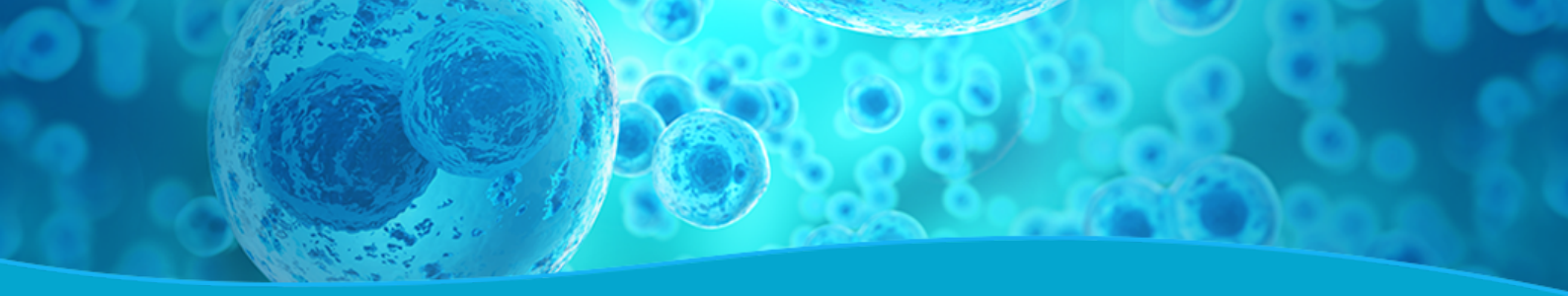

ERA-NET TRANSCAN-2

# NEWSLETTER 6

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TRANSCAN-2

## News From TRANSCAN-2

**TRANSCAN and TRANSCAN-2 success story: BOOSTING TRANSLATIONAL CANCER RESEARCH**

http://ec.europa.eu/research/infocentre/article_en.cfm?artid=39816

## Joint Transnational Call 2017

The 2017 joint transnational call on "**Translational research on rare cancers**" was launched on 5th December 2017, and the submission deadline for pre-proposals was 6th February 2018. Results from the pre-proposal phase were sent on April 2018, and submission deadline for invited full proposals is 30 May 2018.

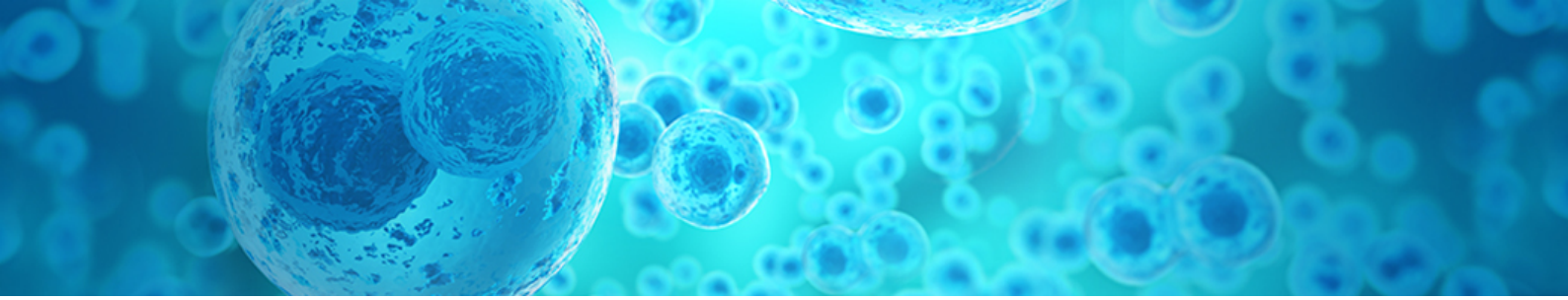
## Joint Transnational Call 2016

This newsletter overviews the results from JTC 2016 on **"Minimally and non-invasive methods for early detection and/or progression of cancer".** 14 projects were chosen to be funded under this call. We wish them all much success.

More information can be found on
http://www.transcanfp7.eu/

This project has received funding from the European Union's Horizon 2020 Research and Innovation Programme under grant agreement no 643638.

