SickKids | Genome Diagnostics

HEREDITARY HEARING LOSS:
USHER SYNDROME

Usher syndrome is a clinically and genetically heterogeneous autosomal recessive disorder characterized by sensorineural hearing deficiencies at birth and later development of progressive retinitis pigmentosa (RP). RP is progressive, bilateral, symmetric retinal degeneration that begins with night blindness and constricted visual fields (tunnel vision) and eventually includes decreased central visual acuity .There are 3 types of Usher syndrome; these types are distinguished by their severity and the age when signs and symptoms appear. Individuals with Usher syndrome type I are typically born completely deaf or lose most of their hearing within the first year of life. Progressive vision loss caused by RP becomes apparent in childhood. Usher syndrome type II is characterized by hearing loss from birth and progressive vision loss that begins in adolescence or adulthood. The hearing loss occurs predominantly in the higher frequencies and ranging from mild to severe . Unlike other forms of Usher syndrome, people with type II do not have difficulties with balance caused by inner ear problems. Individuals with Usher syndrome type III experience progressive hearing loss and vision loss beginning in the first few decades of life. Hearing loss typically begins during late childhood or adolescence, after the development of speech, and progresses over time. By middle age, most affected individuals are profoundly deaf. Vision loss caused by RP also develops in late childhood or adolescence. Individuals may also experience difficulties with balance due to inner ear problems.

GENETICS

All three types of Usher syndrome are inherited in an autosomal recessive manner. A subset of patients have a digenic forms of Usher Syndrome: type ID with heterozygous variants in CDH23 and PCDH15 & type IIC with heterozygous variants in the genes ADGRV1 and PDZD7.

WHO SHOULD BE TESTED?

- Individuals clinically suspected of being affected with Usher syndrome.
- Relatives of a proband with identified pathogenic variant(s) in an Usher syndrome-associated gene.
- Pregnancies at increased risk due to a family history of a Usher syndrome.

TEST METHODS

Complete sequencing of the coding region and flanking intron/exon boundaries of the genes listed below. This is done via NGS of the nine gene Usher syndrome panel. Please refer to our "A Guide to Next-Generation Sequencing" information sheet available on our website, for further details.

INTERPRETATION OF TEST RESULTS

Genetic testing may reveal one or more variants in the Usher syndrome genes, which should be interpreted in the context of the suspected clinical diagnosis, inheritance pattern, clinical findings, family history and other experimental data.

Please refer to our "A Guide to Interpreting Sequence Variations" information sheet available on our website, for further details.

Genes	Types of Usher syndrome
MYO7A	Type IB
USH1C	Type IC
CDH23	Type ID
PCDH15	Type ID
USH1G	Type IG
CIB2	Type IJ
USH2A	Type IIA
ADGRV1	Type IIC
PDZD7	Type IIC
WHRN	Type IID
CLRN1	Type III

For More Information

GeneReviews: Usher syndrome type I: http://www.ncbi.nlm.nih.gov/books/NBK1265/

Usher syndrome type II: http://www.ncbi.nlm.nih.gov/books/NBK1341/

Genome Diagnostics Laboratory: www.sickkids.ca/genome-diagnostics

To locate a genetics center near you:
Canadian Association of Genetic Counsellors (CAGC): www.cagc-accg.ca

National Society of Genetic Counselors (NSGC): www.nsgc.org

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1. A negative result after NGS testing does not rule out the presence of a deletion or duplication. Deletion/duplication testing is available through our laboratory. If clinically indicated, please contact us to discuss this testing.

2. The clinical course or severity of symptoms cannot be predicted by molecular analysis.

3. Test results should be interpreted in the context of clinical findings, family history and other laboratory data.

4. Current molecular testing may not detect all possible mutations for this disease. A negative test does not rule out the possibility of Usher syndrome.

5. This test was developed and its performance characteristics validated by the Molecular Genetics 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.