TGM1 Gene Analysis in Congenital Recessive Ichthyosis (CRI)

Disorder also known as: TGM1 Gene Analysis in Congenital Recessive Ichthyosis (CRI)

Clinical Features:
Most neonates with autosomal recessive congenital ichthyosis present as collodion babies. Collodion babies are born with a taut, shiny, translucent or opaque membrane that encases the entire body and lasts for days to weeks. Affected individuals with severe involvement can have ectropion, eclabium, scarring alopecia involving the scalp and eyebrows, and palmar and plantar hyperkeratosis. After the collodion membrane has been shed, the clinical presentation and severity of congenital recessive ichthyosis may greatly vary between individuals. Congenital recessive ichthyosis encompass a wide spectrum, extending from severe ‘classic’ lamellar ichthyosis with dark brown, plate-like scale without erythroderma to congenital ichthyosiform erythroderma with finer, whitish scale and underlying generalized redness of the skin. The severity of congenital recessive ichthyosis ranges from severe (‘classic’ lamellar ichthyosis) to mild (mild lamellar ichthyosis, mild non-bullous congenital ichthyosiform erythroderma) or almost complete resolution of the skin disorder (so-called ‘self-healing collodion baby’). Although these phenotypes are now recognized to fall on a continuum, the phenotypic classification can be clinically useful for clarifying prognosis and management for individuals and, to some extent, to choose which genes to analyze. A skin biopsy is not necessary to establish the diagnosis of autosomal recessive congenital ichthyosis, and is usually not helpful in differentiating among the different clinical disorders along the spectrum. However, a skin biopsy is useful to differentiate the non-bullous from the bullous forms of ichthyosis. Thus, if blistering is present, histopathological evaluation can be a useful diagnostic tool. Approximately 1 in 225 individuals is a carrier for lamellar ichthyosis/NCIE1 due to variant in the TGM1 gene, and the disorder has been described in all races and ethnicities.

Genetics:
Autosomal recessive.

Test Methods:
Using genomic DNA, variants are identified by bi-directional sequence analysis of the entire coding sequence (exons 2-15) and splice junctions of the TGM1 gene. If sequencing identifies a variant on only one allele, targeted array CGH analysis with exon-level resolution (ExonArrayDx) will be performed 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:
Of patients with non-erythrodermic, mild to severe lamellar ichthyosis, variants in the TGM1 gene account for more than 90% of cases. Missense variants, splice-site variants, and deletions occur throughout the gene, although there are several residues where variants have been reported more than once, and a few that are more common in persons of certain ethnic heritages.

References: