FTD Diagnostic Biomarkers Initiative

Request for Proposals (RFP): Translational Diagnostic Biomarker Development for Frontotemporal Lobar Degeneration (FTLD)

Made possible by the AFTD Holloway Family Fund, Alzheimer's Association, Rainwater Charitable Foundation, and the Robertson Foundation

Frontotemporal Degeneration (FTD) refers to a group of neurodegenerative disorders characterized by progressive atrophy of the frontal and/or temporal lobes, leading to cognitive, behavioral, and language impairments. Clinical diagnoses can include behavioral variant FTD (bvFTD), primary progressive aphasia (PPA), FTD with motor neuron disorder and the related FTLD disorders, corticobasal degeneration (CBD) and progressive supranuclear palsy (PSP).

FTD is the main cause of dementia in people under the age of 60. With the estimated incidence of 15-22 per 100,000 people affected, FTD is considered rare. However, the significant difficulty in getting an accurate diagnosis means the rates of disease are likely much higher. Common misdiagnoses include Alzheimer's or non-specified dementia, primary psychiatric diseases, Parkinson's disease for PSP and CBS, or even mid-life crisis and menopause.

Diagnosis currently relies on physical examination, cognitive assessments, laboratory tests, brain imaging, and patient history. Accurate diagnosis is difficult, time-intensive, and error-prone; as a result, accurate assessments often rely on the expertise of leading FTLD clinicians based at specialized centers. Yet many individuals with FTD and related disorders are never seen by neurologists, let alone specialized centers. In the most common form of FTD – behavioral variant FTD – early symptoms such as impaired decision-making and behavior change can splinter families or trigger unemployment long before the changes are recognized as being caused by a fatal, neurodegenerative disease. Diagnosis is particularly unlikely for people that have limited access to specialist care or are at risk of explicit or implicit bias. FTD disorders progress quickly and necessitate a straightforward path to an accurate diagnosis.

To improve access to diagnosis, different types of tools may be useful at different stages of clinical care. Parameters of potential tools were discussed at the 2023 AFTD Holloway Summit on FTD Biomarkers and with persons with lived experience and AFTD's Medical Advisory Council. Screening tools are needed in primary care, urgent care, and/or the emergency room, to identify people who should be seen by a specialist familiar with FTLD. Affordability and scalability are important to ensure these tools can be used widely. In some cases, a screening or diagnostic tool may have relevant information not only for FTD but for other conditions with overlapping symptomatology or pathology. Such non-specific tools may be more feasible and affordable to deploy in clinics while still serving as invaluable aids in the diagnostic process for FTD. Further, diagnostic tools are needed

for neurology and specialty clinics, to simplify, accelerate, and improve the accuracy of the diagnostic process, and to identify which individuals have which form of FTLD neuropathology.

Biomarkers, or "biological markers," are measurable indicators such as genes, proteins, or other substances that provide critical information about biological processes, disease presence, or treatment responses. Found in blood, cerebrospinal fluid (CSF), other bodily fluids, or tissues, biomarkers are essential in screening and diagnostic tools, enabling healthcare professionals to detect diseases early, and accurately.

Biomarkers are urgently needed as objective tools to improve access to diagnosis of FTD disorders and underlying FTLD pathology by

A) Screening individuals, to identify those in need of evaluation by neurology specialists,

B) Improving diagnostic accuracy compared with similar disorders within specialty clinics, and

C) Identifying types of pathophysiology to inform clinical care and prognosis

The Association for Frontotemporal Degeneration (AFTD) and funding partners invite applications to address these gaps with research studies focused on the development of scalable, accessible diagnostic tools to help screen and diagnose FTLD disorders. This initiative aims to advance diagnostic precision, improve early detection, and enhance patient outcomes by supporting innovative and impactful research projects.

Scope: Diagnostic Biomarkers

Eligible research proposals include, but are not limited to:

- Evaluation or development of low-cost screening biomarkers assessments that could identify individuals in need of evaluation by a neurologist due to suspicion of FTD
- Translation of biomarker assessments into clinically applicable diagnostic tools which are specific to FTD
- Replication studies to validate the utility and reliability of identified human biomarkers for diagnostic use
- Investigation of promising diagnostic biomarkers in understudied populations.
- Development of standardized assays or protocols for diagnostic biomarkers.
- Evaluation or development of a biomarker that could aid in differential diagnosis of FTLD, either distinct forms of FTLD or comparing FTLD to other causes of neurological symptoms.
- Integration of multi-modal approaches (e.g., combining imaging and molecular data) to enhance diagnostic accuracy.

