MBTPS2 Gene Analysis in Ichthyosis Follicularis with Atrichia and Photophobia (IFAP) and Keratosis Follicularis Spinulosa Decalvans (KFSD)

Clinical Features:
Two clinical disorders, Ichthyosis Follicularis with Atrichia and Photophobia (IFAP) with or without BRESK/BRESHECK syndrome, and Keratosis Follicularis Spinulosa Decalvans (KFSD), have been associated with variants in the MBTPS2 gene.

IFAP syndrome is characterized by the triad of follicular ichthyosis, total or subtotal atrichia, and photophobia to variable degree. Congenital atrichia is most prevalent and most affected boys have total atrichia at birth. A subgroup of patients has been described with lamellar rather than follicular ichthyosis. Less common features include nail dystrophy, growth and psychomotor retardation, aganglionic megacolon, and seizures. Female carriers may show features of the disorder, including a linear pattern of follicular ichthyosis, mild atrophoderma, hypotrichosis, and hypohidrosis.[1] Some individuals may have additional features, which constitute BRESK/BRESHECK syndrome. These features include brain anomalies, intellectual disability, ectodermal dysplasia, skeletal deformities, ear or eye anomalies, and renal anomalies, with or without Hirschprung disease and cleft palate or cryptorchidism.[2]

KFSD is a disorder affecting the skin and eyes. In affected men, the skin findings include inflammatory hyperkeratotic follicular papules or pustules on the scalp, eyebrows and elsewhere on the integument. This process leads to progressive scaring alopecia. Eye findings include photophobia and corneal dystrophy. Other findings include hyperkeratosis of the elbows, knees, and palms and soles. KFSD can be distinguished from IFAP due to the nature of alopecia, which is progressive and scaring in KFSD, and congenital and non-scarring in IFAP. Carrier females are usually less severely affected.[3]

Inheritance Pattern/Genetics:
X-linked

Test Methods:
Variant analysis of the MBTPS2 gene is performed on genomic DNA from the submitted specimen using bi-directional sequence analysis of coding exons and corresponding intron/exon boundaries. 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:

Only a few large-scale studies of patients with IFAP with or without BRESK/BRESCHEK and KFSD have been published to date. One study reported distinct variants in MBTPS2 in three multi-generational families with IFAP with typical X-linked inheritance, and in three smaller unrelated families. Minor intra-familial phenotypic variability between affected males was noted; however, the severity between different families varied greatly. Female carriers in all reported families were either phenotypically normal or showed mild features.[1] Another study of IFAP in a large Chinese family identified a missense variant, and affected individuals showed a broad phenotypic spectrum.[5] In one study of nine families with a clinical diagnosis of KFSD, the same variant was identified in three families (26 cases). In the remaining six small families, there was not a clear X-linked mode of inheritance.[3]

References:

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2. Naiki et al., (2011). Am J Med Genet Part A 158A: 97-102.
3. Aten et al., (2010). Hum Mutat 31(10): 1125-1133.
4. Oeffner et al., (2011). Exp Dermatol 20: 445-456.
5. Tang et al., (2011). J Am Acad Dermatol 64 (4): 716-722.