SPARC & U54 REC

Virtual Scientific Presentations

August 10-12, 2021

11:00-12:50pm

DF/HCC Partnership UMB—DF/HCC

Dana-Farber/Harvard Cancer Center
Continuing Umbrella of Research Experiences (CURE)

Launched in 2002, the Continuing Umbrella of Research Experiences (CURE) Program at Dana-Farber/Harvard Cancer Center (DF/HCC) was an important building block in research training initiatives. Under the direction of the DF/HCC Initiative to Eliminate Cancer Disparities (IECD), this inaugural program set the stage to provide underrepresented minority high school and college students with a stimulating and rewarding hands-on research experience that encourages students to pursue education and training in the biomedical sciences and careers in basic, clinical, nursing, and population science cancer research. In 2017 our student training initiatives were expanded to include two NIH funded grants: Summer Program to Advance Research Careers (SPARC) and
Young Empowered Scientists for ContinUed Research Engagement (Yes for CURE).

Dana-Farber/Harvard Cancer Center Initiative to Eliminate Cancer Disparities

The Initiative to Eliminate Cancer Disparities (IECD) is a center-wide initiative that reflects the high level of commitment of the Cancer Center to addressing cancer disparities and health inequities through its research, education and training, and community engagement activities. The goal of the initiative is to integrate this theme throughout all aspects of the organization by facilitating an intentional and dedicated focus on the reduction/elimination of cancer disparities. The IECD focuses on four key areas: Community engagement and education, Reducing barriers to care, Facilitating minority participation in clinical trials, Fostering diversity in cancer researchers

UMass Boston & Dana-Farber/Harvard Cancer Center Partnership (U54)

Since 2002, the UMass Boston/Dana- Farber Harvard Cancer Center (UMB DF/HCC) Partnership has focused on addressing health disparities in minority populations and on improving research, training, and outreach opportunities for students, faculty, and scientists The UMB DF/HCC Partnership's Research Education Core (REC) provides a portfolio of experiential learning and professional development opportunities for students who want to pursue biomedical research and careers. These opportunities come in the form of evidence-based training that fosters the growth and persistence of scientists, especially those from backgrounds underrepresented in the biomedical sciences, across the career continuum from undergraduate through faculty levels.

For more information about the IECD and our student training programs, contact:

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CURE

SPARC
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SPARC and U54 REC Virtual Scientific Presentations

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Isocitrate Dehydrogenase (IDH) Mutant Glioma Survival Update

Mekdem Adebe

Principal Investigator(s): Daniel Cahill, MD, PhD

Scientific Advisor(s): Yosuke Kitagawa, PhD; Lisa Melamed

Massachusetts General Hospital

Previous research has revealed that the genes encoding Isocitrate dehydrogenase (IDH) are frequently mutated in various human malignancies. These malignancies include gliomas, acute myeloid leukemia, cholangiocarcinoma, chondrosarcoma, and thyroid carcinoma. Currently, much is still unknown about IDH mutation. To better evaluate the efficacy of any treatment, we are collecting patient data of those who have received surgical treatments between 2016-2021. The data is based on their anatomical pathology result and aims to track their survival update from IDH mutant glioma and IDH mutant wild-type glioma. Based on our data, we believe that the surgery is beneficial for IDH mutant glioma patients' survival.

The development of a homemade antibody Ly49F

Juliana Adolphe

Principal Investigator(s): Harvey Cantor, MD

Scientific Advisor(s): Andrew Wight, PhD

Dana-Farber Cancer Institute

Both CD4+ and CD8+ T cell lineages contain cells with regulatory activity, but virtually all research efforts to date have focused on CD4 regulatory T cells. The CD8 lineage is known for its cytotoxic effector T cells. Regulatory CD8 T cells are virtually indistinguishable from their effector counterparts, but they can be recognized by the transcription factor Helios and the surface receptor Ly49F. My lab focuses on the specific function and role that Ly49F plays in CD8+ regulatory T Cells. Since Ly49F is poorly characterized and under-researched, many of the reagents have to be produced in-house. This research aims to optimize a method for producing anti-Ly49F antibodies. A high-density hybridoma culture (30 million cells/ml) in a Wheaton Celline Bioreactor was used to hold and grow hybridoma cell lines. Efficacy was measured by gathering the cells produced after 3 days and analyzing the supernatant obtained from those cells. The supernatant was then filtered in order to determine if there is a high level of HBF719/Ly49F antibodies. In conclusion, this method is effective to produce an anti-Ly49F antibody at a preclinical scale. This antibody can now be used to characterize the role played by Ly49F on regulatory CD8 T cells.

Racial and Ethnic Disparities Persist in BRCA Screening and Genetic Counseling

Danielle Ampofo

Principal Investigator(s): Daniela Dinulescu, PhD

Scientific Advisor(s): Allen Green; Hana Abdirahman; Jessica Tall

Brigham and Women's Hospital

Ovarian cancer is the fifth leading cause of cancer deaths in women with most cases diagnosed in late stages due to the absence of specific symptoms, incomplete understanding of precursor lesions, and a lack of sensitivity in current screening methods. Dr. Daniela Dinulescu's laboratory is conducting innovative translational research to improve early tumor diagnosis by identifying precursor lesions in high-risk BRCA carriers and performing non-invasive screening of exosomal ovarian tumor markers in liquid biopsies. Specifically, they have identified key precursors lesions for 3 of the 4 ovarian cancer subtypes, namely that endometriosis is a precursor for endometrioid and clear cell tumors and that fallopian tubal STIC lesions (Serous Tubal Intraepithelial Carcinoma) are precursors for high grade serous cancer (HGSC), which is the most common and deadliest subtype. Recent studies have shown that early screening using ultrasound imaging and blood biomarkers, such as CA125, are not able to reduce mortality for ovarian cancer. Therefore, it is important to be able to detect precursor lesions and early localized tumors using non-invasive biomarker screening and more sensitive imaging. Moreover, genetic screening of deleterious BRCA1 and 2 mutations and risk reduction surgery in BRCA carriers is key for HGSC prevention. However, racial and ethnic disparities in BRCA testing and genetic counseling continue to persist. New strategies are needed to ensure universal access to insurance paying for BRCA testing and genetic counseling, increasing awareness and advocacy for genetic testing, and improving patient-provider communication.

