Abstract

Complement increases release of proinflammatory and proangiogenic mediators by retinal pigment epithelial cells

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Objectives. A mutation in complement factor H (CFH) gene, leading to augmented complement activation, is correlated with development of age-related macular degeneration (AMD). Therefore, the influence of complement on retinal pigment epithelial (RPE) cells was examined concerning their production of proinflammatory and proangiogenic mediators relevant in AMD.

Methods. ARPE-19 cells were cultured with human or fetal calf serum (FCS). Therefore, complement containing native serum as well as the heat-inactivated form with inoperable complement was used. Further, RPE cells were treated with zymosan, a complement activating yeast particle. Serum and zymosan in combination was also tested. Levels of interleukin (IL)-6, -8 and vascular endothelial growth factor (VEGF) in supernatants were examined by ELISA.

Results. Untreated RPE cells produced IL-6, -8 and VEGF constitutively. FCS or human serum led to a concentration dependent release of all mediators. Thereby, FCS increased the cytokine production stronger than human serum, native serum stronger than heat-inactivated. Zymosan only intensified IL-6 and -8 secretion. Combined treatment with serum and zymosan resulted in an additive release of IL-8 and VEGF. In contrast, secretion of IL-6 was synergistic.

Conclusion. The enhanced expression of IL-6, -8 and VEGF by RPE after exposure to complement might explain the correlation between augmented complement production and inflammatory processes accompanying AMD. IL-6 production was strongly increased due to activation of complement within the serum by zymosan. Thus, complement activation could stimulate inflammatory processes by activated RPE cells leading to AMD.

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