



20 | 23 JUNE 2022

Liège | Théâtre de Liège | Belgium

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70th ESCVS
International congress of the European Society
for Cardiovascular and Endovascular Surgery



7th IMAD meeting

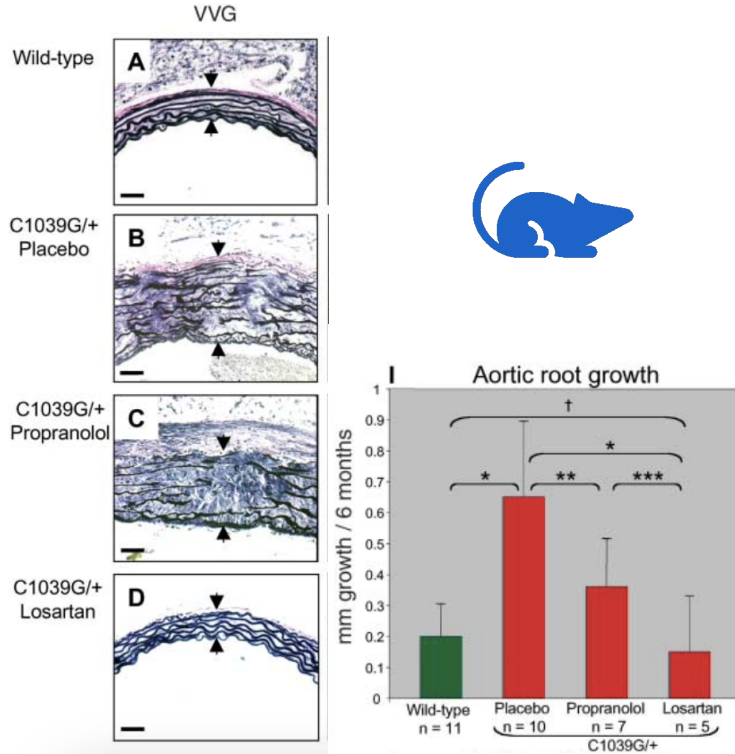
Threats and opportunities with the use of animal models for Marfan syndrome

Julie De Backer, MD, PhD

Ghent University Hospital, Belgium

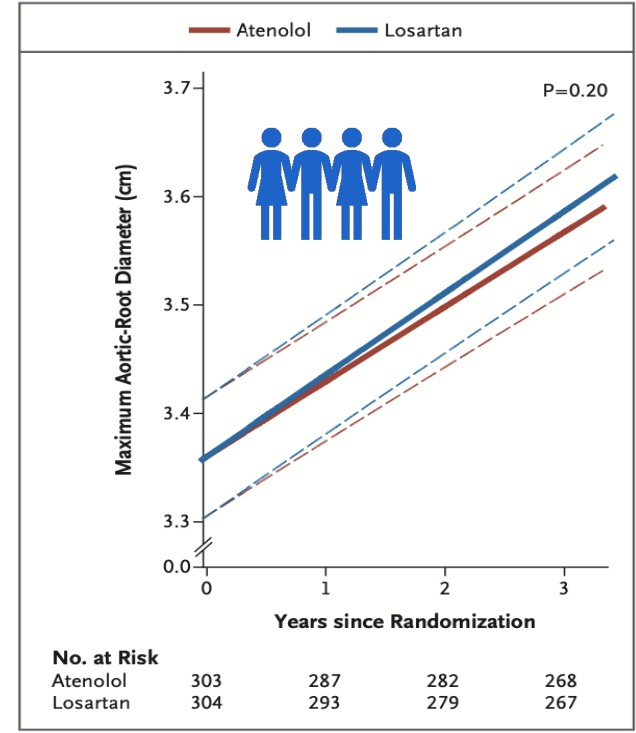
Conflict of interest: none





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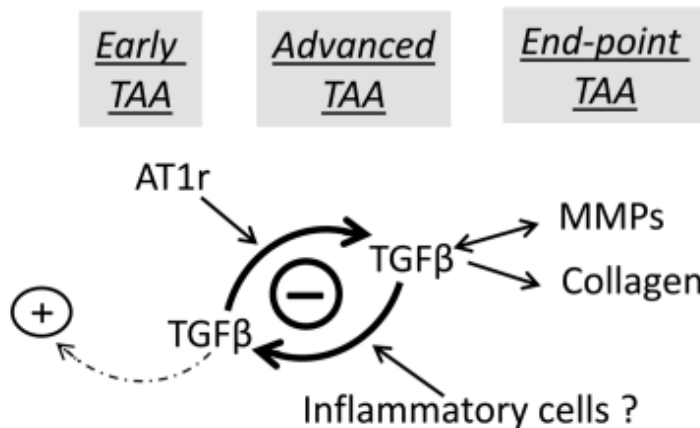


Habashi JP, et al.. Science. 2006

Lacro RV, et al. The New England journal of medicine. 2014



1. Was the concept of increased $\text{TGF}\beta$ signaling too simplistic?



Cook JR, et al. Arteriosclerosis, thrombosis, and vascular biology. 2015

Loss of physiologic SMC $\text{TGF}\beta$ signaling exacerbates MFS-associated aortopathy.

