Noonan-like Syndrome with Loose Anagen Hair: \textit{SHOC2} Gene Deletion/Duplication

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\textbf{Test Code:} DSHOC  \\
\textbf{Turnaround time:} 2 weeks  \\
\textbf{CPT Codes:} 81228 x1  \\
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\textbf{Condition Description}

A mutation in the \textit{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 \textit{SHOC2}. All individuals with mutations had loose anagen hair.

For patients with suspected Noonan-like syndrome with loose anagen hair, 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.

\textbf{References:}

- \textbf{OMIM #607721:} Noonan-Like Syndrome with Loose Anagen Hair

\textbf{Genes}

\textit{SHOC2}

\textbf{Indications}

This test is indicated for:

- Confirmation of a clinical diagnosis of Noonan-like syndrome with loose anagen hair in an individual in whom sequence analysis was negative.
- Carrier testing in adults with a family history of Noonan-like syndrome with loose anagen hair in whom sequence analysis was negative.

\textbf{Methodology}

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region.

Please note that a "backbone" of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient's phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

\textbf{Detection}

Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations. Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

\textbf{Specimen Requirements}

Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

\textbf{Type: Whole Blood}

Specimen Requirements:

In EDTA (purple top) or ACD (yellow 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**

Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of Emory Genetics Laboratory, please submit a copy of the sequencing report with the test requisition.

**Related Tests**

- Sequence analysis of the SHOC2 gene is available and is required before deletion/duplication analysis.
- 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 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.