RESEARCH TOPIC MEM10

Dissecting immune cell diversity in cancer to unveil distinct contributions to therapeutic resistance

Curriculum MEM standard

Research Area

Immuno

Laboratory name

Tumor and Microenvironment Unit

Research Supervisor

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Abstract

Across all cancer types, the overall survival of patients with advanced tumor is limited in most cases. Therefore, the treatment of metastasis is the most needed but highly challenging task in the field of oncology. Considering their success in some types of cancers, immunotherapies, including Immune Checkpoint Inhibitors (ICIs), are now considered as groundbreaking in the treatment of tumors. However, despite efficacy in a portion of cancer patients, yet immunotherapies are ineffective in a significant number of cases and the mechanisms underlying resistance are largely unknown. Importantly, the efficacy of immunotherapies is still limited in metastasis. If we are now aware of the key role played by the tumor microenvironment in disease progression and therapy resistance, still a comprehensive profiling of the TME in metastatic lesions at cellular and molecular level is missing. My proposal provides a perspective for understanding the immune landscape of tumors in different anatomical regions. We will generate knowledge on the regional immune composition to develop site specific therapies. In addition, we will exploit this information to unveil immune-related mechanisms of response and resistance to immunotherapies.

Main technical approaches

Basic skills in cellular biology and molecular biology are required.

Scientific references

1. Edwards, S. C., Hoevenaar, W. H. M. & Coffelt, S. B. Emerging immunotherapies for metastasis. Br J Cancer 124, 37-48, doi:10.1038/s41416-020-01160-5 (2021).2. Syn, N. L., Teng, M. W. L., Mok, T. S. K. & Soo, R. A. De-novo and acquired resistance to immune checkpoint targeting. Lancet Oncol 18, e731-e741, doi:10.1016/S1470- 2045(17)30607-1 (2017).

3. Di Mitri, D. et al. Tumour-infiltrating Gr-1+ myeloid cells antagonize senescence in cancer. Nature 515, 134-137, doi:10.1038/nature13638 (2014).

4. Marelli, G. et al. Lipid-loaded macrophages as new therapeutic target in cancer. J Immunother Cancer 10,doi:10.1136/jitc-2022-004584 (2022).

5. Masetti, M. et al. Lipid-loaded tumor-associated macrophages sustain tumor growth and invasiveness in prostate cancer. J Exp Med 219, doi:10.1084/jem.20210564

Type of contract

PhD scholarship of € 21.000 gross per year awarded by Humanitas University. 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 € 21.000 annui lordi erogata da Humanitas University. 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.

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