DMP1 Gene Testing in Autosomal Recessive Hypophosphatemic Rickets (ARHR)

Disorder also known as: Autosomal recessive hypophosphatemia (ARHP)

Clinical Features:
Autosomal recessive hypophosphatemic rickets is characterized by hypophosphatemia and osteomalacia. Resolution of rickets has been observed after treatment with phosphate and vitamin D substitution. Affected individuals can exhibit bowing of the lower limbs, poor dental development, extraskeletal ossification and elevated serum FGF23 levels. Typically, individuals have normal stature. As an autosomal recessive trait, this disorder affects both males and females. ARHR is phenotypically similar to the more common X-linked form of hypophosphatemic rickets due to loss-of-function variants in the PHEX gene.

Genetics:
Autosomal recessive pattern of inheritance.

Test Methods:
Using genomic DNA obtained from the submitted biological material, the 6 exons (exons 2-6 are coding) and splice junctions of the DMP1 gene are screened by bi-directional sequence analysis. 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:
Sequence analysis of the DMP1 gene is expected to identify all types of variants that have been reported in ARHR to date. It is currently unknown what proportion of individuals with a clinical diagnosis of hypophosphatemic rickets is a result of a pathogenic variant in DMP1.

Variant Spectrum:
To date, six loss-of-function variants have been reported in the DMP1 gene. The types of variants identified include missense, frameshift and splice site variants. All have been reported as homozygous variants identified in consanguineous families.

References: