Research Summaries

Johns Hopkins University

Integrated molecular and clinical analysis of BRAF-mutant glioma in adults

Mutations in the gene BRAF are targetable with FDA-approved therapy. These mutations are frequent in some types of childhood brain cancer, but less understood in adults. Dr. Karisa Schreck et al. (2023) examined BRAF mutations in adult brain cancer. In a cohort study of more than 300 patients, the research team found some types of BRAF mutations are much more common in adults than children, and some types were found in more aggressive cancers than others. They also found that having a specific BRAF mutation (V600E), was associated with sensitivity to FDA-approved targeted therapy, and likely extends life expectancy. This study shows how important it is to look for BRAF alterations in the cancers adults develop, and to consider appropriate targeted therapy.

https://www.nature.com/articles/s41698-023-00359-y

Small molecule haptens trigger immunity against glioblastoma

Keep Punching funded Dr. Amir Ameri et al. (2023) in a project tasked with exploring how the delivery of a small molecule named a hapten to reduce the resistance of primary brain tumors to immunotherapy. The utilization of haptens in other experiments with melanoma have proven to be promising. The researchers injected mice with hapten and in another condition hapten along with immunotherapy in order to assess mouse survival rates. Measurement of the mouse survival rates serve as a way to understand the impact haptens may have on primary brain tumors.

Serum Biomarkers for Monitoring Blood-Brain Barrier Integrity Modulation

Keep Punching in 2023 funded the project of Drs. Kamson, Holdhoff, Knezevic and Viveka Chinnasamy to develop a blood test to track changes in the integrity of the blood brain barrier in patients with gliomas. The project aims to identify promising blood markers to be studied prospectively to guide patient-specific steroid management. A marker that predicts the benefit and duration of steroid therapy may reduce the risk of complications and to optimize symptom management for most patients with brain tumors.

Incidence and clinicopathologic features of H3 K27M mutations in adults with radiographically-determined midline gliomas

Dr. Matthias Holdhoff et al. (2019) conducted a study to gain an understanding of the incidence of the H3 K27M mutation in adult patients with midline diffuse gliomas. In this effort, they reviewed all patients with gliomas in the midline region at The Johns Hopkins Hospital between 2007 and 2017 and used immunohistochemistry to assess their tissue for these genetic variants. The research determined that H3 K27M mutations are fairly common in adults and that although prognosis is thought to be poor with this genetic variation, the data indicated that this idea may not be entirely true as some adult patients exceeded timeline expectations, yet it is poor in children. Based on these findings, treatments that target H3F3A and HIST1H3B/C may be promising.

Immune Dynamic in Aggressive Meningioma

Keep Punching has funded Dr. Sushant Puri's research aimed to identify the immune cells in meningiomas using a cutting-edge technique called long-read sequencing. This will provide novel insights into how these differ across different grades of meningioma. A more comprehensive understanding of the genetics of meningioma will help discover new treatment options for meningioma for which treatment options are limited.

Neuro-Oncology Caregiver Initiative

In 2024, Keep Punching funded Dr. Danielle Bazer's et al. caregiver initiative. This project is designed to gain a greater understanding of the unique challenges that caregivers of patients with brain tumors face. Additionally, they aim to develop a caregiver burn-out screening tool for neuro-oncology caregivers. Ultimately, this project should inform future caregiver research in order to create specific interventions tailored to the needs of caregivers.

Columbia University

Glioblastoma Tumor Tissue Analysis after Clinical Exposure to a New mTOR inhibitor

Recurrent glioblastoma patients have very limited treatment options. A significant percentage of glioblastomas have increased activity of the certain pathways that lead to tumor proliferation.Inhibitors of these pathways have shown poor efficacy. One of the most challenging issues in developing effective treatments is ensuring that the drug crossed the complex blood brain barrier. To overcome this challenge, a novel inhibitor was used. To assess the efficacy of this drug, tissue samples were obtained and analyzed for the presence of multiple biomarkers that serve as proxy measures for proliferation and cell death.

PD-1 inhibitors Pembrolizumab and Nivolumab in Participants with Recurrent or Progressive Gliomas

Beginning in 2015, Dr. Fabio Iwamato conducted research to determine the efficacy of PD-1 inhibitors on glioblastomas. PD-1 is a protein that is found on T-cells. PD-1 inhibitors such as Pembrolizumab and Nivolumab increase the immune response leading to tumor suppressing effects. These drugs have shown promise in other forms of cancer and this research wanted to assess the effects on brain cancer. The goal was to understand the relationship between the number of mutations and the response rate of the brain tumor to the PD-1 inhibitor. Patients with BRAF, PTPN1, and NF mutations were more responsive to the drugs, while PTEN mutations were less receptive.

pERK

Dr. Fabio Iwamato et al. (2021) explored the response of ERK1/2 phosphorylation in patients that responded to the PD-1 inhibitors and those that have received no immunotherapy. They used immunostaining techniques to assess the presence of antigens in a tissue sample. 53 samples from different patients were used. This research was conducted to gain a better understanding of the molecular pathways that are activated as a result of treatment with the inhibitors. This knowledge can provide multiple insights in order to develop treatments as a more comprehensive understanding of the cellular mechanisms has been elucidated.

Immune and genomic correlates of response to anti-PD-1 immunotherapy in glioblastoma

Dr. Fabio Iwamato et al. (2019) explored variations in the responses of patients with glioblastoma to immunotherapy. Patients with various types of cancers may have improved results following immunotherapy, but this response was not observed in patients with glioblastoma. The research found that mutations in the tumor-suppressor gene, PTEN, is associated with immunosuppressive effects. Inhibition of the MAPK pathway has been shown to increase the response to immunotherapy. The potential implications of this research are profound as molecular markers have been identified as targets of interest in the development of treatments along with tailored plans for each patient with glioblastoma.

Use of spatial transcriptomics to evaluate the glioblastoma cell state and the tumor microenvironment in glioblastomas treated with ST101

Keep Punching in 2024 funded Dr. Fabio Iwamato's research on the potential for creating novel therapeutics targeting master regulator proteins. Andrea Califano and Antonio Iavarone in 2010 determined that master regulators are behind the genetic classification of select glioblastomas, specifically C/EBPβ. The current research is going to assess tumor samples from patients with brain tumors using spatial transcriptomics to determine the impact of antagonists of the master regulator.

University of Maryland Medical Center

Patient preferences for reducing adverse events following brain irradiation

Keep Punching in 2015 funded Dr. Mark Mishra's study that evaluated patient preferences relating to brain irradiation ultimately to inform future health practices. He used a discrete choice experiment where patients with primary brain malignancies were given an opportunity to share the side effects that they have experienced due to radiation therapy. The results from this research should provide critical information to physicians and scientists to design care plans that account for the preferences of patients.

LITT

In 2021, Keep Punching funded Dr. Mark Mishra's and Dr. Graeme Woodworth's research on the combination of laser interstitial thermal therapy (LITT) and radiation therapy to treat recurrent gliomas. LITT is a minimally invasive procedure where thermal energy is used to sensitize and treat brain tumors. This method could prove to be advantageous for patients with unresectable and/or recurrent tumors. This clinical trial is designed to assess the safety, feasibility, and early evidence of efficacy of the combination LITT plus radiotherapy and inform future clinical applications.