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ENSURE - Educating students for developing high quality research skills

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ENSURE-project

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How to make a presentation about a scientific report?

Different types of presentations

- CAT: Critically Appraised topic: *short summary of the best available evidence, created to answer a specific clinical question. A **CAT** looks like a short, rigorous version of a systematic review.*
- PICO: Problem, Intervention, Control, Outcome
- Presentation about own research work
- Posterpresentation
- Presentation about science project: pitch

PICO

RESEARCH QUESTION

- PROBLEM
- INTERVENTION
- CONTROL
- OUTCOME

GENERAL OR LOCAL ANESTHESIA AT EVAR?

- PROBLEM: MYOCARDIAL INFARCTION ANESTHESIA AT EVAR
- INTERVENTION: LOCAL
- CONTROL: GENERAL
- OUTCOME: MYOCARDIAL INFARCTION


SOURCES TO SEARCH

- PUBMED
- GOOGLE SCIENCE
- MESH TERMS

LIMITS AND DIVDING THE PAPERS


- META-ANALYSIS
- RCT
- CLINICAL TRIALS
- LIMITS: LANGUAGES, HUMAN

SEARCH


US National Library of Medicine
National Institutes of Health

PubMed

Cardiac events AND endovascular AND anesthesia

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☐ [General anaesthesia is associated with adverse cardiac outcome after endovascular aneurysm repair.](#)
1. Bakker EJ, van de Luitgaarden KM, van Lier F, Valentijn TM, Hoeks SE, Klimek M, Verhagen HJ, Stolker RJ.
Eur J Vasc Endovasc Surg. 2012 Aug;44(2):121-5. doi: 10.1016/j.ejvs.2012.04.028. Epub 2012 May 22.
PMID: 22626989 [PubMed - indexed for MEDLINE]
[Related citations](#)

☐ [Preoperative cardiac evaluation of the vascular surgery patient--an anesthesia perspective.](#)
2. Omar HR, Mangar D, Camporesi EM.
Vasc Endovascular Surg. 2012 Apr;46(3):201-11. doi: 10.1177/1538574412438950. Epub 2012 Mar 9. Review.
PMID: 22407429 [PubMed - indexed for MEDLINE]
[Related citations](#)

☐ [One year outcomes of the United States regulatory trial of the Endurant Stent Graft System.](#)
3. Makaroun MS, Tucheck M, Massop D, Henretta J, Rhee R, Buckley C, Mehta M, Ellozy S; Endurant US Pivotal Trial Investigators.
J Vasc Surg. 2011 Sep;54(3):601-8. doi: 10.1016/j.jvs.2011.03.002.
PMID: 21890702 [PubMed - indexed for MEDLINE]



Contents lists available at SciVerse ScienceDirect

European Journal of Vascular and Endovascular Surgery

journal homepage: www.ejves.com



General Anaesthesia is Associated with Adverse Cardiac Outcome after Endovascular Aneurysm Repair

E.J. Bakker^{a,b}, K.M. van de Luitgaarden^a, F. van Lier^b, T.M. Valentijn^b, S.E. Hoeks^b, M. Klimek^b, H.J.M. Verhagen^{a,*}, R.J. Stolker^b

^a Department of Vascular Surgery, Erasmus Medical Center, Rotterdam, The Netherlands

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- 302 patients infrarenal EVAR
- 2002-2011
- Erasmus MC Rotterdam
- Retrospective cohort study
- Exclusion: acute and hybrid procedures

Material and methods

- Baseline Characteristics
- All had anticoagulant therapy
- Start Heparine or LMWH per case
- Profylac LMWH >12u preoperatief
- Anesthesia type: decide by the anesthesiologist or surgeon, patient → general or locoregional anesthesia
- Endpoint: cardiac events
- Secondary endpoints: other complications, length of stay

Material and methods

- Cardiac measurements
 - ECG and trop-T pre-op, postop 1,3 7.
- Endpoint: 30- days cardiac events:
- Troponine-T elevation

Statistics

- Dichotome: percentages, chi-2
- Continue variables: mean \pm SD \rightarrow ANOVA or Mann-Whitney U – test
- Univariable and multivariable logistic regression model \rightarrow for confounding factors and for associations of cardiac events and type of anesthesia
- The Revised Cardiac Risk score and propensity score were co-variables in model.
- $P < .05$ = significant

Revised Cardiac Risk Index
1. History of ischemic heart disease
2. History of congestive heart failure
3. History of cerebrovascular disease (stroke or transient ischemic attack)
4. History of diabetes requiring preoperative insulin use
5. Chronic kidney disease (creatinine > 2 mg/dL)
6. Undergoing suprainguinal vascular, intraperitoneal, or intrathoracic surgery
Risk for cardiac death, nonfatal myocardial infarction, and nonfatal cardiac arrest: 0 predictors = 0.4%, 1 predictor = 1%, 2 predictors = 2.4%, ≥ 3 predictors = 5.4%

Results

Table 1

Baseline characteristics according to anaesthesia type.

	General (n = 173)	Locoregional (n = 129)	P-value
Demographics			
Mean age (SD)	72 (8)	72 (8)	.75
Male gender (%)	155 (90)	120 (93)	.42
Medical history (%)			
Congestive heart failure	16 (9)	21 (16)	.08
Cerebrovascular disease	28 (16)	15 (12)	.32
Hypertension	122 (71)	75 (58)	.03
Hypercholesterolaemia	162 (94)	112 (87)	.05
Diabetes mellitus	44 (25)	22 (17)	.09
Current smoking	77 (45)	52 (40)	.48
Serum creatinin >2 mg/dL	25 (15)	26 (20)	.22
Ischaemic heart disease	74 (43)	64 (50)	.25
Aortic valve stenosis	6 (4)	3 (3)	.74
COPD	81 (47)	51 (41)	.29
BMI > 30	41 (24)	12 (9)	<.01
Risk indices (SD)			
Revised cardiac risk index	1.9 (1.0)	2.0 (1.0)	.25
ASA class	2.5 (.6)	2.5 (.5)	.59
Medication use (%)			
Anticoagulants	29 (17)	17 (13)	.42
Continuated perioperatively	12 (7)	3 (2)	.11
Aspirin	125 (73)	63 (49)	<.01
Clopidogrel	11 (6)	6 (5)	.62

Abbreviations: SD standard deviation; LVEF left ventricular ejection fraction; COPD chronic obstructive pulmonary disease; BMI body mass index.

- 57% general
- 43% locoregional: 26% epidural en 17% local
- INR >1.8 or therapeutic heparin: 7% vs. 2% (p=0.011)

Results

- Length of stay general vs. locoregional:
 - 3 (2-4) vs. 2 (2-4) days ($p < 0.01$)
- 4 pt (1.3%) died in the general anesthesia group
- 29 pt (9.6%) cardiac event

Results

Table 2
30-day cardiac complications.

	General (<i>n</i> = 173)	Locoregional (<i>n</i> = 129)	<i>P</i> -value
	<i>n</i> (%)	<i>n</i> (%)	
Cardiac events			
Cardiac death	2 (1.2)	0 (0)	.51
Myocardial infarction	6 (3.4)	1 (.8)	.25
Congestive heart failure	2 (1.2)	0 (0)	.51
Arrhythmia	1 (.6)	0 (0)	1.00
Troponin release	12 (6.9)	5 (3.9)	.32
Composite cardiac endpoints			
All cardiac events	23 (13.3)	6 (4.7)	.02
All but troponin release	11 (6.4)	1 (.8)	.02

General versus locoregional: higher risk:

- 30 days cardiac events: OR: 3.8 (CI:1.1-12.9;p=0.03)
- Major cardiac events: OR 13.3; CI 1.2-141.8, p=0.03)

Table 3
30-day major non-cardiac complications.

