

Call for proposals.

Deadline: **March 20<sup>th</sup>, 2018**

# BIOMEDICAL RESEARCH ON AGEING-RELATED DISEASES

**CALL 2018.** SCIENTIFIC RESEARCH

Fondazione  
**CARIPLO**

TUTE SERVARE MUNIFICE DONARE•1816





# BIOMEDICAL RESEARCH ON AGEING-RELATED DISEASES

## BACKGROUND

Estimates about EU population trends in the next 50 years indicate a slight increase in terms of number of individuals, but an important shift towards older ages. It is expected that, by 2060, 30% of the Europeans will be over 65 years old<sup>1</sup>.

Ageing is associated to an increased frequency of adverse conditions associated to the reduction of the physiological reserve necessary to withstand stressors being these endogenous or exogenous. Thus, old people are more prone to hospitalization, adverse treatment-related outcomes, loss of functional independency, institutionalization and increased mortality<sup>2</sup>.

Geriatricians define frailty as a sub-clinical syndrome characterized by the following symptoms: abulia, weight loss, exhaustion, muscle weakness, slow gait speed<sup>3</sup>.

It is crucial distinguishing frailty from conditions of recognized disability or any organ-specific disease. Although such conditions might increase the risk of frailty, it is also true that frail individuals continue to be so even in the absence of disability or other pathologies.

Only recently the scientific community has recognized a clear need to understand the genetic, biological, microbiological and metabolic mechanisms of frailty, together with its clinical manifestations<sup>4</sup>.

In addition, understanding frailty etiology, prevention and treatment becomes even more crucial in order to reduce national healthcare costs<sup>5</sup>.

## AIMS

This call supports research projects aimed to understand biological and pathophysiological mechanisms underlying the geriatric syndrome of frailty. It is also required to develop innovative studies – i.e. aimed to identify innovative biomarkers to promote advances in precision medicine, as well as pharmacological and behavioral studies - that would allow the prevention or mitigation of harmful effects associated to this condition.

Otherwise projects might identify, through the observation of its clinical manifestations, frailty biological causative mechanisms.

In particular, projects must address at least one of the following key priority research areas:

- genomic instability;
- mitochondrial dysfunctions;
- oxidative stress;
- roles of inflammatory factors;
- dysfunctions in cell renewal in specific tissue and apoptosis induction;

1 The 2012 Ageing Report, Economic and budgetary projections for the 27 EU Member States (2010-2060), European Commission, 2012.

2 Fried LP, Williamson J, Kasper J; The epidemiology of frailty: the scope of the problem. In: Coe RM, Perry HM II, eds. Aging. Musculoskeletal Disorders and Care of the Frail Elderly. New York: Springer Publishing Co. 1992.

3 Fried et al.; J Gerontol Med Sci; 2001; 56A(3): M146-M156 and Howlett SE et al.; Age and Ageing; 2013; 42:416-423.

4 Dae Hyun Kim and Sebastian Schneeweiss; Measuring Frailty Using Claims Data for Pharmacoepidemiologic Studies of Mortality in Older Adults: Evidence and Recommendations; Pharmacoepidemiol Drug Saf. 2014 September; 23(9):891-901.

5 Michael J. Rae et al.; The Demographic and Biomedical Case for Late-Life Interventions in Aging; The Science Translational Medicine; 14 July 2010; Volume 2 Issue 40 40cm21.

- the role of neurologic, immunological, musculoskeletal, metabolic, cardiorespiratory, hematologic, endocrine factors and their respective interactions;
- regulation of mood and other psychological factors.

In order to facilitate the uptake of research results in the midterm, projects must be built on effective collaboration between basic and clinical research and explain how a proper merge of the different expertise is likely to allow the development of a global approach to the study of frailty, through the combination of mechanistic studies in pre-clinical models (cellular lines and/or animal models) and clinical studies in well-defined cohorts. To this end it will be necessary to clarify in detail the competencies peculiar per each Partner in addition to the ones of the Leading organization. Furthermore, it must be explained how these different competencies - falling under clinical and basic research - are integrated together in one unique design.

