Ichthyosis Follicularis with Atrichia and Photophobia (IFAP) Syndrome: \textit{MBTPS2} Gene Sequencing

| Test Code: SMBTP | Turnaround time: 6 weeks | CPT Codes: 81479 x1 |

**Condition Description**

Ichthyosis follicularis with atrichia and photophobia (IFAP) syndrome is an X-linked condition characterized by follicular ichthyosis, total or partial atrichia (alopecia), and varying degrees of photophobia. The most prominent feature of the syndrome is congenital atrichia with the majority of affected boys having total atrichia at birth. There have been reports of sparse or thin hair. In more severe cases, other findings of this syndrome may include neurological abnormalities, including seizures and intellectual disability, failure to thrive, nail dystrophy, atopic manifestation, inguinal hernia, aganglionic megacolon, and renal, vertebral, and testicular anomalies. It is inherited in an X-linked manner. Female carriers may be phenotypically normal or may have a milder phenotype including a linear pattern of follicular ichthyosis, hypohidrosis, hypotrichosis, and mild atrophoderma. Phenotypic variability has been reported between families but there is usually very minor variability within a family.

In five out of six unrelated IFAP syndrome patients, missense mutations were identified in the \textit{MBTPS2} gene (Xp22.1).

For patients with suspected IFAP syndrome, sequence analysis is recommended as the first step in mutation identification. For patients in whom mutations are not identified by full gene sequencing, deletion/duplication analysis is appropriate.

References:


**Genes**

\textit{MBTPS2}

**Indications**

This test is indicated for:

- Confirmation of a clinical diagnosis of IFAP syndrome.
- Carrier testing in adults with a family history of IFAP syndrome.

**Methodology**

PCR amplification of 13 exons contained in the \textit{MBTPS2} gene is performed on the patient's genomic DNA. Direct sequencing of amplification products is performed in both forward and reverse directions, using automated fluorescence dideoxy sequencing methods. The patient's gene sequences are then compared to a normal reference sequence. Sequence variations are classified as mutations, benign variants unrelated to disease, or variations of unknown clinical significance. Variants of unknown clinical significance may require further studies of the patient and/or family members. This assay does not interrogate the promoter region, deep intronic regions, or other regulatory elements, and does not detect large deletions.

**Detection**

Clinical Sensitivity: In five out of six unrelated IFAP syndrome patients, missense mutations were identified in the \textit{MBTPS2} gene (Xp22.1). Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical and/or biochemical phenotype.

Analytical Sensitivity: ~99%

**Specimen Requirements**

Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) tube:
- Infants (2 years): 3-5 ml
- Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

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Type: Saliva

Specimen Requirements:

Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.

Related Tests

- Deletion/duplication analysis of the MBTPS2 gene by CGH array is available for those individuals in whom sequence analysis is negative.
- Custom diagnostic mutation analysis (KM) is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- Prenatal testing is available only for known familial mutations to individuals who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.
- X-Linked Intellectual Disability panels are available for 30, 60, and 90 genes.