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HUMANITAS UNIVERSITY

RESEARCH TOPIC MEM5
Single-cell analysis to identify signatures of response to immunotherapy in Diffuse Large B-cell Lymphoma

Curriculum MEM

Laboratory name
Lymphoma Translational Research Lab
Humanitas University Campus, Bldg C

Pre-clinical Supervisor
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Abstract
A variety of novel antibody-based immunotherapies (Bispecifics, Antibody Drug Conjugates) are increasingly used for the treatment of relapsed/refractory Diffuse Large B-Cell Lymphoma. However, response-predicting biomarkers and mechanisms of resistance to immunotherapy remain largely unknown. To address these issues, we designed a translational research project focusing on single cell (sc)RNA-seq and scTCR-seq to characterize the transcriptional and immunological profiles of peripheral blood mononuclear cells. We will perform scRNA-seq and scTCR-seq on longitudinally collected PBMCs to elucidate the contribution of immune cells at baseline and during immunotherapy and to identify relevant receptor clonotypes and track their evolution during treatment. This will allow to (i) identify signatures of response to antibody-based immunotherapy, (ii) increase our knowledge on the mechanisms of resistance to immunotherapy, and (iii) improve the upfront identification of refractory patients.

Main technical approaches
DNA-seq, scRNA-seq, scTCR-seq

Scientific references
Reichel J., Chadburn A., Rubinstein PG., Giulino-Roth L., Tam W., Liu Y., Gaiolla R., Eng K., Brody J., Inghirami G., Carlo-Stella C., Santoro A., Rahal D., Totonchy J., Elemento O., Cesarman E., Roshal M.: Flow-sorting and exome sequencing reveals the oncogenome of primary Hodgkin and Reed-Sternberg cells. Blood 125:1061-1072, 2015

Brief description of the coherence of the project in relation to the PNRR objectives
Antibody-based immunotherapy using bispecific antibodies or antibody drug-conjugate is increasingly used in patients with refractory lymphoma. However, response-predicting biomarkers and mechanisms of resistance to immunotherapy remain largely unknown. We designed a translational research project to characterize peripheral blood mononuclear cells' transcriptional and immunological profiles in lymphoma patients treated with immunotherapy. The project will allow to:

1. Identify signatures of response to antibody-based immunotherapy.
2. Increase our knowledge of the mechanisms of resistance to immunotherapy.
3. Improve the upfront identification of refractory patients.

The proposed project is coherent with the PNRR objectives.

N. of months abroad
6 months, at Institute Of Oncology Research, Bellinzona, Switzerland

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.