AIRC

Associazione Italiana per la Ricerca sul Cancro



Call for Proposals 2017

Start-Up Grant – Reintegration

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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 in cancer research, seeking the opportunity of becoming independent investigators in Italy after a successful research experience abroad. 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 2018 and will provide support for the new unit for a period of 3+2 years (provided that AIRC has available funds and the third year site-visit is successful), allowing it to develop and become competitive for routine mechanisms of funding. The grant is up to € 200.000/year and will be awarded only once in a lifetime.

1. How to Apply

A presubmission inquiry is mandatory for Start-Up grants. The presubmission should 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 cogent case will also have to be presented for the suitability of the candidate for a Start-Up grant. A letter stating the commitment of the Hosting Institution to foster the growth of the new research unit (see below) must accompany the presubmission inquiry. Applicants who meet the eligibility requirements and who present the most competitive presubmissions will be invited to submit a full proposal.

2. Eligibility Criteria

Applicants. Applicants can be of any nationality, are expected to have operated to the highest standards of integrity during their whole career and **should be 35 years old or younger** (born on or after March 2nd 1981) by the time of the presubmission application's deadline. This is a reintegration grant: applicants must have a significant experience in a competitive laboratory outside of Italy, on-going or very recent (must not have been back in Italy for more than twelve months at the time of presubmission application's deadline). They **must have a strong track record** including **at least two first/co-first or last/co-last author primary research papers**, in press or published in the last five years in high level peer-reviewed journals; papers in press must be accepted for publication, not just submitted, by the presubmission deadline. Reviews, editorials, letters to the editor without data, do not count for eligibility.

Researchers applying for a Start-Up grant cannot apply to the other 2017 AIRC Calls.

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 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).

Hosting Institution and affiliation. 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), 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. The Hosting Institution must promote the highest standards of integrity in research, in compliance with the AIRC policy on research integrity.

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

The Hosting Institution will actively favor 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 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. In the letter sponsor and guarantor 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 presubmission preparation). In these publications, the PI must be listed as last author and must be the corresponding author as well. 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.

Research plan. The presentation of a project that is clearly distinct from work performed in laboratories with which the applicant is or was affiliated is required. In case the proposed research involves ideas and materials stemming from the former lab, the former supervisor should agree to this and write a letter of collaboration (see Guide to full proposal preparation).

A Start-Up proposal that has been rejected twice by the same or other applicants in the past cannot be submitted again. See "Resubmission of revised applications" for further details.

The same research project cannot be presented by two or more applicants within the AIRC 2017 Calls.

3. The 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, in monitoring, diagnosis, or treatment of tumors in the near term.

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

- Angiogenesis
- 2. Cancer genetics
- 3. Cancer stem cells
- 4. Cell adhesion, migration, invasion and metastasis
- 5. Cell cycle control and cell division
- 6. Cell death and apoptosis
- 7. Chemotherapy
- 8. Computational biology
- 9. Control of gene expression and epigenetics
- 10. Diagnosis
- 11. DNA damage and repair
- 12. Epidemiology and prevention
- 13. Gene therapy
- 14. Hormone therapy
- 15. Imaging
- 16. Immunotherapy
- 17. Infection, inflammation and cancer
- 18. Metabolism
- 19. Prognosis
- 20. Radiobiology and radiotherapy

- 21. Resistance to therapy
- 22. Signal transduction and intracellular trafficking
- 23. Structural biology
- 24. Targeted therapy and new therapeutics
- 25. Tumor immunology
- 26. 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, AIRC feels that phenomenological, descriptive-at-best, proposals should be discouraged. The following kinds of proposals will receive **low priority and have 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 three clinical trials;
- all phase one and two 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:

- a) proposals aimed at studying: interactions between environmental risk factors, genetic profiles and intermediate biomarkers; the natural history of cancer by linking different phases of the disease to specific biological/genetic profiles;
- b) 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;
- c) pilot clinical studies of new therapeutic drugs, procedures or strategies;
- d) proposals aimed at a critical evaluation of last generation drugs and at elucidating their activity by mechanistic insights;
- e) 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 appropriate provisions for study design, statistical analysis and sample size (whenever applicable), in particular for studies with human subjects (clinical and epidemiological).

For studies involving human subjects, human biological samples or for animal experimentation, the approval of the competent authorities is mandatory; funds will not be granted in the absence of such documentation, even if the research proposal is scientifically approved. See the "Bio-ethical requirements" section of the Guide to proposal

preparation for further details on the documentation required. AIRC does not accept any liability for harm to participants in AIRC funded trials.

Proposals of 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 (see the "Personnel involved in the research" section of the application form), 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. 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 and non-economic oncological research by the Hosting Institution.

5. Funding

Funded projects will officially start on January 2nd 2018 and end on January 1st 2023. The award is up to € 200.000/year. The Start-Up package is intended to support the investigator for a period of 3+2 years. Renewal requests must be submitted yearly (see "Deadlines" below), through appropriate online forms, and will be automatically approved for the second and third year, provided that AIRC has available funds. At the end of the third year, the Pl'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 scientific 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 two years will be granted only if the PI has demonstrated scientific independence and productivity and if the site-visit outcome has been positive.

▶ This grant is meant to cover research costs and the salary for maximum two fellows or technicians and the PI.

The following costs are permitted:

- direct research costs, inclusive of consumables and supplies, "small" bench instrumentation, services, maintenance contracts, publication costs, meetings/travel costs. Such costs should correlate with the number of components of the research unit;
- 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;
- **equipment**. The purchase of large instrumentation will not be looked upon favourably. In any case, it should be thoroughly justified and be of central importance for the development of the project;
- support for fellows/technicians (personnel costs). Support will be provided only for two persons (post-docs or technicians) at 100% of time on the project. Applicants should ascertain that the Hosting Institution can take on fellows;
- **indirect costs.** These are generated by the research project, but cannot be attributed directly and quantitatively to a specific activity. For example, they may include core facilities, personnel of the research team not directly involved in research activities (e.g. secretaries and core-facilities personnel, etc.). Indirect costs are up to 15% of the direct research costs (personnel included)

incurred, not of the total amount that will be granted;

overheads. These are expenses that the Hosting Institution must cover so that the research can be
carried out. They may include, for example, grant management costs, utilities, administrative costs
etc. Overheads are up to 10% of the sum of direct (personnel included) and indirect costs incurred.

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.

Transfer of grant money to other laboratories either in Italy or abroad is not allowed.

At the end of the fifth and last year 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 three months after the termination of the grant (see "Deadlines" section). 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.

Please note that AIRC reserves the right to audit the administrative management of the project at any time.

6. The Review Process

All applications are subjected to an administrative review to verify the compliance with guidelines and eligibility criteria; those that do not conform are triaged out. Presubmission inquiries from researchers who meet the eligibility requirements undergo an initial phase of screening. The proponents of the most competitive presubmissions are invited to submit a full grant application. No detailed feedback will be provided to applicants rejected at the presubmission stage.

For the evaluation of Start-Up applications, AIRC relies on the expertise of reviewers selected from a panel of more than 600 well-established international investigators working in research centers outside of Italy. The AIRC peer review process ensures a fair, independent and expert evaluation of the scientific quality of the applications in compliance with conflict of interest and appearance of conflict rules. When accepting to evaluate an application, reviewers agree that they will maintain the confidentiality of applications and associated materials they have received. The AIRC policy on conflict of interest is available in our website.

The invited full proposals are independently evaluated by three reviewers, who provide a ranking of all applications based on the following review criteria:

- 1. significance and impact on cancer;
- 2. innovation and potential for competition;
- 3. approach and feasibility;
- 4. track record and international standing of the investigator in cancer research;
- 5. leadership, maturity and scientific productivity adequate to establish an independent research group and successfully complete the proposed study;
- 6. Hosting Institution's standing at the international level, resources and facilities available, commitment to support the independence of the PI;
- 7. adequacy of the budget (to determine if the proposed research is doable with the € 200.000/year budget allocated for this programme).

