ImmunoTools *special* Award 2014

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Th17 pathway's immunomodulation as a therapeutic strategy for Multiple Sclerosis

Multiple sclerosis (MS) is a neurodegenerative, autoimmune and demyelinating disease that affects people for decades. The estimated MS prevalence is 70-80 per 100,000 population, which means approximately one million cases worldwide. During the active phase of the disease, CNS demyelination is associated with an inflammatory response mediated by the infiltration of T cells and microglia, which affects the viability of neurons in the brain and spinal cord. The clinical picture is heterogeneous with a variety of neurological symptoms present (aphasia, epilepsy, muscular weakness and and sensory problems). However, despite the effort, there is still not available an effective treatment yet. Moreover, neurodegenerative diseases affecting the CNS are in addition very difficult to treat, mainly because of the difficulty to cross the blood-brain barrier. This problem may be addressed by gene therapy, because it allows the production of the therapeutic molecule directly in the affected organ. Fortunately, several viral vectors have been described to be very efficient in transducing neurons in vivo, and allow transgene expression for years after one single administration.

The key role played by Th17 cells in the development of various autoimmune diseases (Rheumatoid Arthritis, Crohn's Disease or Multiple Sclerosis, etc.), has been recently demonstrated. Moreover, it's also been described that the activity of IL23 is essential to maintain the autoimmune response mediated by Th17 cells. Thus, in MS patients, Th17 cells secrete high amounts of IL23 in comparison to healthy controls, but similar amounts of IL12. Furthermore, the administration of anti-IL23p19 monoclonal antibody inhibits the production of multiple inflammatory cytokines such as IL17, IL-6, IFN-γ, TNF and IL1β and consequently attenuates the development of experimental autoimmune encephalomyelitis. Nowadays, other molecules have also been described to have therapeutic potential for the Th17 pathway, such as IL7, IL21 and IL22. Among them, we are focus on IL7, because signalling mediated by the IL7:IL7R interaction is essential for T cell development and homeostasis of peripheral T cells. Moreover, the association of a polymorphism in the IL7R gene with susceptibility to MS has been reported recently. In addition, in the cerebrospinal fluid of MS patients, expression levels of IL7 and IL7R are higher when compared with controls. Also, IL23 is required to re-express IL7R in Th17 effector and memory cells and it indicates a connection between IL7 and IL23 pathways. Last, IL7R has a differential expression between Th17 cells and Treg

cells, which explains the selective susceptibility of IL7 towards Th17 cells, but not for Treg cells, which is essential, as Th17 and Treg cells seem to represent alternative fates of naive T cells, and an imbalance between Th17 cells and Treg cells would be instrumental in the development of autoimmune diseases.

Therefore, this project is focused on the role of IL23 and IL7 interleukines in the preclinical mouse model of Multiple Sclerosis to study new therapeutic strategies involving the IL23/IL23R and IL7/IL7R signaling pathways, which are strongly associated to several autoimmune diseases. To this end, the antibodies and recombinant proteins from ImmunoTools will facilitate to us to perform in vitro studies including primary cultures of lymphocytes (which requires several survival signals to be maintained), as well as different protein characterization analysis.

ImmunoTools *special* AWARD for **Marcos Tejero Ambrosio** includes 25 reagents

FITC - conjugated anti-human CD3, CD4, CD8, Control-IgG2b,

recombinant human cytokines rh IFNgamma, rh IGF-I, rh IL-6, rh IL-7, rh IL-10, rh IL-17A, rh IL-21, rh IL-22, rh TNFα,

FITC - conjugated anti-mouse CD3e, CD4, CD8a, NK-cells, isotpye control IgG2b,

recombinant mouse cytokines rm IFNgamma, rm IL-6, rm IL-7, rm IL-10, rm IL-17A, rm IL-21, rm IL-22, rm TNFα.

DETAILS