# ERA-NET TRANSCAN-3 Joint Transnational Call (2021)

## Next generation cancer immunotherapy:targeting the tumour microenvironment

## HRB Supplementary Guidance Notes

**Document revised April 19th, 2021 (Modifications in red)**

| Deadline | Key Dates and Times |
|---|---|
| Call Announcement | 06 April 2021 |
| Opening of the on-line submission system for pre-proposals | 20 April 2021 |
| International Networking Event (virtual) | 22 April 2021 |
| Submission deadline pre-proposal | 29 June 2021 (11:00 GMT) |

This document provides additional guidance to researchers based in Ireland applying to this call as part of a transnational consortium. This document must be read in conjunction with the call documents listed in Appendix I, and the FAQ for this call on the HRB website (https://www.hrb.ie/funding/funding-schemes/all-funding-schemes/)

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# 1 Introduction

In the last decades the understanding of the molecular mechanisms responsible for cancer development and progression has significantly improved. This led to the introduction in the clinic of a wealth of targeted therapeutic agents with a corresponding increase in survival and improvement in the quality of life of cancer patients. In this context a major breakthrough is represented by the clinical validation of the concept that the immune system is capable of recognizing cancer cells and controlling tumour growth, which paved the way to the introduction of immunotherapeutic agents in the clinical practice. The high proportion of cancer patients resistant to cancer immunotherapy still remains a huge issue. In this context it is now becoming evident that resistance is largely influenced by the composition of the tumour microenvironment (TME).

Understanding the complexity of TME dynamic dialogs should allow to identify appropriate targets and develop predictive biomarkers of treatment outcome and drug resistance. It is reasonable to predict that targeting the TME will yield the next breakthroughs in cancer immunotherapy.

Under the umbrella of TRANSCAN-3 (ERA-NET: Sustained collaboration of national and regional programmes in cancer research), **Twenty eight** funding organisations have agreed to focus their first Joint Transnational Call (JTC 2021), co-funded by the European Commission, for collaborative research projects on **"Next generation cancer immunotherapy: targeting the tumour microenvironment".** The participating TRANSCAN-3 funding organisations wish to promote innovative interdisciplinary collaboration and truly translational research projects aiming at promoting highly innovative and ambitious collaborative projects in translational cancer research at European and international level.

The expected impact of the call is to improve the efficacy of personalized treatment of cancer patients through the development of new tools and targeted immunotherapy strategies, based on a better understanding of TME functions and of their impact on the disease course.

TRANSCAN-3 supports capacity building activities for promoting the formation and upgrading of multidisciplinary teams in an integrated process: i) exchange/mobility of individual researchers/professionals in order to bring new expertise to an existing multidisciplinary translational team, and/or ii) recruitment of individual researchers/professionals by a translational research team in order to cover expertise and “know-how” unavailable in the existing team. These types of activities, when present, will be supported within the projects which will be selected for funding under TRANSCAN-3 JTC 2021.

# 2 Aims of the Call (See Call Text: http://transcan.eu/opencall.html)

In the context of translational research, this topic at the intersection of laboratory and clinical research in immuno-oncology will comprise **two general aims** which concur to the possible clinical applications. Proposals will have to cover **at least one of the six (6) specific aims** listed below. Approaches should be directed to draw up a multidimensional tumour microenvironment (TME) map paving the road for new efficacious immunotherapy strategies. Projects should be built from a solid and established hypothesis and should be relevant with regards to the possible improvements in clinical practice.

## Aim 1 (three specific aims)

Identification and validation of TME subclasses and their contribution to the resistance mechanisms: Translational research using tumour samples collected from retrospective and/or prospective cohorts of patients.

1.1 Dissection of tumour cells/tumour-infiltrating immune/stromal cells and identification of TME subclasses (single-cell analyses, mass cytometry, imaging, multidimensional immunohistochemistry, etc.) for TME studies (3D culture systems; patient-derived organoids; patient-derived xenografts; syngeneic, genetically modified and chemical carcinogenesis-induced mouse models, etc.).

