# - AIRC -

## Associazione Italiana per la Ricerca sul Cancro

## **CALL FOR PROPOSALS 2015**

Investigator Grant (IG)

1965-2015



Da 50 anni con coraggio, contro il cancro.

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## **Foreword**

The Associazione Italiana per la Ricerca sul Cancro (AIRC) is inviting applications for Investigator Grants (IG) in the area of cancer research. These grants are intended to support the research on cancer by established and independent scientists, leading an existing research unit. The scientific activity must be carried out in a research organization located in Italy, organized under public or private law, whose primary goal is to independently conduct biomedical research (university, hospital or other research center). The grant will be provided for a period of three years, starting January 2<sup>nd</sup> 2016, provided that AIRC has available funds.

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

Only one application, either IG, or MFAG or Start-Up or TRIDEO per applicant can be submitted within the 2015 Calls.

## Eligibility criteria

**Applicants**. Applicants, henceforth defined Principal Investigators (PI), can be of any nationality and are expected to have operated to the highest standards of integrity during their whole career. They should have achieved scientific independence and leadership and, by the submission deadline, they **must have a strong track record. More specifically, to be eligible applicants must have:** 

- 1. **Last- or 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 application deadline. Reviews, editorials, letters to the editor without data, papers published as corresponding or co-corresponding author do not count for eligibility. We are aware that clinicians directly involved in clinical practice may have different authorship conventions, *e.g.* being listed as first authors when leading the research. Therefore, they are eligible to apply even if they don't have last author papers as long as they have first author papers related to their clinical activity.
- 2. A total **active Impact Factor (IF) higher than 20 in the last five years** by the submission deadline. 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.

Applicants who do not meet criterion n. 1 will be triaged out; applicants who do not meet criterion n. 2 are discouraged to apply and may be triaged out, depending on their career stage and area of research.

Also, for your information, an analysis of the results of the four past Calls showed that the probability of success was extremely low (1,6%) when the total IF of all papers published by a PI in the previous five years was below 50.

AIRC reserves the right to reject 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 50% of their time, regardless of their "Effort on project" indicated in the application. 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 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), 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. Any change occurring in the relationship between applicant and the Hosting Institution (e.g. termination, retirement, leave of absence, sabbatical etc.) or in the Hosting Institution legal entity or organization (e.g. changes in Institution name, merging, Legal representative turn-over, changes in addresses) must be promptly notified to AIRC.

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

**Research plan.** A proposal that has been rejected twice (from the same or other applicants) in the past cannot be resubmitted a third time. See "Resubmission of revised applications" for further details.

## The research plan

All proposed research plans must have a clear and strong focus on cancer, and should fall into one of the following research areas:

- 1. 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**, have marginal chances of being funded and may be triaged out:

- studies that are essentially confirmatory in nature or represent marginal "variations-on-thetheme" 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 antitumor 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;
- clinical studies that do not contribute to build or expand an original and independent line of research.

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). If such information is missing or insufficient, the research proposal will be rejected.

For studies involving human subjects, human biological samples or for animal experimentation, the approval of the competent authorities is mandatory; research proposals will not be funded in the absence of such documentation. 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. Failure to provide such information will result in the rejection of the proposal.

## **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.

## **Funding**

Grants are for a three-year period, contingent upon the presentation of yearly renewal requests. Funded projects will officially start on January 2<sup>nd</sup> 2016 and terminate on January 1<sup>st</sup> 2019. Applicants must indicate the requested support in the budget section of the application, providing a detailed financial breakdown of the anticipated expenditures.

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;
- **support for fellows (personnel costs).** Support will be provided only for fellows 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, not of the total amount that will be granted.

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.

Renewal requests must be submitted yearly (see "Deadlines"), 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 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.

For exceptionally competitive PIs (*e.g.* top scorers in the final AIRC ranking, well-established investigators who have demonstrated a long-term commitment to and success in cancer research with consistently outstanding track records and continuous AIRC funding), it will be possible to extend the grant by two additional years, provided that AIRC has funds available. Further details and instructions will be provided by the end of the second year of the grant.

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

## **The Review Process**

All applications undergo an initial administrative review by the staff of the AIRC Peer Review Office for compliance with guidelines and eligibility; those that do not conform will be triaged out. Applications that meet all eligibility requirements undergo a peer review process that ensures a fair, independent and expert evaluation of the scientific quality of the applications.

For the evaluation of IG applications AIRC relies on the expertise of internationally recognized Italian scientists members of the "Comitato Tecnico Scientifico" AIRC (CTS) and a panel of more than 600 well-established international investigators working in institutions outside of Italy. Reviewer assignments are made in compliance with conflict of interest and appearance of conflict rules to ensure a review free from inappropriate influence (*e.g.* no application from a given research Institution is assigned to reviewers from the same Institution). Applicants may request to exclude up to two scientists as reviewers through the online application form.

