Aorta-on-a-chip: a novel tool to gain molecular insights into aneurysm disease

Experimental Vascular Surgery & Medicine Unit

TUM
Disclosure

Speaker name:

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I have the following potential conflicts of interest to report:

☐ Consulting
☐ Employment in industry
☐ Stockholder of a healthcare company
☐ Owner of a healthcare company
☐ Other(s)

✓ I do not have any potential conflict of interest
Outline

- Organs and Tissues-On-Chip introduction
- Applications
- Experimental set-up
Decline in pharmaceutical R&D efficacy


Reason for failure 2013-2015

Percentage failure by therapeutic area


Overcoming the translational problem with better in vitro models

Miniature tissues and organs grown *in vitro* (Micro Physiological Systems)

*Reverse engineer an organ?*

OOC Technology
- Tissue engineering
- Microfluidics
- Human cell sourcing

1. Multicellular architectures
2. Tissue-Tissue interfaces
3. Vascular perfusion
4. Organ-relevant physicochemical microenvironment

Modelling of human physiology and disease
Aorta-on-a-chip: a tool in vascular biology research

- More relevant model of human pathophysiology
- Architecture of the organ
- Organ-relevant physicochemical microenvironment
- EC-SMC crosstalk in vascular diseases
I. Application

- Allows to study different flow patterns and their effects in EC-SMC compartments
  - Discovery of flow-dependent effectors

II. Application _ personalized medicine (Munich Vascular Biobank)

- Biobank of adult primary SMC and EC isolated from patients / donor
- Biobank of iPSCs from patients / donor
  - Aorta-on-a-chip as a disease model

III. Application _ RNA therapeutics testing

Drug Eluting Balloon-delivered anti-29b to halt chronic aneurysm progression in LDLR-/- Yucatan mini-pigs

Li YD et al. Circulation 2018
Aorta-on-a-chip setup & flow

Primary aortic smooth muscle cells

Primary aortic endothelial cells

Chip structure

4-slot OOC

OOC connected to microfluidic pump

Re-circulation: unidirectional flow

Qualitative read-outs: IF

Quantitative read-outs: RNA, protein, secretome analysis

Chip isolation at end point
Aorta-on-a-chip read-outs

Co-culture membrane IF analysis

RNA isolation and expression profile
Increasing High-Throughput

Polydimethylsiloxane

Silicon-based organic polymer

Transparent

Soft, flexible

Very high gas permeability

Absorbs small hydrophobic molecules

Width 800 micron, Height 100 micron
PDMS – syringe pump

Medium Perfusion

Staining protocol

Pecam

Phalloidin
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