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MicroRNA-150 Promotes Pathological Angiogenesis in Age-Related Macular Degeneration by Targeting Stearoyl-CoA Desaturase-2

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Age-related macular degeneration (AMD)—a prominent cause of blindness in older adults—primarily affects the macula, the cone-concentrated area of the central retina. Previous studies have shown that macrophages play a pathogenic role in various diseases associated with aging, including AMD. In order to better understand mechanisms that regulate macrophage aging and the impact of aging on macrophage functionality, we explored the impact of certain microRNAs (miRNAs), key post-transcriptional regulatory factors that have been shown to be dysregulated in patients with advanced AMD, on various metabolic and lipid properties of macrophages. Since one significant difference between old and young macrophages is a shift from an M1-like pro-inflammatory phenotype towards an M2-like proangiogenic phenotype, identifying key miRNAs may provide potential causes for the phenotypic changes. We determined that miR-150 is upregulated in old macrophages and contributes to transcriptomic changes with lipid trafficking and metabolism genes. By detecting specific gene targets for miR-150, we were able to refine our search for potential mechanisms. We identified that stearoyl-CoA desaturase-2 (Scd2), an imperative gene in lipogenesis and biosynthesis of membrane phospholipids, was directly regulated by miR-150. In order to replicate the impact of miR-150 on Scd2, we knocked down Scd2 in murine macrophages and observed that numerous pro-angiogenic factors—contributors to advanced wet AMD—are upregulated. Furthermore, macrophages with a knock down of Scd2 were less capable of inhibiting injury-induced angiogenesis by using an injury-induced choroidal neovascularization model compared to normal macrophages. These results lead to the conclusion that microRNA-150 impacts the pathogenesis of AMD and may serve as a therapeutic target to slow and prevent progression of AMD.