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

Physician: Doctor, Example

Patient: Patient, Example

DOB	5/22/2020
Gender:	Female
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Skeletal Dysplasia Panel, Sequencing and Deletion/Duplication

ARUP test code 2012015

Skeletal Dysplasia Panel Specimen	Whole Blood

Skeletal Dysplasia Panel Interp

Negative

INDICATION FOR TESTING
Suspected skeletal dysplasia.

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 genes tested. This result decreases, but does not exclude, a diagnosis of a skeletal dysplasia. Please refer to the background information included in this report for a list of the genes analyzed and 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 [redacted]

BACKGROUND INFORMATION: Skeletal Dysplasia Panel, Sequencing and Deletion/Duplication

CHARACTERISTICS: Skeletal dysplasias (SD) are a heterogeneous group of >350 disorders characterized by abnormal growth of cartilage or bone. Some may be detectable prenatally while others are not identified until birth or later childhood. Symptoms may include: shortening, bowing, fracturing, thinning, thickening, or under-mineralization of the bones, abnormal ribs, small chest circumference and extra fingers or toes.

EPIDEMIOLOGY: Incidence is 1 in 5000 births.

CAUSE: Pathogenic germline variants in genes associated with cartilage and bone growth.

INHERITANCE: Autosomal recessive, autosomal dominant, X-linked recessive and X-linked dominant dependent on the causative gene.

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

CLINICAL SENSITIVITY: Dependent on the specific SD; 99 percent for achondroplasia and thanatophoric dysplasia; >90 percent for achondrogenesis type 1B, diastrophic dysplasia and campomelic dysplasia.

GENES TESTED: AGPS, ALPL, ARSE, CANT1**, COL1A1, COL1A2, COL2A1, COMP**, CRTAP, DDR2**, DLL3, DYNC2H1, EBP, EVC*, EVC2, FGFR1, FGFR2, FGFR3, FKBP10, FLNA, FLNB, GDF5**, GNPAT, HSPG2**, ICK, IFT80, LBR, LIFR, NEK1, P3H1, PCNT**, PEX7, POR, PPIB, PTH1R**, RUNX2, SERPINH1, SLC26A2, SLC35D1, SOX9, TRIP11, TRPV4**, TTC21B, WDR19, WDR35

* - One or more exons are not covered by sequencing for the indicated gene; see limitations section below.
** - Deletion/duplication detection is not available for this gene.

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. A custom tiled comparative genomic hybridization array (aCGH) was used to detect large deletions or duplications in the indicated subset of genes. 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 diagnosis of a skeletal dysplasia. 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. Single exon deletions/duplications or deletions/duplications less than 1kb may not be detected. Deletions/duplications/insertions of any size may not be detected by massive 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 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 regions are not sequenced due to technical limitations of the assay:
EVC(NM_153717) exon(s) 1

Single exon deletions/duplications will not be called for the following exons:
ARSE(NM_000047) 9;ARSE(NM_001282631) 1;COL1A1(NM_000088) 5;COL1A2(NM_000089) 20,22;EVC(NM_001306092) 12;PEX7(NM_000288) 1

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

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Skeletal Dysplasia Panel Specimen	20-152-400474	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Skeletal Dysplasia Panel Interp	20-152-400474	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