

Brain Tumor Funders' Collaborative (BTFC)

American Brain Tumor Association • Brain Tumour Foundation of Canada
James S. McDonnell Foundation • Pediatric Brain Tumor Foundation • The Sontag Foundation

Request for Pre-Proposals: Immunotherapy for Primary Human Brain Tumors

The Brain Tumor Funders' Collaborative (BTFC) works to identify potential therapies for patients with primary human brain tumors to ultimately increase overall patient survival, increase progression-free patient survival and improve the quality of life of patients affected by a primary brain tumor. Information about the BTFC is available at <http://www.braintumorfunders.org/>.

The current initiative is informed by a BTFC-hosted workshop and planning meetings. Our understanding of immunotherapy for human cancer has evolved significantly over the past 20 years to the point where certain types of cancer have shown meaningful and durable responses to immune-based therapies. For example, melanoma has proven to respond very well to immunotherapy, as have certain blood-borne cancers. Immunotherapy for human brain tumors, on the other hand, is proving more difficult; a better understanding of the complex dynamics among the constituents comprising the neuro-immune system, the tumor, and the brain is required.

To this end, the BTFC is prepared to sponsor research on the role of the neuro-immune system in the origin and progression of the immune responses in primary human brain tumors with the hope of developing immunotherapies for treatment of these tumors in patients. This Request for Pre-proposals focuses on supporting studies on the immune responses in primary brain tumors in pediatric and/or adult human patients.

Background and Rationale

Attempts to use the immune system to control neoplastic disease have a long history. Success has been elusive, but the recent convergence of new techniques in molecular biology, genetic sequencing and RNA/DNA mapping have set the stage for a better understanding of immune mechanisms and their relationship to cancer cells.

Our knowledge of primary brain tumors has similarly expanded in the last decade. This has led to an updated categorization of brain tumors by the World Health Organization (WHO 2016) using, for example, molecular markers such as IDH, 1p/19q for glial tumors and Wnt and SHH activation and TP53 mutational status for medulloblastoma. A better understanding of how low grade glial tumors (WHO Grade II) progress to their more aggressive high grade counterparts (WHO Grade III and WHO Grade IV or glioblastoma) is also emerging and the question remains how the immune system may be influencing or be affected by this process.

A number of immune strategies have been used to explore therapeutic possibilities for primary human brain tumors. These include adoptive T-cell immunotherapy, oncolytic viruses, gene transfer therapy, dendritic cell vaccines, peptide vaccines and checkpoint blockade. However, problems with these therapies have become apparent due to "immunologic escape," "hot versus cold tumors," and unacceptable toxicities, to name a few.

To further its aims, the BTFC is considering supporting a small number of multi-disciplinary team-based projects. Teams should represent the requisite skills to carry out the proposed research including clinical oncology, tumor biology, neuro-immunology, computational modelling, and data science. Other areas of immunotherapy research may also be entertained such as radiation-induced brain tumors in survivors of childhood cancers who received cranio-spinal radiation for their original cancer (leukemias or medulloblastoma).

The BTFC is interested in gaining a better understanding of these immune mechanisms as they apply to human brain tumors of any grade in pediatric and adult populations. Characterization across more than one tumor type, therapeutic approach, and age group are of interest. Potential areas of exploration include, but are not limited to:

- What is needed to make the different kind of immunotherapies efficacious for brain tumor patients?
- What are the differences in the immune characteristics by tumor type or grade?

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- What are the biological factors limiting success of any given approach, such as intra-tumoral/patient heterogeneity, risks of deleterious inflammatory responses, and therapeutic indices?
- What are the immunological implications of progression from low-grade gliomas to high-grade gliomas?
- What escape mechanisms do human brain tumors use to evade immunotherapies?
- What insights can we gain into predictors of response to immunotherapy?
- What insights can we gain into predictors of adverse effects of immunotherapy treatment at a young age?
- How can “big data” be used to better understand the immune system in brain tumors?
- In what ways might immunotherapies be ineffective or detrimental to patients?
- Are treatment strategies impacted by the maturation and senescence of the neuro-immune system?

Submission of Pre-proposal

The BTFC is using a pre-proposal process. Following review of pre-proposals, a limited number of full proposals will be invited for funding consideration. Pre-proposals should provide a concise, yet thorough summary of project goals and methodology, and a description of the proposed collaborative network. The narrative should be written with understandable, jargon-free language as the proposal will be read and reviewed by external advisors, some of whom may have experience with similar studies from non CNS-tumor populations.

