



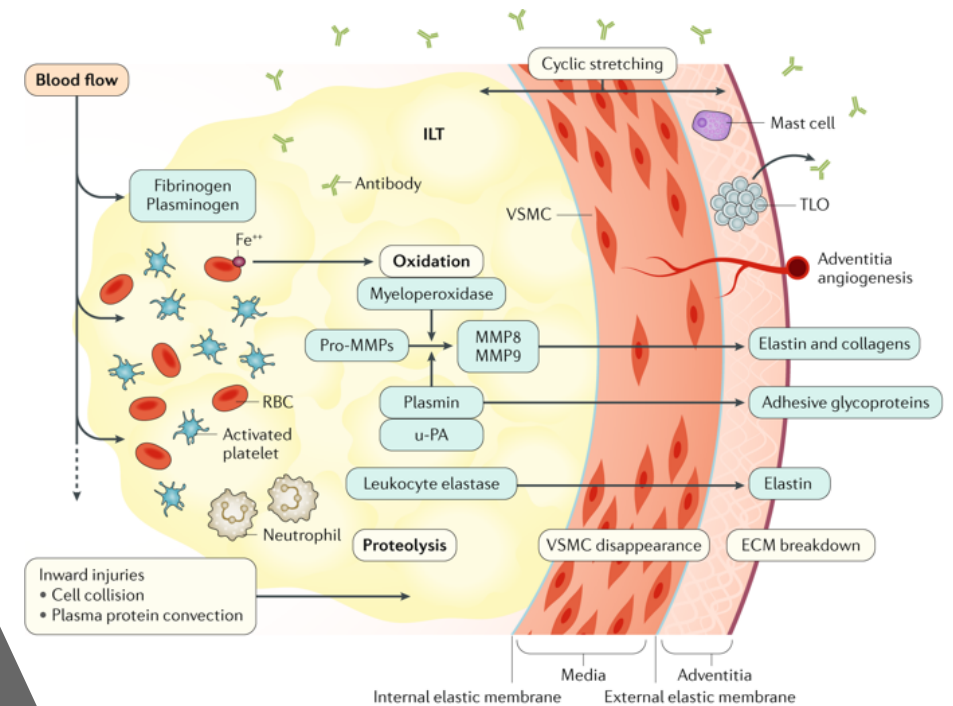
# AAA – does the arterial media and adventia have different roles?

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# Introduction

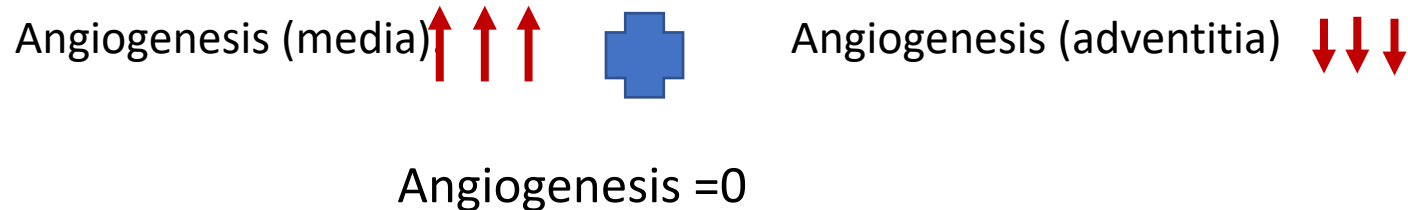
- More than 30 trials for Medical therapy of AAAs (over 10 RCTS) without any success
  - Lack understanding of key processes in AAA pathophysiology
- At least 4 Microarray studies performed to discover novel genes in AAA pathology
  - Whole aortic thickness samples used
    - Lenk et al , *BMC Genomics* 2007
    - Choke et al, *EJVES* 2009
    - Biros et al, *Oncotarget* 2015
    - Gäbel et al, *JAHA* 2017



