

KRT4 and KRT13 Gene Analysis in White Sponge Nevus

Disorder also known as: White Sponge Nevus of Cannon; Hereditary Mucosal Leukokeratosis

Clinical Features:

White sponge nevus (WSN) is a rare autosomal dominant disorder of the non-cornifying squamous epithelia. The clinical hallmarks are white, soft, spongy, thickened plaques on both sides of the oral mucosa and tongue. The mucous membranes of the nose, esophagus, genitalia and rectum may also be involved. Light microscopic examination usually reveals epithelial thickening, parakeratosis, extensive vacuolization of the suprabasal keratinocytes and compact aggregates of keratin intermediate filaments in the upper spinous layers. The disorder usually manifests with whitish mucosal plaques during infancy or early childhood and may be difficult to differentiate from mucosal yeast infections.

Genetics:

Autosomal dominant. Sporadic cases, due to a new variant in a keratin gene, do occur.

Test Methods:

Using genomic DNA obtained from submitted biological material, hot spots for variant in the KRT4 and KRT13 genes are screened for variants by bi-directional DNA sequencing of selected exons. Variants resulting in amino acid substitutions in the ends of the keratin rod domains are sequenced first; if no variant is found the entire coding sequence can be sequenced (at additional cost). If a variant has been found, the result will be confirmed by repeat analysis using sequencing, restriction fragment analysis, or another appropriate method.

Test Sensitivity:

Variants in the KRT4 or KRT13 genes, encoding keratin-4 and keratin-13 of the keratin intermediate filament family, respectively, have been reported in 9 unrelated families to date. Most variants were clustered at variant hotspots areas, which code for the ends of the keratin rod domains. Therefore, sequencing of the hotspot regions of KRT4 and KRT13 is expected to identify the majority of variants in White Sponge Nevus.

References:

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2. Rugg, EL et al. *Nature Genet.* 11: 450-452, 1995
3. Terrinoni, A et al. *J. Invest. Derm.* 114: 388-391, 2000.
4. Witkop, CJ Jr. & Gorlin, R.J. *Arch. Derm.* 84: 762-771, 1961.