

TOPIC PNRR8

Project title	Dissecting the role of innate immunity in emerging infections: impact of soluble and intracellular molecules
Curriculum (standard or clinical)	Standard
Principal Investigator	Diletta Di Mitri
Lab name	Tumor Microenvironment Unit
Main field of interest	Innate immunity, macrophages, regulation of inflammation
Abstract	<p>The lines of research ongoing on in the Unit are focused on the profiling of immune system composition and immune cell dynamics in cancer, infectious and inflammatory diseases by mean of single-cell based technologies including scRNAseq, Cytomass and multiparametric Flow Cytometry. Main scope is the dissection of mechanisms that regulate the innate immune response in pathology, with a specific focus on macrophages. Transgenic and transplantable mouse models are employed to validate human data and test novel therapeutic approaches.</p> <p>This PhD project will investigate the crosstalk between innate immune components and pathogens. Main aim is to unravel novel mechanisms of interaction that can be targeted to prevent or treat infections. Among others, highly pathogenic coronaviruses, including SARS-CoV-2, will be investigated. During this project the PhD student will contribute to the dissection of the mechanism of action of the anti-viral and anti-bacteria activity of phagocytes, as well as the functional consequences of the interaction between pathogens and macrophages.</p> <p>The project will benefit from a collaboration with virologists at Università Vita Salute San Raffaele.</p>
Brief description of the coherence of the Project in relation to the	<p>Among others, this PNRR project has the ambition to fill gaps in knowledge of the biological characteristics on highly diffusible pathogens with a multidisciplinary approach and enhance the level of basic knowledge on highly diffusible pathogens.</p> <p>In particular, the WP1 will to define the molecular and cellular events that</p>

PNRR objectives	<p>mark the interaction between pathogens and target human cells and describe innate and adaptive immune responses elicited by the infection and identify those responses that are either pathogenetic or protective. The PhD project is placed in this line of activities, as it will be focused on the investigation of the role of innate immunity molecules in emerging infections.</p>
PNRR project title	<p><i>One Health Basic and Translational Research Actions addressing Unmet Needs on Emerging Infectious Diseases</i></p>
CUP	<p>B23C22000810006</p>
Scientific references	<ul style="list-style-type: none"> - Lipid-loaded tumor-associated macrophages sustain tumor growth and invasiveness in prostate cancer. Masetti M, Carriero R,Di Mitri D. J Exp Med. 2022 Feb 7;219(2):e20210564. doi: 10.1084/jem.20210564. Epub 2021 Dec 17. PMID: 34919143 - Di Mitri D, et al. Re-education of Tumor-Associated Macrophages by CXCR2 Blockade Drives Senescence and Tumor Inhibition in Advanced Prostate Cancer. Cell Rep. 2019 Aug 20;28(8):2156-2168.e5. doi: 10.1016/j.celrep.2019.07.068. - Stravalaci M, Garlanda C. Recognition and inhibition of SARS-CoV-2 by humoral innate immunity pattern recognition molecules. Nat. Immunol. 2022. Nat Immunol. 2022 Feb;23(2):275-286. doi: 10.1038/s41590-021-01114-w. - Brunetta E, et al. Macrophage expression and prognostic significance of the long pentraxin PTX3 in COVID-19. Nat Immunol. 2021 Jan;22(1):19-24. doi: 10.1038/s41590-020-00832-x. - Salvi V, et al. SARS-CoV-2-associated ssRNAs activate inflammation and immunity via TLR7/8. JCI Insight. 2021 Sep 22;6(18):e150542. doi: 10.1172/jci.insight.150542.
Required skills to carry out the project	<p>Basic skills in cellular biology and molecular biology are required.</p>