RMRP Gene Analysis in Cartilage-Hair Hypoplasia, Metaphyseal Dysplasia without Hypotrichosis, and Anauxetic Dysplasia

Disorder also known as: Metaphyseal chondrodysplasia, McKusick type; Spondylometaepiphyseal dysplasia Menger Type (Anauxetic Dysplasia)

Clinical Features:
Cartilage-hair hypoplasia (CHH) is a pleiotropic disorder characterized by short-limbed dwarfism, cone-shaped epiphyses, metaphyseal flaring and irregularities, sparse and light colored hair of abnormally small caliber, immunological defects manifested by unusual susceptibility to chickenpox, and other hematological anomalies such as neutropenia and anemia. Some patients may also have Hirschsprung disease, impaired spermatogenesis, and increased susceptibility to cancer. Skeletal abnormalities may include incomplete extension at the elbows, chest deformities, lumbar lordosis, joint laxity, bowed legs, genu varum, and excessively long fibula distally relative to the tibia, in addition to dwarfism. Hypoplasia of the cartilage is seen microscopically. Metaphyseal dysplasia without hypotrichosis was initially described as a distinct entity from CHH with identical skeletal features, and lacking hypotrichosis and immunodeficiency. Anauxetic dysplasia is a form of extreme short stature of prenatal onset, hypodontia, and mild mental retardation. Recent data shows that these three disorders are allelic as each condition is caused by pathogenic variants in the RNase MRP (RMRP) gene. The RMRP gene encodes the RNA subunit of a RNA processing enzyme complex (endoribonuclease).

Genetics:
Autosomal recessive

Test Methods:
The RMRP gene consists of a promoter region and an RNA coding region of 267 nucleotides. Using genomic DNA obtained from the submitted biological material the entire sequence will be screened by bi-directional sequencing. Variants found in the first person of a family to be tested are confirmed by repeat analysis using sequencing, restriction fragment analysis, or another appropriate method.

Test Sensitivity:
In previous studies, an RMRP variant was identified in 94% of the patients who fit the clinical description for CHH. The sensitivity for patients with metaphyseal dysplasia without hypotrichosis and anauxetic dysplasia is unknown.

References:

1. Ridanpaa M, et al., Mutations in the RNA Component of RNase MRP Cause a Pleiotropic Human Disease, Cartilage-Hair Hypoplasia Cell 104:195-203 (2001)
2. Bonafe L, et al., RMRP gene sequence analysis confirms a cartilage-hair hypoplasia variant with only skeletal manifestations and reveals a high density of single-nucleotide polymorphisms Clin Genet 61:146-151 (2002)
3. Ridanpaa, M, et al., Worldwide mutation spectrum in cartilage-hair hypoplasia: ancient founder origin of the major 70A□G mutation of the untranslated RMRP Eur J of Hum Genet 10:439-447 (2002).