Sakalihasan et al. *Nat Dis Primers* 2018

# Hypothesis and Aim

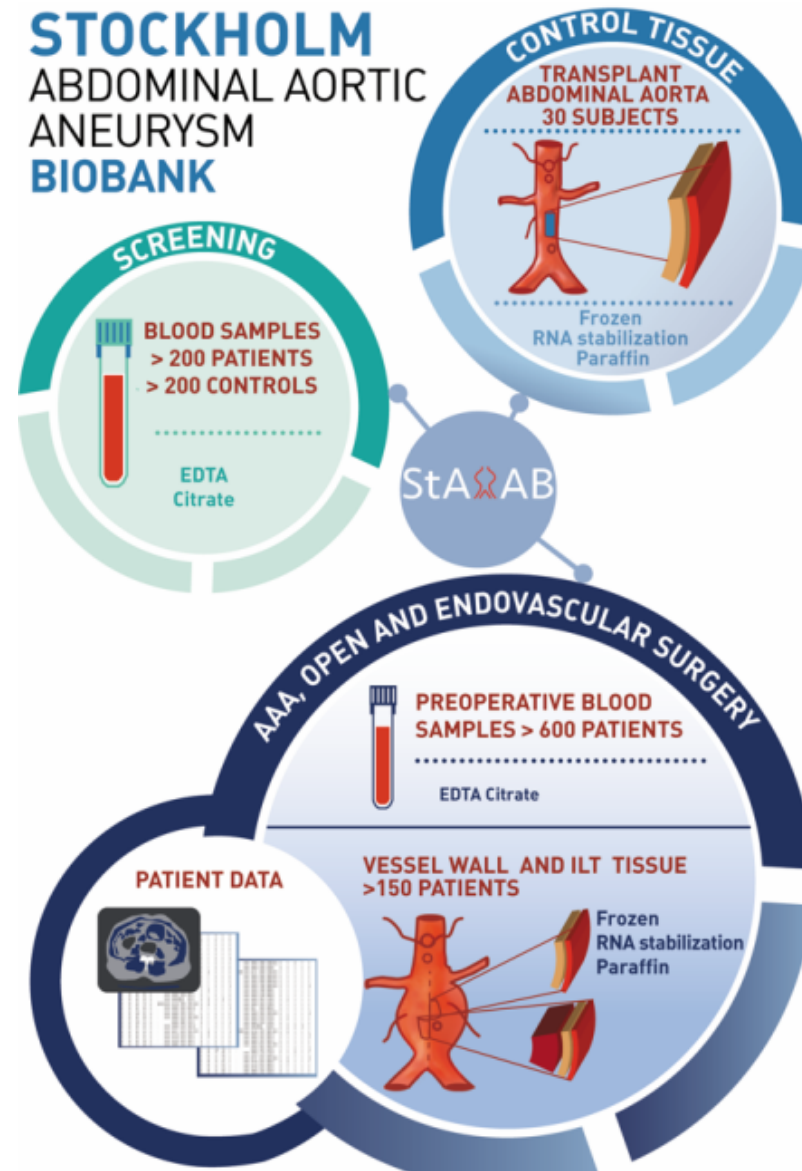
- Hypothesis
  - Processes that occur in the Adventitia and Media differ and can be hidden when whole tissue analysis is performed



