairs

**Program Affiliation:** University Outreach– Baylor University

## University Outreach– Nova Southeastern University

Abstract Number: 108

### **Targeting Interleukin-27 Receptor $\alpha$ in Murine HGSC Cells**

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**Background:** High Grade Serous Ovarian Cancer HGSC has the highest mortality rate among gynecological cancers with 152,000 deaths out of 300,000 confirmed cases each year. The large mortality of HGSC can be attributed to the lack of symptoms until it has progressed to the later stages. Peritoneal spread is the leading cause of death from gynecologic cancers and is associated with abdominal obstruction, intestine, blood vessel obstruction. HGSC first metastasizes to the pelvic organs and blood (Stage 2), then the abdomen (Stage 3), and then beyond (Stage 4). Artificial Intelligence (AI) is a set of algorithms capable of learning without human input and can be used to make new predictions through machine learning. AI was used to determine relationships between HGSC development and the tumor microenvironment by using the TCGA (The Cancer Genome Atlas) dataset to identify potential therapeutic targets. An Explainable Artificial Intelligence (XAI) model was generated to interpret the results. According to the XAI model, IL-27R $\alpha$  is a potential therapeutic target in HGSC patients because the high expression is associated with a lower 5-year survival rate. Interleukin-27 Receptor (IL-27R) is a heterodimeric cytokine receptor composed of Interleukin-27 Receptor  $\alpha$  (IL-27R $\alpha$ ) and glycoprotein 130. IL-27R is shown to display pro-tumor activity. It induces the expression of immune regulatory molecules such as IDO and PD-L1, which leads to immune suppression through decreased T cell response and function, and eventually to tumor cell survival and proliferation. Silencing IL-27R $\alpha$  may be an approach to increase survival rates among HGSC patients.

**Methods:** TCGA Dataset was used to generate a Kaplan-Meier survival curve using the database of HGSC patients (GEPIA). To investigate its therapeutic potential, we silenced IL-27R $\alpha$  in murine HGSC cells lines using siRNA and assessed its impact on tumor proliferation by Clonogenic Assay, migration by Wound Healing Assay, invasion by Matrigel Invasion Assay, and angiogenesis by Tube Formation Assay. **Results:** Silencing IL-27R $\alpha$  by siRNA leads to decreased expression of IL-27R $\alpha$  in ID8 murine HGSC. Silencing IL-27R $\alpha$  expression leads to decreased proliferation, migration, invasion in murine HGSC, and inhibited angiogenesis in endothelial cells.

**Results:** Silencing IL-27R $\alpha$  by siRNA leads to decreased expression of IL-27R $\alpha$  in ID8 murine HGSC. Silencing IL-27R $\alpha$  expression leads to decreased proliferation, migration, invasion in murine HGSC, and inhibited angiogenesis in endothelial cells.

Conclusion: We have shown that IL-27R $\alpha$  is associated with poor survival in patients with HGSC. The silencing of IL-27R $\alpha$  using siRNA in murine HGSC cells reduced colony formation, migration, invasion, and tube formation. IL-27R $\alpha$  is possible therapeutic target for HGSC patients.

Keywords: IL-27R $\alpha$ , High Grade Serous Ovarian Cancer (HGSC), Explainable Artificial Intelligence (XAI), siRNA, RNA-based therapeutics

Program Affiliation: University Outreach– Nova Southeastern University

Abstract Number: 109

### **Cisplatin and the Mu Opioid Receptor Antagonist Methylnaltrexone Inhibit Neurite Growth in Cultured Trigeminal Neurons**

Esha Sultana, Department of Psychology and Neuroscience, Nova Southeastern University; Megan L. Uhelski, Department of Anesthesiology, Critical Care, and Pain Medicine, The University of Texas MD Anderson Cancer Center; Juan P. Cata, Department of Anesthesiology, Critical Care, and Pain Medicine, The University of Texas MD Anderson Cancer Center; Patrick M. Dougherty, Department of Anesthesiology, Critical Care, and Pain Medicine, The University of Texas MD Anderson Cancer Center

**Background:** Cancer patients with head and neck squamous cell carcinoma present with the highest prevalence of pain, requiring the administration of opioids for pain management. Pain is exacerbated in these patients due to perineural invasion, the process through which cancer cells invade the surrounding nerves' perineural spaces. Despite the benefits of pain suppression, Mu-opioid receptor (MOR) overexpression and activation can mediate cancer progression. As a result, MOR may be a potential therapeutic target in cancer treatment. Low doses of the Mu Opioid receptor antagonist, methylnaltrexone (MTNX), has shown to inhibit head and neck squamous cell carcinoma growth in vitro and in vivo. However, the mechanism of MTNX decreasing tumor growth has yet to be elucidated. We aimed to evaluate MTNX and Cisplatin's effect on the functionality of trigeminal neurons implicated in head and neck tumors.

