FONDATION Maladies Rares

CALL FOR PROPOSALS 2024

- SCREENING -

Identifying new therapeutic molecules for rare diseases

Submission deadline for applications: **September 3rd, 2024, 5:00 pm (CET)**

CONTEXT AND OBJECTIVES

To date, 3 millions of persons are affected by a rare disease in France and around 95% of those patients remain without any therapeutic options. The objective of this call is to support research scientific projects that aim at identifying new molecules with potential translation to therapy to develop innovative treatments for patients living with rare diseases.

To reach this objective, three steps of drug discovery will be considered in the call:

1. Projects based on a **high content/throughput screening** (HCS/HTS) approach using compound libraries, towards the discovery of active molecules called “hits” with therapeutic potential.

2. Projects based on a **mechanistic screening** focused on a reduced number of specific signaling pathways to refine the implication of targeted molecules previously identified through a larger screening.

3. Projects based on the **hit to lead** process towards the optimization of preidentified compounds to approach drug-like characteristics.

PROGRAM DESCRIPTION

Prerequisites:

- The project relies on validated preliminary data,
- The biological model is identified and validated by the research team or a collaborating consortium,
- The experimental model is reproducing a physiological relevant pathway in the disease process with clear read-outs,
- The project clearly emphasizes the relevance of the screening assay towards the identification of molecules to reverse the pathogenesis of the disease described.

1. High content / throughput screening

The project should aim at developing a miniaturized automated robust and reproducible assay as a starting point in the process of filtering out potential hits to be optimized as downstream

drug candidates. Clear and measurable read-out(s) must have been identified before submission.

The project could contain two major tasks: miniaturization and automation of the biological model already developed in the lab of the applicant to use it for high throughput/content screening.

The following parameters that should be considered for optimal downscaling must be described in the project:

- Type of assay: target or process based, biochemical, cell-based (primary cells, cell lines or iPSCs; disease-specific and appropriate controls; etc.) and, when possible, validation in whole organism-based assay,
- Detection technology employed (luminescence, fluorescence, etc.),
- Reagents required (cell lines, antibodies, purified proteins, enzyme substrates, etc.),
- Adaptation of the read-out conditions (if necessary),
- Equipment required.

2. Mechanistic screenings

The project should aim at investigating the mechanisms governing the mode of action of a potential therapeutic, focusing on enhancing comprehension of signaling pathways and refining the involvement of targeted molecules previously identified through extensive screening. The project must rely on mechanisms-based screenings that will provide the next generation of therapeutic molecules.

Proposals should concentrate on a limited set of specific signaling pathways for investigation and must showcase a clearly defined hypothesis-driven methodology.

Areas of interest include, but are not limited to, molecular signaling pathways, gene regulation networks, protein-protein interactions, and cellular dynamics.

3. Hit to Lead

The project must rely on promising hits that have been already identified in a previous screening campaign.

Optimization stages of identified hits rely on two major steps:

- Hits confirmation and profiling to confirm a limited series of molecules, by complementary approaches with the aim of ranking and clustering hits (confirmatory testing, dose response curves, orthogonal testing, biophysical testing, secondary screening, giving prioritization through multiple criteria such as patents, synthesis pathways, *in silico* profiling, etc.)
- Lead discovery to evaluate the optimization potential of confirmed hits in order to select the best compounds and to provide a limited optimization of selected compounds towards a proof of concept in an animal model by combining experimental and computer-aided protocols.
  For lead discovery, the projects may include:
  - Validation of hits or candidate drugs (not necessarily from screening, but also already identified in publications) in models of the disease,

- Evaluation of pharmacology (activity/efficacy) and physico-chemical profiles, ADME (Absorption, Distribution, Metabolism, Excretion) and toxicology properties, pharmacokinetic (PK) behavior,
- Limited testing (minimum 3) of analogous compounds to determine a quantitative structure-activity relationship (QSAR),
- Improvement of hits affinities, metabolic half-life, selectivity against other biological targets.

This program is open to research projects covering all rare diseases.

