

**Brain Tumor Funders' Collaborative (BTFC) Call for Applications**  
**Funding for Collaborative Research Teams –**  
**Comprehensive Evaluation of Long-term Survivors of GBM**

The BTFC participates in a number of activities with the aim of identifying forward-looking translational research opportunities where the collective action of funding organizations with a shared commitment to improving the outcomes of brain tumor patients could contribute to advancing the understanding and treatment of devastating brain tumors. Information about the BTFC is available at <http://www.brainumorfunders.org/>.

The current initiative is informed by a series of BTFC-hosted workshops and planning meetings. An issue repeatedly raised in multiple forums was the concern that pre-clinical brain tumor research had become over-reliant on murine-models that do not fully capture the complexity of human gliomas. Progress in brain tumor research could be aided with better understanding of the natural histories of the human disease, a fuller characterization of the molecular and physiological characteristics of human tumors, and an analysis of the individual responses of patients – in terms of the responses to existing or experimental therapies and the natural responses individuals demonstrate in response to pathologies.

To this end the BTFC is prepared to sponsor research taking a more careful and comprehensive analysis of the characteristics of a suite of pertinent factors related to long-term survivors of GBM. For the purposes of this BTFC initiative, the funders are focused on true survivor outliers, and for the purposes of this solicitation long-term survivors are defined as individuals surviving at least 5 years, significantly beyond the most common mean survival statistic of 15 months post-diagnosis.

**Background and Rationale**

For every clinical trial deemed unsuccessful, the survival curves always include a few patients responding favorably to the intervention. In the past, each time the BTFC raised the possibility of studying these patients, the response from researchers was that we could not learn much primarily because of the lack of molecular and physiological markers for distinguishing tumor subtypes. Advances in the genomic, imaging, and molecular tools for characterization of brain tumors now permits the idea of studying long-term survivors. A deeper understanding of characteristics of the tumor, the tumor environment, and the response to therapy evidenced by patients with more favorable outcomes could provide new research and clinical care directions.

The BTFC is interested in more fully characterizing the physiology and the molecular characteristics of the “responsive” patients. Researchers and clinicians now have the ability to distinguish neuronal from mesenchymal GBMs, IDH mutant tumors, and a growing number of other genetic differentiations that may impact tumor response. Ultimately, though, the initially responsive patients are also likely to succumb to recurrent disease. Long term survivors offer us the opportunity to better understand the environment around quiescent tumors, and the triggers by which tumors or the host environment begins to morph toward factors accounting for the inevitable mortality. Long term survivors clearly differ from typical brain tumor patients. The impetus behind this RFA is to identify what factors contribute to the difference. It is hoped that this investigation of long term survivors will yield new questions and suggest new therapeutic directions.

## **Application Guidelines**

*The BTFC funding initiative intends to support a fuller characterization of long term survivors based on the physiological, genetic, and molecular characteristics of not just the tumor, but of the entire organism in which a disease occurs (e.g. immunological changes, altered metabolism). The BTFC believes this broad, holistic approach is critical for understanding patient management and for informing clinical trial designs in the highly heterogeneous, noisy background against which interventions are tested. The complicated nature of the problem addressed by this BTFC initiative and the relatively small numbers of long-term survivors indicates to the BTFC that successful applications will require multi-institutional collaborations and extended community outreach accrual efforts.*

*The BTFC anticipates awarding up to \$1,000,000 per year for up to 2 years to support a major pilot study intended to make rapid progress. The grant contract will be negotiated with a lead sponsoring institution responsible for managing the overall project and all subcontracts. The Sponsoring Grantee Institution must be a non-profit institution with IRS 501(c)(3) status or its equivalent. The BTFC will not provide institutional indirect or overhead costs.*

## **Application Timeline**

|                   |  |
|-------------------|--|
| October 1, 2013   | Deadline for completing on-line letter of intent to apply  |
| November 8, 2013  | Invitations to submit full proposals will be issued  |
| December 15, 2013 | Deadline for uploading PDF of completed applications to the BTFC website. Incomplete or tardy applications will not be considered. |
| January 30, 2014  | Applicants notified of BTFC funding decision.  |
| March 1, 2014     | Earliest anticipated start date  |

***Prior to submitting an application all prospective applicants must complete an online letter of intent to apply by October 1st. [www.braintumorfunders.org/apply](http://www.braintumorfunders.org/apply) Invitations to submit a full proposal will be issued by the BTFC in accordance with the timeline described above.***

**Invited Applications will receive guidelines for proposal preparation.** The central component of the proposal will be a narrative description of the proposed research detailing:

- how study participants will be identified and enrolled

- the scope of tumor and patient characteristics to be acquired
- how the data will be managed
- a plan for the proposed collaboration
- the mechanisms for disseminating study findings
- a plan for making de-identified patient data available to the broader brain tumor research community.

The narrative should be written with understandable, jargon-free language as the proposal will be read and reviewed by the BTFC and by expert external advisors some who may have experience with similar studies from non CNS-tumor populations.

### **Review Process**

Following review of letters of intent, the BTFC will issue invitations and proposal guidelines for full proposals due December 15<sup>th</sup>. Full proposals will be scientifically reviewed by a panel of experts in consultation with the members of the Brain Tumor Funders' Collaborative.