2015 CALL FOR PROPOSALS

Research projects in the field of

Epigenetics and Cancer

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) and Inserm, implements the research section of the cancer plan; the budget allocated to the various actions (call for proposals, call for applicants, support for cohorts, integrated platforms and research centers, etc.) is about €30M in 2015.

On line submission:

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

Deadline: January 29 th, 2015

Contact: plancancer-epig@inserm.fr

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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. Criteria for eligibility and project evaluation

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. Applications from early-stage scientific coordinator are strongly encouraged.

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.

3.a. Criteria for eligibility

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

- The project must meet the objectives of this call for proposals and fall within one of the fields identified in point 2,
- The project must have a duration of 12 to 36 months,
- The consortium must combine at least two teams teams that belong to different research units and/or bodies,
- The project coordinator must be a permanent researcher of a public body or of a higher public education institute. He/she must spend at least 30% of his/her time in the project,
- The management body of the project coordinator must not be an association,
- The application file must be duly completed and include the required documents, and comply with the submission procedures mentioned in point 6.

3.b. Criteria for evaluation

After the eligibility criteria have been verified, the applications are submitted for a written evaluation by international experts and at least one rapporteur from the assessment committee, the members of which cannot be involved in the projects. Projects which do not meet the eligibility criteria will not be assessed. After publication of the list of projects selected, the membership of the assessment 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 co-ordinator.

The criteria for evaluation are:

- 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
  - Complementarity and/or multidisciplinarity of the various teams associated with the project,
  - Organisation of collaboration between candidate groups, planning review document production, holding follow up meetings and formatting results.
- Methodology and feasibility:
  - Methodological relevance,
  - Project environment (human resources, host structure),
  - Credibility of the project's calendar and of the financing requested.

4. Calendar of the call for proposals

Date of publication of the call for proposals:		**October 2014**
Opening of project submission site:		**December 12th, 2014**
Deadline for submitting application files	1. Electronic submission of the complete application **and** 2. Two paper copy (including 1 original) sent by the post	**January 29th, 2015**
Tentative meeting date for the evaluation committee		**End-May 2015**
Tentative date for publishing the results[1]		**June 2015**

[1] Results will be published on the EVA website :
https://www.eva2.inserm.fr/EVA/jsp/AppelsOffres/CANCER/index.jsp

5. Administrative and financial rules

Preliminary article - Definitions:

Granting Act: Funding agreement or letter by which Inserm notifies the Managing Body of its rights and obligations with respect to conduct of the selected Project. The Granting Act takes the form of a notification letter if the body managing the grant is Inserm. These two instruments are hereafter referred to with the generic term "Granting Act".

Research Charity: a private body subject to the Law of 1901 devoting at least 50% of its main activity to research.

Managing Body: Research body managing the grant to conduct the Research Project as submitted in the Application File. The Managing Body is contractually responsible for implementing the Contract and compiling all the scientific and financial reports stipulated in the Granting Act.

Project Coordinator: the person responsible for the scientific conduct of the Project as designated in the Granting Act.

Research body: This term refers to all entities such as public sector research institutions (EPST, EPIC, etc.), institutions of higher learning (universities, etc.), research foundations, health care establishments, and any other body involved in the research field.

Partner: A research team contributing to conduct of the Research Project.

Project: research project addressed in the scientist's Application File and selected by Inserm for funding in the framework of the Cancer Plan.

Rules: these financial rules with their appendices.

5.a. Scope

These Rules apply to Managing Bodies allocated a grant by Inserm to conduct a Research Project, selected in a tender for projects launched by Inserm. Tender procedures are conducted by Inserm under the aegis of the following divisions: ITMO Cancer, the *Département de l'Evaluation et du Suivi des Programmes* (DESP, Department of Programme Evaluation and Monitoring) and the scientific interest group *Institut de Recherche en Santé Publique* (IReSP) within the framework of the Cancer Plan 2014-2019.

