



2017 CALL FOR PROPOSALS

Research projects in the field of multidisciplinary approaches in modeling complex biological processes applied to cancer field (Systems biology)

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 2017.

On line submission:

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

Deadline: June 30th, 2017 (4 pm)

Contact: plancancerbiosys@inserm.fr

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1. Context and objectives of the call for proposals

Systems biology, as the term indicates, is a biology-based interdisciplinary field of study that focuses on the relation and interactions within biological systems (communication of cells at tissue and organ level, metabolism, network of genes and proteins in healthy and pathological conditions). The aim of this call is to propose a functional model at the cellular, tissue or organism level in healthy or pathological situation. The proposed model will be confirmed through experimental approaches using tools from experimental biology to clinical observation.

It is organized by ITMO Cancer of the French National Alliance for Health and Life Sciences (Aviesan) in collaboration with INCa (French National Cancer Institute). Inserm is entrusted with the operational management of this funding call.

The general objective of this call for proposals is to support multidisciplinary upstream research (mathematics, physics, chemistry, computers, biology, *etc.*), in order to make progress towards modelling of complex processes or integrative biology, in the field of cancer. It must in particular allow the development of multidisciplinary integrated teams that interact with clinicians, anatomopathologists and biologists in the field of cancer.









2. Scope of the call for proposals

This call for proposals covers any model, integrating molecular and cellular data to clinical response (predicting the survival of patients). Any model that addresses the various intermediate steps in the continuum will be considered.

The proposals must fall within a multi-scale integration, which, using the analysis of pre-clinical data, will lead to predicting the clinical response, therapeutic evaluation, modeling tumors at a macroscopic and cellular level in order to understand the cellular development and proliferation by integrating the signaling pathways and cellular interactions. Their ambition is to understand the development, growth and changes in tumors and response to the treatment. They should make it possible at an earlier stage to adjust a therapeutic choice by including inter-individual variability.

To implement them, projects will have to call upon multi-disciplinary consortia. The model proposed should be validated experimentally.

The following fields are clearly eligible:

-  **Modelling of major signaling pathways involved in tumor progression incorporating a specific cellular context,**
-  **Integration and modeling of tumor micro-environment and cellular interactions,**
-  **Modelling of interaction networks to predict therapeutic targets,**
-  **Pharmacological models of multi-scale molecular systems (PK-PD) for antineoplastic drugs and their associations in combined therapies, whether or not targeted,**
-  **Modelling of potential new molecular targets for pharmacological research,**
-  **Modelling the response or resistance to treatments,**
-  **Modelling the role of cancer initiating cells,**
-  **Modelling the cellular adaptive dynamics (modeling the change in tissues toward malignancy, clonal evolution, ...),**

- ✚ **Modelling the diagnosis, monitoring, response to treatments and population analysis for an individual estimation,**
- ✚ **Developing models using images or biological "data" of patients.**

The following are out of scope:

- ✚ Projects concerning bioinformatics platform,
- ✚ Clinical trial projects,
- ✚ Projects devoted to traditional imaging approaches,

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 collaboration between participating teams, for the production of required documents (reports and assessments), holding meetings, the progress and the communication of results. Applications from early-stage scientific Coordinators 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 twelve (12) to thirty-six (36) months,
- ✚ The consortium must consist of at least two teams that belong to different research units/institutes,
- ✚ The project Coordinator must be a permanent researcher of a public body, of a higher public education institute, of a public-sector health care institution or of a state-approved research foundation,
- ✚ 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 (See section 5C for detailed information),
- ✚ The Application File must be duly completed and include the required documents, and comply with the submission procedures mentioned in section 6.

3.b. Criteria for evaluation

Once the eligibility criteria are verified, the international experts and at least one reviewer of the evaluation committee will review the applications. Projects that do not meet the eligibility criteria shall not be assessed. After the publication of the list of projects awarded, the participants of the evaluation team shall 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.

The criteria for evaluation are:

✚ Innovation and development:

- Innovativeness of the project (strategy, concept, technology, *etc.*),
- Perspectives in terms of future developments.

✚ Scientific qualities:

- Project relevance and originality,
- Position of the project in national and international context,
- Clarity of the objectives.

✚ Coordinator and participating teams:

- Skills of the coordinator in his/her discipline
- Complementarity and/or multidisciplinary of the various teams associated with the project,
- Organisation of collaborations between the different teams, planning review document production, schedule follow up meetings and result analysis and presentation.

✚ 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

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| Date of publication of the call for proposals: | | April 2017 |
| Opening of project submission site: | | May 15th, 2017 |
| Deadline for submitting Application Files | 1. Electronic submission of the complete application and 2. Two paper copies(including 1 original) sent by post | June 30th, 2017 (4 pm) |
| Tentative date for the evaluation committee meeting | | October 2017 |
| Tentative date for publishing the results¹ | | November 2017 |

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".

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

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 manages 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 education (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'Évaluation 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

Inserm grants funding after the project is selected based on the Application File submitted by the Coordinator.

The Application File includes:

- ✚ A scientific file;
- ✚ The project's budget well divided in the financial annexe (the financial annexe should be signed and stamped). For research charity and research foundation, the budget corresponds to full-costing;
- ✚ The CVs of the project Coordinator and the director(s) of any associated team(s) (all in a single PDF file);
- ✚ The Administrative Form to be filled out on line on the special Application File submission site;
- ✚ Bank account identification for each managing body should be included in the paper version only.

For Research Charities and Research foundations, the following complementary documents should be appended to the Application File:

- ✚ Last year's financial report, all complying to Inserm model;
- ✚ Status updated.