Research project rationales must be developed on solid preliminary data (state of the art and/or applicants' original results), adopt a mechanistic approach and methods adequate to the projects aims and expected results. Special attention will be paid to the research innovativeness respect to the state of the art as well as to the originality of both the hypothesis and applied methods.

In addition, projects must represent training and professional opportunities for young researchers.

Finally, embracing the principles of Responsible Research and Innovation<sup>6</sup>, Fondazione Cariplo aims to promote initiatives fostering communication and interaction between researchers and civil society. In particular, researchers must propose a communication plan inclusive and open to all stakeholders differently implicated in the research. Planned activities are meant to facilitate the activation of a dual exchange between science and society. The communication plan is considered an integral part of the research proposal.

6 The European movement on the theme of Responsible Research and Innovation (RRI) is constantly evolving, as emerges from the debate which has recently led to the so called "Rome declaration on RRI" ([http://www.sis-rri-conference.eu/wp-content/uploads/2014/12/RomeDeclaration\\_Final.pdf](http://www.sis-rri-conference.eu/wp-content/uploads/2014/12/RomeDeclaration_Final.pdf)). In light of the available literature, it is possible to describe RRI as a dynamic and iterative process which intends to match research and innovation to values, needs and expectations of the society. Moreover, RRI aims at actively involving all the stakeholders taking part to activities of research and innovation, making them mutually responsible with respect to both the research process and its results.

## GUIDELINES

### ELIGIBLE APPLICANTS

Beyond the general requirements set out in the *Criteri generali per la concessione di contributi*, it should be noted that this call is intended to all institutions directly carrying out scientific research in the specified field of interest and thus demonstrate to be well endowed in terms of staff and equipment.

Moreover, it is mandatory for the leading institution to have its operational headquarter located in the geographical area of interest of Fondazione Cariplo (Lombardia plus Novara and Verbania districts). This requirement does not pertain to partners.

By submitting a proposal, applicant organizations accept the "portability of the grant". This means that PIs always maintain the rights to require the transfer of the research project to a new eligible institution, for as long as the research objectives are preserved. Any change in the host institution depends on Fondazione Cariplo approval according to the guidelines of this call of proposals.

PIs, both in the leading and in the partner organizations, must be senior researchers with a solid track record in the fields of basic and clinical research. It is also required that PIs actively perform their research at their hosting institution and ensure their participation in the project, with an appropriate commitment to its realization.

Fondazione Cariplo will not accept applications submitted by PIs (both leader PIs and partner PIs) of projects still ongoing and funded in previous calls in the Scientific Research Area (with the exception of calls in partnership with other granting agencies). A project is considered ongoing unless the final grant reports - both the scientific and the economic one - have been uploaded on our website before the deadline of this call.

Finally, each PI can submit only one application<sup>7</sup> under the present call.

### ELIGIBLE PROJECTS:

To be eligible, proposals must:

- be realized in partnership between minimum two eligible institutions. Partnership must guarantee the presence of at least one research group in the team dedicated to basic research and one dedicated to clinic

7 In case several proposals are submitted by the same PI, the first one will be considered eligible.

research. In the partnership one institution must represent the Leading group, while the other/s are going to be considered Partners according to Fondazione Cariplo definition<sup>8</sup>;

- clarify the relevance of the research project in relation to the biological and pathophysiological mechanisms peculiar to the frailty syndrome;
- fall in at least one of the key priority research areas of this call;
- adopt a mechanistic approach, focusing research on causal mechanism related to the frailty syndrome;
- include, train and enhance young researchers<sup>9</sup>;
- prepare a communication plan of activities with the civil society, coordinated by one of the researcher fully included in the working team (for more detail see the *Communication Guidelines*).

Moreover, any proposal with the following characteristics will be considered ineligible:

- purely descriptive projects;
- studies essentially aimed to develop novel methodologies and/or technologies;
- projects with an exclusive pharmacological focus;
- projects with an exclusive basic or clinical focus;
- funding requests aimed to set up new research centres and/or laboratories and/or animal facilities.

In addition, Fondazione Cariplo will not consider eligible a project that has been already submitted to this specific Call twice.

