**Condition Description**

Skeletal dysplasias are a heterogeneous group of more than 450 disorders with complex mechanisms. Clinical and biochemical features continue to be used reliably to assign patients to this general disease category. Identification of the precise genetic defect is important, however, to permit carrier testing and early prenatal diagnosis. Molecular analysis is likely to expand the clinical spectrum of skeletal dysplasia and may also provide data relevant to prognosis and future therapeutic intervention.

Collectively, the incidence of skeletal dysplasia is estimated to be 1 in 5,000 births. Skeletal dysplasia is referred to as generalized disorders of cartilage and bone. Limb malformation consists of hypoplastic or absent bones of the limbs. These abnormalities can be isolated or associated with variety of other anomalies such as septal defects of the heart, renal anomaly, etc.

**References:**

**Genes**

- ARHGAP31, BMP2, BMPR1B, CC2D2A, CDH3, CEP290, CHSY1, ESCO2, FBLN1, FBXW4, FGF10, FGFR2, FGFR3, FMIN, GDF5, GLI3, GNAS, GREM1, HDAC4, HOXD13, IHH, KIF7, LMNB1, LRP4, MGP, MKS1, MYCN, NIPBL, NOG, PIGV, PITX1, PTHLH, RECQL4, ROR2, RPGRIP1L, SALL1, SALL4, SHH, SOX9, TBX15, TBX3, THPO, TP63, WNT3, WNT7A

**Indications**

This test is indicated for:
- Patients for whom there is a suspicion of skeletal dysplasia with limb malformation.

**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

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
- Limb Malformation: Deletion/Duplication Panel