Understanding Brain Function with fMRI

Sydney Bailey

Principal Investigator(s): David Degras-Valabregue, PhD

University of Massachusetts, Boston

Over the past decades, neuroimaging has enabled considerable advances in understanding the structure and function of the brain. In particular, functional magnetic resonance imaging (fMRI) has contributed to answering fundamental neuroscientific questions relating to the functional specialization and integration of the brain, as well as the relationship between outside stimulus and brain function. But even with this technology, many unanswered questions still exist, like how specialized parts of the brain integrate with each other, how neural activity relates to the brain oxygen level dependent (BOLD) signal measured by fMRI, how large-scale hypothesis testing to detect brain activations can be performed, and how the complex spatio-temporal dependence of fMRI data can be accurately modeled. Solving these problems will help make neuroscientific findings more reliable and reproducible and requires an understanding of the link between neural activity and blood flow inside the brain, which is the basis of fMRI. To investigate complex research questions, I will read and analyze several articles on neurobiology, fMRI technology, as well as the collection, preprocessing and statistical analysis of fMRI data. Over the course of the project, I will learn about these theoretical concepts and will gain practical experience with fMRI data analysis through software like Functional Magnetic Resonance Imaging of the Brain (FMRIB) Software Library (FSL). Continued progress in fMRI data analysis will provide a more sound understanding of brain function in healthy and pathological conditions, and has long-term potential to unlock therapeutic applications to neurological disorders and trauma.

Semi-synthesis of Ubiquitinated PTEN Peptides and Recognition by USP7 Deubiquitinase

Bedphiny Deng

Principal Investigator(s): Phillip Arthur Cole, MD, PhD

Scientific Advisor(s): Sam Whedon, PhD; Reina Iwase; Brad Palanski PhD

Brigham and Women's Hospital; Harvard Medical School

PTEN (phosphatase and TENsin homolog) is a phosphatase enzyme, found in almost all human body tissue, that suppresses the growth of tumors in the human body. PTEN is known to be regulated by ubiquitin post translational modifications that influences its enzymatic function, stability, and subcellular localization. However, detailed biochemical understanding for how ubiquitination influences PTEN's function and regulation is lacking due to the difficulties in preparing a site-specifically and stoichiometrically ubiquitinated protein. PTEN monoubiquitination at the Lys13 position has been shown to be regulated by USP7 deubiquitinase. The purpose of this project is to semi-synthesize various ubiquitinated PTEN peptide mimics and evaluate how different mimics can be deubiquitinated by USP7. The development of a method to install a faithful ubiquitin mimic on PTEN will allow us to perform further biochemical experiments to understand the mechanistic details of PTEN regulation. Ubiquitinated PTEN peptides of four different linkages (native isopeptide bond, aminoalanine-cysteine, aminoalanine-alanine, hydrazide) were prepared by ligating the ubiquitin protein expressed and purified from E.coli to the synthesized PTEN N-terminal peptides (residues 1-16) with various ligation handles.The deubiquitinase activity of USP7 to each of the ubiquitinated peptides were determined by tracking release of ubiquitin products using LC/MS and on the SDS-PAGE gel. The importance of this project is to determine if the peptide mimics are recognized the same as the native isopeptide bond by USP7. We can use the faithful ubiquitin peptide linkages to biochemically study ubiquitinated PTEN and apply the knowledge of PTEN regulation by ubiquitination to develop treatments against tumors that have reduced PTEN activity.

Biases in Face Perception Across Development: The Emotions Children Perceive in a Face are Influenced by the Gender of the Face

Wendell Desir

Principal Investigator(s): Vivian Ciaramitaro, PhD

Scientific Advisor(s): Erinda Morina

University of Massachusetts, Boston

How we perceive a face is influenced by different factors that can bias our perception, such as the influence of society, environment, culture etc. Research has shown that, on average, adults tend to perceive male faces as angrier than female faces, but little is known about the developmental trajectory of such biases or when such biases first emerge. Interestingly, Bayet and colleagues (2015) found a bias in perceiving male faces as angrier than female faces in children as young as 5 years of age. To further investigate the development of this bias, we analyzed data collected in children 6-18 years of age through our work at the Living Laboratory at the Museum of Science Boston. We are still in the process of analyzing our data, but we hypothesize that we will observe the same direction of bias in children as previously characterized in adults, with the possibility of a decreased magnitude of bias in younger children compared to older children. This is a critical problem to investigate and ensure people are aware of because implicit biases can result in discrimination and unfair treatment based on gender and other factors. We hope that bringing to light these implicit biases will make individuals more aware and encourage them to take actions to minimize their biases.

