Inserm

La science pour la santé
From science to health

Cross-cutting Programs

Human Development Cell Atlas

HuDeCA 2018

Research projects
In the Field of Human Cell Atlas

Submission deadline: October 18, 2018
Online submission: eva3-accueil.inserm.fr
Contact: hudeca@inserm.fr

TABLE OF CONTENTS

PREAMBLE

Challenges and issues in the field of health and biology are constantly changing and opening up new directions for innovation. In this context and in line with its missions, which consist of accelerating progress in knowledge, supporting integrated and multidisciplinary research, and ensuring a continuum between fundamental and clinical research, Inserm is putting in place cross-cutting scientific programs with the following objectives:

- to build scientific communities in specific high-priority fields and bring forth national interdisciplinary consortia that will build on the skills and expertise of Inserm teams;

- to make French biomedical research a leading player in these fields by accelerating knowledge acquisition, transfer, and value-creation.

These unifying programs aim to create a new dynamic in innovative fields by developing complementary skills for exploring research niches that have as yet been little studied. Funding will only be provided to collaborative projects that spread across a group of activities: several workpackages to be implemented by a consortium of teams. These programs are open to both academic and industrial partnerships with a flexible approach: such partnerships may be agreed across the whole program, or across one or more of the program workpackages only.

Scientific questioning at the frontier of biological knowledge, new technological opportunities, pooling the strengths of Inserm teams working in the field of the cross-cutting program, and potential added benefits in terms of societal value-creation constitute the determining elements for implementing these programs.

1 - OVERVIEW

How diverse are the cells that constitute the human body, and what are their embryonic origins? These are critical questions to address some of the current challenges in science and medicine. Understanding how the hundreds of types of cells in tissues and organs differentiate and self-organize is of crucial importance to understanding normal biological processes of the human body and how they are disrupted in patients with congenital diseases.

By studying several experimental animal models, great progress has been made towards understanding the cellular and molecular mechanisms involved in the development of vertebrates. The use of genetic methods (mutagenesis, transgenesis, homologous recombination, CRISPR-Cas9, etc.) combined with techniques such as 4D imaging, cell culture and molecular biology, has enabled us to determine how different cell types are specified in several organs and how they migrate and interact during morphogenesis, as well as to reassess the roles of genetic and environmental factors. Nonetheless, our knowledge of human embryonic and fetal development remains limited; it relies largely upon anatomical data obtained in the last century and many features specific to humans remain to be discovered or studied in depth.

Recently, new methods have been developed to study aspects of human development without crossing ethical boundaries determined by our societal values. Culturing embryonic stem cells (ESC) and induced pluripotent stem cells (iPSC) has allowed us to investigate some of the early steps in embryogenesis and to study certain processes that control human cellular differentiation *in vitro*. Single-cell transcriptome analysis now provides access to the genetic identity card of each individual cell type at a given moment, enabling its lineage to be traced over time *in vivo*. Finally, new three-dimensional imaging methods make it possible to map cells within developing tissues and organs.

The aim of this state-of-the-art interdisciplinary program is to build a definitive atlas of embryonic and fetal human cell types.

This project is part of an international initiative to map both normal and pathological cells of the human body (Human Cell Atlas or HCA), in adults as well as during development.

The HuDeCA transversal program aims to structure human embryology research in France and to develop unique platforms and databases to contribute significantly to international efforts, including the HCA project. HuDeCA will also help prepare the teams at Inserm to respond to future calls for tenders (in particular, European) in the field of human development. Over the long term, results from this program will serve as a basis for understanding the origins of congenital diseases and malformations, which affect over 28,000 children and fetuses per year in France, i.e. 3% of births, and which also cause many chronic or late-onset diseases in adults.

2 - OBJECTIVES

GENERAL OBJECTIVES OF THE PROGRAM

Thanks to emerging techniques that enable in-depth characterization of single cells, the HuDeCA program aims to establish a spatial and temporal atlas of the different cell types composing the non-pathological human embryo and fetus during gestation. To meet this goal, the teams involved will set up the necessary platforms for specimen collection and analysis using cutting-edge technology, as well as for the storage and sharing of results. This lasting resource will be unparalleled anywhere in the world.