Completed pre-proposals must be submitted electronically via the BTFC website www.brainumorfund.org as a single PDF file and must contain all required information. Pre-proposals are due on Friday, May 11, 2018. Pre-proposals that do not conform to the guidelines will be rejected without review.

Include the following information in this order:

1. BTFC Coversheet

Use [this template](#) or create one that includes the same requested information.

2. Lead institution information

The Sponsoring Grantee Institution must be a U.S. non-profit institution with IRS 501(c)(3) status or equivalent Canadian institution or a state university.

3. Project Manager NIH style bio-sketch

The project manager must have a doctoral degree, including MD, PhD, DrPH, DO or equivalent and hold a full-time faculty appointment with the Sponsoring Grantee Institution. The project manager is the person responsible for communication with the BTFC, and is considered the principal investigator.

4. Details of the proposed research team

Name, title, institution, and a few sentences describing the expertise and role(s) of each member.

5. Proposal narrative (maximum 1000 words)

- Describe the hypothesis and specific aims and outline the approach in detail.
- Describe the methodology of the proposed study.
- Describe how the findings resulting from the proposed studies will advance the current state of knowledge regarding immunotherapeutic approaches and treatment of brain tumor patients.
- Describe the existing research lines (projects, other grants in your labs/institutions) you would be able to leverage for this project.

No more than 10 references to relevant publications may be listed.

Do not include appendices or other attachments.

Figures and tables should be used judiciously, and the accompanying legends should be brief.

6. Estimated budget (maximum of \$250,000 for each project per year for three years)

The intent is that the funds are to be fully expended over three years in support of this research. The BTFC has accelerating progress as its goal and intends for its funds to be used to move the field forward in the near-term. Please do not propose projects that are not ready to ramp up quickly. The BTFC does not intend for projects to extend via no cost extensions. Requests for extensions will be considered on a case-by-case basis and are not guaranteed. The BTFC will not provide institutional indirect or overhead costs.

Review Process

Pre-proposals will be scientifically reviewed by a panel of experts in consultation with the members of the BTFC based on the following criteria:

- **Research Question and Significance:** Is the proposed project addressing an important problem or a critical barrier to progress in immunotherapy for brain tumors? Projects which are likely to result in rapid translation to the clinic will be viewed favorably.
- **Reproducibility and Open Science:** Does the proposed project acknowledge and incorporate data sharing? The BTFC supports the principles of open science. Although a complete data sharing plan is not required at the Pre-proposal stage, there should be acknowledgement of the intent for data sharing within the narrative. Full proposals will require a detailed data management plan that includes sharing of scientific results and protocols through peer-review publication in conjunction with general availability of underlying raw data. The BTFC expects the projects will share both positive and negative findings with the broader neuro-oncology community.
- **Approach and Feasibility:** Is the proposed project feasible within the proposed timeframe? Is the approach reasonable to meet the stated goals of the project?
- **Team:** Is the proposed team well-suited for this project? Do they have the appropriate experience and training?
- **Impact:** If successful, will this project provide a refinement or improvement to our understanding of the immune mechanisms that apply to human brain tumors of any grade in both pediatric and adult populations?

Following successful review of pre-proposals, selected collaborative teams will be invited to submit a full proposal. Guidelines for preparing full proposals will be issued at that time.

For questions, submit an email to info@braintumorfunders.org.

Timeline

March 15, 2018	RFP Announced and Advertised
May 11, 2018	Pre-proposals due no later than 17:00 CDT (22:00 UTC)
June 15, 2018	Invitations to submit full proposals will be issued
July 13, 2018	Full proposals due no later than 17:00 CDT (22:00 UTC)
July – August 2018	Advisory Panel Review
September 2018	Notification and decisions
November 2018	BTFC announces awards
January 2019	Earliest anticipated start date

Frequently Asked Questions

1. Where is the link to submit my proposal electronically?
www.braintumorfund.org/apply
2. The project we are considering includes several university components as well as a for-profit organization. Are there any restrictions on including for-profit businesses as part of the research team?
For-profit businesses cannot be the sponsoring institution
3. The research team we are putting together consists of researchers at multiple institutions. Will the BTFC manage subcontracts or is that the responsibility of the project manager's institution?
Managing subcontracts is the responsibility of the project manager's institution
4. I'm preparing a proposal. What date should I use as the "start date"?
January 2019
5. What are the requirements for font size, margins, and similar requests?
Use your best judgement
6. Are references and image captions included in the word limit?
No, within reason
7. Is there an outline or example of a completed proposal file that I can see?
No
8. Will you accept late proposals?
No
9. I have a question not answered above. Whom should I contact?
Send an email to info@braintumorfund.org