	General (n = 173)	Locoregional (n = 129)	P-value
	n (%)	n (%)	
Non-cardiac complication			
Non-cardiac complications	22	17	
Patients with ≥ 1 complication	20 (11.6)	15 (11.6)	1.00
Mortality			
All-cause	4 (2.3)	0 (0)	.14
Non-cardiac	2 (1.2)	0 (0)	
Pulmonary			
Any pulmonary complication	5 (2.9)	0 (0)	.07
Pneumonia	3 (1.7)	0 (0)	
Aspiration	1 (.6)	0 (0)	
Pneumothorax	1 (.6)	0 (0)	
Renal			
Renal failure requiring intervention	4 (2.3)	0 (0)	.14
Surgical			
Additional surgical procedure required	5 (2.9)	9 (7.0)	.11
Intervention for endoleak	0 (0)	4 (3.1)	
Access site bleeding	2 (1.2)	4 (3.1)	
Arterial embolism	3 (1.7)	1 (.8)	
Other			
Urinary tract infection	2 (1.2)	2 (1.6)	
Access site infection	1 (.6)	2 (1.6)	
Urine retention	4 (2.3)	2 (1.6)	
Sepsis	1 (.6)	1 (.8)	
GI bleeding	0 (0)	1 (.8)	
Stroke / TIA	0 (0)	0 (0)	
Venous thrombo-embolism	0 (0)	0 (0)	

Abbreviations: GI gastro-intestinal; TIA transient ischaemic attack.

2 patients died due to
Pulmonal problems

Problems of this article?

- Retrospective
- Intention to treat
- Patient selection
- Bias

LEVEL OF EVIDENCE

Grade	Recommendation
A	Based on the criterion of at least one randomised, controlled clinical trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation.
B	Based on well-conducted clinical studies but no good-quality randomised clinical trials on the topic of recommendation.
C	Based on evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. (i.e., no applicable studies of good quality)

GUIDELINES ARE ALSO BASED ON THIS SCORE

Presentation about own research work

- What is the key message?
- How much time to present?
- Disclosures
- Introduction to the problem
- Aim and hypothesis
- Methods
- Results
- Conclusion/ key message

HOW CELLS CAN PREDICT AORTIC ANEURYSM GROWTH RATE AND RUPTURE

Kakkhee Yeung, MD, PhD

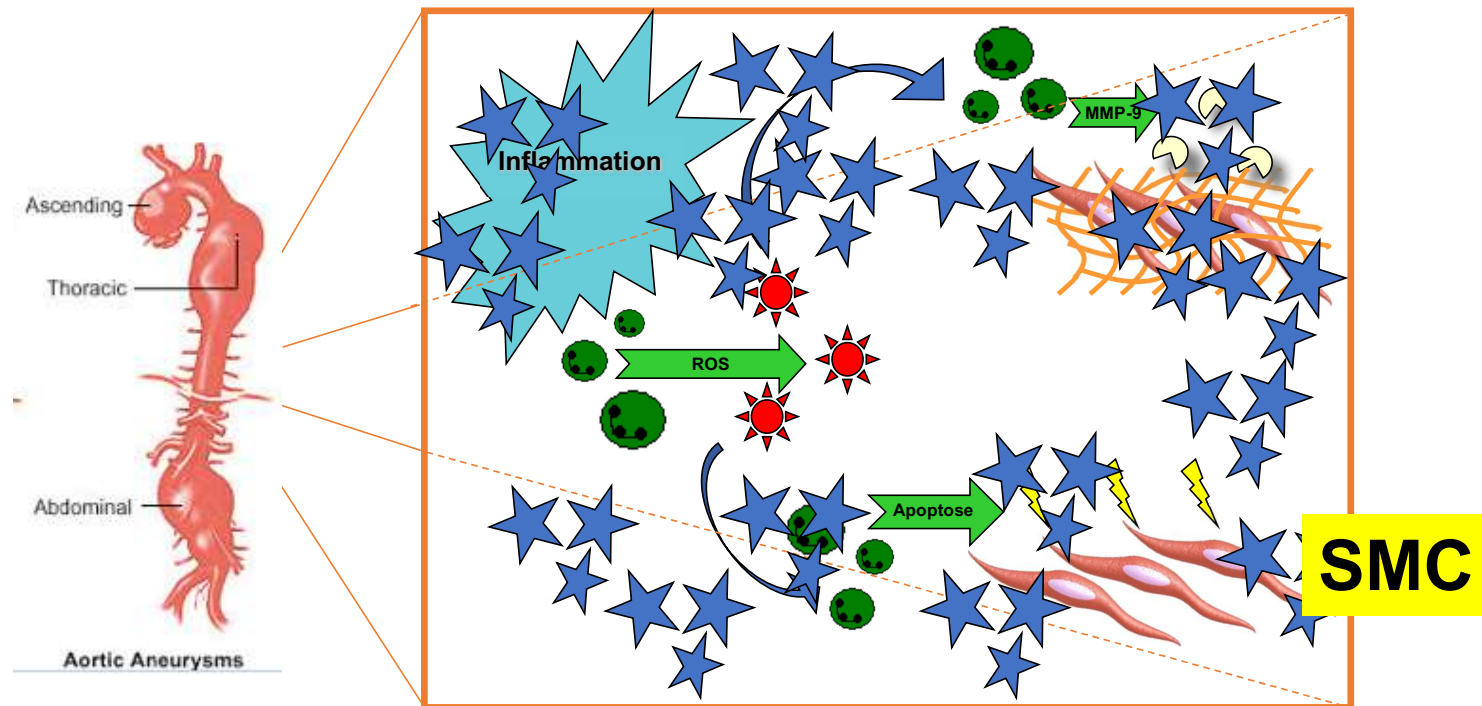
NATALIJA BOGUNOVIC, DIMITRA MICHA, PETER HORDIJK, WILLEM WISSELINK, JAN BLANKENSTEIJN

