SickKids | Genome Diagnostics

CONNECTIVE TISSUE DISORDERS: EHLERS-DANLOS SYNDROME PANEL

Ehlers-Danlos syndrome (EDS) is a heterogeneous group of inherited connective tissue disorders, caused by mutations that disrupt the structure, production, or processing of collagen. EDS is known to affect men and women of all ethnic backgrounds. There are several different types of EDS; all types share common features such as joint hyperlaxity, soft & fragile skin with abnormal wound healing, easy bruising, weak blood vessel walls and some systemic manifestations. The clinical spectrum varies from mild skin and joint hyperlaxity to severe physical disability and life-threatening vascular complications. A review of the different types of EDS can be found in The 2017 International Classification of the Ehlers-Danlos syndromes (Malfait F et al (2017) Am J Med Genet C Semin Med Genet. 175(1):8-26 (PMID: 28306229).

Genetics

Ehlers-Danlos syndrome can be inherited in autosomal dominant, or autosomal recessive or X-linked recessive fashion. The targeted Next-Generation-Sequencing (NGS) panel described below include genes associated with all modes of inheritance.

Who Should be Tested?

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

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 EDS 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 EDS 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.

Gene	Type of Ehlers-Danlos Syndrome (EDS)	Inheritance Pattern
ADAMTS2	Dermatosparaxis EDS*	Autosomal recessive
ATP7A	Menkes Disease (EDS Type IV)	X-Linked recessive
B4GALT7	Spondylodysplastic EDS*	Autosomal recessive
CHST14	Musculocontractural EDS*	Autosomal recessive
COL1A1	Arthrochalasia EDS*	Autosomal dominant
COL1A2	Arthrochalasia EDS*	Autosomal dominant
	EDS, cardiac valvular form	Autosomal recessive
COL3A1	Vascular EDS*	Autosomal dominant
COL5A1	Classic EDS*	Autosomal dominant
COL5A2	Classic EDS*	Autosomal dominant
DSE	Musculocontractural EDS*	Autosomal recessive
FKBP14	Kyphoscoliotic EDS*	Autosomal recessive
PLOD1	Kyphoscoliotic EDS*	Autosomal recessive
SLC39A13	Spondylodysplastic EDS*	Autosomal recessive
TNXB	Classical-like EDS*	Autosomal recessive
ACTA2	Aortic Aneurysm	Autosomal dominant
FBN2	Congenital Contractural Arachnodactyly	Autosomal dominant
PRDM5	Brittle Cornea Syndrome	Autosomal recessive
SMAD3	Loeys Dietz syndrome, Type 3	Autosomal dominant
TGFβ2	Loeys Dietz syndrome, Type 4	Autosomal dominant
TGFβR1	Loeys Dietz syndrome, Type 1	Autosomal dominant
TGFβR2	Loeys Dietz syndrome, Type 2	Autosomal dominant
ZNF469	Brittle Cornea Syndrome	Autosomal recessive

For More Information:

The Ehlers-Danlos National Foundation: www.ednf.org
Ehlers-Danlos Classic type: http://www.ncbi.nlm.nih.gov/books/NBK1244/
Ehlers-Danlos Hypermobility type: http://www.ncbi.nlm.nih.gov/books/NBK1279/
Ehlers-Danlos Vascular type: http://www.ncbi.nlm.nih.gov/books/NBK1494/
Ehlers-Danlos Kyphoscoliotic form: http://www.ncbi.nlm.nih.gov/books/NBK1462/

Genome Diagnostics Laboratory: http://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 EDS.

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.

*Disease names and inheritance patterns as described in (Malfait F et al (2017) Am J Med Genet C Semin Med Genet. 175 (1):8-26 (PMID: 28306229) as well as OMIM (www.omim.org)