RESEARCH ACTIVITY SHEET

2025 PhD selections

YOUR DETAILS

* Name & Surname: Giuseppe Leuzzi

* Affiliation IFOM

PHD PROJECT DETAILS

* Title of the proposed project

Defining the impact of Single Nucleotide Variants (SNVs) on cancer immunity

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

Many cancer-associated Single Nucleotide Variants (SNVs) remain poorly understood and are classified as variants of uncertain significance (VUSs). Understanding the functional impact of these SNVs on immunotherapy response is critical for identifying new biomarkers and therapeutic opportunities to improve cancer treatment outcomes.
Recent advances in genome editing technologies, such as CRISPR-dependent base editing, now enable the precise introduction of cancer-associated SNVs into target genes at scale. This project will leverage these tools to systematically investigate the impact of SNVs in DNA damage response (DDR) and immune-related genes on DNA repair, immune signaling, and tumor immunogenicity. By identifying mutations that drive immune evasion and therapy resistance, this project aims to uncover novel biomarkers for more effective and personalized cancer immunotherapies.

* Indicate the main research area for the project described above Molecular Biology

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

* Provide up to 3 key words for project:

SNVs, Immunotherapy, CRISPR-dependent base editing

YOUR LABORATORY ACTIVITIES DETAILS

* Main topic/s of the lab

DNA damage response, Cancer immunity, High-throughput functional genomics

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

Our lab studies how DNA damage response (DDR) pathways and genomic instability influence immune signaling and tumor immune evasion, aiming to uncover new therapeutic targets to improve cancer immunotherapy. To this end, we employ **high-throughput functional genomics** approaches, such as **CRISPR-based platforms**, to conduct gene knockout (CRISPR-KO) and mutagenesis (CRISPR-BE) **screens** *in vitro* and *in vivo*. These approaches, combined with **multi-omics** and **biochemical tools**, enable us to systematically identify specific DDR factors and single nucleotide variants (SNVs) that modulate tumor immunogenicity and response to immune checkpoint blockade (ICB) therapy.
By integrating these techniques with cellular and molecular biology assays, we dissect the mechanisms by which DDR pathways influence tumor immunogenicity. For example, we use **DNA repair assays** (e.g., metaphase spreads, comet assays, and DNA fiber assays) to study replication dynamics and genomic instability, **gene expression analysis** to evaluate innate immune signaling, and **co-culture systems** to monitor functional interactions between tumor and immune cells. Additionally, we leverage ***in vivo* studies** to evaluate how DDR modulation affects anti-tumor immunity and response to ICB therapy.
By integrating cutting-edge technologies with mechanistic and in vivo studies, we aim to uncover novel DDR targets and biomarkers for immuno-oncology treatments while advancing personalized cancer immunotherapy.

* Recent bibliography (max 5 references)

PMID: 38301646, PMID: 37026695, PMID: 33606978

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

1 Group Leader

Institutional page link

https://www.ifom.eu/en/cancer-research/programs/

Lab website link, if any

https://www.leuzzilab.com

Social media links, if any

https://www.linkedin.com/in/giuseppe-leuzzi-18616455/

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