5.b. Contents

Funding is granted by Inserm after the Project has been selected on the basis of the Application File submitted by the Coordinator according to the criteria for eligibility and evaluation of the text of the corresponding tender for projects.

The Application File includes:

- A scientific file;
- The Project's budget broken down in the financial appendices;
- The CVs of the Project Coordinator and the Director(s) of any associated team(s) (all in a single file);
- The Administrative Form to be filled out on line on the special Application File Submission site.

For research charities, the following complementary documents should be appended to the Application File:

- Last year's accounts together with forecasts and a financial plan, all following Inserm models.

5.c. Managing Bodies

Teams belong to the following bodies:

- Public-sector research institutions (EPST, EPIC, etc.),
- Institutions of higher learning (universities, etc.),
- Research foundations,
- Public-sector health care establishments,
- Other bodies involved in the research field.

The participation of industrial partners and/or foreign teams is possible as long as they provide their own funding in the Project.

The funding of charities (as defined in the 1901 Law) not classified as Research Charities is not allowed. Management by a charity is only possible if it justifies research activity. Public research teams affiliated with a public-sector body or entity must have their grant managed by their associated public body or one of the mixed administrators of their structure.

Similarly, Inserm will check the capacity of charities to finance the part of the cost which is up to them. In the course of the selection process, Inserm may check that any partner charities in the Research Project are in a position to finance the part of the cost of the research not covered by the Inserm grant.

When administrative and financial files are being finalised, charities allocated a grant may be asked for further information.

If the Project involves different teams associated with different bodies benefiting from part of the funds granted, each Managing Body will sign a separate agreement with Inserm.

5.d. Coordinator

If there are multiple teams involved[2], a Project Coordinator must be appointed. Each partner team appoints a scientific leader.

In addition to his/her scientific and technical role, the Coordinator is responsible for organising the collaboration between participating teams and meetings as well as monitoring progress and communicating results. He/she is responsible for compiling the required reports and sending them to Inserm.

The Coordinator must:

- Be a statutory employee of a public-sector research body, a public institution of higher learning or a public health care institution;
- Devote at least 30% of his/her time to the Project.

5.e. Duration of the Project

The Managing Body and the Coordinator undertake that the Project will be completed within the time frame stipulated in the Granting Act notwithstanding possible modifications in duration detailed in Article 6.

This duration corresponds to that in which expenses must be assumed and paid.

The Project must be started in the year of notification of the Granting Act.

[2] Refer to eligibility criteria

5.f. Granting Act

1. Form of the Act

The Act takes the form of:

- Either a grant agreement signed by the Managing Body and Inserm;
- Or a notification letter sent to the beneficiaries if the Managing Body is Inserm.

2. Information that must be mentioned in the Granting Act

The Granting Act is compiled by Inserm on the basis of information in the Application File and the text of the corresponding Tender for Projects.

It must include the following information:

- Title of the Project;
- Duration of the Project;
- Duration of the Granting Act;
- Partners involved in the Project and the Coordinator;
- The total sum granted and how it is to be paid;
- The obligation to send Inserm the reports mentioned in Article ***5h*** of the Rules. How and when these are to be sent are stipulated in the Granting Act;
- Appendices to the Granting Act:
  - Appendix 1: summary of the Project as stipulated in the Application File;
  - Appendix 2: budget
  - Appendix 3: model of the financial justification.

3. Documents constituting the Granting Act

The documents that make up the Granting Act have the following order of precedence, especially in the event of conflicting provisions:

- The Granting Act and its appendices;
- The Rules.

4. Special provisions

Inserm and the Managing Body may include in the Granting Act special obligations and/or exemptions from the Rules that are justified either by specificities of the funded Project or by modification of the Project in the framework of the Tender for Projects or by an agreement between Inserm and one or more of its partners.

5. Notification of the Granting Act

The Granting Act is notified by a letter from Inserm.

6. Modification of the Granting Act

Inserm will compile and sign an additional clause for any modification of the provisions of the Granting Act.