SPECIFIC OBJECTIVES OF THE PROGRAM

Despite its central importance to understanding our origins, normal human embryonic and fetal development remains poorly defined. The advent of "-omics" techniques for single cells and of high resolution imaging in toto paves the way for accurate identification of the different cell types in the human embryo and fetus as they develop. Cells are thereby characterized by multiple parameters, including their location in the embryo and the fetus, the order in which they appear, their chemical properties (nucleic acid, protein, lipid and metabolite composition) and their physical properties (size, shape and mechanical properties). A major challenge will be to obtain high-definition spatial representation, in order to generate a complete 3D image of the cells of the human body at a given moment in time. Using experimental data interfaces from animal models and by sharing imaging data (mapping), it should be possible to establish lineage relationships between different human cell types and to reach a better understanding of how differentiation kinetics are regulated over time. This characterization will make it possible to define their functional capacities, such as a given cell's differentiation potential. Although some of these cell characterization techniques are very new, their use is becoming more and more widespread. However, their application to the study of the human embryo and fetus is currently limited by the scarcity of specimens available for research.

Optimizing the analysis of human embryos and fetuses requires a coordinated effort on the part of developmental biology laboratories. The scientific community must network to establish a national biobank to maximize the use of all available tissue specimens. This physical resource will allow construction of and validation of the atlas, while corresponding databases will need to be built to enable information access and sharing.

The HuDeCA atlas, comprising information about non-pathological embryonic and fetal cells, will serve as a reference point to provide better understanding of the developmental abnormalities underpinning miscarriage, premature birth, or diseases at all stages of life.

The workpackages for the creation of an atlas of the cells of the human embryo and fetus are as follows:

- **Workpackage 1:** construction of a management platform and biobank of human embryonic and fetal cells and tissues;
- **Workpackage 2:** definition of the diverse types of human embryonic and fetal cells and tissues;
- **Workpackage 3:** establishment of the data infrastructure necessary for the release of the digital atlas.

WORKPACKAGE 1: Construction of a management platform and biobank of human embryonic and fetal cells and tissues

Context and objectives

The ethical constraints associated with the collection of human embryonic and fetal tissues for research limit said research to those countries that have proposed a legal framework

(cf. French Decree N° 2007-1220). In the context of developmental biology research, France has long been equipped with a legal framework for oversight of the collection of tissues obtained after voluntary or medical abortions. Academic research teams currently establish partnerships with hospital teams under the supervision of the French Biomedicine Agency, and individually manage the logistics inherent to this work. Nonetheless, this research is necessarily focused on each team's center of interest, such that collection of this rare and precious biological resource is not optimized to best enable research projects of the scientific community as a whole.

Scientific questions and obstacles

The challenge of this workpackage is to collect and store human embryonic and fetal biological specimens associated with standardized annotations, under the appropriate conditions. These human embryonic and fetal cells and tissues will first be made available to the scientific consortium devised to carry out workpackage 2. The challenge is to structure a national biobank for research on the human embryo and fetus in a way that enables significant progress to be made in our understanding of the developmental mechanisms of as many organs as possible in parallel.

Several logistical and organizational obstacles must be overcome:

1. Since specimens are collected across numerous sites, it will be necessary to collaborate with and train the staff involved, in order **to standardize** practices for:
   a. **anonymization** and **consent** for specimen donations;
   b. the **collection** and **storage** of biological samples after **quality control** based on morphology, tissue viability, and molecular biology (at the minimum, establishment of euploidy);
   c. methods of indexing associated data in order to submit them to a **centralized database.**
2. The preparation of samples in anticipation of single cell technologies will require standardized protocols to be developed in line with the criteria of the HCA.
3. The nature of the samples stored will have to be adapted according to the needs of ongoing scientific projects and their different objectives (e.g. freezing tissues or cells before or after dissociation or fixation, nucleic acid or protein extracts, etc.)
4. Specimen management requires traceability of both samples and projects over time and of the resources assigned to them, from distribution to final use.

Deliverables

1. Establishment of a biobank of human embryonic and fetal cells, tissues and organs. The samples must be associated with a minimal parameter set of metadata about the stored specimens (sex, developmental stage, physical state, etc.).
2. Methodological training for handling and processing.
3. A web interface for researchers/users connected to a secure centralized database and with multiple permission levels, including two interdependent modules:
   a. A real-time index of the organs, tissues and cells that are available or assigned to a project, and their related metadata;
   b. An interface for the management of researcher/user needs, including the establishment of connections with the required or selected specimens and their outcomes, if applicable, and monitoring of results.

WORKPACKAGE 2: Definition of the diverse types of human embryonic and fetal cells and tissues

Context and objectives

How can we define the diversity and the future fate of cell types in the human embryo and fetus?

