

## **Brain Tumor Funders' Collaborative (BTFC)**

American Brain Tumor Association ○ Brain Tumour Foundation of Canada  
National Brain Tumor Society ○ Pediatric Brain Tumor Foundation

### **Request for Letters of Intent: Liquid Biopsy for Primary Brain Tumors**

The Brain Tumor Funders' Collaborative (BTFC) is working to identify potential liquid biopsy technology for diagnosis and monitoring of patients with primary brain tumors to ultimately, diagnose patients earlier, improve accuracy of diagnosis, improve clinical monitoring, 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 liquid biopsy for solid tumors has evolved significantly over the past 15 years to the point where cancer and multi-cancer detection tests are working in clinical trials, FDA-approved liquid biopsy tests are currently being used for Non-Small Cell Lung Cancer with specific gene mutations, and approval may be on the horizon for other tests. For example, Grail plans to seek FDA approval for their multi-cancer detection test in 2026. However, brain tumors are often not included in these tests due to challenges with detection and lack of reliable biomarkers.

To this end, the BTFC is prepared to sponsor research on liquid biopsy with the hope of advancing the technology to make liquid biopsy a viable option for brain tumor patient care. This Request for Letters of Intent focuses on supporting studies on liquid biopsy in primary brain tumors in pediatric, adolescent and young adult (AYA) and/or adult patients.

#### **Background and Rationale**

Our knowledge of primary brain tumors has expanded in the last decade. This has led to an updated categorization of brain tumors by the World Health Organization (WHO 2021) and the question remains, how can our improved understanding of brain tumor biomarkers be used for improving the diagnosis and treatment of brain tumor patients?

A number of liquid biopsy strategies have been used to detect the presence of primary brain tumors. These include cerebral spinal fluid (CSF), plasma, and urine, to analyze circulating tumor DNA, extracellular vesicles, and protein. However, challenges remain with sensitivity and specificity of the assays for different brain tumor types.

To further its aims, the BTFC is considering supporting a small number of multi-institutional, multi-disciplinary team-based projects, each in the amount of \$500,000 over a two-year period. Teams should represent the requisite skills to carry out the proposed research including close collaboration between clinical oncology, radiology, tumor biology, computational modelling, and data science.

Projects should be practice-changing and must be focused on liquid biopsy for one or more of the following purposes for human primary brain tumors:

- o Screening or Diagnosis
- o Detection of minimal residual disease
- o Distinguishing progression from pseudoprogression
- o Monitoring for brain tumor progression
- o Monitoring for response or resistance to treatment

Characterization across multiple tumor types and grades, and varied age groups/patient populations are of interest. Potential areas of exploration include, but are not limited to:

- o What factors are most important to make the various kinds of liquid biopsy, sensitive and accurate enough for brain tumor diagnosis and monitoring of treatment response (such as tumor location, BBB, collection methods, sample handling, and analyses)?
- o What are the differences in the extracellular tumor information by tumor type or grade?
- o What is needed/required, in the preclinical setting, to make liquid biopsy techniques reproducible across labs and to prepare the techniques for testing in the CLIA setting?

In the interest of advancing liquid biopsy to clinical utility quickly, the BTFC will prioritize studies focused on CSF and blood sampling as well as ctDNA analytes. Other biofluids and cell-free analytes (cytology is outside of the scope of this RFP) will be considered so long as the investigators present compelling preliminary data to show that the alternative biofluid or analyte can distinguish the presence or absence of brain tumors in significant samples of brain tumor patients compared to healthy controls.

### **LOI Components**

The BTFC is using a letter of intent (LOI) process. Following review of LOIs, a limited number of full proposals will be invited for funding consideration. LOIs 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 LOIs must be submitted electronically via [ProposalCentral](#). The opportunity can be found under the American Brain Tumor Association’s grant opportunities. LOIs are due January 16, 2025. LOIs that do not conform to the guidelines will be rejected without review.

### **Application pages in ProposalCentral**

1. Title Page: Enter a project title (limited to 81 characters) and save to access the other pages of the application.
2. Download Templates and Instructions: This RFP, the sample grant agreement, and biosketch templates can be downloaded from this section.

3. Enable Other Users to Access this Proposal (optional): If personnel other than the Applicant/PI will upload documents, make edits, or review this application, add their email address(es) here and select the appropriate level of access (View, Edit, or Administrator) for each person who will need to access the application.
4. Applicant/PI: The project manager must have a doctoral degree, including MD, PhD, DrPH, DO or equivalent and hold a full-time faculty appointment with the Lead Institution. The project manager is the person responsible for communication with the BTFC and is considered the Lead Principal Investigator.

Information from your ProposalCentral Profile will automatically populate on this page. If any of the required fields are blank, you must update your profile in the Professional Profile tab, including your ORCID identifier.

ORCID (Open Researcher and Contributor ID) is an alphanumeric code to uniquely identify scientific and other academic authors. Registration is free at <https://orcid.org/>.