IG applications are independently reviewed by three reviewers with expertise in the specific area of the research plan: two international reviewers and one member of the CTS. In case the needed expertise is not available within the CTS, a scientist with the appropriate expertise, operating in a research institution either in Italy or abroad, will be recruited to serve as third reviewer. When accepting to evaluate an application, reviewers and CTS members agree that they will maintain the confidentiality of applications and associated materials they have received.

#### The review criteria are:

- a) significance and impact on cancer;
- b) innovation;
- c) approach and feasibility;
- d) leadership and independence, international standing of the investigator in cancer research, track record adequate to successfully complete this study;
- e) environment and standing of the Hosting Institution at the international level (including an analysis of the resources in the Hosting Institution to determine if these are sufficient to grant success to the endeavour);
- f) adequacy of the budget requested.

In case there are major discrepancies among the reviews of an application, an editor is appointed, in observance with conflict of interest rules. Editors do not provide their own review but instead serve as "super partes arbiters", assessing and balancing the three evaluations.

When all reviews have been completed, applications are discussed by all members of the CTS during study section meetings. Scientific final reports of proposals by previously funded applicants are also taken into account during these meetings as a measure of productivity and scientific accomplishments of the PIs. In the final plenary session, all applications are ranked in order of scientific merit (for each application, the scores received from all reviewers are added up to generate the application's global score, which is used to rank the applications). The final ranking and the financial availability of AIRC will determine the recommendation for funding, to be endorsed by the AIRC Board of Directors. All applicants will be notified of the final decision on their application with an official communication from AIRC (the notification date is reported in the "Deadlines" table), and they will have access to the reviewers' comments. The identity of the reviewers will not be disclosed. **The decision concerning the funding of an application cannot be appealed.** 

To avoid conflicts of interests, IG applications submitted by members of the CTS will be reviewed by international reviewers only (at least three); the AIRC Scientific Director will make the funding decision following the indications received from the reviewers.

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.

## **Resubmission of revised applications**

AIRC allows only one resubmission for applications that were not funded. The revised application must include a response to the reviewers' comments in the "Revision" section of the online form. A revised application that has not been approved even after addressing all the issues raised by the reviewers is not considered competitive enough and therefore cannot be submitted a third time. Applicants who fail to receive funding after two submissions (*i.e.* the original and the revised application) may submit a new application only if its research plan is fundamentally different in content and scope from the two that were previously considered not fundable. 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.

An application submitted for the third time (by the same or other applicants) will not be sent out for review and will automatically be rejected, regardless of whether it was presented in the context of a different funding scheme. Example: an MFAG application that has not been funded twice cannot be resubmitted for the third time as an IG application, unless the research plan is fundamentally different.

## **Deadlines**

# DEADLINES ARE STRICTLY ENFORCED: applications submitted after the deadline will not be accepted.

**Deadlines for applications** (by 23:59, Central European Time, of the indicated dates).

New applications	online form release	February 3, 2015
	electronic submission deadline	March 12, 2015
	paper submission (postmark) deadline (*)	March 16, 2015
	notification of results	November 30, 2015
	start of grants	January 2, 2016

- (\*) 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;
- Abstract:
- Budget form, stamped and signed by the PI and the Legal representative;
- Bio-Ethical requirements page, stamped and signed by the PI;
- only if research in humans is planned: Clearance from the Ethics Committee;
- Declaration on affiliation, stamped and signed by the PI and 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 23:59, Central European Time, of the indicated dates).

Renewal for 2nd year of funding	online form release	June 6, 2016
	electronic submission deadline	July 25, 2016
Renewal for 3rd year of funding	online form release	June 5, 2017
	electronic submission deadline	July 24, 2017
Scientific final report	online form release	July 3, 2018
	electronic submission deadline	September 1, 2018
Administrative final report	online form release	January 10, 2019
	electronic submission deadline	March 28, 2019
	paper submission (postmark) deadline	April 1, 2019

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 e-mail.

## **Guide to proposal preparation**

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

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 IG 2015 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 <u>entirely</u> in English. **Applications that do not conform to all the requirements in these instructions will be rejected**.

#### **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: associate professor, staff scientist, etc.). 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) of the PI through the "My personal area" section.

#### Research project

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";
- 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.

#### **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. If the response to the statement "I am affiliated with the Hosting Institution at the application submission deadline" is "No", applicants must provide an official document certifying that for the entire duration of the grant they will be affiliated with the Hosting Institution, where they will work on the project for at least 20% of their time. Please send the document by November 15<sup>th</sup> 2015 (or before the project starts) to: administrative.office@airc.it 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 below. Click on "Add" to list multiple institutions. Applicants must provide official documentation certifying that for the entire duration of the grant they will be: a. working in Italy for at least 50% of their time; b. affiliated with the Hosting Institution; c. working in the Hosting Institution on the research project for at least 20% of their time. In addition, they are expected to provide official documentation of their relationships with all other institutions indicated in the form. If already available at the time of submission, check the box "I am attaching official documentation...", click on "Select" and upload the documents as a single PDF file. If not available at the time of submission, check the corresponding box and send the documentation by November 15<sup>th</sup> 2015 (or before the project starts) to: administrative.office@airc.it

#### **Legal representative**

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 and the Scientific Director are provided automatically by the system based on the Hosting Institution selected in the "Research Project" section. 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.

#### **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 both in alphabetical order and by topic.

To enter the project keywords (at least one, maximum five) please click on the button "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". You will be automatically redirected in the main keywords page: click on "Save" at the bottom of this page to save the record. Repeat this process for each keyword. To exit the window, click on "Close".

#### **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 relevance of the whole line of research. 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.

The Abstract of all research projects funded by AIRC may be made public on AIRC journals and websites.

#### **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.

If it is a resubmission, please 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).** 

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. Exceptionally, and upon presentation of a cogent argument to be included in this section, applicants may request not to have their application reviewed again by one of the previous reviewers. Refer to the "Reviewers to be excluded" section for further details.

An application submitted for the third time with the same research plan (by the same or other applicants) will not be sent out for review.

#### **Proposal Main Body**

This section should not exceed 10 pages (approximately 5000 words), including figures, preliminary data and references. The Proposal Main Body must be attached as a PDF file.

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

- please provide the <u>background and rationale</u> of the proposed research, along with relevant literature references; 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 all 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, the task subdivision is recommended

only for proposals in laboratory research areas only. Proponents of clinical and epidemiological studies should use subdivision in *phases* whenever possible, since 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:
  - o <u>preliminary data</u>. 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;
  - o <u>power calculation</u>. For clinical and epidemiological studies, and whenever appropriate, make sure to have adequate sample sizes to ensure meaningful and statistically significant results;
  - o 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;
  - o <u>a description of facilities and major equipment</u> 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;
  - o <u>a description of the key expertise available in the research team</u> (it is possible to provide this information in the "Description of the work for every unit of personnel" section).

#### 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. PIs are expected to be involved for a significant fraction of their time.

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, Investigator Grants are awarded to a single PI, who has full responsibility for directing the proposed research; they are not meant to support multi-unit projects conducted by a team of independent investigators. 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 pop-up window. In addition to their personal data (name, surname, date of birth, gender, tax code and Hosting Institution), the following information are required:

<u>Role</u>: 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 **support will be provided for fellows only** (not for technicians or collaborators) working 100% of their time on the project.

<u>To be defined (TBD)</u>: 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 compromise the timely start of the work and/or negatively influence the assessment of the feasibility of the research plan. 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.

<u>Title:</u> please choose one from the available entries: Doctor, Professor, Engineer, or leave blank if none applies.

<u>Clinician</u>: 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.

<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 (please indicate the Man/Year effort in the Budget section).

#### The following format <u>must be used</u> for all CVs:

- personal data (name, date and place of birth, citizenship, work address, phone number and email 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).

#### 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, reflecting the organization of the proposal main body, and indicate who will do what in each Task. 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.). 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.

#### **Budget Form and Justifications**

In the three columns, one for each year of support, insert the amount needed for each of the categories allowed.

#### 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 if outside the Hosting Institution);
- publication costs (most likely none in the first year of the project, as it takes time to obtain publishable data);
- meetings and travel costs.

Personnel efforts/costs: please click on "edit costs" to insert the Personnel costs details.

Man/year effort: please indicate the percentage of time that will be devoted to the actual performance of 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. In general, requests for fellowships should not exceed 50% of the total man/year effort. Example: for a research unit where all personnel adds up to a total of 4 man/year effort, no more than two fellowships for two fellows at 100% of their time (= 2 man/year effort) can be requested.

<u>Financial support</u>: please indicate the amount of financial support (e.g. fellowship) requested; support will be provided only for fellows at 100% of time on the project. Financial support can be required, however, only for those fellows who do not have any other fellowship or equivalent source of income. Integration of the AIRC financial support by the Hosting Institution is permitted, but two salaries are not allowed. Applicants should

ascertain that the Hosting Institution can take on fellows under this provision. The general policy of AIRC is to not provide financial support for candidates over 35 years old; in addition, the financial support requested for fellows should be consistent with the gross amount provided to fellows awarded an AIRC/FIRC fellowship for Italy (€25.000/year or, in case the fellow relocates from a different city or region, €30.000/year).