5.c. Managing Bodies

Teams should belong to either of the following bodies:

- ✚ Public-sector research institutions (EPST, EPIC, etc.),

- ✚ Institutions of higher education (universities, *etc.*),
- ✚ Research foundations,
- ✚ Public-sector health care establishments,
- ✚ International research organisations working on French soil.

Research teams affiliated to a public body, a higher education institute, or a public-sector health care institution **must** appoint this managing body (or one of the tutelage of their structure) to manage the grant.

The participation of industrial partners and/or foreign teams is possible as long as they have their own funding, as those teams shall not be funded by this funding call.

The non-research foundations will not be funded (as per the law implemented in 1901). Management by a foundation is possible if at all it justifies research activity. Inserm will check the financial ability of the foundations to verify if it is capable of financing the part of the cost that is not covered by INSERM. 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 involved², 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 **permanent employee** of a public-sector research body, a public institution of higher education 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 period stipulated in the Granting Act, notwithstanding possible modifications in duration detailed in Article 6.

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

The project must be started before June 30th, 2018.

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.

If the project involves several teams belonging to different managing bodies, and receiving a part of the grant, each managing body should be signatory of a convention with Inserm.

² Refer to eligibility criteria.

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 informations:

- ✚ Title of the project in French and in English;
- ✚ 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 is stipulated in the Granting Act;
- ✚ The summary of the project as stipulated in the Application File;
- ✚ The provisional budget of the Project.

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:

- ✚ Granting Act and its appendix:
 - Appendix 1: summary of the project as stipulated in the Application File;
 - Appendix 2: budget of the project;
 - Appendix 3: model of the financial justification;
- ✚ 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

A letter from Inserm notifies the Granting Act.

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, a simple letter sent to the grant's Coordinator or Managing Body notifies prolongation of the duration of the project, agreed to on an exceptional basis.

Prolongation cannot exceed twelve (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 annexe compiled by the Coordinator during application submission.

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 sum that it is intending to attribute to conduct the project.

In this case, a new financial annexe 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 annexe or failure to answer within one month of after sending the E-mail, the grant shall not 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

Since Inserm does not have a financial support counterpart and due to the provisions applied according to the 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 upon signing the agreement with the remaining 20% paid after validation of the reports referred to in Article **5h**.

For **foundations**, a first instalment will be paid upon signing the Agreement. Subsequent payments—up to 80% of the grant—will be made after the validation of interim reports (scientific and financial). The last 20% will be paid after validation of the final reports.

If the Managing Body is **Inserm**, the grant shall be credited in annual blocks.

b) Suspension of payment

In the absence of intermediate and/or final scientific and/or financial reports, Inserm may suspend the payment or even ask for a total or partial reimbursement.

If the project is not started as per schedule or by the date of production of the first scientific report, Inserm will notify the breach to the Managing Body through an acknowledged registered letter. The Managing Body has two (2) months hence to overcome the difficulties since the date of reception of the letter.

If the concerned Managing Body fails to address the problem, the grant shall be cancelled.

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 money should be reimbursed to Inserm within ninety (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 for research 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) per partner. For expenditure of a greater amount, co-funding should 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. Such affectation should be justifiable.

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 part of the Inserm-funded work required for the project to third-party service providers. However, these services must bear execution of only a small part of the project and must comply with public-sector regulations.

Work of these third-party service providers is under the responsibility of the Managing Body.

Services are organized in accordance with the Managing Body terms and conditions, notably in accordance with applicable mandatory prescriptions if required.

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 8% of the project's 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

Reports should be written in French.

1. Scientific reports

The role of the Coordinator is to issue reports (from all Partners) as stipulated in the Granting Act. They are to be sent:

- ✚ An Interim Report six (6) months after the beginning of the Project;
- ✚ A Mid-Term Report half way through the Project for Projects lasting more than two (2) years;
- ✚ A Final Report within two (2) 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. Foundations should 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.

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

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

At the end of the Project, the Managing Body shall return any sum remaining to Inserm (within ninety (90) days from the repayment asked by Inserm).

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 in conducting 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 it is the Finance Director.

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

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 (2) 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 justify all recruitments and all expenditures of the grant;
- ✚ 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 money, various state supervisory bodies may audit the funds.

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 should be sent to Inserm in time (within five (5) 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 forty-five (45) days, the text will be considered validated.

3. Impact analysis

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

5.m. Intellectual property

As funding body 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 amongst themselves regarding 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 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 was freely available from some other source, which has the access and right to it.

5.o. Protection of personal data

Personal information 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 right 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 their best 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 amicable 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 2017 and thereafter.

6. Submission procedure

The completed 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 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 five **(5)** elements:

- ✚ The scientific file (download the scientific document to be used),
- ✚ The financial file (download the Excel file to be used),
- ✚ CV of Coordinator and Director(s) of any associated team(s) (together in a single PDF file),
- ✚ The administrative form (filled on-line in your personal space),
- ✚ The bank account identification (*Relevé d'Identité Bancaire*) (paper format only).

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) to allow the assignment of a user ID and password to reach your personal space on EVA website,
- ✚ The administrative section, as a form to be completed on line,
- ✚ Submission of the required documents by uploading (scientific file, financial annexe and CV of the Project Coordinator and Director(s) of any associated team(s)).

Submission deadline: 30th June 2017, 4 pm

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

6.c. Paper format

Two copies of the application including 1 original signed by the people in charge (Management Body + project scientific Coordinator + teams leaders) should be sent to the following address:

Inserm – DESP
Plan Cancer – “Systems Biology”
101, rue de Tolbiac
75013 Paris

Submission deadline: 30th June 2017, 4 pm (submission date based on the postmark)

7. Publication of the results

The list of the 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: plancancerbiosys@inserm.fr
- for administrative and financial aspects: plancancer.daf@inserm.fr
- for problems related to the electronic submission : eva@inserm.fr