CANCER & AGEING

Call for Projects Fondation ARC 2023

1. CONTEXT

a. Scientific background

Many of the mechanisms causing ageing have been deciphered during the last four decades. These mechanisms appear to be rather complex, yet interventions directed at ageing are emerging, offering the potential opportunity to improve a series of late-onset diseases at once. Cancer is one of the diseases promoted by tissue ageing, which is by far the most important risk factor for many types of cancer in humans, *i.e.*, most malignant diseases arise in individuals over the age of 60, the mean age of death from cancer is above 70 years, and the most frequently detected mutational signatures across malignant tumors are signatures of ageing.

The mechanistic links between cancer and ageing are beginning to emerge. Further investigation of age-related patterns and underlying mechanisms of tumor growth and dissemination is needed to generate innovative strategies aiming at reducing the incidence of ageing-related cancer, improving its early detection and adapting its treatment. We have to decipher how ageing interacts with other parameters (e.g., exposome, genetic background) to modulate disease biology, in tumor cells and in their environment (e.g., through inflammaging, immunosenescence, modified microbiota). In older patients with established tumors, we may explore how biological age measurement could guide the generation of evidence-based therapeutic recommendations and reduce adverse events linked to comorbidities, therefore complementing clinical evaluation. We also need to understand how ageing affects treatment efficacy and to what extent cancer and cancer treatment accelerate ageing. An improved control of ageing effects on cells and tissues may reduce the incidence of cancer, facilitate the treatment of ageing-independent tumors by decreasing the impact of comorbidities, and improve the quality of life of cancer survivors.

b. Fondation ARC's ambition

The ambition of the Fondation ARC is to promote research programs that contribute to improve our understanding of cancer mechanisms and generate innovative strategies to improve cancer prevention, early diagnosis, treatment and survivorship, whatever the age and the gender.

In 2020, the Fondation ARC initiated **a new and major strategic focus on "Cancer & Ageing"** by launching a dedicated "Cancer & Ageing" call for projects in 2022.

Following this successful edition, the Fondation ARC decided to renew the call for projects in 2023.

2. OBJECTIVE

The aim of this call for projects is to support one or several translational programs investigating, through a multidisciplinary approach, the specificities of cancer biology in older patients. Potential outcomes of the projects could include an improved understanding of tumors in older patients, the definition of biological and molecular alternatives to geriatric assessment as tools to guide therapeutic interventions, innovative proposals to reduce adverse events, and improve cancer detection, early diagnosis, care and survivorship in older patients.

3. SCOPE OF THE CALL AND CHARACTERISTICS OF THE PROJECTS

- The project must be relevant to the field of **oncology, with a focus on the link between ageing and cancer;**
- The project must address the **specificity of tumor biology along with individual's biology in older patients with cancer;**
- The project can be focused on **one or several cancer types, one or several therapeutic approaches (e.g. chemotherapy, targeted drugs, immune therapies, radiotherapy, surgery), one or several groups of patients defined by age;** The age range will be defined by each investigator with respect to the scientific question raised.
- **The project should be preferably based on samples and data from an existing clinical trial or cohort**, although the setup of a prospective trial or cohort could be included in the project along with its funding;
- The project must have **two project leaders**: a leader for the **biological part** and a leader for the **clinical part**. **Both will be fully engaged in setting up the project and fully invested in the project monitoring**;
- In addition to its scientific relevance, the project should present the most reliable ethical guarantees and has to be conducted according to the existing legislation.

4. PROJECT DURATION AND FUNDING

Funding will be granted for a period **from 4 to 6 years** and may range from **€1,000,000 to €3,000,000**.

5. ELIGIBILITY CRITERIA

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

- **The project must be in the scope of this call;**
- **The main scientific question must be clearly defined;**
- The application must be written in **English**, unless otherwise indicated;
- For technical reasons, the application must be submitted by either the biological project leader or the clinical project leader. The second project leader must identify him/herself as the team manager of the first associated team;
- The project leaders must hold a full, permanent position in a hospital, university, or research body in France;
- Each team involved in the project must be affiliated with a public research institution (university, public science, and technology research bodies, etc.), a non-profit organization (association, foundation, etc.) or a public health institution (CHU, CH, CRLCC, cooperative groups in oncology, etc.);
- 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, the project leaders 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");
- In case of a prospective clinical trial, 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. The provisional timetable of inclusions or inclusion curves must be detailed (see ANNEX 2 for "Assessment criteria").

Exclusion criteria:

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. Eligible expenses

- Operating costs, including software licenses and fees, and acquisition work in the field: travel costs involved in investigations, etc.
- The funding request must include the costs related to the biological samples (collection, storage, shipment, etc.);
- The funding request may include the cost of a clinical trial (sponsoring, monitoring, insurance, 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 that may arise from the project;
- Publication fees;
- Equipment. Computer 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, clinicians or other staff dedicated to the clinical trial) for a period not exceeding the grant period;
- 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 personnel costs.

b. Non-eligible expenses

- Management body cost's expenses;
- Salaries of PhD students;
- Salaries of clinical personnel employed as individual contractors ("vacataires").
- Traineeship grants for students;
- Office supplies;
- Subscription to scientific societies and/or membership fees;
- Maintenance cost of equipment.

7. PROJECT SELECTION PROCESS

- The review will be done by an *ad hoc* committee composed of international experts in biological and clinical research (cf. ANNEX 2 for "Assessment criteria") who will issue its recommendations. The project leaders will respond to the potential comments raised by the committee and will implement the requested improvements within a period of 10 days (in May 2023);
- 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 for 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 interest.

8. SCHEDULE

- Launch of the call for projects: December 15th 2022
- Deadline for the submission: March 8th 2023
- Examination of projects by an international committee: Spring 2023
- Selection by the Scientific Board of the Fondation ARC: May 2023
- Decision by the Board of Directors of the Fondation ARC: June 2023
- Notification of the results: end of June 2023
- Starting date of the projects: Autumn 2023

9. SUBMISSION PROCEDURE

- The complete application has to be in accordance with this notice and submitted online at:

appelsaprojets.fondation-arc.org

no later than March 8th 2023, midday CET

- Either the biological leader or the clinical leader can submit the project.
- **Be careful:** For the application to be admissible, the project leader must submit it online before the closing date (click on "submit my application package");
- **Until the closing date**, the project leader can re-open/modify the 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 27th, 2023**, 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 the letter from the publisher and the acknowledgment 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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Fondation pour la recherche sur le cancer

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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 8h, 2023, at midday (upload when submitting the application online, at the "Clinical research" step)
2. Scientific signature sheet	Signatures of the associated team leaders and/or persons in charge of the research facilities.	Downloadable online	April 27th, 2023, at noon (to be uploaded online)

Fondation pour la recherche sur le cancer

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ANNEX 2: Assessment criteria

The international *ad hoc* committee will review the applications in line with the 9 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 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