ERA-NET: Aligning national/regional translational cancer research programmes and activities TRANSCAN-2

Joint Transnational Call for Proposals 2015 (JTC 2015) on:

"Immunology and immunotherapy of cancer: strengthening the translational aspects"

Guidelines for Applicants

Submission deadlines

Pre-proposals: 5 February 2016 at 16:00 CET

Full proposals: 26 May 2016 at 16:00 CEST

Useful links

Electronic proposal submission system: http://transcan.cbim.it/
(Online submission will be possible from 15 January 2016)

For further information, please visit

www.transcanfp7.eu or

Contact the **Joint Call Secretariat (JCS)** at:

Ministero della Salute-Istituto Superiore di Sanità,

Italy

E-mail: transcan-jtc2015@iss.it

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Background

Under the umbrella of TRANSCAN-2 (ERA-NET: Aligning national/regional translational cancer research programmes and activities), 15 funding organisations have agreed to launch a Joint Transnational Call (JTC) in 2015 for collaborative research projects on **"Immunology and immunotherapy of cancer: strengthening the translational aspects"**. The participating TRANSCAN-2 funding organisations wish to promote innovative interdisciplinary collaboration and truly translational research projects.

The research projects submitted within this call should be based on novel ideas stemming from consolidated previous results and will be endowed with a strong translational research orientation. Project proposals should also clearly demonstrate the potential health impact as well as the added-value of transnational collaboration. The sharing of relevant results, data sets and/or resources within the transnational research consortia is a prerequisite for funding. The research proposals should be built on an effective, multidisciplinary and multi-professional collaboration between academic, clinical, epidemiological or public health research teams and industry. Researchers' exchanges within the consortium are encouraged.

In order to ensure target-oriented projects, the availability of and/or access to clinical biomaterial banks (cells, tissue, blood, DNA, organs, fluids etc.) and the related clinical data of subjects (patient cohorts with comprehensive clinical documentation and characterisation) must be secured and explained. Biomaterial banks must be maintained with "Standard Operation Procedures" (SOPs for extraction, transport, processing, storage and further usage) and previous use and benefit documented by respective publications.

Proposal submission

TRANSCAN-2 JTC 2015 will be implemented through a two-stage submission procedure: pre-proposals and full proposals. Both pre- and full proposals must be written in English and must be submitted to the Joint Call Secretariat (JCS) by the coordinator of the project through the dedicated electronic submission system exclusively (http://transcan.cbim.it/), as PDF files, using the form to be downloaded from the electronic submission system. Original signed versions of either pre- or full proposal are not required. Please note that full proposals will only be accepted from applicants explicitly invited by the JCS to submit them.

Both pre-proposals and full proposals must be submitted to http://transcan.cbim.it/ **within the deadlines indicated below**.

For pre-proposals submission, the system will open on the 15th of January 2016 at 16:00 (Central European Time, CET).
Pre-proposals must be submitted to and received by the JCS no later than the 5th of February 2016 at 16:00 (Central European Time, CET).

For full proposals submission the system will open on the 14th of April 2016 at 16:00 (Central European Summer Time, CEST).
Full proposals must be submitted to and received by the JCS no later than the 26th of May 2016 at 16:00 (Central European Summer Time, CEST).

Call deadlines will be strictly enforced and the electronic system will not allow submissions after call deadlines. Please take into account that the online data entry may be overloaded on the day of the deadline. It is therefore recommended to upload all the required material in due time.

Eligibility check

Prior to submitting the proposal, applicants should refer to the national/regional eligibility criteria and requirements (see Call text, Annex 4) and should contact their respective national/regional funding organization contact persons for additional clarifications (see Call text, Annex 1).

