Client: ARUP Example Report Only
500 Chipeta Way
Salt Lake City, UT 84108
UNITED STATES

Physician: TEST,

Patient: NF1 NGS, NEG

DOB
Sex: Female
Patient Identifiers: 44132
Visit Number (FIN): 44458
Collection Date: 11/14/2022 11:13

Neurofibromatosis Type 1 and Legius Syndrome Panel, Sequencing and Deletion/Duplication

ARUP test code 3003927

NF1 and LS (SPRED1) Panel Specimen	Whole Blood
NF1 and LS (SPRED1) Panel Interpretation	Negative

RESULT
No pathogenic variants were detected in any of the genes tested.

INTERPRETATION
No pathogenic variants were detected in any of the genes tested. This result decreases the likelihood of, but does not exclude, a diagnosis of neurofibromatosis type 1 or Legius syndrome. Please refer to the background information included in this report for a list of the genes analyzed, methodology, and limitations of this test.

RECOMMENDATIONS
Medical screening and management should rely on clinical findings and family history. If this individual has a family history, determination of a causative familial variant in an affected family member is necessary for optimal interpretation of this negative result. Further testing may be warranted if there is a familial variant that is not detectable by this assay. Genetic consultation is recommended.

COMMENTS
Likely benign and benign variants are not reported.
Variants in the following region(s) may not be detected with sufficient confidence in this sample due to technical limitations:
NONE

This result has been reviewed and approved by Rong Mao, MD.
BACKGROUND INFORMATION: Neurofibromatosis Type 1 and Legius Syndrome Panel, Sequencing and Deletion/Duplication
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 3,000. Prevalence of LS is estimated at 1 in 46,000-75,000.

H=High, L=Low, *=Abnormal, C=Critical

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 99 percent for LS.

GENES TESTED: NF1 (NM_001042492); SPRED1 (NM_152594)

METHODOLOGY: Probe hybridization-based capture of all coding exons and exon-intron junctions of the targeted genes, followed by massively parallel sequencing. Sanger sequencing was performed as necessary to fill in regions of low coverage and to confirm reported variants that do not meet acceptable quality metrics. A proprietary bioinformatic algorithm was used to detect large (single exon-level or larger) deletions or duplications in the indicated genes. Large deletions/duplications confirmed using an orthogonal exon-level microarray. Human genome build 19 (Hg 19) was used for data analysis.

ANALYTICAL SENSITIVITY/SPECIFICITY: The analytical sensitivity is approximately 99 percent for single nucleotide variants (SNVs) and greater than 93 percent for insertions/duplications/deletions (indels) from 1-10 base pairs in size. Indels greater than 10 base pairs may be detected, but the analytical sensitivity may be reduced. Deletions of 2 exons or larger are detected with sensitivity greater than 97 percent; single exon deletions are detected with 62 percent sensitivity. Duplications of 3 exons or larger are detected at greater than 83 percent sensitivity. Specificity is greater than 99.9 percent for all variant classes.

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. Deletions/duplications/insertions of any size may not be detected by massively parallel sequencing. Regulatory region variants and deep intronic variants will not be identified. Precise breakpoints for large deletions or duplications are not determined in this assay and single exon deletions/duplications may not be detected based on the breakpoints of the rearrangement. The actual breakpoints for the deletion or duplication may extend beyond or be within the exon(s) reported. This test is not intended to detect duplications of 2 or fewer exons in size, though these may be identified. Single exon deletions are reported but called at a lower sensitivity. Diagnostic errors can occur due to rare sequence variations. In some cases, variants may not be identified due to technical limitations caused by the presence of pseudogenes, repetitive, or homologous regions. This test is not intended to detect low-level mosaic or somatic variants, gene conversion events, complex inversions, translocations, mitochondrial DNA (mtDNA) mutations, or repeat expansions. 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 U.S. 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.

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VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
NF1 and LS (SPRED1) Panel Specimen	22-318-105101	11/14/2022 11:13:00 AM	11/14/2022 11:14:36 AM	11/14/2022 11:21:00 AM
NF1 and LS (SPRED1) Panel Interpretation	22-318-105101	11/14/2022 11:13:00 AM	11/14/2022 11:14:36 AM	11/14/2022 11:21:00 AM

END OF CHART

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