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

TRANSCAN-2

Preliminary Announcement[1]

The Third Joint Transnational Call for Proposals 2016 (JTC 2016) will be launched in December 2016

The ERA-NET: Aligning national/regional translational cancer research programmes and activities (TRANSCAN-2) is the continuation of the ERA-NET on Translational Cancer Research (TRANSCAN) and has the goal of coordinating national and regional funding programmes for research in the area of translational cancer research. The specific challenge is to promote a transnational collaborative approach between scientific teams in demanding areas of translational cancer research while avoiding the duplication of efforts and ensuring a more efficient use of available resources, to produce significant results of higher quality and impact, and share data and infrastructures. Along this line TRANSCAN-2 will launch the Joint Transnational Call for research proposals (JTC 2016) in December 2016.

The topic of the call will be:

"Minimally and non-invasive methods for early detection and/or progression of cancer"

The call will be published simultaneously by the funding organisations in their respective countries and on the TRANSCAN website: http://www.transcanfp7.eu.

Interested researchers and/or research teams are advised to prepare and make the necessary contacts and arrangements towards preparing applications. Please see below the details of the call topic and an outline of the eligibility criteria. They will be further detailed when the JTC 2016 is published.

[1] *This document is not legally binding and is provided for information purposes only.*

MOTIVATION

Screening of the general population, risk stratification, surveillance of high risk groups, and diagnosis represent different steps of a multimodal approach of early cancer detection, that greatly increase the chances for successful treatment as generally prognosis worsens with advancing stage. Minimally invasive methods, such as the identification of specific biomarkers in body fluids or innovative imaging approaches at early stages of cancer may help to detect the disease before any clinical manifestation, with a better chance to provide therapies with a curative intent. However, there is a certain risk of over-diagnosis and over-treatment.

Cancer screening programmes implemented so far have been designed to test people from the general population with an average risk to develop the disease, mostly in a specific age group. The discovery of highly penetrant gene mutations (e.g. *BRCA*1 and *BRCA*2 for breast cancer, *HNPCC* genes for colon cancer) already paved the way for identifying people with high hereditary risk of cancer. Recent advances in sequencing of the human genome are likely to identify additional risk indicators. For individuals known to be at elevated risk for certain tumour diseases, general cancer screening programmes are not appropriate or start too late in life. Increased knowledge of promising biomarkers, such as serum, urine, faecal or blood-based (genetic, or immunochemical) markers of cancer development, will likely provide efficient tools for risk stratification for targeted screening, i.e. people differing by risk level for developing certain cancer types based on a combination of biomarkers and other risk factors. The benefits of any cancer screening programme will be offset by possible harms, such as false-positives, over-diagnosis, and over-treatment. A screening programme becomes feasible if it does more good than harm at reasonable costs.

The impact of early detection on patient-important outcomes is generally remarkable when dealing with relatively homogeneous, slow-growing tumours, whose precursors can be appropriately identified and removed, e.g. pre-cancerous lesions for cervical and colorectal cancer. However, cancer is a biologically heterogeneous disease, whose behaviour may range from indolent to highly aggressive. Current efforts are increasingly focused on deciphering such complexity and its consequences in terms of disease onset and patterns of disease progression. Within such a context, the broad group of science and engineering disciplines known as ‘omics’, along with imaging techniques, may further add to current knowledge on cancer heterogeneity. Strategies for risk stratification and identification of patients with poor prognosis may result in the administration of more targeted therapies, improved treatment outcomes and more appropriate outcome interpretation. At the same

time, the identification of patients with good prognosis may reduce over-treatment, including potential side-effects of treatment, and thus decrease unnecessary burden to patients and healthcare costs.

Despite major achievements in the understanding of the molecular roots of cancer, validation at the general population level of minimally invasive methods for early detection and prediction of cancer progression remains a poorly explored area. Thus far the interest of the pharmaceutical industry has been strongly focused on areas requiring immediate and effective solutions, i.e., the metastatic setting. These latter efforts are currently paralleled by actions leading to implementation of early detection strategies in groups of people with high risk of cancer and adaptation of treatment strategies according to the risk of progression for patients diagnosed at an early stage of cancer. These actions are particularly attractive at an academic institution level in light of their potential impact on cancer incidence and mortality.

