IRF6 Gene Analysis in Van der Woude and Popliteal Pterygium Syndromes

Disorder also known as: Van der Woude syndrome: VWS; VDWS; lip-pit syndrome, cleft lip and/or palate with mucous cysts of lower lip; Popliteal pterygium syndrome: PPS; cleft lip/palate; paramedian mucous cysts of the lower lip; popliteal pterygium; digital and genital abnormalities; faciogenitalpopliteal syndrome

Clinical Features:
Van der Woude syndrome consists of clefting of the lip, palate, or both. Lip pits are seen in 80% of patients, and mucous cysts of the lower lip also may be observed, although they occur less frequently. The disorder is variable, and affected family members often show diverse phenotypic expression. Hypodontia may be present, and individuals may be missing central and lateral incisors, canines and/or bicuspids.

As with Van der Woude syndrome, cleft lip, cleft palate and lip pits are included in the clinical spectrum of Popliteal Pterygium Syndrome. In addition to the orofacial features, 90% of individuals with PPS have a popliteal web present and ~50% of patients have genital abnormalities. Toenail dysplasia, syndactyly of the toes and digits, and bony deformities also may be present.

Inheritance Pattern/Genetics:
Autosomal dominant

Test Sensitivity:
Sequence analysis detects pathogenic variants in approximately 72% of individuals with Van der Woude syndrome and 97% of individuals with PPS.[1] Whole and partial gene deletions have been reported in a few families with Van der Woude syndrome.[2] Our method is expected to detect the vast majority of existing small intragenic variants as well as large deletions and duplications of one or more exons.

Test Methods:
Using genomic DNA from the submitted specimen, the coding regions and splice junctions of the requested gene are PCR amplified and capillary sequencing is performed. Preferential sequencing of exon 4 can be requested for patients with a clinical diagnosis of PPS. Bi-directional sequence is assembled, aligned to reference gene sequences based on NCBI RefSeq transcript and human genome build GRCh37/UCSC hg19, and analyzed for sequence variants. Concurrent deletion/duplication testing is performed for most, if not all, of the coding exons using exon-level oligo array CGH (ExonArrayDx), and data analysis is performed using

gene-specific filtering. Probe sequences and locations are based on human genome build GRCh37/UCSC hg19. Reported clinically significant variants are confirmed by an appropriate method. Sequence and copy number variants are reported according to the Human Genome Variation Society (HGVS) or International System for Human Cytogenetic Nomenclature (ISCN) guidelines, respectively. Reportable variants include pathogenic variants, likely pathogenic variants and variants of uncertain significance. Likely benign and benign variants, if present, are not routinely reported but are available upon request.

References:

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