SickKids | Genome Diagnostics

Connective Tissue Disorders: Osteogenesis Imperfecta Panel

Osteogenesis imperfect (OI), also known as Brittle Bone disease, is characterized by frequent bone fractures. Individuals with this condition have bones that break easily, often from mild trauma or with no apparent cause. Multiple fractures are common, and in severe cases, can occur even before birth. Milder cases may involve only a few fractures over a person's lifetime. The clinical features of OI represent a continuum ranging from perinatal lethality to individuals with severe skeletal deformities, mobility impairments, and very short stature to nearly asymptomatic individuals with a mild predisposition to fractures, normal dentition, normal stature, and normal life span. There are eight main forms of OI (with many other rare forms also being described), designated type I through type VIII; classification of OI into different types is mostly based on severity of the phenotype. Type I is the mildest form of OI and type II is the most severe, type III is severe and deforming and types IV-VIII are moderately deforming. Individuals with OI may have other features such as short stature, blue sclera, haring loss and dentiogenesis imperfect (discoloured and brittle teeth).

Genetics

OI can be inherited in autosomal dominant (AD) or autosomal recessive (AR) fashion. ~90% of all cases of OI are associated with AD variants in either COL1A1 or COL1A2. The targeted Next-Generation-Sequencing (NGS) panel described below include genes associated with both modes of inheritance.

Who Should be Tested?

- Individuals clinically suspected of being affected with a type of OI
- The relatives of a proband with identified pathogenic variants in an OI gene
- Pregnancies at increased risk due to a family history of OI

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 OI 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 OI 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 Osteogenesis Imperfecta	Inheritance Pattern
COL1A1	Types I, II, III, IV	Autosomal dominant
COL1A2	Types II, III, IV	Autosomal dominant
ALPL	Hypophosphatasia with fractures	Autosomal recessive
BMP1	Type XIII	Autosomal recessive
CRTAP	Type VII	Autosomal recessive
FKBP10	Type XI	Autosomal recessive
IFITM5	Type V	Autosomal dominant
LRP5	Primary Osteoporosis	Autosomal dominant
MBTPS2	IFAP syndrome	X-linked recessive
P3H1	Type VIII	Autosomal recessive
PLOD2	Bruck syndrome (OI-related)	Autosomal recessive
PLS3	X-linked osteoporosis with fractures	X-linked recessive
PPIB	Type IX	Autosomal recessive
SERPINF1	Type VI	Autosomal recessive
SERPINH1	Type X	Autosomal recessive
SP7	Type XII	Autosomal recessive
SPARC	Type XVII	Autosomal recessive
TMEM38B	Type XIV	Autosomal recessive
WNT1	Type XV	Autosomal recessive
XYLT2	Spondyloocular syndrome	Autosomal recessive

For More Information:

Osteogenesis Imperfecta: van Dijk et al (2011) Osteogenesis Imperfecta: A Review with Clinical Examples. Mol Syndromol 2:1–20

Osteogenesis Imperfecta: http://ghr.nlm.nih.gov/condition/osteogenesis-imperfecta

OI Foundation: http://www.oif.org/

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 OI.

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.