NOTE: ***An eligibility check before the pre-proposal submission is mandatory for the following funding organization. Please read national/regional regulations (*****see Call Text, Annex 4*****) and get in touch with the national/regional contact points:***

- ***The Ministry of Health (MOH), Italy***

The JCS will assess proposals to ensure that they meet the call's formal criteria [e.g. date of submission; number of research groups/countries, type of project partners (academic, clinical/public health and industrial/SMEs), document length, and inclusion of all necessary information in English. In parallel, the JCS will forward the proposals to the relevant TRANSCAN -2 national/regional funding organizations that will perform a formal check for

compliance with their respective eligibility criteria. Proposals passing both checks will be evaluated by independent international scientific experts.

Please note that after submission of the proposal it is not possible to amend it or to add further documents.

For additional information, please contact:

JTC 2015 Joint Call Secretariat (JCS) at

Ministero della Salute-Istituto Superiore di Sanità, Italy

E-mail: transcan-jtc2015@iss.it

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Pre-proposal structure

One joint pre-proposal (in English) shall be prepared by the partners and be submitted to the JCS by the project coordinator.

Please note that it is mandatory that the applicants use the pre-proposal application form, a fillable PDF file, provided within the electronic submission system (http://transcan.cbim.it/), and that the pre-proposal complies with the length indicated for each section. Pre-proposals not complying with these rules will be rejected. The proposal must be written in English and must be submitted to the JCS by the project coordinator through the electronic system exclusively.

Pre-proposals must include the following information:

1. Project title (maximum 150 characters, including spaces).
2. Project acronym (maximum 10 characters).
3. Project duration (up to 3 years).
4. Name and full affiliation of the project coordinator designated by the consortium to act as its representative.
5. Names and full affiliations of the principal investigators (only one per partner).
6. Total requested funding (€).
7. Keywords. Please indicate three to seven keywords representing: the scientific content [(type of cancer; specific aim(s) and topic(s) (see Call Text, chapter 2. Aim of the call)]; the methodological and technological approach(es).
8. Project abstract (max 3,000 characters including spaces, equivalent to about ¾ of an A4 page).
   The abstract should contain:
   - Background and rationale
   - Hypothesis
   - Aims (primary and secondary)
   - Methods
   - Expected results and potential impact

9. Adherence of the proposal to the scope, aims and specific topics of the call (see Call Text, chapter 2. Aim of the call). Please, tick box(es).

Aim 1: Identification and validation of shared or personalized mutated human tumor antigenic targets

- Application of "omics" approaches for the identification and validation of immunogenic mutated epitopes in primary and/or metastatic, synchronous as well as metachronous tumor lesions;
- Development of ex-vivo and/or in vivo models to be established starting from patients samples for screening immunogenicity and efficacy of personalized vaccines targeting mutated epitopes.

Aim 2: Development of new and combined immunotherapeutic strategies for cancer patients

- Development of new vaccine formulations for active immunotherapies, including DNA, RNA vaccines, viral vectors as well as heterologous prime-boost combinations;
- Development of combined therapeutic approaches including the above antigen-targeting immunotherapies with *immune compensating* therapies based on irradiation, metronomic chemotherapy and/or anti-immune checkpoint inhibitors and/or adoptive T cell therapies with genetically engineered T cells;
- Development of interventions directed to counteract the role of tumor microenvironment in immune escape and immune evasion;

Aim 3: Translational research for clinical application of cancer immunotherapy.

- Identification of intratumoral and/or peripheral blood biomarkers predictive of the efficacy of cancer immunotherapies and establishment of bioassays to monitor the efficacy of cancer immunotherapy;
- Implementation of new approaches for patient stratification for clinical trials;
- Design and performance of Phase I and Phase II clinical trials for combined cancer immunotherapy strategies;
- Toxicity: understanding and anticipating toxicity problems linked to cancer immunotherapy.

