SickKids | Genome Diagnostics

HEREDITARY HEARING LOSS:
STICKLER SYNDROME

Stickler syndrome is a connective tissue disorder that includes hearing loss that is both conductive and sensorineural (the degree of hearing loss varies among affected individuals and may become more severe over time); ocular findings of myopia, cataract and retinal detachment; distinctive facies that include midfacial underdevelopment and cleft palate (often apart of the Robin sequence). Most individuals with Stickler syndrome have skeletal abnormalities that affect the joints. The joints of affected children and young adults may be loose and very flexible (hypermobile), though joints become less flexible with age. Arthritis often appears early in life and may cause joint pain or stiffness. Problems with the bones of the spine (vertebrae) may also occur, including abnormal curvature of the spine (scoliosis or kyphosis) and flattened vertebrae (platyspondyly). These spinal abnormalities may cause back pain. Variable phenotypic expression of Stickler syndrome occurs both within and among families.

The genes associated with Stickler syndrome are involved in the production of three types of collagen: type II, type IX and type XI. Collagens are molecules that provide structure and strength to connective tissues that support the body's joints and organs. These collagens are components of vitreous, cartilage and other connective tissues.

A similar condition called Marshall syndrome is characterized by a distinctive facial appearance, eye abnormalities, hearing loss, and early onset arthritis. Marshall syndrome can also include short stature, which is typically not seen in Stickler syndrome.

GENETICS

Sticker syndrome can be inherited in an autosomal dominant (AD) or autosomal recessive (AR) fashion. 80-90% of all cases of Stickler syndrome are associated with AD variants in the COL2A1 gene. The targeted Next Generation Sequencing (NGS) panel described below includes genes associated with both modes of inheritance.

WHO SHOULD BE TESTED?

- Individuals clinically suspected of being affected with Stickler syndrome.
- Relatives of a proband with identified pathogenic variant(s) in an Stickler syndrome-associated gene.
- Pregnancies at increased risk due to a family history of a Stickler 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 six gene Stickler syndrome targeted gene 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 Stickler 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 associated with Stickler syndrome	Inheritance Pattern
COL2A1	Autosomal dominant
COL11A1 (also associated with Marshall syndrome)	Autosomal dominant
COL11A2	Autosomal dominant
COL9A1	Autosomal recessive
COL9A2	Autosomal recessive

For More Information

GeneReviews: Stickler syndrome: http://www.ncbi.nlm.nih.gov/books/NBK1302/

Genome Diagnostics Laboratory website: 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 Stickler 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. This test is used for clinical purposes.