RESEARCH TOPIC MEM17
Molecular mechanisms of resistance to immune checkpoint blockade

Curriculum MEM standard

Research Area
Immuno

Laboratory name
Lab of Translational Immunology

Research Supervisor
Enrico Lugli enrico.lugli@humanitasresearch.it
Emilia Mazza emilia.mazza@humanitasresearch.it

Abstract
T lymphocytes in human tumors are characterized by loss of effector functions and proliferation that are otherwise reinvigorated by checkpoint blockade immunotherapy. The molecular mechanisms at the basis of successful immune responses are still under investigation. We have identified novel molecular signals regulating the superior function of T cells leading to successful tumor regression in responding patients, or mediating resistance to therapy in non-responders. Several human samples from cancer patients undergoing clinical trials with immunotherapy are routinely available for this purpose thanks to collaborations with the Humanitas Hospital. We will apply novel genome-wide sequencing technologies and high-dimensional single cell profiling to primary samples to uncover genome organization and regulation of anti-tumor immunity.

Main technical approaches
Cellular and molecular immunology, genomics including at the single cell level, cellular and DNA metabolomics, high-dimensional flow cytometry, bioinformatics (with the support of in-lab expertise) genetic perturbations and functional assays applied to human patients' samples

Scientific references

1. Whiteside SK, et al. Acquisition of suppressive function by conventional T cells limits antitumor immunity upon T(reg) depletion. Science immunology. 2023;8(90):eabo5558.
2. Wischnewski V, et al. Phenotypic diversity of T cells in human primary and metastatic brain tumors revealed by multiomic interrogation. Nat Cancer. 202310.1038/s43018-023-00566-3.

3. Alvisi G, et al. Multimodal single-cell profiling of intrahepatic cholangiocarcinoma defines hyperactivated Tregs as a potential therapeutic target. J Hepatol. 2022;77(5):1359-1372.
4. Galletti G, et al. Two subsets of stem-like CD8(+) memory T cell progenitors with distinct fate commitments in humans. Nat Immunol. 2020. Accompanying commentary by Chu et al "Two parallel worlds of memory T cells".
5. Alvisi G, et al. IRF4 instructs effector Treg differentiation and immune suppression in human cancer. J Clin Invest. 2020;130(6):3137-50.

Type of contract
Scholarship of € 25.000 gross per year awarded by Fondazione Humanitas HFR. This sum is subject to IRPEF income tax and exempt from social security contributions.

Borsa di studio pari a € 25.000 annui lordi erogata da Fondazione Humanitas HFR. Importo soggetto a tassazione IRPEF ed esente da contribuzione previdenziale.

Humanitas University
Via Rita Levi Montalcini, 4
20072 Pieve Emanuele (MI) Italy
Tel +39 0282241 - Fax +39 0282242394
info@hunimed.eu
hunimed.eu
CF 97692990159