



Call for Proposals 2018

Start-Up Grant – *Reintegration*

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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 Start-Up grants in the area of cancer research. The objective of the AIRC Start-Up program is to foster the birth and growth of new research units under the leadership of talented young scientists, with a strong commitment to cancer research, seeking the opportunity of becoming independent investigators in Italy after a successful research experience abroad. With this grant the PI is expected to mature into an independent group leader competitive for funding schemes for established investigators. 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 5-year grant will start on January 2nd 2019 and will initially provide support for the new unit for a period of 3 years. Funding for the last 2 years will be granted only if the PI has set up his/her own lab and has demonstrated scientific independence and productivity in an *ad hoc* site-visit. The grant is up to € 200.000/year (provided that AIRC has available funds) and will be awarded once in a lifetime.

1. How to Apply

A pre-submission inquiry is mandatory for Start-Up grants. The pre-submission must contain a brief description of the proposed work and of the projected achievements, and a description of the qualifications of the applicant, henceforth defined Principal Investigator (PI). A letter stating the commitment of the Hosting Institution to foster the growth of the new research unit (see below) must accompany the pre-submission inquiry. Applicants who meet the eligibility requirements and who present the most competitive pre-submissions will be invited to submit a full proposal.

2. Eligibility Criteria

Only one application, either Investigator Grant (IG), My First AIRC Grant (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 AIRC 2018 Calls.

2.1 Applicants

Applicants 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 70% of their time.

To be eligible for this reintegration grant, applicants must meet the following eligibility criteria:

Have a significant experience in a competitive laboratory outside of Italy, on-going or very recent. Applicants must not have been back in Italy for more than 12 months at the time of the pre-submission application's deadline.

Have a strong track record including at least 2 first/co-first or last/co-last author primary research papers, 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 pre-submission deadline. Primary research papers published as corresponding or co-corresponding author, reviews, editorials, letters to the editor without data, poster abstracts (even if they contain original data or are published on journals with Impact Factor) do not count for eligibility.

Should be 35 years old or younger by the time of the pre-submission application's deadline.

Applications by candidates who do not meet these requirements will be rejected.

2.2 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 not to fund proposals from PIs who, even if jointly affiliated to an Italian and a foreign institution, do not meet criteria for continuous presence in the Hosting Institution in Italy for at least 70% of their time during the funding period. To make sure this requirement is met, supporting official documentation will be requested from all institutions the PI is affiliated with (see “Declaration on affiliation” section in the Guide to proposal preparation).

Any change occurring in the relationship between the applicant and the Hosting Institution (*e.g.* termination, 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.

Preference may be given to investigators aiming to pursue their independent line of research in institutions with which they were not previously affiliated.

The Hosting Institution will actively favour the birth of a **totally independent new research unit**, and provide the facilities, equipment, and infrastructure necessary to carry out the proposed research. An investigator is supposed to sponsor the PI, inviting him/her to set up a new lab in the Hosting Institution; the Scientific Director or equivalent (*e.g.* Department Head) will serve as the guarantor of the entire operation, together with the sponsor. Sponsor and guarantor, together with the Legal Representative must provide a letter that confirms the commitment of the Hosting Institution to foster the growth of the new research unit, describing spaces, laboratories, qualified personnel and resources that will be available to the PI. The letter must include a pledge that they will not be first, last or corresponding authors in publications stemming from research carried out by the PI with Start-Up funds (see “Institutional Commitments” in the Guide to proposal preparation). **In these publications, the PI must be listed as last and corresponding author.** AIRC reserves the right to verify that these conditions are met. Failure to respect this commitment may result in withdrawal of AIRC support to the investigator.

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.

2.3 Research plan

The research project must be clearly distinct from the work performed in laboratories with which the applicant is or was affiliated. In case the proposed research involves ideas and materials stemming from the former lab, the former supervisor should agree to this (see Guide to proposal preparation).

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.

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 at any time, 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: 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.

3. 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 at any time. 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.

4. 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.

