FOUNDATION FOR
Rare Diseases

"Identifying therapeutic molecules for rare diseases"

The Foundation For Rare Diseases (FFRD, Fondation Maladies Rares) is pleased to launch its 2023 call to identify therapeutic molecules for rare diseases that support:

1. **Development of an automated assay and compound screening,**
2. **'Hit to Lead' campaign to develop lead candidates.**

Submission deadline for applications: **August 31, 2023, 5:00 pm (CET)**

Context and objectives

The objective of this call is to support scientific projects that aim at identifying molecules with potential benefit for the treatment of rare diseases in order to develop new therapies for patients living with rare diseases. Indeed, 95% of rare diseases remain to date without any therapeutic options.

In this context, two steps of drug discovery will be considered:

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. The development of the miniaturized robust and reproducible assay is considered as a crucial step and a starting point in the process of filtering out potential hits to be optimized as downstream drug candidates.

2. Projects based on the **hit to lead** process towards the optimization of preidentified compounds to approach drug-like characteristics. At this stage, the crossroads of all skills between the medicinal chemist and the biologist, multidisciplinary teams and competences in pharmacokinetics, physico-chemistry, toxicology, chemo-computing in order to evaluate all the parameters to be optimized will allow to select best compounds with drug-like characteristics.

Program description

1. Development of an automated assay and compound screening

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.

Assay development:
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. This requires downscaling of the assay to adapt it to a multi-well plate format for easy automation. For that purpose, it could be necessary to adapt assay and/or read-out conditions.

For optimal downscaling of the assay, the following parameters should be considered:

- Type of assay: target or process based, biochemical, cell-based (cell lines, differentiated primary 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.)
- Equipment required.

Clear and measurable read-out(s) must have been identified.

Compound screening:
The screening of the Prestwick chemical library (https://www.prestwickchemical.com/screening-libraries/prestwick-chemical-library/) or of an equivalent library may be envisaged in order to validate the assay and to identify potential hits. The screening of larger chemical/natural libraries, such as a part of the French National Chemical Library (https://chembiofrance.cn.cnrs.fr/en/composante/chimiotheque), can be only performed on the fully operational system.

2. Hit to Lead campaign to develop lead candidates

Prerequisites:

- Promising hits must have been identified already in a previous screening campaign.

Hit to lead strategy
Optimization stages of identified hits rely on two major steps:

2.1. Hits confirmation and profiling

Objective: 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.)

2.2. Lead discovery

Objective: 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.
Projects may include:

- validation of hits or candidate drugs (not necessarily from screening, but already also 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.

General information

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:

- High throughput sequencing 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.

The aim of the call is in compliance with the goals set by the International Rare Diseases Research Consortium (IRDiRC).

Overheads are not allowed by the FFRD.

Specific conditions of experimentation

Access to platforms

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 (assay miniaturization/automation, choice of chemical libraries to screen, data analysis in hit selection and validation, hit to lead optimization stages).

The development of the miniaturized assay and the screening will be performed by an experienced FFRD partner platform in close collaboration with the team of the candidate. A period of 6 to 18 months is necessary for assay development and screening or hit selection and characterization.

Information about partners platforms is available on the FFR website: https://fondation-maladiesrares.org/plateformes-partenariats/.

Technical validation

An additional 2-week extension is planned after the submission (see schedule below), in order to allow discussions between the applicant and the platform to optimize, if necessary, the experimental design and to receive **technical validation of the project by the platform** which is mandatory.
A detailed timetable and budget associated with each step of the project must be provided.

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Instructions and Guidelines

Eligibility

The principal investigator 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 investigators.**

Scientific evaluation

Applications will be reviewed by external experts and then selected by a dedicated scientific committee composed of FFRD Scientific Advisory Board members and experts in the field based on the following criteria:

- Relevance of the project and robustness of preliminary data and the scientific plan,
- Originality and innovative aspects of the project,
- Feasibility of the project,
- Clarity of objectives and outcomes of the project,
- Prospects in terms of future development and capitalization of emerging data,
- Integration of the project in the research program of the applicant,
- Positioning of the project in the national and international context.

Results will be communicated by e-mail to the principal investigator.

Funding

FFRD will provide financial support for a:

- maximal amount of 25 k€ per project for assay development and screening,
- maximal amount of 25 k€ per project for hit to lead campaign.

Funding will only cover costs of the platform (services and consumables). Funding is not intended to cover equipment, operating or personnel costs in the applicant laboratory.

Submission and schedule

Applications can only be submitted on the appropriate eAwards platform: https://ffrd.evision.ca/eAwards_applicant/faces/jsp/login/login.xhtml?lang=EN

Provisional schedule:

Launch of the call	June 8, 2023
Submission deadline for application	August 31, 5:00 pm (CET)
Technical validation by platforms	September 14, 2023
Notification of the results	December 2023

Resubmissions and applicants already funded

Applicants resubmitting projects are required to 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 provide a detailed report on the results and impacts of all ended project(s). For ongoing projects, a detailed progress and / or preliminary data report is required.
Report forms are available on the applicant portal or upon request by e-mail at aap-bio@fondation-maladiesrares.com. Please attach all reports to the proposal.

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 (https://www.nature.com/articles/sdata201618).

The project partners are expected to follow IRDiRC policies and guidelines. For more information see http://www.irdirc.org.

Communication

Applicants must be aware that title of funded projects and principal investigator name and affiliation(s) will be published on the FFRD website (http://fondation-maladiesrares.org). The non-confidential abstract may be use for communication purposes by the FFRD.

Acknowledgement 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.