When all evaluations have been submitted, reviewers are invited to read the critiques by the other two reviewers who evaluated the same proposals and make additional comments, if needed. In case there are major discrepancies among the evaluations, an editor may be 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.

For each application, the scores received from all reviewers after the "cross-review" phase and assessment by editors are averaged to generate the application's global score, which is used to rank the applications. Proposals are thoroughly discussed during a plenary session. To confirm the ranking of the applications, shortlisted PIs might be interviewed.

The recommendation for funding, to be endorsed by the AIRC Board of Directors, will be made by the AIRC Scientific Director and the staff of the Peer Review Office, and will be exclusively based on the final ranking and on the financial availability of AIRC.

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.**

Please note that after the awarding of a grant, AIRC reserves the right to site-visit the PIs laboratories and Hosting Institutions at any time.

7. Revised Applications

- ► Revised applications that do not meet all eligibility requirements described in this Call will not be sent out for review.
- ▶ A PI cannot present a Start-Up application more than twice, even with a different research plan.

The revised application must include a response to the reviewers' comments in the "Revision" section of the online form.

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).

	online form release	February 2, 2017
Presubmission enquiry	electronic submission deadline	March 2, 2017
(mandatory)	notification of results	March 27, 2017
	electronic submission deadline	May 8, 2017
Proposals	paper submission (postmark) deadline (*)	May 18, 2017
(only if presubmission approved)	notification of results	November 30, 2017
	start of grants	January 2, 2018

- (*) **For full proposals only,** the following pages are required in paper format and must be mailed by the indicated deadline:
- Title page, stamped and signed by the PI and the Legal Representative;
- Budget form, stamped and signed by the PI and the Legal Representative;
- Bio-Ethical requirements page, stamped and signed by the PI;
- Declaration on affiliation, stamped and signed by the PI and the Legal Representative;
- AIRC policy on research integrity, stamped and signed by the PI and the Legal Representative.

In case candidates are affiliated to a non-Italian Institution at the time of the submission deadline, they can send two separate copies of those documents (one with the signature of the PI and another with the signature of the Legal Representative).

Send all paper documentation to the following address:

AIRC Direzione Scientifica via San Vito, 7 – 20123 Milano

Paper documentation marked with "draft" is not valid. Please print the requested pages only after completion of the online submission.

If these documents are not sent by the indicated deadline, or if AIRC does not receive them, applications will not be sent out for review.

Deadlines for renewals and final reports (by 17:00, Central European Time, of the indicated dates).

Renewal for 2nd year of funding	online form release	June 4, 2018
	electronic submission deadline	July 25, 2018
Renewal for 3rd year of funding	online form release	June 3, 2019
	electronic submission deadline	July 25, 2019
Renewal for 4th year of funding, and progress report (scientific and administrative)	online form release	June 5, 2020
	electronic submission deadline	July 20, 2020
	digitally signed submission deadline	July 30, 2020
Renewal for 5th year of funding	online form release	June 3, 2021
	electronic submission deadline	July 24, 2021
Scientific final report	online form release	July 4, 2022
	electronic submission deadline	September 5, 2022
Administrative final report	online form release	February 1, 2023
	electronic submission deadline	April 3, 2023
	digitally signed submission deadline	April 13, 2023

The deadlines for renewal requests and final reports may be subjected to changes. In this case, PIs will be notified of the new deadlines by email.

9. Guide to Presubmission Preparation

► To apply, click on the "Area Ricercatori" of the site www.airc.it

For researchers who already have an AIRC account: access the "Personal Area" with your username and password.

First-time applicants must register in our system: please click on "Register (for applicants only)" and provide the requested information, including your tax code (*codice fiscale*). The registration will be confirmed by e-mail and a username and password will be provided. Log on in your AIRC account with your username and password.

To launch the application form for the first time: click on "Calls", select "Individual Grants", then click on "Apply" in the Start-Up 2017 section. In the next window, click on "Access the application form". To access the application in progress: click on "Submissions" and then click on "Access the application form".

- ▶ Below you will find a list of the general features of our online system:
 - the system automatically launches the "Principal Investigator" form. All forms that must be filled out
 are listed on the left side of the page. Click on each one of them and fill in all the mandatory fields (in
 bold). Make sure to click on "SAVE" after completing each form;
 - the forms can be filled out in different sessions and the work can be interrupted/resumed at any time;
 - a number of forms must be submitted as PDF files. Each file cannot exceed 2Mb. Any file exceeding such a limit will be automatically rejected by the system. Secure PDF files cannot be uploaded. Documents submitted as PDF files must be written using an A4 format, single spaced, with margins not less than 2 cm and a font not smaller than 12 point (preferably Palatino, Times, Arial). Do not exceed the page limit indicated for each section: the system will not allow the upload of a number of pages beyond the limit;
 - the status of each form is shown on the left: red cross for mandatory forms that are incomplete; yellow circle for not mandatory forms; green mark for completed forms. These same symbols are used in the "Check and Submit" section;
 - the "Check and Submit" section (last title in the list of forms on the left) allows applicants to:
 - a) check and see whether each form has been correctly filled out; for mandatory forms that are incomplete, the information that must be provided is listed;
 - b) view and print the application in its incomplete/complete state. By clicking on "Create draft" and then on "Open submission draft" you can download the PDF draft generated by the system;
 - c) submit the application. Once all mandatory forms are complete, please click on "Submit". Be aware that after clicking on "Submit" it will not be possible to make any further modifications.
 - the complete proposal is automatically assembled as a single PDF file at the end of the online procedure;
 - applicants may designate a Grant Officer from the Hosting Institution to assist in the preparation and submission of the application. However, the PI is fully responsible of the entire proposal content. See the "Research project" section for further details.

The application must be written entirely in English.

Applications that do not conform to all the requirements in these instructions will be rejected.

9.1 Principal Investigator (PI)

The PI is the researcher who is primarily responsible for designing and directing the proposed research.

Please provide the PI's position in the Hosting Institution (examples: assistant professor, staff scientist, etc.) and his/her ORCID identifier, if available. ORCID (Open Researcher and Contributor ID) provides a persistent digital

identifier that distinguishes the PI from every other researcher; for more information visit the website http://orcid.org/. Although not mandatory, we encourage PIs to register into the ORCID website and then insert their ORCID identifier in the corresponding box. All other fields are automatically filled out with information provided during the registration into the AIRC website; to modify the information in any of these fields, please click on the link "My personal data" at the bottom of the page and edit the information in the pop-up window.

Please note: to successfully complete this form, it is mandatory to provide the tax code (*codice fiscale*) and personal and contact data of the PI through the "My personal data" section, which has to be completed and updated.

9.2 Title Page

- ▶ Please fill in the requested fields, entering:
 - the title of the proposal. The title must not exceed 120 characters, small cases, spaces included. It should be neither too specific (with abbreviations of molecules names such as "Role of PGCI in tumor progression"), nor too vague (such as "Analysis of tumor metastatization");
 - the research area. Select one of the 26 Research areas provided in the menu and listed in "The research plan" section of this Call, based on the topic of the research activity that will be carried out with the grant;
 - the Hosting Institution (i.e. the Italian research center where the PI will carry out the research activity). The system automatically lists the institution(s) indicated by the PI in previous applications to AIRC, if any. In case it corresponds to the institution where the research supported with this grant will be carried out, please check the corresponding box, otherwise check the box "Other" and select the correct Hosting Institution from the drop-down menu. The "Address" field is automatically filled in by the system once the Hosting Institution and Department have been selected. If the Hosting Institution is not listed in the menu, please contact our offices administrative.office@airc.it;
 - the Department: please select one of the departments listed in the drop-down menu (unless the form
 indicates "not available"). If the Department is not listed in the menu, please contact our offices
 administrative.office@airc.it;
 - the Laboratory (optional): please indicate the Laboratory, if applicable:
 - Grant Officer (optional): applicants may designate a Grant Officer from the Hosting Institution to assist in the preparation and submission of the application. The name of the Grant Officer, if not already present in the form and selectable from the drop-down menu, must be communicated to AIRC by e-mail airc.direzione-scientifica@airc.it. AIRC will create an account for the Grant Officer and send him/her the access codes to it. The name of the Grant Officer will then appear in the drop-down menu of the application form, allowing the PI to select the name. From their Personal Area the authorized Grant Officers will have access to the PI's application form and will have the possibility of completing and submitting it on behalf of the PI.

