RESEARCH TOPIC MEM 13

Role of chemokine receptors in neutrophil differentiation and effector activities in tumor microenvironment
Curriculum MEM

Laboratory name
Chemokine biology**,** University Campus, Bldg C

Pre-clinical Supervisor
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Abstract
Neutrophils, that are essential to protect the host during infections, are also able to exert tumor-suppressive effects controlling cancer progression but are often subverted in their functions by tumor microenvironment. Our preliminary data indicate that expression of chemokine receptors by neutrophils not only dictates the egress of neutrophils from the bone marrow (BM) and their trafficking to tissues but also their differentiation and activation state.
We will test the hypothesis that targeting chemokine receptors will improve the anti-tumoral activity of neutrophils and can enhance the response to standard therapies and to checkpoint inhibitors in tumors such as melanoma and glioblastoma, where neutrophils are able to inhibit tumor growth and immunotherapies are showing significant promise.

Main technical approaches
FACS analysis
Gene expression
In vivo tumor models

Scientific references
1. Bonecchi R, Mantovani A, Jaillon S. Chemokines as Regulators of Neutrophils: Focus on Tumors, Therapeutic Targeting, and Immunotherapy. Cancers (Basel). 2022 Jan 28;14(3):680.

2. Zippoli M, Ruocco A, Novelli R, Rocchio F, Miscione MS, Allegretti M, Cesta MC, Amendola PG. The role of extracellular vesicles and interleukin-8 in regulating and mediating neutrophil-dependent cancer drug resistance. Front Oncol. 2022 Dec 16;12:947183.

3. Jaillon S, Ponzetta A, Di Mitri D, Santoni A, Bonecchi R, Mantovani A. Neutrophil diversity and plasticity in tumour progression and therapy. Nat Rev Cancer. 2020 Sep;20(9):485-503.

4. Massara M, Bonavita O, Savino B, Caronni N, Mollica Poeta V, Sironi M, Setten E, Recordati C, Crisafulli L, Ficara F, Mantovani A, Locati M, Bonecchi R. ACKR2 in hematopoietic precursors as a checkpoint of neutrophil release and anti-metastatic activity.Nat Commun. 2018 Feb 14;9(1):676.

5. Chemokines and Chemokine Receptors: New Targets for Cancer Immunotherapy. Mollica Poeta V, Massara M, Capucetti A, Bonecchi R.Front Immunol. 2019 Mar 6;10:379.

Brief description of the coherence of the project in relation to the PNRR objectives
The project will provide a significant development of knowledge in the field of inflammation and cancer. It will precisely describe the role of chemokine receptor signaling in neutrophil biology using single-cell technologies, RNA sequencing and multiparametric FACS analysis that will be analysed with artificial intelligence methods such as dimensionality reduction (PCA, tSNE and UMAP). These results will identify new targets for precision medicine of tumor patients

N. of months abroad
6 months, at Department of Microbiology, Immunology and Transplantation Rega - Herestraat 49 - box 1042 3000 Leuven
or
Department of Infection and Immunity, Immuno-Pharmacology and Interactomics Luxembourg Institute of Health

N. of months at the cofounding company
6 months, at Dompè Farmaceutici SPA Via Campo di Pile, 1, 67100 L'Aquila

Type of contract
PhD scholarship of € 18.000 gross per year awarded by Humanitas University PNRR funds under M.D.M. D.D. N. 117/2023 and cofounded by Dompé Farmaceutici.
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 da D.M. 117/2023 e cofinanziata da Dompé Farmaceutici. 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.