



## RESEARCH TOPIC MEM22

### **Negative regulation of the Inteerleukin-1 system by IL-1R8 in tumor infiltrating leukocytes Curriculum MEM**

#### **Laboratory name**

Laboratory of Experimental Immunopathology, IRCCS Humanitas Research Hospital

#### **Pre-clinical Supervisor**

Cecilia Garlanda

[cecilia.garlanda@humanitasresearch.it](mailto:cecilia.garlanda@humanitasresearch.it)

#### **Abstract**

IL-1 family members play a key role in inflammation and innate and adaptive immunity activation. The IL-1 receptor family include molecules with regulatory activity. Among them, IL-1R8 behaves as a negative regulator of the signal transduction by other members of the family. IL-1R8 is expressed by different leukocyte subsets in the tumor microenvironment. In NK cells IL-1R8 acts as a checkpoint inhibiting their maturation and functional activities against cancer.

The aim is to extend the knowledge on the role of IL-1R8 in the functional activity of myeloid cells and lymphocytes and to develop IL-1R8 as a therapeutic target in preclinical cancer models.

The student will be involved in: a) preclinical cancer and metastasis studies; B) in vitro models of IL-1R8 inhibition or silencing (CRISPR/Cas9, siRNA, blocking antibodies) to promote anti-tumor immune responses; C) the study of the relevance in human by studying the expression of IL-1R8 in human cancer and through bioinformatics approaches.

#### **Main technical approaches**

Techniques used include in vivo models of cancer and immunotherapy; leukocyte purification and functional assays; FACS analysis; ELISA; molecular biology; microscopy, bioinformatics.

#### **Scientific references**

1- 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 A, Garlanda C, Mantovani A. IL-1R8 is a checkpoint in NK cells regulating anti-tumour and anti-viral activity. *Nature*. 2017 Nov 2;551(7678):110-114. doi: 10.1038/nature24293.

2-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 MR, Nebuloni M, Roncalli M, Colombo P, Laghi L, Lambris JD, Jaillon S, Garlanda C\*, Mantovani A\*. PTX3 is an extrinsic oncosuppressor regulating complement-dependent inflammation in cancer.



Cell. 2015 Feb 12;160(4):700-14. doi: 10.1016/j.cell.2015.01.004.\*Cocorresponding authors.  
3- Magrini E, ..Garlanda C. Complement activation promoted by the lectin pathway mediates C3aR-dependent sarcoma progression and immunosuppression. Nat Cancer 2021; 2: 218–232.

4 - Mantovani A, et al. Interleukin-1 and Related Cytokines in the Regulation of Inflammation and Immunity. Immunity. 2019 Apr 16;50(4):778-795. doi: 10.1016/j.immuni.2019.03.012. PMID: 30995499

5- Garlanda C, Mantovani A. Interleukin-1 in tumor progression, therapy, and prevention. Cancer Cell. 2021 Aug 9;39(8):1023-1027. doi: 10.1016/j.ccell.2021.04.011

### **Type of contract**

Scholarship of € 21.000 gross per year awarded by Istituto Clinico Humanitas. This sum is subject to IRPEF income tax and exempt from social security contributions.

Borsa di studio pari a € 21.000 annui lordi erogata da Istituto Clinico Humanitas. Importo soggetto a tassazione IRPEF ed esente da contribuzione previdenziale.