9.3 Legal Representative and Scientific Director

The Legal Representative (*Legale rappresentante*) of the Hosting Institution will be responsible, along with the PI, of all the legal and administrative duties of the grant. The information regarding the Legal Representative (mandatory) and the Scientific Director (only if applicable) are provided automatically by the system based on the Hosting Institution selected in the "Title page" section. In case the Director of a Department within the Hosting Institution is duly authorized to sign as Legal Representative of the Institution, check the box "*By flagging this check box you are declaring that the Director of the Department is duly authorized to sign on behalf of the Legal Representative of the Institution*". Please note that by flagging this box the PI certifies that the Director of the Department has power of attorney. Please make sure that all data are correct and up-to-date, and then click on "Save". If they aren't, please notify AIRC by e-mail administrative.office@airc.it and provide an official record (*e.g.* copy of Appointment Decree) as supporting documentation.

9.4 Project Keywords

Project keywords will be used by the AIRC Peer Review Office to assign each application to the most appropriate reviewers. Therefore, a good choice of keywords is extremely important to ensure that reviewers with the most adequate expertise will evaluate the application. Avoid keywords that are too generic or too similar with each other; pick a set of keywords that clearly define the key aspects of your research plan.

Keywords are listed at the end of this Call.

To enter the project keywords (at least one, maximum five) please click on "Enter/Edit Keywords". In the "Manage Project Keywords" pop-up window, keywords are grouped by their first letter: for example, by clicking on the letter "C" in the menu it is possible to visualize all keywords beginning with the letter C, and to select one. Alternatively, type in a specific keyword in the "Search a specific keyword" box and click on "Search". To select a keyword, click on it (the keyword box will turn from grey to blue) and then click on "Save". Repeat this process for each keyword. To exit the window, click on "Close". You will be automatically redirected in the main keywords page: click on "Save" at the bottom of this page to save the record.

9.5 Investigator's Statement

In this section (maximum 3 pages), applicants should make a cogent case to explain why they are suitable candidates for this type of grant, describing why they are ready to establish their own independent research group and how they will manage the relationship with former supervisors. Also, they are invited to explain how the experience abroad contributed to the development of their research, leadership and management skills, and why the selected Hosting Institution is the best place to carry out their line of research.

9.6 Institutional Commitments

Please upload a PDF file of a letter signed by the sponsor, the guarantor of the Hosting Institution (Scientific Director or equivalent, e.g. Department Head) and by the Legal Representative. The letter should describe the level of institutional commitment to foster the applicant's research career and his/her achievement of scientific independence, indicating:

- the extent to which the applicant will be relieved of other responsibilities in order to have at least 70% of his/her time dedicated to the research activity on the AIRC project;
- the laboratory, resources, facilities and equipment that will be available to the PI;
- opportunities for critical professional interactions with senior colleagues;
- the pledge that in all publications relative to the research carried out with the Start-Up package, the PI will be listed as last author and will be the corresponding author as well;
- the commitment to indicate the Start-Up as an independent unit in the Hosting Institution's staff directories, websites, public reports etc.

Each one of these issues must be clearly addressed in the letter; failure to do so may result in rejection of the Start-Up application. Inclusion of additional benefits for the PI (e.g. availability of core facility services free of cost, payment of PI's salary, etc.) is encouraged and will make the presubmission more competitive.

9.7 Revision

Please check the appropriate box ("Yes" or "No") depending on whether the research project submitted within this application is a revision of a previously rejected proposal or not.

Pls whose last application (either IG, MFAG, Start-Up or TRIDEO) was rejected in the past five years have two options:

If the new application is a resubmission, check "Yes" and upload a document with a point-by-point reply to the criticisms and issues raised by the reviewers, explaining how they have been addressed and indicating all changes

(additions, deletions, modifications) introduced in the research plan for this purpose.

▶ Please do not exceed two pages (approx. 1000 words).

If the new application is NOT a resubmission, check "No" and briefly explain in the dedicated box why the research proposal is fundamentally different in hypothesis, methods and scope from the previously rejected application.

▶ The total number of words must not exceed 200.

A Start-Up application submitted for the third time by the same candidate will not be sent out for review, even if the research plan is different.

The Peer Review Office will try to assign revised applications to the same reviewers that evaluated it in the previous Call. However, this is not always possible as some reviewers may not be available in every round of review. Therefore, please make sure to describe (or to report verbatim) all issues raised in the original evaluations, so that new reviewers can understand how the application has been modified to address the criticisms.

9.8 Presubmission Research Plan

Provide an overview of the research activity that will be carried out with the Start-Up grant, highlighting the relevance to cancer. Do not exceed the three-page limit (approx. 1500 words), including key references; attach the document as PDF file.

9.9 PI Education and Training

Click on "Add new record" and list degrees of the PI. The form automatically shows the information inserted in previous applications and stored in the "My Profile" section of your AIRC account. By selecting some or all of these records, they will be uploaded in the current application; please check that all information is present. At any time a record can be modified or completed by clicking on the "Degree" column and filling in the pop-up window. In order to add a new position, click on "Add new record" and indicate the University/Research center, Country, City, Field of research, time frame, and name of the supervisor/mentor (if applicable), then click on "Save".

Do not list post-doctoral positions here, as they should be included in the "PI Research and Professional Experience" section.

9.10 PI Research and Professional Experience

Click on "Add new record" and list all positions held by the PI, including post-doctoral trainings. The form automatically shows the information inserted in previous applications and stored in the "My Profile" section of your AIRC account. By selecting some or all of these records, they will be uploaded in the current application; please check that all information is present. At any time a record can be modified or completed by clicking on the "Position" column and filling in the pop-up window. In order to add a new position, click on "Add new record" and indicate the Institution, City, Country, time frame, position held, and name of supervisor (if applicable), then click on "Save".

9.11 Narrative Biosketch

Please identify up to five major scientific accomplishments of the PI (but no more than five!) and explain how they helped advance the scientific knowledge in oncology. They may be seminal publications, patents, awards, significant teaching/mentoring activities, proprietary software and datasets, authored books.

The goal is not to have a long list of achievements, but rather to focus on those that have impacted most on the field. Upload the document as PDF file (maximum 1 page, approx. 500 words).

9.12 Research Interruptions and Justifications

This section should be completed in case the applicant's research activity has been interrupted for at least 5 months

between 2012 and 2017 due to parental leave, children care, illness or other personal issues. Applicants are invited to describe in detail if/why the career breaks reported may have had a negative impact on their track record. Reviewers are instructed to take this information into account when assessing the scientific productivity of an applicant.

9.13 Publications

The PI must provide the list of papers published in the last five years. To do so, a number of options is available; click on any that applies.

Do not include abstracts, conference papers, book chapters and papers published in journals without IF, unless they are new journals.

Add PubMed publications

Within this interface the system launches a PubMed search and provides a list of PubMed-recorded publications spanning from 2012 to 2017. Enter the PI's first and middle initials, and click on "Find". If the applicant has published with a different last name than that used to register into the AIRC account (e.g. married vs maiden name), check the "Change surname" box, and then click on "Find". Alternatively, search for a specific article by entering its PubMedID in the corresponding box. Once the list of all PubMed publications has been generated, please follow these steps:

- a) Select papers to be included in the application: from the list of all PubMed publications, select the papers published by the applicant and that the applicant wants to include in the proposal by clicking on the box at the left side of each article. Pay special attention to potential homonyms. Do not include abstracts, conference papers, book chapters and papers published in journals without IF, unless they are new journals.
- b) Indicate acknowledgement to AIRC: for each publication, please indicate whether it has an acknowledgement to AIRC by checking the box (the default is "NO").
- c) Certify accuracy of flags, and save records: once all selected publications have been flagged, scroll down to the bottom of the page and check the certification box ("I, the undersigned, certify that all publications have been carefully checked and correctly flagged for authorship. I am aware that any mistake or inaccuracy may impact the evaluation of my track record"). The system automatically recognizes the position of the applicant in the list of authors in each publication (if not, the box "not assignable" will be checked). It is possible to amend this information, if incorrect, by providing supporting documentation from the main page of the Publications (see below). Click on "Add selected publications" and then on "Close" to complete the process.

