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Patient Report

Patient Age/Gender: 34 years Unknown

Specimen Collected: 21-Jun-21 14:58

Alport Syndrome **|Received: 21-Jun-21 14:58** **Report/Verified: 23-Jun-21 13:56**

Procedure	Result	Units	Reference Interval
Alport Syndrome Specimen	Whole Blood		
Alport Syndrome Interp	Positive [i1]		

Test Information

i1: Alport Syndrome Interp

BACKGROUND INFORMATION: Alport Syndrome Panel, Sequencing and Deletion/Duplication

CHARACTERISTICS: Alport syndrome (AS) is characterized by a triad of renal insufficiency, sensorineural hearing loss (SNHL), and ocular findings. The disease spectrum ranges from a slowly progressive disorder with renal insufficiency and SNHL late in life to SNHL in the first decade of life and end-stage renal disease (ESRD) by age 20. All individuals with MYH9-related disease have enlarged platelets and thrombocytopenia; some will also have adult-onset renal disease and SNHL, but cataracts are uncommon.

PREVALENCE of AS: 1 in 50,000 births.

CAUSE: Pathogenic germline variants in COL4A3, COL4A4, and COL4A5 are causative for AS.

INHERITANCE: X-linked for COL4A5, autosomal dominant and autosomal recessive for COL4A3 and COL4A4, and autosomal dominant for MYH9.

PENETRANCE: Complete for males with pathogenic COL4A5 variants and individuals with autosomal recessive COL4A3 and COL4A4 variants. May be incomplete for autosomal dominant COL4A3 and COL4A4 variants. Complete for MYH9-related disease.

CLINICAL SENSITIVITY: Approximately 97 to 100 percent for AS; approximately 98 percent for MYH9-related disease.

GENES TESTED: COL4A3**, COL4A4**, COL4A5, MYH9**
**Deletion/duplication detection is not performed for these genes.

METHODOLOGY: Capture of all coding exons and exon-intron junctions of the targeted genes, followed by massively parallel sequencing. Sanger sequencing performed as necessary to fill in regions of low coverage and confirm reported variants. Multiplex ligation-dependent probe amplification (MLPA) of the COL4A5 gene.

ANALYTICAL SENSITIVITY/SPECIFICITY: The analytical sensitivity of this test is approximately 99 percent for single nucleotide variants (SNVs) and greater than 93 percent for insertions/duplications/deletions from 1-10 base pairs in size. Variants

Test Information

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greater than 10 base pairs may be detected by massively parallel sequencing, but the analytical sensitivity may be reduced. The analytical sensitivity for detection of deletions/duplications by MLPA for this test is 99 percent.

LIMITATIONS: A negative result does not exclude a diagnosis of AS or MYH9-related disease. This test only detects variants within the coding regions and intron-exon boundaries of the targeted genes. Regulatory region variants and deep intronic variants will not be identified and breakpoints of large deletions/duplications will not be determined. Large deletions/duplications are not tested for COL4A3, COL4A4, and MYH9. Single exon deletions/duplications will not be called for the following exons: COL4A5 (NM_000495) 8, 25, 40, 42, 43. 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.