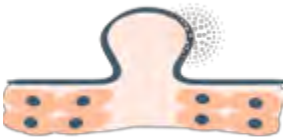
Ehlers-Danlos Syndrome

Precision Panel



Overview

Ehlers-Danlos Syndromes (EDS) are a clinically and genetically heterogeneous group of connective-tissue disorders, where the genetic defect affects collagen and connective-tissue synthesis and structure. It is characterized by hypermobility, cutaneous fragility and hyperextensibility. Since the connective tissue is the tissue that helps body growth as well as serving as a scaffold for cells and organs, Ehlers-Danlos is a pleiotropic syndrome affecting the skin, joints and blood vessels. It has been classically divided into six types (classical, hypermobile, vascular, kyphoscoliotic, arthrochalasis and dermatosparaxis), where the underlying collagen abnormality is different for each type. In some cases, EDS can be life threatening, whereas in others, individuals live a relatively uneventful life. EDS can have phenotypic overlap with conditions such as Marfan disease and cutis laxa.

The Igenomix Ehlers-Danlos Syndrome Precision Panel can be used to make an accurate and directed diagnosis as well as a differential diagnosis of connective tissue disorders due to their overlapping phenotypic features ultimately leading to a better management and prognosis of the disease. It provides a comprehensive analysis of the genes involved in this disease using next-generation sequencing (NGS) to fully understand the spectrum of relevant genes involved.

Indications

The Igenomix Ehlers-Danlos Syndrome Precision Panel is indicated for those patients with a clinical suspicion or diagnosis of EDS presenting with:

- Skin hyperextensibility
- Joint Hypermobility
- Easy bruising
- Retinal detachment
- Mitral valve prolapse
- Hernias and organ prolapse
- Skeletal abnormalities: pectus excavatum, high arched palate, pes planus
- Digestive problems: heartburn and constipation
- Urinary stress incontinence

Clinical Utility

The clinical utility of this panel is:

- The genetic and molecular confirmation for an accurate clinical diagnosis of a symptomatic patient. Clinical overlap exists between different EDS subtypes, as well as with other heritable connective tissue disorders, therefore the diagnosis relies on molecular confirmation with genetic identification of causative genes.
- Early initiation of treatment with a multidisciplinary team in the form of physical therapy and surveillance to prevent vascular complications.
- Risk assessment and genetic counselling of asymptomatic family members according to the mode of inheritance.
- Improvement of delineation of genotype-phenotype correlation.

