



Microbiota against cancer  
International research program

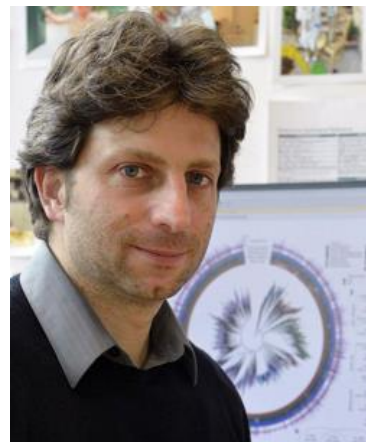
## REVIEW #2

February 2020

**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.**

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**EDITO**



We are very glad to announce almost a year after the kick-off, that the activities in the consortium are progressing as expected and our operative unit already sequenced more than 900 microbiome samples from multiple cohorts and is continuing the sequencing effort with thousands of samples coming from the many cohorts enrolled for the four cancer types that are considered in ONCOBIOME.

**Dr. Nicola Segata,**

*Associate Professor, University of Trento, Italy*

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## **FOCUS ON THE SEGATA LAB INVOLVEMENT IN ONCOBIOME**

Nicola Segata's laboratory at Department CIBIO, University of Trento, employs experimental metagenomic tools and novel computational approaches to study the diversity of the human microbiome across conditions and populations and its role in human diseases. Their work is supported by the European Research Council and by several other European agencies. The projects in the laboratory bring together computer scientists, microbiologists, statisticians, and clinicians and focus on profiling microbiomes with strain-level resolution and on meta-analysing very large sets of metagenomes with novel computational tools.

Relatively new to the field of cancer research he previously performed a large meta-analysis on the link between colorectal cancer and the gut microbiome which spanned many different cohorts and countries. **His team highlighted that there is indeed a strong and reproducible microbiome signature in this type of cancer and also generated few hypotheses on potential mechanisms on the host-microbiome interface.** These results made them

Their main role in the project is to perform most of the metagenomic sequencing for the many cohorts in the ONCOBIOME consortium and to guide the computational analysis efforts. **Metagenomic sequencing of the gut microbiome is performed starting from stool samples and following a series of operations: DNA extraction, preparation of the DNA for sequencing, and sequencing on the most advanced next-generation sequencing machines available today.** They already performed this operation on almost 1,000 samples and will continue to do that at increasing pace. **The key step in the metagenomics is the computational analysis of the sequencing data: his lab developed several open source software tools that are now going to be applied on the ONCOBIOME metagenomic samples to infer at high resolution and accuracy what is the composition of the gut microbiome.**

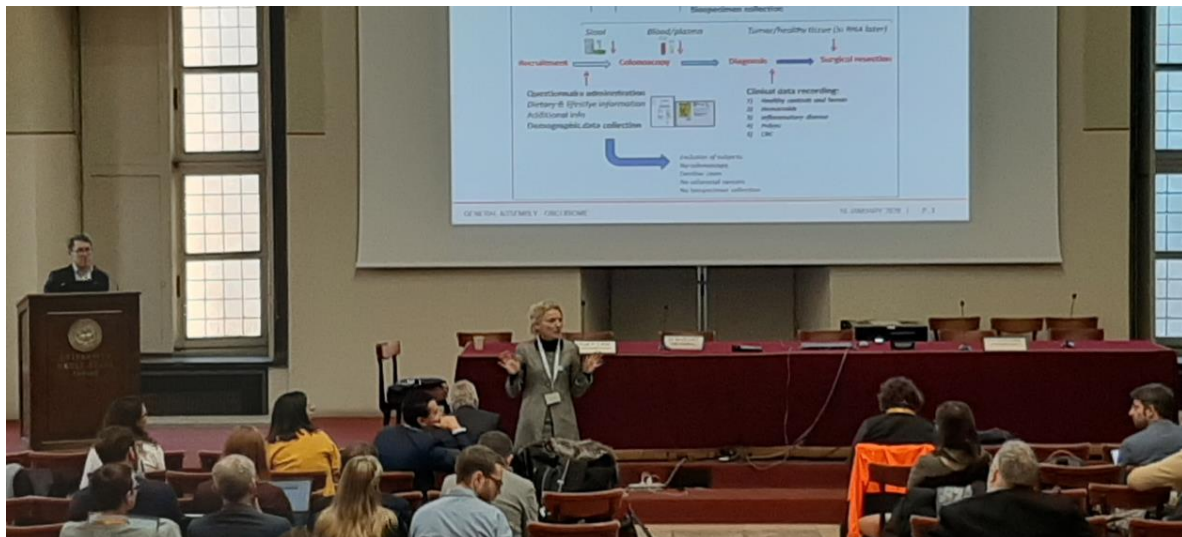
*"We are excited to be part of the project and we look forward to provide our expertise and work to contribute unravelling the diagnostic, prognostic, and treatment potential of the human*

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aware of how the microbiome can be *microbiome in oncology.*" he concluded. crucial in oncology.

