Call for research projects 2025

"Natural History Study of CTBP1-related syndrome / HADDTS"

Maximum budget: **60 000 €** - Maximum duration: **24 months**

Deadline: **05/03/2026 - 5pm** (Paris time)

Your profile must be created on the application platform prior to any application (instructions p3).

Context

Due to the specificities of the field of rare diseases, the HADDTS Foundation and the Foundation For Rare Diseases (FFRD) have agreed on a **partnership to support and stimulate research on CTBP1-related syndrome, also called HADDTS** for Hypotonia, Ataxia, Developmental Delay, and Tooth-Enamel Defects Syndrome (rare diseases network(s): AnDDI-Rares, DéfiScience, ITHACA, DRN-RND, ERN-RND).

The HADDTS Foundation[1] is a non-profit organization dedicated to promoting and supporting research on CTBP genes and advancing scientific understanding of CTBP1-related syndrome / HADDTS, a nano-rare genetic disorder caused by a mutation in the CTBP1 gene. CTBP genes are essential for cellular regulation and repair and are linked to cancer, aging, autism spectrum disorders, and neurodegenerative diseases. Advancing research on CTBP genes therefore has broader implications that extend beyond this nano-rare disease. The HADDTS Foundation also acts as a patient advocacy group, providing a voice for families affected by CTBP-related conditions and supporting them throughout their journey.

FFRD[2] is a private non-profit organization, founded in 2012[3] by five members[4], with the aim of helping to (i) deciphering rare diseases to facilitate diagnosis and accelerate the development of new treatments, (ii) improve the daily lives of people with disease and their loved ones. Its mission is of general interest: to lead, coordinate and support research on rare diseases. It provides free support to patient organizations in their efforts to promote rare diseases research, for example through joint calls for projects such as the one proposed here.

Aim of the call

CTBP1-related syndrome / HADDTS is a **nano-rare genetic neurodevelopmental disorder** caused by pathogenic variants in the CTBP1 gene.
Pathogenic variants in CTBP1 disrupt normal neurodevelopment and cellular function, leading to significant challenges in reaching motor, cognitive, and speech milestones. Scoliosis, as well as feeding and digestive difficulties are also common.

[1] *https://www.haddtsfoundation.org/*
[2] *https://fondation-maladiesrares.org/en/*
[3] *PNMR2 : http://www.sante.gouv.fr/le-plan-national-maladies-rares-2011-14-une-ambition-renouvelee.html*
[4] *AFM-Telethon, Rare Diseases Alliance, Inserm, Conference of University Hospital Directors, Conference of University Presidents*

As the disease progresses, children develop bulbar dysfunction, making them increasingly prone to respiratory diseases and, based on the currently available data and family reports, **HADDTS is considered a life-limiting condition.**
As a nano-rare disorder, CTBP1-related syndrome **critically lacks standardized clinical data**, making it difficult to design clinical trials and evaluate therapeutic efficacy.

This call aims to support **an ambitious natural history research program focusing on CTBP1-related syndrome / HADDTS.** All pathogenic or likely pathogenic CTBP1 variants are of interest and should be taken into consideration, including single variants.

The overarching objective is to establish the first natural history study of CTBP1-related syndrome, in order to:

- better characterise the clinical, neurodevelopmental and behavioural phenotypes over time,
- document the natural course of disease progression (e.g. motor, cognitive, language, orthopaedic, respiratory outcomes),
- identify early prognostic markers and clinically meaningful outcome measures that are feasible to assess in routine care or at home, including caregiver- or self-reported measures,
- generate robust baseline data and endpoints for future interventional trials, including antisense oligonucleotide (ASO) therapies, other gene-targeted approaches, or drug repurposing strategies, in order to identify critical windows of opportunity for intervention,
- improve clinical management and care pathways for affected individuals.

Tools and data available

The HADDTS Foundation has initiated the creation of a **worldwide patient registry** and a collaboration with Simons Searchlight, funded by the Simons Foundation, which has already collected natural history information from 16 families with CTBP1 variants. Participant data are **accessible at no charge** via the Simons Foundation data distribution platform SFARI Base (https://base.sfari.org/) and associated **biospecimens** can also be requested.
The HADDTS Foundation will intensify efforts over the coming months to increase case ascertainment and recruitment prior to the start of the funded project. The HADDTS Foundation and Simons Searchlight will actively **support the selected team with patient recruitment, outreach and communication** to families.

Existing Simons Searchlight instruments for CTBP1-related syndrome include standardized questionnaires and surveys:

- Observer-Reported Communication Ability
- Sleep Supplement Survey
- Children's Sleep Habits Questionnaire
- Pediatric Quality of Life Inventory - Family Impact Module
- Quality of Life Inventory
- Child Behavior Checklist (CBCL)
- Background History Form - Child/Dependent
- Vineland Adaptive Behavior Scales - Third Edition
- National Database for Autism Research (NDAR)
- Seizure History Survey
- Annual Medical History Survey
- Pregnancy and Birth Survey
- Race and Ethnicity Questionnaire
- Additional annual follow-up Medical History Survey (e.g. Brief Development Updates, Communication, Mobility and Social Communication Surveys).

Eligibility criteria

The project must explicitly formulate a **research question**, **addressing natural history study of CTBP1-related syndrome**.
The project must demonstrate its **originality,** feasibility and **the expertise(s)** of the researchers involved.