**Methods:** The study was conducted using trigeminal ganglia from athymic nude mice. Cultures were treated with four treatment conditions: saline, MTNX only, cisplatin only, and MTNX & cisplatin combined. Cells were cultured with Cisplatin for six hours, while MTNX was present continually to replicate the dosing regimen used in tumor-bearing mouse experiments. Cells were fixed with paraformaldehyde and treated with FITC conjugated Beta-III Tubulin for fluorescent imaging. Images were analyzed for neurite growth and number of somas. The stereological approach was conducted by creating an image template in PowerPoint consisting of seven evenly spaced test lines in a square format. Only the regions of neurite extensions that intersected with the template were marked. The number of somas and intersections per image was then counted, and an estimate of average neurite growth length was calculated for each image by using the formula  $\text{Length} = (78.5 \times i)/s$ , where  $i$  represents the number of intersections and  $s$  is the total number of neuron somas present in the image.

**Results:** Conditions with 1.25 uM cisplatin, 1000 nM methylnaltrexone, or 1.25 uM cisplatin and 1000 nM methylnaltrexone were associated with significantly lower neurite outgrowth. There were no significant differences among the three treatment groups.

**Conclusion:** MTNX and Cisplatin decreased neurite outgrowth suggesting administration of opioid antagonists alongside chemotherapy drugs may decrease crosstalk necessary for perineural invasion. Inhibiting cancer metastasis can decrease patient pain outcomes, ultimately reducing the opioid burden.

**Keywords:** Mu Opioid Antagonist, Perineural Invasion, Head and Neck Cancer, Neurite Growth

**Program Affiliation:** University Outreach– Nova Southeastern University

## University Outreach– University of Notre Dame

Abstract Number: 110

### **Synthesis of Azido block copolymers for Targeting and Labeling Micelle**

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Chun Li, Cancer Systems Imaging, University of Texas MD Anderson Cancer Center

**Background:** Polymeric micelles have emerged as promising drug delivery vehicles for targeting cancer cells. These nanoscale micelles can passively target tumors and accumulate in tumor tissues through the enhanced permeability and retention (EPR) phenomenon. The polymers are composed of hydrophobic blocks and hydrophilic blocks, enabling them to self-assemble in aqueous solutions and encapsulate drugs. To enhance the functionality of these micelles, an azido group was introduced to the polymer. This modification enables the polymer to conjugate with targeting peptides, facilitating active targeting to specific receptors or the surface membrane of cancer cells. As a result, the micelles can enhance drug uptake at the target site. Additionally, the polymer can also conjugate with radio-labeling ligands for imaging purposes, aiding in diagnostic applications. The conjugation process was achieved through copper-free click chemistry, ensuring efficient and precise attachment of the ligands to the micellar surface.

**Methods:** Azido-Poly (PEGMA)<sub>20</sub>-b-poly[HEMA-g-( $\epsilon$ -caprolactone)<sub>7</sub>]<sub>20</sub> was synthesized and its structure was confirmed by proton nuclear magnetic resonance (<sup>1</sup>H NMR). The Azido polymer was then mixed with polymers without the azido group, Poly (PEGMA)<sub>20</sub>-b-poly[HEMA-g-( $\epsilon$ -caprolactone)<sub>7</sub>]<sub>20</sub> to create micelles encapsulated inhibitor drug. The size of the micelle was determined by dynamic light scattering (DLS) (ZetaPlus, Brookhaven, NY). Fluorescent dye, sulfo-Cy5-DBCO (ab wavelength 650nm, Lumiprobe, Maryland), was conjugated to the micelle through DBCO-Azide click chemistry. The product was purified through the PD-10 column and then verified by HPLC at the wavelength of 210nm and 650nm. (Viscotek A4000 column.)

**Results:** The <sup>1</sup>H NMR spectra of the initiator and polymers were consistent with the structures we designed. The micelles all have relatively small diameters (40-50 nm) with a narrow polydispersity (< 0.05) and exhibit good homogeneity according to the DLS data. Consistent absorbance peaks at 210nm and 650nm were observed, indicating the successful conjugation of the fluorescent dye to the nanoscale micelles.

**Conclusion:** Azido-Poly (PEGMA)<sub>20</sub>-b-poly[HEMA-g-( $\epsilon$ -caprolactone)<sub>7</sub>]<sub>20</sub> was successfully synthesized. They are able to form homogenous nanoscale micelles with Poly(PEGMA)<sub>20</sub>-b-poly[HEMA-g-( $\epsilon$ -caprolactone)<sub>7</sub>]<sub>20</sub> and encapsulate drugs. The Azido group on the polymer is capable of conjugating with DBCO through copper-free click chemistry, providing the potential of actively targeting the delivery of drugs through peptides, antibody fragments, and targeting ligands conjugation.

**Keywords:** Polymer micelles, Drug delivery, Nanomedicine

**Program Affiliation:** University Outreach– University of Notre Dame

Abstract Number: 111

## **The Role of DKK3 in the Secretome of Cancer-Associated Fibroblasts of Ovarian Cancer**

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**Background:** Ovarian cancer (OC) is the most lethal gynecologic cancer and the fifth leading cause of cancer deaths in women worldwide. A major contributor to ovarian cancer metastasis and therapy resistance is the cancer secretome, which plays an important role in immune response and facilitates cell-cell communication. Past studies have shown that cancer-associated fibroblasts (CAFs) regulate tumor through the secretion of cytokines, recruitment of tumor cells, and activation of inflammation pathways. However, interactions between the CAF secretome, TME, and immune activation are poorly understood. In this study, we aim to determine how DKK3 in the CAF secretome impacts immune cell infiltration and survival in patients with ovarian cancer.

**Methods:** Dickkopf-related protein 3 (DKK3) was identified as a differentially expressed gene in CAFs compared with normal fibroblasts. Kaplan-Meier curves were generated to understand the relationship between DKK3 expression and survival in patients with OC. We then performed an in vitro co-culture assay of T-cells and murine CAF cells to evaluate an immune profiling panel and T-cell killing panel via flow cytometry. The Proteome Profiler Mouse Cytokine Array (BioTechne) was used to determine effect of DKK3 expression on cytokine levels. Finally, we used the Qiagen Ingenuity Pathway Analysis (IPA) software to determine interaction pathways between DKK3 and the tumor microenvironment.

**Results:** Our survival curve analysis demonstrated that increased DKK3 levels in the CAF secretome are correlated with worse survival outcomes in patients with OC ( $p < 0.005$ ). Immunoprofiling revealed DKK3 was also associated with greater levels of T-cell exhaustion marker TIM3. The inhibition of DKK3 in mCAF cells also led to greater cytokine levels of CXCL12, CXCL2, CXCL10, TIMP-1 and CCL5 ( $p < 0.05$ ), and further IPA analysis revealed that DKK3, CXCL12 and CCL5 are regulated by shared TP53 and TWIST1 transcription factors.

**Conclusion:** DKK3-inhibited cells displayed a significant increase in various cytokines levels that are present in ovarian CAFs, which suggests that DKK3 contributes to the immune-suppressive nature of the tumor microenvironment. Furthermore, pathway analysis shows that DKK3 interacts with CCL5 and CXCL12 to impact shared downstream effects on the cellular and molecular levels. Taken together, we show that DKK3 is a potential target for future drug development efforts that aim to treat ovarian cancer. Future efforts should aim to increase technical and biological replicates in the immune profiling and T-cell killing assay.

**Keywords:** Ovarian cancer, cancer-associated fibroblasts, immune filtration, tumor microenvironment

**Program Affiliation:** University Outreach– University of Notre Dame



Abstract Number: 112

### **Psilocybin's Effects on Neuritogenesis in Cancer Associated Neurons**

Josiah Miller, Head and Neck Surgery, University of Texas MD Anderson Cancer Center

**Background:** Psilocybin is the psychoactive component in magic mushrooms. It has been used medically for anxiety and depression but has only been used in cancer research to reduce the stress and worries regarding death. Psilocybin had also been recorded as increasing neurofilament growth.

**Methods:** The plan was to determine if Psilocybin has any positive biological effects in battling cancer. This Experiment investigated if psilocybin causes any structural or functional changes and specifically when looking at the structural changes, examine filament length, branching, and diameter. Additionally, the effect on firing rate of neurons was tested. The measurements used were neurofilament tracing on the Imaris Program and the Maestro Edge Microelectrode Array.