Genes & Diseases

GENE	OMIM DISEASES	INHERITANCE*	% GENE COVERAGE (20X)	HGMD**
ABCC6	Generalized Arterial Calcification Of Infancy, Pseudoxanthoma Elasticum	AD,AR	99	346 of 349
ABL1	Congenital Heart Defects And Skeletal Malformations Syndrome	AD	99.93	8 of 8
ACTA2	Familial Thoracic Aortic Aneurysm, Moyamoya Disease, Multisystemic Smooth Muscle Dysfunction Syndrome, Familial Thoracic Aortic Aneurysm And Aortic Dissection	AD	100	88 of 88
ADAMTS2	Autosomal Recessive Ehlers-Danlos Syndrome Type VII, Dermatosparaxis Ehlers-Danlos Syndrome	AR	95.99	9 of 10
ADAMTSL2	Geleophysic Dysplasia	AR	49.32	18 of 30
AEBP1	Classic-Like Ehlers-Danlos Syndrome Type 2	AR	99.35	9 of 9
ALDH18A1	Autosomal Dominant Cutis Laxa, Corneal Clouding Cutis Laxa And Mental Retardation, Autosomal Dominant Spastic Paraplegia, Aldh18a1-Related De Barsy Syndrome	AD,AR	100	39 of 40
ATP6AP1	Immunodeficiency	X,XR,G	99.2	NA of NA
ATP6V0A2	Autosomal Recessive Cutis Laxa Type II, Wrinkly Skin Syndrome	AR	99.99	55 of 55
ATP6V1A	Autosomal Recessive Cutis Laxa Type IId, Undetermined Early-Onset Epileptic Encephalopathy	AD,AR	99.98	9 of 9
ATP6V1E1	Autosomal Recessive Cutis Laxa, Type IIc	AR	100	2 of 2
ATP7A	Cutis Laxa X-linked, Menkes Disease, Distal X-linked Spinal Muscular Atrophy, Occipital Horn Syndrome	X,XR,G	99.83	NA of NA
B3GALT6	Ehlers-Danlos Syndrome, Spondyloepimetaphyseal Dysplasia With Joint Laxity	AR	65.09	24 of 39
B3GAT3	Multiple Joint Dislocations, Short Stature, Craniofacial Dysmorphism, With Or Without Congenital Heart Defects	AR	99.86	15 of 15
B4GALT7	Ehlers-Danlos Syndrome Spondylodysplastic Type 1, B4galt7-Related Spondylodysplastic Ehlers-Danlos Syndrome	AR	99.92	11 of 11
BGN	Meester-Loeys Syndrome, X-linked Spondyloepimetaphyseal Dysplasia	X,XR,G	99.87	NA of NA
C1R	Periodontal Ehlers-Danlos Syndrome	AD	98.89	16 of 16
C1S	Periodontal Ehlers-Danlos Syndrome	AD	100	12 of 12
CBS	Homocystinuria Due To Cystathionine Beta-Synthase Deficiency, Classic Homocystinuria	AR	99.98	192 of 194
CHST14	Ehlers-Danlos Syndrome, Musculocontractural Type, Musculocontractural Ehlers-Danlos Syndrome	AR	97.7	21 of 22
CHST3	Multiple Joint Dislocations, Short Stature, Craniofacial Dysmorphism, With Or Without Congenital Heart Defects, Spondyloepiphyseal Dysplasia With Congenital Joint Dislocations, Chst3-Related Skeletal Dysplasia	AR	99.97	38 of 38
COL11A1	Fibrochondrogenesis, Marshall Syndrome, Stickler Syndrome Type II	AD,AR	100	104 of 106
COL12A1	Bethlem Myopathy, Ullrich Congenital Muscular Dystrophy, Myopathic Ehlers-Danlos Syndrome	AD	99.97	18 of 19