Blood Test for Triple-Negative Breast Cancer

Tishayne Diaz

Principal Investigator(s): Shannon Stott, PhD; Brian V. Nahed, MD

Scientific Advisor(s): Daniel Rabe, PhD; Elizabeth Flynn; Uyen K

Massachusetts General Hospital

Tumor cells release extracellular vesicles (EVs), small nanometer-sized particles that serve as a potential biomarker for cancer. However, while the use of EVs as a diagnostic tool has been steadily rising in popularity, current methods of isolating EVs are lagging behind. Some of these methods are incapable of isolating EVs at a high enough quantity or quality while also requiring expensive, specialized equipment. The “isolation problem” is one of the major obstacles in the field of EV research and even more so for their potential, widespread use for clinical diagnosis and therapeutic applications. Triple-negative breast cancer is one of the hardest breast cancers to treat and patients could benefit from a blood test to predict the best course of treatment for them. We have a novel microfluidic device, the EVHB-chip, that is capable of capturing those extracellular vesicles from cancer patient’s blood. Here, we will share our project where we modified the EVHB-chip to capture the EVs from triple-negative breast cancer patients. In addition to identifying the right antibodies to acquire these EVs, we validated that we had optimal capture using a model system. Following capture, our downstream assays include imaging the EVs and analyzing their RNA. Once we confirmed our device was working, we tested plasma from patients with triple-negative breast cancer for final validation. We determined that this technique of using the herringbone chip was an effective way of capturing tumor-specific extracellular vesicles and can now be expanded to test more cancer patients.

The PI3K/AKT signaling pathway and radiosensitizing properties of Ipatasertib in HNSCC

Emily Fox

Principal Investigator(s): Henning Willers, MD

Scientific Advisor(s): Xiao Pan, PhD; Aliza Rosenkranz

Massachusetts General Hospital

Enhanced activity of the PI3K/AKT signaling pathway has been shown to promote the growth and survival of head and neck squamous cell carcinoma (HNSCC). It is known that radiation therapy activates this pathway which in turn helps cancer cells survive radiation. The current standard of care for HNSCC, chemotherapy concurrent with radiation, results in a 5-year survival rate of only 50-60%, demonstrating a need for intensified treatments to improve outcomes. Our goal is to develop a novel combination therapy that targets PI3K/AKT-mediated radioresistance, thereby decreasing tumor recurrence and improving survival rates. Specifically, we are investigating the radiosensitizing properties of a pharmacological inhibitor of AKT, ipatasertib, in preclinical HNSCC models. Preliminary results from a novel high-throughput screen suggest that ipatasertib radiosensitizes 1/3 of HNSCCs. My task is to validate the screening results in two selected cell lines, UT-SCC14 and FaDu, by utilizing colony survival assays. A DNA damage assay will also be performed to assess how well irradiated HNSCC cells can repair damage with or without ipatasertib. Thus far, I have assessed the sensitivity of these cell lines to ipatasertib alone and confirmed that UT-SCC14 is more sensitive to AKT inhibition. Experiments using drug/radiation combinations are ongoing. Taken together, these experiments will support a forthcoming NCI clinical trial combining ipatasertib with chemoradiation in HNSCC.

Lymph node responses to biomaterial-based cancer vaccines

Joel Gutierrez Estupinan

Principal Investigator(s): David J. Mooney, PhD

Scientific Advisor(s): Alexander J. Najibi

Harvard University

Biomaterial-based vaccines, such as mesoporous silica rod (MSR)-based vaccines, contain scaffolds loaded with tumor components and immune-activating materials to elicit anticancer immune responses and have demonstrated anti-tumor efficacy in several mouse cancer models. Immunotherapy for cancer is a relatively new research field, and MSR vaccines are still being assessed as such vaccines were developed as recently as 2015. Lymph nodes (LNs) are an essential site for priming T cell responses to infection and vaccines. However, how LNs respond at the cellular and molecular levels to MSR vaccines is not entirely known. Here, we evaluated the cellular spatial arrangement and the extracellular matrix (ECM) in LNs following MSR vaccination using immunohistochemistry and imaging. Myeloid cells, as well as T and B cells, were detected, and certain differences were observed in the LN ECM after in vivo subcutaneous injection of the MSR vaccine (experimental group) and phosphate-buffered saline (control group) in mice. Additionally, monocytes were recognized in LNs after staining protocol optimization with secondary antibodies. With this data, LN responses to biomaterial cancer vaccines can be further understood and used to develop better cancer vaccines and support materials-based vaccine research.

Age as a Factor in the Development and Progression of Breast Cancer in Women

Kiani Jacobs

Principal Investigator(s): Sandra McAllister, PhD

Scientific Advisor(s): Milos Spasic, PhD; Qiuchen Guo, PhD

Brigham and Women's Hospital

The specific effects of age and stress on breast cancer are vaguely known. The root cause of increased breast cancer progression and metastasis in younger women in comparison to older women, and the reason why some treatments work better in younger patients than in older patients, is also currently unknown. This research focuses on the characteristics of triple-negative breast cancer (TNBC) samples from different age groups. Since older patients are more likely to have comorbidities, they are sometimes excluded from clinical trials, which deprives researchers from useful data on older TNBC patients. Therefore, it is difficult to compare TNBC in different age groups. The makeup of tumor cells in young TNBC patients differ drastically from that of older patients, which causes their treatment efficacies to differ. For example, CD8+ T-cells, which can detect and kill abnormal cells, and aSMA, which reflects fibroblast presence in a tumor, are markers used to detect structural differences in young and old populations. In order to investigate the quantity of CD8+ T-cells and aSMA present in young and old tumors, tumor tissue from young and old mice were stained and examined using a microscope. The amount of CD8+ cells found in young tumor cells were significantly less than those found in old tumor cells. Knowing the specific makeup of cancer tissue, a more effective and age-specific form of treatment can be discovered and implemented. This research will help understand how this could be achieved and advance precision medicine.