10. Project description (maximum 20,000 characters including spaces, equivalent to about five pages).

This part should contain:

- Description of the project rationale, in terms of medical need, and of the present state of the art in the field(s)
- Description of the project aims
- Statement of the research hypothesis(es)
- Preliminary data
- Description of methods with specific regards to the study design, the study population(s), intervention/exposure, groups of comparison and expected outcome. Details are also needed regarding the study sample size as defined by *ad hoc* power calculation, and the strategic plan for statistical analysis
- Novelty and originality of the project
- Feasibility of the project: information about the experience of the research consortium partners in the field; management structure and related implementation plan; added value of the proposed transnational collaboration
- Information about the potential impact on cancer recurrence and resistance to therapy with reference to the development, dissemination and use of project results

As annexes, it should contain:

- References (one page maximum, as a separate pdf file)
- Diagrams, working plan, project schedule (e.g. Gantt chart) and figures (three pages maximum, as a separate pdf file)

11. Capacity building activities (if eligible for the funding organization/country) (maximum 2,000 characters including spaces, equivalent to about half of an A4 page).

    Please specify whether the project will include capacity building activities. If so, please describe the nature and purpose of the planned activities taking into account information described in the section 2.2 of Call Text. The budget will have to be mentioned in the financial plans (sections 12 and 13) in the appropriate line.

12. Brief CV for each partner in the research consortium (i.e. the project coordinator and each principal investigator) including a description of the main domain of research and a list of the five most relevant publications within the last five years regarding the proposal (maximum 4,000 characters including spaces, equivalent to about one A4 page).
13. A global financial plan of the project (budget broken down per partner).
14. Individual financial plans: a financial plan per partner and budget justification (**Please note that eligibility of costs is subject to national/regional rules and regulations: refer to the Call Text, Annex 4).**
15. Reviewers (if any) to be excluded from the evaluation of the proposal (up to five). Please note that this information is not compulsory. The CSC will consider these suggestions as it sees fit.

Full proposal structure

The information provided in the pre-proposal application is binding for the entire application process. Thus, any substantial changes between the pre-proposal and the full proposal (e.g. title, acronym, composition of the consortia, objectives of the project, etc.) must be communicated in advance to the JCS with detailed justification and will only be allowed by the Call Steering Committee (CSC) under exceptional circumstances.

Please note that it is mandatory to use the **full proposal application form downloaded from the on-line submission system** (http://transcan.cbim.it/) and to comply with the length indicated.

Full proposals not complying with these rules will be rejected.

Full proposals must include the following information:

- **Project title** (maximum 150 characters, including spaces).
- **Acronym** (maximum 10 characters).
- **Project duration** (up to 3 years).
- **Total requested funding.**
- **Keywords** (3 to 7).

- **Publishable project abstract** (maximum 2,000 characters including spaces, equivalent to about half an A4 page. Please note that if your proposal is selected for funding, the abstract will be published on the TRANSCAN website).

  The abstract should include a concise description of the following:

  a. Background and rationale, i.e. a description of the medical problem and present state of the art in the research field.
  b. Hypothesis, i.e., the hypothesis/es to be tested.
  c. Aims (primary and secondary), i.e. a description of the study aims either primary or secondary, with a maximum of 3 aims (including both primary and secondary).
  d. Methods, i.e. a description of the methods applied.
  e. Expected results and potential impact of the research findings on the disease of interest.

- **Names and full affiliations of each partner** principal investigator.

Project description: This section represents the scientific "core" of the project. The applicants are requested to provide elements on the study characteristics in a more detailed fashion compared to what previously reported in the homonymous sections of the pre-proposal application form and abstract.

1. **Background and rationale** (maximum 4,000 characters including spaces, equivalent to one A4 page). Medical needs and present state of the art in the field of interest.
2. **Preliminary results obtained by the consortium members, if applicable** (maximum 3000 characters including spaces, equivalent to about ¾ of an A4 page. Figures related to the preliminary results, one page maximum, must be uploaded as a separate pdf file).
3. **Specific aims, research hypothesis and preliminary data, experimental design and working plan.** (maximum 12.000 characters including spaces, equivalent to about three A4 pages). This section should contain:

   - Project specific aims (maximum of 3, either primary or secondary). Please list the specific aims of the proposal, not to be confused with the aims of the call.
   - Research hypothesis and supporting data. Supporting (otherwise defined "preliminary") data are not intended as literature-based evidence, unless such evidence is either authored (i.e., one of the applicants is the first, last and/or corresponding author) or co-authored (i.e., one of the applicants is part of the authorship in any position but the first, last and/or corresponding author) by one or more of the applicants. These data are meant to have been generated by research activities carried out by one or more of the members of the consortium. More specifically, the project under evaluation has to be part of a research pipeline in course of development and the applicants have to exhibit a substantial role within such research pipeline.
   - Experimental design, i.e. the strategy that directs researchers towards the study aim(s). Please ensure consistency between each of the project aim and the corresponding experimental design.

