

Hypophosphatasia: *ALPL* Gene Sequencing

Test Code: MSALP

Turnaround time: 6 weeks

CPT Codes: 81479 x1

Condition Description

Hypophosphatasia is a rare disorder characterized by impaired mineralization in bones and/or teeth due to deficiency in serum and bone alkaline phosphatase. At least six clinical forms are currently recognized based on age at diagnosis and severity of features. The highly variable clinical presentation ranges from a severe perinatal form to a mild odontohypophosphatasia form in which only teeth are affected. Clinical features may include prenatal long-bone bowing, infantile rickets with growth failure, craniosynostosis, scoliosis, costochondral enlargements, hypotonia, hypercalcemia and hypercalciuria, bone pain, and premature loss of deciduous teeth.

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Hypophosphatasia is caused by pathogenic variants in the *ALPL* gene. The *ALPL* gene provides instructions for making the enzyme alkaline phosphatase, which is essential in the formation of strong bones and teeth. Perinatal and infantile forms are inherited in an autosomal recessive manner, while milder forms, such as adult hypophosphatasia and odontohypophosphatasia, may be inherited in an autosomal recessive or autosomal dominant fashion. Severe forms of hypophosphatasia affect an estimated 1 in 100,000 newborns and appears most commonly in a Mennonite population in Manitoba, Canada.

References:

1. Genetics Home Reference: <http://ghr.nlm.nih.gov/gene/ALPL2>.
2. GeneReviews: <http://www.ncbi.nlm.nih.gov/books/NBK1150/>.

Genes

[ALPL](#)

Indications

This test is indicated for:

- Individuals with a clinical diagnosis of hypophosphatasia.

Methodology

PCR amplification of 11 exons contained in the *ALPL* gene is performed on the patient's genomic DNA. Direct sequencing of amplification products is performed in both forward and reverse directions, using automated fluorescence dideoxy sequencing methods. The patient's gene sequences are then compared to a normal reference sequence. Sequence variations are classified as pathogenic variants, benign variants unrelated to disease, or variations of unknown clinical significance. Variants of unknown clinical significance may require further studies of the patient and/or family members. This assay does not interrogate the promoter region, deep intronic regions, or other regulatory elements, and does not detect large deletions.

Detection

Clinical Sensitivity: Unknown. Pathogenic variants in the promoter region, some pathogenic variants in the introns and other regulatory element pathogenic variants cannot be detected by this analysis. Large deletions will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's biochemical phenotype.

Analytical Sensitivity: ~99%.

Specimen Requirements

Submit only 1 of the following specimen types

Type: Whole Blood (EDTA)

Specimen Requirements:

EDTA (Purple Top)

Infants and Young Children (2 years of age to 10 years old): 3-5 ml

Older Children & Adults: 5-10 ml

Autopsy: 2-3 ml unclotted cord or cardiac blood

Specimen Collection and Shipping:

Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

Type: Saliva**Specimen Requirements:**

Oragene™ Saliva Collection Kit

Oragene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

Specimen Collection and Shipping:

Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

Type: DNA, Isolated**Specimen Requirements:**

Microtainer

8µg

Isolation using the Perkin Elmer™ Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping:

Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

Related Tests

Hypophosphatasia: *ALPL* Deletion/Duplication