- Find novel mechanisms in AAA pathology

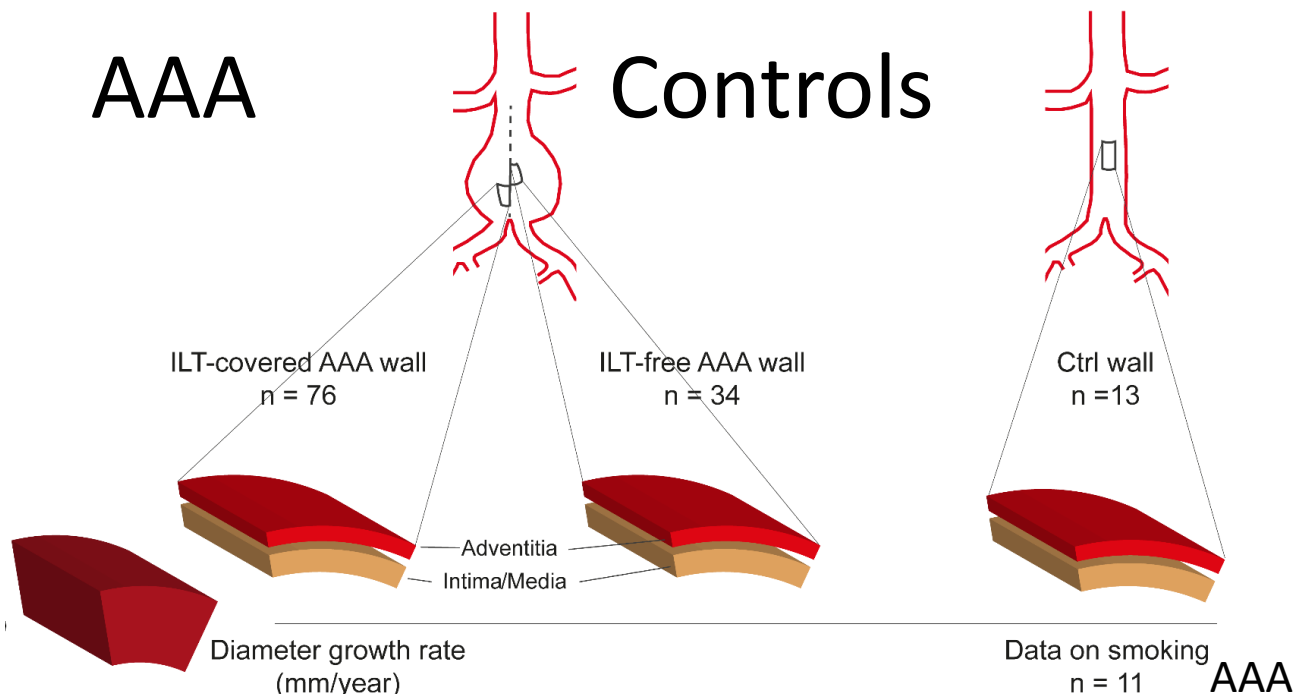
# Method

- > 1000 patients
- > 250 AAA tissue samples
- Patient data
  - Age, sex
  - Comorbidities
  - Growth data (CT or US)
  - CT images



# AAA

# Controls



76 AAA patients

13 Control donor aortas

Total 278 samples

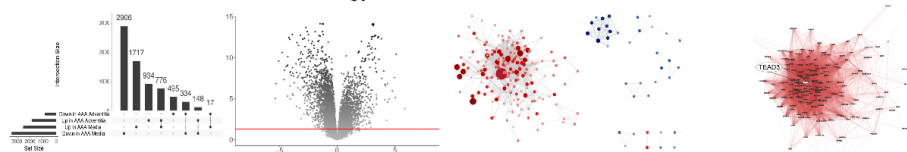
HTA 2.0 microarray

Data on smoking  
n = 75

Differential expression analysis

Gene set enrichment analysis  
Gene ontology network

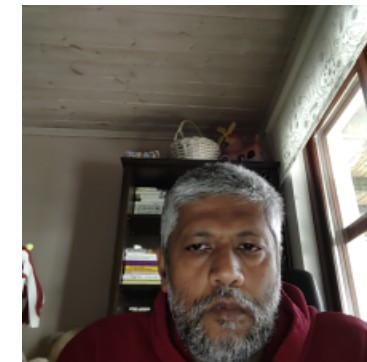
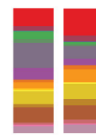
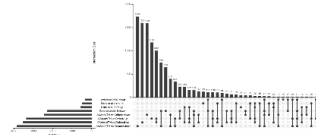
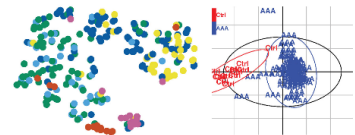
Transcription factor prediction

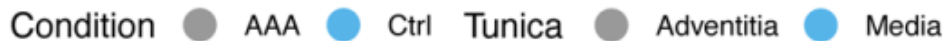
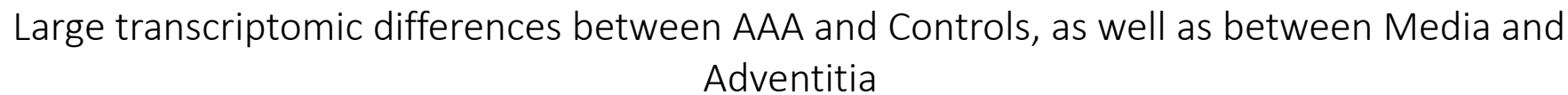


Unsupervised and supervised clustering  
(t-SNE and OPLS-DA)

