Fondation pour la recherche sur le cancer

CALL FOR PROJECTS

PANCREAS 2024

Understand and target pancreatic tumor stroma

-

Call text

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1. Background

With almost 16,000 new cases diagnosed in France in 2023, pancreatic cancer represents a major health issue[1]. Pancreatic cancer is one of the few cancers whose incidence continues to rise, with an increase of 2.3% in men and 3.3% in women each year since 1990. It is estimated that by 2030, it will be the second leading cause of cancer deaths[2]. Despite advances in diagnostic and therapeutic research,

[1] INCa, 2023 – Panorama des cancers en France.

[2] Rahib et al. 2014 – Cancer Res.

pancreatic cancer still has a poor prognosis, with a 5-year survival rate estimated at 11%[1].

Pancreatic cancer is characterized by the presence of a highly developed stroma that can account for 70% to 90% of tumor volume, thus having a significant impact on the biology of this cancer [3,4,5]. The stroma, which represents the non-tumoral part of the tumor, is composed of an extracellular matrix, vessels, nerves, and a cellular component including modified cancer-associated fibroblasts (CAFs) and immune cells[5,6]. It is recognized as an important mediator of disease progression through its direct effects on cancer cells and indirect effects on the tumor's immune microenvironment[3,4]. During pancreatic tumorigenesis, the acellular, cellular and biophysical components of the stroma interact to promote pancreatic adenocarcinoma progression[6].

In addition, the dense pancreatic stroma makes drug penetration difficult. Unlike other solid tumors, where CAFs promote angiogenesis, in pancreatic adenocarcinoma the formation and function of the blood vasculature is inhibited, resulting in a weak and inefficient vascularization in the stroma. Around 80% of intratumoral blood vessels are dysfunctional, and this poor vascularization considerably limits the delivery of therapeutic agents to tumor cells, thus contributing to treatment resistance[6].

To date, no treatment is sufficiently effective in treating pancreatic cancer. The tumor stroma therefore appears to be a relevant therapeutic target. A better understanding of the stroma would enable therapeutic innovations, and for this reason, this line of research represents one of the priorities in the fight against pancreatic cancer.

Since 2022, the ARC Foundation has made pancreatic cancer a major focus of its scientific strategy, by supporting research projects focused on early diagnosis and then early detection of the efficacy of neoadjuvant therapies. This year, the ARC Foundation has decided to continue its support for research into pancreatic cancer, with a particular focus on the specific features of the stroma, with a view to improving therapeutic strategies specific to this cancer.

Funding for the selected projects will be supported by Fonds pour Bertrand Kamal #POURBERTRANDKAMAL.

[3] Hidalgo et al. 2012 – Annals of oncology.
[4] Chu G.C J et al. 2007 – Cell Biochem.
[5] Liot et al. 2021 – Front Immunol.
[6] Jiang et al. 2020 – Front in Oncol.

2. Objective

This call for projects (CFP) aims **to improve understanding of the tumor stroma, anchored in a therapeutic perspective, and develop new treatments for pancreatic cancer.**

3. Scope of the CFP

In the context of this AAP, the notion of pancreatic stroma encompasses: the extracellular matrix, endothelial cells, immune cells and modified cancer-associated fibroblasts (CAF), as well as the nerves innervating the pancreas.

Projects can be in the field of basic, translational or clinical research.

Whatever the field of research, projects must be part of a **therapeutic approach to pancreatic cancer**.

Projects may include, but are not limited to:

- Identification of new therapeutic targets;
- Development of new in vitro or in vivo study models;
- Characterization of the stroma in pancreatic cancer before and after treatment;
- Understanding the role of the stromal microenvironment in therapeutic resistance;
- Developing treatments targeting the stromal microenvironment;
- Etc.

4. Characteristics of the projects

For all projects:

- The proposed project must **be relevant to the field of pancreatic cancer research.**
- The project must **be feasible during the requested funding period.** A description of the project's feasibility, analyses within the allotted time and a timetable of project stages must be included. If necessary, the timetable should include a review of regulatory milestones and negotiations with industry.
- In addition to its scientific excellence, the project must present the most reliable guarantees in terms of ethics, and must be conducted within the framework of existing legislation.
- Projects involving immune cells will only be considered in the context of studying the interaction between immune cells and stroma.

A. Characteristics of basic projects

- The research project must **target the stroma and have a potential therapeutic** impact on pancreatic cancer.

