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 Methods:
Analysis is performed by bi-directional sequencing of the coding regions and splice sites of exons 2-9 of the IRF6 gene. Preferential sequencing of exon 4 can be requested for patients with a clinical diagnosis of PPS. If no variant is found by sequencing, targeted array CGH analysis with exon-level resolution (ExonArrayDx) is available to evaluate for a deletion or duplication of one or more exons of this gene. 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:

Fifty percent of individuals with Van der Woude syndrome and 85% of individuals with PPS exhibit variants in the IRF6 gene.[1] Our method is expected to detect the vast majority of existing small intragenic variants, although sequencing will not detect those rare cases with whole-gene deletions. Large deletions of one or more exons would be detectable by targeted array CGH analysis with exon-level resolution (ExonArrayDx).

References:

1. Kondo, S. et al., (Letter) Nature Genet. 32: 285-89, 2002.
2. Peyrard-Janvid, M. et al., Eur J Human Genet. 13: 1261-7, 2005.
3. Kayano, S. et al., J Hum Genet. 48:662-628, 2003.