To:
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United States

Referred by:
Dr. Example Physician

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OSTEOGENESIS IMPERFECTA CORE PANEL COMPREHENSIVE ANALYSIS REPORT

DATE RECEIVED: 1/2/2021 **DATE REPORTED:** 1/14/2021 **DATE COLLECTED:** 1/1/2021

Patient Name	DOB	Patient ID #
Example, Patient	2/23/2020	X00123
Test Request	**Specimen Type**	**Your Code**
Osteogenesis Imperfecta Core Panel Comprehensive	Peripheral blood	M1234567

SEQUENCING RESULTS:

Pathogenic Variant:	Nucleotide:	Protein:	Consistent with the clinical diagnosis of:
COL1A1 Exon 23 - Heterozygous	c.1588G>A	Gly530Ser	*Osteogenesis Imperfecta*

DELETION / DUPLICATION RESULTS:

Pathogenic Variant:
None

RESULTS: DNA sequencing reveals a c.1588G>A transition in exon 23 of the COL1A1 gene. This change converts a codon for a conserved triple helical glycine (GGT) to a codon for serine (AGT). This change has been previously reported as a COL1A1 pathogenic variant associated with osteogenesis imperfecta (Bateman et al., 1992. Biochem J 288, 131). This finding is consistent with a disease causing variant. We have identified this mutation in six additional individuals. The patient is heterozygous for this variant. Osteogenesis imperfecta caused by COL1A1 is an autosomal dominant disorder. The recurrence risk is 50% for offspring of an individual with a COL1A1 pathogenic variant.

The copy number variation (CNV) analysis reveals no detectable disease causing copy number variation in the genes on the osteogenesis imperfecta core panel.

Genetic counseling is recommended for the interpretation of the results.

METHODOLOGY: All coding exons and exon boundaries of the genes on the osteogenesis imperfecta core panel were analyzed for variations using Illumina MiSeq next generation sequencers. New and putative disease causing single nucleotide variants and small insertions/deletions were confirmed by Sanger sequencing. Additionally, coding exons were analyzed for copy number variations (CNV). CNV detection limit is typically a single exon. The analysis does not detect rearrangements that do not result in copy number variation. The significance of the variants was determined by comparison with wild type sequences, previously reported mutations, and correlation with the protein structures. Genome build GRCh37/hg19 is used. (Note: COL1A1 exon 1 and COL1A1 exon 5 are not covered by the CNV analysis).
Although DNA sequencing and CNV analysis are highly sensitive methodologies, mutation detection may not be 100%.

BACKGROUND: Connective Tissue Gene Tests offers four panel options for osteogenesis imperfecta (OI) testing utilizing NextGen sequencing technology, an OI core panel, a dominant OI panel, a recessive OI panel and a combined dominant and recessive OI panel. In addition to genes associated with the autosomal dominant and autosomal recessive forms of OI, the panels also contain genes for disorders included in the differential diagnosis of OI. Connective Tissue Gene Tests osteogenesis imperfecta core NextGen sequencing panel consists of genes associated with osteogenesis imperfecta core.

Gene	Accession	Disorder	MIM	Inheritance
COL1A1	NM_000088	Ehlers-Danlos syndrome, arthrochalasia type, 1 (EDSARTH1)	130060 166200	AD

- This test was developed and its performance characteristics determined by HNL Genomics (CTGT). It has not been cleared or approved by the FDA. The FDA has determined that such clearance or approval is not necessary. This test is used for clinical purposes. It should not be regarded as investigational or for research. CTGT is certified under CLIA since 2004 to perform high complexity clinical laboratory testing.

		Osteogenesis imperfecta, type I (OI1) Osteogenesis imperfecta, type II (OI2) Osteogenesis imperfecta, type III (OI3) Osteogenesis imperfecta, type IV (OI4)	166210 259420 166220	
COL1A2	NM_000089	Ehlers-Danlos syndrome, arthrochalasia type, 2 (EDSARTH2) Osteogenesis imperfecta, type I (OI1) Osteogenesis imperfecta, type II (OI2) Osteogenesis imperfecta, type III (OI3) Osteogenesis imperfecta, type IV (OI4)	617821 166200 166210 259420 166220	AD
IFITM5	NM_001025295	Osteogenesis imperfecta, type V (OI5)	610967	AD

For additional information, please contact HNL Genomics (CTGT)

at 484-244-2900. Sincerely yours,

Kerry Kocher Brown, Ph.D., FACMG

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