However, prolongation of the duration of the Project, agreed to on an exceptional basis, is notified by a simple letter sent to the grant's Coordinator or Managing Body.

Prolongation cannot exceed 12 months.

5.g. Grant

1. Calculation of the total sum

When the total sum granted is identical to that asked for in the Application File, it includes the budgetary appendix compiled by the Coordinator when the application is submitted.

If the total sum granted by Inserm differs from that asked for in the Application File, Inserm sends the Coordinator an E-mail with the global total of the grant that it is intending to attribute to conduct the Project.

In this case, a new financial appendix is compiled, dated and signed by the Managing Body. Then the Coordinator must conduct the Research Project in line with the instructions of Inserm.

In the event of refusal to compile a new financial appendix or failure to answer within one month of Inserm sending the E-mail, no grant will be attributed.

The grant attributed cannot be less than 25,000 € per team participating in the Project for its entire duration.

2. Value Added Tax

Because of the absence of counterpart to Inserm's financial support and applying the provisions of fiscal instruction 3A-4-08 of 13 June 2008 from the Public Finances Directorate, the grant attributed by Inserm is not subject to VAT.

3. Payment

a) Schedule

For Managing Bodies other than Inserm, 80% of the grant is paid on signing of the agreement with the remaining 20% paid after validation of the reports referred to in Article ***5h***.

For charities, a first payment will be made on signing of the Agreement. Subsequent payments—up to 80% of the grant—will be made after the validation of interim reports (scientific and financial). Payment of the balance of 20% will be made after validation of the final reports.

When the Managing Body is Inserm, credits corresponding to the grant are opened in annual blocks.

b) Suspension of payment

If the project has not been started by the planned date of production of the first scientific report, Inserm will notify the Managing Body of the breach in a registered letter with acknowledgement of reception. This letter will require the Managing Body to overcome the difficulties encountered within two months of reception of this letter.

If the deficient Managing Body has failed to remedy the problem by this deadline, cancellation is announced.

4. Use of the grant

The Managing Body must use the grant paid by Inserm exclusively to conduct the Project stipulated in the granting agreement.

At the end of the Project, any unspent moneys are to be reimbursed to Inserm within 90 days.

5. Eligible expenditure

All expenditure must be directly related to the Project, strictly necessary to its conduct and duly justified.

a) Equipment

Equipment may be bought apart from office materials and furniture.

Apart from funds allocated within the framework of *Actions Equipement des Nouveaux Centres* (New Centre Equipment Actions), Inserm does not fund equipment costing more than a total of 50,000 € (not including tax). For expenditure of a greater amount, co-funding will have to be sought.

b) Staff

Expenses for temporary staff are eligible.

For private-sector establishments, expenses for permanent staff members are eligible as long as these employees are allocated to the Project strictly within the framework of its execution.

Funding doctoral contracts is not allowed unless this is specifically allowed for in the text of the tender for the project concerned.

Expenses for administrative staff are ineligible.

c) Operating costs

Services

The Coordinator may sub-contract out part of the Inserm-funded work required for the Project to third-party service providers. However, these services must only bear on execution of a small part of the Project and must comply with public-sector ordering regulations.

Consortium agreement

The cost of compiling a consortium agreement is eligible if the conditions stipulated in Article ***5m*** of these rules are fulfilled.

Other operating costs

The other operating costs that are eligible are:

- Consumables;
- Project-related travelling expenses for scientists;
- Intellectual property expenses for patents and licenses resulting from execution of the Project;
- Expenses justified by an in-house billing procedure.

d) Management costs

A fraction of general administrative costs generated by the Project may appear in the funded expenses. This fraction is limited to 4% of the Project's grant total cost of eligible expenses and does not need financial justification.

e) VAT

For partners who are not subject to VAT or only partly subject, the unrecoverable part of VAT paid out on eligible expenses constitutes an eligible expense.