Out of Scope:

- Projects testing biomarkers outside the context of diagnosis, such as biomarkers which signal disease modification, severity, or progression
- Animal-based studies
- Early-stage discovery work

Eligibility

The FTD Diagnostic Biomarkers Initiative awards are open to investigators worldwide at:

- Academic or nonprofit research institutions
- For-profit organizations such as biotechnology or diagnostics companies

Collaborative arrangements, e.g., between academia and industry, senior and early-career researchers, or ALS and FTD researchers, are encouraged.

Postdoctoral researchers or fellows/trainees cannot apply as the lead PI but can be key personnel on a project team.

Award Information

Funding period: up to 2 years

Number of awards: Between 2-4 grants will be awarded based on the budgets of the top-ranked, peer-reviewed proposals.

Award Amount: Budget requests between $250,000 to $700,000 (inclusive of direct and indirect costs) will be considered depending on the stage of development and scope of the project. All applications require submission of a detailed budget and corresponding budget rationale. A template for this purpose is provided in the application.

Grant applicants at academic or non-profit institutions may request up to 10% of the approved budget to be allocated to indirect costs. This is inclusive of indirect costs for the implementing institution as well as any subcontracts. This funding mechanism does not cover indirect costs for for-profit organizations.

Application Process

1. AFTD online submission portal account creation: All applications must be submitted through AFTD's online submission portal, which can be accessed on the AFTD website. No paper or emailed applications will be accepted.

2. Eligibility Assessment: Answer all questions on the portal to confirm your eligibility. Interested applicants are encouraged to contact the AFTD Director of Research and Grants (nbjorklund@theaftd.org) with any questions concerning eligibility or proposal scope.

3. Letter of Intent (LOI): Submit a brief summary of the scientific rationale, supporting data, and the specific aims of the proposed work.

4. Full Proposal: If invited, submit the full proposal, including a detailed research plan with clear explanation on how the biomarker could be used in the diagnostic journey, budget, and timeline.

Detailed instructions for the LOI and the Full Proposal are posted on the FTD Diagnostic Biomarkers Initiative RFP webpage.

Selection Process

Applications will be reviewed confidentially by individuals such as staff and/or board members at the AFTD, the other non-profit funding partners, and a Scientific Review Panel of external experts who attest that they do not have a conflict with a given proposal. Please note that funding decisions are final, no appeals will be accepted

Review Criteria: Proposals will be evaluated and prioritized based on the following criteria:

A. **Relevance**: The prospective biomarker, once fully developed, could significantly improve access to diagnosis to FTD disorders. **Of particular interest are accessible and scalable tools that may be used outside of highly specialized clinics**, or tools that could become a gold-standard to which new FTLD diagnostic tools are developed.
B. **Strength of scientific approach and supporting data**: Preliminary data supportive of application along with robust scientific rigor.
C. **Feasibility and strength of research plan:** Study objectives paired with appropriate methods to achieve proposed goals. Thoughtful key measures, statistical analysis plans and go/no-go decision points regarding the next experimental steps.
D. **Qualifications of applicant/team and resources**: The scientific team can carry out the proposed work. The environment and resources are suitable to ensure successful completion of the project.
    a. **Sourcing of biospecimens** must be explained as part of the grant application. If existing samples are expected to be used, this must be arranged prior to application submission. Biomarker developers without access to samples are encouraged to contact AFTD in advance; AFTD may be able to facilitate, but cannot guarantee, introductions to relevant collaborators. Up to 40% of the proposed budget may cover the collection of new biosamples to enable the proposed biomarker research. If new biosample collection is included, the proposal must include a plan for long-term storage and dissemination of excess samples. AFTD strongly encourages investigators to contact BioSEND and NCRAD to explore whether these NIH-funded biorepositories may be leveraged.

E. **Relevance to all populations affected by FTD**.: The scientific team and/or research design have a reasonable plan to include a broad population of research participants; including those most likely unable to access accurate or timely diagnosis.
F. **Appropriateness of budget**.
G. **Overall impact**: Potential to make an impact in the field of FTLD biomarkers and move the field closer to scalable & accessible tools to improve access to diagnosis.

