ImmunoTools *special* Award 2014

Jeremías Galletti, MD, PhD

Immunology Laboratory, Institute of Experimental Medicine,
National Academy of Medicine/CONICET
Pacheco de Melo 3081, (C1425AUM)
Buenos Aires, Argentina

Ocular surface inflammation as a driving force in conjunctival fibrosis after glaucoma surgery

Glaucoma is a sight-threatening disease that affects more than 60 million people and constitutes the second leading cause of blindness worldwide. Glaucoma is characterized by increased intraocular pressure due to impaired aqueous flow out of the eye towards the systemic circulation, and thus its treatment is based on reducing intraocular pressure by topical agents and/or ocular surgery. Medical treatment involves the daily use of one or more ocular hypotensive drugs in the form of eye drops, and it is effective for the initial stages of disease as it can only induce a moderate reduction of the intraocular pressure. Filtration surgery is usually reserved for the advanced cases and it is highly effective in the short term, but failure eventually ensues in most patients due to the unwanted conjunctival cicatricial response that closes the surgically-facilitated aqueous outflow pathway. Clinical evidence suggests that ocular surface inflammation promotes conjunctival fibrosis, especially when triggered by eye drop preservatives, but the molecular & cellular mechanisms that underlie this association are poorly understood.

In this project we propose to evaluate how eye drop preservatives activate the ocular surface epithelium, and in turn, how this phenomenon could facilitate conjunctival fibrosis through fibroblast proliferation and increased collagen deposition in a murine model of glaucoma surgery. We will look at specific intracellular pathways that are known to be involved in the wound healing response and use specific inhibitors to block their activation in vitro and in vivo. We will monitor fibroblast proliferation in vitro with confocal microscopy in organotypic cultures that mimic the conjunctival milieu and also in vivo with the aid of transgenic mice and fluorochrome-labelled cells. We will focus our efforts on the interaction between ocular surface epithelial cells, immune cells and fibroblasts to detect which molecular signals are responsible for the increased fibroblast activity.

The data collected from this project should allow us to determine if two of the main intracellular pathways known to be involved in ocular surface inflammation are responsible for the promotion of conjunctival fibrosis after glaucoma surgery. These results could have high translational value, as they might tell clinicians which phase of the surgical procedure should be most critically targeted by anti-inflammatory therapy and may even uncover new pharmacological targets for the management of the conjunctival cicatricial response. Obtaining the ImmunoTools Award would contribute greatly to the execution of this proposal.

ImmunoTools *special* AWARD for **Jeremías Galletti** includes 25 reagents

FITC - conjugated anti-mouse CD3e, CD4, CD8a, CD11b, CD19, CD44, CD45, CD45R, CD62L, Gr-1, NK-cells, a/b TCR, g/d TCR, isotype control IgG2b,

PE - conjugated anti-mouse CD4, CD8a, CD11b, CD19, CD49d, CD62L, Gr-1, NK-cells, isotype control IgG2b,

APC - conjugated anti- mouse CD3e, CD19 DETAILS more AWARDS