FOXE3 Gene Analysis in Anterior Segment Dysgenesis (ASD) and other Developmental Eye Disorders

Clinical Features:
Anterior segment dysgenesis (ASD) disorders can involve multiple ocular tissues, such as the iris, cornea and lens. Depending on the clinical presentation, these disorders can often be classified into different subtypes. Several subtype examples include Peters' anomaly, which is identified by central corneal opacity and defects of Descemet's membrane and corneal endothelium; posterior embryotoxon, which involves a thickening and opacity at Schwalbe's ring; and aphakia, which is defined by the absence of the ocular lens. Variants in the FOXE3 gene have been associated with a variety of anterior segment dysgenesis disorders including those previously mentioned and others such as congenital cataracts, sclerocornea and coloboma.[1,2,3,4] In addition, FOXE3 variants have also been observed in non-syndromic microphthalmia.[5] Although FOXE3 disorders can be inherited in either an autosomal dominant or recessive pattern, the disease presentation is typically more severe in individuals who are homozygous or compound heterozygotes for recessively-inherited variants.[1]

Genetics:
Anterior segment dysgenesis (ASD) disorders have an autosomal dominant and autosomal recessive inheritance pattern with variable expressivity.

Test Methods:
Using genomic DNA obtained from the submitted biological material, bi-directional sequence of the single coding exon and splice junctions of the FOXE3 gene is obtained and analyzed. Variants found in the first person of a family to be tested are confirmed by repeat analysis using sequencing, restriction fragment analysis or another appropriate method.

Test Sensitivity:
As the majority of reports identifying FOXE3 variants are small case studies involving one or a few families, the precise clinical sensitivity of identifying FOXE3 variants in affected individuals is not clear. However, in a study involving 26 cases of bilateral microphthalmia, recessive variants in the FOXE3 gene accounted for ~15% of cases (4/26).[5] FOXE3 variants also comprised approximately 4% (1/27) of cases involving congenital cataracts.[4] This analysis is expected to detect all currently known variants identified in the FOXE3 gene.

Variant spectrum:
The majority of variants observed in the FOXE3 gene that are associated with an autosomal pattern of inheritance comprise single base pair changes resulting in either missense or nonsense variants or small deletions/duplications resulting in frameshifts.[1,3,5,6] The majority of

variants associated with a dominant pattern of inheritance involve the loss of the normal stop codon, resulting in abnormal protein products of extended length.[1,2,4] To our knowledge, there have been no reported large deletions or duplications involving this gene.

References:

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