During development, the many cell types that make up the human embryo and fetus appear, proliferate and differentiate according to a genetically controlled but non-deterministic timeline. However, the diversity of cell types and the sequence and location of their appearance remain poorly defined. This lack of clarity prevents us from building realistic models of the events that take place in and between the cells and tissues that eventually form the human body.

To determine the nature of both cell types and their interactions, a list of cell-specific characteristics must be established. These can include the molecular composition of each cell type (nucleic acids, proteins, lipids, metabolites, etc.), the stage at which it appears, its physical position in the embryo and fetus, as well as clonal relationships, physical properties (shape, size, mechanical properties, etc.), and developmental capacities. This multidimensional cellular identity card will allow construction of the HuDeCA atlas.

Scientific questions and obstacles

The challenge of workpackage 2 is to develop deploy and cross-reference the multiple technologies needed to define, map, and trace the history of different cell types in the human embryo and fetus. "Omics" techniques, particularly pertaining to single cells, will enable us to establish dynamic molecular identity cards for the various cell types in the embryo and fetus, following their appearance and evolution over time. Imaging techniques will establish the position of the different cell types and confirm the stages at which they appear. The primary *ex vivo* culture of early-stage embryos or cells from embryonic or fetal tissues will be used to determine their physical properties and assess the developmental potential of different cell types. For example, molecular characterization may reveal a new marker that will in turn allow researchers to locate a new cell type using microscopy, whose altered influence on surrounding tissues may be responsible for pathogenesis. **Reproducibility and validation of the data generated will be crucial.**

> Identifying cell types

The recent development of new "-omics" techniques on single cells or nuclei (scRNA-Seq, snRNA-Seq, scATAC-Seq, scBS-Seq, etc.…) offers the ability to better understand the cellular diversity of the human embryo. Applying these techniques to the human embryo is still a challenge and will require data analysis to be standardized and optimized. This will only be possible through fostering new interactions between biologists, computer scientists and biostatisticians. Finally, spatial transcriptomics and proteomics data will have to be generated to support and validate the data on single cells obtained from standardized specimens.

> Mapping cell types

The anatomical study of human embryonic and fetal development has, up to this point, relied on the use of traditional histological techniques (such as embedding, sectioning a few micrometers thick and histological stains of subcellular components such as hematoxylin-eosin). Three-dimensional organization can only be reconstructed following a long, fastidious and imperfect process. This makes it difficult or impossible to interpret imaging data (DTI, MRI, etc.) obtained in utero. New methods rendering tissues transparent and 3D imaging with light-sheet microscopy have been developed and successfully adapted to human embryonic and fetal imaging at a tissue and organ level. Moreover, these methods are compatible with immunolabeling, which makes it easier to identify and locate cells.

Nonetheless, these innovative 3D imaging techniques still require optimization if they are to create exhaustive cell maps of human embryonic development and a reference atlas. First and foremost, the scarcity of specimens means labeling must be optimized and marker "multiplexing" must be possible. Antibody penetration should also be improved to visualize cells all the way through fetal tissues. Likewise, 3D RNA visualization in situ, if it is to benefit from transcriptomic data and to be applicable to the human embryo, requires further technological development. Finally, as current 3D microscopes cannot generate images at the level of whole organisms or large organs, new models will have to be developed in order to resolve this problem.

> Dynamic characterization of human embryos and fetal tissues *ex vivo*

Development is intrinsically dynamic. The accurate determination of the sequence in which cell types appear is greatly limited by the information available regarding the moment of conception of the embryo and the intrinsic limitations of comparisons with other, better-defined species, such as the mouse. To overcome this obstacle, dynamic approaches with living embryonic or fetal cells, tissues and embryos must be developed. These will allow us to **determine the chronology of the cellular events** that lead to the formation of the human embryo and will pave the way for the characterization of other properties such as developmental potential, molecular dynamics (synthesis, degradation and mobility of proteins and RNA), and even the dynamics of shape changes that are controlled by the mechanical properties of the cells and tissues.

Microscopy on living specimens (pre- and peri-implantation) enables cell differentiation to be followed and its chronology to be traced. For example, fluorescent labeling of a protein or an RNA allows us to follow the destiny of a cell. This can be done by introducing proteins or mRNA into cells temporarily (by electroporation or microinjection) or after genome modification. Development involves numerous changes to the shape of the embryo and its organs. Microscopy on living specimens lets us track these morphological changes and their chronology. Deformations are caused by changes in the mechanical forces and properties of the cells and can be determined using biophysical techniques.

