Familial vascular EDS
caused by COL5A1 mutation

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39 year old male visited our policlinic in 2009
→ age 16 y: acute dissection a. subclavia
→ age 18 y: surgery for aneurysm a. coeliacus

- fragile translucent skin, hypermobile joints

Only brother: died at age 34 y from rupture a. iliaca

Mother: died suddenly at age 28, ruptured a. renalis

PA: all massive degenerative changes in vascular tissue

→ Clinical diagnosis: vascular EDS, but no COL3A1 mutation
No mutation detected in TGFBR1, TGFBR2, ACTA2 and SMAD3 genes in DNA diagnostics

Included patient in VASCULOME research project

NGS-based analysis of 550 genes (possibly) linked to vascular disease

OMIM
Pubmed (a.o. GWAS)
KEGG pathways (a.o. TGF-beta, Notch, ECM-receptor interaction)
GO search terms (a.o. VSMC contraction/relaxation)
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• Mutations in *COL5A1* cause Classic EDS \(\rightarrow\) Features of skin & joints, but no vascular disease

• Segregation analysis in family (autopsy material from brother, father & grandparents)

The two affected brothers carry *COL5A1* mutation, but no segregation of other identified variants

\(\rightarrow\) Vascular disease explained by *COL5A1* mutation only?

\(\rightarrow\) Or is there a genetic modifier in this family (grandfather very large rAAA age 78)
Pedigree

Pedigree diagram showing family relationships with genetic and medical information.
Literature

Our patient: p.Gly1537Val

Superior Mesenteric Artery Aneurysm in a 9-Year-Old Boy With Classical Ehlers–Danlos Syndrome

K. de Leeuw,1* J.F. Goorhuis,2 I.F.J. Tielliu,3 S. Symoens,5 F. Malfait,5 A. de Paepe,5 J.P. van Tintel,4 and J.B.F. Hulscher5

Our patient: p.Gly1564Asp
Conclusion

COL5A1 mutation likely the major cause of vascular disease →
Col5A1 protein important role in vascular integrity

COL5A1 gene should be analysed in COL3A1 mutation negative
vascular EDS patients
Acknowledgements

UMC Utrecht
Drs. G. Monroe
Dr. M. Harakalova
Dr. D. Dooijes
Dr. G. van Haaften
Dr. S.N. Slim-van der Crabben
Dr. I.J. Nijman
Dr. A. Vink
Prof. F.L. Moll
Prof. Dr. E. Cuppen
Prof. dr. N. Knoers

VUMC
Dr. A. Maugeri
Dr. G. Pals

Erasmus MC
Dr. D. Majoor-Krackauer
Dr. A. Bertoli-Avella