Fondation pour la recherche sur le cancer

CALL FOR PROJECTS

SIGN'IT 2024

Signatures in Immunotherapy

– Diagnose, predict and follow the response to treatment –

Call text

1. Background

As evidenced recently by the boom of immunomodulators targeting the PD-1/PD-L1 pathway, immunotherapy is a fast-growing field in oncology and a great source of hope for cancer patients. Moreover, therapies using patient-derived immune cells such as CAR-T cells represent an emerging field and a great promise for the future. All these novel approaches achieve major and unexpected results and spark the mobilization of the medical and scientific community. The accumulation of knowledge, clinical trials, practices, and therapeutic achievements make this field an area ready for further investigations. Indeed, more research is urgently needed to improve the treatment of cancer patients with immunotherapy.

In fact, several limitations have been identified. For example, some cancers are less sensitive to immunotherapies and, for a given localization, immunotherapies do not exhibit the same efficacy in all patients. In routine care, several questions have arisen concerning immunotherapy treatments such as treatment response, toxicity, hyper- and pseudo-

progression, resistance, etc. Moreover, immunotherapy combinations have demonstrated their ability to maintain the promise to increase the number of patients achieving long-term

benefit. However, the incredibly huge number of combinations under clinical investigation – which frequently have a poor rational to be assessed – might delay substantial improvement due to trial completion and increase patient exposure to undue toxicities. For these reasons, it is still essential to increase research efforts in this field to deliver the right treatment to the right patient at the right time.

In this context, Fondation ARC has launched a specific call for projects (CFP), SIGN'IT, Signatures in Immunotherapy. After six successful editions since 2018, the program is renewed in 2024.

2. Objectives

As part of its scientific strategy, the ambition of the Fondation ARC is to accelerate the safe deployment of immunotherapies for more indications and more patients (including pediatric and geriatric populations). Thus, this CFP mobilizes French expertise around original, ambitious, and innovative projects aiming at **the identification and/or validation of signatures in cancer patients treated by immunotherapy, by taking advantage of already available samples and data**.

3. Scope of the CFP and characteristics of the projects

a. Scope of the CFP

In the context of this CFP:

- "Immunotherapy" is defined as a therapeutic strategy that aims to (re)activate the immune system's anti-tumor functions.
- "Signature" is defined as an indicator or a combination of indicators (clinical, biological, immunological, genetic, epigenetic, anatomic pathology, medical imaging, etc.) which can predict the tumor response under immunotherapy and help the therapeutic decision-making.

This CFP is open to translational research projects applied to **patients treated for their cancer with immunotherapy/ies including cell therapy, alone or in combination.** In case of a combination therapy, the studied immunotherapy can be associated with another immunotherapy or other treatment(s) (radiotherapy, chemotherapy, targeted therapy, etc.).

Research projects within the scope of this CFP should include:

Experimental controls	Indications	Sample/data collections
Adequate control groups should be used (including, when available, control arms in the case of randomized clinical trials)	Available data showing efficacy for the class of molecule/treatment in the given cancer site(s) (including FDA approval)	- Biological samples: **already collected** and/or **being collected** ***AND/OR*** - Data and/or databases: **already available**

In addition, **verification of the technical validity of signatures** identified in the context of projects is strongly encouraged.

b. Characteristics of the projects

- The translational project must be relevant in the field of cancer research.
- The project can be prospective or retrospective.
- The project must be **feasible within the grant period**. A clear description of the feasibility, a timetable and proven capacity to complete the collection and analysis timely have to be included.
- The **experimental design** must be rigorous and based on a solid research hypothesis, a comprehensive statistical analysis plan, and a well-defined study population having a clear indication of potentially answering the research hypothesis.
- Projects investigating early surrogate markers for treatment response and long-term benefit would be appreciated, in particular projects favoring non-invasive methods such as liquid biopsies and new available tools.
- In addition to their scientific relevance, the projects should present **the most reliable ethical guarantees** and have to be conducted according to the existing legislation.

Projects are expected to **contribute to reproducible science. Discussing a plan to disseminate data and results in the submitted application is strongly recommended**, in particular:

- Sharing of results in public databases, particularly after initial publication;
- Publication of data in addition to the results adhering to FAIR principles;
- Publication of data analysis, methods, and code on established resources (e.g. Github, Zenodo).

