

**Adult and Pediatric Brain Cancer Program  
Department of Cancer Biology  
Dana-Farber Cancer Institute**

**Introduction**

We are in the midst of one of the most remarkable scientific revolutions in history. The mapping of the human genome at the end of the 20th century was a seminal breakthrough that enabled scientists to begin to decipher the molecular basis of life and disease. It opened new avenues of research previously unimagined and spurred the development of sophisticated new technologies that are rapidly transforming our understanding of how cancer develops paving the way for the creation of new cancer therapies targeted to needs of individual patients.

In order to fully exploit the opportunities that now exist, Dana-Farber Cancer Institute has developed a comprehensive multi-faceted Strategic Plan for Research focused on the development of new treatments based on the genetic and molecular understanding of an individual cancer. These improved treatments for patients will come from innovative collaborations that bring together clinicians and basic scientists to solve the most intractable challenges in the clinic. The need for this approach is no where more apparent than in the cancers of the central nervous system and in particular brain cancer.

**Accelerating Research in Brain Cancer**

Primary cancers of the central nervous system account for less than 1.5% of all new cancer cases reported in the United States each year. However, the majority of these cancers are malignant gliomas and for all practical purposes, incurable at this time. High rates of mortality convert these infrequent tumors into the third leading cause of cancer-related deaths among men 15-54 years of age and the fourth leading cause of death for women 15-34 years of age. Multiple factors contribute to the high morbidity of malignant glioma and one of the principle obstacles to successful therapy is the notorious resistance of these tumors to radiation and conventional chemotherapy. A promising avenue is to target the biological pathways that are important for maintaining the cancer cells.

The PI3 kinase pathway is among the most important in glioblastomas. Alterations to this pathway are near-universal in this disease and are essential for tumor growth. Multiple drugs targeting PI3 kinase are either in or entering clinical trials. However, the concern exists that resistance mechanisms may arise against single agents targeting this pathway. The use of combination therapies with two or more agents

targeting this or related pathways may overcome resistance, enabling more effective killing of tumor cells.

The Dana-Farber Cancer Institute has extensive experience in studying the PI3 kinase pathway; indeed, it was discovered at the Dana-Farber by the laboratory of Thomas Roberts. We propose evaluating combination therapies using PI3 kinase inhibitors entering clinical trials, coupled with radiation therapy or additional agents targeting PI3 kinase, MAP kinase, or receptor tyrosine kinase gene families, in mouse models of glioblastoma, to identify synergistic combinations that most effectively kill glioblastoma cells and prevent tumor growth. The results of these preclinical studies will directly inform the design of clinical trials to study these combinations in people with glioblastoma multiforme.

A gift of \$50,000 would provide immediate support to this evolving research and propel it closer to clinical trials that have the potential to benefit patients with this disease.

### **Conclusion**

There has never been a better time to support cancer research at Dana-Farber. Our scientists and clinicians are poised to make significant progress in areas such as brain tumors that would reduce the time it takes to get new drugs into clinical trials. At the same time, the necessity for philanthropic gifts has never been greater. While the government remains an important source of support for basic research the current trend is for resources to be allocated away from biomedical research. Moreover, the government rarely funds the kind of translational research that we are now prepared to do here. Individual gifts are playing an increasingly important role in advancing science that can directly impact clinical care.