Genetic Correlates of Proliferative Vitreoretinopathy

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The experienced retinal surgeon is familiar with the frustrating task of prognosticating and preventing/treating proliferative vitreoretinopathy (PVR) after retinal detachment (RD) surgery. The imperfection of long-described clinical models for predicting PVR leaves the surgeon questioning what underlying predispositions to PVR may exist.1

Rojas and colleagues2 provide insight into this question in their candidate gene association study examining inflammatory genetic markers with the occurrence of PVR after primary RD repair. In their study, Rojas et al. identified single nucleotide polymorphisms (SNPs) in the genes SMAD7 and TNF-α between subjects who developed PVR and those who did not. SMAD7 is an intracellular signaling molecule that results in the downstream inhibition of TGF-β-mediated fibrosis. It is noteworthy that this study could not replicate the previously described TGF-β association. It is very exciting to note the TNF-α association since there are approved drugs that block this proinflammatory cytokine and have even been administered intraocularly.

A major strength of this study is its design, where in the first stage, case-control samples were used to identify SNPs associated with PVR from a panel of 30 candidate genes. Then, in a second stage, the significance of these SNPs was validated in samples from multiple, independent centers. This design avoids the pitfalls of overestimation and false positives, problems common to many association studies.

The authors made commendable efforts to ensure that the baseline characteristics between case and control were similar, although some differences did persist, such as the operative techniques utilized between cases and controls. These discrepancies raise the question of whether other unmeasured variables affected the outcomes of the RD surgery. Regardless of such concerns, the findings of this study are an important contribution to our understanding of the pathobiology of PVR and introduce novel possibilities for more targeted therapies of this complex and befuddling condition.

References