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.

*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.

For each budget category please provide a description/justification of the amounts requested using the "Insert/Edit Notes" boxes. More specifically:

- for each section of the "Direct research cost", provide a financial breakdown, on an item basis:
- 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").

The "Insert/Edit notes" boxes are mandatory sections and must be completed: write n/a if no expenses are foreseen for any particular category of costs.

In the "Institutional Letter of Indirect Costs/Overheads" section at the bottom of the form please upload a letter, in PDF file format, indicating the percentage rate(s) of indirect costs and/or overheads charged by the Hosting Institution, even if the rate is zero. The letter must be dated and signed by the Legal representative. Please note: the rate indicated in the letter must be consistent with the rate indicated in the budget form.

## **Existing/Pending Support**

If the PI is receiving or is expecting to obtain grants from any funding agency during the period of support with the AIRC grant, please list them, 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 IG application. In case already funded research projects overlap or are very similar to the current proposal, 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 cannot be allocated for more than 100% of the time. This applies to the sum of all grants, including those from agencies other than AIRC.

#### PI Education and Training

Click on "Add new record" and list degrees of the PI. For each entry, please indicate the University/Research center, Country, City, Field of research and time frame, then click on "Save".

#### PI Research and Professional Experience

Click on "Add new record" and list all positions held by the PI including post-doctoral trainings. For each entry, please indicate the Institution, City, Country, time frame and the position held, then click on "Save".

#### 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).

### **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 2010 and 2015 due to parental leave, children care, illness or other personal issues. This section allows applicants to report prolonged periods of absence from work that 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.

#### **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.

#### Add PubMed publications

Within this interface the system launches a PubMed search and provides a list of PubMed-recorded publications spanning from 2010 to 2015. 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 PubMed ID 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® publications

From this section it is possible to enter articles that are included in Web of Science® 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®. 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® indexed journals. Mark each paper for authorship and acknowledgement to AIRC. Please upload a PDF file with the letter of acceptance from the journal. **Do not attach the entire manuscript**, unless it is relevant for the proposed research (*e.g.* it contains important preliminary data mentioned in the proposal main body). Finally, check the certification box and click on "Save" to complete the process. The IF of papers in press will not be included in the publications table.

#### Add from MyPub

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 MyPub section of the Personal 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. Please note: papers in press are not included in the track record summary.

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 Thomson Reuters. For this Call, the 2013 Thomson Reuters IF list will be used.

Candidates are required to check all the information and to contact the AIRC Peer Review Office 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 is aware 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 due to their young age. 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 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: <a href="mailto:airc.direzione-scientifica@airc.it">airc.direzione-scientifica@airc.it</a>

All communications made in this regard by May 1<sup>st</sup> 2015 (23:59 Central European Time) will be forwarded to all reviewers evaluating the proposal; communications received after May 1<sup>st</sup> 2015 but before September 1<sup>st</sup> 2015 will be made available only to the members of the CTS, during the study section meetings. Any communication received after September 1<sup>st</sup> 2015 (23:59 Central European Time) will not be taken into consideration.

#### Reviewers to be excluded

Please note: this section is not mandatory. Applicants may indicate investigators they would like to exclude as potential reviewers (no more than two are allowed). Click on "Add reviewer" and enter the requested information, then click on "Save".

In case of a revised application, it is possible to request not to send the proposal to one of the reviewers who evaluated the original application. To do so, click on "Add original application reviewer" and from the "Application" field select the previous, non-approved submission (*e.g.* IG 2014). For each reviewer, the system will provide a statement taken from the "Overall" section of the evaluation form: check the statement by the reviewer you want to exclude, then click on "Save". Applicants are requested to thoroughly justify the request to exclude this reviewer in the "Revision" section of the application.

#### **Bio-Ethical Requirements**

Check boxes as applicable for human and animal experimentation.

#### Research on humans

Please note that human experimentation 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 in 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 grant** and a copy of such authorization must be provided, together with a copy of the informed consent form (if applicable).

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 2012) are NOT acceptable;
- the name of the applicant or of a unit of personnel 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 collaborator's research center.

In any case, if the research deals with human biological samples, genetic materials or data collection, the research proposal should include information about:

- how the samples, materials or data are collected;
- whether the samples, materials or data are collected specifically for the proposed research project;
- how the samples, materials or data are dismissed.

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.

If the approval from the Ethics Committee is not available by the submission deadline, the PI must obtain it **by November 15<sup>th</sup> 2015.** Check the box "I have not obtained the clearance from the competent Ethics Committee/Institutional Review Board yet, but I have requested 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"). Alternatively, please send it to the AIRC Peer Review Office by e-mail (<u>airc.direzione-scientifica@airc.it</u>).

