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Poor anti-VEGF responses linked to genetic variation in immune regulation

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Anti-VEGF therapies are commonly used to stabilize deteriorating vision in patients with wet age-related macular degeneration (wet AMD). Vascular endothelial growth factor, or VEGF, is a signaling molecule that helps maintain blood vessels in the eye and other organs, but its overabundance in wet AMD patients can lead to overgrowth of vessels that causes vision loss. Though reducing VEGF signaling with anti-VEGF therapies has positive effects in many patients, some individuals continue to experience vision deterioration during treatment.

In a study published this week in the *JCI*, Martin Friedlander's lab at Scripps Research Institute investigated whether genetic variation in an immune system component called the complement system may contribute to vision loss during anti-VEGF therapy in some wet-AMD patients.

Prior work suggested that patients who do not respond well to anti-VEGF therapy often expressed variations in the genes encoding complement system proteins, but it was not known whether these variations interacted with VEGF signaling during treatment.

In the current study, researchers examined the these genetic variations in human retinal cells and observed that they led to complement system dysregulation. Blocking VEGF signaling enhanced this dysregulation, providing evidence for a link between VEGF signaling and complement system activation.

These findings suggest that screening wet AMD patients for genetic variations in the complement system may help identify individuals at risk for adverse responses to anti-VEGF therapy.

More information: Lindsay S. Keir et al, VEGF regulates local inhibitory complement proteins in the eye and kidney, *Journal of Clinical Investigation* (2016). DOI: 10.1172/JCI86418