**Next generation sequencing to investigate genetic and molecular bases of rare diseases**

Submission deadline for applications: **February 20, 2024, 5:00 pm (CET)**

**CONTEXT AND OBJECTIVES**

Deciphering genetic and molecular bases of a pathology is mandatory to improve its diagnostic and develop new treatments. Next Generation Sequencing (NGS) technologies are powerful tools toward this objective that is far from being achieved for most rare diseases.

Whole exome sequencing (WES) and whole genome sequencing (WGS) were historically the most used techniques to unravel the cause of genetic diseases. WES allows the identification of genes responsible for monogenic diseases, but WGS is becoming the preferred technique for all gene discovery projects as it covers uniformly exomes and non-coding regulatory sequences such as introns and intergenic sequences.

The “Plan France Médecine Genomique” (PFMG) aims at ensuring an equal assess of all patients affected by a rare disease to WGS to change methods for diagnosis, prevention and treatment of patients. In collaboration with the “Filières de Santé Maladies Rares”, pre-indications were established to perform WGS on patient samples when appropriate. Data are available for both clinicians and patients but also for research programs via the “Collecteur Analyseur de Données”.

However, additional technologies such as RNA sequencing, work on single cells, long read sequencing on targeted genomic DNA or a combination of several techniques are substantial opportunities to identify new molecular bases, identify new biomarkers and therapeutic approaches for diseases with complex mode of inheritance or involving more than a single gene. Efforts are still necessary to improve the understanding of such pathologies and give equal chances to all patients affected by a rare disease.
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.)

**Prerequisites:**
- Projects should focus on human diseases with well-characterized clinical phenotype and for which a genetic basis is postulated but not fully demonstrated,
- Projects need to show potential leading to molecular diagnosis or therapeutic approaches in clinics,
- Applicants must demonstrate the availability of expert bioinformatics hub,
- Projects focusing on disease modifying genes are considered outside the scope,
- Projects for which a pre-indication by the PFMG is existing are not eligible.

**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.

**ACCESS TO TECHNOLOGICAL PLATFORMS**
FFRD has established partnerships with several technological NGS platforms that offer an outstanding range of expertise, skills and services.

For projects using neither conventional WES nor conventional WGS:
- applicants must contact partnering platforms as early as possible to ensure the feasibility of the project and obtain assistance in optimizing the study design,
- a quote for the platform must be submitted at the time of application.

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.

For project using conventional WES or conventional WGS, projects will be oriented through the different partnering platforms of the FFRD after project selection. Applicants do not need to provide a quote at the time of application.

**SAMPLES**

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

For WES and WGS projects, long read sequencing, RNA sequencing, quality check of samples must be available before submission. Funding will be lost if samples cannot be sent in a timely manner.

For other NGS approaches, the applicant must demonstrate the availability of appropriate budget for samples preparation and detail it in the application.

**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.

FFRD is not intended to finance short read WGS for which a pre-indication by the PFMG is existing. Such projects are not eligible to this call. The list of pre-indication is available here: https://pfmg2025.aviesan.fr/professionnels/preindications-et-mise-en-place/

**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 (or evaluated by the FFRD for conventional WES or WGS projects). Funding is not intended to cover equipment, operating or personnel costs from the laboratory of the applicant.

**Overheads are not allowed by the FFRD.**

For information purposes only, projects from 1 k€ and up to 60 k€ were funded through this call during the last 5 years with an average funding of 20 k€ per project.

SUBMISSION AND SCHEDULE

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

Provisional schedule:

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<th>January 9, 2024</th>
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<tr>
<td>Launch of the call</td>
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<tr>
<td>Submission deadline for application</td>
<td>February 20, 2024 - 5:00 pm (CET)</td>
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<td>Notification of the results</td>
<td>End of May – beginning of June 2024</td>
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Results will be communicated by e-mail to the principal investigator.

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 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](mailto: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: http://fondation-maladiesrares.org.

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.