Add Web of Science Core Collection® publications

From this section it is possible to enter articles that are included in Web of Science Core Collection® but not in PubMed (most journals are present in both databases, but there are few exceptions; the drop-down menu does not list PubMed journals). For each record, please provide the title, list of authors, journal, year and month of publication, volume, pages. Select the journal from the drop-down menu, which provides all journals listed in Web of Science Core Collection®. Mark each paper for authorship and acknowledgement to AIRC. Please upload the page of the article where the role of the author in the published work is certified (not the entire manuscript). Finally, check the certification box and click on "Save" to complete the process.

Add papers in press

Use this section to submit articles already accepted for publication but not yet available online. For each record, please provide the title, list of authors, journal, year. Select the journal from the drop-down menu, which lists all Web of Science Core Collection® indexed journals. Mark each paper for authorship and acknowledgement to AIRC. Please upload a PDF file with the letter of acceptance from the journal. Please attach only the pages that report the authorship of the PI and make this information clearly visible (e.g. highlighting the name of the

applicant). Do not attach the entire manuscript. Finally, check the certification box and click on "Save" to complete the process.

Add from My Profile - Publications

This interface lists all publications previously entered into the system (either when submitting an application, or when submitting a grant renewal request, or directly into the publication section of the My Profile Area). By selecting some or all of these publications, they will be uploaded in the current application; please make sure the flags are correct.

All publications entered from any of the above sections will be listed in the "Publications" main page. From here, it is possible to edit the information relative to each paper by clicking on the title of the publication. Once in the "Edit publication flags" window, please check the appropriate authorship box and, if different from the default provided by the system, upload the page of the article where the role of the author in the published work is certified (e.g. for a second or third author who is in fact a co-first author, please upload the PDF file of the page where it is stated that the PI "equally contributed to this work"). To complete the process, click on the certification box and click on "Save" to complete the process.

The system will automatically process all publications data to generate the complete **list of publications** reporting the IF and the PI's **track record summary** in the PDF file of the application. The PI track record summary is intended as a quick assessment of the **productivity in the last five years** and of the international standing of the PI, in order to facilitate the work of reviewers. Active IF is calculated as the sum of IFs of all articles where the applicant is first, last or corresponding author in the last five years.

The PI is responsible for uploading the most accurate information regarding publications and authorship. The IF assigned to each article, regardless of the publication date, is the latest provided by the Journal of Citation Reports (JCR) by Clarivate Analytics (previously the Intellectual Property and Science business of Thomson Reuters). For this Call, the 2015 JCR IF list will be used.

Candidates are required to check all the information and to contact the AIRC Peer Review Office (<u>airc.direzione-scientifica@airc.it</u>) before the deadline of the Call in order to correct any possible inaccuracy or mistake.

Even though the Impact Factor is internationally acknowledged as an important objective criterion that allows for an estimate of peer-recognition of the work of a given investigator, AIRC acknowledges that it is not an absolute standard to evaluate scientific productivity. Moreover, several circumstances mitigate the relevance of the IF; for example, some important, recently established journals may not be impacted yet or have "artificially low" IF. Also, for some research areas with very specialized, limited readership (e.g. medicinal chemistry) the best journals have low IF compared to others in more popular research arenas. Reviewers are carefully instructed by AIRC to give due consideration to all caveats associated with the IF when assessing an applicant's track record and scientific productivity.

In the full submission phase only: in case additional papers are accepted for publication after the submission deadline, the PI may request permission from the AIRC Peer Review Office to add this supplementary information to his/her application.

Please prepare a **single PDF file** containing a copy of the acceptance letter and a copy of the manuscript, and e-mail it to: <u>airc.direzione-scientifica@airc.it</u>

All communications made in this regard **by June 1**st **2017** (23:59 Central European Time) will be forwarded to all reviewers evaluating the proposal; communications received after June 1st 2017 will not be taken into consideration.

9.14 Presubmission Online Submission

Applicants are advised to not leave submission to the last minute, as heavy server load might affect system performance.

At any time during the application process a PDF draft file of the presubmission enquiry can be generated and checked: go to "Check and submit" (on the lower left of the main page), click on "Create draft" and then on "Open submission draft". It is strongly suggested that after all forms have been correctly filled out, and prior to proceeding with the final submission, the PDF Draft and its content are carefully read, controlled and verified.

To submit the application, go to "Check and submit". All mandatory sections of the application form must be completed and must have the green "OK" label before finalizing the submission. Only after having ascertained that all data are correctly reported in the PDF Draft of the presubmission, please click on "submit".

Applicants will receive a confirmation of the submission by e-mail. The final PDF file of the presubmission enquiry will be available in the "Your submissions archive" section of the Personal Area, and a copy should be saved for future reference.

- ▶ The application cannot be modified after the electronic submission deadline.
- ▶ The evaluation of the proposal is only based on the information present in the application.
- ▶ No detailed feedback will be provided to applicants rejected at this stage.

10. Guide to Full Proposal Preparation

▶ This section is only for applicants officially notified that their presubmission enquiry has been successful.

Click on the "Area Ricercatori" of the site www.airc.it. Log on in the "Personal Area" with your username and password.

To launch the full application form click on "Submissions" and then click on "Access the application form".

The full submission application comprises:

- the presubmission enquiry forms. All the information entered in these forms during the presubmission
 phase cannot be changed, with the exception of the Publications form, which can be modified in order to
 submit updated information with the full proposal;
- a set of new forms. Below is a detailed description of the information required in the new forms.

Please note that the same general instructions described in the Guide to presubmission preparation apply for the full proposal preparation, *e.g.* do not attach PDF files bigger than 2 Mb, etc.

10.1 Declaration on Affiliation

In this section applicants must indicate whether they are already working in the Hosting Institution. It is not mandatory to be located in the Hosting Institution at the submission deadline; however, should the application be funded, PIs are expected to be affiliated with the Hosting Institution from the beginning of the project and for the entire duration of the grant. Applicants are also required to list all institutions (in Italy or abroad) they are affiliated with.

Affiliation with the Hosting Institution

Check "yes" if you are already affiliated with the Hosting Institution by the submission deadline. The Legal Representative of the Hosting Institution will have to sign this declaration; by signing it, he/she confirms that the PI is affiliated with the Hosting Institution and declares that, in case the application is funded, the PI will be affiliated with and will be allowed to carry out the research project in the Hosting Institution for the entire duration of the grant.

Check "no" if you are not affiliated with the Hosting Institution by the submission deadline. The Legal Representative of the Hosting Institution will have to sign this declaration; by signing it, he/she confirms that the PI will be affiliated with the Hosting Institution by the start date of the project and declares that, in case the application is funded, the PI will be affiliated with and will be allowed to carry out the research project in the Hosting Institution for the entire duration of the grant.

Affiliation with other institutions

If the response to the statement "The Hosting Institution is the only institution I am affiliated with" is "No", please list any additional institution the PI is involved with (in Italy or abroad), either selecting it from the drop-down menu or indicating it in the text box underneath, and then Click on "Add".

Repeat the process to list multiple institutions. Applicants must provide the following documentation in a single PDF file:

- An official letter signed by the Legal Representative of the Hosting Institution (meaning the Institution
 where the PI will carry out the project) certifying the amount of time the PI will spend in the Hosting
 Institution and the percentage of time that the PI will devote to the project.
- For each of the other institutions the PI is affiliated with (in Italy or abroad): an official letter signed by an institution's official certifying the amount of time the PI will spend in that institution.

