Molecular Genetics Service Profile
Stickler dysplasia

Introduction

◊ Stickler dysplasia (MIM 108300) is an autosomal dominant connective tissue disorder affecting the ocular, orofacial and articular systems. Major clinical features include early-onset severe myopia with congenital vitreous anomalies, spontaneous retinal detachments, cleft palate, flat facial profile, hearing loss and early-onset degenerative joint disease.

◊ Stickler dysplasia shows considerable genetic heterogeneity. Mutations in *COL2A1, COL11A1 and COL11A2* have been identified in Stickler dysplasia patients. A few families have been reported with no linkage to either of these three loci (Wilkin DJ et al; 1998). *COL2A1* seems to be the major gene involved in Stickler dysplasia.

◊ Genotype-phenotype correlations: The classical phenotype is usually due to mutations in *COL2A1*. If the hearing loss is more significant, mutations in *COL11A1* can be found. In the absence of ocular involvement, a mutation in *COL11A2* should be considered. The type of congenital vitreous anomaly seems to be different between *COL2A1* and *COL11A1* related Stickler dysplasia (Snead MP et al; 1999).

Contact details for the laboratories carrying out the genetic test for Stickler dysplasia
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Reasons for referral

◊ Mutation analysis in patients for confirmation of a clinically suspected diagnosis of Stickler dysplasia. Screening for unknown mutations is labour intensive, therefore we cannot accept urgent referrals of this type.

◊ Evaluation of at-risk relatives for management reasons and genetic counselling. In this case the mutation in the index case must be known.

◊ Prenatal diagnosis (preferentially offered after genetic counselling). The mutation in the parent must be known.

Samples

◊ Minimum 100μg of genomic DNA from peripheral lymphocytes (or cultured cells) from your local laboratory. Blood samples (minimum of 5ml in EDTA) can also be sent to our laboratory by express mail (DHL/FedEx//TNT/UPS).

◊ Prenatal samples must be sent with a sample from both parents. For prenatal diagnosis: please contact our laboratory in advance.

Technical

◊ Testing strategy: All patients are tested for *COL2A1* (Ghent). If normal, *COL11A1* and/or *COL11A2* are tested depending on the clinical phenotype (Oulu).

◊ Mutation scanning of exons 1-54 of *COL2A1* by fluorescent bidirectional sequencing.

◊ Mutation scanning of exons 14-68 of *COL11A1* by fluorescent bidirectional sequencing.

◊ Mutation scanning of exons 1-66 of *COL11A2* by fluorescent bidirectional sequencing.

Target turn-round time

◊ Mutation scanning of *COL2A1* – 3 months. Mutation scanning of *COL11A1* and *COL11A2* – 20 weeks. Routine, single mutation test - 4 weeks. Urgent, single known mutation test - 2 weeks. Prenatal diagnosis – 2 weeks (*COL2A1* only). Turn-round times are from the receipt of all required samples and information, including appropriate clinical information and radiographs. Relevant clinical-radiographic expertise is currently offered at no cost through the use of the secure online submission system (the **ESDN Case Manager**). Testing is only performed after clinical and radiographic evidence has been reviewed using the **ESDN Case Manager**. To obtain a username and password for the **ESDN Case Manager** please email info@esdn.org.

Cost

◊ Full mutation screen – €6300. (This includes €1000 for *COL2A1,* €2500 for *COL11A1* and €2800 for *COL11A2*).

References

◊ Wilkin DJ, Mortier GR *et al*. (1998). *Am J Med Genet.* **80**: 121-127.

◊ Snead MP *et al*. (1999). *J Med Genet* **36**: 353-359.

◊ Annunen S et al. (1999). *Am J Hum Genet*: **65**: 974-983.

ESDN Administrator contact details

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