Projects should provide the approval of the Ethical Committee<sup>10</sup>. In case of animal experimentations Fondazione Cariplo requires a copy of the Ministry of Health authorization. By all means the authorization has to be notified to Fondazione Cariplo before the final report on the project.

The total cost of the project can only include costs related to the realization of the proposed studies, respecting the eligibility criteria and the thresholds listed below:

- A03 - "Equipment and software"  
This entry cannot exceed 20% of the additional costs<sup>11</sup>. It covers fully the costs for newly acquired equipment and software that must be clearly motivated in accordance to the specificity of the project. In this category

can also be included renting costs as well as building expenses for the installation of the new equipment.

- A04 - "Other amortizable costs"  
This entry can only include patent costs.
- A06 - "Temporary staff"  
This entry can only include research personnel costs. The cost of administrative staff is not allowed.
- A07 - "Sub-contractors and consultants"  
This entry should also include audit costs, where applicable<sup>12</sup>. Exclusively certificated auditors are considered eligible.
- A08 - "Materials and supplies"  
This entry cannot include costs related to stationery and photocopies.
- A09 - "Overheads"  
This entry cannot exceed 5% of the additional costs<sup>13</sup>.
- A10 - "Travel, publication and dissemination costs"  
This entry cannot exceed 15% of the additional costs<sup>14</sup> and can only include travel expenses and conference participation fees for the research personnel involved in the project, scientific publications.

The grant will cover 100% of project costs. Requested funding should range from 200,000 to 400,000 euros. Please note that it is not required to explicit organizations' co-funding expressed in terms of personnel costs in the budget form.

## PROPOSAL SUBMISSION PROCEDURE

Applications must be submitted by 5:00 p.m. on March 20<sup>th</sup>, 2018. Leading organizations must submit applications for all partners accessing the online platform available on Fondazione Cariplo's website. First-time applicants need to register and require their username and password.

Fondazione Cariplo will consider ineligible applications submitted on paper or using forms different from the specific ones available online.

8 Please check the *Guidelines for presentation* available on line.

9 The term "young researcher" in this Call for proposals indicates graduate fellows, PhD students and post-docs not older than 35 years of age, at the Call's deadline.

10 In case the approval is not available by the Call's deadline, the leading organization will be requested to send it together with the preliminary fulfillment, penalty the grant revocation.

11 Sum of: A03, A04, A06, A07, A08, A10.

12 With the sole aim of ascertaining whether the obligation to perform a financial audit applies or not, the amount which has to be considered is obtained multiplying the eligible costs detailed in the Budget (sum of entries A06, A07, A08, A09 and A10) by the coefficient 1.25 (which represents an estimate of the co-funding generally guaranteed by the hosting institution, mainly in the form of permanent staff). It is also recommended to refer to chapter 10 of the *Grant management and reporting guide* and to the *Guidelines for audit*; both documents are available on the *Grant management and reporting* page of Cariplo Foundation's website.

13 See footnote 11.

14 See footnote 11.

In order to apply for this grant, applicants are required to fill in integrally all the online forms organized as below:

- Leading organization details (fill in the form with in details; or check and update your organization's details if already registered);
- Project section<sup>15</sup>;
- Additional information;
- Budget section<sup>16</sup>.

In addition, the Leading organization must upload all compulsory documents as it is indicated in the *Guidelines for Presentation*:

- Project Form<sup>17</sup>, PDF format;
- Budget Form<sup>18</sup>, PDF format;
- Project Dissemination Form<sup>19</sup>, PDF format;
- Letter of commitment from the hosting institution;
- Partnership agreement;
- Documentation of the applicant organizations<sup>20</sup>.

Please note that the "Project Form", the "Budget Form" and the "Project Dissemination Form" are the only documents subjected to meritocratic analysis.

Before submitting a proposal, applicants are kindly invited to carefully read the documents listed below and available on Cariplo Foundation's website at [www.fondazionecripilo.it](http://www.fondazionecripilo.it):

- *Criteri generali per la concessione di contributi*;
- *Guidelines for Presentation*;
- *Grant management and reporting guide*;
- *Communication guidelines*;
- *Acknowledgement guidelines for academic papers*;
- *Intellectual property rights policy*;
- *Open access policy*.