For rare cancers, the French National Cancer Institute (INCa) and the FFRD have defined jointly the following criteria:

- Projects concerning primary malignant tumors should be addressed to INCa,
- Projects concerning benign tumors as well as systemic rare diseases involving tumor development will be evaluated within this call.

Only one project per research team will be funded for the current call.

INVOLVEMENT OF TECHNOLOGICAL PLATFORMS

FFRD has established partnerships with several technological platforms that offer an outstanding range of expertise, skills and services.

Working with a partnering platform for high content/throughput screening projects is mandatory. Mechanistic screenings and hit to lead campaigns could be performed in the lab of the applicant.

Principal investigators must contact FFRD partner platforms for a detailed description of services and costs that could fit the objectives of their project and to obtain assistance in optimizing the technical design.

The list of the partnering platforms is available on the FFRD website: https://fondation-maladiesrares.org/en/plateformes-partenariats/.

If specific needs are not covered by partnering platforms, please contact the FFRD at aap-bio@fondation-maladiesrares.com in order to evaluate the eligibility of another platform and conditions of services.

ELIGIBILITY

The principal investigator of the study must belong to a French research team**,** affiliated to academia (research team working in universities, other higher education institutions or research institutes) and/or to clinical/public health sector (research team working in hospitals/public health organizations).
Early career scientists are encouraged to apply as principal investigator.

EVALUATION

Applications will be reviewed by at least two national or international academic experts in the field and selected by a dedicated scientific committee composed of FFRD Scientific Advisory Board members and experts in the field based on the following criteria:

- Relevance and significance of the project,
- Project quality and scientific soundness,
- Feasibility of the project,
- Innovation,
- Quality of the applicant and quality of the laboratory.

FUNDING

Funding will only cover costs of the platform (services and consumables) based on the quote provided in the application for high content/throughput screening projects.
For mechanistic screenings and hit to lead campaigns, FFRD will only cover services and consumables. Funding is not intended to cover equipment or personnel costs in the applicant laboratory.

FFRD will provide financial support for a maximum of 40 k€ per project.

SUBMISSION AND SCHEDULE

Applications can only be submitted on the FFRD Synto online platform: https://ffrd.syntosolution.com/.

Provisional schedule:

Launch of the call	June 11, 2024
Submission deadline for application	September 3, 2024 - 5:00 pm (CET)
Technical validation by platforms*	September 17, 2024
Notification of the results	December 2024

*For high content/throughput screening projects, an additional 2-week extension is planned after the submission, in order to allow discussions between the applicant and the platform to optimize, if necessary, the experimental design.

Applicants resubmitting projects must provide a detailed answer to the comments provided by the scientific committee of the FFRD at the previous session and highlight changes in the revised version.
Applicants belonging to a research team already funded by the FFRD since 2017 must have provided a detailed report on the results and impacts of all ended project(s). For ongoing projects, a progress and / or preliminary data report is required.
Report forms are available on the applicant portal (tab “Documentation”) or upon request by e-mail at aap-bio@fondation-maladiesrares.com. Please attach all reports to the proposal in the appropriate section.

FAIR policy / IRDiRC policies and guidelines

By submitting a project to this call, applicants will adhere to the FAIR guiding principles for scientific data management and stewardship.
The aim of the call is in compliance with the goals set by the International Rare Diseases Research Consortium (IRDiRC). Applicants are expected to follow IRDiRC policies and guidelines.

COMMUNICATION

Applicants must agree that title and non-confidential abstract of funded projects as well as principal investigator name and affiliation(s) will be published on the FFRD website: https://fondation-maladiesrares.org/projets-de-recherche-laureats/.

ACKNOLEDGEMENT POLICY

Applicants must acknowledge the FFRD in all communications related with the project (posters, oral communication, scientific publications, etc.) as a funding source using the following terms “Foundation For Rare Diseases” or “Fondation Maladies Rares” and/or using the appropriate logo (available upon request).
Reference(s) of the publication(s) must be sent to the FFRD by e-mail to aap-bio@fondation-maladiesrares.com.

CONTACT

Please contact aap-bio@fondation-maladiesrares.com for any question related with this call.