UPDATE ON PREDICTING AAA GROWTH RATES AND RUPTURE RISK FROM SMOOTH MUSCLE CELL BEHAVIOR

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PROBLEM

- Still not able to predict Rupture or Growth rates of Aneurysms and Dissections
- Endovascular repair → 30% reintervention rates
- Are we able to select patients for treatment?
- Do we get to a medical treatment?

New insights from cell specific analysis

AORTIC WALL STRUCTURE

VASCULAR SMOOTH MUSCLE CELLS (SMC)

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

- Disturbed SMC function
- Weakening of the aortic wall

LIVE PATIENT SPECIFIC SMC CELL LINES

Open aneurysm repair

Aortic biopsy → Tissue explant protocol → Patient specific SMC

STUDIES ON SMC BEHAVIOR AND AAA BEHAVIOR PREDICTION

1. Study of SMC function: Contraction of SMC
2. Cell-specific DNA or RNA analysis → Finding new mutations
3. Building a patient cell specific Bio-engineered scaffold to study the interaction of SMC with EC and production of ECM
4. Cell-specific wall strength of live aortic tissue

1. CONTRACTION OF SMC

- Graph showing contraction (%) of Smooth Muscle Cells (SMC), Smooth Muscle Tissue (SMT), and Aorta (Ao)
11/14/2018

LOW CONTRACTION IS CORRELATED WITH HIGHER AAA GROWTH RATE

\[ R^2 = 0.719, \ p = 0.045 \]

In 3 of 7 patients pathogenicity confirmed!

2. FINDING NEW MUTATIONS

1 x ‘splice error’ and 2x amino acid change were shown

3. STUDY OF SMC AND ECM IN 3D BIO-ENGINEERED VESSEL

Lower contraction in SMC with genetic variant

Cell growth degrades the scaffold, leading to the production of an original extracellular matrix

3. BIO-ENGINEERED VESSEL: ANISOTROPY

A parameter of order in the system

More straight matrix and not a network of ECM in AAA patients

4. NANOIDENTATION:

Cell and aortic wall specific strength
CONCLUSION

- Our preliminary results show that a disturbed function: contraction and ECM production of SMC have a key role in aortic aneurysm development.
- SMC can be made of skin biopsies.
- Our new cell specific analysis can lead to discovery of new mutations.
- Our bio-engineered vessel scaffolds can be used to study SMC function and the reaction to any stimulation therapy.
- Smooth muscle cells are a new focus for medical therapy.