AIM OF THE CALL

Translational research proposals of the TRANSCAN-2 JTC 2016 call must focus on:
"Minimally and non-invasive methods for early detection and/or progression of cancer"
Minimally invasive methods refer to techniques that have limited physical damage, burden and pain associated with the detection method, resulting in less anticipated stress, a higher screening/clinical care uptake, and more efficient and cost-effective screening and care. The studied methods should be sensitive for early detection of cancer, its staging and prediction of progression. Examples are: individual or combination of molecular, immunochemical, proteomic or genetic markers in body fluids and blood or cell samples, as well as macroscopic, microscopic and molecular imaging techniques (e.g. improved ultrasound technology, molecular imaging with contrast agents, fluorescence imaging, radiolabelling). This call excludes invasive methods, such as image-guided biopsy or surgery.
In the context of translational cancer research, this topic will comprise three specific aims. Proposals will have to cover at least one of the specific areas listed under each undermentioned aim.

Aim 1: Risk stratification to distinguish groups by susceptibility for development or progression of cancer based on molecular biomarkers and established cancer risk factors, such as age, medical history, anthropometrics (e.g., body mass index, waist

circumference), and lifestyle related determinants (e.g., diet, physical exercise, environmental exposure and medication)

- Risk stratification for cancer development (susceptibility to develop cancer) using minimally invasive methods (imaging, biomarkers assessment in body fluids) to identify high risk groups of individuals who will benefit most from a more intensive and/or invasive screening.
- Risk stratification for cancer progression (biomarker(s) or clinical characteristic(s) with a prognostic value, i.e. that provides information on the likely outcome of the cancer in (untreated) individuals). Detection of tumour promoting subpopulations, those with enhanced ability to drive tumour progression.

Aim 2: Validation of multiparametric methods, using the combination of promising[2] biomarkers (genomic, proteomic, metabolomic and imaging markers) to improve our capability for early detection or progression of cancer

Different tumour markers show different sensitivity towards different types of tumours. Combining multiple markers significantly increases the ratios of positive cancer diagnosis. Even though the increase in sensitivity when combining markers and tools might be accompanied by a decrease in specificity, tumour markers combinations may still play an important role in early tumour detection as well as in prediction of cancer progression. As high throughput genomic assays become more accessible, working with largescale data sets requires user-friendly and powerful tools and techniques to help researchers manage, analyse and integrate big data from genomics. The development and implementation of adequate bioinformatics techniques are of essential importance. Biomarkers that are suitable for automated measurement are promising tools.

- Molecular tumour markers: increase sensitivity of detecting genetic, epigenetic or proteomic markers, including circulating tumour cells (CTC techniques), exosomes, tumour DNA, circulating free DNA in plasma and other fluids, micro RNA and integration with metabolomic assays.
- Imaging markers: such as low radiation CT scans or intravenously delivered fluorescent peptide probes.
- Bioinformatics techniques: techniques for mining complex genomic/biomarkers data.

[2] Biomarkers that already have shown to have predictive value, but need to be validated in an independent heterogeneous target population

Aim 3: Improve clinical evidence of the minimally invasive methods

Important criteria to evaluate a biomarker are described in the ACCE model. It is important to acknowledge these criteria when describing the outcome measures and future directions of the project plan.

- Analytical validity, clinical validity, and clinical utility: Evaluation (or describe the planning) of the impact of minimally invasive methods on patient outcome (less invasive detection, increased life expectancy, or reduced morbidity) and properties such as sensitivity and specificity. Ethical, legal, and social implications (could also be considered): Evaluation of implication and implementation aspects, e.g. acceptance of personalised screening based on risk stratification.