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## BACK ON THE FIRST ONCOBIOME GENERAL ASSEMBLY



**In January 16-17, 2020 the first General Assembly (GA) of ONCOBIOME has been held in the Aula Magna of the Rectorate of University of Turin organized by the local Partners, Dr Alessio G. Naccarati (IIGM) and Dr Francesca Cordero (University of Turin) and their staff.**

The GA was preceded by three lectures open to the general audience held by experts on the field of microbiome, metabolism and cancer: Dr George Zeller, Prof Patrice Cani, Scientific Advisory board members of the EU Project, and Prof Guido Kroemer, partner of the Project. These three excellent conferences were focused on the functional links between metabolism, immunity and the microbiota as well as significant advances in the field of metagenomics analyses and their implementation for the accurate diagnosis of colorectal cancer.

After this successful opening and the Steering Committee meeting to overview the current status of the Project, the GA has finally started with the presence of about 50 members: 17 partners across 9 countries. Sections were organized either according to the investigated cancers in the Project or by specific issues, such as the database creation. In the evening, a social dinner has been offered to the participants at the Ristorante Arcadia where they have got the occasion to continue their discussion in a pleasant atmosphere. The second and conclusive day during the Scientific Advisory Board meeting, the members of ONCOBIOME have organized smaller workshops dedicated to specific

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topics to implement the communication between partners and the organization of the Project.

## Significant advances made by the consortium

All the ethical considerations have been addressed according to the European guidelines and solved to allow a transversal translational research and facilitate the acceleration of inter country exchanges. The methodology and processes from stool harvesting, DNA extraction and DNA sequencing have been streamlined across the partners.

Janne Lethtio's team at the Karolinska Institute together with Francesca Cordero, University of Turin, Italy, made considerable progress in establishing the data base to accommodate all cohorts results in the ONCOBIOME iCloud abiding by the GDPR rules.

GENTURIS has identified a repository of stool samples stored in the setting of whole population based-systemic diagnosis of hematuria (FIT) and early diagnosis of colorectal cancer in The Netherlands that could subserve as a tool to address whether dysbiosis precedes the development of extraintestinal malignancies.

The breast cancer groups (University of Cambridge in UK; Marburg University and GBG in Germany) are mainly focusing on triple negative breast cancer cohorts treated with neoadjuvant platinum salt-based chemotherapy +/- anti-PDL-1 Ab, while french partners are analyzing early breast cancers at diagnosis.

The Erlangen group of melanoma experts are collecting stool samples after primary resistance to immune checkpoint blockade, which will be instrumental to analyze the impact of gut dysbiosis in the future therapeutic pipeline of 2L advanced melanoma patients.

A collection of stools and plasma from elite patients (exhibiting markedly pronounced responses to their therapy) and hyper progressors is being performed to allow deep metabolomics and culturomics. Pioneering results linking distinct commensals to precise metabolic profiles or metabolites (prebiotics) were presented.

HalioDX biotech Cie involved in the development of diagnosis tools is providing its expertise for WP3 aimed at analyzing MG profiles together with immunoscore (IS and IS-IC) and tumor genetics in multivariate regression analyses in colon, lung and breast cancers.

EverImmune devoted efforts in the preclinical studies showing the efficacy and safety of oral gavages with *A. muciniphila*, across several cancer mouse models in the avatar (gut humanized) preclinical platform.



## Perspectives

Given the success of the dissemination and website of ONCOBIOME initiative, extra-cohorts outside the H2020 network intend to join the endeavor and will increase the accrual for accelerated stool biobanking and metagenomics (such as Seerave Foundation, Dr Tim Spector UK, Dr Ole Thorlacius-Ussing, Denmark), efforts that our group can accommodate given the progress made in the technology reducing the cost per sample. In this regard, Gustave Roussy Transfer is drafting a collaborative framework to discuss the potential valorization of the findings in and outside the consortium.

The SAB was pleased to meet the investigators and recommended to prospectively demonstrate the deleterious role of antibiotics in cancer patients amenable to immune checkpoint blockade. Even if this recommendation falls outside the endpoints of ONCOBIOME as initially written, the Canadian and IGR physicians agreed and will abide by this recommendation to launch a specific and parallel study in their hospitals.

Workshops will be reconducted in AACR San Diego (April 2020), and IHMC Barcelona (June 2020). Meanwhile, small ONCOBIOME entities sharing their expertise or specimen will reconvene individual sessions.

**The next yearly meeting will be organized in Paris, Centre de Recherche Les Cordeliers, in January 4 and 5, 2021, local organizer Prof. Guido Kroemer, Sylvère Durand, amphitheater Gustave Roussy.**



## ONCOBIOME WEBSITE IS NOW ONLINE

Visit [www.oncobiome.eu](http://www.oncobiome.eu) to be updated on the latest ONCOBIOME news.

## KEY DATES

Meet the ONCOBIOME team at the following events:

- AACR The Microbiome, Viruses, and Cancer / Orlando / Feb 21th – 24th
- Translational Microbiome Conference / Boston / Apr 21st - 23rd
- AACR / San Diego / Apr 24th – 29th
- ASCO / Chicago / May 29th – Jun 2nd

- EACR / Torino / Jun 17th – 20th
- IHMC / Barcelona / Jun 29th - 30th

## KEY FIGURES



**17**

teams across 9 european countries and Montréal



**9000**

cancer patients



**25 000**

stool biobanking



**15**

million euros

Contact : [a-brion@unicancer.fr](mailto:a-brion@unicancer.fr)

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