AIRC
Associazione Italiana
per la Ricerca sul Cancro

Call for Proposals 2018

Investigator Grant (IG)

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Guide to proposal preparation, **Tips for applicants, Eligible costs and Keywords** are available at:
https://www.direzionescientifica.airc.it/Calls/Default.aspx

Foreword

The Associazione Italiana per la Ricerca sul Cancro (AIRC) is inviting applications for Investigator Grants (IG) in the area of cancer research. These grants are intended to support the research on cancer by established and independent scientists with a strong commitment to cancer research, leading an existing research unit. The scientific activity must be carried out in a research organization located in Italy, organized under public or private law, whose primary goal is to independently conduct biomedical research (university, hospital or other research center). This grant will start on January 2nd 2019 and will provide support for a period of 5 years (provided that AIRC has available funds and that the evaluation of the third year progress report has been positive).

Applicants, henceforth defined Principal Investigators (PIs) cannot have more than one active AIRC grant at the same time in the following categories: Investigator Grant (IG), Start-Up Grant, My First AIRC Grant (MFAG) or TRansforming IDEas in Oncological research award (TRIDEO). Nevertheless, they can apply to this Call if their active grant is in its final year.

1. Eligibility Criteria

Only one application, either IG, MFAG or Start-Up per applicant can be submitted within the 2018 AIRC Calls.
The same research project cannot be presented by two or more applicants within the 2018 AIRC Calls.

1.1 Applicants

PIs can be of any nationality and are expected to have operated to the highest standards of integrity during their whole career. PIs must be involved in the project for at least 20% of their time. They should have achieved scientific independence and leadership and, by the submission deadline, they **must have a strong track record.**

More specifically, applicants must meet the following two eligibility criteria:

1. **applicants must have at least one last- or co-last-author primary research paper, in press or published in the last 5 years** in high level peer-reviewed journals; papers in press must be accepted for publication, not just submitted, by the application deadline. For this eligibility criterion, papers published as corresponding or co-corresponding author, reviews, letters to the editor without data and editorials do not count. We are aware that clinicians directly involved in clinical practice may have different authorship conventions, *e.g.* being listed as first authors when leading the research. Therefore, they are eligible to apply even if they don't have last author papers as long as they have first author papers related to their clinical activity.
2. **applicants must have a total active Impact Factor (IF) higher than 30 in the last 5 years** by the submission deadline. Active IF is calculated as the sum of IFs of all publications where the applicant is first, last or corresponding author in the last 5 years, including papers accepted for publication by the application deadline. For this eligibility criterion, reviews, letters to the editor without data and editorials count and are included in the calculation of the active IF. Applicants who do not meet this requirement are discouraged to apply and may be triaged out, depending on their career stage and possible career interruptions.

Please note that poster abstracts do not count for both eligibility criteria, even if they contain original data or are published on journals with Impact Factor.

1.2 Hosting Institutions

For the entire duration of the grant applicants must operate in the Hosting Institution, *i.e.* a research organization (such as university, hospital or other research center), irrespective of its legal status (organized under public or private law), located in Italy, whose primary goal is to independently conduct non-economic biomedical research and to disseminate its results. Possible revenues coming from non-economic research activity must be completely reinvested in the non-economic research activities. Where the Hosting Institution also pursues economic activities, the financing, the costs and the revenues of those economic activities must be accounted for separately. Shareholders, members

or other individuals that can exert a decisive influence upon the Hosting Institution cannot enjoy a preferential access to the intellectual property of the results generated by the non-economic research activity.

AIRC reserves the right to exclude proposals in which the PI, although jointly affiliated to an Italian institution and an institution abroad, does not meet criteria for substantial presence, *i.e.* at least 50% of their time, in the institution in Italy. To make sure this requirement is met, supporting official documentation will be requested from all institutions the PI is affiliated with.
Any change occurring in the relationship between applicant and the Hosting Institution (*e.g.* termination, retirement, leave of absence, sabbatical etc.) or in the Hosting Institution legal entity or organization (*e.g.* changes in institution name, merging, Legal Representative turn-over, changes in addresses) must be promptly notified to AIRC.

