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 #613482: 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**

**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:**

Orangene™ 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: DNA, Isolated**

**Specimen Requirements:**
Microtainer
8µg
Isolation using the Perkin Elmer™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**

- 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.