FOUNDATION FOR
Rare Diseases

# “GenOmics of Rare Diseases 2022”

The Foundation For Rare Diseases (FFRD, Fondation Maladies Rares) is pleased to launch its 2022 call for research projects dedicated to applications of **next generation sequencing to unravel genetic and molecular bases of rare diseases.**

Submission deadline for proposals: **January 19, 2023, 5:00 pm (CET)**

## Rationale

Deciphering the genetic and molecular bases of rare diseases is still far from being completed. It remains of paramount importance to elucidate the pathogenic mechanisms of rare diseases to improve their diagnostic and ultimately for the development of innovative therapies. Next Generation Sequencing (NGS) technologies are powerful tools to achieve this objective.

While whole exome sequencing (WES) allows the identification of genes responsible for monogenic diseases, whole genome sequencing (WGS) may ultimately become the preferred technique for all gene discovery projects. Indeed, it covers uniformly exomes and non-coding regulatory sequences such as introns and intergenic sequences. WGS is also a strategy of choice for the detection of complex structural variants.
However, WGS is still a high-cost technology that requires important resources for analysis and interpretation of genomic variants could be challenging. Hence, expected benefits of conducting a WGS project must be carefully considered and balanced with the chances of success with WES technology for each project.

Due to technical limitations, most of the research focused until recently on highly penetrant monogenic diseases while they represent only a small part of rare diseases. Emerging technologies now allow the study of complex inheritance involving more than a single gene. Identification of genetic bases of rare diseases with non-coding, somatic and complex inheritance is just beginning.

Combination of several approaches could also be helpful such as:
- WGS and RNA-seq with adapted bioinformatic tools, which may allow identification of non-coding variants with evidence of altered gene expression and help to decipher how gene expression is regulated by noncoding RNA,
- deep sequencing and comparative studies, which could highlight hypotheses of constitutive and somatic mosaic mutations,
- study of miRNA expression and epigenetic changes, which can explain the etiology of diseases and/or phenotypic variability of diseases.

Constant cutting-edge technological improvements like single cell approaches are offering substantial opportunities to identify new molecular bases of rare diseases, identify new biomarkers and therapeutic approaches.

## Program description

The goal of this call is to support **hypotheses driven research projects aiming at exploring genetic and molecular bases of rare diseases by the use of NGS approaches** (WES, WGS, RNA-seq, small RNA-seq, ChIP-seq, Methyl-seq, etc.)

Priority will be given to projects that:
- focus on well-characterized clinical phenotypes for which a genetic basis is postulated but not fully demonstrated,
- that show potential leading to molecular diagnosis or therapeutic approaches in clinics,
- for which applicants can demonstrate the availability of expert bioinformatics hub.

Projects based on exome sequencing of modifying genes are henceforth considered outside the scope of this call.

Successful applicants will have a facilitated access to the latest improvements and most appropriate techniques developed by experienced sequencing academic platforms and private companies. Information about our partner platforms is available on the website (https://fondation-maladiesrares.org/les-plateformes/). If specific needs are not covered by partners, please contact us by e-mail at aap-bio@fondation-maladiesrares.com in order to evaluate conditions of services.
For projects using neither conventional WES nor conventional WGS, technical conditions must have been discussed with partner platforms before submission to ensure feasibility of the project. Applicants have to provide a detailed budget based on a quote provided by a platform of the sequencing and data analysis.

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.

Overheads are not allowed by the FFRD.

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

## Instructions and Guidelines

### Submission and schedule

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

Applications will be evaluated by external referees and selected by a scientific *ad hoc* committee, composed of members of the Scientific Advisory Board of the FFRD and NGS experts. Results will be communicated by e-mail to the principal investigator.

Provisional schedule:

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| Launch of the call | November 22, 2022 |
| Submission deadline | January 19, 2023, 5:00 pm (CET) |
| Evaluation and selection process | January – April 2023 |
| Notification of results | April 2023 |

### Eligibility criteria

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 investigator.**

This program is intended for qualified existing biosamples only analysis and will not support participant enrollment, consent or biosample collection for new studies. Consents for research purpose sample analysis must be obtained before application.

### 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 using: aap-bio@fondation-maladiesrares.com.
Please attach all reports to the proposal.

If these items are not fully answered,
the submitted project will not be considered for funding.

## Funding

The FFRD provides financial support for NGS and bio-informatics analyses performed by one of its partner platform. Funding will only cover partner platform costs and is not intended to cover equipment, running costs or personnel costs in the research laboratory.
Please clearly indicate the part(s) of your project for which you request financial support.
Possible co-funding of projects must be specified.

## Samples

For WES and WGS projects, quality check of sample must be available before submission.
Project funding will be lost if samples cannot be sent in a timely manner.
For other NGS approaches, the principal investigator must demonstrate the availability of appropriate budget for samples preparation and detail it in the proposal.

## FAIR policy

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).
Applicants submitting projects agree that the genomic data obtained through funding from the FFRD will be released, as much as possible, after anonymization into a national shared database of rare variations, that will be linked to the RD-Connect platform, a project funded by the European Commission as a contribution to the IRDiRC goals and guidelines.

## Communication

Applicants must be aware that title of funded projects and principal investigator name and affiliation(s) on the FFRD website (http://fondation-maladiesrares.org).

## Acknowledgement Policy

Applicants must acknowledge the FFRD in all communications on 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.

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

## Contact

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