

American Brain Tumor Association * Brain Tumour Foundation of Canada * Brain Tumor Society Children's
Brain Tumor Foundation * Goldhirsh Foundation * James S. McDonnell Foundation
National Brain Tumor Foundation * Sontag Foundation

Request for Pre-Proposals New Mechanisms for Preclinical Development and Testing of Agents for Glial Tumors

Background

The identification of successful treatments for human gliomas remains elusive despite the dedicated and heroic efforts of researchers, clinicians, patients, and families. For most patients the tumors are lethal. The reasons for this record of failure in the development of new therapies are well recognized by the research community. The aggressive nature of gliomas, the logistical difficulties in delivering drugs and biomolecules across the blood-brain barrier to the malignant cells, the functional uniqueness of the human brain, and the lack of ecologically valid experimental models all contribute to the lack of progress against these devastating tumors.

Other hurdles contribute to the lack of progress. The preclinical pipeline for the identification and testing of potential new therapies is fragmented among different populations of research scientists and clinicians. The current system is dated and fails to take optimal advantage of the biomedical community's emerging capacity for discovering, testing, and developing novel therapies. The disconnection between the experimental systems used at the laboratory bench and the clinical realities of patients often means that compounds showing promise in early phases of pre-clinical research fail in later stages of clinical investigation. The new tools of genomics, proteomics, complex systems biology, and informatics need to be brought to bear on the quest for new brain tumor therapeutics. Such efforts will require new collaborations assembling skills and expertise not traditionally associated with brain tumor research.

For the past two years a group representing private funders supporting brain cancer research (the Brain Tumor Funders' Collaborative, the BTFC) convened a series of workshops with researchers and clinicians. We discussed the challenges and opportunities for progress in the clinical treatment of adult and pediatric glioma patients. On the basis of those conversations, the funders reached several conclusions:

- The focus of any new funding initiative is on *both* pediatric and adult gliomas.
- Translating knowledge acquired from basic science into effective clinical applications requires new preclinical research systems that are more predictive of the human response. Developing such systems may require entirely new ways of conceiving of therapeutic target identification and drug design and development.
- Scientists and clinicians working in the brain tumor field are frustrated by the limitations of their efforts, and some are contemplating new approaches, new ways to assemble information, and/or new colleague connections. With an opportunity for financial support, such investigators will be able to design novel, innovative, approaches to the problem of moving promising results from basic and pre-clinical research to drug development and clinical applications.
- This new funding initiative is designed to yield novel, effective treatments for brain tumor patients. It is focused on supporting teams translating preclinical results into clinical

applications and integrating the disciplines of basic science with clinical medicine. The investigators making up a collaborative team need to be drawn from different disciplines and different institutions, and might even require contributions from nonprofit and for-profit organizations. It is unlikely that any one institution will have the disparate expertise required to successfully compete for funding.

- BTFC funds can be used by collaborative teams for ongoing planning and team discussions as part of a comprehensive research design. We recognize, through our own experiences, that building collaboration requires hard work, time, and administrative support.
- Only pre-proposals from new collaborative teams with the requisite skills needed for designing and testing new research systems will be seriously considered. Pre-proposals packaging old wine into new bottles will be rejected early in the review process.

Brain Tumor Research Initiative: Who is eligible?

- New collaborative networks of researchers and clinicians proposing novel systems for moving pre-clinical research into clinical applications are eligible. Eligible research networks can focus on adult and/or pediatric preclinical initiatives. Pre-proposals focusing on developing mechanisms appropriate to both adult and pediatric glial tumors are strongly encouraged.
- Proposed teams should include clinical expertise as well as expertise in brain tumor research and expertise from other fields such as, but not limited to, genetics, stem cell research, physics, mathematics, and complex systems.
- Pre-proposals should be submitted on behalf of the collaborative network by one individual identified as the project manager. Grant contracts will be negotiated with a single US-based 501(c)(3) or equivalent Canadian institution identified as the sponsoring institution accepting responsibility for the scientific, administrative, and financial management of the overall project including all subcontracts.
- Collaborative components, other than the sponsoring institution accepting and administering the grant, need not be not-for-profit institutions. Collaborative components may be located outside the U.S. or Canada.

Scope of Grants

- Collaborative networks proposing novel systems for preclinical glioma research may request funding for up to a total not exceeding \$2 million to be expended between 3 and 5 years.
- The total budget for any given year should not exceed \$600,000. Applicants can expect that all budget requests will be heavily scrutinized during the review process.
- Continued funding for each year beyond the first year is dependent upon satisfactory annual review by a panel comprised of BTFC representatives and scientific experts. Review criteria will be developed for each project according to the goals and milestones articulated in the proposal (see next bullet). The exact nature of the annual review (i.e. written progress report or site visit) will be determined for each project after the grants are awarded.
- The research goals must include time-lines and benchmarks measurable in real-world outcomes; all goals must be clearly articulated and measurable within the project timeline.

Outcomes measures must be directly relevant to the development of patient therapies and achieving improved clinical outcomes.

- The pre-proposal must detail the collaborative aspects of the project by specifically addressing intellectual property issues such as, but not limited to, data-sharing and joint publication.
- Pre-proposals must specifically explain how participation in the network yields a whole significantly greater than the sum of its parts. Pre-proposals must explicitly describe how information exchange among the groups contributing to the research project will be fostered through such activities as workshops, inter-site visits, internet forums, or other collaborative mechanisms appropriate to the proposed project.
- Each unit of the collaborative network must submit a brief letter (one page) stating a commitment to participate in the proposed collaborative activities.
- Each funded network must commit to sending representatives to participate in an annual workshop, the expenses for which will be covered by the BTFC. The annual meeting will also include representatives from the funding organizations and other invited participants.

Submission of Pre-proposal

Pre-proposals must first be submitted in the form of an initial Letter of no more than five (5) pages of narrative. A listing of collaborators with a paragraph not exceeding 100 words describing his/her expertise and proposed contribution to the collaborative, a NIH style bio-sketch of the project manager, the collaborative support letters, and a proposed budget overview are the only allowable attachments. The pre-proposal is intended to provide a concise, yet thorough summary of project goals and methodology, and a description of the proposed collaborative network including name, title, institution and areas of expertise of each proposed member. Completed pre-proposals must be submitted electronically via the BTFC website www.braintumorfunders.org as a single PDF file. The PDF file must contain all required information. Pre-proposals will be reviewed against the criteria outlined above. Each pre-proposal must be accompanied by a 250 word abstract describing the proposed project in language accessible to a general, non-scientific audience. Pre-proposals not conforming to the guidelines will be rejected without review. Following successful review of the pre-proposal, selected collaborative teams will be invited to submit a full proposal. Guidelines for preparing full proposals will be issued at that time.

Review Process

Pre-proposals will be scientifically reviewed by a panel of experts in consultation with the members of the Brain Tumor Funders' Collaborative. When pre-proposal review is completed, the BTFC will issue invitations for full proposals including all guidelines for full proposal preparation. The BTFC anticipates invitations for full proposals will be issued on or by mid-October, 2005.

Timeline:

August 8, 2005	Pre-proposals DUE by 5:00 P.M. CDT
Mid- October 2005	Invitations to submit full proposals will be issued
November 14, 2005	Full proposals DUE by 5:00 P.M. CST
On or about January 16, 2006	BTFC announces awards