Amsterdam UMC, AMSTERDAM, THE NETHERLANDS

DISCLOSURES

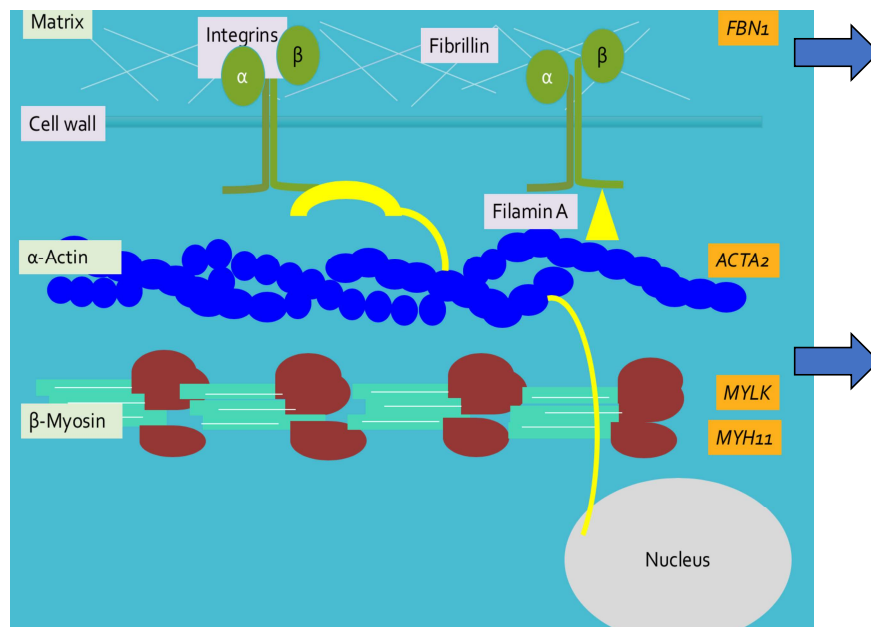
- National funding: ICAR-AIO grant
- Dekker Senior Clinical Scientist, Dutch Heart Foundation

PATHOPHYSIOLOGY OF AORTIC ANEURYSMS: KEY ROLE FOR SMOOTH MUSCLE CELLS



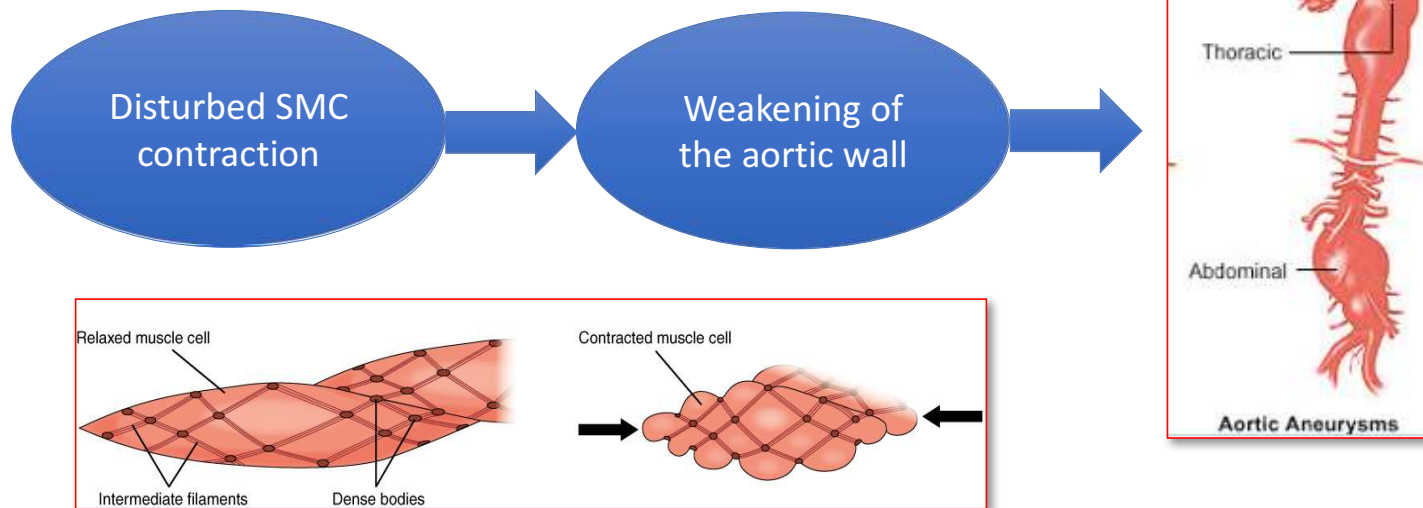
GENETIC MUTATIONS INVOLVING SMC

- Mutations in genes of the mechano-transduction complex: smooth muscle cells + environment