     Experimental Design AIM 1

     Experimental Design AIM 2 (if applicable)

     Experimental Design AIM 3 (if applicable).
   - Work plan, including a general overview of the entire consortium, and the rationale of the work packages, i.e., one or more subset/s of the entire study tasks assigned to one or more specific partner/s for execution. Task assignment will obey to rules dictated by the

specific expertise of the consortium members and the way they complement each other within the study proposed.

- Synthetic description of the work plan at the work package level: please, fill the fields in accordance to the column headings.

4. **Methods, power calculation and statistical analysis, expected outcome and risk analysis** (maximum 8,000 characters including spaces, equivalent to about two A4 pages).

   a. Methods: this section should include a detailed description of the study methods. To this aims, details on the following issues are required:

   - Study Design: the applicants are requested to be clear about the type of study being proposed. Most commonly, the proposals will fall into one of the following two main categories i.e., (i) observational study or (ii) intervention trial.Once the main category has been defined (i.e. observational or intervention study), further elements will help characterize the study design.

     If an observational study is proposed, the applicants will be required to add specific details on whether the study is conceived as prospective, retrospective or mixed and whether by design is intended as a cohort, case-control, case-control nested within a cohort or cross-sectional study. For studies with a mixed design, the applicants are requested to be clear about which parts of the study will be retrospective (i.e. based on patient data already collected and stored biological specimens), and which will include patients (and their specimens) to be recruited prospectively; and indicate the number of patients (or samples) in each of these groups.

     Since observational studies are particularly prone to confounding and bias, these aspects will have to be carefully considered when designing the study and, later on, carefully addressed in a dedicated section of this application, i.e., section d., namely, “Contingency plan including potential bias, anticipation of problems and possible solutions”. Since possible solutions to confounding and bias may derive by an appropriate use of the statistical tools, the applicants may refer to these issues also in the statistical analysis section, i.e. section b.

     If an intervention trial is proposed, details related to the study design have to be provided regarding the trial phase and type. Such details have to be extended, though not necessarily limited to, the use of randomization (yes/no and specific details on the procedures applied), type of masking (if any), characteristics of the control group/s, parallel group assignment/cross-over. By their nature, randomized clinical trials are less prone to, though not immune, from bias. Actually, the use of randomization procedures, when properly applied, minimizes the chance of selection bias. However, this latter is not the only bias which potentially attempts to the methodological quality of a trial. Again, the issues related to “potential bias, anticipation of problems and possible solutions” have to be considered when defining the study design and specifically addressed in the dedicated section, i.e. section d.

   - Study population(s): Study population(s) should be described exhaustively, i.e., based on clearly stated inclusion and exclusion criteria.

   - Intervention/exposure: Clearly describe the interventions, and how they will be administered to patients within the trial. Please specify the drug dose and mode of administration, and the use of additional intervention(s) if applicable.

   - Outcome of interest: Clearly define all important endpoints (outcome measures), which, in clinical trials, will usually include efficacy, safety (toxicity) and compliance (adherence) to the interventions.

     Specific details on the procedural aspects will be added depending on the adherence of the proposal to the specific scopes, aims and topic of the call, as specified in the pre-proposal application, section 9, i.e., “Adherence of the proposal to the scope, aims and specific topics of the call”.

If questionnaires will be used (for example to obtain information on lifestyle characteristics), please state whether you will be using established and validated ones, or developing your own.