For proposals that involve a for-profit company, the following must be provided:

1. Company description and history, mission statement, milestones, scientific and financial goals, and future plans

2. Annual report or audit

Key Dates 2026

- AFTD Online Submission Portal Opens: February
- Letter of Intent Due: March 6
- Full Proposal Invited: March 26
- Full Proposal Deadline: May 12
- Award Announcements: Expecting fall of 2026

Contact Information

For inquiries, please contact:

Nicole Bjorklund

Director of Research & Grants

nbjorklund@theaftd.org

Expectations for successful applicants:

Publication of Research Results

In accordance with generally accepted standards applicable to scientific publication, and subject to any third-party obligations, the Recipient and Grantee agree to submit for publication any results or other work, arising directly from the performance of research that is funded in whole or in part by this award, which would be useful to scientists working on FTD-related research. Furthermore, as maximizing the distribution of these publications through free, online access is the most effective way of ensuring that the research funded in whole or in part by AFTD can be accessed, read and built upon, AFTD encourages Recipient to make available any research papers accepted for publication in a peer-

reviewed journal by electing an open access publication option or by depositing an electronic copy in an open repository such PubMed or Creative Commons as soon as possible.

Resource Sharing

Recognizing that the sharing of research outputs, including reagents, code, software, protocols and research tools, contributes to advancing scientific discussion and enhances the value of our sponsored research programs, AFTD encourages Recipient and Grantee to make available nonproprietary research materials developed in the course of the work funded through this award with as few restrictions as possible.

Data Sharing and Management

AFTD supports adherence to the FAIR (Findability, Accessibility, Interoperability, and Reusability) guiding principles of data stewardship and expects grant recipients to plan for the appropriate sharing of data, following the general principles of data stewardship outlined in the NIH 2023 Data Management and Sharing Policy. Applicants are therefore required to provide a concise Data Management and Sharing (DMS) plan that includes the following elements:

- *Data type – Summarize the type and estimated amount of scientific data expected to be generated in the project*
- *Related tools, software, and/or code – Indicate whether specialized tools are needed to access or manipulate shared scientific data to support replication or reuse, name(s) of the needed tool(s) and software, and specify how needed tools can be accessed.*
- *Standards – Describe what standards, if any, will be applied to the scientific data and associated metadata (i.e., data formats, data dictionaries, etc.).*
- *Data preservation and access – Give plans and timelines for data preservation and access, including the repository where scientific data and metadata will be archived and how the scientific data will be findable and identifiable*
- *Access, distribution, or reuse considerations – Describe any applicable factors affecting subsequent access, distribution, or reuse of scientific data (e.g., informed consent)*
- *Oversight of data management and sharing – Indicate how compliance with the DMS Plan will be monitored and managed*

The NIH has provided samples of DMS plans as well as a format template page you may find helpful for writing your data management plan. AFTD recognizes that some scientific data may be proprietary, or that the extent of data sharing may be constrained by restrictions imposed by licensing limitations or other terms. Applicants should provide justification for any such restrictions on data sharing. If you have questions or concerns about how data sharing expectations apply to for-profit organizations, please contact AFTD to discuss.

Funding Restrictions

In general, AFTD grants are available to scientists and researchers worldwide. However, as a U.S.-based charity, AFTD adheres to U.S. laws and regulations. Consequently, AFTD will not provide funding to any individual or entity that: (i) is subject to U.S. comprehensive or targeted sanctions, or if awarding funding would violate such sanctions; (ii) appears on the U.S. List of Specially Designated Nationals, or is owned or controlled by individuals or entities on this list; or (iii) is otherwise restricted under U.S. laws related to combating terrorism.

Potential return on investment

Funding agreements may include provisions for repayment in connection with downstream commercial milestones achieved by a funded research product, such as net sales, licensing, acquisition, or other changes in control. Specific terms related to repayment will be determined on a case-by-case basis and discussed during the grant contracting process.

You are welcome to contact us to discuss your proposed project prior to submission or for answers to questions about eligibility, the submission process, or the online portal.

We look forward to receiving your innovative proposals to advance the diagnosis of FTD.