Produced by MIZS, SI and CSO-MOH, IL

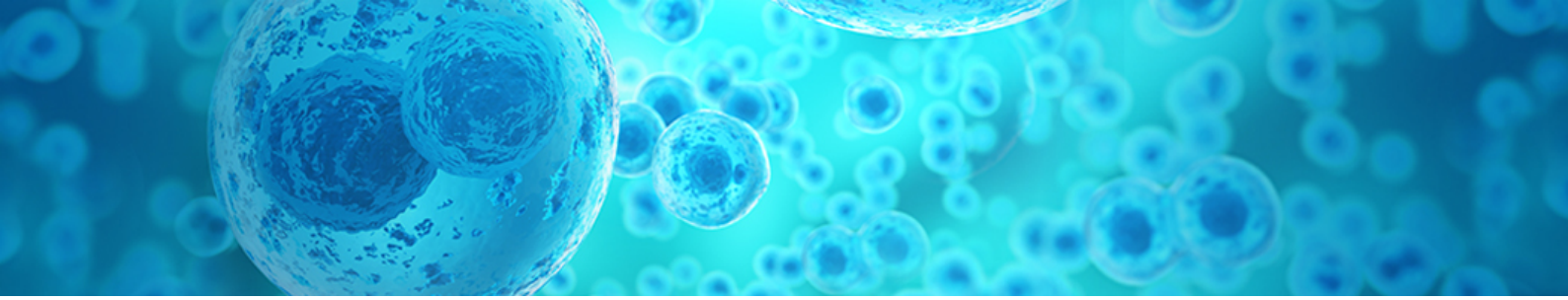


# Outcome of the Joint Transnational Call 2016 (closed call) - OVERVIEW OF THE 14 FUNDED PROJECTS

The 2016 Joint transnational call on **"Minimally and non-invasive methods for early detection and/or progression of cancer"** primarily aimed to fund studies on 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). The second aim was validation of multiparametric methods, using the combination of promising biomarkers (genomic, proteomic, metabolomic and imaging markers) to improve our capability for early detection or progression of cancer. The final aim was the improvement of clinical evidence of the minimally invasive methods.

The call was motivated by the notion that 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. This approach greatly increases 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.

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. So far, the interest of the pharmaceutical industry has been strongly focused on areas requiring immediate and



effective solutions, i.e., the metastatic setting. This effort is currently in parallel with 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.

**At the completion of the Call, 14 transnational projects were selected for funding, with a total requested budget of 15,2 Mio €.**

In Table 1, Figure 1, and Figure 2 you can find some of the call statistics.

**Table 1: Number of submitted (pre/full/funded) proposals under JTC-2016**

| | Proposals | Countries | PIs |
|---|---|---|---|
| Eligible pre-proposals | 110 | 21 | 543 |
| Eligible full proposals | 38 | 16 | 205 |
| Funded proposals | 14 | 12 | 70 |

