



Disease Information

Canavan Disease is an autosomal recessive neurodegenerative disease caused by mutations in the *ASPA* gene, which codes for the enzyme aspartoacylase. Deficiency of this enzyme causes accumulation of N-acetylaspartic acid in the central nervous system and disrupted myelination. Onset occurs in infancy with hypotonia, progressive loss of motor control, and macrocephaly. Most developmental milestones are not achieved and patients usually do not survive past childhood. Approximately 1/57 members of the Ashkenazi Jewish population carry a Canavan Disease mutation.¹ Three mutations account for 99% of those detected in this group but they are rare in other groups.² A fourth mutation accounts for approximately 50% of Canavan alleles in the non-Ashkenazi Jewish.²⁻⁴ More than 50 disease-causing mutations, including gross deletions, have been reported.

Testing Benefits & Indications

Molecular testing for a small number of mutations is highly sensitive in the Ashkenazi Jewish population, but not in other ethnic groups. Biochemical carrier screening is not available for screening purposes. The Canavan AMPLIFIED test provides a detection rate of ~99% across all ethnicities. This enables the greatest possible carrier risk reduction for high-risk or mixed-ethnicity couples, expands options for prenatal diagnosis, simplifies carrier testing in the extended family, and clarifies or confirms biochemical diagnoses. Indications for testing are:

- carrier testing for high-risk, anxious, or mixed-ethnicity couples
- prenatal diagnosis for known carrier couples
- mutation identification in affected patients

The following table shows revised or post-test carrier risks by ethnicity, assuming a negative Ambry Test result and no family history of the disease.

Ethnicity	Canavan Carrier Risk before Test	Revised Carrier Risk after Canavan AMPLIFIED
Ashkenazi Jewish	1/57	1/5601
Other populations at general risk	unknown; <1/57	<1/5601

Test Description

The Canavan AMPLIFIED test is performed by PCR-based double-stranded automated sequencing in the sense and antisense directions of exons 1-6 of the *ASPA* gene, plus at least 20 bases into the 5' and 3' ends of all the introns. Concurrent analysis for gross deletions/duplications of any exon is performed by MLPA®. Specific mutation analysis for known family mutations in *ASPA* is also available.

Mutation Detection Rate

Approximately 99% of mutations are detectable by Canavan AMPLIFIED regardless of the patient's ethnicity.

Turn-Around-Time

Canavan AMPLIFIED 14 – 28 days
 Specific mutation analysis 10 – 14 days

Specimen Requirements

BLOOD: Collect 3-5 cc from adult or 2 cc minimum from child into EDTA purple-top tube (first choice) or ACD yellow-top tube (second choice). Store at room temperature or refrigerate. Ship at room temperature.

BLOOD SPOT: Minimum of one complete spot approximately 0.5 inch in diameter on S&S 903 collection paper or similar. Store in a clean plastic bag at room temperature. Ship at room temperature.

SALIVA: Collect 2 ml into Oragene™ DNA Self-Collection container. Store and ship at room temperature.

DNA: Send 20 µg in TE at 50-100 ng/µl. Store frozen and ship on ice or dry ice.

PRENATAL: Prenatal testing is available. Please call an Ambry Genetic Counselor to discuss your case.

CPT Codes

Canavan AMPLIFIED 83891, 83894, 83898, 83900, 83901, 83904, 83909, 83912
Specific mutation analysis 83891, 83894, 83898, 83904, 83909, 83912

References

¹Feigenbaum A et al. *Am J Med Genet.* 2004;124:142-147.

²Kaul R. et al. *Am J Hum Genet.* 1994;55:34-41.

³Sisternans EA et al. *Eur J Hum Genet.* 2000;8:557-560.

⁴Kaul R et al. *Am J Hum Genet.* 1996;59:95-102.