Details have to be provided regarding the planning for the management and retention of biological samples, specifying whether cooperation with existing or creation of new biobanks is envisaged.

b. The proposed sample size has to be clearly supported in terms of power calculation. *Sample size* statements should be clear, unambiguous and capable of being replicated by a reviewer. Therefore, provide all the necessary quantitative information used for the sample size estimate; and make sure that the target sample size and (when relevant) number of events are likely to be achievable in the study time frame. With specific regard to studies with a mixed design, the applicants are required to be clear about which parts of the study will be retrospective (i.e. based on patient data already collected and stored biological specimens), and which would include patients (and their specimens) to be recruited prospectively; and indicate the number of patients (or samples) in each of these groups. If questionnaires will be used (for example to obtain information on lifestyle characteristics), please state whether you will be using established and validated ones, or developing your own. For clinical trials, this section is expected to include referrals to the number of patients to be assessed for eligibility, to be allocated to the trial arms, the expected rate of loss to follow-up. Feasibility of recruitment is a key issue, thus the applicants are requested to provide evidence that the intended recruitment rate is achievable and specify whether and how the collaboration with the partners in the research consortium will facilitate the recruitment. Please specify the plans for monitoring of recruitment and contingency planning for recruitment problems. It is important that the *statistical analyses* section in the proposal is correct. It is strongly recommended that applicants work closely with colleagues such as medical statisticians or bioinformaticians, who have sufficient knowledge/expertise in study design, i.e. clinical trials and/or observational studies, including studies of prognostic markers (when appropriate). Applicants should be aware that reviewers are likely to take confused statistical statements and incorrect use of terminology as an indication that statisticians have not been involved closely in the planning. The lesson is that genuine, not token, involvement is needed (where a statistician or bioinformatician simply 'approves' the design before submission, without evaluating it carefully). With specific regard to clinical trials, interim analyses and stopping rules have to be anticipated and appropriately motivated. For studies which involve different cancer types or major subtypes, the applicants should consider describing how the different types will be handled in the statistical analyses.

c. A referral to the expected outcome has to be included. In specific regard to the intervention trials, this section has to include some justification for the expected treatment outcome.

d. Contingency plan including potential bias, anticipation of problems and possible solutions.

5. **Novelty and originality of the proposal** (maximum 2,000 characters including spaces, equivalent to about half a A4 page). The applicants are requested to underline the importance of their proposals in terms of novelty and originality.

6. **Project feasibility, consortium governance and management of project coordination** (maximum 5,000 characters including spaces, equivalent to about one A4 page). This section should include:

   - A description of the infrastructures and resources relevant to the implementation of the work plan, concept of data and material acquisition and storage, availability of biological resources, data management and elaboration.

   - A description of the research consortium governance and management as well as of project coordination. This should include: i) a description of the governance and

management structure and of project coordination planning (meeting, monitoring, etc.); ii) an outline of responsibilities and project effort (expressed in person months) of each participating research group per work package.

7. **Potential impact in reference to the development, dissemination and use of the project results** (maximum 3,000 characters including spaces, equivalent to about ¾ of an A4 page).
8. **References** (maximum 4,000 characters including spaces, equivalent to about one A4 page).
9. **Timeline and milestones** (maximum 2,500 characters including spaces, equivalent to about half an A4 page). This section should include a graphic representation of the project time plan and the milestones (Gantt chart) on a 12-month basis, that is, at 12, 24 and 36 months. **The chart must be uploaded as a separate PDF document.**
10. **Diagram** which compiles the work plan, the contribution of the partners to each work package and their interactions (Pert diagram). **The diagram must be uploaded as a separate PDF document.**
11. **Added value of the collaboration in the proposed transnational project** (maximum 2,000 characters including spaces, equivalent to about half an A4 page). This section should describe the quality of the transnational research consortium, illustrating:
    a. the level of expertise of the individual partner research teams in the field(s) of the proposal (team scientific track record, publications, patents, etc.);
    b. the quality of the collaboration between the research teams and added value of the research consortium with respect to the individual team.
12. **Description of past and ongoing research projects** of each participating group related to the present topic: specify in the table the funding or co-funding sources (include at least: title, ID number, amount and duration of funded project, correlation to the requested proposal, funding agency). Participation of at least one of the research partners in former TRANSCAN calls (JTC 2011, JTC 2012, JTC 2013, JTC 2014) select when applicable.
13. **Description of existing or potential patents** (own or third party) and present/future position with regard to intellectual property rights, both within and outside the consortium (i.e. freedom to operate, barriers to sharing materials or results), if applicable (maximum 2,500 characters including spaces, equivalent to about half an A4 page).
14. **Ethical and legal issues**. Ethical and legal issues, according to national/regional regulations, if applicable (e.g. informed consent, data protection, material transfer obligations, use of animals) (maximum 2,500 characters including spaces, equivalent to about half an A4 page).
15. **Brief CVs for each research partner** (i.e., the project coordinator and each principal investigator) including a description of the main domain of research and a list of the five most relevant publications within the last five years, demonstrating the competence to carry out the project (maximum 4,000 characters including spaces, equivalent to about one A4 page, for each partner).
16. **Capacity building activities (optional section)** (maximum 4,000 characters including spaces, equivalent to about one A4 page):

