PROJECT 1

DoS: Marco E. Bianchi

Title: CXCR4-mediated antitumor immunization

Curriculum: Basic and Applied Immunology and Oncology

Link to OSR/UniSR personal page:https://www.unisr.it/docenti/b/bianchi-marco-emilio

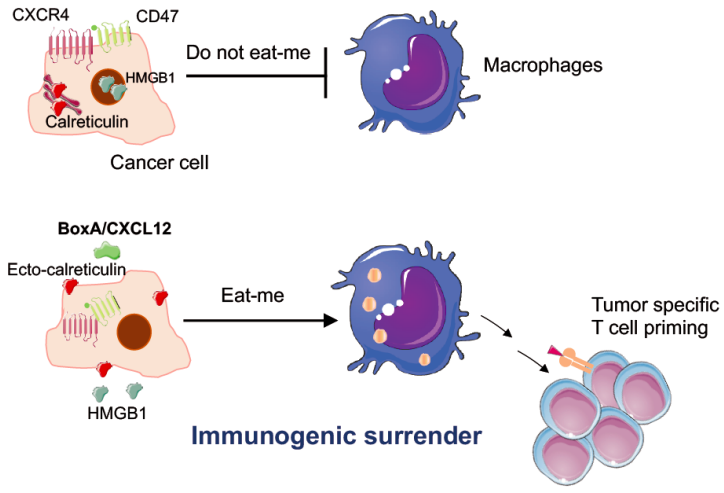
Project description (*Number of characters, including spaces*: 2.000 - 3.000):
We offer a PhD position, funded by an AIRC project started in 2021, to further investigate the molecular and cellular mechanisms of a novel immunosurvellaince process that we named Immunogenic Surrender.

Current work in our lab (1) has unveiled an antitumor activity of CXCR4, a G-Protein Coupled Receptor, which weighs on the risk/benefit balance of promoting tissue (re)growth. Tissue regeneration and cancer progression often recapitulate developmental processes, involving the same pathways and key players. The alarmin HMGB1 and the chemokine CXCL12 promote the regeneration of multiple tissues via the activation of CXCR4 (2,3). CXCR4 activation also promotes cancer growth and invasion (1,3).

We have found that CXCR4 activation flags tumor cells to immune recognition (1). Both CXCL12, a natural CXCR4 ligand, and BoxA, a fragment of HMGB1, promote the exposure of Damage Associated Molecular Patterns and the internalization of CD47, a “don’t eat me” signal. This leads to phagocytosis of tumor cells by macrophages, and protective T-cell-dependent antitumor immunity. We called this process Immunogenic Surrender because tumor cells turn themselves in to the immune system, thereby subjecting a rapidly growing (but “illegal”) tissue to immunological scrutiny.

The project consists in understanding which cells mediate Immunogenic Surrender in vivo, focusing on macrophages (either tumor-resident or monocyte-derived) and DCs. The location of the consequent interaction of macrophages/DCs with CD4 cells (in cancer tissue vs lymph nodes or spleen) is also of interest. Finally, we want to understand whether the state of the target cancer cells (proliferating vs non-proliferating vs dead)plays a role.

Although this is primarily a project of basic immunology and cell biology, there is a potential translational application to cancer therapy.



Skills to be acquired by the student:

- work with cancer models developed in-house

- learn about immune responses to cancer, and how to measure them by flow cytometry and cell imaging assays

References (max. 3)

1. Mezzapelle R… and Bianchi ME (2021) CXCR4 engagement triggers CD47 internalization and antitumor immunization in a mouse model of mesothelioma. EMBO Mol Med, in press
2. Tirone M, … Bianchi ME* and Vénéreau E* (*equal contribution). High Mobility Group Box 1 orchestrates tissue regeneration via CXCR4. J Exp Med 2018, 215: 303-18. doi: 10.1084/jem.20160217
3. Bianchi ME and Mezzapelle R (2020) The chemokine receptor CXCR4 in cell proliferation and tissue regeneration. Front Immunol 11:2109. doi: 10.3389/fimmu.2020.02109. PMID: 32983169