1.2 Definition of the contribution of TME to resistance mechanisms and identification of new therapeutic targets through multiomics (epigenomic, transcriptomic, proteomic, metabolomics, study of the microbiome and virome, etc.) to assess functional characteristics of TME-tumour cell interplay within the primary tumour and/or metastases (e.g. the underlying signaling, the transcriptional landscape, the cell-cell communication, the network regulation of immune cells, etc.), to identify candidate TME targets and to assess the activity of pathway-targeting agents.

1.3 Development of tools capable of predicting treatment efficacy and tumour recurrence using minimally or noninvasive techniques (generation of algorithms modelling the network dynamics,predictive models based on artificial intelligence, integrating -omics data and network approaches).Development of robust noninvasive biomarkers of disease course (radiomics,cell-free circulating tumour DNA,miRNA signatures,circulating tumour cells,etc.)Sex/gender impact must be considered.

## Aim 2 (three specific aims)

Targeting TME to improve efficacy of immunotherapy in human patients **(NB: Irish partners are not eligible for HRB Funding for Aim 2.3. Furthermore, HRB will not support clinical trials and interventions as an approach in any of the other aims.)**

2.1 Development of new precision therapeutic strategies that may prevent human tumour recurrence or resistance (T-cell-based cancer immunotherapies, immune checkpoint blockers (ICBs), chimeric antigen receptor (CAR)-T-cells, preventive and therapeutic vaccines, etc.).

2.2 Evaluation in translational studies of the impact of TME on treatment efficacy and patient outcome (clinical utility of specific TME feature detections or identifications, clinical utility of specific intratumour or peripheral blood immune biomarkers, sex/gender impact, etc.).

2.3 Phase I and II clinical trials (combinations of available treatments, new therapeutic strategies, new administration schemes, etc.) targeting, or preventing resistance of multiple TME features. Particular attention should be given to gender balance inclusion in order to intercept sex/gender differences and to determine if there is an association between sex/gender and treatment response.

## Irish partners are not eligible for HRB funding for:

- Aim 2.3 which seeks applications for Phase I&II clinical trials is explicitly out of scope for HRB funding. Furthermore, HRB will not support clinical trials and interventions as an approach in any of the other aims.
- Proposals involving basic biomedical research

- Proposals seeking to evaluate a definitive intervention or stand-alone feasibility studies in preparation for a future definitive intervention
- Proposals from Irish partners that include Human Embryonic Stem Cell Research will be deemed ineligible.

# 3 Eligibility criteria

**Non-compliance with the eligibility rules detailed below will lead to rejection of the entire proposal without further review.**

Only transnational projects will be funded: each consortium must involve funded partners from at least **three different countries** participating in this call. Each proposal must **involve a minimum of three and a maximum of six partners** (principal investigators) eligible for funding. In addition, a consortium must not involve more than two (2) partners from the same country (in such cases the minimum number of research groups must be four, coming from three different countries).

A wide inclusion of research teams from all the countries/regions participating in the call is encouraged, with a particular attention to research teams from Latvia, Slovakia and Turkey, in order to strengthen the European translational cancer research area.

Project partners not eligible for funding (e.g., from non-funding countries or not fundable according to national/regional regulations of the participating funding organisations) may participate in projects provided that they demonstrate, with the full proposal submission, that their economic and human resources have already been secured and will be available at the start of the project. No more than one partner with its own funding is allowed in consortia with at least three partners eligible for funding. Project partners not eligible to be funded cannot be consortium coordinators and, like funded members, must accept all TRANSCAN-3 rules and guidelines.

Applications must be submitted by the coordinator. The coordinator and each individual partner will be funded by the funding organization from their country/region that is participating in the TRANSCAN-3 JTC 2021 and are therefore subject to national/regional eligibility rules.