B. Characteristics of translational projects

- The research project must **target the stroma and have a potential therapeutic** impact on pancreatic cancer.
- The project **must involve at least 2 teams.**
- The project may be based on existing cohorts and/or on existing clinical trials (ancillary study).
- The project may be prospective (use of material to be collected) or retrospective (use of previously collected material).
- The study design must be rigorous, based on a sound research hypothesis, a complete statistical analysis plan and a well-defined study population with an indication of the potential response to the research hypothesis.

C. Characteristics of clinical projects

- The research project must **target the stroma and have a potential therapeutic** impact on pancreatic cancer.
- The project **must be a phase 1 and/or 2 clinical trial.**
- The proposed trials may involve monotherapy or combination therapies, **with one of the therapies being evaluated having to target the stroma.**
- The project **must involve at least 2 teams.**
- A strong scientific rationale (biological evidence) supporting the hypothesis and objective of the trial is required.
- Clinical trial evaluation criteria must be clearly defined.
- Drugs with marketing authorization but whose authorization does not cover pancreatic cancer will be accepted.
- Drugs without marketing authorization will only be accepted if the pharmaceutical company undertakes to make them available free of charge.
- The project may be associated with the creation of a biological collection to reinforce the biological concept under study.
- The study design must be rigorous, based on a sound research hypothesis, a complete statistical analysis plan, a well-defined study population and a justification of the initial research hypotheses. The projected inclusion schedule must be detailed (see ANNEX 2 "Expertise criteria").

5. Project duration and funding

The duration and maximum amount granted will be specific to the type of research:

- For a basic research project: **maximum €450,000** over 3 years
- For a translational research project: **maximum €600,000** over 3 or 4 years
- For a clinical research project: **maximum €1,000,000** over 3 to 5 years

6. Eligibility criteria

Applications that do not meet the eligibility criteria will not be considered.

- The project must fall within the scope of this call for proposals.
- Unless otherwise specified, the application must be written entirely in English.
- The same researcher/clinician can only be **involved in one project under the present AAP** but can be associated with several projects.
- The application must be submitted by the project leader, who will be the coordinator recognized by the teams associated with the project. He/she undertakes to commit him/herself fully to setting up and monitoring the project.
- The project leader must hold a permanent position in a French hospital, university, or research establishment (civil servant or permanent contract); failing this, the project leader must provide proof of a temporary position covering the period of the grant applied for.
- Each of the teams involved in the application, including the trial sponsor (if applicable), must belong to a public research organization (university, EPST, EPIC…), a non-profit organization (associations, foundations…) or a public health establishment.
- The participation of foreign and/or private partners is possible as long as they provide their own funding for the project.
- Where applicable, and in order to ensure project feasibility, availability and access to samples and patient clinical data must be secured and detailed (see ANNEX 1 for "Mandatory documents").
- Where applicable, project sponsors must enclose the following documents (see ANNEX 1 for "Mandatory documents"):
    - A letter of commitment in principle from the sponsor to carry out the trial if the project is selected for funding.
    - A commitment in principle from the pharmaceutical company specifying the conditions of participation, and in particular the free provision of medicines without marketing authorization.

7. Exclusion criteria of the CFP

- Projects whose intellectual property is exclusively industrial (particularly in the case of research backed by industrially-promoted clinical trials).
- For translational projects: funding will not be provided for work specific to clinical trials (trial set-up, promotion, patient enrolment, investigation, etc.). Only data collection and analysis carried out as part of ancillary studies in support of clinical trials will be taken into account (collection, storage and analysis of samples, data analysis, modeling, statistical analysis, etc.).
- Phase III clinical trials.

8. Funding procedure

A. Eligible expenses

- Operating costs, including computer licenses and royalties, and field acquisition work (travel expenses related to surveys, etc.);
- Clinical trial costs, in particular:
    - Academic promotion of the trial (administrative procedures to open the trial, insurance, eCRF, follow-up, etc.), patient enrolment;
    - Purchase of drugs studied in the trial (only if they have market authorization).
    - Costs related to biological samples (collection, storage, dispatch to storage center).
- Services are authorized. However, private service providers (start-ups, biotech companies, etc.) must not claim any intellectual property rights on the results that emerge from the projects;
- Publication costs ;
- Equipment;
- Computer hardware (computers, accessories and software), provided this is justified in the financial application;
- Recruitment of non-permanent staff (post-doctoral researchers, engineers, technicians, datamanagers or other professionals dedicated to the clinical trial) for a period not exceeding that of the grant.
- Mission expenses (participation in conferences, congresses, etc.). Except in exceptional circumstances, and subject to justification, mission expenses may not exceed 4% of the total amount.