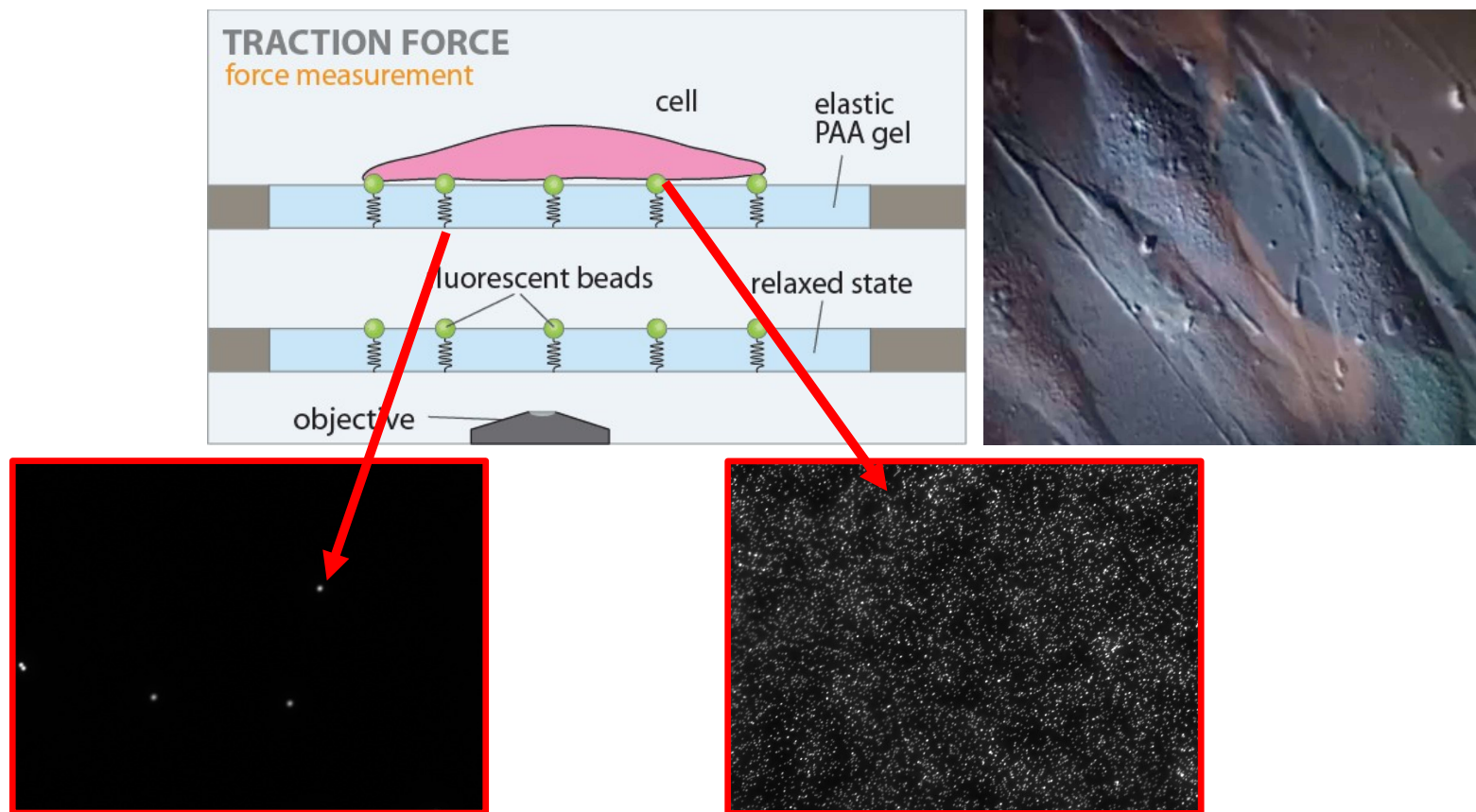
20% Familial thoracic aneurysms

SMOOTH MUSCLE CELLS HAVE A KEY ROLE IN AORTIC ANEURYSM DEVELOPMENT

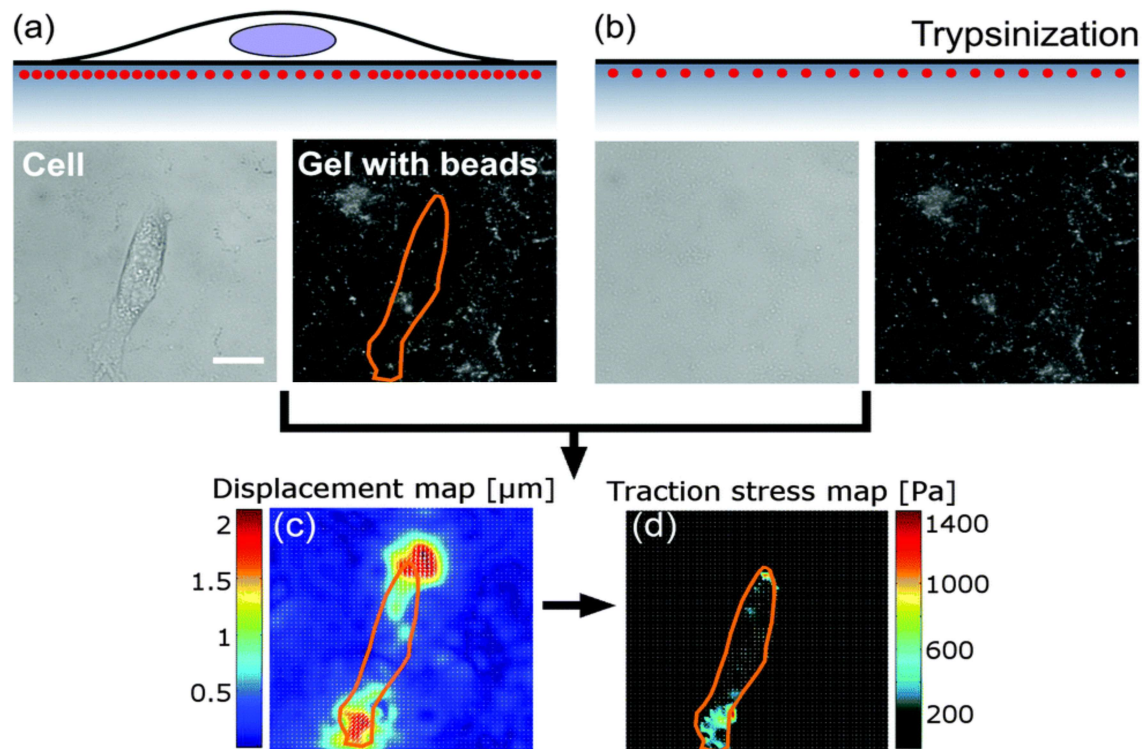


DEVELOPED METHODS TO
STUDY SMC CONTRACTION

TRACTION FORCE MICROSCOPY



TRACTION FORCE MICROSCOPY OUTPUT

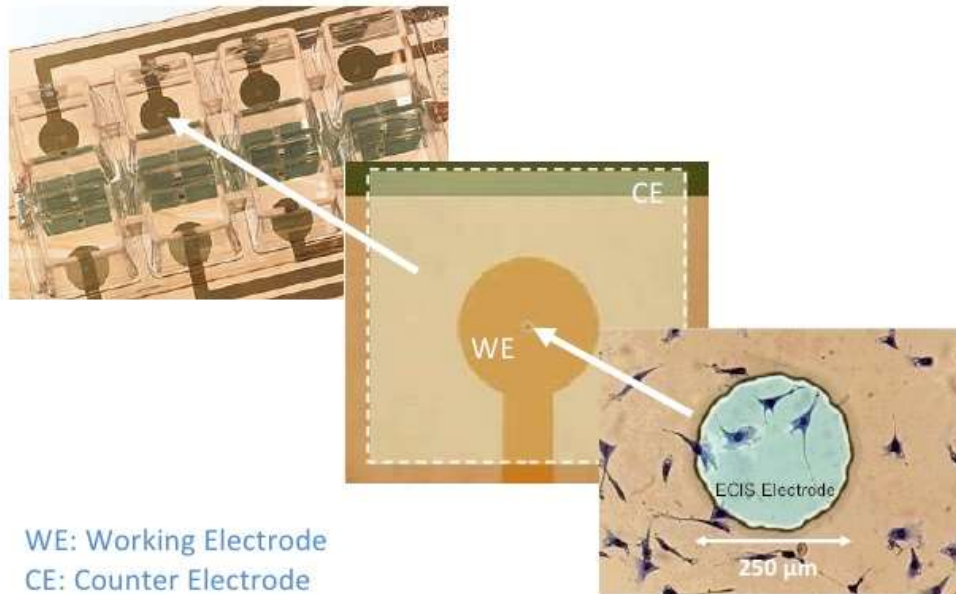


ECIS

electric cell-substrate impedance sensor

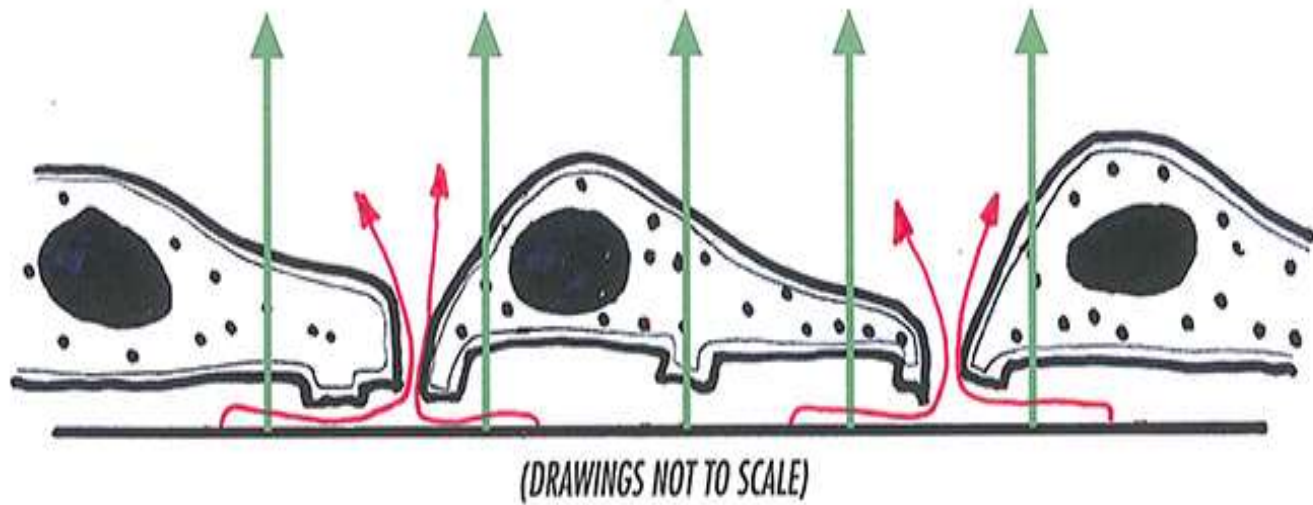


The ECIS Electrodes



WE: Working Electrode
CE: Counter Electrode

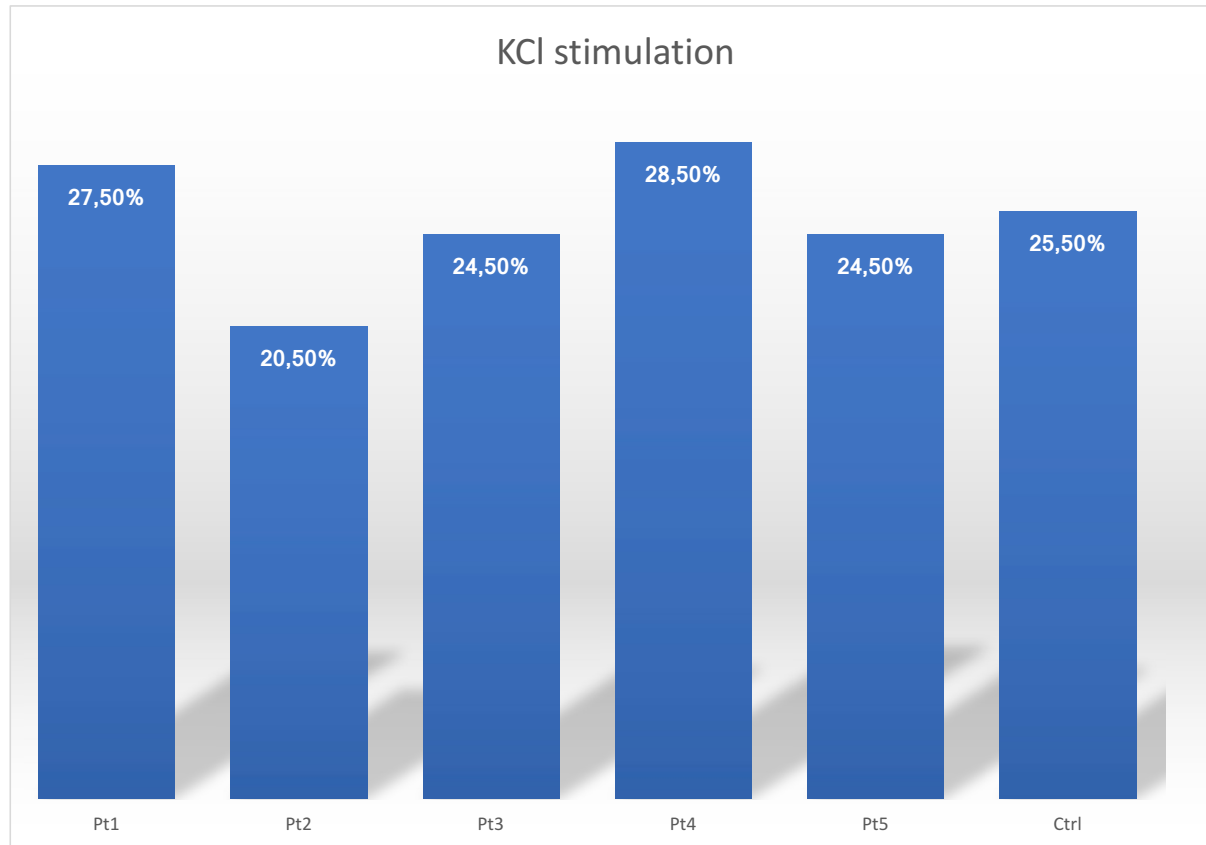
Resistance of a cell monolayer



PILOT STUDY

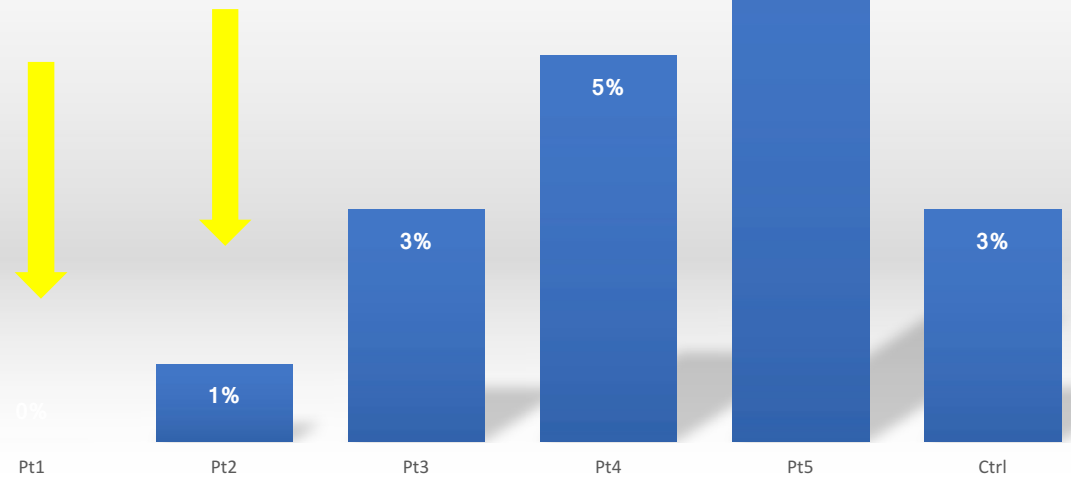
Patient #	Clinical presentation	ASA classification	Aneurysm type	Aneurysm size (mm)	Aneurysm growth	Medication
