CONNECTIVE TISSUE LABORATORY
Center for Medical Genetics – Ghent University Hospital - MRB – De Pintelaan 185 – B-9000 Ghent, Belgium
Department Chair: Prof. A. De Paepe – Supervisor Connective Tissue Lab: Prof. P. Coucke
Receipt of samples: Tel: 0032-(0)9-332 24 77 – Fax: 0032-(0)9-332 65 49
Website: http://medgen.ugent.be – e-mail: connective_tissue@medgen.ugent.be

CLINICAL INFORMATION SHEET

Marfan syndrome
and related aortic aneurysm syndromes

Patient information

Name:
First Name(s):
Sex: ☐ M ☐ F
Date of Birth (dd/mm/yyyy): / /
Address:

Referring Physician:
Referring Center:

SAMPLE:
☐ EDTA blood ☐ DNA ☐ Skin biopsy ☐ Chorionic villi
☐ Heparin blood ☐ RNA ☐ Aortic biopsy ☐ Amniocytes
☐ Buccal swab ☐ Fibroblasts ☐ Paraffin embedded material
☐ Other:

Date (dd/mm/yyyy): / /
Sample arrived:

Suspected diagnosis

☐ Marfan syndrome
☐ Ehlers-Danlos syndrome
☐ Loeys-Dietz syndrome
☐ Shprintzen-Goldberg syndrome
☐ Beals-Hecht syndrome or congenital contractural arachnodactyly
☐ Arterial tortuosity syndrome
☐ Familial (thoracic) aortic aneurysms syndrome
☐ Bicuspid aortic valve
☐ Other:

This checklist is meant to guide genetic testing for the Marfan syndrome or testing in the setting of (familial) thoracic aortic aneurysm/dissection and/or arterial tortuosity. Since both entities are not mutually exclusive, both check-lists may be used for a single patient in some cases.
Selecting the most likely gene to be screened in order to explain the underlying clinical presentation in your patient highly depends on adequate and correct clinical data. We therefore kindly ask you to be as precise and specific as possible.
The differential diagnosis in patients referred for additional genetic testing with a clinical presentation characterized by aortic (root) aneurysm/dissection and/or arterial tortuosity is extensive. You will find an overview of possible diagnosis below. Please indicate what diagnosis you suspect in your patient and/or make sure to fill out the checklist as complete as possible so that we can set up the appropriate genetic testing.

CLINICAL SUMMARY

PEDIGREE

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Differential diagnosis	Gene	Discriminating features
Marfan syndrome (MFS)	FBN1	Aortic root dilatation, presence of ectopia lentis, systemic features (table 1) (diagnostic criteria Box 1)
Loeys-Dietz syndrome (LDS)	TGBR1/2	Bivid uvula/cleft palate, arterial tortuosity, hypertelorism, diffuse aortic and arterial aneurysms, craniosynostosis, clubfoot, cervical spine instability, thin and velvety skin, easy bruising
Shprintzen-Goldberg syndrome (SGS)	FBN1 and other	Craniosynostosis, mental retardation, hypertelorism, proptosis
Congenital contractural arachnodactyly (CCA)	FBN2	Crumpled ears, contractures
Weill-Marchesani syndrome (WMS)	FBN1 and ADAMTS 10	Microspherophakia, brachydactyly, joint stiffness, short stature
Ectopia lentis syndrome (ELS)	FBN1, LTBP2, ADAMTS4	Lack of aortic root dilatation
Homocystinuria	CBS	Thrombosis, mental retardation
Familial thoracic aortic aneurysm syndrome (FTAA)	TGFBR1/2	Lack of Marfanoid skeletal features,
	ACTA2	levido reticularis, iris flocculi, CVA
	Smad3	Osteoarthritis, arterial tortuosity, soft skin
	MLCK	Gastro-intestinal abnormalities
FTAA with bicuspid aortic valve (BAV)		Lack of Marfanoid skeletal features, levido reticularis, iris flocculi
FTAA with patent ductus arteriosus (PDA)	MYH11	Lack of Marfanoid skeletal features, levido reticularis, iris flocculi
Arterial tortuosity syndrome (ATS)	SLC2A10	Generalised arterial toruosity, arterial stenosis, facial dysmorphism
Ehlers-Danlos syndromes (vascular, valvular, kyphoscoliotic type)	COL3A1, COL1A2, PLOD1	Middle sized artery aneurysm, severe valvular insufficiency, translucent skin, dystrophic scars, facial characteristics
Cutis laxa	ELN (AD)	Cutis laxa with variable involvement of internal organs (lung, aorta), association with BAV
	FBLN4 (AR)	Cutis laxa, emphysema, arterial tortuosity, aortic aneurysm, joint laxity, pectus excavatum, diaphragmatic hernia, bone fragility