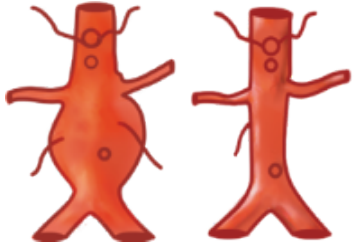
Comparison with previous studies  
microarray, AAA vs Ctrl

Cell type deconvolution  
(CIBERSORT)

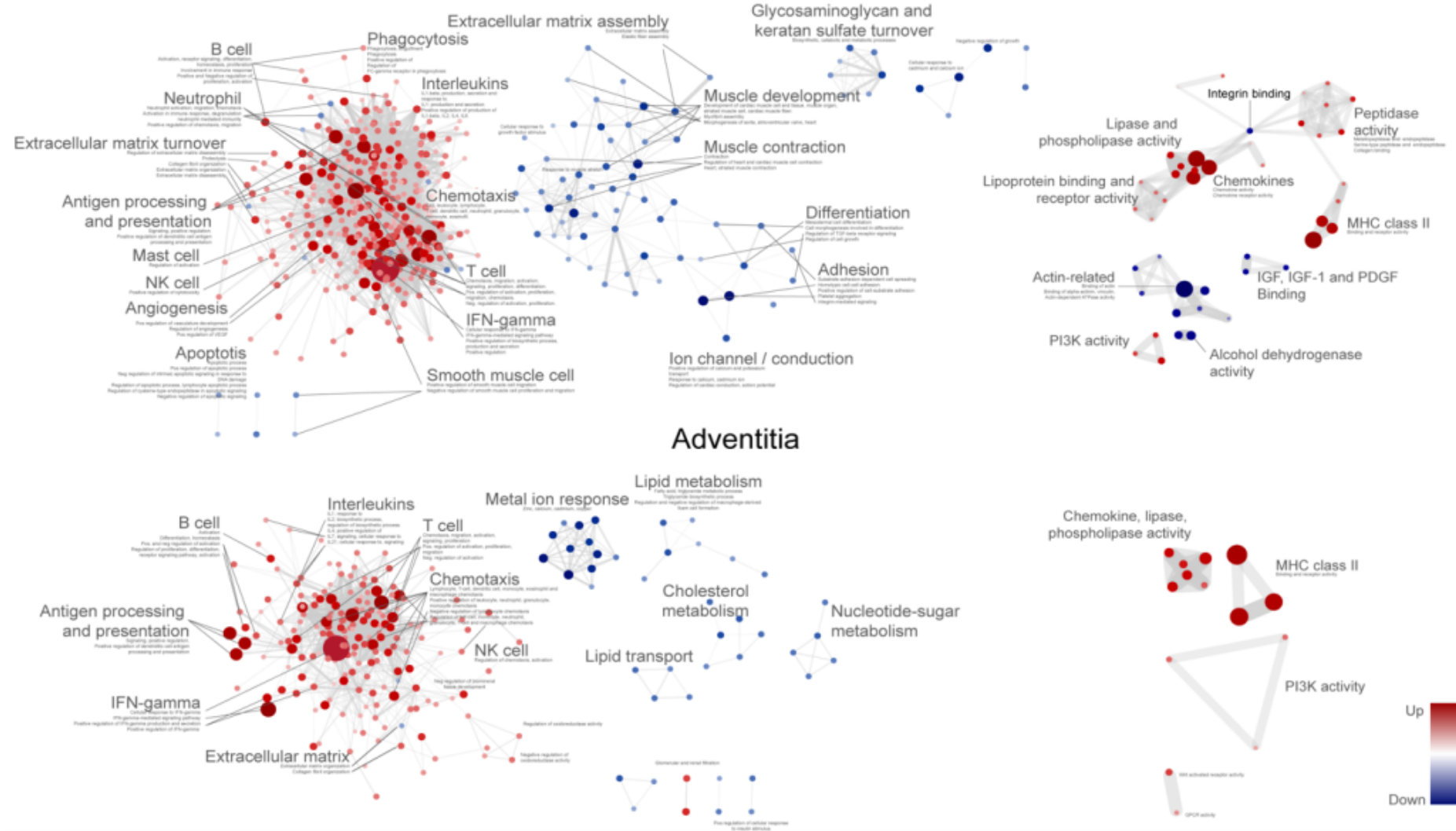








AAA vs Control



Transmural: Adaptive and Innate immunity

Media: Increased proteolysis, angiogenesis, apoptosis and Decreased muscle contraction, development, differentiation

