IMPACT REPORT

UCLA Neuro-Oncology Program
David Geffen School of Medicine at UCLA

Activity Summary 2015

Uncle Kory
FOUNDATION

We've got brain cancer surrounded.

IMPACT REPORT: UCLA NEURO-ONCOLOGY PROGRAM
DAVID GEFFEN SCHOOL OF MEDICINE AT UCLA

In 2014 the Uncle Kory Foundation (UKF) made its first financial contribution to support brain cancer research to the UCLA Neuro-Oncology Program. The foundation contributed $250,000 in discretionary funding to be applied to its highest priority endeavors aimed at eliminating brain cancer. The discretionary nature of this funding is critical because it allows the program to be responsive to the most time sensitive aspects of its work. These funds dramatically impacted the program's ability to affect discovery, execute promising clinical trials, and evaluate outcomes in order to develop better treatments.

Over the past year the Uncle Kory Foundation has provided the UCLA Neuro-Oncology Program with $250,000 in discretionary funding to be applied to its highest priority endeavors aimed at eliminating brain cancer. The discretionary nature of this funding is critical because it allows the program to be responsive to the most time sensitive aspects of its work. These funds dramatically impact the program's ability to affect discovery, execute promising clinical trials, and evaluate outcomes in order to develop better treatments.

DISCOVERY

The UCLA Neuro-Oncology Program's discovery process entails hypothesis generation and testing as well as basic and translational research. The program's researchers utilize vast resources of tissue, imaging, and outcome evaluation. This discovery research might be performed within the program or in collaboration with other researchers at UCLA or outside the institution. The Program also utilizes the provisional materials gained from its clinical trials to generate or test hypothesis for discovery. The discovery process results in publications, grant applications and, most important, the development of new clinical trials and their evaluation, with an aim of offering better treatments to patients. The UCLA Neuro-Oncology Program typically publishes 20-30 manuscripts each year in such high impact journals as Science, PNAS, New England Journal of Medicine, Nature, and others. The program's grant funding comes from the National Institute of Health and private foundations.

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Out of the $250,000 generously provided by the Uncle Kory Foundation, $50,000 went to the program's researchers to perform advanced imaging analysis on more than 300 patients (more than 3,000 scans) in longitudinal modeling. It is hoped that this data will provide new ways to determine the benefits of therapies in smaller sample sizes, allowing for more opportunities to achieve FDA approval and make greater advances in treating brain cancer.

PROMISING CLINICAL TRIALS

The only way to eliminate brain cancer is to treat patients with novel or research-informed approaches to disease, taking into account better evaluations of the benefits of particular treatments. Currently the UCLA Neuro-Oncology Program offers about 20 different clinical trials to patients with malignant brain cancer. Different types of trials are distinguished by the mode of action, phase of study, and trial sponsor.

In general, three types of modalities are explored with clinical trials run in the UCLA Neuro-Oncology Program. They include targeted therapy, immune therapy, and gene transfer therapy. Targeted therapy combines the power of next-generation sequencing to define populations of brain cancer patients who possess the target and can be treated with an agent that inhibits it. These agents can include small molecules or antibodies. Immune therapies include vaccines and immune checkpoint inhibitors. Gene therapy agents include viruses that can play multiple roles, including creating susceptibilities by delivering a new gene and causing a secondary immune response to foreign antigens expressed in tumor cells.

CLINICAL TRIALS: PHASES OF STUDY

The UCLA Neuro-Oncology Program is involved in early to late phase studies. The earliest is a phase I or first in-human study. A special environment, including skilled and vigilant staff, needs to be in place to runs these studies, as they require close follow-up of patients and rapid recognition of possible toxic effects of therapy. Many times these are the most important studies, as they will define the dose and schedule for a potential therapy; if incorrect, they will lead to ineffective therapies. Proper

design and execution of these studies increase the likelihood of success. Other trials include phase II and phase III studies. These also require a highly skilled staff and the ability to take on a larger subject load. Finally, the program physicians believe that it is humane to provide the opportunity for compassionate-use trials (similar to the EGFRviii vaccine that KH received). This allows patients to received unapproved agents that might prove beneficial that would otherwise not be available due to rigid enrollment criteria. Patients are not charged for this approach.
Trials are sponsored by federally funded consortia, pharmaceutical and biotech companies, and the investigator. Only the pharmaceutical- and biotech company-sponsored trials are fully funded. The federally funded consortia must be subsidized by the parent institution (e.g., the UCLA Neuro-Oncology Program). The investigator-sponsored studies require full funding from grants, philanthropy, or a combination of both. Compassionate use is completely covered by philanthropy.

Of the funding provided by Uncle Kory Foundation, $150,000 allowed the UCLA Neuro-Oncology Program to hire a new research coordinator and clinical trials coordinator, thereby increasing the capacity for clinical trials, particularly the compassionate-use and investigator-initiated trials.

CRITICAL INFRASTRUCTURE

Most of the program's important findings about which therapies are beneficial, how best to use therapies, and what constitutes useful biomarkers come from well conducted clinical trials in which carefully collected provisional materials are correlated with outcomes. Unfortunately, only 10 percent of patients enter clinical trials. In order to increase the number of patients in trials where provisional materials can be gathered to accelerate discovery, the UCLA Neuro-Oncology Program initiated three distinct, yet interdependent pieces of infrastructure— tumor tissue archive, imaging archive, and outcomes archive—that enable every patient to be a part of the cure for glioblastoma. More than 7,000 brain cancer patients are cataloged in what is the largest data set in the world. Data and provisional materials from these archives have been used heavily in discovery, and have garnered mention in more than 100 publications by the programs' researchers.

$50,000 provided by the Uncle Kory Foundation allowed the program to hire an additional research assistant to help with the brain tumor translational research and to aid with tissue collection and processing for development of invitro and invivo models used by the program's investigators in their discovery.

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**

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