

RESEARCH ACTIVITY SHEET

2025 PhD selections

YOUR DETAILS

* Name & Surname

Luigi Nezi

* Affiliation IEO

PHD PROJECT DETAILS

* Title of the proposed project

The modulatory role of the gut microbiome on the balance between antigen-specific and bystander immune responses in solid tumors.

* Short description of the project (up to 300 words)

Immunotherapy improved life perspectives of many patients with solid tumors, however, benefits are still limited to a few cancer types and very heterogeneous. In this regard, we were among the first to demonstrate that gut microbiota plays a crucial role in the response to immune checkpoint blockers (*ICB, Gopalakrishan et al. Science 2018*) and our most recent studies revealed that the clinical outcome is the results of local (gut) and systemic interactions between microbial derived factors and the immune system (*Macandog et al. Cell Host&Microb 2024; Ballerini et al. Nat Biomed. Eng. 2025*). In this project we will further develop these concepts, focusing on the balance between immune responses directed against different bacterial antigens and how they influence the antitumor immunity.

* Indicate the main research area for the project described above Immunology

If needed indicate a second research area for the project described above

* Provide up to 3 key words for project:

Anti-tumor immunity, Gut microbiome, Bacterial Antigens

YOUR LABORATORY ACTIVITIES DETAILS

* Main topic/s of the lab

Microbiome and Antitumor Immunity

* Short description of the lab activity (up to 500 words)

Our current research aims to improve efficacy and safety of the immunotherapy by manipulating the gut microbiome. We dedicate great efforts to establishing new clinical studies that meet urgent clinical needs while generating knowledge and reagents to move the seek for better therapies forward. Once at the bench, we model the complexity of the interactions between microbes, immune system and tumors by complementary in vivo and in vitro approaches, leveraging on my expertise on pre-clinical mouse models and a visionary drive to create novel patient-derived ex vivo platforms by mixing culturomics and microfluidic tissue-engineering.

As a scientist, I am convinced that we have in our hands the knowledge and the technology to impact the lives of patients.

* Recent bibliography (max 5 references)

A gut-on-a-chip incorporating human faecal samples and peristalsis predicts responses to immune checkpoint inhibitors for melanoma. Ballerini M, [...] Manzo T, Rasponi M, <u>Nezi L.</u> Nat Biomed Eng, 2025

Longitudinal analysis of the gut microbiota during anti-PD-1 therapy reveals stable microbial features of response in melanoma patients. Macandog ADG, [...], Ascierto PA, Manzo T, <u>Nezi L</u>. Cell Host Microbe, 2024

Location and condition based reconstruction of colon cancer microbiome from human RNA sequencing data. Sambruni G, Macandog AD, [...] <u>Nezi L*</u>, Schaefer MH*. Genome Med. 2023. *Corresponding author.

GZMKhigh CD8+ T effector memory cells are associated with CD15high neutrophil abundance in non-metastatic colorectal tumors and predict poor clinical outcome.

Tiberti S, [...], Lugli E, <u>Nezi L*</u>, Manzo T* Nat Commun, 2022 *Equal contribution.

Accumulation of long-chain fatty acids in the tumor microenvironment drives dysfunction in intrapancreatic CD8+ T cells.

Manzo T*, [...] Navin NE, Caprioli RM, Greenberg PD, Draetta G, <u>Nezi L*</u> J Exp Med, 2020 *Equal contribution.

* Group composition: total members, and roles distribution (PhD, postdoc, technician, etc.)

3 postdoc (wet), 3 postdoc (computational), 1 PhD student, 1 Research Assistant, 1

Master student

Institutional page link

https://www.research.ieo.it/research-and-technology/principal-investigators/luigi-nezi/

Lab website link, if any

Social media links, if any

If you prepare a video to promote your lab/project, please include the link below