
AIRC
Associazione Italiana
per la Ricerca sul Cancro



Metastatic disease: the key unmet need in oncology Second edition

5 per Mille – Call for Proposals

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Guide to proposal preparation and keywords are available at:
<https://www.direzionescientifica.airc.it/Calls/Default.aspx>

Foreword

The explosion of new technologies, the clever merging of interdisciplinary approaches and the growing list of rationally designed clinical trials are favoring significant progresses in the understanding and treatment of cancer. The ultimate goal of timely translating research results into real benefits for the patients is becoming more and more achievable through the development of a successful seamless research pipeline stretching from fundamental discoveries to clinically measurable applications. Unfortunately this goal is far from being attained especially if one thinks of the major hurdles that we are still facing in oncology, the most prominent example being metastatic disease.

Metastasis, *i.e.* the ability of primary tumors to spread in the body, is a central "Hallmark of Cancer". It is a still largely unknown and imperfectly understood biological and pathological event that occurs irrespective of the cellular origin of cancer, takes place in both blood cancers and solid tumors and has dire consequences. Malignant cells from primary tumors can seed distant sites early, and later may progress into difficult-to-treat, usually lethal tumors. The presence of metastatic disease has important repercussion on patient's prognosis and treatment. It is a crucial component of tumor-related morbidity; little is known on how to prevent it and it accounts for more than 90% of cancer deaths, thus strikingly affecting not only the quality of life but also patients' survival.

The Associazione Italiana per la Ricerca sul Cancro (AIRC) believes that time has come to tackle this major issue. AIRC deems essential to better understand the fundamental mechanisms of metastatic process, especially bearing in mind the goal of developing novel biology-based methods for early diagnosis and treatment of metastatic disease. To this end it launches the second edition of the Special Program on **Metastatic disease: the key unmet need in oncology** and invites applications aimed at investigating metastatic disease.

The aim of the Call is to finance outstanding programs that can have significant impact on improving understanding metastatic disease and transferring the knowledge, within their duration, to the clinical setting. Programs must be structured as «from the bench to the bedside», where the «bedside», *i.e.* a real clinical achievement/applicability, is a must and should not merely represent a perspective development of the research. Therefore, the actual transfer of knowledge will be considered paramount towards feasibility.

It is expected the programs to be interdisciplinary in nature, requiring a team science approach. Applications should include a thorough description of the complementary expertise provided by each participating group. An appropriate governance structure must be in place.

Successful applications will be funded for a total of 7 years, with assessments and site visits at the end of the third and of the fifth year (3+2+2).

The total budget allocated for this Call is in the range of € 10 million/year; it is projected that 3-5 grants will be awarded.

1. How to Apply

In the initial phase of the Call applicants must submit a **pre-submission enquiry** which includes a Letter of Intent (LOI). Selected applicants will be invited to submit a **full proposal**. Pre-submissions and full proposals will be evaluated by a dedicated Study Section composed of outstanding non-Italian experts with complementary expertise on the metastatic disease.

2. Eligibility Criteria

Applicants. Given the sizable amount of the grants and the interdisciplinary nature of the Call, it is expected that proposals will be structured under the coordination of a single proponent/coordinator (hereafter referred to as the **Principal Investigator, PI**) with the participation of **Group Leaders (GLs)** with competence in various specific areas. The PI and all GLs must have achieved scientific independence and leadership, and must have a strong track record in oncology as demonstrated by last-author publications in high level peer reviewed journals. In addition, the PI and all GLs, regardless of their nationality, must be affiliated with and operate in Hosting Institution(s) in Italy from the beginning of the program and for the entire duration of the grant.

Applicants who have not been funded within the first “Call on metastatic disease” can apply to this Call.

Hosting Institutions. The Call is open to proposals both from single Institutions and multi-institutional, the latter when the outstanding goals of the proposal can only be achieved through such a setting.

For the entire duration of the grant, applicants (PI and GLs) must operate in Hosting Institution(s), *i.e.* a research organization (such as university, hospital or other research center), irrespective of its legal status (organized under public or private law), located in Italy, whose primary goal is to independently conduct non-economic biomedical research and to disseminate its results. Possible revenues coming from non-economic research activity must be completely reinvested in the non-economic research activities. Where the Hosting Institution(s) 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(s) cannot enjoy a preferential access to the intellectual property of the results generated by the non-economic research activity.