COL1A1	Caffey Disease, Ehlers-Danlos Syndrome Type VII, Osteogenesis Imperfecta, Arthrochalasia Ehlers-Danlos Syndrome, Classical Ehlers-danlos Syndrome, Dermatofibrosarcoma Protuberans	AD	99.98	1156 of 1159
COL1A2	Ehlers-Danlos Syndrome Arthrochalasia Type 2, Ehlers-Danlos Syndrome Cardiac Valvular Form, Osteogenesis Imperfecta	AD,AR	100	576 of 581
COL2A1	Achondrogenesis Type II, Czech Dysplasia, Epiphyseal Dysplasia, Multiple, With Myopia And Conductive Deafness, Kniest Dysplasia, Osteoarthritis With Mild Chondrodysplasia, Platyspondylic Lethal Skeletal Dysplasia Spondyloepimetaphyseal Dysplasia, Stickler Syndrome, Autosomal Dominant Otospondylomegaepiphyseal Dysplasia, Dysspondyloenchondromatosis, Multiple Epiphyseal Dysplasia	AD,MU	100	583 of 583
COL3A1	Ehlers-Danlos Syndrome Type IV, Polymicrogyria With Or Without Vascular-Type Ehlers-Danlos Syndrome, Vascular Ehlers-Danlos Syndrome	AD,AR	100	676 of 676
COL5A1	Ehlers-Danlos Syndrome Classic Type 2, Ehlers-Danlos Syndrome Type 1	AD	99.08	191 of 195
COL5A2	Ehlers-Danlos Syndrome Classic Type 2	AD	100	45 of 45
COL6A1	Bethlem Myopathy, Ullrich Congenital Muscular Dystrophy	AD,AR	99.96	182 of 186
COL6A2	Bethlem Myopathy, Ullrich Congenital Muscular Dystrophy	AD,AR	100	223 of 225
COL6A3	Bethlem Myopathy, Dystonia, Ullrich Congenital Muscular Dystrophy	AD,AR	99.63	232 of 232
CRTAP	Osteogenesis Imperfecta Type VII	AR	99.98	29 of 30
DCC	Familial Horizontal Gaze Palsy With Progressive Scoliosis With Impaired Intellectual Development, Familial Congenital Mirror Movements	AD,AR	94	39 of 39
DSE	Musculocontractural Ehlers-Danlos Syndrome	AR	99.94	3 of 3
EFEMP2	Autosomal Recessive Cutis Laxa Autosomal Recessive Type Ib	AR	99.99	17 of 17
ELN	Autosomal Dominant Cutis Laxa, Supravalvular Aortic Stenosis, Williams-Beuren Syndrome, Familial Thoracic Aortic Aneurysm And Aortic Dissection, Williams Syndrome	AD	99.99	95 of 96
FBLN5	Autosomal Dominant Cutis Laxa, Autosomal Recessive Cutis Laxa Type 1	AD,AR	97.43	23 of 23
FBN1	Marfan Lipodystrophy Syndrome, Marfan Syndrome, Mass Syndrome, Stiff Skin Syndrome, Weill-Marchesani Syndrome, Familial Thoracic Aortic Aneurysm And Aortic Dissection, Glaucoma-Ectopia Lentis-Microspherophakia-Stiff Joints-Short Stature Syndrome, Neonatal Marfan Syndrome, Shprintzen-Goldberg Syndrome	AD	100	2836 of 2845
FBN2	Congenital Contractural Arachnodactyly	AD	100	115 of 115
FKBP14	Ehlers-Danlos Syndrome With Progressive Kyphoscoliosis, Myopathy,and Hearing Loss	AR	99.98	7 of 8
FLNA	Cardiac Valvular Dysplasia, X-linked, Frontometaphyseal Dysplasia, Melnick-Needles Syndrome, Otopalatodigital Syndrome Type I and Type II, Melnick-Needles Syndrome, X-linked Ehlers-Danlos Syndrome	X,XR,XD,G	100	NA of NA
FLNB	Atelosteogenesis, Type I, Atelosteogenesis Type III, Boomerang Dysplasia, Larsen Syndrome, Spondylocarpotarsal Synostosis Syndrome	AD,AR	100	124 of 124
GGCX	Pseudoxanthoma Elasticum-Like Disorder With Multiple Coagulation Factor Deficiency, Combined Deficiency Of Vitamin K-Dependent Clotting Factors	AR	100	62 of 62
GORAB	Geroderma Osteodysplastica	AR	96	17 of 18
LOX	Familial Thoracic Aortic Aneurysm And Aortic Dissection	AD	95.47	8 of 8
LTBP4	Autosomal Recessive Cutis Laxa Type Ic, Duchenne Muscular Dystrophy	AR	97.45	27 of 27
LZTS1	Ehlers-Danlos Syndrome		99.73	6 of 6
MYLK	Familial Thoracic Aortic Aneurysm And Aortic Dissection	AD	99.95	50 of 50
NOTCH1	Adams-Oliver Syndrome, Familial Bicuspid Aortic Valve	AD	99.83	178 of 179
P3H1	Osteogenesis Imperfecta Type VIII	AR	94.6	NA of NA
PIEZO2	Distal Arthrogryposis Type 5 With Impaired Proprioception And Touch, Gordon Syndrome, Marden-Walker Syndrome	AD,AR	96.93	37 of 37
PLOD1	Ehlers-Danlos Syndrome Type V	AR	100	36 of 36
PLP1	Pelizaeus-Merzbacher Disease, Spastic Paraplegia Type 2	X,XR,G	100	NA of NA
PRDM5	Brittle Cornea Syndrome	AR	99.86	13 of 13
PYCR1	Autosomal Recessive Cutis Laxa Type IIb, Type IIIb, Geroderma Osteodysplastica	AR	100	44 of 44
RIN2	Macrocephaly, Alopecia, Cutis Laxa, And Scoliosis, Rin2 Syndrome	AR	99.6	4 of 4
ROBO3	Horizontal Gaze Palsy With Progressive Scoliosis	AR	99.88	45 of 45
SKI	Shprintzen-Goldberg Craniosynostosis Syndrome	AD	99.66	39 of 39
SLC39A13	Slc39a13-Related Spondylodysplastic Ehlers-Danlos Syndrome	AR	100	9 of 9
SMAD2	Buschke-Ollendroff Syndrome, Osteopoikilosis	-	100	19 of 19