If the requested documentation is already available at the time of submission, check the box "I am attaching the following documentation...", click on "Select" and upload the documents as a single PDF file. If it is not available at the time of submission, check the corresponding box and send the documentation preferably by **December 15**th

2017 and, in any case, before the project starts; use the specific link available in the submission section of your personal area in the AIRC website. Please note that, should the application be approved, funds will not be granted unless all the requested documentation is uploaded.

10.2 AIRC Policy on Research Integrity

Please read the AIRC policy on research integrity and check the corresponding box. The PI and the Legal Representative of the Hosting Institution will have to sign this document; by signing it, they certify that they will comply with ethical principles of good scientific practice and engage in honest behaviour, as described in this policy.

10.3 Abstract

Extreme care must be placed on the Abstract preparation. The Abstract must provide an immediate understanding as to why the research plan is proposed, which approach will be undertaken and **the potential impact of the whole line of research on cancer**. A particular care must be dedicated to the last aspect: please explain why the proposed research has a clear objective that is consistent with the AIRC mission and will likely lead to advances in cancer biology, in monitoring, diagnosis, or treatment of tumors in the near term. Avoid long introductions and do not include references.

The Abstract must be structured into the following sections: Background, Hypothesis, Aims, Experimental Design, Expected Results and Impact on Cancer. Either type in the text directly into each box, or use a Word processor and then cut and paste each section into the corresponding box. Please note: the system allows plain text only; special characters will be maintained but formatted text (e.g. bold, superscripts, etc.) will be automatically converted into plain text. **The total number of words for the entire abstract must not exceed 500**; for convenience, the total word count is provided at the bottom of the page and is updated in real time. When all sections have been filled out, click on "Save". All sections will be assembled automatically into one page in the PDF file of the application.

Information on all research projects funded by AIRC may be made public on AIRC journals and websites.

10.4 Reference Letters

Please upload at least two reference letters. Furthermore, we require one letter to be written by the (former) supervisor at the institution abroad stating that he/she is aware that the candidate is applying to this grant. In case the proposed research involves ideas and materials stemming from the former lab, the supervisor should make clear whether he/she intends to collaborate.

Each letter should be in letterhead paper, dated and signed, and must not exceed one page in length (approx. 500 words, font size 12). Please upload the three letters in a single PDF file.

In case the persons who write the letters prefer not to include them in the application, please upload a pdf file with a statement indicating that, in order to maintain confidentiality, the letters will be sent separately to the AIRC Peer Review Office. The letters should be quoted as "Start-Up Grant Submission 2017 – reference letter" and e-mailed by May 8th 2017 to: airc.direzione-scientifica@airc.it

The AIRC Peer Review Office will forward the letters to the reviewers assigned to the application.

10.5 Proposal Main Body

This section should not exceed 10 pages and should be structured as follow: 8 pages of written text including references (approximately 4000 words), and 2 pages with figures.

The Proposal Main Body must be attached as a single PDF file.

Describe in detail the proposed research, intended to have a duration of five years, according to the following guidelines:

 please provide the <u>background and rationale</u> of the proposed research, along with relevant literature references and explain the <u>impact on cancer</u>; avoid lengthy, paper-like, introductions. The bibliography should be limited to only those citations essential to the application. List all references

- together at the end of the proposal main body, **employing the format used by the journal** *Cancer Research*: **for any reference, give the title and authors.** Example: Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. Cell 2011; 144:646-74. When available, we strongly encourage to include a paper identification code (PubMedID or doi);
- please describe the <u>experimental design</u> and the methodologies that will be employed. If the methodology is new or unusual, describe it in sufficient details for evaluation. Description of cumbersome experimental details and protocols, however, is not encouraged and generally detracts from the quality of the proposal. The research plan should be organized in *tasks*. Given existing difficulties in splitting clinical and epidemiological proposals into tasks, these types of studies should be divided into *phases*, whenever possible: this facilitates the work of reviewers and, in general, results in a better appreciation of the real value of the proposal. When the description of the research can be subdivided in tasks/phases, each numbered item must describe a precise part of the project with its own experimental design and methodological approach. The objective (milestone) of each task/phase and the experimental design (including methods and time-frame) should be clearly identifiable and will be examined by the reviewers to evaluate the feasibility of the project;
- make sure to include a section on potential <u>pitfalls and caveats</u>, discussing the potential difficulties
 and limitations of the proposed procedures, and suggesting alternative approaches to achieve the
 objectives;
- please describe the feasibility of the project, by providing:
 - preliminary data. Pay particular attention to this point, as reviewers always evaluate whether enough preliminary data are provided to support the working hypotheses. Include figures (not just written descriptions) of relevant preliminary data. Reviewers will be asked whether the preliminary data leading to the proposed work are scientifically sound and whether they represent a solid premise for the proposed experiments;
 - power calculation. For clinical and epidemiological studies, and whenever appropriate, make sure to have adequate sample sizes to ensure meaningful and statistically significant results.
 Make sure that the power calculation and analysis are clear and accurately described;
 - a description of the <u>PI's expertise</u>, qualification, past experience and accomplishments that are directly relevant to the projected success of the proposal;
 - a description of facilities and major equipment available for the research. This is particularly important, as many international reviewers may not be familiar with Italian research institutions.
 To this aim, it would be useful to provide a link to the lab and/or Hosting Institution webpage, when available in English;
 - a description of the key expertise available in the research team (it is possible to provide this information in the "Description of the work for every unit of personnel" section).

10.6 Personnel Involved in the Research

This form must be filled out for all persons directly involved in the project, including the PI. Do not list secretaries and/or administrative staff, or personnel involved for less than 20% of their time. Please pay particular attention to the allocation of manpower: reviewers will determine whether it is reasonable for the amount and type of work proposed.

The "core research team" is the research unit directed by the PI, comprising the PI and internal staff (fellows, technicians, collaborators working in the Hosting Institution). The term "External collaborations" is used for scientists external to the core team and/or not affiliated with the Hosting Institution and collaborating with the PI, and for companies involved in the project. Even though scientific collaborations are not discouraged, Start-Up Grants are awarded to a single PI, who has full responsibility for directing the proposed research. Also, please note that the term "collaboration" means a scientific collaboration, not a kind of labor contract.

Begin by completing the information relative to the PI: click on the name of the PI, fill in the indicated fields, then click

on "Save".

Core team members

To insert a new member of the research unit, click on "Add new core team member" and fill in the fields in the popup window. In addition to their personal data (name, surname, date of birth, gender, tax code and institution), the following information are required:

ROLE: please choose one from the available entries: fellow; technician; internal collaborator (for any personnel working in the same laboratory, Department or Institution as the PI, and working/collaborating with the PI on the proposed research plan). Please note that **financial support for salaries will be provided for fellows or technicians** (not collaborators) working 100% of their time on the project. Support can be requested for a maximum of two fellows or technicians.

TO BE DEFINED (TBD): check this box if a fellow, technician or internal collaborator has not been identified yet, and enter the requested information. Add TBD personnel sparingly, since a high percentage might negatively influence the assessment of the feasibility of the research plan and/or compromise the timely start of the work. For each TBD personnel please upload one page containing a brief description of the qualifications/skills necessary for the project that the TBD should have.

TITLE: please choose one from the available entries: Doctor, Professor, Engineer, or leave blank if none applies.

CLINICIAN: for each personnel, including the PI, choose "yes" only if directly involved in clinical practice (*i.e.* examining and treating patients). In general, fellowship support should not be awarded to clinical fellows, since it is quite rare that physicians taking care of patients may be involved on a specific research project at 100% of their time. Exceptions may be possible if thoroughly justified in the "Personnel costs justifications" section of the budget form.