The ability to **culture embryos and tissues *ex vivo*** is a prerequisite to the application of these techniques. During its development pre-implantation, the embryo can be cultured *ex vivo* until the blastocyst stage in a relatively simple way. Recent technological advances allow the embryo to be cultured during the peri-implantation stages and thus pave the way for the dynamic study of these embryonic stages. Technological efforts are still needed to extend the limits of *ex vivo* embryo culture. The culture of explanted or reconstituted tissues from primary cells also enables the dynamic study of human development.

Deliverables

1. Genetic, epigenetic, proteomic and metabolome expression maps at the single-cell level.
2. Definitions of the different cell types that make up a given tissue or organ.
3. New multiplexing techniques for RNA and marker proteins.
4. Novel 3D microscopy methods for large biological specimens.
5. Techniques that make it possible to create a timeline of human embryonic and fetal development (dynamic microscopy using fluorescent markers, cell behavior, mechanical properties, etc.).
6. Culture protocols for diverse primary human embryonic and fetal cells and tissues (excluding derivations from embryonic and induced pluripotent stem cells).
7. Human embryo culture (for research purposes only) beyond pre-implantation stages.

WORKPACKAGE 3: Establishment of the data infrastructure necessary for the release of the digital atlas

Context and objectives

The objective of this workpackage is to link three types of data: the results of workpackage 2 (proteome, transcriptome, metabolome, images); their analyses and rendering in the form of a dynamic atlas; and their annotation using the data and metadata of the specific specimens used to obtain them. A dynamic atlas of the prenatal human body at a cellular level will generate a massive amount of digital data. In line with their sensitive nature and/or their quantity, they demand the development of specific solutions.

Scientific questions and obstacles

One of the main challenges is to process and integrate numerous parameters at the individual cellular scale, then apply them to the embryo or fetus as a whole. This will require new technological advances as well as integrative computer science-based approaches. Another challenge is enabling access to a modular, flexible system allowing future technological advances to be integrated (data format and size, data types, etc.).

To meet these challenges, **several obstacles** must be overcome:

1. The atlas must be interoperable or enable the results within it to be integrated into the HCA project.
2. Ontologies (keywords, trees, etc.) must be defined using current standards and periodically updated in line with user feedback, thus enabling data to be organized/sorted, compared and queried.
3. Conducting searches in a database will involve making the information obtained from all of the other workpackages available in real time.
    a. The process of submitting and accessing data and metadata should be simple yet secure, with a restricted access portal for input, integrating version storage and management.
    b. The traceability of specimens, which is vital, will allow researchers to match samples to the results they have generated, deposition of which to the project will be mandatory for publication or any further use of its resources.
    c. The submission of alignments (as opposed to raw data) obtained through high-throughput sequencing in *.bam format must be made to a public research archive such as the European Genome-phenome Archive or the Sequence Read Archive in order to complete a project.
    d. The **protection of personal data** must be ensured and demonstratable for all specimens processed using high-throughput sequencing.
4. Permanence of the data and results, their storage and/or the archiving of secondary data must be ensured and demonstratable by publicly funded European institutions.

Certain technological obstacles are particularly constraining when it comes to processing and visualization of imaging data.

5. Development of algorithms/software to facilitate and automate cell segmentation and cell counting in 3D.
6. Facilitation of the sharing of imaging data and of the visualization and interpretation of such data by developing 3D web interfaces.
7. Transfer of imaging data to, or its compatibility with, virtual reality or augmented reality applications will enable faster and more accurate data analysis and will make them simpler to understand.

Deliverables

1. Permanent, modular, interoperable, online yet secure, controlled-access databases with unmodifiable links to data and metadata from the specimens used to generate the results.
2. Centralization of "-omics" data and microscopy data (or permanent access paths) with separate pipelines for the collection, storage and distribution of results.
3. Graphical interface and website (access portal) to access data.
4. Dynamic and topological 3D atlas of human embryonic and fetal development.
5. Methodological training.

3 - PROGRAM PERSPECTIVES

Although the aim of the HuDeCA program is initially to create an atlas of normal human development, it may be extended in the future to the study of pathological embryos and fetuses, in order to better understand the etiology of congenital malformations and diseases.

Intended audience: cell biologists, geneticists, statisticians

4 - OPERATIONS OF THE CROSS-CUTTING PROGRAM

GOVERNANCE AND ORGANIZATION

The cross-cutting program: based on the formation of a scientific consortium, organized around scientific workpackages, each composed of a number of scientific teams that may vary depending on the objectives. This consortium will be led by a scientific coordinator and guided by the heads of each workpackage.

