**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 saponsins 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

**Genes**

*PSAP*

**Indications**

This test is indicated for:

- Confirmation of a clinical diagnosis of *PSAP*-related disorders in an individual in whom sequence analysis was negative.
- Carrier testing in adults with a family history of *PSAP*-related disorders in whom sequence analysis was negative.

**Methodology**

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region. Please note that a “backbone” of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient’s phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

**Detection**

Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations. Results of molecular analysis must be interpreted in the context of the patient’s clinical and/or biochemical phenotype.

**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:

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

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Special Instructions**

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

Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of EGL Genetics, please submit a copy of the sequencing report with the test requisition.

**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.