



RESEARCH TOPIC-MEM17

TO EVALUATE THE ROLE OF INNATE IMMUNITY IN TUMOR IMMUNOEDITING AND IN RESPONSE TO CANCER IMMUNOTHERAPIES

Curriculum MEM Standard

Laboratory name: Laboratory of experimental immunopathology, Humanitas University

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Abstract

Cancer-related inflammation, including the presence of inflammatory leukocytes in the tumor microenvironment (TME) is recognised as a hallmark of cancer. Neutrophils are present in the TME but their role in cancer remains poorly understood and controversial. Recently, our group revealed the clinical significance of tumor-associated neutrophils in patients with colorectal cancer (Galdiero MR et al, 2016) and that neutrophils play an essential role in the induction of a novel antitumor response in mice and selected human tumors (Ponzetta A et al, 2019).

Using a multitask approach, combining state-of-the-art technologies, genetically engineered mice, models of primary carcinogenesis and investigation in human samples, our project aims to dissect the role played by neutrophils in the process of tumor immunoediting (the process in which the host immune system shapes the tumor fate) and in response to cancer immunotherapies. Our project can pave the way for innovative therapeutic approaches.

Main technical approaches

- Animal handling (Murine models of carcinogenesis)
- Blood and tissues sampling from mice
- Cellular Biology (purification and culture of cells from blood and tissues, culture of cell lines)
- Flow cytometry
- Molecular Biology (PCR, Real-time PCR, RNAsequencing)
- Bioinformatics analysis

Scientific references

1. Neutrophils driving unconventional T cells mediate resistance against murine sarcomas and selected human tumors.

Ponzetta A, Carriero R, Carnevale S, Barbagallo M, Molgora M, Perucchini C, Magrini E, Gianni F, Kunderfranco P, Polentarutti N, Pasqualini F, Di Marco S, Supino D, Peano C, Cananzi F, Colombo P, Pilotti S, Alomar SY, Bonavita E, Galdiero MR, Garlanda C, Mantovani A, Jaillon S. Cell. 2019. Jul 11;178(2):346-360.

2. IL-1R8 is a checkpoint in NK cells regulating anti-tumor and anti-viral activity.

Molgora M, Bonavita E, Ponzetta A, Riva F, Barbagallo M, Jaillon S, Popović B, Bernardini G, Magrini E, Gianni F, Zelenay S, Jonjić S, Santoni S, Garlanda C, Mantovani A. *Nature*. 2017. Nov 2;551(7678):110-114.

3. Occurrence and significance of tumor-associated neutrophils in patients with colorectal cancer.

Galdiero MR, Bianchi P, Grizzi F, Di Caro G, Basso G, Ponzetta A, Bonavita E, Barbagallo M, Tartari S, Polentarutti N, Malesci A, Marone G, Roncalli M, Laghi L, Garlanda C, Mantovani A, Jaillon S. *Int J Cancer*. 2016 Jul 15;139(2):446-56.

4. PTX3 is an extrinsic oncosuppressor regulating complement-dependent inflammation in cancer. Bonavita E, Gentile S, Rubino M, Maina V, Papait R, Kunderfranco P, Greco C, Feruglio F, Molgora M, Laface I, Tartari S, Doni A, Pasqualini F, Barbati E, Basso G, Galdiero M.R, Nebuloni M, Roncalli M, Colombo, P., Laghi, L., Lambris J.D, Jaillon S, Garlanda C, Mantovani A. *Cell*. 2015. Feb; 160(4):700-14.

5. Neutrophils in the activation and regulation of innate and adaptive immunity.

Mantovani A, Cassatella MA, Costantini C, Jaillon S. *Nat Rev Immunol*. 2011 Jul 25;11(8):519-31.

Type of contract

PhD scholarship of € 18.000 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.

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