



Microbiota against cancer
International research program

REVIEW #1

July 2019

First and bigger network and biobanking of cancer patients stools for building up gut oncomicrobiome signatures for a better diagnosis and treatment of malignancies in Europe.

EDITO



Beyond its role in regulating multiple physiological functions that impact health, the intestinal metagenome is implicated in cancer initiation, progression and responses to therapies, even for extraintestinal neoplasia.

Hence, there is an urgent need to fully identify and functionally characterize minimalist commensal ecosystems relevant to cancer, with reliable and robust methods, to validate cancer-associated gut microbiome fingerprints of high clinical relevance, and to develop diagnosis tools that will become part of the oncological arsenal for the optimization and personalization of therapy.

Based on retro-and pro-spective studies, with large discovery and validation cohorts enrolling > 9,000 cancer patients across 10 countries, ancillary to ongoing innovative clinical trials or FDA/EMA approvals across 4 frequent cancer types, ONCOBIOME will pursue the following aims :

1. Identify and validate core or cancer-specific Gut OncoMicrobiome Signatures (GOMS) associated with cancer occurrence, prognosis, response to, or progression on, therapy (polychemotherapy, immune checkpoint inhibitors, dendritic cell vaccines) or adverse effects.
2. Decipher the functional relevance of these cancer-associated gut commensal ecosystems in the regulation of host metabolism, immunity and oncogenesis.
3. Integrate these GOMS with other oncology hallmarks (clinics, genomics, immunomics, metabolomics).
4. Design optimal companion tests, based on those integrated signatures to predict cancer occurrence and progression.

With high carat interdisciplinary experts, ONCOBIOME expects to validate cancer or therapy-specific Gut OncoMicrobiome Signatures (GOMS) across breast, colorectal, melanoma and lung cancers adjusting for covariates, to unravel the mode of action of these GOMS in innovative platforms, thus lending support to the design of cancer preventive campaigns using well characterized pre-and pro-biotics.

Dr. Laurence Zitvogel,

MD, PhD, Professor of Immunology and Biology at University Paris Saclay, Oncologist at Gustave Roussy (GR) and Director of an INSERM Unit 1015

SET THE STAGE OF THE COHORTS ACROSS COUNTRIES

Oncobiome is a 5 year programm project coordinated by Laurence ZITVOGEL, MD, PhD, Professor of Immunology and Biology at University Paris Saclay, Oncologist at Gustave Roussy (GR) and Director of an INSERM Unit 1015, along with Dr Mélodie BONVALET, Pharm. D, PhD in the operational management of the consortium and Dr François EISINGER heading the ethical committees. Algoe is the consulting agency coordinating the portal of the EU and all 17 partners.

(University of Trento in Segata's group, Karolinska Institute (Engstrand platform), CRUK and at the Masaryka University (Dr Eva Budinska)).

The role of the composition of the gut microbiota in cancer incidence will be studied thanks to the swedish National Registry, the french LUNGPREVAL cohort, the french Clinic of the Risk (Dr Delaloge, GR) and the GENTURIS association in the Netherlands.

Lung, breast, colon and melanoma cancer cohorts and related stool and tumor sample biobanking are under the liability and clinical direction of France (UNICANCER, GR, Montréal), UK-Germany-France (CRUK, Erlangen, Berlin, Marburg, GR), Italy-Czech Republic (Milan, Torino, Masaryka), Netherlands-Germany (Nijmegen Radboud, Erlangen) respectively.

The impact of the microbiome repertoire in the efficacy of cancer vaccines will be evidenced by Dr J. De Vries at Radboud University and Dr Schuler at Erlangen University.

Dr Stefan Michiels heads the epidemiology and bioinformatics of the french studies and will contribute to building up the landscape and format of the clinical data base for the consortium and recording of the translation research findings to eventually transfer to a iCloud the concatenation of the clinical data bases for final centralization and interpretation of the data at the Karolinska Institute, Sweden in Dr Lehtiö's department. The first kick off meeting was held in Gustave Roussy in January 2019.

The other partners will gather all relevant clinical and biological parameters (multi-omics) to be aligned with GOMS in order to perform multivariate analyses predicting prognosis, responses and toxicity to chemo-or immuno-therapy.

High carat platforms of metabolomics (G. Kroemer, University Paris Descartes/INSERM, culturomics, L. Zitvogel, GR and mouse models (avatar platforms, GR) are currently up and running to analyze elite patients and hyperprogressors (outliers of our cohorts).

The DNA extraction of cancer patients stools and the metagenomics analyses will be performed using a harmonized methodology across four centers

Biotech Cies involved in the development of diagnosis tools (such as the immunoscore Cie, HaliDX, France) or OncoBax live biotherapeutics (EverImmune, SAS France) are in the forefront to transform validated data into products.

Cross- fertilizations within the MICROBIOME networks of 2018 H2020 call Important collaborative networks are being settled with the other selected program projects of the same call i.e Prof. Jonel Trebicka (MICROB-PREDICT), and Prof. Alessio Fasano (GEMMA).

Oncobiome SAB members
Giorgio Trinchieri (NIH, USA), Miriam Merad (Mount Sinai, USA), Nathalie Varoquaux (Astra Zeneca), Duskho Erlich (INRA, France), Willem de Vos (Wageningen, Netherlands), Patrice Cani (Louvain, Belgium), Christian Blank (NKI, Netherlands), Eric Vivier (Innate Pharma, France), Zoltan Szallasi (Harvard Medical School, USA), Jonel Trebicka (Frankfurt, Germany), Alessio Fasano (Harvard Medical School, USA), Georg Zeller (Heidelberg, Germany).

KEY DATES

The second Oncobiome meeting will take place at the University of TORINO, Italy, organized by Dr Alessio Naccarati mid-January 2020.

At this occasion, Oncobiome will deliver the GOMS in 2L locally advanced or metastatic lung cancer patients (Dr Routy, Dr Derosa, Dr Bonvalet, GR-Montréal, data mining by Dr Iebba, Dr A. Thomas, Dr N. Segata) as well as melanoma GOMS associated with the efficacy or resistance to DC-based vaccines (Dr J. De Vries).

KEY FIGURES



17

teams across 9 European countries and Montréal



9000

cancer patients



25 000

stool biobanking



15

million euros

4 STATUTS OF DISEASE PROGRESSION