6. Fungibility

The grant paid by Inserm is fungible under the operating expenses ticket. Budget can only be transferred for staff costs with the agreement of Inserm.

7. Other provisions

If the amount of the grant paid by Inserm does not cover all expenses incurred in executing the Project, the Managing Body undertakes to complement the funding to ensure the Project's proper execution, either from its own resources or by means of one or more co-financing agreements.

In this event, the Managing Body will tell Inserm about any co-financing agreed to subsequent to notification of the agreement together with the name of the co-financer and the sum of the co-financing.

5.h. Scientific and financial reports

1. Scientific reports

The Coordinator is to issue reports as stipulated in the Granting Act.
They are to be sent:

- An Interim Report six months after the beginning of the Project for Projects conducted by ITMO Cancer and DESP;
- A Mid-Term Report half way through the Project for Projects lasting more than two years;
- A Final Report within two months of completion of the Project.

Failure to produce interim or final scientific reports will entail reimbursement of all sums paid by Inserm.

Scientific review of interim or final reports may lead Inserm to ask for complementary information and financial support may be suspended or terminated in the event of failure to adhere to the Project or use of the funds for some other project.

2. Financial reports

Financial reports are compiled as stipulated in the Granting Act and the Rules; these present the expenses allowed throughout the duration of the Project.

Charities send an interim financial report on the anniversary date of the Granting Act.

Managing Bodies will issue a Final financial Report within two months of completion of the Project.

Financial reports are signed by the Coordinator together with a financial manager in such a way as to represent the Managing Body.

They are to be sent to Inserm by the grant's Managing Body.

Costs related to the certification of expenditure by an external auditor are eligible expenses.

At the end of the Project, any sums remaining will be paid back to Inserm by the Managing Body.

5.i. Other undertakings on the part of the Coordinator and the Managing Body

The Coordinator is obliged to tell Inserm about any substantial change to the Research Project vis-a-vis the contents of the Application File/Granting Act as well as about any difficulties encountered with conduct of the Project.

The Coordinator also undertakes to take an active part in operations to monitor the Project organised by Inserm/ITMO Cancer (dissemination workshops, colloquia, etc.).

The Managing Body will inform Inserm of any change of address or bank details.

5.j. Organiser - assigned accountant

The organiser of grants and credit transfers is Inserm's Président Directeur Général or by proxy its Director of Finance.

The assigned accountant for payments is Inserm's Head Accountant (*Agent Comptable Principal*).

5.k. Technical and financial supervision

At any point during the Project, Inserm reserves the right to organise site visits in concert with the Managing Body and the Project Coordinator.

Use of the grant paid under the aegis of the Granting Act may, throughout the Project and for two years after its termination, be controlled or audited by Inserm or by an agent appointed by Inserm, by means of a document review or an on-site inspection.

The Managing Body will be expected to be able to justify allocation of funded staff members to the Project as well as all expenditure on the grant.

The Managing Body must be ready to provide all administrative, accounting and legal documents as well as receipts related to use of the grant.

Attention is drawn to the fact that, since this grant corresponds to public moneys, the funds may be audited by various state supervisory bodies.

5.l. Publications – communication

1. Publications

All publications resulting from the Research Project must mention this financial support in the following terms:

"With financial support from ITMO Cancer AVIESAN (*Alliance Nationale pour les Sciences de la Vie et de la Santé*, National Alliance for Life Sciences & Health) within the framework of the Cancer Plan"

or

"With financial support from IReSP within the framework of the Cancer Plan"

Any publications are to be sent to Inserm in a timely fashion (within five days of publication).

2. Dissemination of the abstract

The Coordinator will authorise the dissemination of the abstracts (in both English and French) contained in the Application File. Before dissemination, the texts will be sent by E-mail to the Coordinator for validation of their contents. In the absence of any response within 45 days, the texts will be considered validated.

3. Impact analysis

The Coordinator undertakes to compile—for subsequent posting on the ITMO Cancer Web site—an impact analysis summarising what the funded Project contributes to the fight against cancer.