The budget is freely allocated, particularly regarding the proportion devoted to financing personnel.

B. Non-eligible expenses

- Management fees for managing organizations ;

- Salaries of thesis students ;
- Internship allowances and bonuses ;
- Vacations ;
- Office supplies ;
- Subscriptions to learned societies and/or membership fees ;
- Equipment maintenance costs.

9. Project selection process

Projects will be appraised as follows:

- An *ad hoc* international committee will examine the applications (see ANNEX 2 "Appraisal criteria") and issue its recommendations. The project leader will respond to comments made by the committee, and will make the requested improvements within approximately 10 days (around the second half of September 2024);

- The Scientific Board of the ARC Foundation, in the light of the expert appraisals carried out by the *ad hoc* committee, will select the applications and make its recommendations to the Board of Directors, which will vote on the funding.

All applications are appraised in compliance with the confidentiality agreement and the procedure for preventing and managing conflicts of interest established by the Fondation ARC.

10. Provisional timetable of the CFP

- Call for projects launched: March 1, 2024
- **Return of complete applications:** June 10, 2024, noon
- Projects appraised by an international ad hoc committee: summer 2024
- Selection by the Scientific Council of the ARC Foundation: September 2024
- Decision by the ARC Foundation Board of Directors: October 2024
- Notification of results: end October 2024
- Start of projects: autumn 2024

11. Submission procedure

- **The complete application must comply with these instructions** and be submitted online at :

appelsaprojets.fondation-arc.org
no later than noon on June 10, 2024

- 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 acknowledgement of receipt will be sent by email to the project leader, upon validation of the online application.
- The **mandatory documents** required for scientific and technical assessment of the project, **has to be submitted online by June 10, 2024 or September 2, 2024** (see ANNEX 1 "Mandatory files").

- Optional supplemental information: Until September 2nd, 2024, the project leader can supplement the application package, in the annex tab, 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.

12. 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
If applicable: Sponsor's commitment in principle	A letter from the legal representative of the institution agreeing in principle to act as sponsor if the project is selected to be funded. In this letter the sponsor should also agree to making the results obtained publicly available.	Free format, generated by the applicant	September 2, 2024, at midday (upload online)
If applicable : Pharmaceutical company's commitment in principle	An agreement in principle from the pharmaceutical company to supply the drug if the project is selected for funding. Drugs without marketing authorisation must be provided free of charge.	Free format, generated by the applicant	September 2, 2024, at midday (upload online)
If applicable: Letter of commitment to provide samples Certified by: trial sponsor **or** bio-bank 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	June 10, 2024, noon (upload online)
Scientific signature sheet	Signatures of the associated team leaders and/or persons in charge of the research facilities.	Downloadable online	September 2, 2024, at midday (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
   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.
   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

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ANNEX 3: Summary of project features

Basic research project	Translational research project	Clinical research project
Unless otherwise specified, the application must be written entirely in **English.** The project must: - Fall within the scope of this CFP. - Target the stroma and have a potential therapeutic impact on pancreatic cancer. - Be feasible during the requested funding period. - Present the most reliable guarantees in terms of ethics and be conducted within the framework of existing legislation. *Projects involving immune cells will only be considered in the context of studying the interaction between immune cells and stroma.*		
€450,000 over 3 years	**€600 000 over 3 or 4 years**	**€1 000 000 over 3 to 5 years**
No minimum number of teams involved	Minimum 2 teams involved	Minimum 2 teams involved
	The project may : - Be based on existing cohorts and/or on existing clinical trials (ancillary study). - Be prospective (use of material to be collected) or retrospective (use of previously collected material).	- Phase 1 and/or 2 clinical trials. - Treatments as monotherapy or in combination, **with one of the treatments being evaluated necessarily targeting the stroma.** - Clearly defined clinical trial evaluation criteria. - May be associated with the creation of a biological collection to reinforce the biological concept under study. - A detailed timetable for inclusion is required.
Mandatory annexes: - Signature form for scientific managers (**September 2, 2024**)	**Mandatory annexes:** - Signature form for scientific managers (**September 2, 2024**) - Letter of commitment to provide samples (June 10, 2024)	**Mandatory annexes:** - Signature form for scientific leaders (**September 2, 2024**) - Letter of commitment in principle from the sponsor (**September 2, 2024**) - If using drugs without marketing authorization: Letter of commitment in principle from the pharmaceutical company (**September 2, 2024**)