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

Physician: arup, arup

Patient: ALPORT NGS, Neg Report

DOB	10/10/1980
Gender:	Unknown
Patient Identifiers:	32170
Visit Number (FIN):	32479
Collection Date:	8/17/2021 08:43

Alport Syndrome Panel, Sequencing and Deletion/Duplication

ARUP test code 3002685

Alport Syndrome Specimen	Whole Blood
Alport Syndrome Interp	Negative

INDICATION FOR TESTING
Carrier status or a diagnosis of Alport syndrome

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

INTERPRETATION
No pathogenic variants were identified by massively parallel sequencing of the coding regions and exon-intron boundaries of the genes tested. No large exonic deletions and duplications were identified in the COL4A5 gene; large deletion/duplications are not tested for the COL4A3, COL4A4, and MYH9 genes. This result decreases the likelihood of, but does not exclude, a diagnosis of Alport syndrome or MYH9-related disease. Please refer to the background information included in this report for the clinical sensitivity and limitations of this test.

RECOMMENDATIONS
Medical screening and management of this individual should rely on clinical findings and family history. Genetic consultation is recommended.

COMMENTS
Likely benign and benign variants are not included in this report.

This result has been reviewed and approved by [redacted]

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 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 may not be detected based on the breakpoints of the rearrangement, and will not be called for the following exons: exons 8, 25, and 40 (NM_000495), and exons 42 and 43 (NM_033380) of the COLA5 gene will not be detected. 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.

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Alport Syndrome Specimen	21-229-102667	8/17/2021 8:43:00 AM	8/17/2021 8:44 06 AM	8/17/2021 10:29:00 AM
Alport Syndrome Interp	21-229-102667	8/17/2021 8:43:00 AM	8/17/2021 8:44 06 AM	8/17/2021 10:29:00 AM

END OF CHART

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