Noonan-like Syndrome with Loose Anagen Hair: SHOC2 Gene Sequencing

Test Code: SSHOC
Turnaround time: 6 weeks
CPT Codes: 81405 x1

Condition Description

A mutation in the SHOC2 gene (10q25) has been shown to cause a consistent phenotype called Noonan-like syndrome with loose anagen hair. Affected individuals have an unusual combination of features observed in disorders of the neuro-cardio-facial-cutaneous disorders family. Characteristics in affected individuals include facial features somewhat similar to Noonan syndrome (NS), macrocephaly, growth hormone deficiency, mild psychomotor delay with ADHD that improves with age, and hair anomalies including easily pluckable, sparse, thin, slow growing hair (loose anagen hair). Most individuals also have increased skin pigmentation with eczema or ichthyosis. Other features can include enlarged CSF spaces, webbed neck, short stature, ptosis, epicanthal folds, hypertelorism, low-set posteriorly rotated ears, widely spaced nipples, pectus deformities, and cardiac anomalies, especially mitral valve dysplasia and septal defects.

In studies, approximately 4% of individuals with Noonan characteristics who were negative for mutations in other NS genes were found to have a mutation in SHOC2. All individuals with mutations had loose anagen hair.

References:
- OMIM #607721 Noonan-Like Syndrome with Loose Anagen Hair

Genes

SHOC2

Indications

This test is indicated for:
- Confirmation of a clinical diagnosis of Noonan-like syndrome with loose anagen hair

Methodology

PCR amplification of 8 exons contained in the SHOC2 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 studies, approximately 4% of individuals with Noonan characteristics who were negative for mutations in other NS genes were found to have a mutation in SHOC2. All individuals with mutations had loose anagen hair. 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 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.

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.

Special Instructions
Submit copies of diagnostic biochemical test results with the sample, if appropriate. Contact the laboratory if further information is needed.

Related Tests
- Deletion/duplication analysis of the SHOC2 gene by CGH array is available for those individuals in whom sequence analysis is negative.
- Analysis of the SOS1, PTPN11, RAF1, and KRAS genes is available for Noonan syndrome.
- 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 to individuals who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.