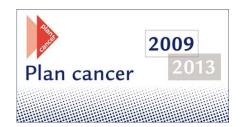


2013 CALL FOR PROPOSALS



Mesure 3, Actions 3.2 et 3.6 Mesure 5, Action 5.4

Research projects in the field of Epigenetics and Cancer

This call for proposals is organized by the Cancer ITMO of the French National Alliance for Life and Health Sciences (AVIESAN) in collaboration with the Institut National du Cancer (French National Cancer Institute). Operational management and follow-up have been entrusted to Inserm.

On-line submission:

https://www.eva2.inserm.fr/EVA/jsp/AppelsOffres/CANCER/BS/index_F.jsp

Deadline: June 10, 2013

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Epigenetic and Cancer

1. Context and objectives of the call for proposals

Cancer is the number one cause of mortality in France and its individual and collective impact is substantial. The major advances in the last few years concerning our understanding of cancers as well as in therapeutic development, underline the importance at this stage of our knowledge in considering new fields able to modify the approaches for prevention, screening and new treatments, beyond genetics.

Research efforts carried out to date have shown the complexity of the mechanisms in the cancerization process which cannot be explained by studies that are targeted solely on isolated factors, mutations, deletions or translocations of single genes.

Understanding the mechanisms that control gene expression and stability of the genome in its multiple dimensions represents major leverage in the generation of tumors and their progression. In this regards, one must consider the factors responsible for the locking and unlocking of the human genome, of which the nature is considered as epigenetic in the sense that their action is exerted without changing the DNA sequence by allowing the propagation of specific states over several cell generations. These epigenetic modifications can be modulated and therefore become new targets of interest for the development of new therapies. The work on these epigenetic modifications goes beyond the framework of the isolated cancer cell and also concerns the peri-tumor cell environment therefore leading to integrated approaches. Such studies are essential in order to expand our understanding of cancers and innovate in the areas of prevention, diagnosis and offer therapeutic approaches that benefit patients. Such approaches are beginning to emerge and developing them as well as evaluating their potential is required.

The purpose of this call for proposals is a better understanding of the epigenetic mechanisms associated with cancer by exploiting in particular recent progress such as the obtaining of high-quality reference maps of the epigenome. These proposals should make it possible to open doors to innovative concepts that participate in untangling the processes involved in tumor development and its possible recurrence.

2. Scope of the call for proposals

Research questions that fall under the scope of epigenetics are highly demanding, in terms of scientific and technical know-how as well as research infrastructures. In this context, the Cancer ITMO is launching this call for proposals of which the objective is to promote the implementation of the critical mass in terms of resources and skills needed to conduct the epigenetics project in the field of cancer. The interdisciplinary nature in which epigenetics operates, which is multi-scale, requires national cooperation between teams with different thematic fields, (and even internationally with funding from the countries concerned) in order to be able to treat and integrate multiple data.

Whenever possible, the research project must demonstrate pooling or a combination of preexisting knowledge, such as: Quality biological and clinical resources, explicit consents, sequencing data, proteomic data, technologies, resources and skills in bioinformatics, validation experimental models, etc.

This call for proposals does not intend to fund a pure mapping project which is already covered in the framework of the International Human Epigenome Consortium (IHEC). The objective is rather to promote innovative research in the field of epigenetics, by following the orientations of IHEC (cf. http://ihec-epigenomes.org/) as much as possible in the quality and methodological criteria. As such, in order to allow for the integration of the results obtained into existing data sets in order to create a global analysis, applicants will have to comply with the same rules as those that exist in IHEC, with regards to collecting equipment, data and management thereof.

Research questions that address the following are eligible:

- the role of epigenetics in the appearance of cancers and their progression;
- pertinent epigenetic mechanisms in liaison with the appearance of cancers and their progression;
- development of experimental models exploring the epigenome and the epigenetic mechanism during transformation or progression;
- functional analysis for validating data on experimental models for results of epigenomic data (for example: analysis of methylation of DNA, analysis of the modification of histones- or transcriptional analysis associated with functional analysis, etc.);
- exploration of the epigenetic characteristics of cells in the tumor microenvironment able to favor tumor progression, for example immune cells, vascular cells, etc.
- Influence of the environment and behavior of people on modifications of the epigenome including normal cells subjected to carcinogen agents;

- Factors that have an impact on the epigenetic profile of an individual, such as very early events, during gestation or infant stage that can create increased susceptibility to developing cancers, nutrition, exposure to infectious agents or behaviors at risk (tobacco, alcohol, etc.);
- Epigenetic mechanisms common to different pathologies (i.e. obesity and cancer) or associated with therapeutic resistance.

The following are out of scope:

- Epigenetic dimension approaches that do not fall under an integrated epigenomic scope;
- pure large-scale map approaches;
- Clinical trials.

3. Participation particulars

3.a. <u>Duration of the projects</u>

The projects may have a duration of 12 to 24 months.

3.b. Eligible teams

The projects shall associate at least two teams that belong to different disciplines, different research units and/or bodies.

- ♣ The teams shall belong to the following bodies:
 - Public research bodies (EPST (French Public Establishments for Scientific and Technological Research), EPIC (French Public Industrial and Commercial Establishment), etc.);
 - Higher education institute (University, schools);
 - Research foundations:
 - Healthcare institutions.
- ♣ The participation of industrial partners and/or foreign teams in possible as long as the latter provide their own funding in the project.

