

Phenylketonuria (PKU): PAH Gene Sequencing

Test Code: SK

Turnaround time: 4 weeks

CPT Codes: 81406 x1

Condition Description

Phenylketonuria (PKU) results in an inability to metabolize the amino acid phenylalanine to tyrosine. If dietary phenylalanine is not metabolized, the amino acid accumulates to neurotoxic levels resulting. If untreated, the condition results in mental retardation, seizures, microcephaly and behavior abnormalities. PKU is among the disorders tested by newborn screening and treated by dietary restriction. The incidence of PKU is approximately 1 in 10,000 live births.

PKU is autosomal recessive disorder and caused by mutations in the *PAH* gene (12q22-q24) leading to deficiency of phenylalanine hydroxylase. Disease severity, clinical phenotype, and effectiveness of treatment differs among the different *PAH* mutations and correlates with the level of *PAH* enzyme activity. Complete or near complete absence of enzyme activity results in classical phenylketouria (PKU), which requires strict dietary restraint of phenylalanine for life. Milder enzyme deficiencies can result in non-PKU hyperphenylalaninemia (non-PKU HPA) or variant PKU. Carriers of PKU are unaffected.

For patients with mutations not identified by full gene sequencing, a separate deletion/duplication assay is available using a targeted CGH array XM.

Visit www.ThinkGenetic.com for patient-friendly information on [phenylketonuria](#).

References:

- [GeneReviews Clinical Summary](#)

Genes

[PAH](#)

Indications

This test is indicated for:

- Patients with a biochemical diagnosis of PKU.
- Individuals with biochemical test results indicating carrier status of PKU.
- Individuals who are at risk to be carriers of PKU, when the proband is unavailable for testing.

Sequencing is not appropriate for prenatal samples in which familial mutations have not been identified.

Methodology

The 13 exons and flanking regions of *PAH* are amplified by PCR and sequenced in both the forward and reverse directions. Patient gene sequences are compared to a normal reference sequence. Sequence variations are then classified as previously described mutations, novel mutations, or variations of unknown significance. This analysis may detect novel variants of unclear effect, which may require further studies.

Detection

This assay will detect over 95% of sequence variants in the coding region and splice junctions. Mutations in the promoter region, some mutations in the introns, and other regulatory elements cannot be detected by this analysis. Large deletion and insertion mutations will not be detected by this assay. It is possible that some patients with a typical presentation may not carry a mutation detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's biochemical phenotype.

Specimen Requirements

Submit only 1 of the following specimen types

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.

Type: Saliva

Specimen Requirements:

Oragene™ Saliva Collection Kit

Orangene™ 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: 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.

Special Instructions

Submit copies of diagnostic biochemical test results with the sample. Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside EGL Genetics, please submit a copy of the sequencing report with the test requisition. Contact the laboratory if further information is needed.

Related Tests

- Organic Acid Analysis (OA) and Plasma Amino Acid (AA) Analysis are used in the diagnoses of a patient with PKU.
- Deletion/Duplication Assay is available separately for individuals where mutations are not identified by sequence analysis. Refer to the test requisition or contact the laboratory for more information.
- Custom Diagnostic Mutation Analysis (KM) is available to determine the carrier risk in family members when the PKU mutations have been identified. Please contact the laboratory genetic counselor to arrange testing.
- Prenatal testing is available to couples who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.