5. Funding

The Start-Up grant is intended to support the investigator for a period of 5 years. Funded projects will officially start on January 2nd 2019 and end on January 1st 2024. **The award is up to € 200.000/year.**

The following costs are eligible:

- Direct research costs:
 - a) Consumables and supplies
 - b) Small bench instrumentation
 - c) Equipment: the purchase of large instrumentation will not be looked upon favourably. However, if it is of central importance for the development of the project, it can be requested only if thoroughly justified.
 - d) Services
 - e) Maintenance
 - f) Publications
 - g) Meetings and travels
 - h) Personnel: support for up to 2 units of personnel (only PhD students, early-stage researchers, research nurses and technicians) at 100% of time on the project
 - i) Salary for the PI (partial or full). It can be requested only if strictly necessary, *i.e.* only in case the Hosting Institution cannot afford to pay his/her stipend. In this case, the salary support will be negotiated with and given to the PI by the Hosting Institution, which will have all the administrative responsibility.
- 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 PI's research activity and his/her achievement of a true scientific independence and leadership will be evaluated through an *ad hoc* site-visit to the Start-Up laboratory. A detailed progress report (scientific and administrative) will be required. Instructions regarding the site-visit will be communicated to the PI in due time. Funding for the last 2 years will be granted only if the PI has set up his/her own lab, has demonstrated scientific independence and productivity, and if all this is reflected in the positive assessment by the site-visitors.

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.

6. The Review Process

6.1 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.

6.2 Pre-submission evaluation

AIRC has appointed a dedicated Start-Up Study Section composed of outstanding non-Italian experts with complementary expertise covering various cancer research areas. The Study Section is in charge of the entire review process, including the evaluation of the pre-submissions. The identity of the reviewers will not be disclosed.

Each pre-submission is evaluated by three members of the Study Section who select the most meritorious applications, based on the review criteria listed below, indicating whether the applicant should or should not be invited to submit a full proposal. All applicants will be notified on the outcome of the first round of evaluation and will receive the reviewers feedback.

6.3 Full proposal evaluation

Full proposals are independently reviewed by at least three members of the Study Section with expertise in the specific area of the research plan, who act as *primary reviewer*, *secondary reviewer* or *discussants*. The primary reviewer might also ask to recruit a *reviewer specialist*, should he/she think that the expertise available within the Study Section may not be sufficient for a thorough assessment of the research proposal. The reviewer specialist is recruited from a panel of more than 600 well established international investigators working in institutions outside of Italy. Each member of the Study Section provides a score, while the reviewer specialist only expresses a priority for funding.

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.

The review criteria are:

1. significance and impact on cancer;
2. innovation;
3. approach and feasibility;
4. PI's track record and international standing in cancer research;
5. PI's leadership, maturity and scientific productivity adequate to establish an independent research group and successfully complete the proposed study;
6. quality of the Hosting Institution: environment, international standing, resources, facilities, infrastructures and commitment to support the independence of the PI;
7. adequacy of the budget requested.

When all evaluations have been submitted, reviewers are invited to read the critiques by the other reviewers who evaluated the same proposals and, if they deem necessary, to make additional comments.

6.4 Interview

When all reviews are completed, applications are ranked in order of scientific merit (the *preliminary score*, which is used to rank the applications at this stage, is calculated as the mean of the scores received from the reviewers who evaluated the application). Based on the preliminary ranking, a shortlist of candidates will be invited to an **interview in Milan on September 19th 2018**. All applicants are requested to hold this day; all candidates will be notified by the end of July 2018. The interview will include a short presentation followed by Q&A with the members of the committee. Further details will be provided to the shortlisted candidates. The final ranking, which is based on the *final score* of each application, is calculated as the mean of the scores received from all reviewers during the discussion.

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, and they will have access to the reviewers' comments. **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.

7. Revised Applications

A PI cannot present a Start-Up application more than twice, even with a different research plan.

In addition, 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 (e.g. 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 (full submission only).

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.

8. 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).

Pre-submission enquiry (mandatory)	Publication of Call and application form release	February 1, 2018
	Online submission	March 2, 2018
	Notification of results	April 17, 2018
Full proposal (only if pre-submission is approved)	Full submission form release	April 17, 2018
	Online submission	May 21, 2018
	Online submission with digital signatures of the PI and Legal Representative	May 31, 2018
	Papers in press (*)	July 1, 2018
	Interview	September 19, 2018
	Notification of results	November 30, 2018
	Start of grants	January 2, 2019

(*) Communications regarding these papers will be forwarded to all reviewers evaluating the proposal.

AIRC has modified its procedures for the signature of the full 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.