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Patient Report

**Patient Age/Gender:** 0 hours Female

**Specimen Collected: 30-Sep-20 16:34**

**Osteogenesis Imperfecta by NGS |Received: 30-Sep-20 16:34 Report/Verified: 30-Sep-20 17:05**

| | Result | Units | Reference Interval |
|---|---|---|---|
| Osteogenesis Imperfecta Specimen | See Note | | |
| Osteogenesis Imperfecta Interp | See Note f1 i1 | | |

## Result Footnote

f1: Osteogenesis Imperfecta Interp

Section 79-1 of New York State Civil Rights Law requires informed consent be obtained from patients (or their legal guardians) prior to pursuing genetic testing. These forms must be kept on file by the ordering physician. Consent forms for genetic testing are available at www.aruplab.com. Incidental findings are not reported unless clinically significant but are available upon request.

## Test Information

i1: Osteogenesis Imperfecta Interp

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.

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

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i1: Osteogenesis Imperfecta Interp

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

Test developed and characteristics determined by ARUP Laboratories. See Compliance Statement C: aruplab.com/CS