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

Physician: TEST,

Patient: FAM NGS FE, POS

DOB
Sex: Male
Patient Identifiers: 44261
Visit Number (FIN): 44588
Collection Date: 11/15/2022 10:30

Familial Targeted Sequencing, Fetal

ARUP test code 3005869

Maternal Contamination Study Fetal Spec	Fetal Cells
Maternal Contam Study, Maternal Spec	Whole Blood For quality assurance purposes, ARUP Laboratories will confirm the above result at no charge following delivery. Order Confirmation of Fetal Testing and include a copy of the original fetal report (or the mother's name and date of birth) with the test submission. Please contact an ARUP genetic counselor at (800) 242-2787 extension 2141 prior to specimen submission.
FAM NGS FE Specimen	Cultured CVS
FAM FE Interp	Positive RESULT Positive for the requested pathogenic variant in the COL1A1 gene. PATHOGENIC VARIANT Gene: COL1A1 (NM_000088.4) Nucleic Acid Change: c.3207+1G>A; heterozygous Inheritance: Autosomal dominant INTERPRETATION The familial pathogenic variant, c.3207+1G>A, was detected in the COL1A1 gene in this prenatal sample by massively parallel sequencing. This variant was previously reported to be associated with osteogenesis imperfecta in the family; therefore, this fetus is predicted to be affected. Evidence for variant classification: The COL1A1 c.3207+1G>A variant (rs1555572239) is reported in the literature in individuals and families affected with osteogenesis imperfecta (Chen, 2022; Higuchi, 2021; Peng, 2012). This variant is also reported in ClinVar (Variation ID: 488809), but is absent from the Genome Aggregation Database, indicating it is not a common polymorphism. This variant disrupts the canonical splice donor site of intron 43, which is likely to negatively impact gene function. Based on available information, this variant is considered to be pathogenic. RECOMMENDATIONS Genetic consultation is indicated. COMMENTS Reference Sequence: COL1A1 (NM_000088.4)

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

REFERENCES
Chen P, et al. Phenotypic spectrum and molecular basis in a Chinese cohort of osteogenesis Imperfecta with mutations in type I collagen. Front Genet. 2022;13:816078. PMID: 35154279.

Higuchi Y, et al. Genetic analysis in Japanese patients with osteogenesis imperfecta: genotype and phenotype spectra in 96 probands. Mol Genet Genomic Med. 2021;9(6):e1675. PMID: 33939306.

Peng H, et al. A novel splicing mutation in COL1A1 gene caused type I osteogenesis imperfecta in a Chinese family. Gene. 2012;502(2):168-71. PMID: 22565191.

BACKGROUND INFORMATION: Familial Targeted Sequencing, Fetal

METHODOLOGY: Probe hybridization-based capture of all coding exons and exon-intron junctions of the targeted gene(s) region(s), followed by massively parallel sequencing. Variants in genes, other than the gene(s) region(s) specifically requested, were not evaluated. 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. Specificity is greater than 99.9 percent for all variant classes.

LIMITATIONS: A negative result does not exclude all genetic diagnoses in this fetus. This test only evaluates the specified familial variant(s) of interest and other pathogenic or likely pathogenic variants by massively parallel sequencing related to the condition of interest within the targeted gene(s) region(s). Refer to Targeted Sequencing Gene List for complete list of genes available for this test and any gene-specific technical limitations. Deletions/duplications/insertions of any size may not be detected by massively parallel sequencing. Regulatory region variants, deep intronic variants, and large deletions/duplications will not be identified. 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, aneuploidies, 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.

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Maternal Contamination Study Fetal Spec	22-319-104026	11/15/2022 10:30:00 AM	11/15/2022 10:31:13 AM	11/15/2022 10:35:00 AM

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

Maternal Contam Study, Maternal Spec	22-319-104026	11/15/2022 10:30:00 AM	11/15/2022 10:31:13 AM	11/15/2022 10:35:00 AM
FAM NGS FE Specimen	22-319-104026	11/15/2022 10:30:00 AM	11/15/2022 10:31:13 AM	11/15/2022 10:35:00 AM
FAM FE Interp	22-319-104026	11/15/2022 10:30:00 AM	11/15/2022 10:31:13 AM	11/15/2022 10:35:00 AM

END OF CHART

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