1	70 yo male with abdominal and back pain	5	rAAA, pararenal	55	--	Ascal, statin
2	75 yo male with abdominal pain extending to the perineum	4	sAAA, juxtarenal	86	6mm in 3 months	Ascal, statin
3	64 yo male, incidental finding	1	asymptomatic AAA, juxtarenal	63	--	Ascal, statin
4	75 yo male, incidental finding	3	asymptomatic AAA, juxtarenal	59	24mm in 8 years	Ascal, statin, lisinopril, metoprolol, hydrochloorthiazide, amlodipine, pantozol
5	68 yo male	3	asymptomatic AAA, infrarenal	57	--	Ascal, statin
6	63 yo male	1	commercial available cells	-	-	-

SMC WERE CONTRACTILE



Noradrenaline stimulation

Ruptured and symptomatic AA
less contractile

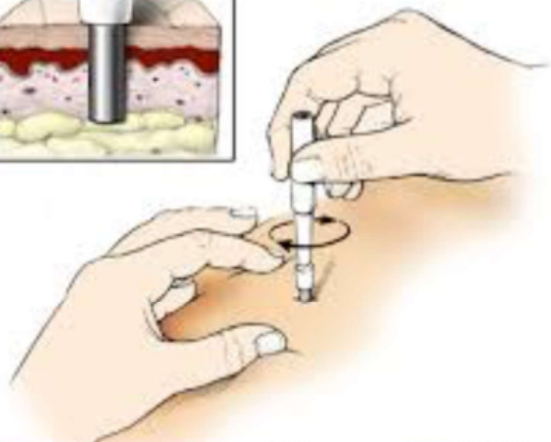
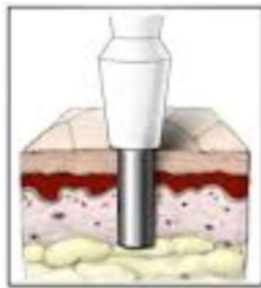