Hosting Institutions must provide proper working spaces, laboratories, equipment, qualified personnel and resources to allow the project execution. AIRC reserves the right to verify that these conditions are met.

The Hosting Institution must promote the highest standards of integrity in research, in compliance with the AIRC policy on research integrity available on the AIRC website.

1.3 Research plan
All proposed research plans must have a clear objective that is consistent with the AIRC mission and will likely lead to advances in cancer biology, monitoring, diagnosis, or treatment of tumors in the near term. Projects must have a duration of 5 years, with a budget consistent with this time-frame: 3-year projects will be rejected.

Research plans should fall into one of the following research areas:

- Angiogenesis
- Cancer genetics
- Cancer stem cells
- Cell adhesion, migration, invasion and metastasis
- Cell cycle control and cell division
- Cell death and apoptosis
- Chemotherapy
- Computational biology
- Control of gene expression and epigenetics
- Diagnosis
- DNA damage and repair
- Epidemiology and prevention
- Gene therapy
- Hormone therapy
- Imaging
- Immunotherapy
- Infection, inflammation and cancer
- Metabolism
- Prognosis
- Radiobiology and radiotherapy
- Resistance to therapy
- Signal transduction and intracellular trafficking
- Structural biology
- Targeted therapy and new therapeutics
- Tumor immunology
- Tumor microenvironment

In principle, AIRC believes that rigid guidelines on the research plan should not be provided for this type of grant since investigator-driven discovery is one of the most potent engines of scientific progress.

At the same time, phenomenological, descriptive-at-best, proposals are discouraged. The following kinds of proposals will receive **low priority and have very marginal chances of being funded**:

- studies that are essentially confirmatory in nature or represent marginal "variations-on-the-theme" of well-established concepts in cancer research;
- studies contemplating descriptive screenings of molecules and/or phenotypes without mechanistic insights and/or elements of innovative discovery. These include purely descriptive microarray and proteomic profiling studies that are not associated with a strong strategy for clinical application, or the generation of chemical compounds without validating their anti-tumor activities in pharmacological and biological studies;
- generation of reagents and/or optimization of technologies, or creation of services/technological facilities in the absence of a coherent and innovative research plan;
- chemical and/or viral carcinogenesis studies not embodied in the framework of mechanistic studies;
- requests for on-going routine collection of current statistics, such as cancer registry;
- descriptive epidemiology studies;
- health economics proposals;
- all phase III clinical trials;
- all phase I and II clinical trials that are company-driven, with the PI or the Hosting Institution deprived of the intellectual property, of the possibility of publishing the results and of freely exchanging data, reagents and information. This does not exclude collaborative studies with industry.

As for **clinical and epidemiological studies**, AIRC has interest in the following type of studies:

- proposals aimed at studying interactions between environmental risk factors, genetic profiles and intermediate biomarkers;
- proposals aimed at studying the natural history of cancer by linking different phases of the disease to specific biological/genetic profiles;
- clinical studies of innovative procedures (*e.g.* molecular, imaging etc.), aimed at evaluating in clinical practice the efficacy of diagnostic and therapeutic approaches, in terms of outcome and quality of life;
- pilot clinical studies of new therapeutic drugs, procedures or strategies;
- proposals aimed at a critical evaluation of last generation drugs and at elucidating their activity by mechanistic insights;
- clinical trials on types of cancer or treatment that generally receive low financial support from other funding agencies, such as studies on rare tumors and/or orphan drugs.

All proposals must contain thorough descriptions of study design, statistical analysis and sample size (whenever applicable), in particular for clinical and epidemiological studies with human subjects.

For studies involving human subjects, human biological samples or animal experimentation, the approval of the relevant institutional or national authorities is mandatory. AIRC reserves the right to check compliance with this requirement anytime, including after the termination of the grant. AIRC does not accept any liability for harm to participants in AIRC funded trials.