External collaborations

To insert a collaborating scientist external to the core team and/or not affiliated with the Hosting Institution, or a company involved in the project, click on "Add new external collaboration" and fill in the fields in the pop-up window. In both cases a formal letter of collaboration is required and must be uploaded as PDF file. In the letter of collaboration, the role on project, the expertise and/or reagents that will be provided should be described in detail. Also in this document, the external collaborators should indicate whether specific agreements have already been made with the PI in terms of: a) management of the resources; b) intellectual property rights; c) authorship in publications resulting from the collaborative effort. Letters of collaboration provided by companies should also state that: a) the PI has the full property of data and results; b) the company has no right to veto the publication of results at any time; c) 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 of any type of economic interest. The letter should also indicate under what provision (free or not) the company provides its product(s) to the PI.

Description of the Work for each Unit of Personnel

Click on "Select" and upload a PDF file; please do not exceed 2 pages (1000 words).

Please divide this document into tasks/phases, reflecting the organization of the proposal main body, and indicate who will do what in each task/phase. Describe in a <u>concise</u>, but complete manner, the work that each unit of personnel (both core team members and external collaborators) will perform. If necessary, provide evidence of the skills of key team members citing a couple of significant papers that attest to their expertise. Please indicate the position held by each person (e.g. investigator, post-doc, staff scientist, technician, etc.) and if the Hosting Institution will cover the salary of Personnel for whom a financial support is not requested. Do not list undergraduate students, secretaries and/or administrative staff, but do include scientific personnel that might be involved for less than 20% of their time.

10.7 Budget Form and Justifications

The Start-Up package is intended to support the investigator for a period of 3+2 years. Funding for the last 2 years of the project is contingent upon a positive assessment of the PI's research activity and achievement of a true scientific independence and leadership at the end of the third year, through an ad hoc site-visit to the Start-Up laboratory.

In the five columns, one for each year of support, insert the amount needed for each of the categories allowed. The budget requested cannot exceed € 200.000/year. If the grant is awarded, AIRC will provide detailed instructions on the dates within which funds must be spent for each year of support.

Budget categories allowed

DIRECT RESEARCH COSTS (EXCLUDING PERSONNEL). The standard way of budget calculation, based on an itemized list of actual costs, must be employed. Enter the amount of money needed for research costs, divided into the following subcategories:

- consumables and supplies (examples: plasticware, reagents, chemicals, animals if applicable, etc.);
- "small" bench instrumentation (examples: electrophoresis power supplies, microcentrifuges, PCR machines, etc.);
- services (examples: sequencing, microarray, histology, patent filing costs, etc.);
- maintenance contracts (examples: service contracts for large instruments, animal facilities contracts);
- publication costs (most likely none in the first year of the project, as it takes time to obtain publishable data);
- meetings and travel costs.

EQUIPMENT. Indicate the support requested. Please remember that purchase of large instrumentation is not looked upon favourably by AIRC. In any case, it should be thoroughly justified and be of central importance for the development of the project.

▶ PI SALARY AND PERSONNEL: This grant is meant to cover the salary for maximum two fellows or technicians and the PI.

PI SALARY. Please click on "edit costs" to insert the PI costs details.

MAN/YEAR EFFORT. Please indicate the percentage of time that will be devoted to the actual performance of the work. **The PI must be at least at 70% of the time on the project.**

FINANCIAL SUPPORT (partial or full). Please indicate the amount of financial support requested for the PI's salary, if any. The financial support of the PI salary 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. In the justification notes please indicate the type of financial support (*i.e.* type of contract).

PERSONNEL EFFORTS/COSTS. Please click on "edit costs" to insert Personnel costs details.

<u>Man/Year effort:</u> Please indicate the percentage of time that will be devoted to the work. Fellows for whom a salary is requested must be at 100% of their time on the project. AIRC discourages the habit of listing many units of personnel at marginal fractions of their time: therefore, make sure to have a sizable number of units of personnel devoting at least 75% of their time to the project. PhD students (or equivalent) can be listed as 100%, as the time commitments to courses is not taken into account.

<u>Financial support:</u> Please indicate the amount of financial support (e.g. fellowship or other contracts permitted by the applicable law) requested; support will be provided only for **fellows or technicians at 100% of time** on the project

(a maximum of two). Applicants should ascertain that the Hosting Institution can take on fellows as indicated in the application, under the type of financial support requested.

The general policy of AIRC is **to provide fellowships to researchers in the early stages of their career**; the financial support requested should be consistent with the gross amount provided to fellows at the same career level at the Hosting Institution. Integration of the AIRC financial support by the Hosting Institution is permitted, but two salaries are not allowed.

In case an AIRC/FIRC fellowship is awarded to one of the unit of personnel for whom financial support has been requested in this grant application, the PI will be allowed to use the financial support for another unit of personnel, if needed. In case, the name of the new fellowship recipient must be provided when submitting the budget adjustment or the grant renewal request.

<u>Curriculum Vitae:</u> please upload a **one page CV in English** as a PDF file. CV must be added only for personnel working at least at 75% of their time on the project, with the exclusion of technical staff.

- ▶ The following format must be used for all CVs:
 - personal data (name, date and place of birth, citizenship, work address, phone number and e-mail address);
 - education (list, in reverse chronological order, all degrees obtained);
 - research experience (list, in reverse chronological order, all positions held, describing very briefly two sentences maximum – the main focus of the research activity);
 - · technical skills and competences;
 - awards;
 - publications (please provide only a selection of the most relevant, with a maximum of five).

INDIRECT COSTS. As defined in the "Funding" section of this Call, indirect costs will be supported up to 15% of the direct research costs (personnel included). Please enter the percentage charged by the Hosting Institution (from 0 to 15; 0,1 decimals are allowed); the system will automatically calculate the corresponding amount.

OVERHEADS. As defined in the "Funding" section of this Call, overheads will be supported up to 10% of the sum of direct (personnel included) and indirect costs. Please enter the percentage charged by the Hosting Institution (from 0 to 10; 0,1 decimals are allowed); the system will automatically calculate the corresponding amount.

The signature of the Legal Representative in the paper copy of the Budget form (see "Deadlines" and "Final Full Proposal submission") will be considered an official confirmation that the amounts indicated in the "Indirect costs" and "Overheads" are those applied by the Hosting Institution in agreement with the guidelines of this Call.

- ► For each budget category, a description and justification of the amounts requested in the "Justification notes" box must be provided. More specifically:
 - for each section of the "Direct research cost", provide a financial breakdown, on an item basis;
 - for "PI Salary": the PI salary can be requested only if strictly necessary (*i.e.* only in case the Hosting Institution cannot afford to pay his/her stipend). Please, specify if the financial support will cover the salary in full or partially: in the latter case please indicate the percentage of the salary paid on the grant and the percentage contributed by the Hosting Institution;
 - for "Personnel costs": describe under what type of provision (*e.g.* fellowship, contract etc.) the fellows for whom financial support is sought will be hired. Use this section to justify exceptions for requesting financial support for clinicians (see the section "Personnel involved in the research").

10.8 Existing/Pending Support

In this section please list grants that the PI will or might receive from any funding agency during the period of

support with the AIRC grant. In particular:

- Existing support: the PI has already obtained a grant;
- Pending support: the PI has applied and he/she is waiting for the decision by the funding agency.

Please list all grants, regardless of whether they overlap with the current proposal or not. For each grant, indicate: the funding agency, project title, duration, total amount of funding (in Euros) and degree of overlap (in terms of research plan) with the project presented with this Start-Up application. In case of overlap provide a justification for requesting additional support from AIRC in the apposite box; also, please provide name and percentage of time committed of all personnel listed in the current application (including the PI) that are also involved in the other grant. A single unit of personnel should not be allocated for more than 100% of the time. This applies to the sum of all grants, including those from agencies other than AIRC. Reviewers will be asked to verify that the proposal does not represent a duplication of projects already funded by or submitted to AIRC or other funding agencies. AIRC reserves the right to ask supplementary documentation to other funding agencies in order to verify possible overlaps.

10.9 Bio-Ethical Requirements

► Check boxes as applicable for human and animal experimentation.