<sup>15</sup> In the Project Section applicants are required to enter information about the project and the organizations making up the partnership. Fondazione Cariplo may use this information for internal and external communications, and for analysis about performance of the call. Applicants are required to enter information in Italian using a language that is understandable to a lay person.

<sup>16</sup> The budget section requires the indication of the costs according to the different entries and divided per year, partner and action (WP).

<sup>17</sup> The detailed project shall be prepared in accordance with the template relating to the call that can be downloaded from the section Additional Information under Online Forms.

<sup>18</sup> The detailed budget form shall be prepared in accordance with the template relating to the call that can be downloaded from the section Additional Information under Online Forms

<sup>19</sup> The project dissemination form shall be prepared in accordance with the template relating to the call that can be downloaded from the section Additional Information under Online Forms.

<sup>20</sup> Applicants are advised to read the document Guidelines for presentation available on line.

By submitting a proposal, applicants acknowledge, agree and accept that the award of the grant requires the irrevocable acceptance of all policies mentioned above and respect of aforementioned Guide and Guidelines.

## EVALUATION PROCESS

All proposals submitted before the deadline and according to the formal requirements described above will follow a two-step evaluation process:

### I. Preliminary Control

This step is meant to check that all required documents are correctly submitted and they are consistent with the call's guideline. At this stage officers will also check all Organisations' eligibility. This is equally valid for leading organizations as well as partners. Independent experts will evaluate the project consistency with the scientific aims of the call. The review panel will be composed by international experts on frailty and aging. Applications considered eligible enter the peer review stage. All applicants ineligible will be notified. Organizations will receive a formal letter explaining in detail the reasons for the exclusion. This information will also be available on line on Fondazione Cariplo's web platform. Please note that consistency with the scientific.

### II. Peer Review

Eligible applications will be evaluated by independent experts in a peer review process ensuring scientific expertise and impartiality. The review panel will be composed by international experts on frailty and aging. Each proposal will be assessed by 3 reviewers including at least one clinical researcher and one basic research scholar. Reviewer-project matching will be made according to the indications provided by applicants in the keywords section. This logic is meant to ensure the identification of the most suitable reviewers for the project.

The final score given to the project reflects the following scores and weight:

#### 1. DESCRIPTION (weight 5%)

- knowledge of the state of the art;
- clarity of aims and strategies.

#### 2. APPROACH (weight 20%)

- presence of a plausible rationale and robust preliminary data;
- adoption of an interdisciplinary approach;
- adoption of a mechanistic approach;
- presence of adequate back-up plans;
- adequacy of the monitoring plans.

#### 3. INNOVATION (weight 20%)

- originality of the research question;
- innovativeness of the experimental approaches;
- expected impact on the state of the art.

#### 4. OUTCOMES (weight 20%)

- expected impact on scientific and medical community;
- health benefits in the elderly in the medium term.

#### 5. INVESTIGATORS AND ENVIRONMENT (weight 10%)

- PIs' scientific leadership;
- track record and adequacy of the PI and team competencies (leading organization and partner);
- level of consolidation of the collaborations with national or international research centres and/or the ability to build new partnerships;
- nature and strength of the partnership between basic or preclinical and clinical research centres.

#### 6. YOUNG RESEARCHERS (peso 10%)

- engagement of young researchers<sup>21</sup>;
- presence of training programmes for young researchers.

#### 7. DISSEMINATION (peso 5%)

- presence of a coordinator, chosen among the members of the research team;
- consistency with the *Communication guidelines*;
- consistency with the Responsible Research and Innovation principles<sup>22</sup>.

#### 8. BUDGET AND DURATION (10%)

- budget adequacy and internal coherence;
- adequacy of the proposed duration.

The final ranking ultimately represents the list of the best projects worth of funding.

At the end of the review process, all applicants will receive official communication together with reviewers' feedback. All these documents will also be available in the dedicated area on Fondazione Cariplo's website.

## AVAILABLE BUDGET

The budget available for this call for proposals is 4 million euros.

Please note that all documents cited in this call are available online at [www.fondazionecripilo.it](http://www.fondazionecripilo.it).

<sup>21</sup> See footnote 9.

<sup>22</sup> See footnote 6.

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