Strategies for Increasing Genetic Screening and Cancer Prevention in BRCA Carriers

Ketura Luldy Jean Louis

Principal Investigator(s): Daniela Dinulescu, PhD

Scientific Advisor(s): Allen Green, Hana Abdirahman, Jessica Tall

Brigham and Women's Hospital

Early detection of ovarian and breast cancer presents significant clinical challenges especially for carriers with deleterious BRCA1 and BRCA2 genetic mutations that confer increased lifetime risk for both diseases. Early detection can save lives and cancer prevention in women with precursor lesions and high-risk BRCA mutations is particularly important for improving prognosis. Many factors contribute to early detection and cancer prevention for breast and ovarian cancer and those include 3D mammography in conjunction with MRIs for younger women with dense breasts, evaluation of family history and genetic counseling, in addition to more complex socio-economic aspects of access to genetic screening and risk reduction surgery. Together with their clinical collaborators, the Dinulescu laboratory has made key contributions and changed the medical paradigm for ovarian cancer screening in high-risk BRCA carriers by identifying the existence of the cell of origin and precursor lesions (i.e., STIC) in the fallopian tube. Detailed evolutionary analysis in patients has now identified a window of 7 years on average between the development of STIC precursor lesions to the development of ovarian carcinoma followed by rapid metastasis to the peritoneum. These results have implications for cancer prevention in high-risk BRCA carriers. Monitoring early tubal lesions and markers have to be included in our efforts towards early detection in high-risk carriers. Moreover, changes in clinical practice are needed to eliminate racial/ethnic disparities and better facilitate early access to BRCA testing and risk-reducing surgery, especially among black BRCA carriers.

Improving breast cancer detection with computer-aided diagnosis

Isabelle Lara

Principal Investigator(s): Daniel Haehn, PhD

University of Massachusetts, Boston

Breast cancer is one of the main causes of death for women today, so much so that researchers are branching out of the traditional approach of human diagnosis to explore computer-aided diagnosis (CAD). CAD systems include artificial intelligence (AI) and other biomedical imaging tools such as conventional neural networks (CNNs). A previously existing web-based framework for annotating breast cancer images will be connected to a cancer detection algorithm (DeepSight, v1.0, manufactured by Intel labs at UMass Boston) to create a pipeline for intelligent annotations. For this, we will use traditional image processing, Python, JavaScript, Unix command line, and machine learning basics such as clustering. When analyzing images through the classifier, if there is a clear indication of growth present in the breast, then the pipeline is successful. CAD systems are the future of medicine, mainly due to their abilities to actively identify early stages of breast cancer which will hopefully result in higher survival rates after more years of use.

Choline kinase A regulates homologous recombination

Thi Le

Principal Investigator(s): Alejandro Gutierrez, MD, PhD

Scientific Advisor(s): Kimberly Bodaar, MD; Natsuko Yamagata

Boston Children's Hospital

Chemotherapy using drugs called alkylating agents is key to treat relapsed/refractory acute leukemias. Tumor cells can develop resistance, which creates the critical need to develop effective therapies. We wanted to know why tumor cells become resistant to nitrogen mustard, a typical alkylating agent. Preliminary data showed that choline kinase A depletion induces nitrogen mustard sensitivity in T-ALL but not in normal hematopoietic progenitors. Therefore, choline kinase A is required for nitrogen mustard resistance. Loss of choline kinase A (CHKA) causes sensitivity to drugs inducing a specific type of DNA damage called DNA adducts. Mammalian cells are known to be capable of repairing DNA adducts using a repair pathway called homologous recombination (HR). CHKA is not known to have a role in HR, but based on our data, we hypothesize that CHKA regulates HR.

To see if CHKA function is required for repairing DNA damage through homologous recombination, we are testing whether cells with genes consisting of two modified GFP sequences - each of which independently makes the cells not fluorescent - can become fluorescent. Two strands of GFP genes were assembled: one has I-SceI site mutant, the other with a missing 5' end. The homologies within the DNA allows them to align. The endonuclease I-SceI will cut the gene strand, then homology-directed repair, if it happens, should make the cells fluorescent. We will test this in cells with CHKA present and cells with CHKA knockout. The result of this research will be important in learning the underlying mechanism in which CHKA responds to DNA damage.

MYC-driven Pediatric Medulloblastoma

Eden Lifshatz

Principal Investigator(s): Pratiti (Mimi) Bandopadhayay, MBBS, PhD

Scientific Advisor(s): Adam Boynton, PhD; Leslie Lupien, PhD; Madison Chacon, MS; Rushil Kumbhani

Dana-Farber Cancer Institute

Medulloblastoma is a common malignant brain tumor that presents in children. Current standard of care such as radiation, surgery, and chemotherapy are associated with major side effects such as cognitive deficits. The major issues stemming from the standard of care have motivated scientists to pursue new effective therapies for medulloblastomas that will lead to improved patient outcomes. Medulloblastoma is divided into four distinct molecular subgroups and the Bandopadhayay lab focuses on Group 3, or MYC-driven, medulloblastoma. Group 3 medulloblastomas are primarily characterized by amplifications in the MYC oncogene, and these MYC-driven tumors have the worst prognosis of all medulloblastomas and are associated with resistance to standard therapy. This has led researchers to develop new target therapies such as BET bromodomain inhibitors (BETi), which are currently being tested in clinical trials at the Dana-Farber Cancer Institute. While these targeted therapies hold promise for the treatment of MYC-driven medulloblastoma, cancer cells often develop resistance to targeted therapies over time. Current research is thus aimed at understanding the mechanisms cancer cells employ to become resistant, and how to overcome them. The Bandopadhayay lab utilizes a variety of methods such as CRISPR/Cas9 screening, gene expression profiling, and ORF screening to identify genes that drive resistance, and may therein serve as new vulnerabilities that can be targeted in combination therapies.