The proposal must be original and cannot contain copied texts, ideas and figures from other sources unless properly referenced. At AIRC we are aware that plagiarism may be accidental and that parts of an application (*e.g.* material and methods) may include material originally produced by the PI. However, AIRC may verify documents with anti-plagiarism software and proposals that contain blatantly and substantially copied materials will be rejected.

A proposal that has been rejected twice (from the same or other applicants) in the past cannot be resubmitted a third time and will be rejected. See "Revised applications" for further details.

2. Intellectual Property

For inventions arising from an AIRC funded project, grant money can be used to cover the costs for filing a patent application within the European Union (EU), but not to extend a patent to non-EU countries. Intellectual property and patents resulting from research carried out with AIRC grants will be solely owned and managed by the grantee and the Hosting Institution. All royalties and revenues deriving from the results of an AIRC grant must be reinvested in independent, non-economic oncological research.
Proposals for clinical studies that are property of companies producing drugs or diagnostic tools and that receive economic support from such companies will not be accepted. Drug supply and economic support from companies do not preclude AIRC evaluation, provided that the PIs have the full property of data and results, and that companies have no right to veto the publication of results anytime. A statement that the management of the study, data acquisition and analysis and data property are completely independent of any company producing/marketing drugs or diagnostic tools or with any type of economic interest in the study must be included in the application, together with the indication on whether the company provides its product(s) to the PI for free or not. Projects will not be funded without such information.

3. Disclosure of Financial Conflicts of Interest

PIs are required to disclose any financial conflict of interest with the proposal. Appropriate measures will be taken against applicants who have deliberately or recklessly failed to disclose conflicts of interest. These may include the termination of the grant, the obligation to return grant money to AIRC, the ineligibility to apply to future AIRC grants and the exclusion from AIRC review panels and other bodies.

4. Funding

Grants are for a 5-year period: they will officially start on January 2nd 2019 and terminate on January 1st 2024.

The following costs are eligible:

- Direct research costs:
    a) Consumables and supplies
    b) Small bench instrumentation
    c) Services
    d) Maintenance
    e) Publications
    f) Meetings and travels
    g) Personnel: support only for PhD students, early-stage researchers and research nurses at 100% of time on the project
- Indirect costs
- Overheads

First year of funding. Once awarded, the grant is assigned to the PI to carry out the project described in the application. Funds will be made available to the Hosting Institution under terms and conditions that AIRC will provide once the application is approved. Funds must be at the grantee's disposal within 30 days from the time the Hosting Institution has access to them.

Each year the PI must submit a renewal request. Funding for subsequent years will depend on the submission of the renewal requests. It has to be endorsed by the AIRC Board of Directors, provided that AIRC has available funds.

Year 3. At the end of the 3rd year the project will be evaluated through a detailed progress report (scientific and administrative). A site visit might be also scheduled. Funding for the last 2 years will be granted only after a positive assessment.

Year 5. A scientific final report will be required and will strongly impact on the evaluation of future AIRC grant applications**.** An administrative final report must be submitted within 3 months after the termination of the grant.
Transfer of grant money to other laboratories either in Italy or abroad is not allowed.

Further information about the terms and conditions of the grant, including renewal requests, scientific and administrative final reports, will be provided once the application is approved.

AIRC reserves the right to audit the administrative management of the project anytime and up to 10 years after the project is concluded.

5. The Review Process

5.1 Eligibility check

All applications are subject to an administrative review to verify compliance with guidelines and eligibility criteria; those that do not conform will be rejected at this stage.
Eligible applications undergo a peer review process that ensures an expert, fair and independent evaluation of their scientific quality. Only the most scientifically meritorious applications, identified through the peer review process in a rigorous and objective manner as described below, will be funded.

5.2 Full proposal evaluation

For the evaluation of IG applications, AIRC relies on the expertise of internationally recognized Italian scientists members of the "*Comitato Tecnico Scientifico-progetti*" AIRC (CTS-projects) and a panel of more than 600 well-established international investigators working in institutions outside of Italy. Applicants may request to exclude up to 2 scientists as reviewers through the online application form.

