

Filaggrin ProGenotyper[®] Test

Test Name: Filaggrin ProGenotyper[®] Test

Alternative Names: Filaggrin Mutation Test

Test Code: 403100

CPT Code: 83890, 83898x3, 83891x3, 83904x6, and 83912

Clinical Utility:

The test detects the presence of loss of function or null mutations in the filaggrin gene. Individuals with mutations in FLG are at higher risk of developing atopic dermatitis with or without ichthyosis vulgaris. The prevalence of IV is 1 in 250-400 individuals. Patients with a null mutation in this gene may be candidates for targeted lipid-replacement therapy.

Specimen Requirement:

- 2 mL of whole blood (EDTA)
- Ship overnight at ambient temperatures

Background:

This assay detects the presence of heterozygous or homozygous mutations or wildtype sequence at six prevalent sites of known null mutations or at additional sites in the portions of the filaggrin gene sequenced.

Filaggrin is a major protein in the epidermis, localized in the keratohyalin granules of the keratinocytes. It is expressed as a large protein that is then proteolytically cleaved into multiple individual filaggrin molecules; these are encoded by a gene with 10-12 repeats. The cleaved products aggregate the keratin cytoskeleton, causing the transformation of the granular cells into flattened squames. The cornified cell envelope on the external surface prevents water loss and impedes entry of allergens and infectious agents. Aberrant expression of filaggrin has been implicated in a number of keratinizing disorders, including atopic dermatitis. The five most common European ancestry mutations show a strong association with moderate to severe childhood atopic dermatitis. In Asian populations, the sixth mutation, S2554X, was found to be associated with atopic dermatitis.

Units and Reference Range:

Results are presented as either WT-no null mutation detected, HET (one copy of WT and one copy of mutation containing sequence), or MUT (both copies carry a mutated sequence) for the region sequenced (approximately codons 413-531; 741-916, and 2419-2565).

Method:

1. DNA is isolated from whole blood.
2. Regions of the filaggrin gene are amplified by PCR from the genomic DNA, and the products of each fragment are purified.
3. Cycle sequencing is performed with one or two sequencing primers per FLG fragment, depending on the size of the PCR fragment.
4. These products are purified and run on the ABI3130 or 3730 Genetic Analyzer.
5. The sequenced areas are analyzed for heterozygous or homozygous null mutations in comparison with the reference sequence, NG_016190.

List of prevalent mutations detected:

R501X	2282Δ4
1249insG	E2422X
R2447X	S2554X

Related Tests for Atopic Dermatitis:

403068	Complete Atopic Dermatitis Panel
403071	Atopic Dermatitis Food IgE Panel
403069	Atopic Dermatitis Microbial Panel
403070	Atopic Dermatitis Autoimmunity Panel
00001	Total Serum IgE
000042	Eosinophil cationic protein (ECP)
002102	Soluble E-Selectin

References:

1. Basu K, Palmer CAN, et.al. 2008. Filaggrin null mutations are associated with increased asthma exacerbations in children and young adults. *Allergy*. 63:1211-1217.
2. Chen H, Ho JCC, et. al. 2008. Unique and recurrent mutations in the filaggrin gene in Singaporean Chinese patients with ichthyosis vulgaris. *Journal of Investigational Dermatology*. 128:1669-1675.
3. McGrath JA and Uitto J. 2008. The filaggrin story: novel insights into skin-barrier function and disease. *Trends in Molecular Medicine*. 14:20-27.
4. Sandilands A, O'Regan GM, Liao H, et al 2006. Prevalent and rare mutations in the gene encoding filaggrin cause ichthyosis vulgaris and predispose individuals to atopic dermatitis. *J Invest Dermatol*. 126(8):1770-5.
5. Smith FJ, Irvine AD, Terron-Kwiatkowski A, et al. 2006. Loss-of-function mutations in the gene encoding filaggrin cause ichthyosis vulgaris. *Nat Genet*. 38(3):337-42.
6. Weidinger S, O'Sullivan M, et.al. 2008 Filaggrin mutations, atopic eczema, hay fever, and asthma in children. *J Allergy Clin Immunol*. 121:1203-1209.

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