5. Institution & Contacts: The Lead Institution must be a U.S. or Canadian non-profit institution or university. The Institution information will automatically populate from the Applicant/PI's primary institution in their Professional Profile. Applicants should verify that the information is accurate. Applicants must select a Grant Officer (if any are listed) or add a Grant Officer by entering their email address.
6. Key Personnel: Key Personnel can include collaborators, co-investigators, and patient advocates who are integral to the research project. A minimum of one co-investigator or collaborator, who is located at a separate institution from the PI and a minimum of one patient advocate are required. Do NOT include the Applicant/PI on this page.

To add Key Personnel, enter their email address and, in the pop-up window, select the appropriate role for that person. Other information will be populated if the key person has a ProposalCentral account. You must complete the other required fields if empty. Click Save and close the pop-up window. Repeat for each Key Personnel on the project.

7. Research Focus: Select the applicable tumor type(s) and patient population(s) for this project.
8. Attachments:
  - o Applicant/PI Biosketch: Limited to 5 pages in NIH standard format (such as Arial, 11 point or larger). The Biosketch may include, in Section A, details from ongoing and completed research support that is relevant to the project.
  - o Project Team Description (maximum 300 words): Describe the expertise and roles of the Key Personnel named on the project, and how the team will work together to accomplish the project goals, including proposed frequency of communications and meetings.
  - o Proposal narrative (maximum 1,200 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 liquid biopsy approaches for the diagnosis 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.
- Figures and tables should be used judiciously, and the accompanying legends should be brief (legends not included in the 1,200-word limit).
- An impact statement describing how the results of this work will be practice changing and useful in the clinical management of brain tumors.
- No more than 10 references to relevant publications may be listed (not included in the 1,200-word limit).

Do not include appendices or other attachments.

### **LOI Submission**

1. **Validate:** Validate is a required step for the system to check for the required components of the LOI. If the system indicates that required information is missing, click the component in the list to go to the associated page in the application.
2. **Signature Pages:** Click the Print Signature Pages button and obtain the required signatures on page one of the document (electronic signatures are accepted). Save the signed and dated signature page as a PDF and upload it to the Attachments section of your LOI.

#### **Required signatures include:**

- Applicant/PI
  - Signing Official (designated by the Institution)
3. **Submit:** When your application is complete, click the Submit button. By clicking submit, you confirm that all the information in your application is accurate and all documents uploaded correctly, including the signed signature page. You will receive an email confirming the submission of your application. You may view your submitted application in the Proposals tab in your ProposalCentral account by selecting “Submitted” in the Proposal Status drop-down menu.

### **Review Process**

LOIs will be administratively reviewed for completeness and responsiveness to the research focus, by staff of BTFC member organizations. LOIs will then be scientifically reviewed by a panel of experts in consultation with the members of the BTFC based on the following criteria:

- o **Research Question and Significance:** Is the proposed project addressing an important problem or a critical barrier to progress in liquid biopsy for brain tumors? Projects which are likely to result in rapid translation to the clinic will be viewed favorably.

- o Approach and Feasibility: Is the proposed project feasible within the proposed timeframe? Is the approach reasonable to meet the stated goals of the project?
- o Team: Is the proposed team well-suited for this project? Do they have the appropriate experience and training?
- o Impact: If successful, will this project provide a refinement or improvement to our understanding for the use of liquid biopsy for human brain tumors of any or all grades, in any or all patient populations (pediatric, adolescent and young adult, and/or adult) If successful, does this project have the potential to be practice changing and improve the clinical management of brain tumors?

Following the successful review of LOIs, selected applicants will be invited to submit a full proposal. Guidelines for preparing full proposals will be issued at that time.

### Questions

Questions regarding the LOI components and submission may be sent to [grants@abta.org](mailto:grants@abta.org). Please include BTFC grant application in the subject line.

### Full Application information

The following information is not required for the LOI stage, but will be required if invited to submit a full application:

- o Grant Budget: Maximum of \$250,000 per year for two years, direct costs only.
- o Biosketches and letters of support from co-PIs, co-investigators, collaborators, and patient advocates named on the project.
- o A brief description of how the project, if successful, will progress to clinical validation. A successful project may be considered for an additional year of funding, at an amount yet to be determined, to support the initial steps for carrying out this additional work.
- o Data Management and Sharing Plan: The BTFC supports the principles of open science. The full proposal will require a detailed data management plan that includes the sharing of scientific results and protocols through peer reviewed publication and submission of underlying raw data to data repositories. The BTFC requires that the grantees share both positive and negative results of the project with the broader neuro-oncology community.
- o Letters of Support from the lead/sponsoring institution and collaborators.

### Timeline

November 14, 2024	RFP Announced and Advertised
January 16, 2025	LOIs due no later than 17:00 CDT (22:00 UTC)
March 18, 2025	Invitations to submit full proposals will be issued
April 15, 2025	Full proposals due no later than 17:00 CDT (22:00 UTC)

July 2025	Notification and decisions
September 1, 2025	Earliest start date
September 2025	BTFC announces awards

The members of the Brain Tumor Funders' Collaborative, the American Brain Tumor Association, Brain Tumor Foundation of Canada, National Brain Tumor Society, and Pediatric Brain Tumor Foundation are proud to provide funding for the 2025 grants, with additional support from and Anonymous Family Foundation, Dragon Master Initiative, The Glioblastoma Research Organization, The Sontag Foundation, Southeastern Brain Tumor Foundation, and StacheStrong.

