ImmunoTools *special* Award 2017

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Immunomodulation of the Th17 pathway as a therapeutic strategy to avoid the demyelination associated with Multiple Sclerosis

Multiple sclerosis (MS) is a demyelinating, inflammatory and neurodegenerative disease of the central nervous system (CNS). Approximately 2.5 million people worldwide suffer from this pathology that causes serious physical problems in young adults and especially in women. The symptomatology is quite heterogenous, wich includes sensorial and visual affectations, motor disability, fatigue, pain and cognitive deficits, and there is a direct correlation between the succession of clinical manifestations and the disemination of CNS lesions. The etiology of the disease is unknown, but it is known to exist a combination of genetic susceptibility and external factors such as viral infections, metabolic and environmental factors. The lesios produced by this pathology to the CNS can be summarized in an infiltration of immune cells through the blood-brain barrier, promoting inflammation, gliosis and neuroaxonal degeneration, resulting in an interruption in nerve signalling.

Like other autoimmune diseases such as Psoriasis or Chron´s disease, in the MS it has been seen that the Th17 cell pathway is a key element of this immunopathology, in which there is an uncontrolled performance of the pathway generating a situation of chronic inflammation.

The aim of the present project is to modulate the previously mentiones pathway through a gene therapy strategy, selecting as regulatory targets two interleukins (IL), IL-23 and IL-21, which have a big relevance in the evolution of the disease. The interaction of the IL-23 and IL-21 with their respective transmembrane receptors results in differentiation, amplification and induction of the immune Th17 response. So based on this fact, we try to block these interactions by administering their respective receptors in their soluble form (sIL23R, sIL21R). The IL-23 blockade has already been studied and we observed that it was very effective, so we now focus on the blockade of IL-21 and the combined blockade of the two ILs by the combined administration of adenoassociated viral vectors (AAVs).

On the other hand, recently, we have decided to work with a new immunomodulatory molecule, IL-37. IL-37 is a new anti-inflammatory IL belonging to the IL-1 family. It has been observed that this IL is able to reduce proinflammatory cytokine levels such as IL-17 or IL-6. In addition, it has been observed that IL-37 is able to inhibit the proliferation of Th17 cells, so it would be a suitable molecule to combine with sIL23R, which inhibits the differentiation of this cell pathway.

With the previous information, we have to do several in vitro assays of interaction of the soluble receptors with their respective IL (sIL23R/IL23, sIL21R/IL21), as well as in vitro studies of effectiveness and characterization of the cloned hIL-37 molecule in viral vectors. On the other hand, the final objective is to know the therapeutic effectiveness of all moleculas both in monotherapy and in combination to find some functional synergism by intravenous (IV) administration of AAVs vectors encoding the molecules in the EAE (Experimental Autoimmune Encephalomyelitis), model of MS. In vivo studies will carry out a clinical score of mice as well as numerous ex vivo studies, including immunohistochemistry, in which we need many reagents that you have.

In summary, this project treats about an immunomodulation of the Th17 cell pathway by targeting IL-23 and IL-21 and using as the main immunomodulator the recent molecule IL-37. So for this project both the antibodies and recombinant proteins of ImmunoTools will be a great help to us to realize different in vitro studies, as well as to facilitate the studies of samples obtained in the in vivo assays.

ImmunoTools *special* AWARD for **Angel Edo Salvador** includes 25 reagents

FITC - conjugated anti-mouse CD3e, CD4, CD45

PE - conjugated anti-mouse CD8a, CD11b, CD80

mouse ELISA-set, for 96 wells: mouse IL-6, mouse IL-17A, mouse TNF-a (each 4 reagents)

recombinant mouse cytokines: rm IFN-gamma, rm IL-1beta, rm IL-6, rm IL-10, rm IL-17A, rm IL-21, rm TNFa DETAILS more AWARDS