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PATIENT REPORT

Patient Age/Sex: Male

Specimen Collected: 20-Jul-22 15:15

Birt-Hogg-Dube Syndrome by NGS, DelD | **Received: 20-Jul-22 15:15** **Report/Verified: 21-Jul-22 11:10**

Procedure	Result	Units	Reference Interval
FLCN Interp	See Note [i1]		
FLCN Specimen	Whole Blood		

Test Information

i1: FLCN Interp

BACKGROUND INFORMATION: Birt-Hogg-Dube Syndrome (FLCN) Sequencing and Deletion/Duplication

CHARACTERISTICS: Birt-Hogg-Dube syndrome (BHDS) is characterized by cutaneous manifestations, pulmonary cysts (typically with history of pneumothorax), and various renal tumors.

EPIDEMIOLOGY: Approximately two individuals per million in the general population are estimated to have BHDS.

CAUSE: BHDS is caused by heterozygous pathogenic germline variants in the FLCN gene.

INHERITANCE: Autosomal dominant

PENETRANCE: Approximately 90-95 percent of individuals with a single pathogenic FLCN variant will develop at least one feature of BHDS.

CLINICAL SENSITIVITY: Approximately 96 percent

GENE TESTED: FLCN (NM_144997)

METHODOLOGY: Probe hybridization-based capture of all coding exons and exon-intron junctions of the FLCN gene, 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.

Test Information

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LIMITATIONS: A negative result does not exclude a diagnosis of Birt-Hogg-Dube syndrome or FLCN-associated tumors. This test only detects variants within the coding regions and intron-exon boundaries of the FLCN gene. 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) variants, 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.