SMAD3	Loeys-Dietz Syndrome Type 3, Aneurysm-Osteoarthritis Syndrome, Familial Thoracic Aortic Aneurysm And Aortic Dissection	AD	100	128 of 128
SPARC	Osteogenesis Imperfecta Type XVII	AR	100	4 of 4
TGFB2	Loeys-Dietz Syndrome Type 4, Familial Thoracic Aortic Aneurysm And Aortic Dissection	AD	99.9	41 of 44
TGFB3	Loeys-dietz Syndrome 5; Lds5 , Familial Thoracic Aortic Aneurysm And Aortic Dissection	AD	100	34 of 35
TGFBR1	Loeys-Dietz Syndrome, Type 1a Loeys-Dietz Aortic Aneurysm Syndrome, Familial Thoracic Aortic Aneurysm And Aortic Dissection	AD	94	96 of 100
TGFBR2	Loeys-Dietz Syndrome Type 1b, Familial Thoracic Aortic Aneurysm And Aortic Dissection	AD	99.9	165 of 166
TNFRSF1A	Tumor Necrosis Factor Receptor 1 Associated Periodic Syndrome	AD	95.77	111 of 112
TNXB	Classical-like Ehlers-Danlos Syndrome Type 1	AD,AR	92.75	29 of 33
ZNF469	Brittle Cornea Syndrome	AR	99.91	79 of 79

*Inheritance: AD: Autosomal Dominant; AR: Autosomal Recessive; X: X linked; XLR: X linked Recessive; Mi: Mitochondrial; Mu: Multifactorial.
**Number of clinically relevant mutations according to HGMD

Methodology

Contact us

Call +34 963 905 310 or send an email to supportspain@igenomix.com for any of the following objectives:

- Get more information about the test.
- Request your kit.
- Request a pick up of the kit after collecting the sample.

References

1. Scheper MC, Nicholson LL, Adams RD, Tofts L, Pacey V. The natural history of children with joint hypermobility syndrome and Ehlers-Danlos hypermobility type: a longitudinal cohort study. *Rheumatology (Oxford)*.
2. Malfait, F., Wenstrup, R. J., & De Paepe, A. (2010). Clinical and genetic aspects of Ehlers-Danlos syndrome, classic type. *Genetics in medicine: official journal of the American College of Medical Genetics*, *12*(10), 597–605. https://doi.org/10.1097/GIM.0b013e3181eed412
3. Malfait, F., Francomano, C., Byers, P., Belmont, J., Berglund, B., Black, J., Bloom, L., Bowen, J. M., Brady, A. F., Burrows, N. P., Castori, M., Cohen, H., Colombi, M., Demirdas, S., De Backer, J., De Paepe, A., Fournel-Gigleux, S., Frank, M., Ghali, N., Giunta, C., … Tinkle, B. (2017). The 2017 international classification of the Ehlers-Danlos syndromes. *American journal of medical genetics. Part C, Seminars in medical genetics*, *175*(1), 8–26. https://doi.org/10.1002/ajmg.c.31552
4. De Paepe, A., & Malfait, F. (2012). The Ehlers-Danlos syndrome, a disorder with many faces. *Clinical genetics*, *82*(1), 1–11. https://doi.org/10.1111/j.1399-0004.2012.01858.x
5. Ritelli, M., & Colombi, M. (2020). Molecular Genetics and Pathogenesis of Ehlers-Danlos Syndrome and Related Connective Tissue Disorders. *Genes*, *11*(5), 547. https://doi.org/10.3390/genes11050547
6. Miller, E., & Grosel, J. M. (2020). A review of Ehlers-Danlos syndrome. *JAAPA : official journal of the American Academy of Physician Assistants*, *33*(4), 23–28. https://doi.org/10.1097/01.JAA.0000657160.48246.91