

00329 Valproic Acid Reduces Inflammation in the Post-operative Conjunctiva

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Aims: We aim to determine the effect of valproic acid (VPA) on the inflammatory response following experimental conjunctival surgery.

Methodology: Experimental conjunctival surgery was performed as described for the mouse model of glaucoma filtration surgery (GFS). VPA was injected into the operated site after surgery at 300µg/ml in 5µl volume. PBS was injected in parallel experiments as controls. Blebs were harvested and pooled into 5 groups (n=5) on day 2 post-surgery to assess the inflammatory response, which is measured by analyses of cytokine levels, macrophage infiltration and capacity of VPA to suppress the effects of archetypal tumor necrosis factor-alpha, TNF-A, on primary mouse conjunctival fibroblasts. Cytokines were determined using the MCYTOMAG-70K multiplex assay. Macrophages were measured by flow cytometry analysis of CD45/ F4/80-labeled cells. Mouse conjunctival fibroblasts were treated with TNF-A for 48h before the culture supernatants were recovered for cytokine analysis. Statistical analyses were performed using either two-tailed Student's t-test or one-way ANOVA.

Result: VPA-treated blebs contained significantly less chemokines (CXCL1 and CCL2), interleukins (IL-1A, -1B, -2, -5, -6, -9, -10, and -15), and other cytokines (GM-CSF and M-CSF). Notably, IL-5, -6, -10 were reduced by more than 2-fold compared to PBS controls. VPA also reduced the recruitment of CD45+F4/80+ cells by 3-10% (n=5, mean 6.5% reduction, p=0.0055). In fibroblasts co-treated with TNF-A, VPA significantly suppressed TNF-A induction of chemokines (CCL2, CCL5, and CCL10), interleukins (IL-1A, -1B, -2, -5, -10, -12 and -15) and other cytokines (VEGF, IFN-?). Comparing TNF-A with TNF-A+VPA treatment, CCL5 was the most suppressed, by 4.89-fold, (p=3.70e-15, n=3).

Conclusion: VPA is able to reduce the production of a myriad of proinflammatory chemokines and cytokines as well as the recruitment of macrophages in the operated conjunctiva. This property, together with its capacity to suppress collagen production, suggests that VPA will be an effective adjunct to GFS for improving surgical success.