Complement stimulates Retinal Pigment Epithelial Cells to undergo Pro-inflammatory

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Changes as in Early Age-Related Macular Degeneration

<u>Purpose.</u> A polymorphism in the complement factor H gene, leading to increased complement activation, is associated with the development of age-related macular degeneration (AMD). We therefore examined the effect of human complement sera (HCS) on retinal pigment epithelial (RPE) cells with respect to pro-inflammatory mediators relevant in early AMD.

<u>Methods.</u> RPE cells were treated with HCS or heat-inactivated (HI)-HCS as a complement-deficient control. Cells were stained for C5b-9 using immunocytochemistry and immunofluorescence, and cell viability was determined. Interleukin (IL) -6, -8 and monocyte chemoattractant protein-1 (MCP-1) were quantified by ELISA and their expression was determined by RT-PCR. Intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1) and tumour necrosis factor- α (TNF- α) were analysed by western blotting. The intracellular distribution of nuclear factor (NF)- α 8 was investigated by immunofluorescence.

<u>Results.</u> Concentration-dependent increased staining for C5b-9 was observed after HCS treatment, whereas cell viability decreased. ELISA and RT-PCR analysis revealed increased secretion and expression of IL-6, -8 and MCP-1. Western blot analysis showed a concentration-dependent enhancement in ICAM-1, VCAM-1 and TNF- α in response to HCS, and immunofluorescence staining revealed cytosolic to nuclear translocation of NF- $\hat{\kappa}$ B.

<u>Conclusions.</u> This study suggests that complement may stimulate RPE cells to create a proinflammatory environment via NF-kB activation which may support early AMD development.

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