



UNIVERSITÀ DEGLI STUDI DI MILANO

D-MEM



PhD-UNIMI

Doctorate program
Milan
**EXPERIMENTAL
MEDICINE**

New mechanisms controlling macrophages functions: role of MS4A proteins

Nuovi meccanismi di regolazione della funzione macrofagica: il ruolo delle proteine MS4A

TUTOR: **Borroni Elena Monica**

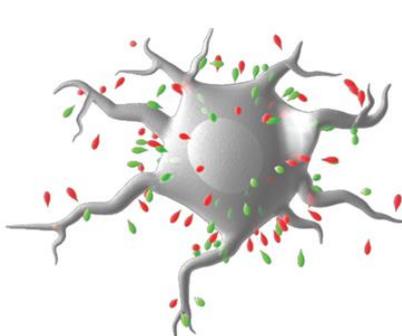
LABORATORY: **Laboratory of Leukocyte Biology**

DEPARTMENT: **Medical Biotechnologies and Translational Medicine (BioMeTra)**

Macrophages are a specialized class of innate immune cells with multifaceted roles in all stages of inflammation, homeostasis, and wound healing. Regardless their origin, macrophages can polarize towards a wide range of context-dependent activation states ranging from pro-inflammatory (M1) to pro-resolving/wound healing (M2), that permits adoption of the appropriate functional phenotype to restore physiological equilibrium, also known as macrophage plasticity. The analysis of transcriptional profiles associated with M2 polarization identified three members of a tetraspannin-like family, the MS4A4A, MS4A6A and MS4A7 proteins, which are further enhanced by anti-inflammatory molecules, such as glucocorticoids. Consistent with this, Ms4a4a deficiency impaired expression of M2 polarization markers in murine bone-marrow-derived (BMDM) and peritoneal macrophages, suggesting a role of MS4A4A on macrophage plasticity. However, the molecular mechanisms underlying MS4A4A activities, as well as the biological relevance of Ms4a4a expression on M2 macrophages, are largely undefined. By a two-hybrid system, our lab discovered that MS4A4A interacts a key molecule in macrophage biology, represented by the Fc γ receptor signaling chain, which mediates macrophage activation in response to immune complexes in autoimmune diseases, such as rheumatoid arthritis (RA). Interestingly, MS4A4A expression has been reported in a subset of CD163+ macrophages infiltrating the inflamed synovium in RA patients in response to glucocorticoids, key agents in controlling active RA symptoms. However, the MS4A4A/Fc γ R interaction, as well as its functional relevance, is still unexplored.

This project will define the molecular contribution of MS4A4A and other myeloid MS4A family members in moulding the multimolecular complexes whose constitution is responsible for the integration of different signal transduction pathways defining macrophage functions and their plasticity.

TASKs for you to solve.....



TASK 1.

Role of Ms4a4 in macrophage polarization

TASK 2.

Role of Ms4a4a in Fc-gamma receptor-mediated functions

TASK 3.

Role of Ms4a4a in Fc-gamma receptor signaling

TASK 4.

Role of Ms4a4a in TEMs organization and their dynamic remodeling

contact:

elena.borroni@unimi.it