The Impact of mutated CALR-ASXL1 on Myeloproliferative Neoplasms

Brenda Loc

Principal Investigator(s): Ann Mullally, MD

Scientific Advisor(s): Frederike Kramer, PhD

Brigham and Women's Hospital

Myeloproliferative Neoplasms (MPN) are blood cancers that constitutively activate the JAK-STAT signal transduction pathway resulting in the overproduction of red blood cells, white blood cells, or platelets. JAK2, CALR, and MPL are frequently mutated in patients with myeloid malignancies. The presence of the additional sex combs like 1 (ASXL1) mutation is associated with poor prognosis, worsening a patient's condition. Currently, it is unknown how mutations in ASXL1 cooperate with the MPN driver mutations. In order to elucidate these possible connections, mouse models with the ASXL1/CALR, ASXL1, and CALR mutations were analyzed using complete blood counts (CBC), flow cytometry, and microscopic imaging. It was discovered that the double mutant mice had a lot more platelets, lower numbers of red blood cells, and consistent white blood cell levels. Single mutant CALR mice had high platelet levels in comparison to the control mice, and single ASXL1 mutant mice did not have blood disease. Results indicate that double mutant mice tend to have more severe symptoms than the single mutant mice, which is applicable to patients with blood diseases. Given that mice models are excellent representations of the human genome, we will be able to acquire critical information that will allow patients with myelodysplastic syndromes, chronic myelomonocytic leukemia, and acute myeloid leukemia to have access to more potential therapeutics.

The Effect of Aspirin in Colorectal Cancer Prevention

Timothy Long

Principal Investigator(s): David A. Drew, PhD

Scientific Advisor(s): Connor Geraghty, PhD

Massachusetts General Hospital

Colorectal cancer is one of the most common and fatal cancers globally with a five-year survival rate of 63% for all stages. Aspirin regimens are known for the prevention of adenomas and neoplasias in patients with an elevated risk for colorectal cancer. Additionally, aspirin irreversibly inhibits PTGS1 (COX-1) and PTGS2 (COX-2), which are necessary in cellular proliferation and survival in colorectal tumors. However, the mechanism of action of aspirin's chemopreventive properties in terms of gene inhibition and expression are not fully understood. Understanding these properties is important because aspirin can prevent numerous cancers like colorectal, breast, and lung cancers. Leveraging this mechanism of aspirin could allow for increased efficiency in preventative treatments for cancer by understanding how the genes of interest are inhibited. Furthermore, by understanding the impact aspirin has on expression of the genes of interest, specific patients can be identified for an aspirin chemoprevention regimen based on who can benefit the most. To better understand the mechanism of action of aspirin and its chemopreventive properties, a qPCR analysis will be run to measure any inhibition or expression of the genes of interest caused by aspirin or differences in aspirin dosage. The results of the analysis will be used to guide later studies on the effect of aspirin on gene expression. Aspirin is hypothesized to dose-dependently influence the expression of the targeted genes. Through this work we will improve our understanding of molecular targets for aspirin chemoprevention with the goal of increasing efficacy and decreasing the occurrence of colorectal adenomas.

Uncovering the Health Care Experience of Brazilian Immigrant Cancer Patients in Massachusetts (MA)

Beatriz Louzado

Principal Investigator(s): Eduardo Siqueira, PhD

Scientific Advisor(s): Laura Warwick, MD; Anne Revette, PhD; Kirsten Meisinger, MD; Elisa Tristan-Cheever, MPH

University of Massachusetts, Boston

In order to cater to certain communities, people rely on research to form treatments, itineraries, and even to further research on various topics. In Massachusetts (MA), accommodating the Brazilian community is challenging as they are often labeled as Latinx members, and grouped with several other ethnicities who have their own singular itineraries. This situation makes it difficult to better treat Brazilians taking into consideration their specific socio-economic and cultural aspects. Due to the unavailable public data in reference to that, our study aims to identify the treatment pathways of Brazilian immigrant cancer patients in MA, and potential barriers and facilitators along the access to healthcare. As an underserved community, it can often be very difficult to find and reach out to these individuals due to reasons such as language barrier. By conducting this research, we allow for Brazilians to gain a voice in medicine. We will interview twenty Brazilian cancer patients in MA who were treated or are in treatment. These interviews have questions about personal information, patient's access to care, and continuity and coordination of care provided to them by health care services in MA. We expect to find different trends and themes that could lead to a larger study that delves into treatment pathways that are specific to the Brazilian community, which can also help reduce cancer health disparities in the state as a whole.

Knowledge, Awareness, Practices and Acceptability of the HPV Vaccine Among College Students at a Majority-Minority University in Massachusetts

Maryann Mucemi

Principal Investigator(s): Ana Cristina Lindsay, PhD, MPH, DDS

University of Massachusetts, Boston

The human papillomavirus (HPV) vaccine is the best preventative measure against HPV infection. Despite recent increases in vaccination rates, HPV remains the most common sexually transmitted infection in the United States (US). Unvaccinated college students are at high risk of HPV infection given changes in lifestyle and social norms resulting from the transition to more independence. Although the ideal time for receiving the HPV vaccine is in late childhood and early adolescence, catch-up vaccination is recommended at ages 26 and 21 for women and men, respectively, who have not been previously vaccinated. However, evidence shows that HPV vaccination remains low among college students, and rates might be especially low among minority and foreign-born students. Therefore, the objective of this cross-sectional study is to examine HPV knowledge, awareness, and behaviors (KAB), and acceptability of the HPV vaccine among undergraduate college students attending a majority-minority university in Massachusetts. Data will be collected using an IRB-approved anonymous online survey administered to a sample of ~300 college students between August and December 2021. Data will be analyzed to describe the prevalence and factors associated with HPV KAB and acceptability of the HPV vaccine and to compare findings among racial ethnic minority groups. Understanding college-aged individuals' HPV KAB and acceptability of the HPV vaccine is critical to developing effective on-campus health education and vaccine promotion interventions, and ultimately reducing the risk of HPV and HPV-related cancers.

