ImmunoTools *special* Award 2014

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The role of Bone Morphogenetic Proteins in human $CD4^+$ T cell activation and polarization

The Bone Morphogenetic Proteins (BMPs) form a conserved group of secreted growth factors belonging to the Transforming Growth Factor beta (TGF-β) superfamily. First discovered by their potential to induce ectopic bone and cartilage formation, BMPs play an essential role orchestrating the embryogenic development and also participate in the homeostasis of a wide array of organs in the adult state, including the hematopoietic and immune systems. Consequently, it is not surprising that a large number of disorders have been associated to alterations in this pathway. These pathologies include fibrodysplasia ossificans progressiva, rheumatoid arthritis, multiple sclerosis, airway inflammation and vascular diseases, among others. In addition, aberrant expression of BMP ligands has been found in several types of cancer.

In relation to the immune system, it is well documented that BMPs participate in modulating hematopoietic stem cell differentiation and homeostasis, but also in regulating different aspects of more defined immune cell lineages. In this line, my group and others have established that BMP signaling plays a pivotal role during T cell development within the thymus. Recently, it has been described that the activation of the BMP pathway promotes the acquisition of several effector functions in mature T cells. Besides to control general aspects of T cell activation, such as cytokine production and proliferation, some evidences suggest that BMP signaling may participate in the differentiation of mature T cells towards the Th17 and Treg cell subtypes.

Since these later studies were carried out in the mouse model, the aim of this project will be to confirm these evidences in human in order to better understand the role of BMPs during T cell activation and polarization. In 2012, a model for antigen-specific

$CD4^+$ T cell priming in vitro was described by Federica Sallusto's lab (*Nature. 2012 Apr 26;484(7395):514-8*). Briefly, different microorganisms that specifically induce a certain Th response can be loaded in blood monocytes that, once irradiated, are able to differentiate naive $CD4^+$ T cells in culture. Taking advantage of this elegant model, we will study the modulation of the BMP signaling pathway on human $CD4^+$ T cells during their antigen-specific polarization towards the different Th cell types. We will study as well the possible effects of enhancing or inhibiting BMP signaling during this process by addition of BMP ligands or specific inhibitors (Noggin, DMH1, etc), respectively.

I strongly believe that the ImmunoTools AWARD will provide us a great deal of help to tune up in our lab this interesting model in order to bring more light to the current knowledge on how human helper T cells are generated in response to different pathogens. In addition, these results could be extended to those autoimmune diseases associated to a certain Th response, such as Th17 in rheumatoid arthritis in which, interestingly, BMPs are increased.

ImmunoTools *special* AWARD for **Víctor Manuel García Martínez**

includes 22 reagents

FITC - conjugated anti-human CD45RB, CD105, Annexin V,

PE - conjugated anti-human CD3, CD25, CD45RA,

PerCP - conjugated anti-human CD4,

APC - conjugated anti-human CD3, CD25, CD62L, CD69,

human IL-4 ELISA-set for 96 wells, human IL-12p40 differential (detect IL-12p40 but not IL-12p70) (each 3 reagents),

recombinant human cytokines: rh BMP-2, rh BMP-7, rh IL-2, rh Noggin, rh TSLP

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