#### 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), and a copy of the authorization must be provided. More specifically:

- If the authorization was obtained before Italy incorporated the Directive 2010/63/EU into its national law with the D.Lgs. 26/2014, please provide a copy of the approval of the local Animal Ethics Committee or Institutional Animal Care and Use Committee, together with a certification that the proposal was sent to the Ministry of Health under the "Regime di comunicazione" protocol. In case a special authorization was required ("Decreto autorizzativo in regime di deroga"), please provide such authorization.
- If the authorization was obtained after Italy incorporated the Directive 2010/63/EU into its national law with the D.Lgs. 26/2014, please provide the authorization by the Ministry of Health.

In any case, the authorization to carry out in vivo studies **must be valid for the entire duration of the grant**; if it expires during the course of the research project, a new approval must be provided to AIRC.

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.

If the authorization is not available by the application submission deadline, the PI must obtain it by November 15<sup>th</sup> 2015. Check the box "I have not obtained the clearance from the Ministry of Health yet, but I have requested 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". Alternatively, please send it to the AIRC Peer Review Office by e-mail (airc.direzione-scientifica@airc.it).

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.

#### **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.

#### **Final Full Proposal Submission** (online and by regular mail)

Online submission

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 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.

#### Paper submission

For paper submission, please print only these pages:

- Title page;
- Abstract;
- Budget form;
- Bio-Ethical requirements page;
- only if research in humans is planned: Clearance from the Ethics Committee;
- Declaration on affiliation.

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 and the Declaration on affiliation: by signing the Title page, the PI and the Legal representative acknowledge and agree to all terms and conditions of this Call. 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 reviewed.

Adenovirus Caveolin

Adhesion dynamics CD133/Stem cell markers

Adjuvant therapy Cell adhesion and/or cell adhesion molecules

Aging Cell cycle

AIDS/HIV/Kaposi Cell cycle checkpoint G1/S
ALL Cell cycle checkpoint G2/M

AML Cell differentiation and/or differentiation therapy

Androgen and/or receptors Cell migration, motility and/or invasion

Aneuploidy Cell polarity
Angiogenesis and/or vasculogenesis Cell signaling
Animal models Centrosome

Anti-angiogenic therapy Cervix or endometrial ca.

Antibody/mAb therapy Chemistry
Apoptosis Chemokines

Aromatase and/or inhibitors Chemotherapy and/or chemotherapic drugs

ATM pathway Chromatin remodeling
ATR pathway Circulating tumor cells
Autoimmunity/Autoantibodies Clinical practice guidelines

Autophagy Clinical trials

B cells CLL bcl2 family CML

BCR-Abl/Abl Colorectal and/or Intestinal ca.

Beta-catenin/Wnt pathway Combination therapy

Biochemistry Comparative genomics hybridization (CGH)

Bioinformatics Computational biology

Biomarkers Computer Tomography (CT Scan)

Biomolecular modelling Costimulatory molecules

Biophysics COX2
Bladder tumor Crosstalk

Body mass index (BMI) and/or obesity Crystallography

Bone disease CTL

Bone morphogenetic protein (BMP)

Cyclic AMP

BRAF/RAF kinases Cyclins and/or inhibitors

Brain and/or nervous system tumors Cytogenetics and/or chromosome alterations

BRCA Cytokines/Interleukins

Breast ca. Cytokinesis
Burkitt lymphoma Cytoskeleton
C.elegans Dendritic cells
Cachexia Diagnosis
Cadherins Diet

Cancer stem cells DNA damage

Carcinogenesis DNA double strand break repair (DSBR)

Caspases DNA methylation

DNA recombination Genomics
DNA repair Genotoxicity

DNA replication Glioma and/or glioblastoma

DNA single strand break repair (SSBR) Glucocorticoids and/or receptors

Docking Glucose metabolism and/or Warburg effect

Drosophila Glycoproteins and/or glycosylation

Drug delivery Golgi

Drug discovery and/or development G-proteins and/or GPCR

Drug response and/or resistance Granulocytes

Drug screening Growth factors and/or receptors

Drug toxicity Growth induction and/or growth arrest
EGF and/or receptors GVDH and/or Graft versus Tumor

Embryonic development Gynecological tumors
Endocrinology Head and neck ca.