Each IG application is independently reviewed by three reviewers with expertise in the specific area of the research plan: 2 international reviewers and one member of the CTS-projects. In case the needed expertise is not available within the CTS-projects, a scientist with the appropriate expertise will be recruited from the international reviewers panel to serve as third reviewer.

In all stages of the review process reviewer assignments will be made in compliance with conflict of interest and appearance of conflict rules to ensure a review free from inappropriate influence. Upon accepting the request to evaluate an application, reviewers agree that they will maintain the confidentiality of the application and associated materials they have received. The AIRC policy on conflict of interest is available in our website.

To avoid conflicts of interests, IG applications submitted by members of the CTS-projects will be reviewed by international reviewers only (at least three).

The review criteria are:

1. significance and impact on cancer;
2. innovation;
3. approach and feasibility;
4. PI's leadership and independence, international standing in cancer research, track record adequate to successfully complete this study;
5. quality of the Hosting Institution: environment, international standing, resources, facilities and infrastructures;
6. adequacy of the budget requested.

When all evaluations have been submitted, reviewers are invited to read the critiques by the other two reviewers who evaluated the same proposals and, if they deem necessary, to make additional comments. In case there are major discrepancies among the evaluations, an editor is appointed, in observance with conflict of interest rules. Editors do not provide their own review but instead serve as "*super partes* arbiters", assessing and balancing the three evaluations.

After the "*cross-review*" phase and assessment by editors, applications are discussed by all members of the CTS-projects during a study section meeting. Scientific final reports of proposals by previously funded applicants are also taken into account during these meetings as a measure of productivity and scientific accomplishments of the PIs. In the final plenary session, all applications are ranked in order of scientific merit (for each application, the scores received from all reviewers are added up to generate the application's global score, which is used to rank the applications). The final ranking and the financial availability of AIRC will determine the recommendation for funding, to be endorsed by the AIRC Board of Directors.

All applicants will be notified of the final decision on their application with an official communication from AIRC (the notification date is reported in the "Deadlines" table) and they will have access to the reviewers' comments. The identity of the reviewers will not be disclosed. **The decision concerning the funding of an application cannot be appealed.**

After the awarding of a grant, AIRC reserves the right to site-visit the PIs laboratories and Hosting Institutions anytime.

6. Revised Applications

AIRC allows only one resubmission for applications that were not funded, regardless of whether they were previously presented in the same or different funding schemes (IG, MFAG, Start-Up etc.). Please note that:

- revised applications that do not meet all eligibility criteria described in this Call will not be sent out for review;
- revised applications must include a response to the reviewers' comments in the "Revision" section of the online form.

Applicants who fail to receive funding after 2 submissions (*i.e.* the original and the revised application), even after addressing all the issues raised by the reviewers, **may submit a new application only if its research plan is fundamentally different** in content and scope. More specifically:

- a new application should include substantial changes in all sections of the research plan;
- there should be fundamental changes in the questions being asked and/or the outcomes examined;
- changes to the research plan should produce a significant change in the direction and approach for the research project;
- rewording of the Title and Abstract does not constitute substantial changes in scope, direction or content.

7. Deadlines

Deadlines are strictly enforced: applications submitted after the deadline will not be accepted.

Deadlines for applications (by 17:00 Central European Time, of the indicated dates).

Publication of Call and application form release	February 1, 2018
Online submission	March 8, 2018
Online submission with digital signature of the PI and Legal Representative	March 20, 2018
Papers in press (*)	May 1, 2018
	September 1, 2018
Notification of results	November 30, 2018
Start of grants	January 2, 2019

(*) Communications received by May 1st 2018 will be forwarded to all reviewers evaluating the proposal; communications received after May 1st 2018 and by September 1st 2018 will be made available only to the members of the CTS-projects during the study section meeting.

AIRC has modified the procedures for the signature of the applications, by introducing the digital signature. **Both the PI and the Legal Representative must digitally sign the application**: refer to the FEA instructions ("Firma Elettronica Avanzata") for details. If the digitally signed applications are not submitted by the indicated deadline, they will not be sent out for review.

Deadlines for renewal requests and final reports will be communicated in the award letter.