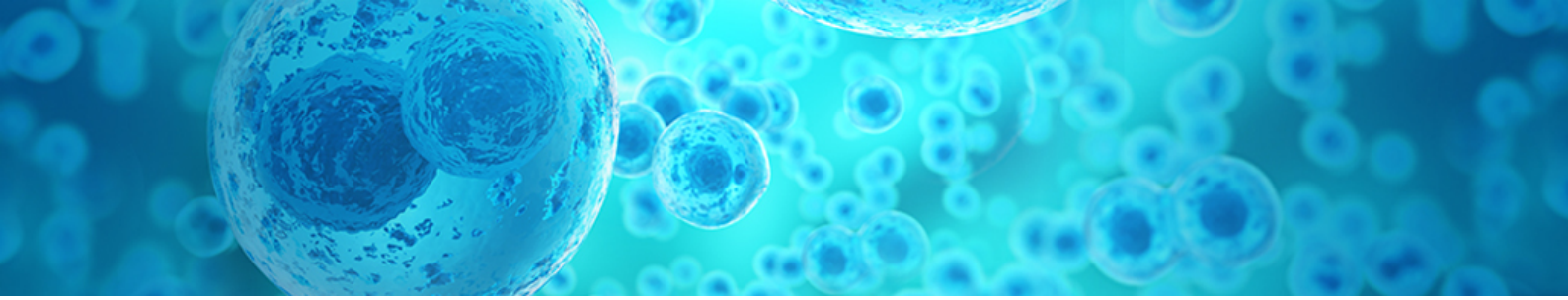


**Figure 1:** Gender ratio of the 70 Principal investigators involved in the 38 full proposals and 14 funded projects

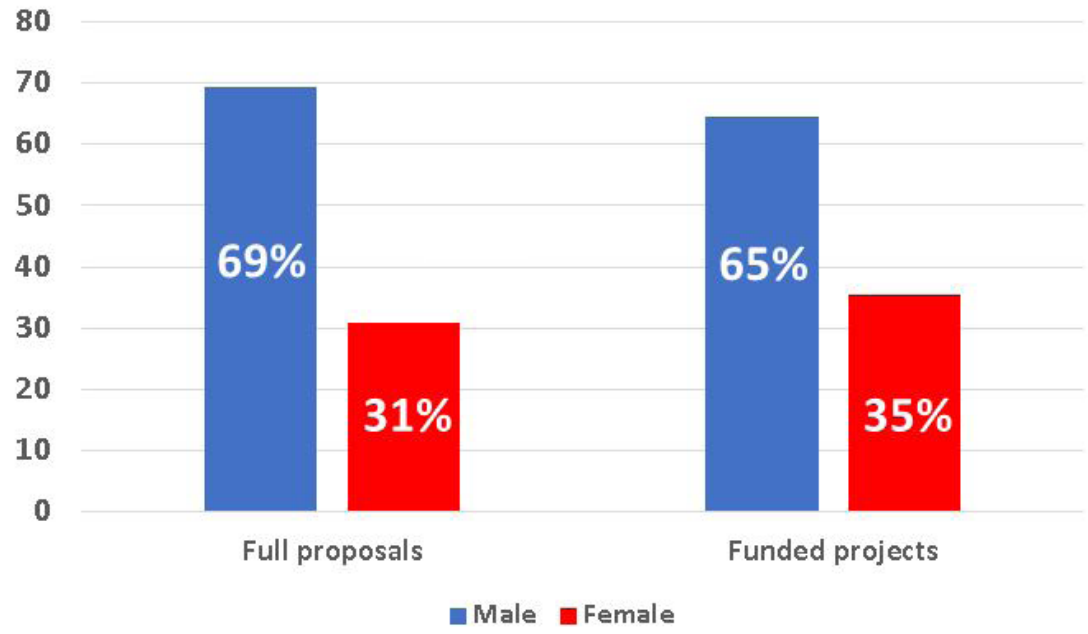
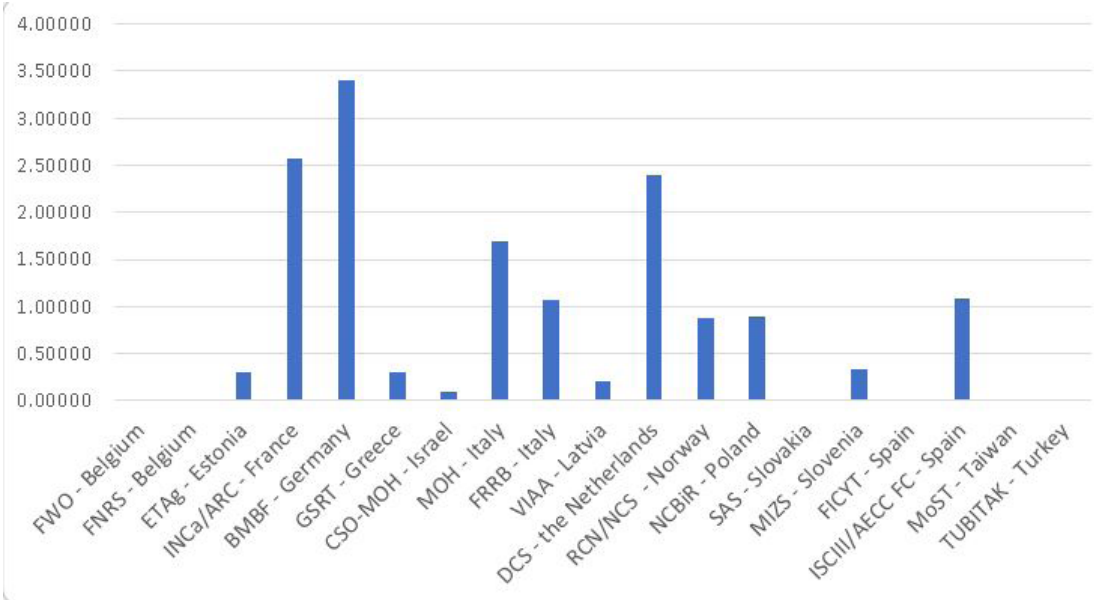
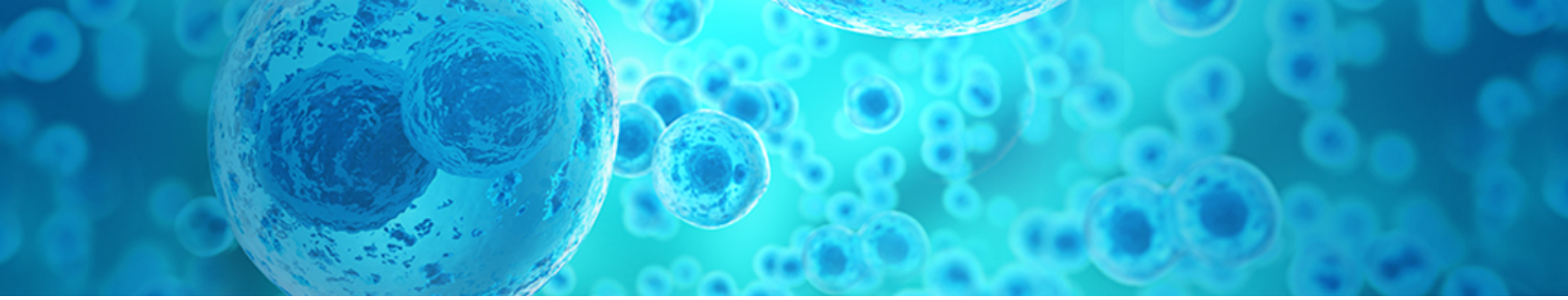



