

## Retinal pigment epithelial cells respond to complement by an augmented production of vitronectin

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**Objectives:** Genetic studies have demonstrated the role of activated complement on the alternative pathway during the development of age-related macular degeneration (AMD). The extracellular matrix component vitronectin can protect against activated complement. Drusen appear in the retina between the retinal pigment epithelial (RPE) cell layer and Bruch's membrane. Drusen are hallmarks of early and late AMD and contain high amounts of vitronectin. Therefore this study addressed the influence of complement on the vitronectin production by RPE cells.

**Methods:** ARPE-19 cells as model for RPE cells were cultivated with increasing amounts of human serum as complement source in its naïve and heat (and thereby complement) inactivated form. In another series of experiments zymosan as an activator of the alternative pathway of complement was tested alone and in combination with naïve human serum. Vitronectin was assayed in situ by immunohistochemistry, on protein level by western blot and by PCR after reverse transcription of total RNA.

**Results:** A constitutive production of vitronectin by RPE cells was detected by all three tests. With naïve human serum increased vitronectin protein was found by immunohistochemistry and western blot while the number of mRNA transcripts was not significantly altered. The vitronectin production was further enhanced with the combination of zymosan and naïve human serum while heat inactivated serum showed lesser effect.

**Conclusion:** Activated complement lead to an augmented vitronectin production by RPE cells on post-transcriptional level. Enhanced complement activation during AMD might also contribute in vivo to an enhanced production of vitronectin by RPE cells. On the one hand this can cause protection against activated complement but on the other hand the increased retinal vitronectin might contribute to thickening of Bruch's membrane and may facilitate the development of drusen.

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