    a) Description of capacity building activities and relevance to the objectives of the proposal;

    b) Description of the involved candidate [CV, background (scientific, medical, etc.); scientific production; current work; coherence of the training with the CV,];

    c) Description of the host team (expertise in the field, qualification in research of the responsible person);

    d) Justification of the additional separate budget needed for these specific activities.

17. **Clinical Trial Description (if applicable**):Clinical trial synopsis Clinical trial flow chart: The chart must be uploaded as a separate PDF document.
18. **Global financial plan** (whole budget broken down per year and per partner). Please follow regional/regional rules and regulations on the eligibility of costs, detailed in the Call Text, Annex 4. Sum of year 1-3.
19. **Individual financial plans** for each partner and budget justification. Sum of year 1-3. This table should include the costs of the clinical trial, if applicable. Please note that eligibility of costs is subject to national rules and regulations: refer to the Call Text, Annex 4.
20. **Signed declaration** by the project coordinator and by all the principal investigators (signed PDF), partners in the project, declaring they keep track record of evidence that each of their respective team members agreed to participate in the proposal submitted. Please note: All the scanned signature pages should be assembled in a single PDF file that **must be uploaded as a separate pdf file.**

    If signatures are provided on different pages, all the pages should be assembled in a single PDF document.

Please note that additional information may be requested by national/regional funding organisations, in accordance with their respective eligibility criteria.

Important reminders for all applicants

Applicants should refer to the national/regional eligibility criteria and requirements (see Call text, Annex 4) and should contact their respective national/regional funding organisation contact persons (see also Call text, Annex 1) prior to submitting the application. An **eligibility check** is mandatory for some national/regional funding organizations before the submission deadline (see above).

The JCS will assess proposals to ensure that they meet the call's formal criteria [e.g. date of submission; number of participating research groups, type of project partners (academic, clinical/public health and industrial/SMEs), and inclusion of all necessary information in English, document length]. In parallel, the JCS will forward the proposals to the relevant TRANSCAN national/regional funding organisations that will perform a formal check of compliance with their respective eligibility criteria. Proposals passing both checks will be forwarded to independent international scientific experts for evaluation.

Please note that once the JTC 2015 is closed it is not possible to amend an application or add additional documents.

Start of the project and Consortium Agreement

In order to ensure a proper conduct of the project activities, a Consortium agreement (CA) must be signed among the partners before the official start date of the project. The CA should address the following issues: governance structure and decision making process, responsibilities between the partners and subsequent liability, reporting, ownership and use of research results, IPR, publications, confidentiality. Upon request, a copy of the CA will be made available to the concerned TRANSCAN-2 JTC 2015 funding organizations.

A common start date for the funded project will be agreed by the consortium partners. The agreed date will be the reference date for yearly and final reports and extensions. The official start date shall be communicated by the project coordinator to the JCS and shall appear in the consortium agreement.