To ensure a minimal level of standardized phenotyping, it is expected that **at least one structured remote assessment** (e.g. videoconference interview with the family and/or clinician) will be conducted for each participant enrolled in the study.
In-person clinical evaluations performed by the local treating physician (e.g., neurological examination, imaging, standardized motor assessments) using the standardized clinical evaluation forms provided by the research team are strongly encouraged and will be considered an asset. Investigators are strongly encouraged to make use of existing medical records and imaging (e.g. brain MRI, EEG) and to integrate them in a standardized, de-identified format into the study dataset, in accordance with applicable ethical and data protection regulations.

The principal investigator of the project ("lead applicant" – P.I.) must be a **researcher**, belonging to an **academic public research organization**[5]. It is expected that the bearer will be statutory and hold a permanent position. Otherwise, the applicant will have to provide proof of an employment contract with the organization managing the allocated funds. The said employment contract must run for the entire duration of the research project plus 6 months.

There must be a clear match between the main methodology used in the project and the expertise of the principal investigator.

Funding

Thanks to the HADDTS Foundation, this call for research projects provides for financial support up to **60 000 €**, for a maximum duration of **24** months.
Funding support can cover, **if it is entirely and exclusively dedicated to the research experiments**, the costs of:

- Fixed-term contract staff (excluding administrative staff),
- Equipment, up to a maximum of €2,000 (any excess to be justified precisely in the application form),
- Consumables,
- Travels, up to a maximum of €2,000 (possible overage to be justified precisely in the application form),
- Open-access publication fees (article processing charges),
- Provision of services/Subcontracting, if they relate only to the execution of a very limited part of the project (maximum 10% of the budget).

No environmental costs or management fees are eligible.
Funding must be **realistic, reasonable, detailed line by line,** and **fully justified**.
For any question regarding the budget, please see: Guideline to Eligible Expenses

Co-financing of the selected project is possible as long as no conflict of interest exists.

[5] ***Public research organization***: *The public research sector includes entities, organized under public law, that carry out research and experimental development (R&D) for the government, higher education institutions or non-profit institutions (associations and foundations).*

The lead applicant will be responsible for the management of the allocated funds, including, where applicable, the agreement and distribution to the partner teams.

An agreement will be established between the organization managing the research programme (organization of the main leader) and FFRD. **The management organization will not be able to charge any management fee on the amount granted**. *FFRD manages the financial support provided by the HADDTS Foundation and oversees the scientific and budgetary aspects of the winning projects. FFRD does not charge any fees on the sums entrusted to it by the HADDTS Foundation; these will be paid in full to the winning projects.*

Submission process, Selection and Schedule

The application form, in English, must be completed at https://ffrd.syntosolution.com/ before **05/03/2026**, **5pm** (Paris time).
You must have already created your profile on the application platform before submitting (a delay may be necessary). Technical support for the platform is available from 9am to 6pm until March 4th, 2025.

The joint selection by the HADDTS Foundation and FFRD will take place on the basis of:

- validation of the eligibility criteria by FFRD,
- of the priorities of the HADDTS Foundation,
- evaluations by independent external experts (see Annex).

The managing directors of the HADDTS Foundation and the external experts sign a confidentiality and a non-conflict-of-interest agreement.
The reports, documents and filings sent to the managing directors of the HADDTS foundation are confidential.

Scientific and financial follow-up

The HADDTS Foundation is committed to this approach with gravity and a strong sense of responsibility. The budget that its Board of Directors will commit to the selected projects comes exclusively from donations. These include donations from members, as well as funds donated by friends and families, sometimes following the death of one of their own, in a gesture of solidarity with those who are waiting and hoping. PIs are expected to adhere to this commitment.

Half of the grant will be paid at the start of the project.
For projects longer than one year, the PI will have to share briefly by email, every 6 months, on the progress of the project (a few lines).
A complete scientific and financial report must be produced by the PI at mid-term, in order to justify the correct progress of the work and trigger the payment of 40% of the grant.
A final scientific and financial report must be produced by the PI 1 month after the end of the project in order to trigger the payment of the remaining 10% of the grant.

Project outcomes must be published through scientific publications and public communications. Results will be published in open-access, peer-reviewed journals, within a reasonable timeframe, to ensure equity in knowledge sharing and help address access gaps in rare disease fields. All publications, presentations and communications arising in whole or in part from the funded project must mention the support of the HADDTS Foundation in the acknowledgements.

Annex

Evaluation criteria

1. **Interest and importance of the research project to meet the missions of the association.**

Does this study address an important problem? Innovative potential of the expected results for exploitation and for future relevant applications? Is there a sufficient body of evidence for high quality research that supports the rational? How is the project positioned regarding international competition in the field?

2. **Quality and feasibility**

Soundness of the concept, clarity, originality, and pertinence of the objectives. Are the conceptual framework, design, methods techniques, and analyses adequately developed, and appropriate for the aims of the projects?
Coherence and effectiveness of the work plan, including appropriateness of the timeframe, allocation of task and resources (financial, human, and technological resources linked to the laboratory's infrastructure).
Does the applicant acknowledge potential problem areas and consider alternative strategies?
Effectiveness of the proposed measures to exploit and disseminate the project results.

3. **Quality of the applicant**

Ability of the applicant to conduct the research based on the quality of the CV, on its publications and on the quality of the laboratory. Competence and experience of participating research partners. Does the applicant have the right network of collaborators to undertake this type of project? If not, is it important for the Organization to attract this researcher because of their skills or previous work on related subjects?

4. **Budget**

Budget and cost-effectiveness of the project (rational distribution of resources in relation to project's activities, partner responsibilities, and time frame).