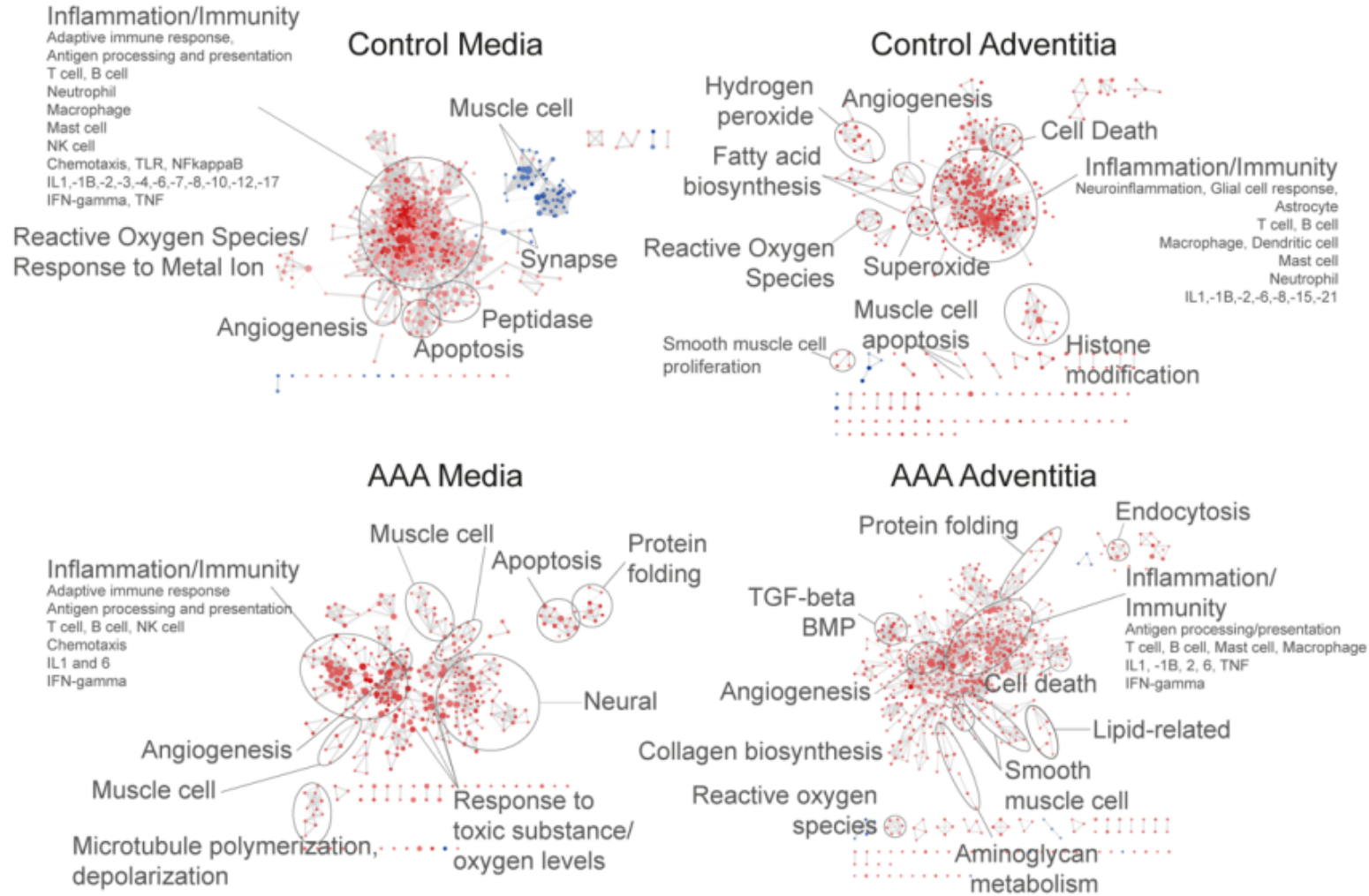
Adventitia: Decreased lipid- and metal ion response-related processes