The scientific expert committee: responsible for selecting the letters of intent, producing recommendations for the directions of the cross-cutting program, advising on alignments across the teams for the formation of workpackages, and approving the final scientific project. It is composed of international outside experts and directors of the relevant Inserm thematic institutes.

The scientific monitoring committee: responsible for monitoring the progress of the scientific project. It is composed of the consortium scientific coordinator and the scientific leads from each workpackage.

The program management committee: responsible for managing the running of the program, including the budget, and for approving proposals from the scientific monitoring committee for activities relating to the implementation of the overall program strategy. It is composed of the legal representative of the coordinating institution and the director of the thematic institute relevant to the theme of the program, in this case the Cell biology, development and evolution Institute.

ESTABLISHING THE CROSS-CUTTING PROGRAM

Preparing the cross-cutting program

A working group composed of field experts[1] has compiled a list of the relevant scientific issues inorder to bring together complementary skills. Their discussions have culminated in the proposed program definition.

Putting in place the consortium

The consortium is organized around workpackages. Participation in the different workpackages will take place in two stages: an initial selection of candidates by the scientific expert committee on the basis of letters of intent (see Evaluation criteria p. 13), followed by a stage of co-construction of workpackages (see p. 12).

1.Composition of the working group: Alain Chedotal (Paris), Anne Dubart-Kupperschmitt (Villejuif), Heather Etchevers (Marseille), Pierre Gressens (Paris), Bernard Jegou (Rennes), Robert Kelly (Marseille), Jean-Léon Maitre (Paris), Michel Samson (Rennes), Sabine Sarnacki-Feray (Paris), Shahragim Tajbakhsh (Paris), Manuela Tavian (Strasbourg), Stéphane Zaffran (Marseille)

Submission of the letter of intent

A single researcher or a research team may submit a letter of intent. This will specify the program workpackage being applied for and will describe the way in which the skills and expertise of the researcher or the team may contribute to overcoming one or more of the conceptual and/or technological obstacles identified as high-priority scientific components of the cross-cutting program.

Co-construction of the workpackages

Following selection of letters of intent, the coordinating institution (Inserm), based on the proposals and recommendations of the scientific expert committee, will invite the selected candidates to group themselves by workpackage and contribute to drafting a scientific project. This project will be presented to the steering committee and the scientific expert committee, as part of a discussion seminar.

Following this seminar, and taking onboard the committee recommendations, the consortium scientific coordinator will file a final scientific project with the coordinating institution (Inserm) that details the contribution of each team, the objectives, and the expected added benefits. Following formation of the program, a 3-year funding plan will be detailed and external funding sources identified.

Monitoring the consortium

The steering committee will organize an annual general meeting that brings together, in addition to its own committee, the scientific expert committee and the scientists involved in the consortium. During this meeting, participants will present and discuss the progress of the cross-cutting program, the next stages to tackle and, if necessary, propose new directions for research.

5 - ELIGIBILITY CRITERIA AND EVALUATION OF LETTER OF INTENT

ELIGIBILITY CRITERIA

- the letter of intent to participate in the consortium must respond to the objectives of this call for projects and fit into at least one of the workpackages described above;
- the researcher must be a researcher or tenured teacher-researcher working within an official Inserm team. He must, for the purposes of the project, propose a collaboration with at most a researcher or a team from Inserm or an other institution, with the agreement of such party;
- the researcher must specify:
  - their time commitment to the project;
  - the resources, particularly in terms of staff or equipment, that they intend to use as part of the cross-cutting program, in agreement with the responsible party from the partner institutions.

EVALUATION CRITERIA

After verifying eligibility, letters of intent will be submitted for evaluation by the scientific expert committee. Letters of intent not meeting the eligibility criteria will not be evaluated. The evaluation criteria are as follows.