Endocytosis Heat shock proteins (HSP)

Endoplasmic reticulum (ER) Hedgehog pathway

Endothelial cells Hematologic malignancies

Epidemiology Hematopoiesis

Epigenetics Hematopoietic stem cells

Epithelial mesenchyme transition (EMT) Hepatitis B virus (HBV)

Epstein-Barr Virus (EBV) Hepatitis C virus (HCV)

Estrogens and/or receptors Hepatocellular carcinoma (HCC)

Exosomes and/or endogenous microvescicles HER1-2-3-4

Extracellular Matrix (ECM)/Stroma Hereditary DNA repair disorders

Fas and/or FasL Hereditary tumors
FGF and/or receptor Herpes virus

Flow cytometry High Mobility Group Proteins (HMG)

Fluorescence in situ hybridization (FISH)

Hippo pathway

Fluorescence resonance energy transfer (FRET) Histone modifications

Focal Adhesion/FAK HLA/Major Histocompatibility Complex (MHC)

Folate and/or receptor Hodgkin's lymphoma

Functional genomics Homologous recombination

Functional validation of target genes Hormones

Fusion genes Human Papilloma Virus (HPV)

Gastric ca. Hypoxia/Hypoxia-inducibile Factors (HIF-1)

Gene alteration/gain or loss Immune escape
Gene expression and/or profile Immunization
Gene regulation Immuno-editing

Gene therapy Immunohistochemistry

Genetics Immunosuppression and/or suppressor cells

Genome wide screening/GWAS Immunotherapy

Genomic imprinting In vitro imaging and/or live cell imaging

Genomic/Genetic instability

In vivo imaging

Infection Monoclonal antibodies (mAbs) and/or immunoconjugates

Inflammation and/or inflammatory cytokines Mouse models
Inhibitor of apoptosis proteins (IAPs) mRNA processing
Innate immunity mRNA translation

Insulin Multidrug resistance (MDR)

Insulin-like growth factor (IGF) and/or receptors

Mutation (somatic and/or germline)

Integrins and/or Integrin-linked kinase (ILK) Myc

Interferons Myeloma

Ion channels Nanotechnology/Nanoparticles

Jak/Stat pathwayNetrin receptorsKidney ca.Neuroblastoma

Kinase/Kinome Neuroendocrine tumors
Lentivirus Next generation sequencing

Leukaemia NF-kB family
Lipid metabolism Nitric oxide

Liver development and/or regeneration NK and/or NKT cells
Loss of heterozygosity (LOH) NMR spectroscopy

Lung ca. Non apoptotic cell death

Lymphatics and/or lymphangiogenesis Non melanoma skin tumors

Lymphocyte differentationNormal stem cellsLymphomasNotch pathwayMacrophages and/or monocytesNuclear medicineMagnetic resonance imaging (MRI)Nuclear receptorMAP KinasesNuclear structures

Mass spectrometry Oncogenes

Mathematical modeling Oncogenic virus/Viral oncology

Matrix metalloproteases (MMP) and/or inhibitors

Organic compounds

MDM2 Osteopontin

Medulloblastoma Osteosarcoma

Melanoma Ovarian ca.

Membrane biology Oxidative stress and/or Reactive Oxygen Species (ROS)

Mesothelioma p21 - activated kinases (PAK)

MET/HGF p53, p63, p73
Metabolism/Metabolomics Palliative care
Metallo-drugs Pancreas ca.

Metastasis PDGF and/or receptors

Microarrays Pediatric tumors

Microenvironment Peptides as drugs
microRNA PET and/or PET-CT

Microscopy Phage display

Minimal Residual Disease (MRD) Phagocytes and/or phagocytosis

Mitochondria Pharmacogenetics/Pharmacogenemics

Mitosis Pharmacokinetics

Pharmacology Staging
Phosphatases Statistics

Phospholipids Stress response

Phosphorylation SUMO and/or sumoylation

PI3K/Akt/PTEN/mTOR pathway Surgery

Poly-ADP-ribose polymerase (PARP)

Polymorphisms/SNPs

Synthetic lethality

Post-translational modification

Systems biology

Precancerous lesions

T cells/TCR

Preclinical studies

T helpers

Prevention and/or chemoprevention Target therapy

Prognosis Telomera and/or telomerase

Prostaglandins Testis ca.

Prostate ca. TGF and/or receptors

Proteasome Thymoma
Protein microarrays Thyroid ca.

Proteomics Thyroid hormone

Radionuclide therapy Tissue microarrays (TMA)
Radiosensitivity and/or resistance TNF and/or receptors

Radiotherapy Tolerance

Radiotoxicity Toll-like receptors (TLR)

RAS/RAS inhibitors Topoisomerase

Rb/Rb family TRAIL

Response and/or resistance to therapy Transcription

RET Transcription factors
Retinoic acid and/or receptors Transformation assays
Retrospective studies Transgenic mice
Rho GTPases family Translesion synthesis

Risk factors Translocation

RNA binding proteins Transplantation

RNA splicing Treg cells

Sarcoma Triple negative breast ca.