**Results:** The preliminary variables examined were the dose dependent effect of Psilocybin and the alteration in effect when cancer cells are present. With increasing the amount of Psilocybin there was an increase in number of segments and number of branch points with a decrease in segment length while maintaining the overall filament length.

**Conclusion:** This means that the neurofilament network is becoming more interconnected with microbranching and decreasing the length filaments travel away from the soma. The next step is rerunning the experiments with the cancer associated neurons to confirm results while also examining the electrical and protein expression changes to determine more clearly the effect of Psilocybin on a structural and functional level.

**Keywords:** Psilocybin, Cancer, Structural, Electrical, Imaris

**Program Affiliation:** University Outreach– University of Notre Dame

Abstract Number: 113

## **Use of ATR-PARP inhibitor combination therapy to treat and generate an immune response in PARP inhibitor resistant breast cancer is questioned**

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**Background:** To treat breast cancer tumors independent of BRCAness, PARP inhibitors (PARPi), such as Olaparib, are used as first-line maintenance therapies. However, novel combination therapies, such as PARPi and ATR inhibitor (ATRi) combinations, are being developed in clinical trials due to inevitable tumor PARPi resistance. Although PARPi-ATRi is too cytotoxic for first-line maintenance therapy, this study further elucidates this combination's efficacy in re-sensitizing PARPi-resistant recurrent tumors. Furthermore, in addition to causing unresolved genomic lesions, ATRi/PARPi-ATRi treatments are potentiated in the context of immunotherapy: this study also further assesses whether cytosolic DNA fragments created by ATRi/PARPi-ATRi can trigger the cGAS-STING pathway for a Type I Interferon (IFN) response, such as the production of CCL5 and CXCL10 chemokines, promoting T-cell chemotaxis and antitumor effects.

**Methods:** 4T-1 mouse cells (Wild-Type or 4 uM Olaparib resistant) were cultured and exposed to ATRi (AZD6738) or PARPi(Olaparib)-ATRi treatments at various concentrations for 24 hours. Following RNA extraction and cDNA synthesis, qRT-PCR analyzed CCL5, CXCL10, and IFN $\beta$  gene expression. Treated cells were stained with crystal violet. Western blot of ATR pathway proteins (p-CHK1, RPA32/p-RPA32) was conducted.

**Results:** It is verified ATRi induces DNA damage at high concentrations from presence of p-CHK1, RPA32/p-RPA32 ATR pathway proteins in Western blotting. ATRi-PARPi exhibits synergy in inhibiting cell survival greater than ATRi or PARPi alone, viewed via staining. However, ATRi-PARPi does not show synergy in promoting a Type 1 IFN response of CCL5, CXCL10, and IFN $\beta$  expression. Our data showed that ATRi and ATRi-PARPi can induce Type 1 INF response in WT cells but not in PARPi resistant cells.

**Conclusion:** Unexpectedly, cell death and immune response appears separate. We speculate the generation of DNA fragments from the damaged genome in the ATRi-PARPi treatment or in the resistant line is not as efficient as the ATRi alone or in WT cells, leading to differential effects in Type 1 interferon induction. To gain mechanistic understanding, the effect of ATRi and ATRi-PARPi on DNA damage signaling and cytosolic DNA accumulation should be examined using Western blot and Picogreen. Alternative signaling pathways such as ATM, DNA-PK or AKT should be analyzed to explain p-CHK1 and p-RPA32 in the presence of ATRi or ATRi-PARPi. Observations need to be confirmed in additional cell lines, cancer types, and replicates. Further testing in pre-clinical animal models will potentially guide the choice of ATRi in PARPi resistant tumors.

**Keywords:** PARP inhibitor resistance, PARP inhibitor, ATR inhibitor, Type 1 Interferon response

**Program Affiliation:** University Outreach– University of Notre Dame

## UPWARDS Summer Program

Abstract Number: 114

### **Anaplastic Thyroid Cancer: Gender Discrepancy and Treatment Strategies**

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**Background:** Anaplastic Thyroid Cancer (ATC) is a rare subtype known for its malignancy and difficulty to treat. ATC is characterized by elevated PDL-1 expression and prominent infiltration of dysfunctional and immunosuppressive cells. Previous studies have demonstrated that the incidence of ATC is significantly higher in women; however, men often present with more aggressive disease and poorer prognosis. In this study, we focus on uncovering the mechanisms underlying sex-based differences in ATC to improve treatment strategies and outcomes.

