# Patient-specific aorta-on-a-chip models for thoracic aortic aneurysm and dissection

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## SCOPE OF THE METHOD

| | |
|---|---|
| **The Method relates to** | Human health |
| **The Method is situated in** | Basic Research, Translational - Applied Research |
| **Type of method** | In vitro - Ex vivo |
| **Specify the type of cells/tissues/organs** | Endothelial and vascular smooth muscle cells derived from iPSCs, generated from PBMCs or fibroblasts |

## DESCRIPTION

### Method keywords

Aorta-on-a-chip
Microfluidic device
blood vessel
Human induced Pluripotent Stem Cell

### Scientific area keywords

Cardiogenetics
thoracic aortic aneurysm
vascular biology
Induced pluripotent stem cells

### Method description

Thoracic aortic aneurysm (TAA) involves the progressive enlargement of the thoracic aorta, posing a significant risk for life-threatening aortic dissection and/or rupture. Currently, mouse models are frequently used to investigate and target the molecular defects underlying TAA, due to the difficulty in collecting native aortic samples from patients and especially control individuals. However, murine *in vivo* studies are often

lengthy, and drug testing results have not always translated to patient outcomes. The existing vascular smooth muscle cell (VSMC) or endothelial cell (EC) monocultures are simplified and fail to replicate the complex multilayered and multicellular structure of the aorta adequately. To address this, we aim to develop and validate the first iPSC-derived TAA aorta-on-a-chip models using induced pluripotent stem cells (iPSCs). PDMS chips will be seeded with the key cell types found in the ascending aorta, with pressure and shear stress applied to mimic the native environmental conditions. Once the patient model is established, we will demonstrate its ability to recapitulate established cellular and molecular disease processes and drug responses.

### Method status

Still in development

## PROS, CONS & FUTURE POTENTIAL

### Advantages

• Using patient-derived iPSCs provides complete genetic background and allows a more accurate representation of human disease mechanisms,
• By including key cell types and mimicking the complex structure of the aorta, the model will offer more comprehensive insights into disease mechanisms and drug responses,
• Applying pressure and shear stress to the chips replicates the native physiological conditions, enhancing the model's accuracy in simulating the disease environment.

### Challenges

• There can be significant variability between iPSC lines, which may affect the reproducibility and consistency of the model,
• While the model aims to replicate the aortic environment, it may still lack some nuances of the *in vivo* conditions, such as interactions with other cell types, and hormones,
• The long-term stability and functionality of the model is yet to be established.

### Modifications

Introduce other relevant cell types such as fibroblasts, immune cells (e.g., macrophages), and pericytes to more closely mimic the cellular diversity of the native aorta.

### Future & Other applications

• Study other types of aneurysms, such as abdominal aortic aneurysms.
• Study the effects of high blood pressure on the aorta and its cellular components.
• Assess the cardiovascular toxicity of new drug candidates, reducing the risk of adverse effects.
• Use the model to predict how individual patients might respond to specific drugs, enhancing personalized treatment plans.

## REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

*Coordinated by*

sciensano

VUB

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Vlaanderen
verbeelding werkt

bruxelles environnement
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