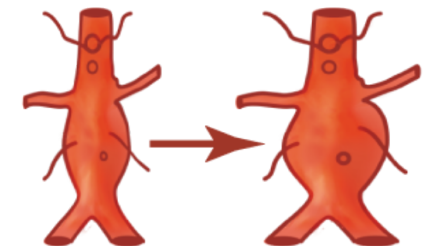
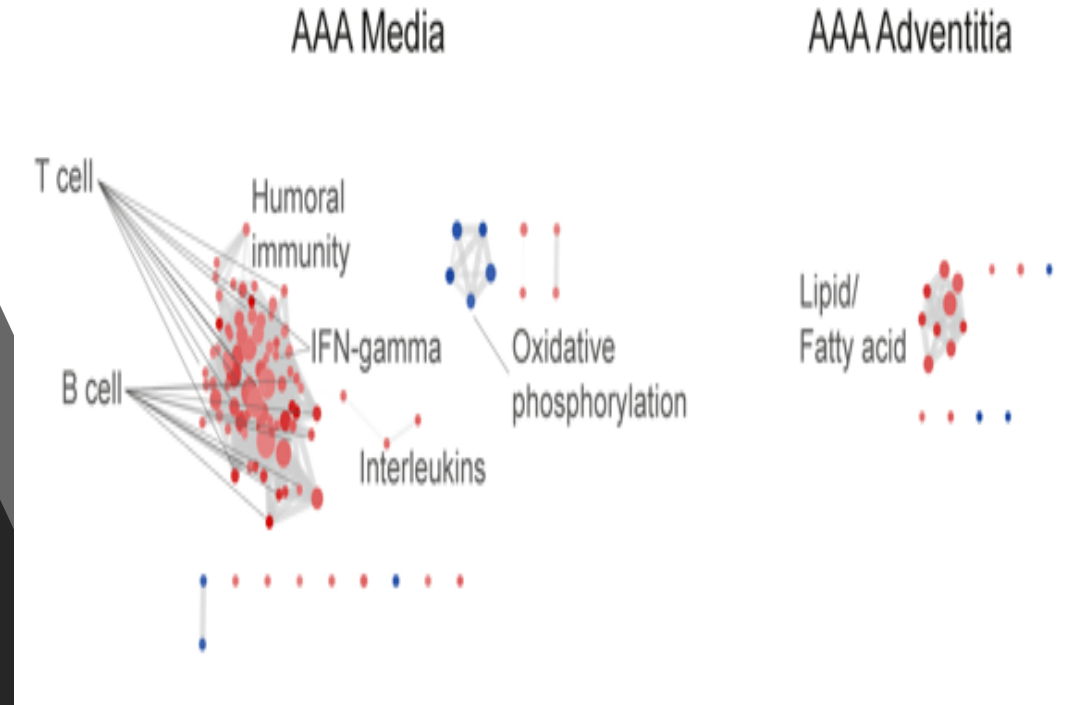
## Effect of Smoking

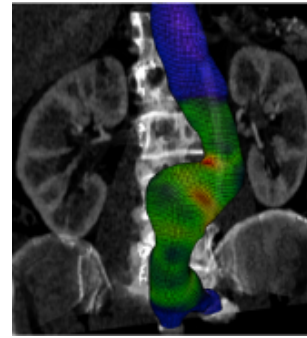


Smoking causes oxidative stress in all tissues, AAA-like transcriptome in controls and increased inflammation in AAA

# AAA Growth -24 patients

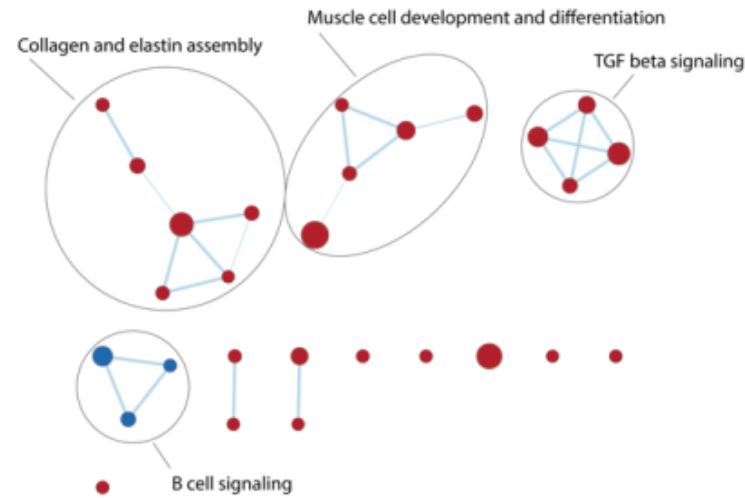
- Fast diameter growth rate correlates with adaptive immunity in Media and lipid/fatty acid in Adventitia





