

Keratin Gene Analysis in Epidermolytic Palmoplantar Keratoderma

Disorder Also Known As: Vörner Syndrome; including epidermolytic palmoplantar keratoderma with tonotubular keratin

Clinical Features:

EPPK results in diffuse, yellowish palmar and plantar hyperkeratosis ('keratoderma') with a red border. Patients may have blistering in affected areas triggered by trauma, such as friction; however, the blistering often appears to improve with age. A rare variant with characteristic electron microscopic findings ("tonotubular keratin") has been reported in Northern Europe.

There are also patients whose disease primarily affects the palms and soles, but who also have relatively mild generalized involvement. Some of these patients have been found to have variants in KRT1, which typically causes epidermolytic ichthyosis. Other patients with focal plaques of palmoplantar keratoderma (callus-like) have been found to have variants in the KRT16 gene, which typically causes pachyonychia congenita.

Inheritance Pattern/Genetics:

Epidermolytic palmoplantar keratoderma is an autosomal dominant disorder typically caused by a heterozygous variant in the KRT9 gene, which is almost exclusively found in the skin of palms and soles. Rarely, variants in the KRT1 or KRT16 genes have been observed.

Test Methods:

The KRT9 gene is screened for variants by bi-directional sequence analysis. Since all variants reported to date cluster at two variant hotspots encoding the ends of the central rod domain, including the common variant R162W, analysis is limited to these regions.

See the information sheets and requisition form for KRT1 testing in epidermolytic ichthyosis and KRT16 testing in pachyonychia congenital for methods of those tests.

Test Sensitivity:

If there is a variant in the coding sequence of KRT9 in an individual, the methods employed by GeneDx will identify the variant approximately 99% of the time. However, because palmoplantar keratoderma is a very heterogeneous disorder, it is possible that a patient with the disease will not have a variant in this gene, but in a different gene for which screening was not done.

Most variants in keratin genes are missense variants that affect the ends of the rod domains of the keratin proteins and affect stability of keratin intermediate filaments. There is a common KRT9 variant in Vörner disease, R162W, which has been described in many patients.

References:

1. Reis et al. Keratin 9 gene mutations in epidermolytic palmoplantar keratoderma (EPPK). *Nat Genet.* 1994; 6(2):174-9
2. Terrinoni et al. Identification of the keratin K9 R162W mutation in patients of Italian origin with epidermolytic palmoplantar keratoderma. *Eur J Dermatol.* 2004;14(6):375-8.
3. Kon et al. L457F missense mutation within the 2B rod domain of keratin 9 in a Japanese family with epidermolytic palmoplantar keratoderma. *Br J Dermatol.* 2006;155(3):624-6.