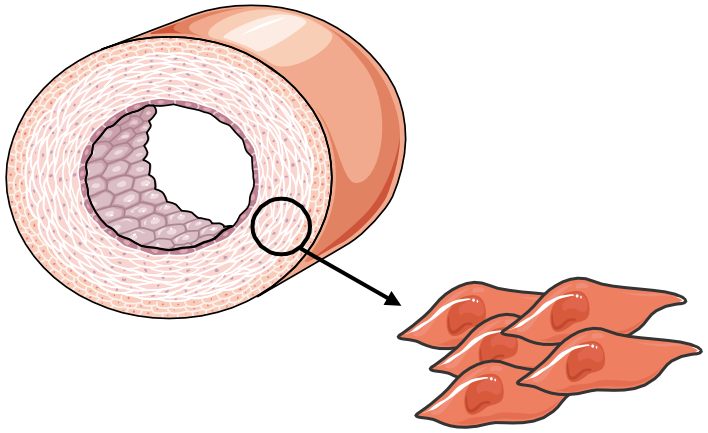
(Phospho)proteomic screen to investigate the underlying mechanism of altered *in vitro* contractility of vascular smooth muscle cells derived from abdominal aortic aneurysm patients

Karlijn Rombouts[1,2], Tara van Merrienboer[1,2], Natalija Bogunovic[1,2], Jolanda van der Velden[2], Kak Khee Yeung[1,2]
Department of Surgery, Amsterdam University Medical Centers, Amsterdam Cardiovascular Sciences, location VU medical center and AMC, Amsterdam, the Netherlands
Department of Physiology, Amsterdam University Medical Centers, Amsterdam Cardiovascular Sciences, location VU medical center, Amsterdam, the Netherlands

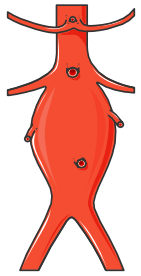
Dekkerbeurs 2019T065 Senior clinical scientist grant

Funded by Hartstichting

Smooth Muscle Cells (SMC) dysfunction plays a paramount role in AAA pathophysiology



Smooth muscle cells



Abdominal Aortic Aneurysm

- Smooth muscle cell death
- Impaired extracellular matrix production
- Loss of contraction proteins

Research aim:

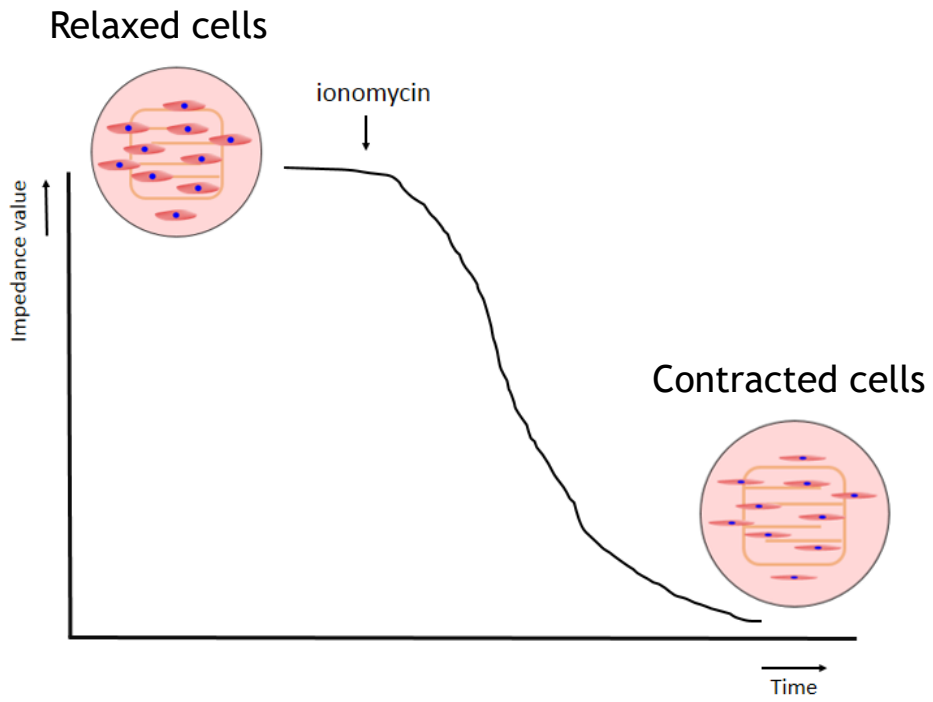
Is *in vitro* contractility affected in SMC derived from AAA patients?