Screening Tumor antigen
Senescence Tumor dormancy

Signal transduction inhibitors Tumor suppressor genes siRNA and/or non coding RNA Tumor-stroma interaction

Small molecule inhibitors

Tyrosine kinase receptors (TKR) and/or inhibitors

Smoking Ubiquitin and/or ubiquitination

Soft tissue tumors Ultrasound

Solid tumors Urokinase-Plasminogen System (uPA, uPAR, PAI)

SPECT Vaccine

Spheroids/3D cultures VEGF and/or receptor

Src family Virology

Von Hippel-Lindau (VHL)
Wilms' Tumor Gene (WT1)
Xenopus

Yeast

Zebrafish

Adhesion and stroma

Adhesion dynamics

Cadherins

Caveolin

Cell adhesion and/or cell adhesion molecules

Cell migration, motility and/or invasion

Cell polarity

Cytoskeleton

Extracellular Matrix (ECM)/Stroma

Focal Adhesion/FAK

Integrins and/or Integrin-linked kinase (ILK)

Matrix metalloproteases (MMP) and/or inhibitors

Microenvironment

Osteopontin

Tumor-stroma interaction

Urokinase-Plasminogen System (uPA, uPAR, PAI)

Angiogenesis

Angiogenesis and/or vasculogenesis

Endothelial cells

Hypoxia/Hypoxia-inducibile Factors (HIF-1)

Lymphatics and/or lymphangiogenesis

VEGF and/or receptor

Von Hippel-Lindau (VHL)

Cell death and apoptosis

Apoptosis

Autophagy

bcl2 family

Caspases

Fas and/or FasL

Inhibitor of apoptosis proteins (IAPs)

Mitochondria

Non apoptotic cell death

p53, p63, p73

Senescence

TRAIL

Clinical topics

Cachexia

Computer Tomography (CT Scan)

Diagnosis

Drug toxicity

Endocrinology

GVHD and/or Graft versus Tumor

Magnetic resonance imaging (MRI)

Metastasis

Minimal Residual Disease (MRD)

Nuclear medicine

Palliative care

PET and/or PET-CT

Prognosis

Retrospective studies

**SPECT** 

Staging

Survival analysis

Ultrasound

Transplantation

Genes, proteins and miscellanea

ATM pathway

ATR pathway

BCR-Abl/Abl

Bone morphogenetic protein (BMP)

BRAF/RAF kinases

**BRCA** 

Embryonic development

Endocytosis

Endoplasmic reticulum (ER)

**Epigenetics** 

Epithelial mesenchyme transition (EMT)

Exosomes and/or endogenous microvescicles

FGF and/or receptor

Glucocorticoids and/or receptors

Glucose metabolism and/or Warburg effect

Glycoproteins and/or glycosylation

Golgi

Heat shock proteins (HSP)

High Mobility Group Proteins (HMG)

Ion channels

Lipid metabolism

Liver development and/or regeneration

MDM2

Membrane biology

Myc

Netrin receptors

Nitric oxide

Oncogenes

p21 - activated kinases (PAK)

Phosphatases

Phospholipids

Poly-ADP-ribose polymerase (PARP)

Proteasome

RNA binding proteins

Stress response

SUMO and/or sumoylation

Telomere and/or telomerase

Topoisomerase

Ubiquitin and/or ubiquitination

Wilms' Tumor Gene (WT1)

Genetics

Aneuploidy Pharmacogenetics/Pharmacogenomics

Centrosome Polymorphisms/SNPs

Chromatin remodeling Post-translational modification

Cytogenetics and/or chromosome alterations RNA splicing

DNA damage siRNA and/or non coding RNA

DNA double strand break repair (DSBR)

Synthetic lethality

DNA methylation

Transcription

DNA recombination Transcription factors
DNA repair Transformation assays

DNA replication Translesion synthesis

DNA single strand break repair (SSBR)

Translocation

Functional genomics Tumor suppressor genes

Fusion genes

Gene alteration/gain or loss

Gene expression and/or profile

Gene regulation

Genomic imprinting

Genetics

Genomics

Genome wide screening/GWAS

Genome wide screening/GW/18

Genomic/Genetic instability

Genomic/Genetic instability

Hereditary DNA repair disorders

Histone modifications

Homologous recombination

Loss of heterozygosity (LOH)

microRNA

Mitosis

mRNA processing

mRNA translation

Mutation (somatic and/or germline)

Nuclear structures

## **Immunology** Autoimmunity/Autoantibodies Tolerance B cells Toll-like receptors (TLR) Chemokines Treg cells Costimulatory molecules Tumor antigen COX2 Tumor dormancy CTL Vaccine Cytokines/Interleukins Dendritic cells Granulocytes Hematopoiesis HLA/Major Histocompatibility Complex (MHC) Immune escape Immunization Immuno-editing Immunosuppression and/or suppressor cells Immunotherapy Infection Inflammation and/or inflammatory cytokines Innate immunity Interferons Lymphocyte differentation Macrophages and/or monocytes Monoclonal antibodies (mAbs) and/or immunoconjugates NF-kB family NK and/or NKT cells Phagocytes and/or phagocytosis Prostaglandins