Research on humans

Please note that the term "Research on humans" is not limited to clinical studies with healthy volunteers and/or patients. **It includes use of human biological samples** (commercially available human cell lines *e.g.* from ATCC are exempt), human genetic material and human data collection (*e.g.* genetic information, health, etc.). If the research plan includes Research on humans, the approval of the local Ethics Committee or Institutional

If the research plan includes Research on humans, the approval of the local Ethics Committee or Institutional Review Board (IRB) is mandatory.

▶The authorization must be valid for the entire duration of the human studies as planned in the research proposal.

The approval document issued by the Ethics Committee MUST indicate:

- the date when the IRB meeting was held; approvals obtained more than 3 years ago, i.e. prior to 2014, are NOT acceptable, unless the study protocol is still active (supporting documentation might be requested to verify this is the case);
- the name of the applicant or of a unit of personnel or of a collaborator included in the application;
- a clear reference to the studies described in the proposal (e.g. the title of the application).

In case biospecimens have been obtained by external sources/collaborators, the clearance documents must be provided by the Ethics Committee of the collaborator's research center.

If the IRB approval is available at the time of submission, check the box "I have obtained the clearance from the competent Ethics Committee/Institutional Review Board..." and upload it as PDF file by clicking on "Select" under the "Research on humans: clearance from Ethics Committee" header. Please indicate the date the approval was released and, if available, the date it expires; check the box "Valid for the duration of the project" if this is the case (supporting documentation might be requested to verify this condition is met).

If the approval from the Ethics Committee is not available by the submission deadline, we encourage PIs to submit their request to the IRB as soon as possible in order to avoid delays in the payment of the grant, if funded: grants will start only after the provision of the approval to AIRC. Check the box "I have not obtained the clearance from the competent Ethics Committee/Institutional Review Board yet, but I will provide it..." and, when available, upload it as PDF file in the "Submissions" section of the AIRC account (click on "The following required actions are pending" and on the link "Upload required document") possibly by **December 15th 2017.**

Research on animals

Experimentation on animals (vertebrates, cephalopods and foetal forms of mammals) must conform to all regulations protecting animals used for research purposes. The animal protocol(s) must be evaluated and authorized by the competent authorities (*i.e.* the Italian Ministry of Health, if the animal experimentation will be carried out in the Hosting Institution or in the research lab of a collaborator based in Italy, according to the D.Lgs. 26/2014), and a copy of the authorization must be provided.

▶The authorization must be valid for the entire duration of the animal studies as planned in the research proposal.

If the authorization is available at the time of the application submission, check the box "I have obtained the clearance from the Ministry of Health ..." and upload it as PDF file by clicking on "Select" under the "Research on animals: Clearance from Ethics Committee" header. Please indicate the release and expiration date of the authorization in the appropriate boxes.

If the authorization is not available by the submission deadline, we encourage Pls to submit their request to the Ministry of Health as soon as possible in order to avoid delays in the payment of the grant, if funded: grants will start only after the provision of the approval to AIRC. Check the box "I have not obtained the clearance from the competent Ethics Committee/Institutional Review Board yet, but I will provide it..." and, when available, upload it as PDF file in the "Submissions" section of the AIRC account (click on "The following required actions are pending" and on the link "Upload required document") possibly by **December 15th 2017.**

Research supported by AIRC that involves animal experimentation must comply with the principle of the Three Rs (3Rs) to Replace, Reduce and Refine the use of animals in research, as required by national and international rules. Please upload a document in the "Research on animals: Principles of the 3Rs" section, describing how the three Rs have been implemented in the research plan (e.g. explain why the anticipated results and benefits of the proposed research justify the use of animals, and why methods avoiding the use of living animals cannot be used; provide details and justification on the number of animals proposed for the research plan; describe all actions that will be taken to avoid or minimize pain and distress; etc.).

By signing the Bio-Ethical requirements page in the PDF file of the application, the applicant declares that the research studies are accurately described in the proposal and conform to all regulations protecting animals used for research purposes, including those of the D.Lgs. 26/2014, and that the experiments described in the proposal will be performed following the guidelines described in: Wolfensohn S, Lloyd M: "Handbook of Laboratory Animal Management and Welfare, 4th Edition" (Wiley-Blackwell, 2013).

Please note: Ethics Committee(s) approval(s) for human and/or animal research are not necessary for the assessment of the scientific merit of an application, during the review; however, **if the application is approved, funds will be granted only if the required Ethical Committee certifications have been sent to AIRC.** AIRC is not responsible for any inaccuracy in the ethical documentation provided and does not accept any liability for harm to participants in AIRC funded trials.

10.10 Final Full Proposal Submission

(online and by regular mail)

Proposal PDF draft

At any time during the application process a PDF draft file of the proposal can be generated and checked: go to "Check and Submit" (on the lower left of the main page), click on "Create draft" and then on "Open submission draft". It is strongly suggested that after all forms have been correctly filled out, and prior to proceeding with the final submission, the PDF Draft and its content are carefully read, controlled and verified.

Online submission

Do not leave submission to the last minute, as heavy server load might affect system performance.

To submit the application, go to "Check and Submit" (on the lower left of the main page). All mandatory sections of the application form must be completed and must have the green flags before finalizing the submission.

Only after having ascertained that all data are correctly reported in the PDF Draft of the proposal, please proceed to the proposal submission by clicking on "submit".

Applicants will receive a confirmation of the submission by e-mail. The final PDF file will be available in the "Your submissions archive" section of the Personal Area, and a copy should be saved for future reference.

- ▶ The application cannot be modified after the electronic submission deadline.
- ▶ The evaluation of the proposal is only based on the information present in the application.

Paper submission

For paper submission, please print only these pages:

- Title page, signed by the PI and the Legal Representative. In case candidates are affiliated to a non-Italian institution at the time of the submission deadline, they can send two separate copies of this document (one with the signature of the PI and another with that of the Legal Representative);
- Budget form;
- Bio-Ethical requirements page;
- Declaration on affiliation;
- AIRC policy on research integrity.

Sign and stamp in the appropriate spaces: the signatures of the PI and of the Legal Representative are both required in the Title page, the Budget form, the Declaration on affiliation and the AIRC Policy on research integrity: by signing the Title page, the PI and the Legal Representative acknowledge and agree to all terms and conditions of this Call and certify that all information present in the application is correct. In addition, the Legal Representative declares that, should the application be funded, the PI will be affiliated with the Hosting Institution for the entire duration of the grant and will be allowed to carry out the research project in the Hosting Institution. The applicant's signature is required in the Bio-Ethical requirements page as well. Paper documentation marked with "draft" is not valid. Please print the requested pages only after completion of the submission online.

Please send all paper documentation required to the following address:

AIRC, Direzione Scientifica Via San Vito 7, 20123 Milano

If these documents are not sent by the indicated deadline, or if AIRC does not receive them, applications will not be sent out for review.

List of Keywords

Acute Lymphoblastic Leukemia (ALL) Acute Myeloid Leukemia (AML)

Adenovirus Adjuvant therapy Aging and cancer AIDS/HIV/Kaposi

Androgen and/or receptors

Aneuploidy

Angiogenesis and/or vasculogenesis

Animal models Anti-angiogenic therapy Antibody/mAb therapy

Apoptosis

Aromatase and/or inhibitors

ATM pathway ATR pathway

Autoimmunity/Autoantibodies

Autophagy
B cells
bcl2 family
BCR-Abl/Abl
Biochemistry
Bioinformatics
Biomarkers

Biomolecular modelling

Biophysics Bladder tumor

Body mass index (BMI) and/or obesity

Bone disease

BRCA

Bone morphogenetic protein (BMP)

BRAF/RAF kinases

Brain and/or nervous system tumors

Breast ca.
Burkitt lymphoma
C.elegans
Cachexia
Cadherins
Cancer evolution
Cancer stem cells
Carcinogenesis
Caspases

CD133/Stem cell markers

Cell adhesion and/or cell adhesion molecules

Cell cycle

Caveolin

Cell cycle checkpoint G1/S Cell cycle checkpoint G2/M

Cell differentiation and/or differentiation therapy

Cell migration, motility and/or invasion

Cell polarity Cell signaling Centrosome

Cervix or endometrial ca.

