

HUNTER DISEASE

Hunter disease (mucopolysaccharidosis type II) is a lysosomal storage disease caused by deficiency of the enzyme iduronate-2-sulphatase. A deficiency of this enzyme causes accumulation of the products dermatan sulphate and heparan sulphate in lysosomes which leads to cell death. Hunter disease can vary from mild to severe, depending on the level of enzyme deficiency. Characteristics of the disease include dwarfism, enlarged liver and spleen, cardiovascular disorders and deafness.

GENETICS

Mutations in the *IDS* gene located at Xq28 cause the loss of the iduronidate sulfatase enzyme. A pseudogene *IDS2* also exists 20 kb from the active *IDS* gene. The pseudogene *IDS2* shares homology to exon 2, intron 2, exon 3, intron 3 and intron 7 of the *IDS* gene.

Mutations that have been reported in the *IDS* gene in Hunter patients include gene rearrangements caused by recombination with the *IDS2* gene (10% of patients), deletions of certain exons or the entire *IDS* gene (10% of patients) or small mutations including insertions, deletions and point mutations (80% of patients).

An accurate biochemical test is available for the diagnosis of Hunter disease consisting of the analysis of iduronate-2-sulfatase activity in plasma, leucocytes or cultured cells. This test should be considered before molecular analysis is undertaken. Molecular identification of the mutation in individuals with a confirmed diagnosis can be used for carrier testing and prenatal diagnosis in the family. This test is not reliable for identifying carriers.

POTENTIAL OUTCOMES & INTERPRETATION OF TEST RESULTS

Sex of Patient	<i>IDS</i> Gene Mutation	Explanation
Male	None detected	This result does not support a diagnosis of Hunter disease
Male	Mutation detected	This result confirms a diagnosis of Hunter disease
Female	None detected / none detected	This individual is unlikely to be affected with, or a carrier of Hunter disease
Female	Mutation detected / none detected	This individual is a carrier of Hunter disease and may transmit a mutation to offspring

TEST METHODS

- Complete sequencing of the 9 exon coding region and flanking exon/intron boundaries of the *IDS* gene to identify point mutations.
- Quantitative testing of the *IDS* gene to detect larger deletions or duplications, using MLPA (Multiplex Ligation-dependent Probe Amplification).
- Southern blot analysis to detect rearrangements between the *IDS* gene and the *IDS2* pseudogene.

WHO SHOULD BE TESTED?

- Individuals clinically/biochemically suspected of being affected with Hunter disease
- Women with a family history of Hunter disease, to determine carrier status
- Pregnancies at risk due to a family history of Hunter disease

For More Information

Online Mendelian Inheritance in Man <http://www.ncbi.nlm.nih.gov/omim/> Item # 309900

GeneReviews online clinical information resource <http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=hunter#hunter>

To locate a genetics center near you, please visit the Canadian Association of Genetic Counsellors website at www.cagc-accg.ca or the National Society of Genetic Counsellors website at www.nsgc.org



1. Current molecular testing may not detect all possible mutations for this disease. A negative test does not rule out the possibility of Hunter disease, or the possibility the individual is a carrier.

2. We strongly recommend that biochemical analysis be done on these patients, as it can be a useful complement to molecular testing.

3. It is often helpful to first identify the mutation(s) in an affected family member or parent of the affected family member. If the familial mutation can be identified, only the familial mutation will be tested for.

4. This test was developed and its performance characteristics validated by the Genome Diagnostics Laboratory at the Hospital for Sick Children. It has not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. This test is used for clinical purposes.