



THE OCULAR IMMUNOLOGY
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High Levels of IL-12 in the Aqueous Humor and Vitreous of Uveitis Patients

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Introduction There is considerable experimental evidence for the concept that T-lymphocytes and cytokines play a major role in the pathogenesis of uveitis. T lymphocytes have been demonstrated to be the most abundant cell type in uveal tissue, retina, aqueous humor and vitreous of patients with intraocular inflammation. Studies have implicated that the pathogenic cell in experimental autoimmune uveitis may be CD4+Th1-like.

IL-12 is a potent immunoregulatory molecule that is critically involved in a wide range of diseases. It is mainly produced by monocytes, macrophages, B cells and connective tissue type mast cells. IL-12 is a heterodimeric cytokine comprising p35 and p40 chains. Its presence drives CD4 cells towards type-1 (Th1) cells that mediate delayed-type hypersensitivity, activates macrophages, and switches antibody production from IgM to IgG2. Other potential direct effects of IL-12 include regulation of the homing of T cells and other inflammatory cells to a particular organ via modulation of adhesion molecules. Further, it acts as a T-cell growth factor and it suppresses induction of counter-regulatory cytokines such as IL-4, IL-5 and TGF- β . It is known that the main antitheses of IL-12 are IL-4 and IL-10. IL-4 drives CD4 cells towards type 2 (Th2) cells that mainly provide help for B cells by promoting antibody class switching from IgM to IgG1 and IgE.

IL-10 has primarily been described as a cytokine- synthesis inhibitor factor. It acts as a negative regulator for IL-12-induced inflammation. Monocytes, B lymphocytes, Th0- and Th2-lymphocytes are the main sources for IL-10. Its secretion has been shown to be enhanced by high levels of IL-12.

We measured the levels of IL-12 and IL-10 in the aqueous humor and vitreous in 22 patients with uveitis to determine whether or not the levels of these cytokines are significantly different from those of normal aqueous and vitreous.

Results: Cytokine levels found in the anterior chamber and the vitreous are presented in pg/ml (medium;range). The highest IL-12 levels were found in patients with active uveitis (108.5pg/ml; 72-293pg/ml). IL-12 in patients with moderate uveitis or in remission of their disease was lower (32pg/ml;15-

94pg/ml), than in patients with active disease ($p>0.001$), but higher than in the control group (10.5pg/ml;9-14pg/ml). IL-10 was detectable in only three of 22 uveitis patients (12pg/ml;9-23).

Conclusion: We found statistically significant differences of IL12- levels in the various patient groups (active versus inactive versus control). These results support the idea that these uveitis cases represent Th1-T lymphocyte mediated diseases, in which IL-12 plays a pivotal role in the initiation and maintenance of the intraocular inflammation. The high levels of IL-12 in the vitreous and/or aqueous humor of our uveitis patients suggest that susceptibility or resistance to ocular autoimmunity may be connected to a genetic predisposition to an elevated Th1 response.