

RESEARCH ACTIVITY SHEET

2025 PhD selections

YOUR DETAILS

* Name & Surname

Giuseppe Leuzzi

* Affiliation IFOM

PHD PROJECT DETAILS

* Title of the proposed project

Uncovering DDR Factors that influence tumor immunogenicity

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

The immune system plays a critical role in defending against cancer by identifying and eliminating tumor cells. However, as tumors evolve, they acquire mutations and chromosomal alterations that modify their ability to provoke immune responses—a phenomenon known as tumor immunogenicity. Understanding the molecular mechanisms behind this phenomenon is crucial for improving immunotherapy outcomes and developing new immuno-oncology strategies.

Recent studies have shown that DNA damage response (DDR) pathways play a key role in modulating tumor immunogenicity. Yet, the specific DDR factors involved remain poorly understood. This project aims to identify the DDR factors that regulate tumor immunogenicity, characterize the molecular mechanisms by which they do so, and explore their therapeutic potential as targets for cancer immunotherapy.

Using CRISPR-Cas9 screening platforms developed in our lab, we will systematically identify DDR factors that modulate tumor immunogenicity. Advanced cellular and molecular biology techniques will then be used to determine how these factors influence the DNA damage response, cancer cell-intrinsic innate immunity, and tumor-immune interactions. Co-depletion experiments will help us investigate the functional relationships among these DDR factors, while in vivo studies will clarify their roles in anti-tumor immunity and responses to immune checkpoint blockade (ICB) therapy.

This multidisciplinary project seeks to uncover novel immuno-oncology strategies and identify new therapeutic targets to enhance the effectiveness of 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:

DNA damage response (DDR), CRISPR screening, Immunotherapy

YOUR LABORATORY ACTIVITIES DETAILS

* Main topic/s of the lab

DNA damage response (DDR), 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

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

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