The Hosting Institutions must promote the highest standards of integrity in research, in compliance with the [AIRC policy on research integrity](#).

AIRC reserves the right to exclude proposals in which the PI or GLs, although jointly affiliated to an Italian institution and institution abroad, do not meet criteria for substantial presence, *i.e.* at least 50% of their time, in the institution in Italy. To make sure this requirement is met, supporting official documentation will be requested from all institutions the PIs and the GLs are affiliated with.

Any change occurring in the relationship between applicants and the Hosting Institutions (*e.g.* termination, retirement, leave of absence, sabbatical etc.) or in the Hosting Institution legal entities or organizations (*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. Programs must be interdisciplinary in nature, requiring a team science approach.

Notwithstanding the broad and «bottom-up» nature of this Call, some types of proposals **are excluded and will not receive consideration**:

- Basic research- or translational research-only proposals, which do not contemplate actual transfer to the clinical setting within the duration of the grant;
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- Clinical research-only proposals, without an innovative laboratory research component;
- Proposals including any type of Phase III and Phase IV clinical trials;
- Proposals that could be financed through the regular calls of AIRC (Investigator Grants, Start-Up Grants, My First AIRC Grants);
- Generic «brain gain» programs, e.g. programs aimed at bringing researchers working abroad back to Italy, if such programs are not embedded in a proposal that meets all other requirements of the Call;
- Generic proposals which are not hypothesis-driven and do not portray measurable outputs;
- «Core» funding for research and/or clinical institution;
- Open-ended programs unlikely to be accomplished within the specific time frame of 7 years;
- Drug development programs (drug discovery programs are admissible);
- Proposals of clinical studies that receive economic support from companies producing drugs or diagnostic tools (unless the intellectual property is retained by the PI/GL and the company has no right to veto the publication of results at any time).

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. AIRC reserves the right to check compliance with this requirement anytime, including after the termination of the program. AIRC does not accept any liability for harm to participants in AIRC funded trials.

3. Intellectual Property

For inventions arising from an AIRC funded program, 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 grantees and the Hosting Institutions. All royalties and revenues deriving from the results of a «5 per Mille» research program must be reinvested in independent and non-economic oncological research.

Drug supply and economic support from companies do not preclude AIRC evaluation, provided that the PI and/or GLs demonstrate to have the full property of data and results, and that companies have no right to veto the publication of results at any time.

Supporting documentation will be required in the full submission and proposals will not be funded without such information.

4. Partnership

In the full submission, a partnership plan addressing the following issues must be in place:

- **Governance and organizational structure of the team:** a deputy-PI, a program manager and a steering committee must be appointed. The steering committee must include the PI (chairman), the deputy-PI and selected Group Leaders; the role of this committee is to assist the PI in overseeing the program, for example by proposing solutions to manage changes in the proposed plan or conflicts between participants;
 - **Advisory board:** the PI must create an external advisory committee of 2 to 4 scientists working outside of Italy; they will monitor the program, providing independent feedback and recommendations;
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- **Retreats:** the PI must organize regular meetings with all GLs (including a kick-off meeting) and yearly retreats with all members of the program, the advisory board and representatives of AIRC. At the end of each meeting the advisory board must write a report and send it to AIRC;
- **Procedures for resolving conflicts;**
- **Intellectual property:** an agreement between the PI, all GLs and their Hosting Institutions about the intellectual property of data obtained through this funding scheme must be in place.

5. Disclosure of Financial Conflict of Interests

In the full submission, PIs and GLs are required to disclose any financial conflicts of interest with the proposal. Appropriate measures will be taken against applicants who have deliberately or recklessly failed to disclose conflicts of interest, including: the termination of the grant; the obligation to return grant money to AIRC; the ineligibility to apply to AIRC grants; the exclusion from AIRC review panels and other bodies.

