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

Physician: TEST,

Patient: OINGS, PROD Val

DOB	5/17/2021
Gender:	Female
Patient Identifiers:	30542
Visit Number (FIN):	30848
Collection Date:	5/18/2021 10:21

Osteogenesis Imperfecta and Low Bone Density Panel, Sequencing

ARUP test code 3001607

Osteogenesis Imperfecta Specimen	Whole Blood
Osteogenesis Imperfecta Interp	Negative

INDICATION FOR TESTING
Confirm diagnosis.

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. 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 and the limitations of this test.

RECOMMENDATIONS
Medical screening and management 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 Yuan Ji, Ph.D.

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.

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

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

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	21-138-105410	5/18/2021 10:21:00 AM	5/18/2021 10:21:13 AM	5/18/2021 10:24:00 AM
Osteogenesis Imperfecta Interp	21-138-105410	5/18/2021 10:21:00 AM	5/18/2021 10:21:13 AM	5/18/2021 10:24:00 AM

END OF CHART

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