4. Eligibility criteria

Applications not in accordance with eligibility criteria will not be considered.

Complete applications must be submitted online by the deadline at appelsaprojets.fondation-arc.org

- **The project must be in the scope of this CFP.**
- Unless otherwise stated, **the application and all files must be written in English**.

- The application must be submitted **by the project leader**, who is the coordinator recognised by the associated teams. She/he will be fully engaged in setting up the project and fully invested in the project monitoring.
- The project leader must hold a full, permanent position in a hospital, university or research body in France; failing that, the project leader must hold a temporary position covering the grant period.
- As a project leader, a given researcher **can only submit one project among the two Fondation ARC's CFPs that are simultaneously open** as described in Box 1 below.
- Each team involved in the application must be affiliated with a public research institution (university, public science and technology research bodies etc.) or a non-profit organisation (association, foundation etc.) or a public health institution.

- Foreign and industrial/commercial partners can participate as long as they provide their own funding for the project.
- **To ensure the project feasibility, the availability and access to the samples and to the clinical data of patients must be secured and described.** To this end:
    1) The project leader should attach a letter of commitment from the sponsor or from the biobank operation manager or from the pathologist in charge of the collection (see ANNEX 1 for "Mandatory files");
    2) A clear description of the study design should be included, with a provisional timetable of inclusions. The project should also contain inclusion curves and a description of the specific clinical context (see ANNEX 2 for "Assessment criteria").

Box 1:

The Fondation ARC's CFPs "Programmes labellisés 2024" and SIGN'IT 2024 "Signatures in Immunotherapy" are simultaneously open for submission.

The project leader can only apply to one of the two CFPs.

Projects in the scope of SIGN'IT 2024 "Signatures in Immunotherapy" must imperatively be submitted to this CFP.

For further information concerning the Fondation ARC's CFPs: https://www.fondation-arc.org/liste/appel-projet

5. Exclusion criteria of the CFP

- Clinical trials: tasks directly dedicated to the execution of a clinical trial (inclusion of patients, collection of blood samples, biopsies, etc.) will not be funded. **Only the analyses conducted as part of ancillary studies related to clinical trials will be eligible for funding** (sample analyses, data analyses, modelling, statistical analyses, etc.);
- Projects in which the intellectual property is exclusively industrial (in particular in case of research studies associated with a clinical trial with industrial sponsorship).

6. Funding procedure

a. Project duration and funding

Funding is granted for a period of **24 or 36 months**.
The maximum amount that can be applied for is **€600,000**.

b. Eligible expenses

- Operating costs, including software licenses and fees, and acquisition work in the field (travel costs involved in investigations, etc.);

- Service provisions are allowed. However, private sector service companies (start-up, biotech, etc.) should not claim any intellectual property rights in relation to the results and potential signatures that may arise from the project;

- Publication costs;

- Equipment;

- Computers hardware (computers, accessories and software) can be covered by the funding only if it is justified in the financial application;

- Recruitment of non-permanent staff (post-doctoral researchers, engineers, technicians, data manager or other) for a period not exceeding the grant period;

-Travel expenses (attending symposiums, conferences etc…). Except for a particular situation (evidence must be provided), business expenses must not exceed 4% of the total requested budget.

- Expenses related to experiments on pre-clinical models will only be covered if they are justified and necessary for the project's progress.

There are no restrictions on how the budget is allocated, particularly how much is dedicated to personal cost.

c. Expenses not covered by the grant

- Management fees for managing organizations;

- Salaries of doctoral students;

- Salaries of civil servants and permanent staff;

- Vacations;

- Internship allowances and bonuses;

- Office supplies;

- Subscriptions to learned societies and/or membership fees;

- Equipment maintenance costs.

7. Selection of the projects

The assessment of the projects will be conducted as follows:

- An *ad hoc* committee composed of international experts will review the applications (cf ANNEX 2 for "Assessment criteria") and will issue its recommendations. The project leader will respond to the potential comments issued by the committee and will **make the requested improvements within a period of 2 weeks** (first weeks of May 2024);
- The Fondation ARC's Scientific Board, based on the expert assessments conducted by the *ad hoc* committee, will select applications and make its recommendations to the Board of Directors, which will then vote the funding.