Functional MRI Data Analysis: Overview

Jawahir Noor

Principal Investigator(s): David Degras-Valabregue, PhD

University of Massachusetts, Boston

Functional MRI (fMRI) has been extensively used for studying brain activity by detecting changes associated with blood flow. In this report, we provide a brief overview of fMRI data analysis, specifically the problem of human brain mapping and its significance in neuroscience. Brain mapping is important because it helps us understand how the brain works and specifically its functional specialization. Many challenges remain in mapping the human brain, that is, detecting which brain regions become differentially activated when performing a given motor, cognitive, or psychological task. For example: the variability of the hemodynamic response function across the brain, the complex spatio-temporal dependencies in the data, and the large-scale hypothesis testing required to detect brain activations. Functional MRI employs MRI to image dynamic changes in brain tissue that are caused by changes in neural metabolism; specifically, fMRI, relies on blood oxygenation level dependent (BOLD) changes in the brain tissue. An important modelling and statistical hypothesis testing method that is used in almost all areas of neuroimaging is the General Linear Model (GLM). GLM models an observed signal which could be a BOLD time-series in a given brain voxel, in terms of one or more explanatory variables, also known as regressors. Collected data then undergoes preprocessing, which involves recognition of outlier data followed by multiple steps to correct for noise, motion, signal drifts, slice timing discrepancies, and spatial distortions. This summer we analyzed a sample fMRI data set based on the flanker task, which is used to assess cognitive control.

Qualitative Data Analysis of Interviews in the "Move Together Boston." Digital Intervention for Black/African American Women Breast Cancer Survivors

Shree Patel

Principal Investigator(s): Julie Wright, PhD; Catherine Marinac, PhD

Scientific Advisor(s): Meghan Underhill-Blazey, PhD, APRN; Barbara Halpenny, MA; Jessica Whiteley, PhD

University of Massachusetts, Boston; Dana-Farber Cancer Institute

Studies have shown that in the United States, breast cancer accounts for more cancer deaths in women than any other cancer except lung cancer. Black/African American women have a higher risk of mortality when diagnosed with breast cancer than women from other racial backgrounds. Reducing sedentary time and increasing physical activity can contribute to improving health outcomes in addition to reducing risk for breast cancer and breast cancer recurrence. Digital health interventions are one strategy to help individuals reduce sedentary time and increase physical activity. The purpose of this qualitative analysis is to obtain the perspectives of Black/African American breast cancer survivors about their needs and preferences to promote sitting less and moving more. This study is a part of a larger study which aims to create a family dyad-based digital intervention for Black/African American breast cancer survivors and their first-degree relatives that helps to reduce sedentary time and increase physical activity. A total of nine interviews were conducted with breast cancer survivors. These interviews were recorded after participants provided consent and notes were also taken of the interviews. Interviews and field notes were content analyzed to identify common themes between the interviews. Data analysis is underway and key themes will be summarized as well as exemplar quotes provided. Findings from the interviews will inform the development of the digital health intervention.

Effects of Microenvironment on Mantle Cell Lymphoma Growth and Drug Response

Romaisa Shahid

Principal Investigator(s): Mark Murakami, MD

Scientific Advisor(s): Nezha Senhaji, PhD

Dana-Farber Cancer Institute

Mantle cell lymphoma (MCL) is an aggressive form of B-cell non-Hodgkin lymphoma accounting for 5% of cases in the United States. Despite considerable advances in treatment leading to increased rates of complete remission (CR) and improved survival, virtually all patients relapse and eventually become treatment-refractory. This suggests that a population of lymphoma cells persists in the face of treatment and ultimately triggers relapse. Treatment strategies capable of eradicating these residual lymphoma populations therefore represent an unmet medical need, whose fulfillment requires broader understanding of MCL biology. Signals from the tumor microenvironment (TME) have been reported to promote cell proliferation, survival, and drug resistance in MCL and many related disorders. Though the detailed pathogenic role of the TME has yet to be clearly defined in MCL, published reports have implicated cross talk between MCL and stromal cells in disease progression through promotion of cell survival and growth, thereby reducing their sensitivity to targeted therapies (3, 2). Here we aimed to optimize a short-term ex vivo culture system of primary patient-derived MCL cells. Cells were isolated from peripheral blood or bone marrow by Ficoll-Paque and cultured in the presence or absence of HS-5 stromal cells and with or without cytokines (interleukin-10, B-cell activating factor, insulin-like growth factor-1, and interleukin-6). Culture conditions were iteratively adjusted to achieve levels of viability most conducive to sensitive assay of functional drug sensitivity. These optimized conditions will be used to test the efficacy of targeted drug therapies that are used in clinical settings. Ultimately, we will also use these conditions to test ex vivo doses of venetoclax and acalabrutinib that recapitulate in situ drug levels plus additional combinational partners and novel therapies.

AI used in the detection of breast cancer

Patricia Somera

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The medical field increasingly uses artificial intelligence and machine learning methods to detect diseases such as breast cancer. These methods, especially when paired with human experts such as gynecologists and radiologists, allow for early detection of breast cancer when they look at mammographic images, which is crucial for successful treatment. We are working on an intelligent breast cancer diagnostic pipeline that combines an existing web-based annotation called DeepHealth, which allows us to annotate mammographic images as Dicom files, with a state-of-the-art lesion detection algorithm. Our machine learning algorithm of choice is DeepSight, a mammography research software which runs on two supercomputers at UMass Boston. We will connect the annotation tool to DeepSight by using the images from Deepsight to be annotated to Deephealth so experts can highlight lesions and compare them to the automatic detection result. Improvements in early detection could help in the long run by having fair and consistent screening instead of push-backs due to false-positive rates.

The role of transposons in mood disorders

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Transposable Elements (TEs) are also known as “jumping genes” or transposons, which are DNA sequences that can move from one location on the genome to another and change its position within a genome, sometimes creating or reversing mutations and modifying the whole amount of DNA held within one copy of a single complete genome. For decades most scientists thought transposons were useless or junk DNA; however, recent discoveries indicate that TEs can regulate the function of neurons. Also, TEs are expressed and active in the brain, challenging the dogma that neuronal genomes are static and revealing that they are susceptible to somatic genomic alterations. Recently, the identification of active TEs in several different human brain regions suggests that TEs play a role in normal brain development and adult physiology and quite possibly in psychiatric disorders. This review will show there is potential involvement of transposable elements in mood disorders, specifically Major Depressive Disorder (MDD) and Bipolar Disorder (BD).

