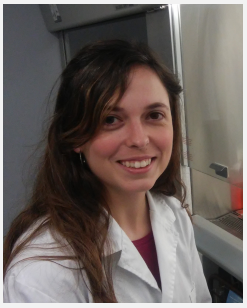
ImmunoTools *special* Award 2017



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Regulatory B cell induction by human adipose tissue-derived Mesenchymal Stem Cells: Optimization of the method

Renal transplantation is the unique curative option for patients suffering from end-stage renal disease, but rejection after transplantation cannot be totally avoided. However a small percentage of patients (0.03%) spontaneously develop long term tolerance to their allograft without immunosuppressive drugs. The study of biomarkers in those patients showed an increased B cell-related gene signature, specially related to regulatory B cells (Breg). In fact, Breg have been attributed immune regulatory functions not only in the acquisition of tolerance in renal transplantation but also in autoimmune diseases such as systemic lupus erythematous, rheumatoid arthritis or multiple sclerosis.

Tracking of Breg in vivo or their induction in patients can be envisaged as a monitoring parameter or cellular therapy in these situations. However, there is no consensus on a unique phenotype for the Bregs although it is of general acceptance that the main mechanism of action is through IL-10 secretion. In vitro induction of IL-10-producing B cells has been achieved using products derived from bacteria (LPS, CpG), or using a bacterial-free polyclonal stimulation (anti-CD40 + anti-Immunoglobulin + cytokine) that activates memory B cells at the same time.

Nevertheless, if the goal is to modulate the immune system in a clinical setting, the ideal situation is the induction of Breg without bacterial products in addition to non-activation of the other B lymphocytes. In this sense, our group is working with Mesenchymal Stem Cells (MSC), a type of multipotent stromal cells found in all the tissues that are immunoprivileged due to their low expression of HLA and costimulatory molecules. They have been under the spot light during the last years because they also have immunoregulatory properties in a variety of immune cells like T lymphocytes, macrophages, natural killer or dendritic cells. We demonstrated that when MSC are co-cultured with B cells with a determined cocktail of cytokines they

induce high IL-10-producing B cells while maintaining most of B cells in a naïve phenotype. These Breg can inhibit T cell proliferation.

As said above, despite the knowledge acquired on this cell subset we are still lacking a unique defining phenotype or a key transcription factor (like FoxP3 in Tregs) that would allow the proper identification and isolation. This delay in the identification of a human Breg phenotype is due, among other factors, to non-conserved extracellular markers between mouse and human Bregs. Finding a determined phenotype for human Breg could be directly applied in the clinical setting for the monitoring of tolerance or rejection in kidney transplanted patients, in addition to being of utmost importance if we want to generate Bregs *in vitro* for their use in cell therapy as well as inducing them *in vivo* to overcome several pathological situations.

AIMS

- Optimization of the induction of human Bregs in a system free of bacterial components.
- Study the mechanism of action of MSC in the induction of Bregs.
- Unravel a specific Breg signature.

ImmunoTools antibodies can help us to characterize both Breg and MSC, as well as the other immune cells used in functional assays. With a diverse the recombinant human cytokines from ImmunoTools, we could test different combination of stimuli cocktails for B cells that have been previously described in the literature or not. In addition, human IL-10 and TNF-α ELISA-sets will be of great importance in order to determine the level of induction of Breg or the maintenance of their naïve phenotype.

ImmunoTools *special* AWARD for **Laura Carreras-Planella**

includes 25 reagents

APC - conjugated anti-human CD29, CD31, CD44, Control-IgG1

FITC - conjugated anti-human CD20, CD31, CD54, CD62L, CD72, CD105, isotype control IgG1

PE - conjugated anti-human CD34, CD62P, CD72, isotype control IgG1

human IL-10 ELISA-set, for 96 wells, (each 4 reagents)

recombinant human cytokines: rh BAFF/sCD257, rh sCD40L / CD154, rh CTLA-4 / CD152, rh IL-4, rh IL-10, rh IL-21

DETAILS more AWARDS