

PROJECT 1DoS: Renato OstuniTitle: Dissection and therapeutic exploitation of macrophage diversityCurriculum: Gene and Cellular Therapy

Link to OSR/UniSR personal page:

<https://research.hsr.it/en/institutes/san-raffaele-telethon-institute-for-gene-therapy/genomics-of-the-innate-immune-system.html>**Project description** (*Number of characters, including spaces: 2.000 - 3.000*):

Macrophages

The development of single-cell genomic technologies has revolutionized our understanding of cellular heterogeneity and tissue organization. In this context, cells of the innate immune system - such as macrophages - provide paradigmatic examples of how complex environmental inputs are integrated into a wide array of phenotypic and functional states. On the one hand, cell heterogeneity underlies the multifaceted activities of resident macrophages during homeostasis, tissue damage and regeneration. On the other hand, rational manipulation of macrophage diversity via cell and gene therapy approaches is of extreme relevance for the treatment of cancer. In this project, the candidate will employ technologies for spatial RNA-sequencing and combine them with multiparametric immunofluorescence to map the sub-tissular localization and transcriptional heterogeneity of innate immune cells. Specifically, she/he will dissect the complex network of physical and soluble interactions of macrophages with stromal and stem cell niche components in the bone marrow and the pancreas, target organs of primary relevance for cell and gene therapies. The candidate will also determine how tissue perturbations, such as those associated to cancer development or chemotherapy, impact on cell-cell dynamics. If successful, this project will reveal fundamental principles of tissue organization and immune homeostasis.

Skills to be acquired by the student:

The candidate is expected to develop critical thinking and appropriate degrees of scientific independence and organization/presentation skills. She/he will gain experience with bulk, single-cell and spatial transcriptomics, as well as with advanced tissue imaging methods. By closely interacting with an existing network of computational biologists, she/he will gain familiarity with data analysis tools and will learn to productively operate in an interdisciplinary context.

References (max. 3)

Determinants, mechanisms, and functional outcomes of myeloid cell diversity in cancer. Caronni N, Montaldo E, Mezzanzanica L, Cilenti F, Genua M, Ostuni R. **Immunol Rev.** 2021

Adaptation and memory in immune responses. Natoli G, Ostuni R. **Nat Immunol.** 2019

Heterogeneity of neutrophils. Ng LG, Ostuni R, Hidalgo A. **Nat Rev Immunol.** 2019