What is the underlying mechanism of affected SMC contractility and how is this involved in AAA development and progression?

Figures from Servier medical ART

Measuring SMC contraction using ECIS

Electric Cell-substrate Impedance Sensing (ECIS) measures impedance value based on electrode coverage



Ionomycin stimulus (Ca^{2+} ionophore inducing influx of Ca^{2+})
→ SMC contraction → Drop in impedance value

jove

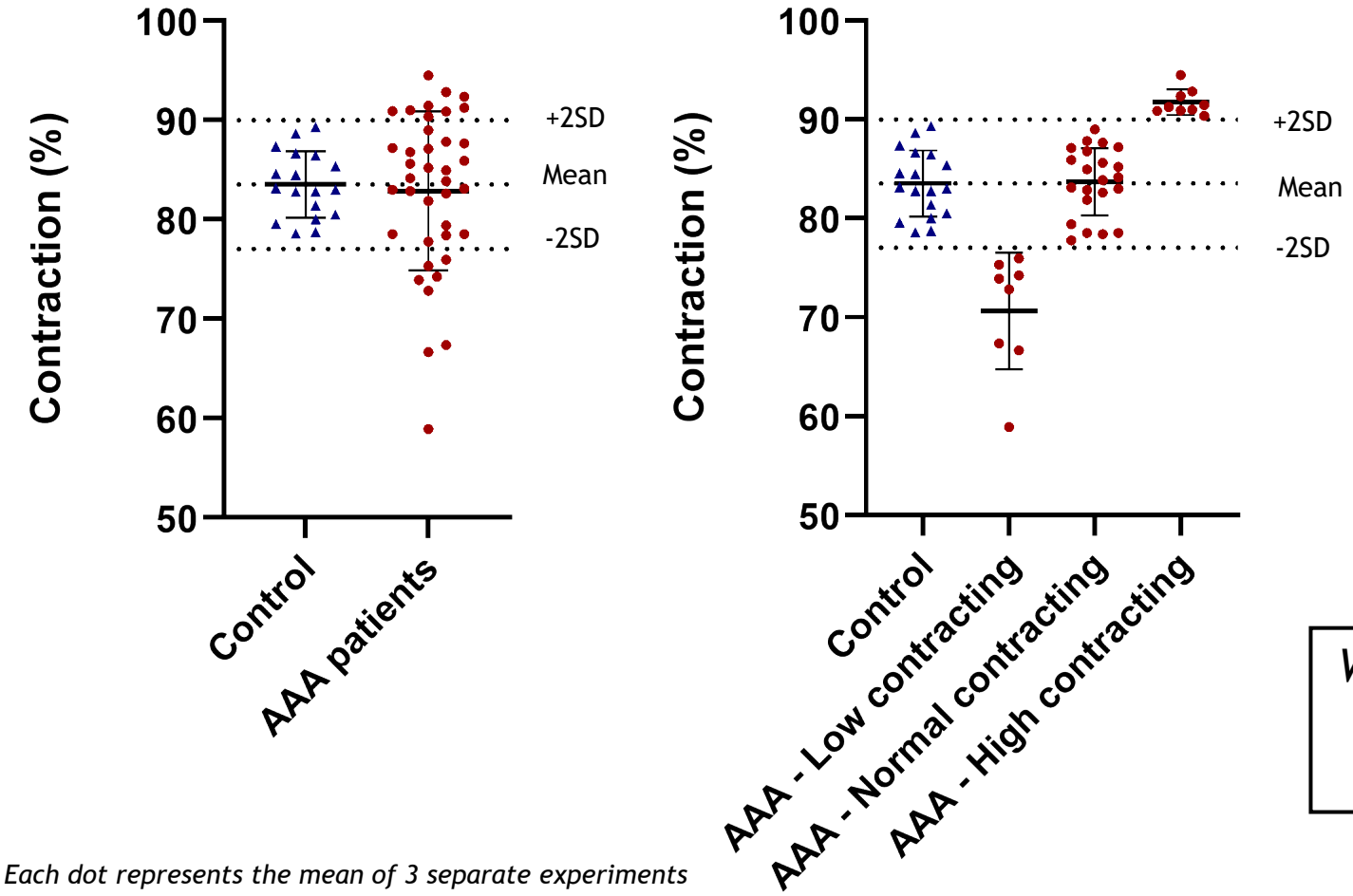
Isolation of Primary Patient-specific Aortic Smooth Muscle Cells and Semiquantitative Real-time Contraction Measurements *In Vitro*

