SickKids | Genome Diagnostics

Connective Tissue Disorders: Bone Involvement Panel

Connective tissue disorders (CTDs) comprise a genetically and clinically heterogeneous group of disorders characterized by changes in the physical properties of the skin, joints, blood vessels, ligaments and tendons. They can also involve other organs and organ systems including the eyes, heart, lungs, kidneys & gastrointestinal tract. Clinical features may include loose joints, abnormal wound healing, fragile bones, abnormal growth, abnormal skin and cardiovascular problems. Age of onset, rate of symptom progression and extent of disability are variable. Our CTDs sequencing panel encompass several different connective tissue disorders.

Genetics

CTD's are inherited in an autosomal dominant, autosomal recessive and X-linked manner. The 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 a CTD.
- The relatives of a proband with identified pathogenic variants in an CTD-associated gene
- Pregnancies at increased risk due to a family history of CTD

Test Methods

Complete sequencing of the coding region and flanking intron/exon boundaries of the genes listed (see attached). This is done via NGS of the targeted gene panels.

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 CTD 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 web-site, for further details.

Genes associated with Connective Tissue disorders with Bone Involvement

See table on page 2

For More Information:

Murphy-Ryan et al (2010) Genetics in Medicine: 12 (6):344-354

Connective Tissue Disorders: www.nlm.nih.gov/medlineplusconnectivetisuedisorders.html

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 CTD.

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.

ARSE	Chondrodysplasia punctata group	X-linked recessive
CBS	Homocystinuria	Autosomal recessive
COL11A1	Stickler type II; Fibrochondrogenesis	Autosomal recessive/dominant
COL11A2	Fibrochondrogenesis type 2	Autosomal recessive/dominant
COL2A1	Stickler type I; Achondrogenesis, type II	Autosomal dominant
COL9A1	Stickler type IV; Multiple epiphyseal dysplasia type VI	Autosomal recessive/dominant
COL9A2	Stickler type V; Multiple epiphyseal dysplasia type II	Autosomal recessive/dominant
COL9A3	Multiple epiphyseal dysplasia type III	Autosomal dominant
COMP	Multiple epiphyseal dysplasia type I; Pseudoachondroplasia	Autosomal dominant
DDR2	Spondylometaepiphyseal dysplasia, short limb-hand type	Autosomal recessive
DYM	Dyggve-Melchoir-Clausen disease; Smith-McCort dysplasia	Autosomal recessive
EBP	Chondrodysplasia punctate; MEND syndrome	X-linked recessive/dominant
EIF2AK3	Wolcott-Rallison syndrome	Autosomal recessive
FBN1	Fibrillimopathies including Marfan syndrome; Acromelic dysplasias	Autosomal dominant
FBN2	Congenital contractural arachnodactyly	Autosomal dominant
FGFR3	FGFR3 chondrodyplasia group; Craniosynostosis syndromes; Polydactyly-Syndactyly-Triphalangism group	Autosomal dominant
FLNB	Filamin group and related disorders	Autosomal recessive/dominant
HSPG2	Perlecan group	Autosomal recessive
IFT122	Cranioectodermal dysplasia I	Autosomal recessive
IFT43	Cranioectodermal dysplasia III	Autosomal recessive
IFT80	Short-rib thoracic dysplasia 2 with or without polydactyly	Autosomal recessive
LBR	Campomelic dysplasia and related disorders	Autosomal recessive/dominant
LIFR	Stuve-Wiedemann syndrome	Autosomal recessive
MATN3	Multiple epiphyseal dysplasia type V; Spondyloepimetaphyseal dysplasia	Autosomal recessive/dominant
NEK1	Ciliopathies with major skeletal involvement	Autosomal recessive
NKX3-2	Spondylo-megaepiphyseal-metayseal dysplasia	Autosomal recessive
NSDHL	CHILD syndrome; CK syndrome	X-linked recessive/dominant
PEX7	Rhizomelic chondrodysplasia punctata	Autosomal recessive
PTH1R	Metaphyseal dysplasias; Neonatal osteosclerotic dysplasias	Autosomal recessive/dominant
SHOX	Langer mesomelic dysplasia; Leri-Weill dyschondrosteosis	X-linked dominant
SLC26A2	Sulphation disorders group	Autosomal recessive
SLC35D1	Schneckenbecken dysplasia	Autosomal recessive
SLC39A13	Spondylodysplastic Ehlers-Danlos Syndrome	Autosomal recessive
SOX9	Campomelic dysplasia	Autosomal dominant
TRAPPC2	Spondyloepiphyseal dysplasia tarda	X-linked recessive
TRIP11	Achondrogenesis, type IA	Autosomal recessive
TRPV4	TRPV4 group	Autosomal dominant
TTC21B	Short-rib thoracic dysplasia 4 with or without polydactyly; Nephronophthisis 12	Autosomal recessive/dominant
WDR19	WDR19 related disorders	Autosomal recessive
WDR35	Short-rib thoracic dysplasia 7 with or without polydactyly; Cranioectodermal dysplasia 2	Autosomal recessive

Group/Name of disorder provided from: Bonafe et al. (2015) PMID: 26394607 as well as OMIM *www.omim.org)