- protective role for SMC $\text{TGF}\beta$ signaling during early development

(Wei H, et al. J Am Heart Assoc. 2017)



2. Was losartan not the right TGF β inhibitor?

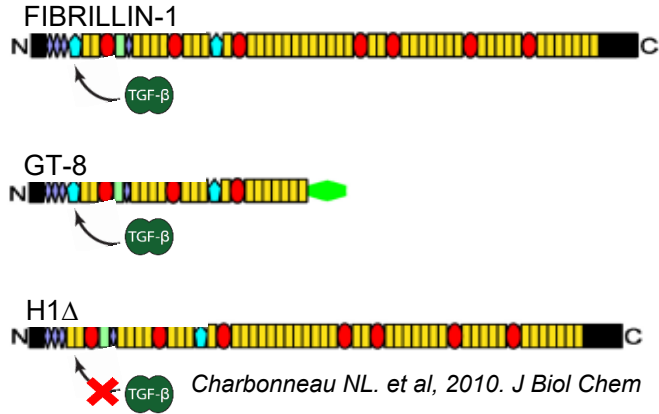
- Dosage: x100!
- Half-life – irbesartan better? – cfr AIMS trial
- Timing

Mullen M, et al. Lancet. 2020



3. Did the mouse models fail us?

- 1 variant vs >1000
- Dissection versus aneurysm models
- Background
- genome 99% similar to human
- good genetic/molecular toolbox
- Small size - large scale/high throughput
- cost-efficient model

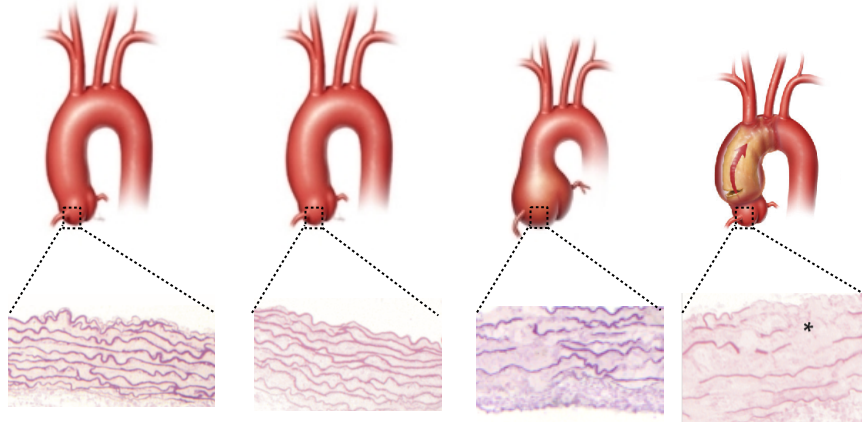


Wild-type

H1Δ/+

GT-8/+

GT - 8/H1Δ



Microdissection Aneurysm Aneurysm/dissection

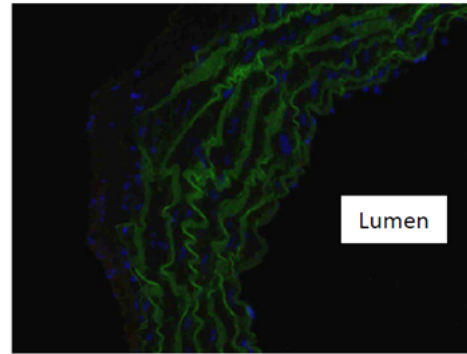
Proteomics – scRNAseq – cell culture – (synchrotron) imaging
⇒ Mechanism of aortic dissection – targeted treatment

Preliminary results

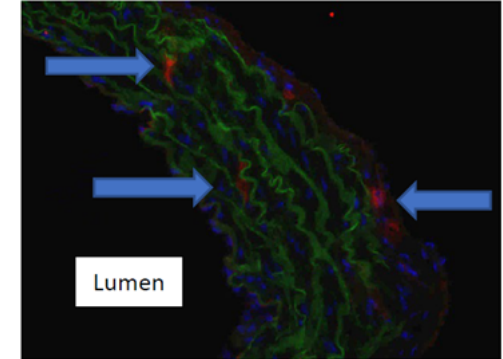
Proteomics analyses:

Cellular: VCAM-1

Molecular: HTRA1



WT



Fbn1^{GT-8/+}

Conclusions

- We need animal models
 - To study disease mechanisms
 - To identify new treatment targets
- Lessons learned from translation to humans need to be taken into account

Thank you!

Ghent University

Lisa Caboor

Violette Deleeuw

Griet Desmet

Karo De Rycke

Marina Horvat

Laura Muiño Mosquera

Patrick Sips

OHSU Portland

Eric Carlson

Lynn Sakai



@judbacke



Julie.debacker@ugent.be