

## WNT10A Gene Analysis in Ectodermal Dysplasia

**Also Includes:** Odonto-onycho-dermal dysplasia (OODD), Schöpf-Schulz-Passarge Syndrome (SSPS)

### **Clinical Features:**

A broad spectrum of clinical features has been found in ectodermal dysplasia patients who have compound heterozygous or homozygous variants in WNT10A, with the most consistent clinical feature being severe oligodontia of permanent teeth. Both generalized hypohidrosis and hyperhidrosis have been reported. Excessive or reduced sweating involving palms and soles can occur. Skin is usually dry, while nails may be normal in shape and texture, or thinned, flat, convex, slow growing, or even absent at birth but develop later in childhood. Palmoplantar findings range from normal skin to severe hyperkeratosis. Scalp, body, and facial hair may be sparse. Photophobia has been described in a few patients. Patients with OODD have, in addition to oligodontia and abnormal teeth, dystrophic nails, erythematous lesions of face, and palmoplantar hyperkeratosis with hyperhidrosis. Hair may or may not be involved. SSPS is characterized by hidrocystomas (eyelid cysts) in association with other findings of ectodermal dysplasia. Heterozygotes frequently manifest mild symptoms (see below).

### **Inheritance Pattern:**

WNT10A belongs to a highly conserved gene family encoding secreted signaling molecules. While WNT10A variants are associated with autosomal recessive ectodermal dysplasia, it has been shown that over half of obligate heterozygotes for WNT10A variant display clinical symptoms of ectodermal dysplasia, including mild oligodontia or a few abnormally shaped permanent teeth, nail dystrophy, and other mild hair, skin, and palmoplantar symptoms of ectodermal dysplasia.

### **Test Sensitivity:**

Variants in the WNT10A gene have been reported in up to 25% of individuals with hypohidrotic ectodermal dysplasia who do not have an EDA gene variant, and 9% of unselected patients with ectodermal dysplasia.<sup>1</sup> The method used by GeneDx to screen the WNT10A gene is expected to identify nearly all variants that occur in the coding and flanking splice sites of the gene.

### **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. 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:

1. Bohring et al. *Am J Hum Genet.* 85:97-105, 2009
2. Adaimy et al. *Am J Hum Genet.* 81:821-828, 2007
3. Wright JT, Grange DK, Fete M. Hypohidrotic Ectodermal Dysplasia. 2003 Apr 28 [Updated 2017 Jun 1]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. *GeneReviews*® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2018. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK1112/>