**Figure 2:** JTC 2016 Spent budget (M€) for funded projects per funding organisation





## Topics of JTC-2016 funded projects

According to the tumour classification by organ site (World Cancer Report 2014, International Agency for Research on Cancer, WHO), the 14 funded projects can be grouped as follows:

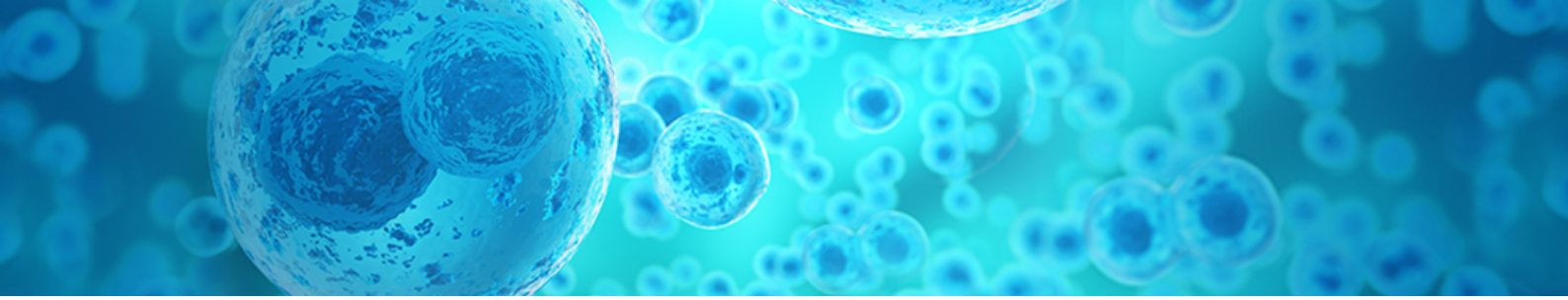
### LUNG CANCER

**CLEARLY - Validation of multiparametric models and Circulating and imaging biomarkers to improve Lung cancer EARLY detection [Lung cancer].** CLEARLY focuses on validation of a multifactorial "bio-radiomic" protocol for early diagnosis of lung cancer that combines circulating biomarkers and radiomic analysis: (a) assess the role of molecular and cellular biomarkers (exosomes, protein signatures, CTCs, microRNA) and radiomic signature, as complementary to assist early detection of lung cancer by LDCT, using bioinformatics techniques; (b) assess the prognostic role of CTCs including the role of cells epithelial mesenchymal transition (EMT) and (c) standardize a method for genomic analysis of CTCs for early detection of treatment resistance.