The Fondation ARC guarantees that each application will be assessed under confidentiality agreements, in compliance with its procedure for preventing and managing conflicts of interests.

8. Provisional timetable of the CFP

- Launch of CFP: **November 21th, 2023**
- Return of complete packages: **March 6th, 2024 midday**
- Examination of projects by an international *ad hoc* committee: **April-May 2024**
- Return of modified packages as recommended by the *ad hoc* committee: **mid-May, 2024**
- Selection by the Scientific Board of the Fondation ARC: **May 2024**
- Decision by the Board of Directors of the Fondation ARC: **June 2024**
- Notification of results: **end of June 2024**
- **Project start: Automn 2024**

9. Submission procedures

- The **complete application package**, **including all files** (see ANNEX 1 "Mandatory files") required for scientific and technical assessment of the project, have to be in accordance with this notice and submitted **online** at:

  appelsaprojets.fondation-arc.org

  no later than March 6th, 2024 midday
- **Be careful:** For the application to be admissible, the project leader has to submit it online before the closing date (click on "submit my application package").
- **Until the closing date**, the project leader can re-open/modify his/her application **as many times as desired**.
- An acknowledgment of receipt will be sent by email to the project leader upon validation of the online application.
- **Optional supplemental information:** until **April 14th, 2024**, the project leader can supplement, in the annex tab, the application package with the following documents:
  - Publication update: manuscripts that are in review or have been accepted for publication (please attach letter from the publisher and acknowledgement of receipt);
  - Notification of changes in the administrative situation;

- Notification of acceptation/use of any grant obtained from another funding organization.

10. Contact

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ANNEX 1: Mandatory files

To be admissible, the application must be submitted online at appelsaprojets.fondation-arc.org along with the mandatory files indicated in the table below:

Mandatory files	Content	Format	Deadline for online submission
1. Commitment letter Certified by: • Trial sponsor OR • Biobank operational manager OR • Pathologist in charge of sample collection	• Availability and number of biological samples and/or data included in the project; • Agreement allowing access to these biological samples and/or data; • Conditions and expected date for the provision and/or transfer of the samples and/or data; • Terms of agreements on intellectual property rights; • Compliance with regulations concerning data storage (French Data Protection Authority [CNIL] declaration, etc.); • Quality accreditation of the organization (indicate any potential NF or ISO accreditations).	Free format, generated by the applicant	March 6th, 2024, **at midday** (to upload in the online application, section "Clinical research")
2. Referring staff	List of referring staff for the different disciplines/fields (clinical, immunology, genetics, epigenetics, anatomic pathology, biostatistics, bioinformatics, medical imaging, etc.).	Downloadable online	
3. Scientific signature sheet	Signatures of the associated team leaders and/or persons in charge of the research facilities.	Downloadable online	April 14th, 2024, **at midnight** (to upload online)

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ANNEX 2: Assessment criteria

The international *ad hoc* committee will review the applications in line with the 8 assessment criteria listed below, with a special attention to the quality of experimental design and statistical plan, studied population and feasibility of the work plan.

1. **Global scientific quality of the project and impact**
   Overall scientific quality and innovativeness
   Clarity of hypotheses and objectives
   Potential scientific and medical impact

2. **Relevance and originality of the project**
   Relevance of the project to the objective of the CFP
   Originality of the project

3. **Clarity of the biological hypotheses and the objectives**
   Clarity and appropriateness of the experimental design.
   Clear definition of the studied population.

4. **Quality of methodology, statistical analysis and the studied population**
   Appropriateness of the statistical methodologies.
   Comprehensiveness and quality of statistical analysis plan.
   Anticipation of potential problems, and proposal of alternative approaches

In case of study based on clinical trials: Pertinence in the selection of the patients and samples; Justification of the sample size; Clear synopsis and/or study protocol.

5. **Competence of the applicants and quality of the research collaborations**
   Competence and expertise of the applicant and his/her team.
   Consistency and complementarity between the associated teams

6. **Feasibility of the work plan**
   Clarity of the work plan.
   Overall feasibility of the work plan.
   Appropriateness of the research environment, staff, and infrastructures.
   (If applicable) provisional patient inclusion plan.

7. **Funding sustainability**
   Appropriateness of the project's financial plan.

8. **Ethical issues**
   Accordance with the legislation in force
   Respect for good clinical practice