Natalija Bogunovic[*,1,2,3], Karlijn B. Rombouts[*,1,2], Kak Khee Yeung[1,2]

[1] Department of Vascular Surgery, Amsterdam UMC, Vrije Universiteit Amsterdam [2] Department of Physiology, Amsterdam Cardiovascular Sciences, Amsterdam UMC, Vrije Universiteit Amsterdam [3] Laboratory of Experimental Cardiology, Department of Cardiology, Leiden University Medical Center

[*] These authors contributed equally

SMC contraction more variable in AAA-SMC vs. C-SMC



- AAA patients (open repair) n = 39
- Control (post mortem heart beating kidney donor, non-dilated aorta) n = 18

- No reference for normal SMC contraction: Mean controls ± 2SD

What is the underlying mechanism of affected SMC contractility and how is this involved in AAA development and progression?

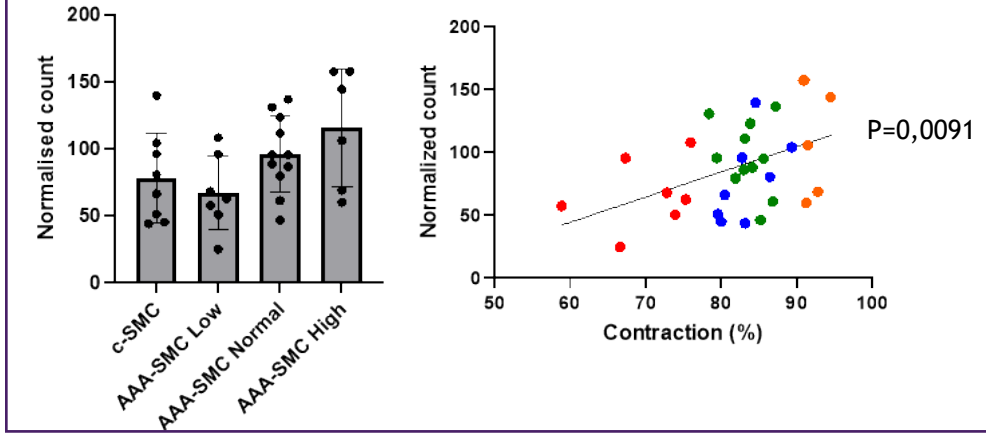
Each dot represents the mean of 3 separate experiments

Proteomics screen to find proteins and pathways that might regulate SMC contraction

Proteomics screen to find proteins and pathways that might regulate SMC contraction