**RESTING - Non-invasive prognostic markers for Resected Early-STage NSCLC: role of circulatING and exosomal miRNAs and free circulating DNA [Lung cancer].** To evaluate the prognostic value of exosomal and cell-free miRNAs in relation to disease free survival (DFS) and overall survival (OS) in a prospective case series of resected early-stage (stages IA-IIIA) NSCLC patients. Secondary goals: to analyze the role of fcDNA in relation to DFS and OS; to analyze the association between exosomal and cell-free miRNAs and fcDNA and their combinations in relation to patient outcome.

### TUMOURS OF THE NERVOUS SYSTEM

**GLIOMA-PRD - Multiparameric Analysis of the Evolution and Progression of Low-Grade Glioma (LGG) [Glioma].** This project focuses on Lower Grade Gliomas and how to integrate imaging and molecular heterogeneity into a tool to be used in the routine clinical practice for easily predicting LGGs progression. Predicting the prognosis using such high dimensional and heterogeneous data required specific approaches.

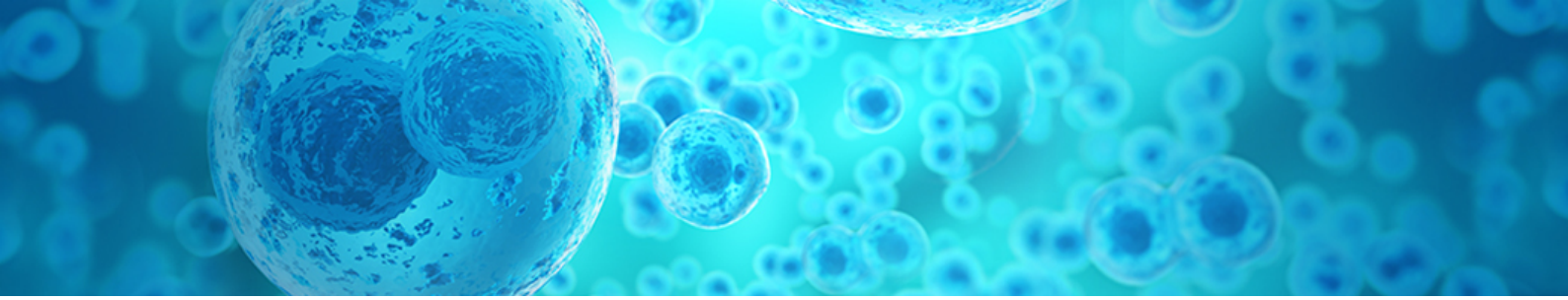


## HAEMATOPOIETIC AND LYMPHOID MALIGNACIES

**iMMunocell - Single-cell immunophenotypic and transcriptomic profiling for minimally-invasive detection of early multiple myeloma [Multiple myeloma].** The primary aim is to develop new minimally-invasive methods that identify individual patients at risk of developing active MM, towards treating disease causation instead of symptomatology. This will be accomplished through longitudinal and periodic single-cell characterization of circulating tumor cells (CTCs) and immune subsets, during patients' transition from benign into malignant disease stages. Our secondary aims are to i) evaluate clonal heterogeneity over time with unprecedented single-cell resolution, ii) generate in-depth knowledge on the pathogenesis and dissemination of smoldering into active MM, iii) generate large datasets on single-CTC-RNAseq, ATACseq and immunoscores from SMM patients, and iv) develop minimally-invasive algorithms to tailor pre-emptive (immuno)therapies.

**NOVEL - Employing NGS technology for improved, non-invasive early detection, staging and prediction of progression in lymphoma patients [Lymphoma].** B-cell non-Hodgkin lymphomas (B-NHL) are more frequent in healthy individuals with a family history of lymphoma and in immunocompromised patients. The aims are: 1. To detect early disease through screening procedures in populations at risk. 2. To risk-stratify individuals carrying pre-lymphomatous conditions or indolent lymphomas for progression to overt disease. 3. To refine diagnosis and staging in B-NHL.