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Check-list for (Familial) Aortic Aneurysm/Dissection and/or arterial tortuosity

Suspected clinical diagnosis (see list above):	
Maximal aortic diameter	mm
Age at measurement	yrs
Localisation of the maximum dilatation	
Sinus Valsalva	☐
Sinotubular Junction	☐
Ascending Aorta	☐
Aortic arch	☐
Descending Aorta	☐
Abdominal Aorta	☐
Aortic dissection:	
thoracic type A – type B	A -B
abdominal	☐
Arterial tortuosity	☐
Peripheral arterial dissection: please specify	
Bicuspid Aortic Valve	☐
Other cardiovascular lesions (please specify):	
Other systemic features (please specify): • Ocular: • Osteo-articular: • Central Nervous: • Skin: • Gastro-intestinal:	

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Revised Ghent Criteria for Diagnosis of Marfan syndrome and related conditions

In the absence of family history:

(1) Ao (Z≥2) + EL = MFS
(2) Ao (Z≥2) + FBN1 = MFS
(3) Ao (Z≥2) + Syst (≥7pts) = MFS
(4) EL + FBN1 with known Ao = MFS

In the presence of family history:

(5) EL + FH of MFS (as defined above) = MFS
(6) Syst (≥7 pts) + FH of MFS (as defined above) = MFS
(7) Ao (Z≥2 in adults, Z≥3 in children) + FH of MFS (as defined above) = MFS

Z: Z-score (aortic root diameter corrected for age and BSA); EL: ectopia lentis; FBN1: Fibrillin 1 mutation; Syst: systemic score (see below); FBN1 with known Ao: FBN1 mutation linked to aortic aneurysm in other patients/families (Loeys et al, Journal of Medical Genetics 2010)

Required clinical data

Aortic diameter at the level of the sinus of Valsalva	mm
Age at measurement	yrs
Height	cm
Weight	kg
Ectopia Lentis	Y/N
Systemic score	/20
Family History: please specify	

Systemic features	Yes	No	NE	Score
Wrist AND thumb sign	☐	☐	☐	3
Wrist OR thumb sign	☐	☐	☐	1
Pectus carinatum deformity	☐	☐	☐	2
Pectus excavatum or chest asymmetry	☐	☐	☐	1
Hindfoot deformity	☐	☐	☐	2
Pes Planus	☐	☐	☐	1
Pneumothorax	☐	☐	☐	2
Dural ectasia	☐	☐	☐	2
Protrusio acetabuli	☐	☐	☐	2
Reduced US/LS AND increased arm/height AND no severe scoliosis	☐	☐	☐	1
Scoliosis or thoracolumbar kyphosis	☐	☐	☐	1
Reduced elbow extension	☐	☐	☐	1
Facial features (3/5) (dolichocephaly, enophthalmos, downslanting palpebral fissures, malar hypoplasia, retrognathia)	☐	☐	☐	1
Skin striae	☐	☐	☐	1
Myopia > 3 diopters	☐	☐	☐	1
Mitral valve prolapse (all types)	☐	☐	☐	1
TOTAL SCORE	**/20**			

Maximum total: 20 points; score> 7 indicates systemic involvement