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A role for IL-17 in age-related macular degeneration

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In a recent article[1], Ambati and colleagues discussed the immunological aspects of age-related macular degeneration (AMD) pathogenesis and inflammation-directed therapeutics to treat AMD.

Based on the current literature and evidence, they deliberated that AMD could be caused by various factors, such as immune-mediated retinal damage (for example, interleukin-1β (IL-1β), IL-6 and IL-18), the pro-inflammatory components of drusen (for example, β-amyloid), complement activation (for example, C1q, C3 and C5 activation), proliferative angiogenic responses causing neovascularization (for example, IL-1β, IL-6, tumour necrosis factor (TNF) and vascular endothelial growth factor A (VEGFA)), and geographic atrophy caused by prolonged VEGFA-specific antibody therapy[1]. However, we would like to add that the IL-17 signalling pathway is also likely to be important in the pathogenesis of AMD.

IL-17 is a signature cytokine of the T helper 17 (T_H17) cell subset and has a crucial role in promoting inflammation in various autoimmune and inflammatory diseases[2]. In addition to T_H17 cells, γδ T cells and innate lymphoid cells (ILCs) also produce IL-17. Recently, several reports have demonstrated the involvement of IL-17 in the pathogenic inflammation of AMD[3–5]. Liu *et al.*[3] reported that complement component 5a (C5a) is increased in the circulation of AMD patients and that it promotes IL-17 and IL-22 expression by human $CD4^+$ T cells. These authors found significantly elevated levels of IL-17 and IL-22 in patients with AMD compared with control individuals who did not have AMD. Furthermore, in laser-induced experimental choroidal neovascularization — which has characteristic features of AMD — Hasegawa *et al.*[4] showed that IL-17 has a strong potential for stimulating neovascularization in a VEGF-independent manner. Importantly, the authors reported that γδ T cells and $THY1^+$ ILCs, but not T_H17 cells, were the relevant source of IL-17. In line with the findings of Liu *et al.*[3], IL-1β in combination with high-mobility group box 1 (HMGB1) induced IL-17 production by γδ T cells. Tuo *et al.*[5] demonstrated that intravitreous administration of recombinant TNF-inducible gene 6 protein (TSG6) could stabilize retinal lesions in mice that are deficient in both CC-chemokine ligand 2 (CCL2) and CX_3C-chemokine receptor 1 (CX_3CR1) by modulating the expression of several ocular immunological genes and, in particular, *Il17a*. IL-17 is also known to promote VEGF-mediated angiogenesis by enhancing VEGF-induced growth of vascular endothelial cells[6].

All of these reports point towards the possibility that IL-17 could be involved in the pathogenesis of AMD by promoting retinal angiogenesis and neovascularization. Therefore, as a proof-of-concept, IL-17-targeted therapies could be explored, at least in experimental models.

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Competing interests statement
The authors declare no competing financial interests.