**PSAP-related Disorders: PSAP Gene Sequencing**

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

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**Condition Description**

The PSAP gene (10q22.1) codes for a glycoprotein called prosaposin (pSap). Prosaposin is a precursor for four saposins proteins (Saps) A-D. Mutations in the PSAP gene can affect either the entire pSap protein or one of the Sap proteins. All of the conditions caused by mutations in the PSAP gene are inherited in an autosomal recessive manner. Combined saposin deficiency, also known as prosaposin deficiency, is caused when loss of prosaposin results in deficiency of saposins A-D, usually due to two loss of function mutations in the PSAP gene. PSAP-related disorders are clinically and metabolically variable neonatal condition characterized by an acute generalized neurovisceral dystrophy and caused by the storage of multiple sphingolipids. SapA deficiency results in atypical Krabbe. SapB deficiency results in metachromatic leukodystrophy. SapC deficiency results in atypical Gaucher disease. There are currently no known human diseases caused by loss of SapD alone.

**References:**

- OMIM #176801: PSAP gene  
- OMIM #611721: Combined saposin deficiency  
- OMIM #611722: Atypical Krabbe due to saposin A deficiency  
- OMIM #249900: Metachromatic leukodystrophy due to saposin B deficiency  
- OMIM #610539: Atypical Gaucher disease due to saposin C deficiency

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**Genes**

PSAP

**Indications**

This test is indicated for:

- Confirmation of a clinical/biochemical diagnosis of PSAP-related disorders
- Carrier testing in adults with a family history of PSAP-related disorders

**Methodology**

PCR amplification of 14 exons contained in the PSAP 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: 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.

**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.

**Special Instructions**

Submit copies of diagnostic biochemical test results with the sample, if appropriate. Contact the laboratory if further information is needed.

**Related Tests**

- **Krabbe Disease:** Full Gene Sequencing & Deletion/Duplication
- **Krabbe Disease:** Galactocerebrosidase Activity, Dried Blood Spot
- **Gaucher Disease:** Biomarker Panel (ACE, CHITO, TRAP)
- **Gaucher Disease:** GBA Full Gene Sequencing & Common Mutation Panel
- **Gaucher Disease:** Angiotensin Converting Enzyme (ACE)
- **Gaucher Disease:** Chitotriosidase (CHITO)
- **Gaucher Disease:** Tartrate Resistant Acid Phosphatase (TRAP)
- **Gaucher Disease:** Enzyme Assay
- **Metachromatic Leukodystrophy:** Full Gene Sequencing & Deletion/Duplication
- **Metachromatic Leukodystrophy**

**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 to adult couples who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.