SMOOTH MUSCLE CELLS NEEDED

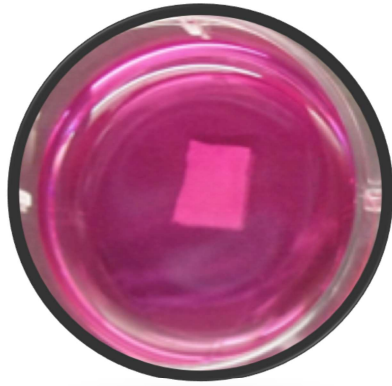
- Research on mutations only possible in smooth muscle like cells
 - Aortic Biopsy: invasive and expensive
 - Through stem cells: expensive and slow

Transdifferentiation of Human Dermal Fibroblasts to Smooth Muscle-Like Cells to Study the Effect of *MYH11* and *ACTA2* Mutations in Aortic Aneurysms

Kak K. Yeung,^{1,2*} Natalija Bogunovic,^{1,2} Niels Keekstra,¹ Adriaan A. M. Beunders,¹ Jorrit Pals,³ Kim van der Kuij,³ Eline Overwater,³ Willem Wisselink,¹ Jan D. Blankensteijn,¹ Victor W.M. van Hinsbergh,² Rene J.P. Musters,² Gerard Pals,³ Dimitra Micha,^{3*†} and Behrouz Zandieh-Doulabi^{4†}