Chitosan Functionalized EGaIn Nanoparticles

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Photodynamic therapy is used in cancer treatment due to its favorable effect on multidrug resistant cancer cells and its low toxicity on healthy cells. Photodynamic therapy makes use of ligand-functionalized-metal-nanoparticles ability to target specific cancer cells and photoreact to release desired drugs. Liquid metal is a popular new material for photodynamic therapy and less toxic, therefore we will optimize the functionalization of the eutectic Gallium Indium (EGaIn) surface. Herein, we report on the synthesis of chitosan covered liquid metal, specifically eutectic Gallium Indium (EGaIn) nanoparticles as a function of pH. Chitosan is dissolved in acetic acid or glycolic acid with varying amounts of NaOH to adjust the pH within the range from 3 to 7. EGaIn is added to each solution and ultrasonicated to generate chitosan coated EGaIn nanoparticles with a desired size of less than 200 nm. UV-Vis Spectroscopy and Raman Spectroscopy are used to confirm the attachment of chitosan onto the EGaIn nanoparticles. Dynamic Light Scattering (DLS) and Scanning Electron Microscope (SEM) are used to determine the morphological properties such as shape and size of the nanoparticles. In conclusion, we discovered that the optimal pH for synthesizing chitosan functionalized EGaIn nanoparticle was pH 5 for acetic acid solvent and pH 3 for glycolic acid solvent as these conditions generated the most desirable size of nanoparticle, approximately 200 nm or less. With a nanoparticle size of approximately 200 nm or less, existing cancer treatment drugs such as verteporfin could be attached to the nanoparticle and used in photodynamic therapy in the treatment of cancers.

How do Mammalian Stress granules and P bodies interact with one another and the role of UBAP2L?

Tiffany Ye

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Stress granules (SGs) and processing bodies (PBs) are visible membraneless ribonucleoprotein-based cellular compartments that assemble in response to stress. We are trying to determine the mechanisms by which UBAP2L, a protein involved in ubiquitination, contributes to the formation of SGs with attached PBs upon stress. However, UBAP2L has yet to be studied from the perspective of SGs with PBs and docking PBs. Filling in this gap in knowledge is important because determining how the mammalian SGs and PBs respond to stress and understanding the interaction may help us explain the stress response, which pertains to different diseases. This research investigates how UBAP2L contributes to the formation of SGs with attached PBs upon stress. The approach involved taking two cell lines, one wild type and one knockout with UBAP2L, that were treated with Arsenite as the stressor. The number of SGs, PBs, SGs with PBs, and PBs docking were counted and compared. In the UBAP2L knockout there was a decrease in the amount of SGs, PBs, SGs with PBs, and PBs docking when compared to wild type. These results will help us understand the relationship between UBAP2L and SGs and PBs, which may contribute to understanding how mammalian cells respond to stress.

Regulation of Capicua by the ERK signaling pathway

Wootchelmine Christalin

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Capicua (Cic) is a transcriptional repressor downstream of the extracellular signal regulated kinase (ERK) pathway. Phosphorylation of Cic by ERK is a critical regulatory event in ERK signal transduction that leads to the downregulation of Cic function. This results in relief of repression of Cic target genes that regulate growth and tissue patterning, leading to the proper development of multiple organs in Drosophila. Loss of function mutations in the Cic gene has been observed in different tumors such as breast cancer and oligodendroglioma. From previous mammalian and fly studies, four potential mechanisms have been proposed to explain Cic downregulation: loss of DNA binding, export to cytoplasm, protein degradation, and loss of binding to corepressors. However, the exact molecular mechanisms by which ERK phosphorylation controls Cic repressor activity are still not well understood. In this study, the potential ERK-dependent phosphorylation sites on the Drosophila Cic were identified by in vitro kinase assay followed by mass spectrometry. Alanine mutagenesis of the putative sites was done to create mutant Cic variants. We are currently focused on functionally validating these Cic variants by using UAS-GAL4-driven tissue-specific overexpression, specifically looking at wing venation patterns and the ventralization phenotypes of dorsal appendages in Drosophila, which are under Cic regulation. These functional screens in vivo have revealed a region in Cic that is required for its downregulation via ERK phosphorylation. The mutant Cic variants resulted in stronger overexpression phenotypes, compared to wild-type Cic. This research will uncover the molecular mechanisms of ERK-dependent control of Cic repressor activity.

CG14767 as a novel regulator of the Hippo/Yorkie tumor suppressor pathway

Saja El-Saudi

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The Hippo pathway is a conserved signaling pathway essential for the proper regulation of organ growth in Drosophila and vertebrates. It is known that when there is an activation of the Hippo pathway, there is no abnormal cell proliferation. However, if the Hippo pathway is inactive and an over-expression of yorkie or yorkie-specific genes occur during that inactivation period, this can lead to abnormal cellular proliferation. For this reason, the Hippo pathway is known as a tumor suppressor pathway. Mass spectrometry was performed to learn about the interactors of the yorkie protein, and the interactome of the yorkie protein was identified. This data was then used to focus on some of the novel regulators of yorkie. CG14767 was identified as one of the novel regulators of yorkie. CG14767 is an uncharacterized protein and its function in Drosophila is not majorly known. Our research is attempting to uncover the role of the CG protein in the Hippo/Yorkie tumor suppressor pathway. To do this, a coimmunoprecipitation assay has been performed that shows the binding between this protein and Yorkie, and it has been discovered that it is indeed dependent upon that. Moreover, colocalization studies have also been performed and they show that these two proteins colocalize well. With the coimmunoprecipitation assays and colocalization studies in mind, the current research focuses on whether this uncharacterized protein has any genetic effect on the Yorkie induced overgrowth. Whether it suppresses or enhances the overgrowth, this will tell us if it is a novel interactor of this Hippo pathway or not. Further research can be done to learn more about the molecular role of CG14767 at the cellular and signaling levels.