Each consortium must involve at least **one basic or pre-clinical research team and one clinical team**. It is also recommended to include **an expert team in methodology, biostatistics or bioinformatics**, depending on the type of work planned. The consortium may also involve other teams with specialised skills and know-how (biobanks, model systems, technological platforms, etc.) or expertise (epidemiology and molecular epidemiology, early phase clinical trials, public health, ethical legal and social implications (ELSI), etc.). The consortium should have sufficient critical mass to achieve ambitious scientific, technological and medical goals and, along with the particular contribution of each research team, should clearly demonstrate its transnational added value. The translational nature of the research results is the key goal of TRANSCAN-3, therefore the consortium should also clearly demonstrate a knowledge transfer towards clinical, public health and/or industrial applications.

The duration of the projects shall not exceed three (3) years.

For up to date information on which countries are participating in this call, together with country-specific specific eligibility requirements, see: http://www.transcan.eu/opencall.html

Joint transnational research proposals may be submitted by academic research groups (from universities or other higher education or research institutions), clinical/public health sector research groups (from hospitals/public health and/or other healthcare settings and health organisations) enterprise's research groups (depending on national/regional eligibility rules), with particular emphasis on small and medium -sized enterprises. The eligibility of the afore-mentioned institutions, together with details of eligible costs (personnel, material, consumables, equipment, travel money, etc.), are subject to the individual administrative requirements of individual funding organisations http://www.transcan.eu/opencall.html

## 3.1 Eligibility of researchers based in Ireland

**All proposals for HRB funding must be from a recognised HRB Host Institution and will be subject to a HRB eligibility check following submission to the centrally coordinated peer review to ensure:**

1. The Lead Applicant(s) (Principal Investigator(s)/Partner) from Ireland is from a recognised HRB Host Institution. A HRB Host Institution[1] is a research performing organisation that is approved by the HRB for the purpose of receiving and administering HRB grant funding and is responsible for compliance with all general and specific terms and conditions of awards. In order to be eligible to apply for funding, an Institution must be an approved HRB Host Institution no later than two calendar months before the closing date of a call. A list of currently approved HRB Host Institutions and information on the application process for research performing organisations to be approved as HRB Host Institutions can be found on the HRB website (Policy on Approval of Host Institutions).
2. The Lead Applicant (Principal Investigator/Irish Partner) named on the proposal
    a) holds a post (permanent or a contract that covers the duration of the award) in a recognised research institution in the Republic of Ireland (the "Host Institution") as an independent investigator, **or**
    b) is a contract researcher recognised by the Host Institution as an independent investigator who will have a dedicated office and research space for the duration of the award, for which he/she will be fully responsible, **or**
    c) is an individual who will be recognised by the Host Institution upon receipt of the TRANSCAN-3 award as a contract researcher as defined above. The lead applicant does not necessarily need to be employed by the Host Institution at the time of the application submission.
3. The Lead Applicant has demonstrated research independence through securing at least one peer-reviewed, independent research grant as a Principal Investigator or as Co-Investigator and is a senior author (first, last or corresponding or in those fields where alphabetic order authorship is the norm, joint author) in peer-reviewed scientific journals.
4. The Lead Applicant is not requesting their own salary.

[1] Policy on Approval of Host Institutions

5. Should a Lead Applicant (Irish Partner) wish to collaborate with an Irish Principal Investigator from another or its own Host Institution in Ireland, the Irish Principal investigator should be included in the consortium as a separate partner while respecting the eligibility requirements of partners from a participating country, see Section 3 above.

Any queries on eligibility should be raised with the HRB well in advance of the call deadline.

# 4 Funding

Whilst joint applications will be submitted involving groups from different countries, individual research groups in successful projects will be funded by the individual TRANSCAN-3 funding organisation(s) within their country. The maximum amount that funders in each participating country will contribute to their successful applicants can be found in the TRANSCAN-3 Guidelines for Applicants document: http://transcan.eu/opencall.html

## 4.1 Funding for Irish researchers applying to the HRB

For successful bids involving applicants based in recognised host institutions in Ireland, the total available for the research component carried out in Ireland will be a maximum of €370,000 over 36 months (inclusive of overheads and pension contributions). For applicants in Ireland the award will cover the costs of salary-related costs, small equipment costs, travel, direct running costs, FAIR data management costs, dissemination and knowledge exchange costs and overheads.

