Client: Example Client ABC123
123 Test Drive
Salt Lake City, UT 84108
UNITED STATES

Physician: Doctor, Example

Patient: Patient, Example

DOB	7/5/2022
Gender:	Male
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Osteogenesis Imperfecta and Low Bone Density Panel, Sequencing

ARUP test code 3001607

Osteogenesis Imperfecta Specimen	Whole Blood

Osteogenesis Imperfecta Interp	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 osteogenesis imperfecta or a monogenic form of low bone density. 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 by NGS with sufficient confidence in this sample due to technical limitations: None

This result has been reviewed and approved by [redacted]

BACKGROUND INFORMATION: Osteogenesis Imperfecta and Low Bone Density Panel, Sequencing

CHARACTERISTICS: Although osteoporosis is present in 10 percent of the US population, monogenetic causes of osteoporosis, such as osteogenesis imperfecta (OI), are rare. OI is defined by a continuum of phenotypes ranging from individuals with perinatal lethal OI, severe skeletal deformities, dentinogenesis imperfecta (DI) and severe short stature to individuals with normal stature, dentition and lifespan but mild predisposition to fractures. This panel targets monogenic forms of OI and low bone density; it excludes genes causative for hypophosphatemic rickets and osteopetrosis.
EPIDEMIOLOGY: 6 to 7 per 100,000 for OI.
CAUSE: Varies depending on causative gene; pathogenic germline variants in COL1A1 and COL1A2 are causative for 90 percent of OI.

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

INHERITANCE: Varies depending on causative gene; autosomal dominant for COL1A1 and COL1A2.

CLINICAL SENSITIVITY: Greater than 90 percent for OI and unknown for other monogenic causes of low bone density.

GENES TESTED: ALPL, ANO5, BMP1, CASR, CLCN5, COL1A1, COL1A2, CREB3L1, CRTAP, CYP27B1, FKBP10, GORAB, IFITM5, LRP5*, P3H1, P4HB, PLOD2, PLS3, PPIB, SEC24D, SERPINF1, SERPINH1, SLC34A3, SP7, SPARC, TMEM38B, WNT1.

* - One or more exons are not covered by sequencing for the indicated gene; see limitations section below.

METHODOLOGY: Targeted 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 confirm reported variants. Human genome build 19 (Hg 19) was used for data analysis.

ANALYTICAL SENSITIVITY: 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, but the analytical sensitivity may be reduced.

LIMITATIONS: A negative result does not exclude a monogenic form of OI or low bone density. This test only detects variants within the coding regions and intron-exon boundaries of the targeted genes. Regulatory region variants, large deletions/duplications/inversions and deep intronic variants will not be identified. 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. Non-coding transcripts were not analyzed.

The following region is not sequenced due to technical limitations of the assay:
LRP5 (NM_002335) exon 1

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
Osteogenesis Imperfecta Specimen	23-313-151250	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Osteogenesis Imperfecta Interp	23-313-151250	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

END OF CHART

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