The molecular basis of size regulation in late-stage axolotl limb regeneration

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The axolotl (Ambystoma mexicanum) is frequently used to study regeneration because of its ability to reliably regenerate fully patterned limbs that are almost identical to intact, un-amputated limbs. There are two stages of regeneration. During the first stage, a blastema forms and the limb is initially patterned. During the second stage, the fully patterned “tiny limb” grows in size until it is proportional to the size of the animal. The goal of this project is to identify the potential molecular mechanism by which growth and size are regulated in the regenerate. There are several growth factors that are known to drive growth during the blastema stage of regeneration, and many of these growth factors, including BMPs, also have an elevated expression in the tiny limb. This project tests whether BMP signaling is required for growth during the tiny limb stage of regeneration using, in vivo, molecular biology, and biochemistry-based assays. To do this, we used a BMP inhibitor to treat axolotls during the tiny limb stage of regeneration. We found that the inhibition of BMP caused a decrease in the growth of the tiny limb without impacting the overall growth of the body length. This indicates that BMP signaling is required for growth in the tiny limb stage of regeneration. Next, we will determine if the inhibition of BMP signaling decreases growth in the tiny limb by impacting cell size, cell proliferation or cell death, by performing immunofluorescence and histochemistry on regenerated limb tissues.

A qualitative content analysis of opioid use smartphone apps

Baby Lenga Kalemba

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Health care providers in the United States have been using opioids as analgesics for pain treatment for centuries in patients who experience mild to chronic pain from cancer treatments, sports injuries, and surgical procedures. However, according to the Center for Disease Control and Prevention (CDC) and the National Center for Health Statistics (NCHS), prescription painkillers are commonly misused and overdosed by their users, making opioid overdose a national crisis. In 2019 the NCHS reported that among all ages and gender, more than 49,860 Americans died from opioid overdose alone, including prescription and illicit opioids. Moreover, the recent COVID-19 pandemic distracted the delivery of health care services, leaving a significant number of people with opioid use dependency with a lack of access to providers and, therefore, treatment. The smartphone applications which currently exist were developed to serve as mobile health (mHealth) technologies to combat the opioid crisis. Whether these apps/mobile health technologies are for the public or are only accessible through recommendations from clinicians is unclear. Given that there is a consistent rise in accessibility of smartphone app users, the purpose of this review is to conduct a qualitative content analysis examining if the content in Android apps has shifted since the onset of the COVID-19 pandemic. The content analysis will focus on the top fifteen apps on the Android Play Store. Apps were identified by using keywords such as “opioids,” “opioid prevention,” and “opioid overdose.” The apps will then be coded by two independent raters who will identify themes, resolve discrepancies, and eventually reach a consensus on the kinds of content provided by these apps. Ensuring that there is correct and safe content within the app environment is essential because smartphone apps serve as tools to help combat the high rate of opioid overdose by facilitating bystander administration of drugs, providing information, or helping with recovery.

Assessing cultural appropriateness of digital health apps for Black/ African American breast cancer survivors.

Tyrza Milord

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Research shows that Black/African American breast cancer survivors have a higher mortality rate than White breast cancer survivors. Some of the barriers Black/African American breast cancer survivors face are accessibility, distrust in the health care system, economic barriers, lack of resources, and lack of a support system. Less sedentary time and more physical activity can improve breast cancer survivors’ quality of life and potentially cancer outcomes. Digital health interventions, such as apps, might be one way to provide breast cancer survivors support to sit less and move more. The present study assesses 76 apps identified through a keyword search (physical activity or sedentary time or breast cancer) in Google Play and/ or Apple Store. Apps were assessed using an adapted rating scale to evaluate if content was culturally tailored or appropriate to Black/African American breast cancer survivors. The app review results are pending. The frequency of adequate cultural appropriateness in ratings tailored for Black or African American breast cancer survivors will be described. Preliminary findings indicate that apps are not culturally tailored to the Black community. The information gathered from the evaluation will help create an app tailored explicitly to Black or African American breast cancer survivors. This app will then allow the Black community to feel supported and represented. Additionally, it will provide resources and a social network to its participants and encourage them to move more and engage in physical activity.

TISMO: syngeneic mouse tumor database to model tumor immunity and immunotherapy response

Nofal Ouardaoui

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Syngeneic mouse models are tumors derived from murine cancer cells engrafted on genetically identical mouse strains. They are widely used tools for studying tumor immunity and immunotherapy response in the context of a fully functional murine immune system. Large volumes of syngeneic mouse tumor expression profiles under different immunotherapy treatments have been generated, although a lack of systematic collection and analysis makes data reuse challenging. We present Tumor Immune Syngeneic MOuse (TISMO), a database with an extensive collection of syngeneic mouse model profiles with interactive visualization features. TISMO contains 600 in vitro RNA-seq samples from 49 syngeneic cancer cell lines across 23 cancer types, of which 191 underwent cytokine treatment. TISMO also includes 1,525 in vivo RNA-seq samples from 68 syngeneic mouse tumor models across 19 cancer types, of which 832 were from immune checkpoint blockade (ICB) studies. We manually annotated the sample metadata, such as cell line, mouse strain, transplantation site, treatment, response status, and uniformly processed and quality-controlled the RNA-seq data. Besides data download, TISMO provides interactive web interfaces to investigate whether specific gene expression, pathway enrichment, or immune infiltration level is associated with differential immunotherapy response. TISMO is available at http://tismo.cistrome.org.

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