**TRANSCALL2 - Integration of genetic biomarkers and early Minimal Residual Disease to improve risk stratification and cure in childhood Acute Lymphoblastic Leukemia. [Acute Lymphoblastic Leukemia].** The use of minimally invasive methods to screen the childhood ALL population for new molecular markers at diagnosis and the combination of genetic information with MRD monitoring in the early treatment phases, will allow the improvement of risk stratification and subsequent clinical decision making for improved personalized precision treatment of children and adolescents with ALL. The Research plan comprises 5 related work packages: 1) Infrastructure and methods; 2) New biomarkers in precursor B-cell ALL; 3) New biomarkers in precursor T-cell ALL; 4) Clinical impact of host genetic heterogeneity; 5) Circulating 'free' DNA for MRD monitoring in serum.

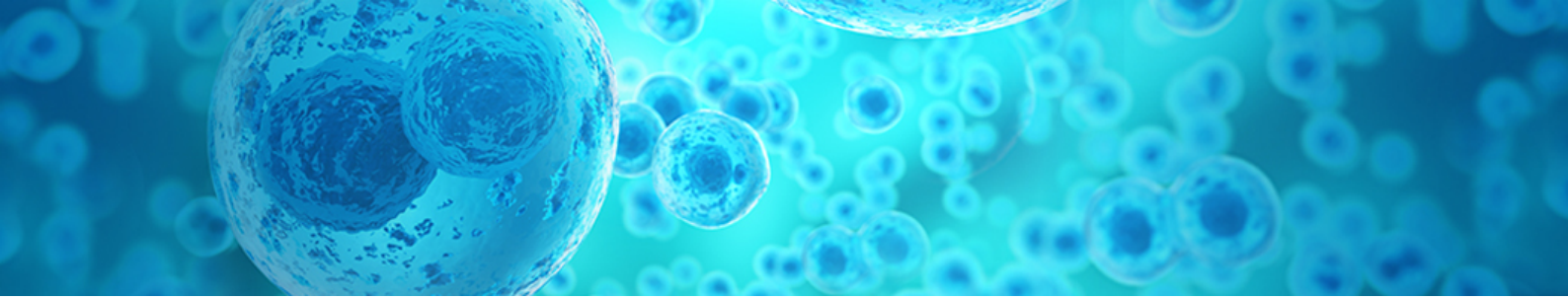


## COLORECTAL CANCER

**ABC-Cancer - Airborne Biomarkers for Colorectal Cancer [Colorectal cancer].** Recently, volatile organic compounds (VOCs) from biological fluids, including blood, urine and breath, have been proposed as potential biomarkers for various diseases. State-of-the-art analytical technologies based on mass spectrometry (MS) can identify thousands of VOCs in biological media, known as the volatilome, and past studies have linked certain VOCs with specific diseases like cancer. The driving hypothesis for this proposal is that CRC, as well as its pre-cancerous stages, leads to the generation of specific VOCs that manifest in faeces and exhaled breath, thereby offering the opportunity to identify potential biomarkers or patterns that can be implemented in CRC screening, diagnosis and monitoring.

**THRuST - Early detection of relapses in stage II-III colon cancer patients by following a personalized molecular signature from a blood test [Colon cancer].** Proof of concept of longitudinally following up an individualized tumour molecular signature from cfDNA analysis in post-surgery stage III CC patients.

**SCRAtCH - Microbiota-based screening of anal cancer in HIV-infected individuals [Anal cancer].** Primary: to identify in HIV-infected men who have sex with men (MSM) a set of anal-associated bacterial biomarkers to improve the accuracy of anal cytology for the diagnosis of biopsy-proven high degree squamous intraepithelial lesions (HSIL). Bacterial biomarkers may include bacterial species, proteins and metabolites. Secondary: to externally validate the diagnostic accuracy of the microbiota-based screening of HSIL in an external cohort of HIV-infected MSM and women. Third: to generate a model that allows linking metabolically active bacteria to proteins being actively expressed and subsequently to fluxes of metabolites being produced in the context of anal cancer in HIV patients and to identify potential targets for therapeutic interventions.



