Early Infantile Epileptic Encephalopathy Type 10: *PNKP* Gene Sequencing

**Test Code:** SPNKP  
**Turnaround time:** 4 weeks  
**CPT Codes:** 81479 x1

### Condition Description

Shen et al. (2010) describes an autosomal recessive disorder, early infantile epileptic encephalopathy type 10, characterized by microcephaly, early-onset intractable seizures and developmental delay in seven families. Additional variable behavioral problems, especially hyperactivity, were reported. Mutations were identified in all seven families in the *PNKP* gene (19q13.4). *PNKP* encodes a protein involved in DNA repair.

For patients with suspected early infantile epileptic encephalopathy, sequence analysis is recommended as the first step in mutation identification. For patients in whom mutations are not identified by full gene sequencing, deletion/duplication analysis is appropriate.

### References:
- OMIM #605610: *PNKP* gene  
- OMIM #613402: Early Infantile Epileptic Encephalopathy

### Genes

*PNKP*

### Indications

This test is indicated for:
- Confirmation of a clinical diagnosis of early infantile epileptic encephalopathy.  
- Carrier testing in adults with a family history of early infantile epileptic encephalopathy.

### Methodology

PCR amplification of 16 exons contained in the *PNKP* 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 mutations, 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. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations 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 clinical and/or biochemical phenotype.

**Analytical Sensitivity:** ~99%

### Specimen Requirements

Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) tube:  
- Infants (2 years): 3-5 ml  
- Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Type: Saliva**

Specimen Requirements:

Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.
Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Related Tests**

- Deletion/duplication analysis of the *PNKP* gene by CGH array is available for those individuals in whom sequence analysis is negative.
- Custom diagnostic mutation analysis (KM) is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- Prenatal testing is available only for known familial mutations to individuals who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.