5.m. Intellectual property

As funder and issuer of tenders for projects and grants, Inserm does not acquire any intellectual property rights. All intellectual property rights related to work on the Project and its results accrue to the Managing

Body. If there is more than one Managing Body, they will have to agree among themselves about the allocation of intellectual property rights.
Compiling a consortium agreement is highly advisable if:

- The overall total of the grant amounts to more than €250,000;
- More than three partners are involved in the Project.

It is obligatory if a private-sector Managing Body becomes a partner in the Project.

5.n. Confidentiality

Inserm undertakes to preserve the confidentiality of all information acquired in the course of execution of the project, notably that contained in the Activity Report, hereafter referred to as the "Information". Inserm is not allowed to disclose anything at all in any form to any third party (apart from the Cancer Plan Steering Committee) without written permission from the Coordinator.

Nevertheless, Inserm will not be bound to secrecy for a specific point of information if it can prove that:

- The information is in the public domain without there having been infraction of the grant agreement or the Rules;
- The information was already known to Inserm on the date of signing of the agreement;
- The information becomes freely available from some other source which has the right to it.

5.o. Protection of personal data

Information of a personal nature collected in the Application File will be processed by computer to compile documents and help with the administrative and financial monitoring of Research Projects. In compliance with the Information Technology & Privacy Law of 6 January 1978 as amended in 2004, persons on whom data are collected have rights of access to, rectification of and deletion of information about themselves. These rights can be exercised by application to Inserm, Legal Affairs Department, 101 rue de Tolbiac - 75013 PARIS.

5.p. Settlement of disputes

For any conflict between Inserm and the Managing Body relating to interpretation or execution of the Granting Act, both parties undertake to bring their dispute to conciliators appointed by each of them (unless they can agree on a single conciliator) before recourse to any court.

The conciliator(s) will do all they can to settle the difficulties and bring the parties to amiable resolution within sixty (60) days of the date of their appointment.

In the absence of amiable resolution, the administrative judge will be convened to rule on the dispute related to application of the Granting Act.

5.q. Date of implementation of these Rules

These Rules come into force on the date of their publication and apply to grants allocated by Inserm in the framework of scheduling tenders for projects for 2015 and thereafter.

6. Submission procedure

The complete application file is submitted in electronic format AND in paper format.
Both formats are identical except for the signatures which are required only on the original paper version.

6.a. Application file

The application must include all of the elements that are required and needed for the scientific, technical and financial evaluation of the project. Applicants are recommended to produce a scientific and technical description of the project proposal in English. If the scientific and technical description is written in French, an English translation may be requested within a deadline compatible with the evaluation process milestones.

The applicant's file is composed of 5 elements:

- The scientific file (download the scientific document to be used)
- The financial file (download the Excel file to be used)
- PI and Co-PI Resumes (together in a single file)
- The administrative form (you have to fill it on-line in your personal space)
- The bank information (Relevé d'Identité Bancaire) (paper format)

6.b. Electronic submission procedure

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

This submission procedure from the EVA website of INSERM will include:

- Identification of the candidate (surname, forename and e-mail),
- The administrative section, as a form to be completed on line
- Submission of the required documents by uploading (scientific dossier, financial appendices and CV of the project co-ordinator and heads of the participating groups).

Submission deadline: Januray 29th, 2015

Applicants are strongly advised not to wait until the proposals closure deadline to submit their project proposal.

6.c. Paper format

Two copies of the application dossier including 1 original signed by the people in charge (management body + project scientific coordinator + teams leaders) sent to the following address:

Inserm – DESP
Plan Cancer – “Epigenetics and Cancer”
101, rue de Tolbiac
75013 Paris

Submission deadline: January 29th, 2015 (submission date based on the postmark)

7. Publication of the results

The list of projects financed will be published on the EVA website of INSERM. For these projects, the abstract will be published later, and 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.

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
- for problems relative to the electronic submission : eva@inserm.fr