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FUNDING REPORT

Duke Medicine

A Guided Immunotoxin Missile for
Treatment of Malignant Brain Tumors

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There are approximately 15,000 new cases of glioblastoma multiforme (GBM) in the U.S. each year, and the standard of care treatment gives only an average survival of 15 months after diagnosis. Once the tumors have failed standard of care treatment, there truly are no additional treatments.

Two novel immune approaches have been developed at the Preston Robert Tisch Brain Tumor Center at Duke. Guided by principal investigator Darell Bigner, M.D., Ph.D. The two approaches recently received nearly \$7 million in funding from the National Cancer Institute.

The funding supports additional animal and human studies for two separate immunotherapies – one using a modified polio virus and another using a bacterial immunotoxin to attack lethal glioblastoma tumors – that are already showing promise in early clinical trials.

The polio virus therapy is currently in a phase 1 study and was the subject of a lengthy report on 60 minutes in March. The therapy uses deactivated poliovirus, which is predisposed to selectively attach to tumor cells and not healthy cells. After surgically injecting the modified virus into the brain tumor, the immune system goes to work, attacking the virus-infused tumor.

IMMUNOTOXIN MISSILE

The collaboration between Dr. Ira Pastan at the National Cancer Institute and Dr. Bigner's team at Duke, has helped develop an immunotoxin missile that identifies two of the most important "driver-oncogene" molecules present in 95% of glioblastomas, EGFRwt and EGFRvIII. These two molecules, cause the uncontrolled growth and proliferation of glioblastoma cells. To help increase the effectiveness and avoid the blood brain barrier, the team has developed a new methodology to appropriately place multiple small tubes directly into a patients tumor by using PET and MRI scanning to ensure the immunotoxin



missile has gone to the right place in the tumor. The immunotoxin will kill tumor cells with very high efficiency and will trigger the body's immune system to kill the remaining tumor cells. This is the only guided immunotoxin treatment that targets both of these molecules. Previous treatments have only been able to attack cells with one of these two gene products.

The grant from the National Cancer Institute will help fund the production of the clinical grade immunotoxin, obtain an Investigational New Drug Permit from the FDA, and carry out Phase I and II clinical trials.

The hope is that this will be a highly effective treatment, which will ultimately be compatible with the poliovirus treatment after all the clinical trials necessary for FDA approval of both agents are complete. It is anticipated by combining the two treatments there will be a significant increase in high quality survival and cures.

UNCLE KORY FOUNDATION GRANT

While the National Institute grant will help accelerate the immunotoxin research, there is still additional funding needed to help expand the number of patients in the trials. To date, four patients have been treated successfully, all of who are doing well with no significant side effects. The short-term goal is to determine the ideal dose for treatment. The team will be increasing the administered dose after treating two patients at each higher dose. Once they determine the maximum tolerated dose, they will treat 20 patients at that dose to determine the true response rate. The Uncle Kory Foundation (UKF) will be providing the Preston Robert Tisch Brain Tumor Center at Duke a \$100,000 grant to specifically cover patient expenses as part of expanding this trial.

Ultimately, by combining these two immunotherapies (poliovirus and immunotoxin missile) in a treatment that circumvents the blood brain barrier, and has seen early success, we are hoping this will lead to longer lifespans and potentially a cure for this terrible disease.



THE UNCLE KORY MISSION

The Uncle Kory Foundation looks forward to collaborating with like-minded individuals and organizations to inspire and bring hope to those who are facing such life-altering challenges. GBM accounts for approximately 17 percent of all brain tumors and increases in frequency with age, affecting more men than women. Unfortunately for all of them, the prognosis is grim, as few will live to see 3 years after diagnosis. Most patients will live only 6-18 months. The entire family is affected by the devastating news. The Uncle Kory Foundation's mission is to advance innovative and collaborative brain cancer research to specifically improve the survival rate and treatment of those diagnosed with Glioblastoma (GBM).

For more information or to make a donation, please visit [UNCLEKORY.ORG](https://www.unclekory.org)