3.c. Coordinator

For each project submitted, the participating teams shall designate a scientific coordinator for the project. In addition to his or her scientific and technical role, the coordinator is responsible for setting up the procedures for the collaboration between the participating teams, for the production of the required documents (reports and assessments), holding meetings, the progress and the communication of results. The project coordinator must spend at least 30% of their time on the project. Applications from early-stage investigators are strongly encouraged.

3.d. <u>Management body</u>

For each project submitted, the participating teams shall designate their management body to receive the funding (which can be different from the body that the coordinator belongs to).

The management body is contractually liable to Inserm for implementing the contract, forwarding all of the financial and scientific reports provided for in the agreement.

For projects that involve several teams that belong to different bodies, and which benefit from a portion of the funds awarded, each management body shall sign an agreement concluded with Inserm.

4. Criteria for eligibility and project evaluation

After the eligibility criteria have been verified, the application files are submitted for written evaluation by international experts and a representative of the evaluation committee of which the members cannot be involved in the projects. Projects that do not meet the eligibility criteria shown in point 4a will not be evaluated.

After publication of the list of projects selected, the membership of the evaluation committee will be posted on the EVA website of Inserm. The opinions of the committee and experts will be sent at the request of the project coordinator.

4.a. Criteria for eligibility

In order to be eligible, the projects must satisfy the following conditions:

- The application file must be duly completed and include the required documents, and comply with the submission procedures mentioned in point 7;
- The project must meet the objectives of this call for proposals and fall within one of the identified fields:
- The project must have a duration that is compliant with the duration mentioned in point 3.a;
- A calendar of key stages must be presented. This calendar will be the primary element for monitoring results;
- The project coordinator must spend at least 30% of his/her time on the project.

4.b. Criteria for evaluation

- Innovation and development:
 - Innovative nature (strategy, concept, technology, etc.);
 - Perspectives in terms of later developments.
- Scientific qualities:
 - Project relevance and originality;
 - Positioning of the project in the national and international context;

- · Clarity of the objectives.
- Coordinator and participating teams:
 - Skills of the coordinator in his/her discipline (applications from early-stage investigators are encouraged);
 - Complementarity and/or multidisciplinarity of the various teams associated with the project;
 - Organization of the collaboration between the candidate teams, scheduling for the production of summary documents, holding meetings for follow-up and for putting the results into form.
- Methodology and feasibility:
 - Methodological pertinence;
 - Project environment (human resources, host structure);
 - Credibility of the project's calendar and of the funding requested.

General provisions for funding

Funding is awarded for the duration of the project (24 to 36 months).

The funding awarded to each project shall be provided in the form of a grant within the framework of an agreement between Inserm and the management body designated in the application file.

- The minimum amount requested per benefitting team must be greater than €25,000.

The Inserm grant can be used to finance:

- Equipment (< €50,000 exc. tax),
- Post-doctoral researchers,
- Missions,
- Provisions of service,
- Operations and various consumable items,
- Personnel costs for temporary staff and post-doctoral researchers; Management costs, for a maximum of 4% of the grant awarded by Inserm. (teams which are managed by Inserm will not include management costs).

Funding of PhD students is not allowed in this call for proposals. Budgetary items shall be fungible during the execution of the project, after approval obtained from Inserm.

5. Calendar of the call for proposals

Publication date for	April, 2013 April 15, 2013	
Opening of the proposal submission website:		
Deadline for submitting application files	 Electronic submission of the complete application file and Paper copy (including 1 original) sent by the post to: 	June 10, 2013
Tentative meeting of	End of September 2013	
Tentative date for p	October 2013	

6. Submission procedure

6.a. Electronic submission procedure

Website: https://www.eva2.inserm.fr/EVA/jsp/AppelsOffres/CANCER/BS/index_F.jsp

This submission procedure, using the EVA website of Inserm, includes:

- identification of the candidate, last name, first name and email),
- the administrative portion which is a form to be completed online
- filing via uploading the requested documents (scientific document, financial notes and the résumé of the project coordinator and of the managers of the participating teams).

Submission deadline: June 10, 2013

It is strongly recommended that you do not wait until the proposal closing deadline to submit your project proposal.

6.b. Application file

The application file must include all of the elements that are required and needed for the scientific, technical and financial evaluation of the project. It is recommended that a scientific and technical description of the project proposal be provided in English. In the event the scientific and technical description is written in French, a translation into English may be requested within a timeframe that is compatible with the evaluation process deadlines.

The complete dossier is submitted in electronic format and in paper format.

Both formats are identical except for the signatures which will be required only on the original paper version.

6.c. Paper format

Two copies of the application file including 1 original signed by the persons in charge (management body + scientific coordinator of the project), and sent to the following address:

Inserm – DESP
Plan Cancer – AAP Epigénétique et Cancer
101, rue de Tolbiac
75013 Paris

Submission deadline: June 10, 2013 (submission date based on the postmark)

7. Publication of the results

The list of projects funded will be published on the EVA website of Inserm. For these projects, the abstract will be published later; each applicant will be contacted in order to confirm the content or provide a publishable version.

Results will be communicated in writing to the coordinators and to the legal representatives of the management bodies.

8. Contacts

For further information, please contact:

- for scientific and technical aspects: plancancer-epig@inserm.fr
- for administrative and financial aspects: plancancer.daf@inserm.fr

Please do not hesitate to refer to the application guide.