Lab Dept: Anatomic Pathology

Test Name: NEUROFIBROMATOSIS TYPE 1-LIKE (SPRED1) SEQUENCING

General Information

Lab Order Codes: SPRED

Synonyms: Legius syndrome; Neurofibromatosis Type 1-like Comprehensive Analysis; SPRED1 Testing, NFLS

CPT Codes: 81405 – SPRED1 (sprout-related, EVH1 domain containing 1 (eg, Legius syndrome), full gene sequencing (Molecular Pathology Level 6)
81404 – SPRED1 Deletion/Duplication (Molecular Pathology Level 5) (if appropriate)

Test Includes: Testing is DNA based including complete sequencing and copy number analysis; no NF1 testing previously done. Complemented with MPLA to detect copy number changes.

Logistics

Test Indications: Physical characteristics consisting of mainly multiple CAL-spots, freckling and relative macrocephaly. Some patients also have learning disabilities or hyperactivity. In none of the adult patients identified so far, neurofibromas or central nervous system tumors were observed (Brems et al, 2007). A Noonan-like dysmorphology was observed in some individuals. In the five multi-generation families initially ascertained, several affected individuals fulfilled the NIH diagnostic criteria for NF1. The disorder is caused by germline loss-of-function mutations in SPRED1. At the recent European NF meeting in Killarney (Ireland), it was decided by the community to refer to this condition as “Legius syndrome”. SPRED 1 is a member of the SPROUTY/SPRED family of proteins that act as negative regulators or RAS-RAF interaction and mitogen-activated protein kinase (MAPK) signaling.

Lab Testing Sections: Anatomic Pathology - Sendouts

Referred to: University of Alabama, Medical Genomics Laboratory, Dept of Genetics (UAL) (Test 1C)

Phone Numbers: MIN Lab: 612-813-6280

STP Lab: 651-220-6550

Test Availability: Monday - Thursday

Turnaround Time:	3 – 4 weeks, specimens are batched and run once or twice weekly
Special Instructions:	Restricted draw times, see Test Availability. Requests must include request form with referring or genetic counselor's name and address, billing information, completed informed consent and **phenotypic checklist**. All forms can be found at Spred1Req form.pdf.

Specimen

Specimen Type:	Whole blood
Container:	Lavender top (EDTA) tube
Draw Volume:	10 mL (Minimum: 3 mL) blood
Processed Volume:	Same as Draw Volume
Collection:	Routine venipuncture
Special Processing:	Lab Staff: **Do Not** centrifuge. Specimen should remain in original collection container. Specimen should remain at room temperature and received at reference lab within 60 hours of collection. Send Monday-Thursday via UPS or Federal Express marked "priority". Specimens must be packaged to prevent breakage and absorbent material must be included in the package to absorb liquids in the event that breakage occurs. Also, the package must be shipped in double watertight containers. Please contact the reference lab prior to sample shipment and provide them with the date of shipment and the tracking number of the package, so that sample delivery can be better ensured within the 60 hour window.
Patient Preparation:	None
Sample Rejection:	Mislabeled or unlabeled specimens; frozen specimens, contaminated specimens, absence of referring physician and address, absence of billing information, absence of informed consent, absence of phenotypic checklist

Interpretive

Reference Range:	Interpretive report
Critical Values:	N/A
Limitations:	N/A

Methodology:	RNA/cDNA based core assay resulting in the full characterization of SPRED1 mutation. If NF1 testing was performed previously, the complete SPRED1 coding region is analyzed by sequencing exons 1-7 starting from the sample submitted for NF1 testing. In addition, DNA copy number analysis by MPLA is performed. Mutations screened for include truncating mutations (nonsense, frameshift, splice mutations), missense mutations, multi-exon deletions or duplications and total gene deletions.
References:	University of Alabama Medical Genomics LaboratoryJanuary 2013 (205) 934-5562 Fax (205) 996-2929
Updates:	1/15/2013: Updated CPT coding and inclusion of Deletion/Duplication.