Quality and originality of the proposed research

- Quality and originality of the proposed research
  - Clarity of objectives and research hypotheses
  - Innovative nature and advancement on current state of the art
- Skills/expertises
  - Relevance of skills to the program objectives
  - Possibility of combining skills within a broad network
- Excellence of the research team(s)
  - International recognition
  - Skills of the team leaders within their discipline
- Quality of the research environment
  - Human resources to be used by the program
  - Infrastructure available to carry out the program
- Innovation/competition: Innovative nature of the project in relation to international scientific issues or in relation to international competition
- Expected added benefits
  - Impact of added benefits in terms of knowledge and overcoming technological obstacles
  - Role of the project in the consortium construction in response to international calls

6 - ELIGIBILITY CRITERIA OF THE FINAL PROJECT

To be considered eligible, the final project must satisfy the following conditions:

- the project must respond to the objectives of the cross-cutting program;
- each workpackage must include at least two teams with complementary skills, at least one of which must come from an Inserm research unit;
- the consortium coordinator must be significantly involved in the project.

7 - PROGRAM CALENDAR

Date of publication of the project submission		**September 2018**
Opening of the project submission website		**September 18, 2018**
Submission deadline for the letter of intent	Online submission of the letter of intent	**October 18, 2018**
Meeting of scientific expert committee to select the letters of intent		**December 2018**
Co-construction of the workpackages		**January 2019**
Seminar and presentation of the workpackages		**February 2019**
Submission deadline for the final project	Project submission to the coordinating institution	**March 2019**

8 - OPERATING PROCEDURES OF THE CONSORTIUM

COORDINATION OF THE CONSORTIUM

The coordinating institution of the consortium is Inserm. Inserm is responsible for implementing the chosen project within the cross-cutting program and, if necessary, formalizing collaboration between the partner institutions (public or private), in particular by drawing up an agreement relating to the consortium, the production of project deliverables –including the production of scientific reports–, the organization of progress meetings, and the communication of results. The partner institutions designate the public or private entities in which the partner units are involved as part of the cross-cutting program. The partner units designate in particular the research units, services, and teams involved in fulfillment of the project and placed under the responsibility of one or more partner institutions.

If non-Inserm partner units are involved in the consortium, they must have prior consent for their administrative supervision.

DURATION OF THE PROJECT

Duration of the project is 3 years.

SCIENTIFIC REPORTS

The scientific coordinator of the consortium will provide scientific reports to the coordinating institution according to the Charter of good practices and the procedures defined below.

They will be sent as per the following schedule:

- a progress report 6 months after the project has started;
- a report halfway through the project;
- a final report no later than 2 months after the end of the project.

The scientific evaluation of intermediate and final scientific reports by the steering committee may lead Inserm to request additional information, to suspend the project, or to end financial support if the project is not being run properly or funding is being used for another project.

RESPONSIBILITIES OF THE SCIENTIFIC COORDINATOR

The consortium scientific coordinator must inform Inserm and its partners, if necessary, via the steering committee, of any substantial modification of the research project or any difficulties hindering project completion.

The consortium scientific coordinator must also participate actively in the project monitoring procedures organized by Inserm (presentation seminars, colloquia, etc.).

PUBLICATIONS – COMMUNICATION

All publications resulting from the research project must include the following fundingstatement:

- **“Inserm cross-cutting program HuDeCA 2018”:** for English-language journals;
- « **Programme transversal Inserm HuDeCA 2018 » :** for French-language journals, press releases...

These publications are sent to Inserm for reference as soon as possible and at the latest five (5) days following publication.

INTELLECTUAL PROPERTY

The results of the project belong to Inserm and to the project partner institutions.The rules of ownership and the use of results from the project are defined as follows:

- between various partners in the context of a joint research facility: the applicable rules are those generally in force between the said various partners (in particular those of a joint research agreement);
- between various partners associated with several research structures, these rules will be defined in a separate consortium agreement.

9 - RULES FOR SUBMISSION

SUBMITTING THE LETTER OF INTENT

The submission of your application involves a mandatory stage: registration on the Eva Inserm website and online submission of the letter of intent. This submission procedure, through the Eva Inserm website, includes:

- providing candidate information (surname, first name and email) enabling you to receive a user code and password providing access to a secure Eva personal space;
- uploading the letter of intent to the Eva website.

Submission deadline: October 18, 2018

You are strongly advised not to wait for the closing deadline before submitting your letter of intent.

SUBMISSION OF THE FINAL PROJECT

This will be submitted to the coordinating institution, Inserm.

10 - PUBLICATION OF RESULTS

The list of candidates selected from the letters of intent will be published on the Eva Inserm website.

11 - CONTACTS

For further information you can contact:

- in relation to scientific and technical matters: the Cell biology, development and evolution Institute (**hudeca@inserm.fr**);
- for questions relating to online submission (**eva@inserm.fr**).

101, rue de Tolbiac
75654 Paris cedex 13
inserm.fr