RESEARCH TOPIC MEM22
Unravelling the role of the innate immune response in resistance to anti-cancer therapies

Curriculum MEM

Laboratory name
Tumor microenvironment Unit
IRCCS Humanitas

Pre-clinical Supervisor
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Abstract
Immune checkpoint blockade (ICB) has revolutionized cancer care yet is ineffective in most patients. Predicting which patients will respond to ICB and personalizing the therapy to improve response are major challenges. We and others have discovered that macrophages infiltrating tumors can promote cancer progression in association with poor ICB response. Still whether specific subsets of macrophages, and more in general if a definite tumor microenvironment (TME), are predictive of ICB efficacy and which are the mechanisms behind this remain unexplored. Our objective is to determine how cells in the TME limit the efficacy of anti-cancer immunotherapies and to develop novel therapies. We will explore the link between TME and ICB efficacy in samples from patients and in murine models using single cell-based approaches, including scRNAseq and Imaging Mass Spectometry. Our work will provide insight in the TME to identify patient-specific approaches that improve therapeutic efficacy in cancer.

Main technical approaches
Basic knowledge of cellular and molecular biology techniques. Expertise in analysis of data from single cell-based approaches (scRNAseq, Imaging Mass spectrometry) will be considered as a plus.

Scientific references
Marelli G, Morina N, Portale F, Pandini M, Iovino M, Di Conza G, Ho PC, Di Mitri D. Lipid-loaded macrophages as new therapeutic target in cancer. J Immunother Cancer. 2022 Jul;10(7):e004584. doi: 10.1136/jitc-2022-004584. PMID: 35798535

Alvisi G, Termanini A, Di Mitri D, Lugli E, Lleo A. Multimodal single-cell profiling of intrahepatic cholangiocarcinoma defines hyperactivated Tregs as a potential therapeutic target. J Hepatol. 2022 Jun 20:S0168-8278(22)00370-1. doi: 10.1016/j.jhep.2022.05.043

Masetti M., Carriero R, Di Mitri D. Lipid-loaded tumor-associated macrophages sustain tumor growth and invasiveness in prostate cancer. JEM 2021.

Di Mitri D, De Bono J, Alimonti A. Re-education of Tumor-Associated Macrophages by CXCR2 Blockade Drives Senescence and Tumor Inhibition in Advanced Prostate Cancer. Cell Reports. 2019 Aug 20;28(8):2156-2168.e5. doi: 10.1016/j.celrep.2019.07.068.

Di Mitri D, Alimonti A. Tumour-infiltrating Gr-1+ myeloid cells antagonize senescence in cancer. Nature. 2014 Nov 6;515(7525):134-7. doi: 10.1038/nature13638. Epub 2014 Aug 24. PubMed PMID: 25156255.

Brief description of the coherence of the project in relation to the PNRR objectives

Among the objectives of the PNRR project, personalized medicine plays a key role. The present proposal aims at unveiling the mechanisms behind cancer resistance to immunotherapies. The hypothesis is that each patient may have a different tumoral microenvironment, which contributes specifically to hinder (or support) therapy. Discovering which mechanisms are involved in this will permit to identify the most appropriate therapies for each patient and to reveal targets predictive of response that in turn allow a stratification of patients.

N. of months abroad

6 months, at CNIO in Madrid, Cancer Immunity group, Dr. Maria Casanova Acebes

Type of contract

PhD scholarship of € 18.000 gross per year awarded by Humanitas University on institutional funds and cofounded with PNRR funds under M.D.M. D.D. N. 118/2023.
This sum is exempt from IRPEF income tax according to the provisions of art. 4 of Law no. 476 of 13th August 1984, and is subject to social security contributions according to the provisions of art. 2, section 26 and subsequent sections, of Law no. 335 of 8th August 1995 and subsequent modifications.

Borsa di dottorato pari a € 18.000 annui lordi erogata da Humanitas University su fondi istituzionali e fondi da D.M. 118/2023. Importo non soggetto a tassazione IRPEF a norma dell'art. 4 della L. 13 agosto 1984 n. 476 e soggetto, in materia previdenziale, alle norme di cui all'art. 2, commi 26 e segg., della L. 8 agosto 1995, n. 335 e successive modificazioni.