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Patient Report

Patient Age/Gender: 49 years Male

**Specimen Collected: 21-Jun-21 15:00**

**NF1 and LS(SPRED1) by NGS, DelDup |Received: 21-Jun-21 15:00 Report/Verified: 23-Jun-21 13:58**

| Procedure | Result | Units | Reference Interval |
|---|---|---|---|
| NF1 and LS (SPRED1) Panel Specimen | Whole Blood | | |
| NF1 and LS (SPRED1) Panel Interpretation | Positive [f1 i1] | | |

## Result Footnote

f1: NF1 and LS (SPRED1) Panel Interpretation

Section 79-1 of New York State Civil Rights Law requires informed consent be obtained from patients (or their legal guardians) prior to pursuing genetic testing. These forms must be kept on file by the ordering physician. Consent forms for genetic testing are available at www.aruplab.com. Incidental findings are not reported unless clinically significant but are available upon request.

## Test Information

i1: NF1 and LS (SPRED1) Panel Interpretation

BACKGROUND INFORMATION: Neurofibromatosis Type 1 Sequencing and Deletion/Duplication and Legius Syndrome Sequencing Panel

CHARACTERISTICS: Common clinical findings of neurofibromatosis type 1 (NF1) include cafe au lait macules, axillary and inguinal freckling, cutaneous fibromas, Lisch nodules, choroidal freckling, and learning disabilities. Less common findings of NF1 include optic or other CNS gliomas, vasculopathies, tibial pseudarthrosis, scoliosis, somatic overgrowth, and malignant peripheral nerve sheath tumors. The following symptoms of Legius syndrome (LS) overlap with findings in NF1: cafe au lait spots, axillary and inguinal freckling, learning disabilities, ADHD, developmental delays, and macrocephaly. Neurofibromas, Lisch nodules, and CNS tumors are not typically observed in LS.

EPIDEMIOLOGY: Incidence of NF1 is 1 in 3000. Prevalence of LS is estimated at 1 in 46,000-75,000.

CAUSE: Pathogenic germline variants in the NF1 gene (for NF1) or SPRED1 gene (for LS).

INHERITANCE: Autosomal dominant; 50 percent of pathogenic NF1 variants are de novo.

PENETRANCE: Complete after childhood for NF1.

CLINICAL SENSITIVITY: Approximately 90 percent for NF1 and 89 percent for LS.

GENES TESTED: NF1 and SPRED1**

**-Deletion/duplication detection is not available for this gene.

METHODOLOGY: Multiplex ligation-dependent probe amplification (MLPA) of the NF1 gene. Capture of all coding exons and exon-intron junctions of the NF1 and SPRED1 genes, followed by massively parallel sequencing. Sanger sequencing was performed as necessary to fill in regions of low coverage and confirm reported variants. Human genome build 19 (Hg 19) was used for data analysis.

ANALYTICAL SENSITIVITY/SPECIFICITY: The analytical sensitivity for MLPA is greater than 99 percent. The analytical sensitivity of sequencing is approximately 99 percent for single nucleotide variants (SNVs) and greater than 93 percent for

## Test Information

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insertions/duplications/deletions from 1-10 base pairs in size. Variants greater than 10 base pairs may be detected, but the analytical sensitivity may be reduced. LIMITATIONS: A negative result does not exclude a diagnosis of NF1 or LS. This test only detects variants within the coding regions and intron-exon boundaries of the NF1 and SPRED1 genes. Large deletions/duplications in SPRED1 are not assessed. Regulatory region variants and deep intronic variants will not be identified, and breakpoints of large NF1 deletions/duplications will not be determined. Deletions/duplications/insertions of any size may not be detected by massively parallel sequencing. Diagnostic errors can occur due to rare sequence variations. In some cases, variants may not be identified due to technical limitations in the presence of pseudogenes, repetitive, or homologous regions. This assay may not detect low-level mosaic or somatic variants associated with disease. Interpretation of this test result may be impacted if this patient has had an allogeneic stem cell transplantation. Noncoding transcripts were not analyzed.

This test was developed and its performance characteristics determined by ARUP Laboratories. It has not been cleared or approved by the US Food and Drug Administration. This test was performed in a CLIA certified laboratory and is intended for clinical purposes.

Counseling and informed consent are recommended for genetic testing. Consent forms are available online.