Complement stimulates Retinal Pigment Epithelial Cells to undergo Pro-inflammatory Changes as in Early Age-Related Macular Degeneration

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Purpose. 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.

Methods. 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)-ƙB was investigated by immunofluorescence.

Results. 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-ƙB.

Conclusions. This study suggests that complement may stimulate RPE cells to create a pro-inflammatory environment via NF-ƙB activation which may support early AMD development.

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