Chemistry

Chemoimmunotherapy

Chemokines

Chemotherapy and/or chemotherapic drugs

Chromatin remodeling

Chronic Lymphocytic Leukemia (CLL) Chronic Myeloid Leukemia (CML)

Circulating tumor cells Clinical practice guidelines

Clinical trials

Colorectal and/or Intestinal ca.

Combination therapy

Comparative genomics hybridization (CGH)

Computational biology

Computer Tomography (CT Scan)

Costimulatory molecules

COX2 CRISPR/Cas9 Crosstalk Crystallography Cyclic AMP

Cyclins and/or inhibitors

Cytogenetics and/or chromosome alterations

Cytokines/Interleukins

Cytokinesis Cytoskeleton

Cytotoxic T Lymphocytes (CTL)

Dendritic cells Diagnosis Diet

DNA damage
DNA double strand break repair (DSBR)

DNA methylation DNA recombination DNA repair DNA replication

DNA single strand break repair (SSBR)

Docking
Drosophila
Drug delivery

Drug discovery and/or development Drug response and/or resistance

Drug screening
Drug toxicity
EGF and/or receptors
Embryonic development

Endocrinology Endocytosis

Endoplasmic reticulum (ER)

Endothelial cells Epidemiology Epigenetics

Epithelial mesenchyme transition (EMT)

Epstein-Barr Virus (EBV) Estrogens and/or receptors

Exosomes and/or endogenous microvescicles

Extracellular Matrix (ECM)/Stroma

Fas and/or FasL Fatty acids FGF and/or receptor Flow cytometry Fluorence imaging system

Fluorescence in situ hybridization (FISH)

Fluorescence resonance energy transfer (FRET)

Focal Adhesion/FAK Folate and/or receptor Functional genomics

Functional validation of target genes

Fusion genes Gastric ca.

Gene alteration/gain or loss Gene expression and/or profile

Gene regulation Gene therapy Genetics

Genome wide screening/GWAS

Genomic imprinting

Genomic/Genetic instability

Genomics Genotoxicity

Glioma and/or glioblastoma Glucocorticoids and/or receptors

Glucose metabolism and/or Warburg effect

Glycoproteins and/or glycosylation

Golgi

G-proteins and/or GPCR

Granulocytes

Growth factors and/or receptors Growth induction and/or growth arrest GVHD and/or Graft versus Tumor

Gynecological tumors
Head and neck ca.
Heat shock proteins (HSP)
Hedgehog pathway
Hematologic malignancies

Hematopoiesis

Hematopoietic stem cells Hemostasis and thrombosis Hepatitis B virus (HBV) Hepatitis C virus (HCV)

Hepatocellular carcinoma (HCC)

HER1-2-3-4

Hereditary DNA repair disorders

Hereditary tumors Herpes virus

High Mobility Group Proteins (HMG)

Hippo pathway Histone modifications

HLA/Major Histocompatibility Complex (MHC)

Hodgkin's lymphoma
Homologous recombination

Hormones

Human Papilloma Virus (HPV)

Hypoxia/Hypoxia-inducibile Factors (HIF-1)

Immune escape Immunization Immuno-editing Immunohistochemistry

Immunosuppression and/or suppressor cells

Immunotherapy

In vitro imaging and/or live cell imaging

In vivo imaging

Inflammation and/or inflammatory cytokines

Inhibitor of apoptosis proteins (IAPs)

Innate immunity

Insulin

Insulin-like growth factor (IGF) and/or receptors Integrins and/or Integrin-linked kinase (ILK)

Interferons
Ion channels
Jak/Stat pathway
Kidney ca.
Kinase/Kinome
Lentivirus
Leukaemia
Lipid metabolism
Lipidic mediators

Lipooxygenases

Liquid biopsy

Liver development and/or regeneration

Loss of heterozygosity (LOH)

Lung ca.

Lymphatics and/or lymphangiogenesis

Lymphocyte differentation

Lymphomas

Macrophages and/or monocytes Magnetic resonance imaging (MRI)

MAP Kinases Mass spectrometry Mathematical modeling Mathematical oncology

Matrix metalloproteases (MMP) and/or inhibitors

MDM2

Medulloblastoma Melanoma Membrane biology Mesothelioma MET/HGF

Metabolism/Metabolomics

Metallo-drugs Metastasis Microarrays Microbiome Microenvironment microRNA Microscopy

Minimal Residual Disease (MRD)

Mitochondria Mitosis

Monoclonal antibodies (mAbs) and/or immunoconjugates

Mouse models mRNA processing mRNA translation

Multidrug resistance (MDR) Mutation (somatic and/or germline)

Myc Myeloma

Nanotechnology/Nanoparticles

Netrin receptors Neuroblastoma Neuroendocrine tumors Next generation sequencing

NF-kB family Nitric oxide NK and/or NKT cells

NMR spectroscopy Non apoptotic cell death Non melanoma skin tumors Normal stem cells

Notch pathway Nuclear medicine Nuclear receptor Nuclear structures Nucleophosmin (NPM)

Oncogenes

Oncogenic virus/Viral oncology

Organic compounds Osteopontin Osteosarcoma Ovarian ca.

Oxidative stress and/or Reactive Oxygen Species (ROS)

p21 - activated kinases (PAK)

p53, p63, p73 Palliative care Pancreas ca. Pathology

Patient-derived xenografts (PDX)

Patient risk stratification PDGF and/or receptors Pediatric tumors Peptides as drugs

Peroxisome proliferator-activated receptor (PPAR)

PET and/or PET-CT

Phage display

Phagocytes and/or phagocytosis

Pharmacogenetics/Pharmacogenomics

Pharmacokinetics Pharmacology Phosphatases Phospholipids

Phosphorylation

Photodynamic tharapy and photodetection

Photonics

PI3K/Akt/PTEN/mTOR pathway Poly-ADP-ribose polymerase (PARP)

Polymorphisms/SNPs

Post-translational modification

Precancerous lesions Preclinical studies

Prevention and/or chemoprevention

Prognosis Prostaglandins Prostate ca. Proteasome Protein microarrays

Proteomics

Radionuclide therapy

Radiosensitivity and/or resistance

Radiotherapy Radiotoxicity RAS/RAS inhibitors Rb/Rb family

Response and/or resistance to therapy

RET

Retinoblastoma

Retinoic acid and/or receptors

Retrospective studies Rho GTPases family

Risk factors

RNA binding proteins

RNA splicing Sarcoma Screening Senescence Side effects

Signal transduction inhibitors siRNA and/or non coding RNA

Small molecule inhibitors

Smoking

Soft tissue tumors

Solid tumors **SPECT**

Spheroids/3D cultures

Src family Staging **Statistics**

Stress response

SUMO and/or sumoylation

Surgery

Survival analysis Synthetic lethality Systems biology T cells/TCR

T helpers

Target therapy

Telomere and/or telomerase

Testis ca.

TGF and/or receptors

Thymoma Thyroid ca. Thyroid hormone Tissue microarrays (TMA) TNF and/or receptors

Tolerance

Toll-like receptors (TLR)

Topoisomerase

TRAIL Transcription Transcription factors Transformation assays Transgenic mice Translesion synthesis

Translocation Transplantation Treg cells

Triple negative breast ca.

Tumor antigen Tumor dormancy

Tumor-inflitrating Lymphocytes (TIL)

Tumor suppressor genes Tumor-stroma interaction

Tyrosine kinase receptors (TKR) and/or inhibitors

Ubiquitin and/or ubiquitination

Ultrasound

Urokinase-Plasminogen System (uPA, uPAR, PAI)

Vaccine

VEGF and/or receptor

Virology

Von Hippel-Lindau (VHL) Wilms' Tumor Gene (WT1) Wnt/beta-catenin pathway

Xenopus Yeast Zebrafish