

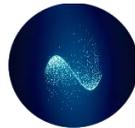


DNA DILIGENCE

SUMMARY REPORT

CONNECT THE DOTS – GET TO THE ROOT – REVERSE ENGINEER

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Hypermobile Ehlers-Danlos Syndrome (EDS3)

Hypermobile Ehlers-Danlos syndrome is an inherited connective tissue disorder that is caused by defects in a protein called collagen. It is generally considered the least severe form of Ehlers-Danlos syndrome (EDS) although significant complications can occur. Common symptoms include joint hypermobility, affecting both large (elbows, knees) and small (fingers, toes) joints; soft, smooth skin that may be slightly elastic (stretchy) and bruises easily; and chronic musculoskeletal (muscle and bone) pain.

An important gene associated with Hypermobile Ehlers-Danlos Syndrome is [COL1A1](#) (Collagen Type I Alpha 1 Chain), and among its related pathways/superpathways are [Signal Transduction](#) and [Integrin Pathway](#).

[Collagen Formation](#)

[Collagen Degradation](#)

[ECM proteoglycans](#)

[Glycosaminoglycan metabolism](#)

Glycosaminoglycans (GAGs) are sulfated glycans capable of regulating various biological and medical functions. Heparin, heparan sulfate, chondroitin sulfate, dermatan sulfate, keratan sulfate and hyaluronan are the principal classes of GAGs.

Examples of these mimetics are the sulfated fucans and sulfated galactans found in brown, red and green algae, sea urchins and sea cucumbers.

Compounds for COL1A1 Gene

Glycosaminoglycans, Lysine, Proline, Clove, Valerian, Thymus glandular, Zinc, Calcium, Vitamin A, other Amino acids

Ehlers Danlos Syndrome with Glycosaminoglycan Abnormalities [\[R\]](#)

Bone and connective tissue disorders caused by defects in glycosaminoglycan biosynthesis: a panoramic view [\[R\]](#)

Upstream Target Genes

NID2 Gene - Nidogen 2 - cell-adhesion protein that binds collagens I and IV and laminin and may be involved in maintaining the structure of the basement membrane

PILRA Gene - Paired Immunoglobulin Like Type 2 Receptor Alpha - PILRA is thought to act as a cellular signaling inhibitory receptor by recruiting cytoplasmic phosphatases like PTPN6/SHP-1 and PTPN11/SHP-2

Compounds for PILRA:

PTPN11/SHP2 SHIP Modulators:

- Resveratrol [\[R\]](#)
- **Cryptotanshinone (Dan shen) [\[R\]](#)**
 - Capparis ovata (Capers) [\[R\]](#)
 - Ashwagandha [\[R\]](#)
 - Licorice [\[R\]](#)

- Beta glucan ([R](#))

Support:

VEGF receptor (VEGFR) inhibitors ([R](#)) ([R](#)) ([R](#))

- **Polysaccharides**
 - Artemisia annua (Chinese wormwood)
 - Viscum album (European mistletoe)
 - **Curcuma longa (curcumin)**
 - Scutellaria baicalensis (Chinese skullcap)
- Resveratrol and proanthocyanidin (grape seed extract)
 - Magnolia officinalis (Chinese magnolia tree)
 - Camellia sinensis (green tea)
 - Ginkgo biloba
 - Quercetin
 - Zingiber officinalis (ginger)
 - Panax ginseng

Matrix Metalloproteinase (MMP) 2 Inhibitor/Collagenase ([R](#))

- **Curcumin**
 - Allicin
 - **Sulforaphane**
 - Green Tea Extract
 - Ashwaganda
 - Red Marine Algae
 - Fucoidan
 - Passion Flower
 - Progesterone
- EPQ – Ascorbic Acid, Lysine, Proline, Green Tea Extract, Quercetin

Human Neutrophil Elastase Compounds (ELANE): ([R](#))

- Green tea
- Caffeic acid
- Devil's claw

- Strawberry
- Pomegranate
- Nigella sativa
 - Lupeol
 - Ursolic acid
- Oleanolic acid
 - Oleic acid
- β -1,3-glucan
- Nattokinase
 - Tamarind
 - Quercetin
- Grapeseed extract
- Phloretin (Manchurian apricot)
 - Resveratrol
 - Genistein
 - Myrtle
 - Thyme
- Catechins (wine, tea and chocolate)
 - Chalcones
 - Rutin
 - Naringenin
 - Hesperidin
 - Myricetin
 - Kaempferol
 - Skullcap
 - Luteolin
 - Propolis
 - Astragalus
 - Delphinidin
 - Boswellic acid
- MCT coconut oil
 - St. John's wort

SHP-2 is the main target for Collagen and EDS3

Type I collagen limits VEGFR-2 signaling by a SHP2 protein-tyrosine phosphatase-dependent mechanism 1 [\[R\]](#)

The Protein Tyrosine Phosphatase SHP-2 Regulates Interleukin-1-induced ERK Activation in Fibroblasts [\[R\]](#)

The tyrosine phosphatase SHP2 controls TGF β -induced STAT3 signaling to regulate fibroblast activation and fibrosis [\[R\]](#)

PHPS1 Specifically Inhibits Shp2-Dependent Signaling [\[R\]](#) (PHPS1 = **Endocannabinoid**)

Fatty acids as natural specific inhibitors of the proto-oncogenic protein Shp2 [\[R\]](#)

Cellular and Molecular Mechanisms in the Pathogenesis of Classical, Vascular, and Hypermobility Ehlers–Danlos Syndromes [\[R\]](#)

Genes for Signal Transduction SuperPath

DHRS9 Gene - Dehydrogenase/Reductase 9

IDH3G Gene – Isocitrate
Dehydrogenase (NAD(+)) 3 Non-Catalytic Subunit Gamma

UQCRC1 Gene - Ubiquinol-Cytochrome C Reductase Core Protein 1

[These are Citric acid cycle genes]

Therapeutics

Liver extracts, Vitamin B Complex, CoQ10, TUDCA [\[R\]](#)

NAD(+), Alpha-ketoglutarate, Hydro-citric acid (Garcinia), Manganese, Magnesium [\[R\]](#)

Genes for Integrin Pathway SuperPath

COL13A1 Gene - Collagen Type XIII Alpha 1 Chain

[Binds **heparin** (**Nattokinase**). At neuromuscular junctions, may play a role in **acetylcholine** receptor clustering]

Therapeutics

Focal Adhesion Kinase (FAK) Inhibitors:

- Resveratrol ([R](#))
- **Genistein** ([R](#))
- **Hesperadin** ([R](#))
 - ATP ([R](#))
- Liverwort ([R](#))([R](#))

AKT ([R](#))

- Resveratrol
 - ATP
- **Genistein**
- Andrographis
- **Withaferin A**
 - Garcinia

Actin/N-WASP inhibitors: **Sulforaphane**, Ashwagandha, Propolis

Caspase 3 Modulators: Withaferin A (Ashwagandha), Glycyrrhizic acid (Licorice), Spermidine

cyclic adenosine monophosphate (cAMP) Modulator: Forskolin, Luteolin