The HRB component of the budget for the project cannot exceed €370k (including overheads and pension contributions)

**Funding available is inclusive of overheads and pension contributions**

a) Personnel
   i. Salary-related costs in line with the IUA most recent scale for funded personnel
   ii. Stipends and fees (EU rate only)
b) Small equipment costs (not expected to exceed €10k)
c) Travel costs
d) Direct running costs (including travel, or mobility costs)
e) FAIR data management costs: Data stewardship costs (e.g. service/fees from data steward, access to secondary data, costs of making data FAIR, ets.)
f) Dissemination and knowledge exchange activities
g) Overheads contribution

# 5 Application Process

In order to start the application procedure, please go to http://www.transcan.eu/opencall.html and follow the instructions provided. A Pre-proposal Application Form can be downloaded from the call webpage http://www.transcan.eu/opencall.html along with the **call text** (detailing the aim and scope

of the call, eligibility and submission details, the evaluation process and assessment criteria, reporting requirements), **Guidelines for Applicants** and **National Contact Points**. These documents **must be consulted** in addition to the HRB Guidance Notes and HRB Frequently Asked Questions documents on this page. Please refer also to HRB Grant Policies.

The Pre-proposal Application Form includes all information required. Please complete all fields within the required format and length. The submission must be made through the dedicated electronic submission system PT-Outline exclusively, at: https://ptoutline.eu/app/transcan2021

Both pre-and full proposals must be written in English and must be submitted by the coordinator of the proposal.

Please note that proposals submitted by post, email, fax or any other means will not be accepted and will be rejected without further review.

Applicants from Ireland in consortia invited to submit a full proposal will be required to provide additional information to the HRB at the time of the full application submission deadline. This will include justification for their requested budget, and clarification on deliverables assigned to the partner from Ireland. A template requesting the information required from applicants from Ireland will be provided by the HRB.

It is the responsibility of the applicants in each country to ensure that their host institution(s) have reviewed and approved the budget prior to submission. Please allow sufficient time for these additional processes. Any late applications will be rejected.

# 6 Timeframe

| Deadline | Key Dates and Times |
|---|---|
| Call Announcement | 06 April 2021 |
| Opening of the on-line submission system for pre-proposals | 20 April 2021 |
| Submission deadline pre-proposal | 29 June 2021 (11:00 GMT) |
| Communication of the results of the pre-proposal assessment and invitation for full proposal stage | 05 November 2021 |
| Opening of the submission system for full proposals | 19 November 2021 |
| Submission deadline full proposals | 20 December 2021 (11:00 GMT) |
| Communication of the funding decisions to the applicants | Expected for May 2022 |
| Expected project start (also subject to regional/national procedures | October/November 2022 |

# 7 Contacts for Further Information

**For general information, please contact the Joint Call Secretariat (JCS):**

Silvia Paradisi
Ministero della Salute - Istituto Superiore di Sanità, Italy

e-mail: jtc2021@transcan.eu

**For country- specific information for Irish Partners, please contact the HRB, Ireland:**

Dr Louise Drudy
Project Officer: International Cooperation, Evaluation & Targeted Programmes
Research Strategy and Funding Directorate

e-mail: ldrudy@hrb.ie

**The HRB reserves the right to reject any application that does not meet the terms of this call. The decision of the HRB Board in respect of any grant application is final and cannot be appealed or reviewed.**

**In view of the overwhelming evidence that both active and passive smoking of tobacco are injurious to health, the HRB is unwilling to fund applications from individuals applying for, holding, or employed under a research grant from the tobacco industry.**

**The HRB cannot fund research using human embryonic stem cells or tissues or intended to create human embryos solely for the purpose of research or for the purpose of stem cell procurement, including by means of somatic cell nuclear transfer.**

# Appendix 1

# Call documents

| Call Documents | Websites |
|---|---|
| Call Text | http://transcan.eu/opencall.html |
| Guidelines for Applicants, National/Regional Regulations | http://transcan.eu/opencall.html |
| Pre-proposal Application Form | http://www.transcan.eu/opencall.html |
| Submission website (opened from April 20th to June 29th 2021 | https://ptoutline.eu/app/transcan2021 |