

Noonan-Like Syndrome with Loose Anagen Hair via *SHOC2* Gene Sequencing – Test #381

Brief Description of Clinical Features: Noonan-like syndrome with loose anagen hair (OMIM 607721) is a rare disorder characterized by an association of Noonan syndrome and loose anagen hair. The most common clinical features are reduced growth, cognitive deficits, hyperactive behavior, and hair abnormalities consisting of easily pluckable, slow-growing hair (Mazzanti et al. Am J Med Genet 118A:279-286, 2003). Trichogram findings include abnormally shaped anagen bulbs lacking root sheaths (Tosti et al. Dermatologica 182:247-249, 1991). Additional features suggestive of Costello or Cardiofaciocutaneous syndromes have been reported. These include darkly pigmented skin with eczema or ichthyosis, hypernasal voice, and cardiac anomalies including dysplasia of the mitral valve and septal defects (Cordeddu et al. Nat Genet 41:1022-1026, 2009).

Genetics: A mutation in the *SHOC2* gene causes Noonan-like syndrome with anagen hair (Cordeddu et al. 2009). Several patients with the *SHOC2* mutation presented as newborns or young infants with clinical features suggestive of Costello syndrome or Cardiofaciocutaneous syndrome. All patients tested to date share a missense mutation in the *SHOC2* gene, defined as c.4 A>G and resulting in the amino acid substitution p.Ser2Gly. This mutation occurred *de novo* in all reported patients for which parental testing was performed.

Description of this Particular Test: The SHOC2 protein positively regulates the RAS-MAPK signaling pathway. This test involves bidirectional sequencing using genomic DNA of all coding exons (exons 1-8) of the *SHOC2* gene. The full coding region of each exon plus ~50 bp of flanking non-coding DNA on each side are sequenced. As requested, we will also sequence only exon 1 (Test #100) which contains the c.4 A>G mutation.

Reference Sequences: Genomic: NC_000010.10 mRNA: NM_007373.3 Protein: NP_031399.2 (CCDS 7568.1)

Indications for Test: Patients with symptoms suggestive of Noonan-like syndrome with loose anagen hair and patients with Noonan syndrome who are negative for mutations in the genes that are commonly mutated in this disorder.

Sensitivity of Test: Unknown at this time.

Turnaround Time: Maximum of 40 calendar days, although many tests are completed in 2-3 weeks.

Specimen Requirements: See page 4 of the Requisition Form.

Prices: Sequencing of the full *SHOC2* gene \$ 660 Sequencing of Exon 1 only (Test #100) \$190

CPT Codes:

Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1	83891 \$ 40
Amplification x10	83898 \$180	Sequencing x10	83904 \$ 260
Separation x1	83894 \$ 60	Interpretation/Report x1	83912 \$ 90

Accreditation Info. CLIA ID #: 52D1027685 (expires 1/18/13) (CAP#: 7185561, AU ID: 1407125 expires 12/20/12)

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