T cells/TCR T helpers

TNF and/or receptors

Methods

Animal models Proteomics

Biochemistry Spheroids/3D cultures

Bioinformatics Statistics

Biomolecular modelling Systems biology

Biophysics Tissue microarrays (TMA)

C.elegans Transgenic mice

Chemistry Xenopus
Comparative genomics hybridization (CGH) Yeast
Computational biology Zebrafish

Crystallography

Docking

Drosophila Risk factors

Epidemiology Aging

Flow cytometry Biomarkers

Fluorescence in situ hybridization (FISH)

Body mass index (BMI) and/or obesity

Fluorescence resonance energy transfer (FRET) Carcinogenesis

Functional validation of target genes Diet

Immunohistochemistry Genotoxicity

In vitro imaging and/or live cell imaging Metabolism/Metabolomics

In vivo imaging Organic compounds

Mass spectrometry Oxidative stress and/or Reactive Oxygen Species (ROS)

Mathematical modeling Precancerous lesions

Microarrays Prevention and/or chemoprevention

Microscopy Risk factors

Mouse models Screening

Nanotechnology/Nanoparticles Smoking

Next generation sequencing

NMR spectroscopy

Phage display

Protein microarrays

Signaling and cell cycle

Androgen and/or receptors RAS/RAS inhibitors

Beta-catenin/Wnt pathway Rb/Rb family

**RET** Cell cycle

Cell cycle checkpoint G1/S Retinoic acid and/or receptors

Cell cycle checkpoint G2/M Rho GTPases family

Cell differentiation and/or differentiation therapy Src family

Cell signaling TGF and/or receptors Crosstalk Thyroid hormone

Cyclic AMP Tyrosine kinase receptors (TKR) and/or inhibitors

Cyclins and/or inhibitors

Cytokinesis

G-proteins and/or GPCR

EGF and/or receptors Estrogens and/or receptors

CD133/Stem cell markers Folate and/or receptor

Growth factors and/or receptors

Growth induction and/or growth arrest

Hedgehog pathway

HER1-2-3-4

Hippo pathway

Hormones

Insulin

Insulin-like growth factor (IGF) and/or receptors

Jak/Stat pathway Kinase/Kinome

**MAP Kinases** MET/HGF

Notch pathway

Nuclear receptor

PDGF and/or receptors

Phosphorylation

PI3K/Akt/PTEN/mTOR pathway

Stem cells

Cancer stem cells

Circulating tumor cells Hematopoietic stem cells

Normal stem cells

Types of tumors

ALL Soft tissue tumors

AML Solid tumors

Bladder tumor Testis ca.

Bone disease Thymoma

Brain and/or nervous system tumors Thyroid ca.

Breast ca. Triple negative breast ca.

Burkitt lymphoma

Cervix or endometrial ca. Therapies

CLL Adjuvant therapy

CML Anti-angiogenic therapy

Colorectal and/or Intestinal ca.

Antibody/mAb therapy

Gastric ca. Aromatase and/or inhibitors

Glioma and/or glioblastoma Chemotherapy and/or chemotherapic drugs

Gynecological tumors Clinical practice guidelines

Head and neck ca. Clinical trials

Hematologic malignancies Combination therapy

Hepatocellular carcinoma (HCC) Drug delivery

Hereditary tumors Drug discovery and/or development

Hodgkin's lymphoma Drug response and/or resistance

Kidney ca. Drug screening
Leukaemia Gene therapy
Lung ca. Metallo-drugs

Lymphomas Multidrug resistance (MDR)

Medulloblastoma Peptides as drugs
Melanoma Pharmacokinetics
Mesothelioma Pharmacology
Myeloma Preclinical studies
Neuroblastoma Radionuclide therapy

Neuroendocrine tumors Radiosensitivity and/or resistance

Non melanoma skin tumors Radiotherapy
Osteosarcoma Radiotoxicity

Ovarian ca. Response and/or resistance to therapy

Pancreas ca. Signal transduction inhibitors
Pediatric tumors Small molecule inhibitors

Prostate ca. Surgery

Sarcoma Target therapy

#### Viruses

Adenovirus

AIDS/HIV/Kaposi

Epstein-Barr Virus (EBV)

Hepatitis B virus (HBV)

Hepatitis C virus (HCV)

Herpes virus

Human Papilloma Virus (HPV)

Lentivirus

Oncogenic virus/Viral oncology

Virology