ImmunoTools *special* Award 2014

Guillermo Docena, PhD

IIFP Institute of Immunology and Physiopathology
Buenos Aires, Argentina

Immunomodulation of intestinal inflammation

An aberrant immune response has been described in different chronic inflammatory disorders that affect the intestine of patients. Food allergy and inflammatory bowel disease (IBD) are two immune-related disorders that affect the intestinal mucosa and are highly prevalent nowadays. In food allergy a Th2-biased immune response is responsible for the elicitation of IgE antibodies, which upon binding to specific receptors on mast cells and exposure to the allergen develop cell degranulation and release of potent pro-inflammatory components. If circulating basophils are activated, anaphylaxis is induced, and a life-threatening condition may arise. In IBD, colonic lamina propria T cells are responsible for the Th1 immune response that characterizes the mucosal inflammation. A chronic and persistent inflammation may develop tissue fibrosis (with activation of fibroblasts, release of metalloproteases and collagen accumulation), which may progress to fistula, stenosis or colon cancer. Different factors have been implicated in the transition from healthy to inflamed or neoplastic tissue. Our group studies the role of galectin-1 (Gal-1) in the regulation of the mucosal immune response. Activated T cells that are sustained in the colonic tissue are key contributors to the inflammatory setting of the intestinal mucosa that promotes the tissue remodelling of IBD. It has previously been described that Gal-1 acts as a broad anti-inflammatory factor by selectively deleting pathogenic Th1 and Th17 cells, promoting the differentiation of tolerogenic DCs. The control of these cells promotes the remission in these patients.

Regarding food allergy we have seen that the induction of regulatory T cells (Treg) revert the allergic inflammation and control de Th2 cells in a food allergy mouse model. Gal-1 has been described as a key factor in the differentiation of Treg. The literature reflects that Tregs are down-regulated in patients with food allergy. Therefore we are developing different strategies to induce therapeutic Treg that control the intestinal allergic inflammation.

Besides, Gal-1 exerts protective effects in a murine model of colitis and might be effective in the treatment of human IBD. We propose to characterize the Gal-1-linked glycome of circulating and mucosal T cells in the mouse model using biochemical, molecular biology and immunological approaches. Based on these findings we propose to develop a novel immunomodulatory strategy with the administration of a highly stable recombinant Gal-1 protein directly into the inflamed intestinal mucosa. These therapeutic approaches could serve to dampen the exuberant inflammation by selectively deleting or dampening the pathogenic activated T cells, and allowing regulatory T cells to restore homeostasis.

In this project we analyze human and mouse intestinal specimens, peripheral blood cells and murine cells isolated from different organs. We perform cell analysis by flow cytometry, ELISA and westernblotting. Besides, different cell cultures are carried out to activate and characterize the cell fate, or to induce cell death. Therefore different antibodies conjugated to fluorochromes (for Tcells, dendritic cells, NK cells and plasma cells), cytokines and chemokines are used. Annexin V is currently used to analyze early apoptosis in cells that have been exposed to the pro-apoptotic Gal-1.

ImmunoTools *special* AWARD for **Guillermo Docena** includes 25 reagents

FITC - conjugated anti-human CD3, CD38, Annexin V,

PE - conjugated anti-human CD4, CD62L, CD80, Annexin V,

PerCP - conjugated anti- human CD8,

APC - conjugated anti-human IL-6,

recombinant human cytokines rh IL-10, rh IL-17A, rh IL-17F,

human TNFa ELISA-set for 96 wells (each 3 reagents),

FITC - conjugated anti-mouse CD8a,

PE - conjugated anti- mouse CD19, Gr-1,

APC - conjugated anti-mouse NK-cells,

recombinant mouse cytokines rm GM-CSF, rm IL-2, rm IL-5, rm IL-10, rm IL-17E / IL-25, rm MIP3a / CCL20, rm TNFa

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