Novel mutations in FZD4 with Familial Exudative Vitreoretinopathy
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Incomplete retinal blood vessel formation is the hallmark of a group of diseases including retinopathy of prematurity (ROP) and familial exudative vitreoretinopathy (FEVR). These conditions can cause a failure to vascularize the peripheral retina and is the unifying feature seen in all affected individuals, but by itself usually causes no clinical symptoms. The visual problems in ROP and FEVR result from secondary complications due to the development of leaky blood vessels, formation of new unwanted vessels and traction of the retina that can cause hemorrhages. These features cause a reduction in visual acuity and in 20% of cases can lead partial or total retinal detachment, causing blindness if untreated.

We have been using FEVR as a genetic model to understand this group of diseases. FEVR is a well-defined inherited disorder of retinal vessel development. It is reported to have a penetrance of 100% (likelihood of person with a mutation to develop the characteristics of that mutation), but clinical features can be highly variable, even within the same family. Severely affected patients may become blind during the first decade of life, while mildly affected individuals are not aware of symptoms and only diagnosed by fluorescein angiographic photography. FEVR is genetically versatile, and can present dominant, recessive or X-chromosome linked traits. Three loci have been mapped and two genes (FZD4 and LRP5) identified in dominant FEVR. The purpose of this study was to characterize clinical features and screen for the FZD4 gene in a panel of 13 FEVR patients.