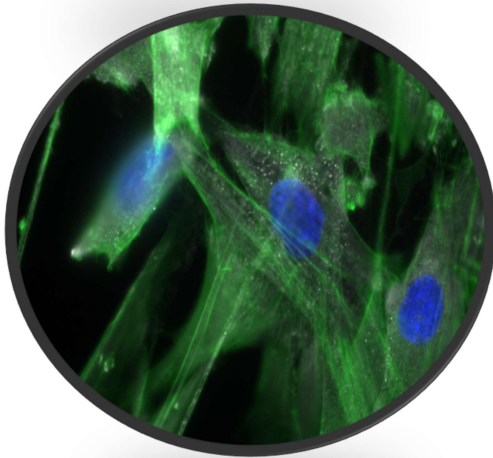


Smooth muscle cells



+5 ng/mL TGF β

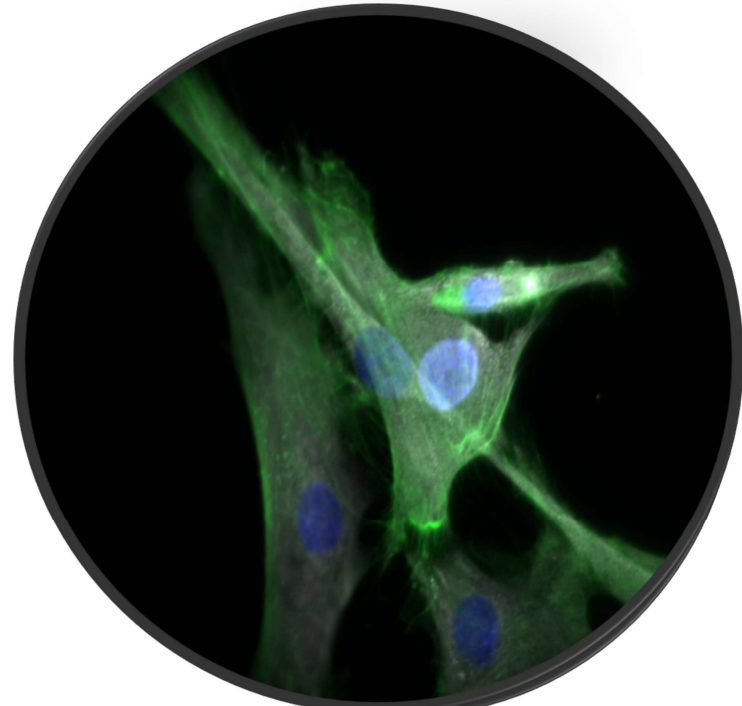
2 weeks



Primary SMC

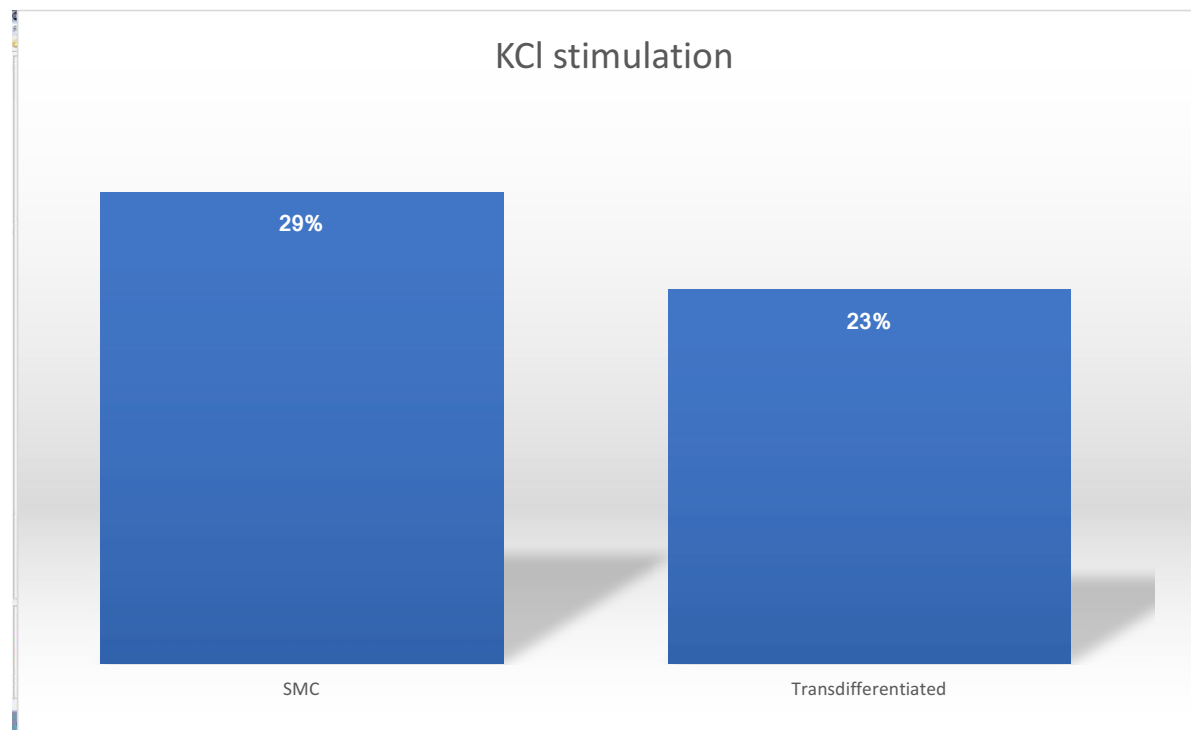


Calponine

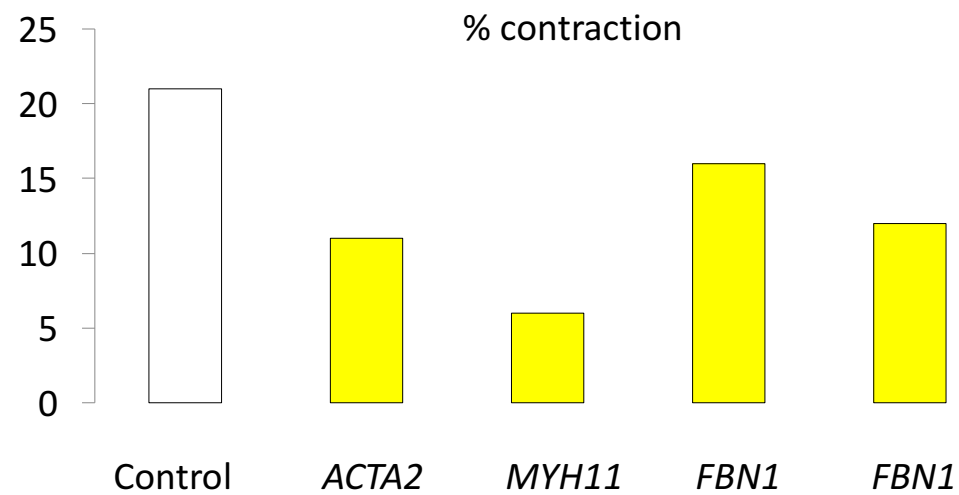
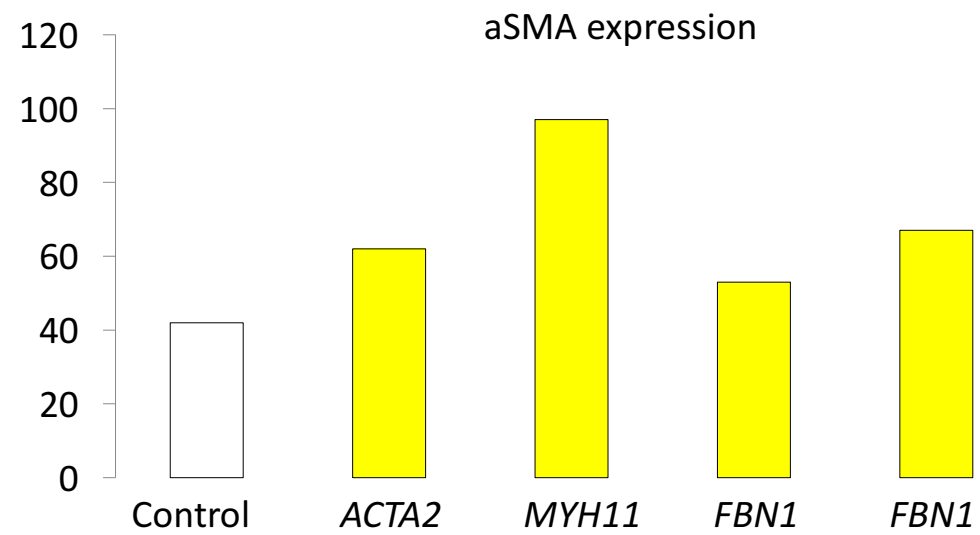


transdifferentiated SMC

Do the transdifferentiated SMC from the skin biopsy contract the same?



Pt.2 symptomatic AAA SMC (black) and transdifferentiated (pink)



CONCLUSION

- Our preliminary results show that a disturbed contraction of SMC has a key role in aortic aneurysm development
- SMC can be made of skin biopsies with nearly similar contraction of SMC of the aorta
- SMC from ruptured or symptomatic aneurysms have lower contraction forces
- Smooth muscle cells are a new focus for medical therapy

POSTER PRESENTATION

- Short introduction
- Problem
- Methods
- Key results by depictive figures
- Conclusion

Transdifferentiation of Dermal Fibroblasts to Smooth Muscle Like Cells: A New Method to Study the Contractile Forces in the Aortic Aneurysm

K.K. Yeung, N. Bogunovic, R.J.P. Musters, D. Micha, G. Pals, W. Wisselink, J.D. Blankensteijn, B. Zandieh-Doulabi
VU University Medical Center, Amsterdam, the Netherlands

contact: k.yeung@vumc.nl

BACKGROUND

Research on the pathogenesis of aortic aneurysms has revealed mutations in proteins of the extracellular matrix and deficient in smooth muscle cell (SMC) proteins as key underlying mechanisms. Mutations associated with familial aortic aneurysms have been found in *MYH11* (myosin heavy chain 11), *ACTA2* (smooth muscle actin alpha 2) and *MYLK* (myosin light chain kinase), which are proteins that are integral parts of the contractile apparatus of aortic SMC (Fig 1). Currently, SMC can only be obtained with an invasive aortic biopsy and thus, a different method would be preferable to investigate SMC function and their mutations.

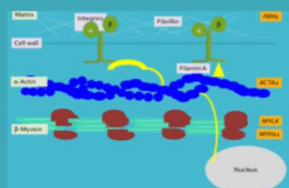


Fig 1.
The mechano-transduction complex

AIM

To transdifferentiate dermal fibroblasts into SMC to investigate contraction and pathogenic variations

METHODS

Harvesting of dermal fibroblasts of 7 healthy donors and 7 aortic aneurysm patients with *MYH11* or *ACTA2* mutation.

Transdifferentiation:
Cell culture of dermal fibroblasts → 14 days seeded on matrigel with HAMF10 nutrient mix with horse serum (HS) and 5 ng/mL TGFβ.



Fig 2. Contraction of matrigel

- qPCR on RNA and western blot of αSMA, smoothelin, calponin, SM22
- Imaging of SMC markers + cytoskeleton
- Contraction assay and traction force microscopy
- Splice site prediction

RESULTS



Fig 3. αSMA expression after 14 days transdifferentiation with and without TGFβ. Dark bars=healthy donors; Light bars=aneurysm.



Fig 5. Splice error in transdifferentiated SMC of *MYH11*, shown by a double band on agarose gel electrophoresis.

Fig 4. αSMA (green): note the similar morphology of the primary aortic SMC and the transdifferentiated SMC. No αSMA in the control cells.

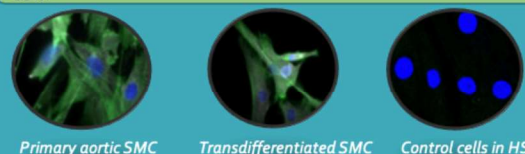
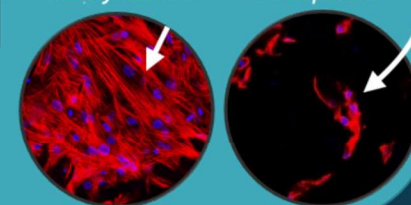


Fig 6. Example of SMC traction force microscopy

Note the disturbed actin filaments

F-actin cytoskeleton

Healthy volunteer MYH11 patient



CONCLUSION

Direct conversion of human dermal fibroblasts into SMC-like cells is a highly efficient method to investigate the pathogenic effect of a (splice) variant in proteins of the SMC contractile apparatus. Our findings suggest a disturbed contraction of SMC in aortic aneurysm formation caused by a defective F-actin cytoskeleton.