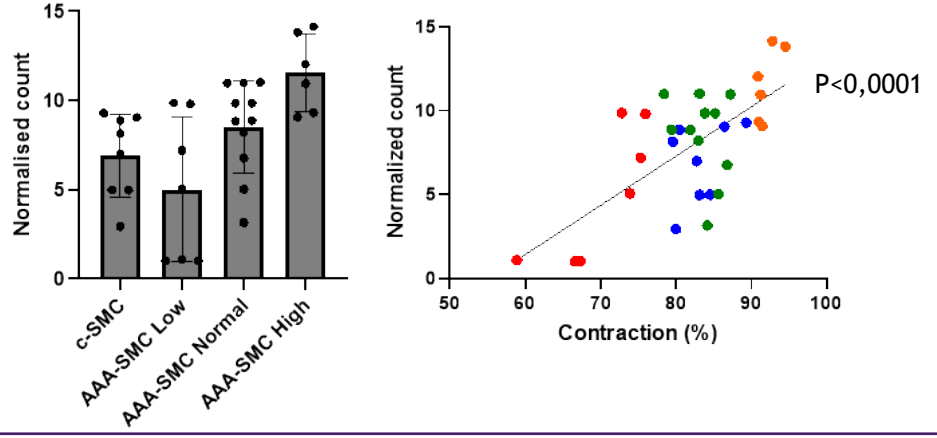
Protein A

Cell-to-cell and cell-to-matrix interactions



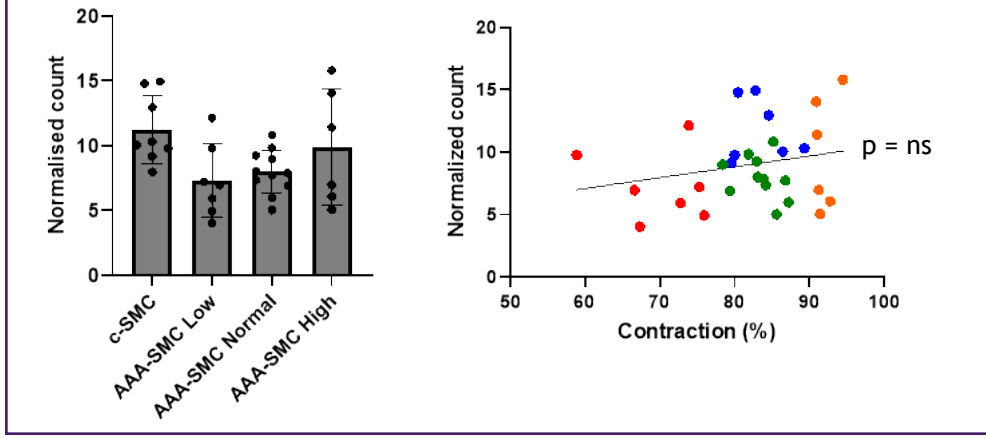
Protein B

Actin cytoskeleton organization



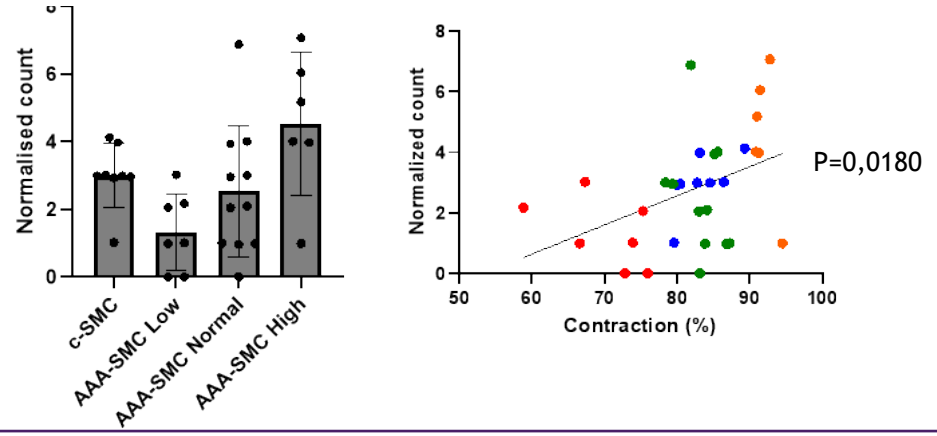
Protein C

Adds glucose monomers to glycogen molecule (energy storage)



Protein D

Intracellular calcium homeostasis



C-SMC
AAA-SMC low contracting
AAA-SMC normal contracting
AAA-SMC high contracting

Concluding remarks and future experiments

- Impaired contraction is seen in SMC derived from AAA patients compared to healthy, control SMC, and might therefore be involved in AAA development and progression.

- Can we restore or decrease the contraction of SMC?
  - *Knock down and overexpression of proteins found by proteomics screen to find the underlying mechanism of affected AAA-SMC contractility*

- We aim to find a target to development novel non-invasive treatment options for AAA patients.

Acknowledgement

- Kak Khee Yeung
- Jolanda van der Velden
- Natalija Bogunovic
- Ed Eringa
- Peter Hordijk
- Albert van Wijk
- Tara van Merrienboer
- Lan Tran

Funded by Hartstichting

Dekkerbeurs 2019T065 Senior clinical scientist grant