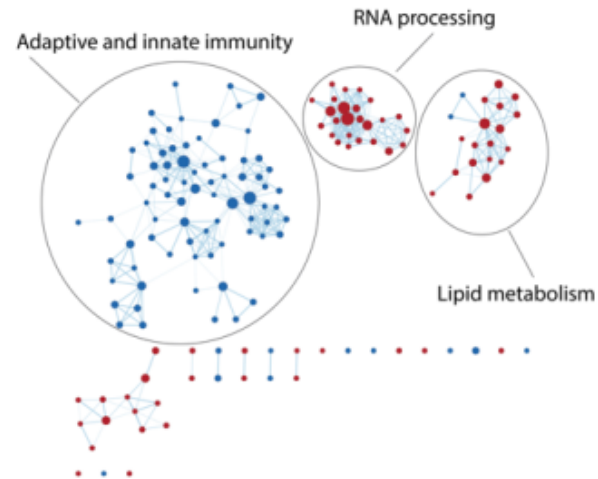
# Aortic Biomechanics

Media



Finite Element Analysis  
peak wall rupture risk  
Wall stress / Wall strength

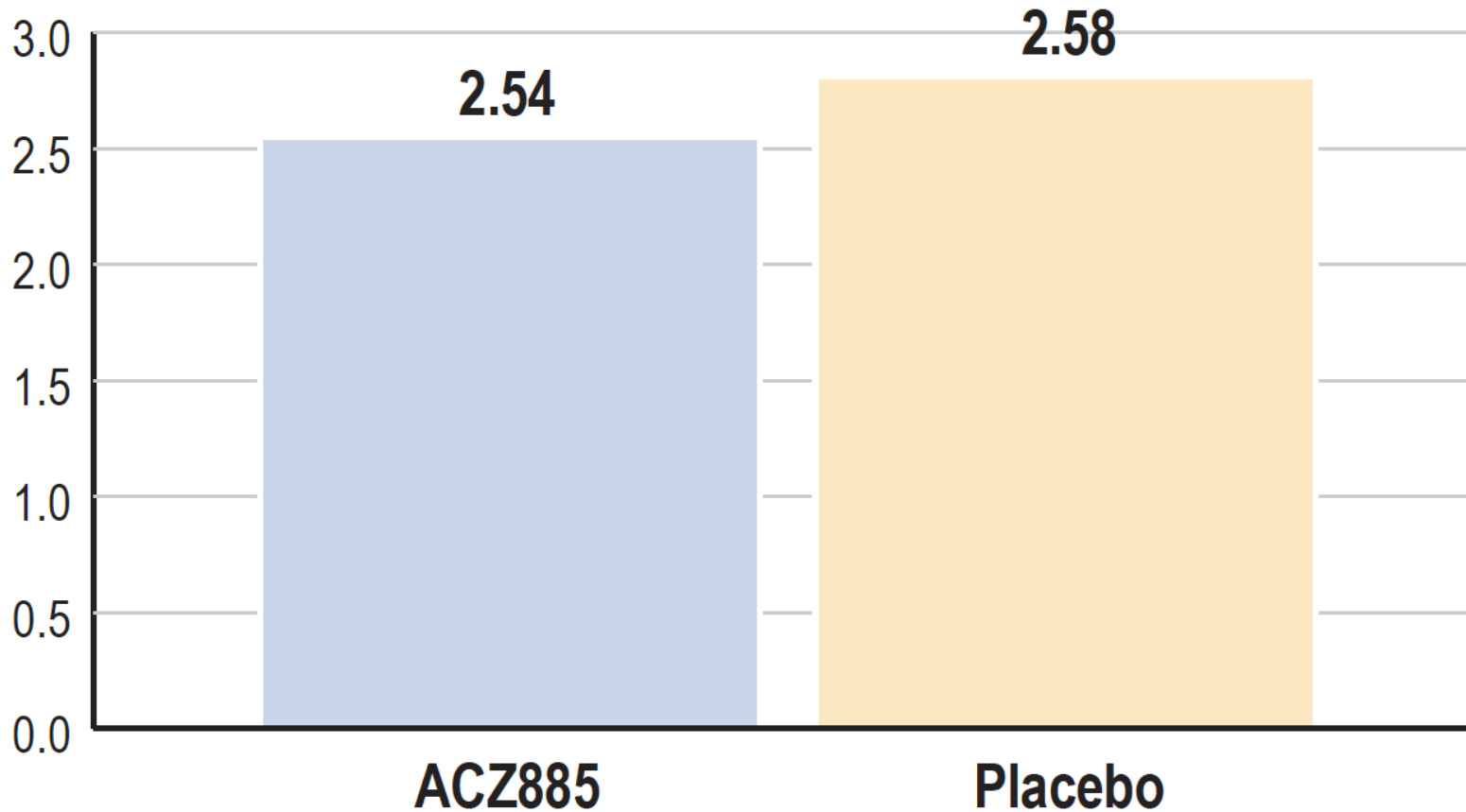
Adventitia



More significant effects on the media

## Growth Per Year of AAA After 12 Months of Treatment

Growth of abdominal  
aorta (mm/year)



Novartis study

Left renal  
vein

Stopped Early

section