Projects should be built from solid and established research and should be relevant with regard to possible improvements in clinical practices. Projects should describe how the research results would fit in current screening programmes and/or (inter)national clinical cancer detection and diagnostic guidelines and how they can be implemented in the future. Proposals reach high impact if they meet the following requirements:

a) There is a clear added value of the transnational collaboration.
b) They are presented by a sustainable network/consortium. As TRANSCAN-2 can only support the consortium until the end of the project, it is stimulated to describe a plan for future collaboration and to guarantee the sustainability of the consortium with regard to the next translational steps and long term data accessibility for all partners.
c) They are focussed on cancers without established screening programmes. Screening programmes for rare or very aggressive tumour types or subtypes, may have high impact as these are often discovered in a late stage, which is associated with a high mortality rate.

The following types of research projects are excluded from the call:

1. Analysis of preclinical models (cell lines and animal models) only.
2. Phase III and IV clinical trials.
3. Studies not compliant with the COMMISSION REGULATION (EC) No 800/2008 (link), with specific reference to the articles 30, 31, 32, and 33. For full reference, please see also the COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT, THE COUNCIL, THE EUROPEAN ECONOMIC AND SOCIAL COMMITTEE AND THE COMMITTEE OF THE REGIONS of 20.12.2011 (link). Studies not compliant with the Commission Regulation (EU) No 651/2014 of 17 June 2014 (link).

The national/regional funding organisations listed below have agreed to participate in the TRANSCAN-2 Joint Transnational Call for proposals 2016 (JTC 2016):

- Research Foundation - Flanders (FWO), Belgium
- Fund for Scientific Research (FNRS), Belgium, French speaking community
- Estonian Research Council (ETAg), Estonia
- National Cancer Institute (INCa), France
- ARC French Foundation for Cancer Research (ARC Foundation), France
- Federal Ministry of Education and Research (BMBF), Germany
- General Secretariat for Research & Technology (GSRT), Greece
- The Chief Scientist Office of the Ministry of Health (CSO-MOH), Israel
- Ministry of Health (MoH), Italy
- Alliance Against Cancer (ACC), Italy
- Lombardy Foundation for Biomedical Research (FRRB), Italy
- State Education Development Agency (VIAA), Latvia
- Dutch Cancer Society (DSC), Netherlands
- Research Council of Norway (RCN), Norway
- Norwegian Cancer Society (NCS), Norway
- National Centre for Research and Development (NCBR), Poland
- Slovak Academy of Sciences (SAS), Slovakia
- Spanish Association Against Cancer (AECC), Spain
- The Foundation for the support of the Applied Scientific Research and Technology in Asturias (FICYT), Spain
- Ministry of Science and Technology (MoST), Taiwan
- Scientific and Technological Research Council (TUBITAK), Turkey

Pending decision:

- *National Institute of Health Carlos III (ISCIII), Spain*
- *Ministry of Education Science and Sport (MIZS), Slovenia*
- *Ministry of Education, University and Research (MIUR), Italy*

MAIN ELIGIBILITY CRITERIA

Only transnational projects will be funded. Each research consortium asking for funding must involve a minimum of three (3) research groups and a maximum of seven (7) research groups (with the exception if Estonia, Latvia, and Slovakia are involved, then there can be a maximum of ten (10)). The groups must be from at least three (3) different countries participating in the call. In addition, a consortium must not involve more than two (2) research groups from one country (in such cases the minimum number of groups must be 4, coming from 3 different countries). Up to 1 (one) research group from a country not participating in this call may be included in a consortium, if this group is able to secure its own funding. In order to strengthen the European translational cancer research area, 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 Estonia, Latvia, Slovakia. 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. Consortia 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, ELSI, etc.). Consortia 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-2 and, therefore, the consortium should also clearly demonstrate a knowledge transfer towards clinical, public health and/or industrial applications. While applications will be submitted by the coordinator, the individual research groups will be funded by the funding organisation from their country/region that is participating in the TRANSCAN-2 JTC 2016. The applications are therefore subject to eligibility criteria of national/regional funding organisations. In case of ineligibility of one of the teams, the eligibility of the consortium as a whole would be at stake. Upon the call publication, applicants will have to refer to the annexes of the document “Call text” containing all the specific national/regional eligibility criteria and will have to contact their respective national/regional funding organisation contact points for additional clarification.

For further information, please visit the TRANSCAN website:

http://www.transcanfp7.eu