Skeletal Dysplasia With Increased Bone Density: Sequencing Panel

Test Code: MM172
Turnaround time: 6 weeks
CPT Codes: 81405 x1, 81408 x1, 81479 x1

Condition Description

Skeletal dysplasias are a heterogeneous group of more than 450 disorders with complex genetic etiologies. Clinical and radiographic features can be used reliably to assign patients to general disease categories, but reaching a specific diagnosis, especially at a young age, may be difficult. Identification of the precise genetic defect is important, however, to permit appropriate genetic counseling, anticipatory guidance, and early prenatal diagnosis.

Collectively, the incidence of skeletal dysplasias is estimated to be 1 in 5,000 births. Skeletal dysplasias with increased bone density are characterized by hypermineralization of some or all of the skeleton.

References:

Genes
ANKH, CA2, CLCN7, COL1A1, CTSK, DLX3, FERMT3, GALNT3, HPGD, LEMD3, LRP4, LRP5, OSTM1, RASGRP2, SOST, TBXAS1, TCIRG1, TGFβ1, TNFRSF11A, TNFRSF11B, TNFSF11, TYROBP

Indications

This test is indicated for:
- Patients for whom there is a suspicion of skeletal dysplasia with abnormal radiographic findings indicating increased bone density.

Methodology

**Next Generation Sequencing:** In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

Detection

**Next Generation Sequencing:** Clinical Sensitivity: Unknown. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions/duplications will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical/biochemical phenotype.

Analytical Sensitivity: ~99%.

Specimen Requirements

Submit only 1 of the following specimen types

**Type: Whole Blood**

Specimen Requirements:
- In EDTA (purple top) tube: Infants (2 years): 3-5 ml
- Older Children & Adults: 5-10 ml.

Specimen Collection and Shipping: Ship sample at room temperature with overnight delivery.

**Type: Isolated DNA**

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Specimen Requirements:

In microtainer: 60 ug

Isolation using the Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping: Refrigerate until time of shipment in 100 ng/ul of TE buffer. Ship sample at room temperature with overnight delivery.

**Related Tests**

- Comprehensive Skeletal Dysplasia Panel
- Skeletal Dysplasia With Increased Bone Density: Deletion/Duplication Panel