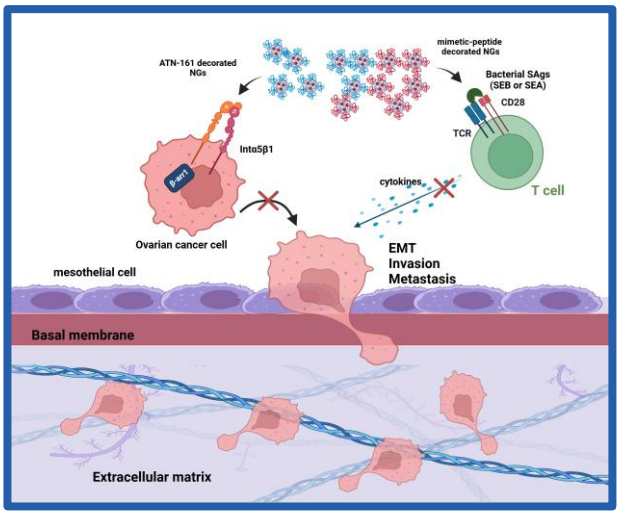
Ministero dell'Università e della Ricerca

PRIN

Project title: Dissecting how microenvironment remodelled by tumor and stromal cells facilitate ovarian cancer metastasis: interaction between integrins and microbiome



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Description

Integrins serve as signaling molecules and mechanotransducers that regulate cancer progression, especially in high-grade serous ovarian cancer (HG-SOC). Integrin β1 (Intβ1) influences intraperitoneal spread and metastasis towards the omentum. Various proteins, including the scaffolding protein β-arrestin1 (β-arr1), associate with the integrin adhesion complex to modulate intracellular activation. β-arr1 is essential for invasive signaling, pericellular proteolysis, and the communication with stromal cells in the metastatic niche. Additionally, Staphylococcus aureus in the female reproductive tract produces superantigen toxins (SAgs) that stimulate T cells, promoting inflammatory responses that may enhance metastatic progression.

Aims

By using HG-SOC cells, omental-derived mesothelial cells (MCs), T cells, and 3D organotypic models, we aim to:

1. Define the interaction between β-arr1/Intβ1 and Staphylococcus aureus-mediated SAgs, which bind the T cell receptor and CD28 costimulatory molecule on T cells, in reinforcing invasive signaling and interaction with MCs, gaining access to the submesothelial matrix.

3. Evaluate the feasibility of targeting Intαβ1 with ATN161 **and CD28, with p1TA and p2TA mimetic peptides,** as free therapeutics and as functionalization of engineered polymer nanoparticles, to interrupt tumor/stroma signaling reciprocity.

Expected results

The expected outcomes of the project are to **shed light on n** cooperation between oncobiome and cell-autonomous **intβ1** signalling in driving HG-SOC metastatic processes, **which may be pharmacologically tractable, and provide a relevant model platform for translational studies.**

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