CALL FOR PROJECTS

SIGN'IT 2022

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, hyperprogression, pseudoprogression, 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 in order 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 four successful editions since 2018, the program is renewed in 2022.

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 immunotherap(y/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 (including FDA approval)	- Biological samples: **already collected** and/or **being collected** *AND/OR* - Data and/or databases: **already available**

b. Characteristics of the projects

- The 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 and have a plan to disseminate their data and results, in particular:

- Sharing of results in public databases, particularly after initial publication;
- Publication of data in addition to the results adhering to FAIR principles (https://www.go-fair.org/);

- 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 2022" and "SIGN'IT 2022, 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 2022 "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.
- Equipment;
- Computers hardware can be covered by the funding only if mentioned in the provisional budget;
- Recruitment of non-permanent staff (post-doctoral researchers, engineers, technicians, data manager or other) for a period not exceeding the grant period;
- 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;
- Travel expenses (attending symposiums, conferences etc...). With the exception of a particular situation (evidence must be provided), travel expenses must not exceed 4% of the total requested budget.

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

- Salaries of PhD students;
- Traineeship grants for students;
- Management body cost's expenses;
- Office supplies;
- Subscription to scientific society and/or membership fees;
- Maintenance cost in case of equipment purchase.

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 approximately 10 days (in the second half of May 2022);
- The Fondation ARC's Scientific Board, based on the expert assessments conducted by the *ad hoc* committee, will select the 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. Timetable of the CFP

- Launch of CFP: **December 17th, 2021**
- Return of complete packages: **March 8th, 2022 midday**
- Examination of projects by an international *ad hoc* committee: **mid-May 2022**
- Return of modified packages as recommended by the *ad hoc* committee: **May 23rd, 2022**
- Selection by the Scientific Board of the Fondation ARC: **June 2022**
- Decision by the Board of Directors of the Fondation ARC: **June 2022**
- Notification of results: **end of June 2022**

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 the March 8th, 2022 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 **May 10th, 2022**, 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

signit@fondation-arc.org
Fondation ARC pour la recherche sur le cancer
Direction scientifique – PReTI
9 rue Guy Môquet
94803 VILLEJUIF Cedex

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ANNEX 1: Mandatory files

To be admissible, the application has to 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 operations 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 8th, 2022, at midday (to be uploaded online)
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	May 10th, 2022, at noon (to be uploaded online)
3. Scientific signature sheet	Signatures of the associated team leaders and/or persons in charge of the research facilities.		

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ANNEX 2: Assessment criteria

The international *ad hoc* committee will review the applications in line with the 5 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. Project quality and impact

- Overall scientific quality and innovativeness of the project.
- Clarity of hypotheses and objectives.
- Potential scientific and medical impact of the project (potential breakthroughs or exceptionally significant outcomes).
- Project's relevance and competitiveness in the national and international context.
- Ethical quality of the research: project implementation in accordance with the existing legislation.
- Plan for dissemination of the results (including how and by when data will be shared according to FAIR principles, https://www.go-fair.org/) and transfer into practice.

2. Project leader and associated teams

- Competence and expertise of the applicant and his/her team.
- Complementarity of the teams involved in the project and the scientific added value of the collaboration.

3. Financial plan

- Appropriateness of the project's financial plan.

4. Quality of experimental design, statistical analysis plan and study population

- Clarity and appropriateness of the experimental design.
- Clear definition/description of the study population.
- Appropriateness of the statistical methodologies to address the study endpoints (e.g. description of null- and alternative hypothesis, statistical models/tests, training/testing/validation set, method for multiple testing correction, provenance of prior distributions/effect sizes).
- Comprehensiveness and quality of statistical analysis plan listing the consecutive analytical steps, which methodology used on which data, to test which hypothesis.

- In case of studies based on any clinical trials:
    - Pertinence in the selection of the patients and samples (representativeness of the study population);
    - Justification of the sample size (statistical power analysis required, or clear reasoning why not possible, in case of "inherited" sample size from existing clinical trial, corresponding sample size justification has to be explained);
    - Clear synopsis and/or study protocol (to be uploaded in "Clinical Research" step in the online application).
- Anticipation of potential scientific or methodological problems, and appropriateness of the proposed alternative approaches ("plan B").

5. Quality and feasibility of the work plan

- Clarity of the work plan and its management over the funding period.
- Overall feasibility of the research plan including milestones' accomplishment on time and on budget.
- Appropriateness of the research environment, staff involved and infrastructures supporting project's implementation.
- In case of studies associated with a clinical trial: provisional timetable of inclusions, inclusion curves and description of the specific clinical context.