## Frequently Asked Questions

### Where should I submit my proposal?

The BTFC grant opportunity is available in [ProposalCentral](#), among the ABTA's grant opportunities

### 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/lead institution.

### 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 PI/project manager's institution

### I'm preparing a proposal. What date should I use as the "start date"?

September 1, 2025

### What are the requirements for font size, margins, and similar requests?

For biosketches, use NIH standard format. The project narrative is limited to 1,200 words. Use your best judgement on font size, font type, and margins for the project narrative.

### Are references and image captions included in the word limit?

No, but LOIs are limited to 10 reference and image captions should be within reason

### Is there an outline or example of a completed proposal file that I can see?

No sample proposals are available.

### Will you accept late proposals?

No. Applicants are encouraged to plan on submitting early to allow time for potential delays.

### I missed the LOI deadline, may I submit a full proposal?

No. Full Proposals will accepted by invitation only and are based on the outcome of the LOI review.

### **I have a question not answered above. Whom should I contact?**

Send an email to [grants@abta.org](mailto:grants@abta.org), please include “BTFC grant application” in the subject line.

## **Frequently Asked Questions about Including a Patient Advocate in your Research**

### **Why is a Patient Advocate required for BTFC grants?**

The Brain Tumor Funders Collaborative has a strong commitment to including the patient voice in research. Patient Advocates provide the patient perspective in the design and implementation of research projects funded through these grants, ensuring that the BTFC funds research that has the greatest potential to have a positive impact on patients.

### **Who can serve as a Patient Advocate on my project?**

Patient Advocates can be anyone who has a strong personal connection to primary brain tumors. They can be patients who have been diagnosed with brain tumor or a caregiver, family member, or friend of someone who has been diagnosed.

Patient Advocates that you work with should have a basic understanding of research or willingness to learn.

### **How do I find a Patient Advocate to serve on my project?**

Ask other researchers and clinicians at your institution or collaborators if they have worked with patient advocates and if they have recommendations.

Most of the member organizations in the Brain Tumor Funders Collaborative work with patient advocates regularly and may be able to connect you to someone who can serve on your project. A full list of organizations in the BTFC can be found at <https://www.braintumorfunders.org/>. You can also reach out to [grants@abta.org](mailto:grants@abta.org). ABTA staff can also connect you with the partner organizations who may have an advocate with relevant experience to serve on your project.

### **How can I involve a Patient Advocate in my project?**

- Be sure to include a patient advocate in your project early on. They will be most helpful when they are given time to learn about the project.
- Communicate with the patient advocate regularly during the project to keep them informed of the progress. Communications may be via email, video calls, or in person.
- Have clearly defined roles and responsibilities for the advocates (see below for ideas).
- Seek Input from the advocates on your project, as they have valuable perspectives.

### **What roles can Patient Advocates play in my project?**

Patient Advocates vary in the variety of skills, experiences and knowledge they bring to the team. Depending on the nature of your project and the background of the advocate(s), there may be other ways that they can assist other than those mentioned here.

During Application Submission you may want the Patient Advocate to:

- Provide feedback on the impact of your project on patients by identifying the translation potential of your research (i.e., how meaningful or important is the outcome to patients).

- Work with you to develop and review the scientific and patient impact sections to help communicate the importance of your project to patients and their families.
- Work with you to develop and review the lay summary and impact statement of the application to ensure terminology is understandable to a general, non-scientific audience and to convey the importance and overall impact of your project on liquid biopsy research for brain tumor patient care.
- Work with them to define their role in the project.

During and after the Research Project:

- Provide feedback on the findings and any potential changes to the project plan.
- Participate in the project team update/planning meetings, seminars and other events important to your project's success. They will add the patient perspective to the discussions and their involvement in these meetings will allow them to learn more about the project and identify other ways they can contribute.
- Speak in the community about your ongoing research and its importance to patients. To maximize impact and enhance understanding, the researcher and an advocate can make the presentation as a team. This can include the required presentations at the end of the grant.
- Work with you to create educational materials, events, webinars and teleconferences for local, regional, and national groups and organizations to inform them of the research you are conducting and its importance to brain tumor patients.

**How often should I and the other researchers on the project meet with the Patient Advocate(s)?**

The frequency of the meetings should be driven by the research plan and how often the team meets to discuss the progress. Patient advocates should be active participants, not infrequent or secondary participants. Your Project Team Description should include details on how often the research team will meet with the advocates and the type(s) of meetings that will occur.

**How should Patient Advocates be compensated?**

Compensation will vary depending on the involvement of the patient advocate in your project. At a minimum, the patient advocate should be compensated for the out-of-pocket expenses incurred to attend meetings and conferences (mileage, parking, etc.). If the patient advocate will have specific deliverables for your project, honoraria or consulting fees are encouraged. Compensation should be agreed upon during the development of the application and included in the grant budget.