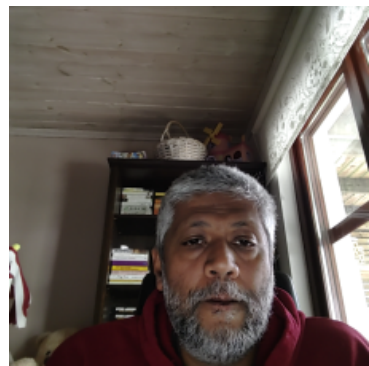
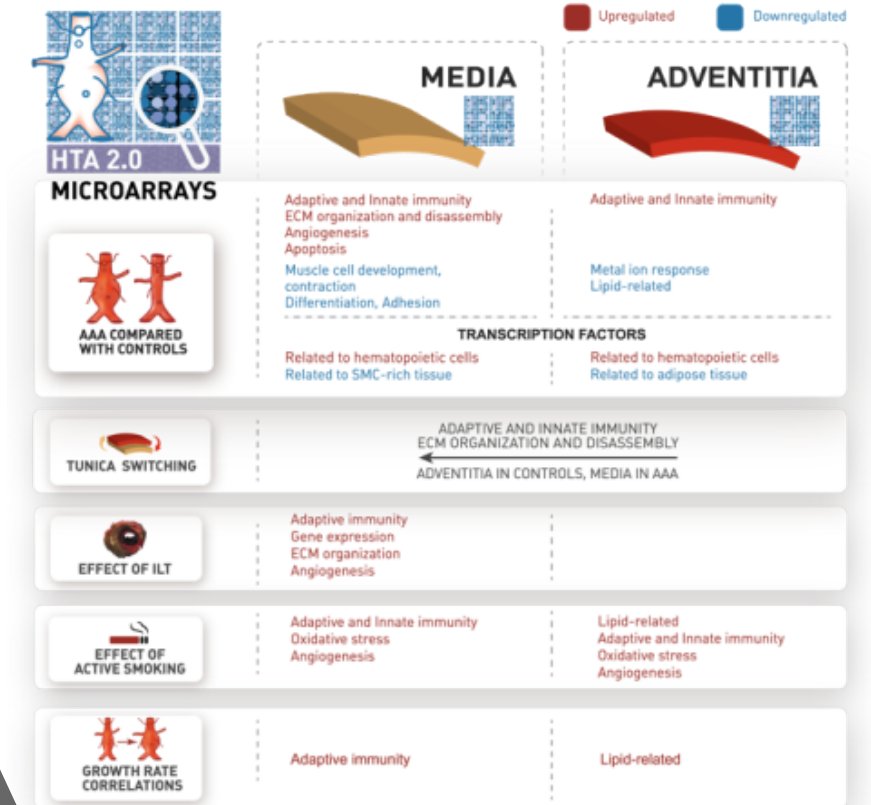
\*Drug penetration

\* Correct outcome



# Summary

- Separate Media and Adventitia analysis can give new insights
- Smoking – control aortas express “Aneurysm genes”
- Biomechanics and Gene expression





# ATVB

Arteriosclerosis, Thrombosis, and Vascular Biology



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