Presentation about science project – 3 min PITCH

- Problem + impact → Why?
- What are you going to do about it?
- How are you going to do it?
- Expected results

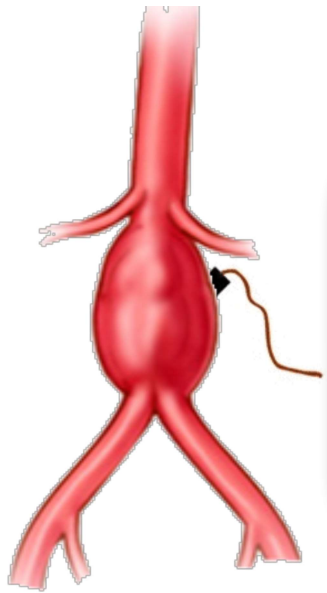


THE KEY ROLE OF SMOOTH MUSCLE CELL FUNCTION IN AORTIC ANEURYSMS



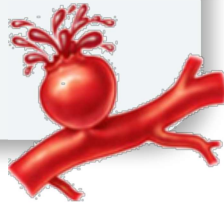
Kak Khee Yeung, MD, PhD, FEBVS
Vaatchirurg
Amsterdam UMC

Aortic aneurysms: unsolved problem



90%

Mortality rate after
rupture



2-8% of population > 65 jr

60%

Do not reach the hospital

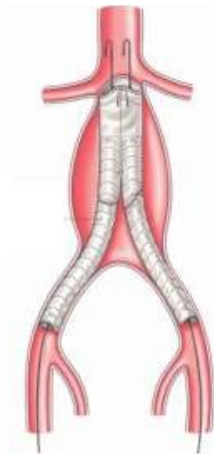
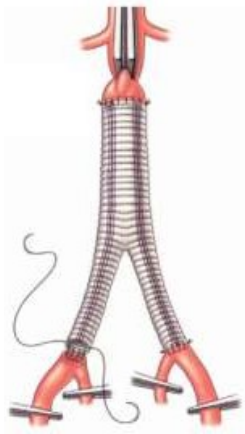


50%

Will only survive surgery

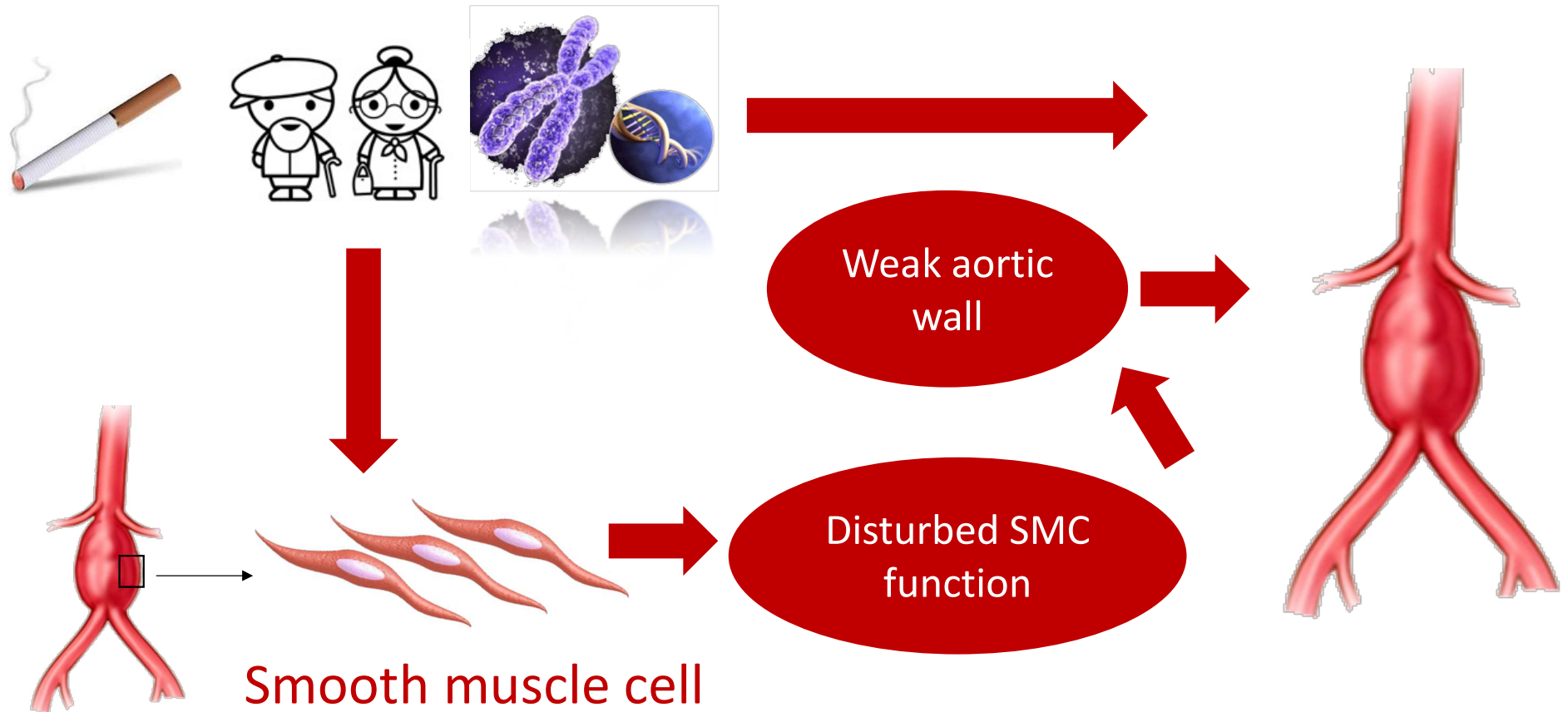


**Current treatment = symptomatic
Surgery**



**Prevention, better selection
Pharmacological treatment**

Hypothesis

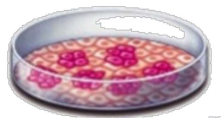
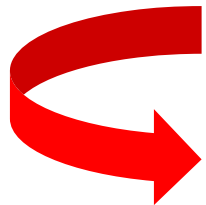


Expected results & impact

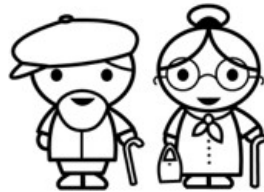
Dekker Fellowship Clinical Scientist



Molecular pathways



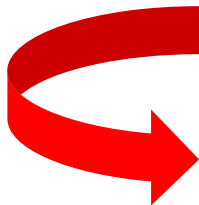
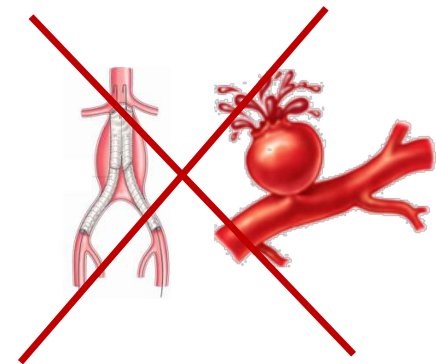
New in-vitro aneurysm models



Better selection of high risk patients



New targets



Pathophysiology of other cardiovascular diseases

Workshop

CAT or PICO

- Problem
- Search on the pubmed
- References 30-40
- Introduction/background
- Hypothesis
- Aim
- Method
- Expected results
- 3 pgs
- Figures

3min pitch about a big project

- Problem to get attention
- Your aim
- What are you going to do
- What to expect

Or present your own work by presentation or poster