ImmunoTools *special* Award 2014

Amiel Olivos-Ortiz, PhD student

Supervisor: Prof. Dr. Thierry Calandra
Co-Supervisor: Dr. Thierry Roger

Infectious Diseases Service, Department of Medicine, Centre Hospitalier Universitaire Vaudois and University of Lausanne, 1011 Lausanne, Switzerland

Regulation of Dendritic Cell Migration by Macrophage Migration Inhibitor Factor (MIF)

MIF was described in the late 60's as a cytokine released by activated T cells that inhibit macrophage random migration *in vitro*. It is now well established that MIF acts as a pro-inflammatory cytokine playing a central role in the control of innate and adaptive immune responses. MIF is constitutively expressed and stored in intracellular pools in virtually all cell types, including the immune cells. MIF is released upon stimulation with microbial ligands and stress. MIF exerts its functions by interacting with a membrane receptor complex composed of CD74 and CD44 with or without CXCR2 and CXCR4, thereby triggering the activation of the ERK1/2 and p38 MAPK and PI3K/Akt signaling pathways. MIF also acts inside the cytosol by interacting with and modulating the activity of p53 and CSN5/JAB-1.

MIF promotes host defences by sustaining the expression of TLR4, the signalling subunit of the LPS receptor complex, and by counteracting p53-mediated LPS-induced cell apoptosis. In agreement, *MIF* gene knockdown, anti-MIF antibodies and MIF small molecule inhibitors impair host defences against infections, while protect from septic shock in preclinical models. Increased MIF expression is associated with the onset of different inflammatory pathological conditions. Moreover, carriage of MIF high expression gene alleles have been associated with increased susceptibility to or severity of infectious diseases and autoimmune and inflammatory diseases. MIF has also been implicated in the development of tumorigenesis by favoring cell cycle progression and by promoting cell motility and invasion. Therefore, MIF represents an attractive therapeutic target for numerous pathological conditions.

DCs are a particular type of professional antigen presenting cells (APCs) that capture, process and present antigens to T-cells and B-cells, thereby initiating immunity and conferring memory and tolerance. A central feature for of DCs is their migration capability.

Migration of DCs to inflamed sites followed by their recruitment to LN is a crucial and integral event necessary for the onset of adequate immune responses. Curiously, almost nothing is known about the impact of MIF on the function of DCs. In our laboratory, we are interested in the study of the mechanisms that regulate innate immune responses and the pathogenesis of sepsis. The aim of my project is to elucidate the impact of MIF on the behaviour of DCs, with a particular interest on the impact of MIF on the migration of DCs.

If I am awarded with the ImmunoTools *special* Award 2014, the fluorochrome-conjugated antibodies to mouse CD antigens would be invaluable to discriminate and sort DCs from other leukocyte subsets. The results obtained from these studies will help to understand the role of MIF during DC responses. Identification of new mechanisms controlling the homing and the recruitment of DCs to inflammation sites will help to develop new therapeutic strategies for the control of infectious and inflammatory diseases.

ImmunoTools *special* AWARD for **Amiel Olivos-Ortiz** includes 25 reagents

FITC - conjugated anti-mouse: CD11b, CD19, CD44, CD45, CD45R, CD62L, Gr-1, a/b TCR, g/d TCR, isotype control IgG2b,

PE - conjugated anti-mouse: CD11b, CD19, CD62L, Gr-1, NK-cells, isotype control IgG2b,

APC - conjugated anti-mouse: CD3e, CD4, CD11b, CD19, CD45, CD62L, Gr-1, NK-cells, isotype control IgG2b

DETAILS more AWARDS