**Methods:** Following inoculation of C57BL/6 male and female mice subcutaneously with an ATC cell line, tumors were collected and analyzed at different time points by flow cytometric analyses. Fecal microbiome from individual mice over the course of ATC progression were assessed by 16S rRNA sequencing. ATC-bearing mice were treated with androgen receptor (AR) inhibitor or immune checkpoint inhibitors (ICIs) (anti-PD-1 and anti-CTLA-4). To understand the connection between gender and microbiome in ATC, fecal microbiome transplant (FMT) was utilized.

**Results:** Our data shows that males display accelerated ATC growth characterized by high infiltration of exhausted T cells compared to females. Interestingly, AR inhibition and ICI treatment appear to be effective in both sexes and depend on time of administration. 16S rRNA sequencing revealed significant differences in microbial composition between males and females over the course of tumor growth, suggesting contribution of sex-related microbiota in ATC progression. In fact, male microbiome predisposes mice to more aggressive ATC tumor growth.

**Conclusion:** In summary, impaired immune activation and microbial dysbiosis may drive differences in tumor growth in males compared to females in ATC. Thus, AR inhibition, ICI and FMT treatment could be promising therapeutic strategies for ATC.

**Keywords:** Anaplastic thyroid cancer (ATC), gender discrepancy, therapeutic approaches

**Program Affiliation:** UPWARDS Summer Program

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## **Pembrolizumab Enhances the Anti-Leukemia Activity of Antigen Specific Cytotoxic T Lymphocytes**

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**Background:** Acute myeloid leukemia (AML) is a type of cancer that affects the blood and bone marrow and is one of the deadliest malignancies. AML occurs when the body makes too many immature white blood cells, which cannot fight infections normally. AML has a 5-year overall survival rate of <35%. Adoptive T cell therapy is a type of immunotherapy that uses cytotoxic T lymphocytes (CTLs) to fight cancer. CTLs are a type of white blood cell that helps the body fight off infections and cancer, by recognizing and attacking cells that are infected with viruses or have become cancerous. In this project, we used a medication called Pembrolizumab. It is a type of cancer treatment that helps the immune system fight cancer. By blocking PD-L1 from binding to its ligand, PD-1, Pembrolizumab can allow the immune system to recognize and attack cancer cells more effectively. The goal of this project is to determine how Pembrolizumab affects and enhances the killing of AML by PR1 and CG1 antigen specific CTL's in vitro and in vivo.

**Methods:** We expanded CG1 and PR1 specific CTLs. We used cytotoxicity assays to determine specific lysis. For the in vivo experiments, we used (NOD SCID gamma) NSG mice engrafted intravenously with HLA-A2 transduced U937 leukemia cells. The expression of immune checkpoint molecules by the CTL and residual AML was measured using standard flow cytometry for human (h) CD45, hCD3, hCD33, and mouse CD45 antibodies. We investigated normal tissue samples to ensure that pembrolizumab does not affect surrounding normal tissues.

**Results:** In vitro cytotoxicity assays showed that the addition of pembrolizumab to antigen-specific CTL resulted in an increase in leukemia killing compared to cells treated with CTL alone. Following the addition of pembrolizumab, colony forming unit (CFU) assays showed fewer colony formations, hence enhanced killing of AML by CTL. In vivo mouse models showed enhanced killing of AML in mice treated with CTL+pembrolizumab. In vitro CFU assays using HLA-A2+ healthy donor bone marrow showed similar bone marrow CFUs between pembrolizumab treated and CTL only treated groups, indicating no change in the specificity of the antigen specific CTL after adding pembrolizumab. Immunohistochemistry staining of mouse tissues showed no added tissue necrosis between CTL and CTL+pembrolizumab groups, indicating that pembrolizumab does not alter CTL specificity to normal tissue.

Conclusion: Pembrolizumab enhances in vivo killing of AML by CG1- and PR1-CTL, with no added toxicity. This strategy could prove beneficial in the setting of adoptive T-cell immunotherapy for AML.

Keywords: Acute Myeloid Leukemia, Pembrolizumab, Cytotoxic T Lymphocytes, PR1 Antigen Specific CTL, CG1 Antigen Specific CTL

Program Affiliation: UPWARDS Summer Program