**Limb Malformation: Deletion/Duplication Panel**

**Test Code:** MD174  
**Turnaround time:** 2 weeks  
**CPT Codes:** 81228 x1

**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**

\[ \text{ARHGAP31, BMP2, BMP1B, CC2D2A, CDH3, CEP290, CHSY1, ESCO2, FBLN1, FBXW4, FGF10, FGFR2, FGFR3, FMIN1, GDF5, GLI3, GNAS, GREM1, HADC4, HOXD13, IHH, KIF7, LMBR1, LRP4, MGP, MKS1, MYCN, NIPBL, NOG, PIGV, PITX1, PTHLH, RECQL4, ROR2, RPGRIP1L, SALL1, SALL4, SHH, SOX9, TBX15, TBX3, TBX5, THPO, TP63, WNT3, WNT7A} \]

**Indications**

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

**Methodology**

**Deletion/Duplication Analysis:** DNA isolated from peripheral blood is hybridized to a gene-targeted CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes that cover the entire genomic region. Please note that a “backbone” of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient’s phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

**Detection**

**Deletion/Duplication Analysis:** Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations. Results of molecular analysis must be interpreted in the context of the patient’s clinical and/or biochemical phenotype.

**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

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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: 10 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.

**Special Instructions**

Please include radiographic findings for expert review at EGL Genetics.

**Related Tests**

- Limb Malformation: Sequencing Panel
- Skeletal Dysplasia: Sequencing Panel