Krabbe Disease: GALC Gene Deletion/Duplication

Test Code: LD
Turnaround time: 2 weeks
CPT Codes: 81228 x1

Condition Description

Krabbe disease is an autosomal recessive neurodegenerative disorder caused by a deficiency of the enzyme galactocerebrosidase. It is part of a group of disorders known as leukodystrophies, which result from the abnormal formation of myelin, the protective covering of nerve cells. When the enzyme galactocerebrosidase is deficient it produces toxic substances in the brain resulting in myelin loss, change to brain cells, and neurological damage.

Krabbe disease is characterized by the onset of progressive neurologic deterioration leading to early death. Symptoms of Krabbe disease usually become apparent before two years of age (85%-90% of individuals) or between six months and the fifth decade for those with slower disease progression (10%-15% of individuals). Early symptoms of Krabbe disease include: irritability, excessive crying, stiffness, arrest of motor and mental development, loss of developmental milestones, feeding difficulties, unexplained fevers, hypersensitivity to stimulus, progressive weight loss, and seizures. As the condition progresses, symptoms may include: back arching, jerking of the arms and legs, severe and rapid deterioration of mental and motor function, loss of vision and hearing, and loss of the ability to move or speak. Neuroimaging studies (MRI and/or CT scans) often reveal progressive, diffuse, and symmetrical cerebral atrophy; however, in the early stage of the disease, the MRI and CT scans can be normal.

Mutations in the GALC gene cause a deficiency of the enzyme galactosylceramidase. Diagnostic sequencing analysis of the GALC gene coding region is available for patients with Krabbe disease and their at-risk relatives on a clinical basis.

For questions about testing for Krabbe disease, call the Emory Genetics Laboratory at 470-378-2200. For further clinical information about lysosomal storage diseases, including management and treatment, call the Emory Lysosomal Storage Disease Center at (404) 778-8565 or (800) 200-1524.


References:

Genes

GALC

Indications

- Confirmation of a clinical diagnosis of Krabbe Disease
- Prenatal testing for known familial mutations.
- Assessment of carrier status in high risk family members - known mutation analysis.

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. Array CGH will not detect point mutations 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) or ACD (yellow 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.

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 of Emory Genetics Laboratory, please submit a copy of the sequencing report with the test requisition. Contact the laboratory if further information is needed.

Related Tests

- **Known Mutation Analysis (KM)** is available to test family members.
- Prenatal testing is available for known familial mutations only. Please call the Laboratory Genetic Counselor for specific requirements for prenatal testing before collecting a fetal sample.