6. Funding

Successful applications will be financed through the revenues of «5 per Mille» donations for a total of 7 years. The budget granted will be communicated directly to the PI, who will be the sole responsible for the year by year allocation of the budget to each Group Leader. The allocation of the budget to each Group Leader will be indicated to AIRC who, in the case of multi-institutional grants, will directly fund each single Institution. **AIRC will closely monitor the scientific progress and the administrative handling of the grants.**

Funding can be requested in all categories of expenses, including:

- personnel (for the duration of the project);
- direct research costs, services and supplies;
- instruments, including technological platforms necessary for the project. The acquisition of new platforms will be carefully evaluated during the reviewing process;
- indirect costs and overheads.

First year of funding. Once awarded, the grant is assigned to the PI and GLs to carry out the program described in the application. Funds will be made available to the Hosting Institutions under terms and conditions that AIRC will provide once the application is approved. Funds must be at the grantees' disposal within 30 days from the time the Hosting Institutions have access to them. PIs will be responsible for the allocation of the budget to each GL.

Every year the PI must:

- submit two six-month progress reports in which he/she authorizes the payment to each research unit, as AIRC will provide funds in six-month instalments;
- organize a retreat with all members of the program, the advisory board and representatives of AIRC. At the end of the retreat the advisory board must write a report and send it to AIRC;
- submit a renewal request taking into account the recommendations received by the advisory board during the retreat (the renewal request must be submitted by GLs as well);
- submit an administrative report within three months after the termination of each year of funding.

Funds will be granted each year to each research unit only after the endorsement by the advisory board and the approval of the above documents by AIRC.

Yearly renewals of the awarded grants will be dependent on the availability of funds through net receipt of «5 per Mille» revenues from the competent Ministries.

Year 3 and 5. At the end of the 3rd and 5th year the program will be evaluated through a progress report and/or site-visit. Funds for the following years will be granted only after a positive assessment.

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

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

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

7. The Review Process

Eligibility. 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. Eligible applications undergo a peer review process that ensures a fair, independent and expert evaluation of their scientific quality. Only the most scientifically meritorious applications, identified through the peer review process in a rigorous and objective manner as described below, will be funded.

LOI evaluation. AIRC has appointed a dedicated Study Section composed of outstanding non-Italian experts with complementary expertise on the metastatic disease. The Study Section is in charge of the entire review process, including the evaluation of the LOIs. Each LOI is evaluated by members the Study Section who select the most meritorious, based on the review criteria listed below, indicating whether the applicant should or should not be invited to submit a full proposal. All applicants will be notified on the outcome of the first round of evaluation.

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

The review criteria are:

- relevance to the goals of the Call;
- quality of the research program (including analysis of caveats and contingency plans);
- actual transferability to the clinical setting;
- quality of the proponent(s);
- quality of the proposing institutions;
- feasibility (including demonstrated capability of assembling teams with all required expertise for performing the project).

Proposals are expected to be **strongly mechanism-based and hypothesis-driven** and will be exclusively judged on the basis of their excellence. Given the special nature of the Call, AIRC will give priority (among comparably outstanding proposals) to those proposals in which explicit plans are made to enrol **physician scientists** specifically dedicated to the program.

When all reviews are completed, applications are ranked in order of scientific merit (the *preliminary score*, which is used to rank the applications at this stage, is calculated as the mean of the scores received from the three reviewers who evaluated the application). Proposals are thoroughly discussed by all members of the Study Section during the plenary session. The final ranking is based on the final score of each application, which is calculated as the mean of the scores received from all reviewers during the discussion.

The final ranking and the financial availability of AIRC will determine the recommendation for funding, to be endorsed by the AIRC Board of Directors.

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

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 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 PI and GLs laboratories and Hosting Institutions, at any time.

8. Deadlines

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

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

Pre-submission enquiry (Letter Of Intent)	Publication of Call and online form release	June 13, 2018
	Electronic submission deadline	July 17, 2018
	Notification of results	October 23, 2018
Full Proposals (if pre-submission approved)	Electronic submission deadline	December 4, 2018
	Digitally signed submission deadline	December 18, 2018
	Papers in press (*)	February 1 2019
	Notification of results	April 30, 2019
	Start of grants	July 1, 2019

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

For full proposals only: AIRC has modified the procedures for the signature of the applications and requires digital signatures. The PI, each GL and the Legal Representatives must digitally sign the full application. If the digitally signed applications are not submitted by the indicated deadline, they will not be sent out for review.

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