## OESOPHAGEAL CANCER

**ESCEND - Detection of Early esophageal cancer by near-infrared fluorescence molecular endoscopy [Oesophageal cancer].** ESCEND aims to shift the paradigm in EC early diagnosis and enhance current endoscopic performance by adding highly sensitive and quantitative fluorescence molecular endoscopy (FME) in real time. Based on exciting preliminary data using fluorescent agents targeting dysplasia and neoplasia and approved for experimental clinical use, ESCEND will advance evidence on minimally invasive FME, which is on the verge of clinical translation and with immense clinical impact and commercialization potential.

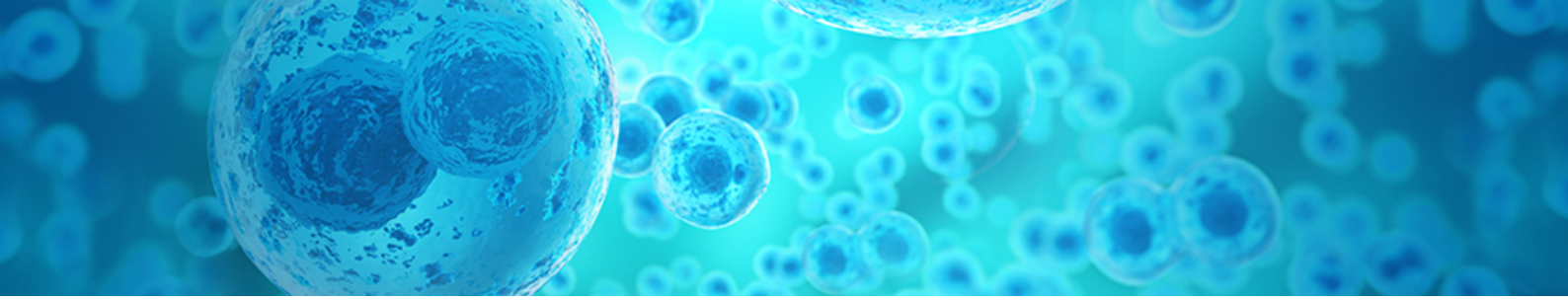
## CANCERS OF THE MALE REPRODUCTIVE ORGANS

**PROSCANEXO - Exploitation of extracellular vesicles for precision diagnostics of prostate cancer [Prostate cancer].** The overall aim of PROSCANEXO is to establish technically and clinically validated noninvasive tools for PCa diagnosis and prognosis based on the analysis of EV counts and molecular cargo in patients' biofluids.

**PROLIPSY - Early Detection of Prostate Cancer by Liquid Biopsies [Prostate cancer].** The primary aim of this research proposal is to improve blood-based detection of PCa patients by testing of circulating tumour cells (CTCs), tumour-derived exosomes and circulating cell-free DNA (cfDNA) as Liquid biopsies.

## CANCERS OF THE FEMALE REPRODUCTIVE ORGANS

**BioEndoCar - Biomarkers for diagnosis and prognosis of endometrial carcinoma. [Endometrial cancer].** We hypothesize that discrete panels of metabolites and proteins are associated with early Endometrial cancer (EC) and aggressive EC, where bioinformatics combined with statistical modelling allows development of diagnostic and prognostic models with high sensitivity and specificity. We thus aim to identify diagnostic metabolite and protein biomarker signatures for early detection of cancer in asymptomatic high-risk population and prognostic biomarkers for selection of patients with poor prognosis.



## OTHER CANCERS

**NIRBTEST - New strategies to detect cancers in carriers of mutations in RB1: blood tests based on tumor-educated platelets, or extracellular vesicles [Retinoblastoma].** The aim of this project is to develop non-invasive blood tests, either platelet- or EV-based, for early detection and stratification of tumors in RB1-mutation carriers (NIRBTEST: Non-Invasive RB1 cancer TEST). As secondary aims, we will i) initiate the systematic and comprehensive biobanking of blood and cancerous tissues from RB1-mutation carriers with SPMs and ii) determine non-cancerous (no-SPM) baseline in heritable Rb-survivors.