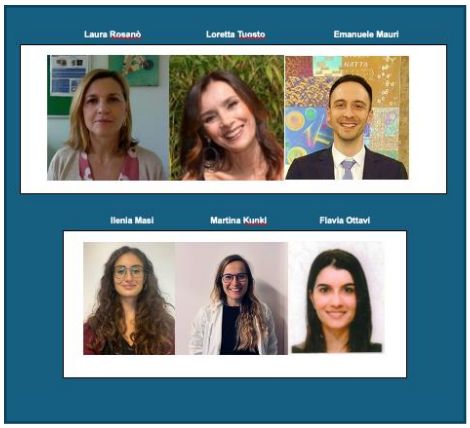
Project title: Improving ovarian cancer immunotherapy by the combination of Discoidin Domain Receptor 2 blockade and bispecific antibodies targeting CD28 and tumour-associated antigens



Partners:

- IBPM-CNR: Laura Rosanò (UO)
- Università di ROMA "La Sapienza": Loretta Tuosto (PI)
- Politecnico di MILANO: Emanuele Mauri (UO)

laura.rosano@cnr.it

Description:

Immunotherapy is an emerging cancer treatment, but responses to checkpoint blockade in high-grade serous ovarian cancer (HG-SOC) have been disappointing, despite the presence of tumor-infiltrating T lymphocytes (TILs). Tumor-targeted recombinant bispecific antibodies (BsAbs) are being developed to selectively recruit and activate tumor-specific T cells by binding to tumor-associated antigens (TAAs) and costimulatory receptors on T cells, with CD28 being a key receptor for T cell activation. The fibroblasts in the tumor microenvironment (TME) can hinder immunotherapy efficacy by secreting collagens that exclude TILs. Additionally, abnormal activity of collagen receptors like Discoidin Domain Receptors (DDR) 1 and 2 is linked to immune exclusion.

Aims:

Using HG-SOC cells, T cells, and 3D organotypic models, we will evaluate the therapeutic efficacy of combinatory CD28xTAA bispecific antibodies (BsAbs) and DDR2 inhibitors, both as free therapeutics and functionalized on engineered polymer nanoparticles. We aim to assess:

1. Tumor-specific T cell responses and the effects on HG-SOC cell proliferation, EMT, invadopodia, ECM deposition, and invasion.
2. Tumor-immune system interactions driving tumor growth and progression in organotypic models.

Expected results:

The expected outcomes of the project are to establish innovative immunotherapeutic strategies combining the blockade of DDR2 with the use of CD28xTAA BsAbs to improve the safety and efficacy of HG-SOC therapies. The project seeks to establish a preclinical platform for testing additional immunotherapeutic approaches in vitro and generating preclinical data for translation into animal models. This will be achieved by utilizing HG-SOC-specific T cells, 3D organotypic models, and nanotechnologies.

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