FLG Gene Analysis in Ichthyosis Vulgaris with or without Atopic Dermatitis

Disorder also known as: IV; Ichthyosis simplex; Autosomal dominant ichthyosis

Clinical Features:
Ichthyosis vulgaris (IV) is the most common type of ichthyosis with an estimated prevalence of 1 in 250 to 400 individuals. The disorder initially presents with dry skin and mild to moderate scaling during infancy or early childhood. Fine, white, flaky scales cover the extensor surfaces of the extremities with sparing of the groin and flexural areas. The scales are usually larger on the lower legs, with detached, outward turning edges. The palms and soles appear hyperlinear with accentuated skin markings due to mild hyperkeratosis. Cracking and painful fissures of the heels are common. In more severe disease, scaling extends to large areas of the trunk, scalp, forehead and cheeks, and there may be itchiness and heat intolerance. Clinical symptoms and severity depend on season and climate, improving during the summer and with increasing humidity, and worsening in a dry, cold environment. Ichthyosis vulgaris is frequently associated with keratosis pilaris and features of atopic disease: atopic dermatitis (AD), asthma, and hay fever. Atopic dermatitis is encountered in as many as 25 to 50% of IV patients, and can obscure the characteristic sparing of the flexures. However, the group of patients with atopic dermatitis who also have ichthyosis vulgaris is small.

Genetics:
Autosomal semi-dominant (co-dominant), with more subtle features in heterozygotes (penetrance up to 90%), and severe disease with complete penetrance in individuals with a FLG variant affecting both alleles (homozygotes or compound heterozygotes).

Test Methods:
Using genomic DNA obtained from the submitted biological material, bi-directional sequence of exon 3 of the FLG gene is analyzed to specifically evaluate for the presence of the common R501X and c.2282_2285delCAGT variants. 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:
A recent study found that of 26 white IV patients analyzed, about 69% had 2 null FLG alleles and 27% were heterozygous for a FLG variant. Analysis for the 2 common hot spot variants in FLG as performed at GeneDx will identify the underlying genetic cause in the vast majority (80%-90%) of white IV patients of North/West-European decent. However, almost 20 other
variants in FLG have been reported in various different population groups to date, and those variants would not be identified by the GeneDx test.

References: