Electronic Supplementary Material (ESI) for Lab on a Chip.

Supplementary information for:

Organs-on-Chips with Combined Multi-Electrode Array and Transepithelial Electrical Resistance Measurement Capabilities

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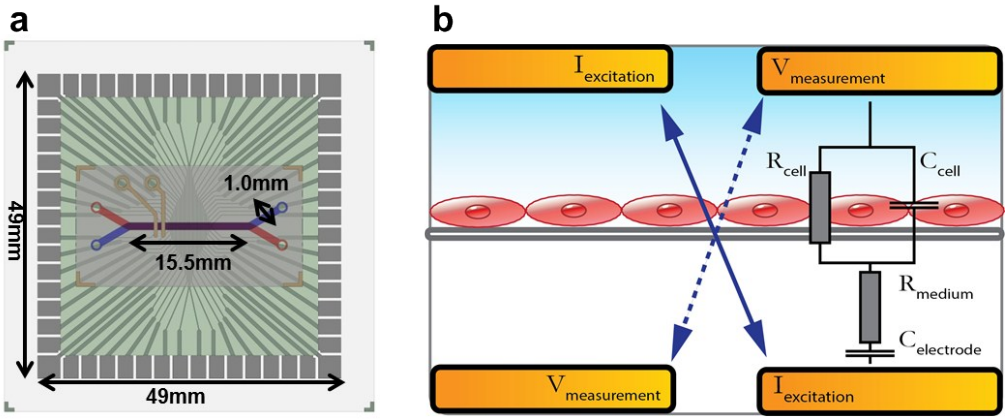
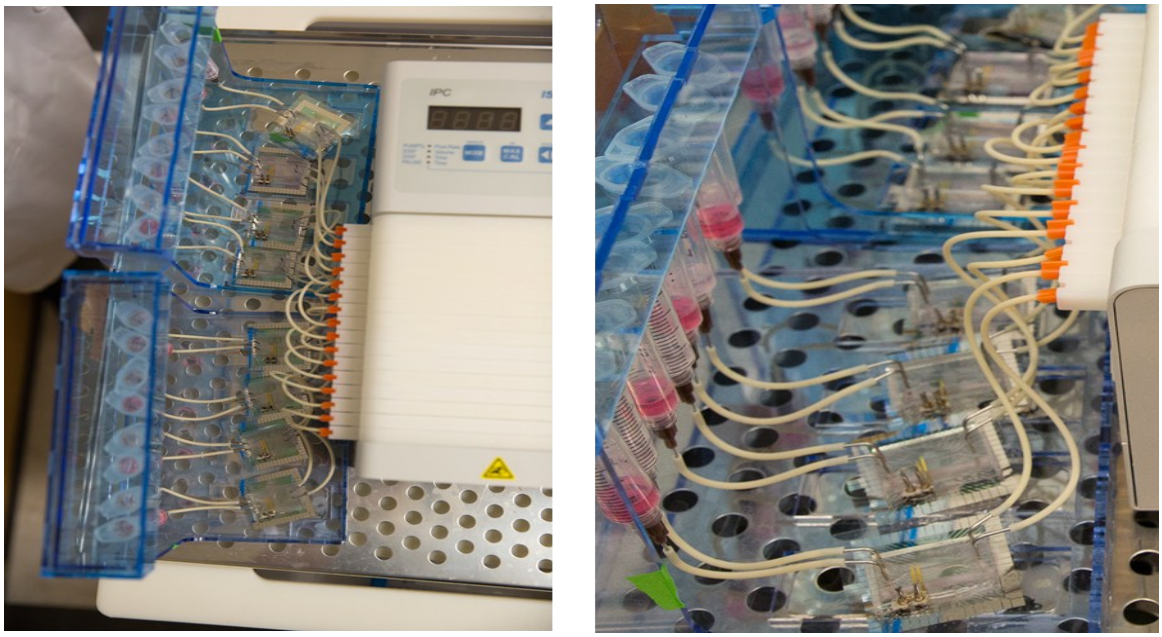
SIFig. 1



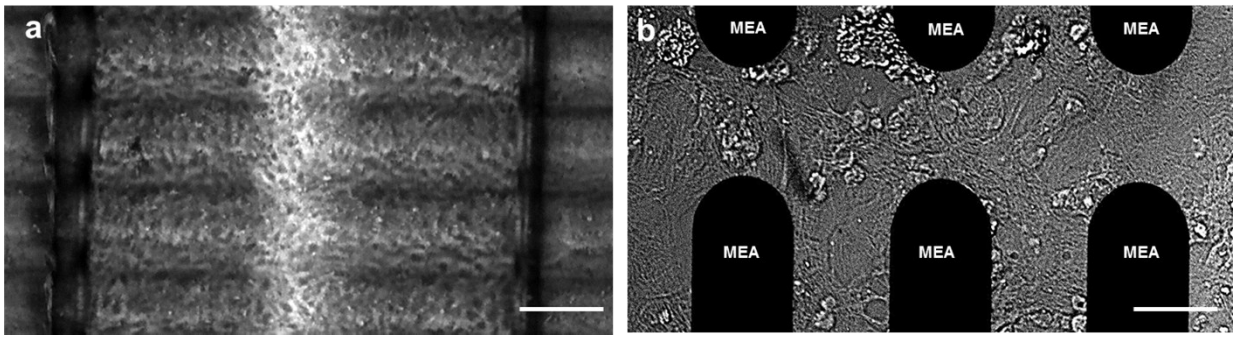
SIFig. 1 – Chip design – a. CAD view demonstrates the two microfluidic channels in the chip. b. Impedance spectroscopy using four-point probe measurements where the impedance over the cell layer can be modelled by the illustrated equivalent circuit.

SIFig. 2



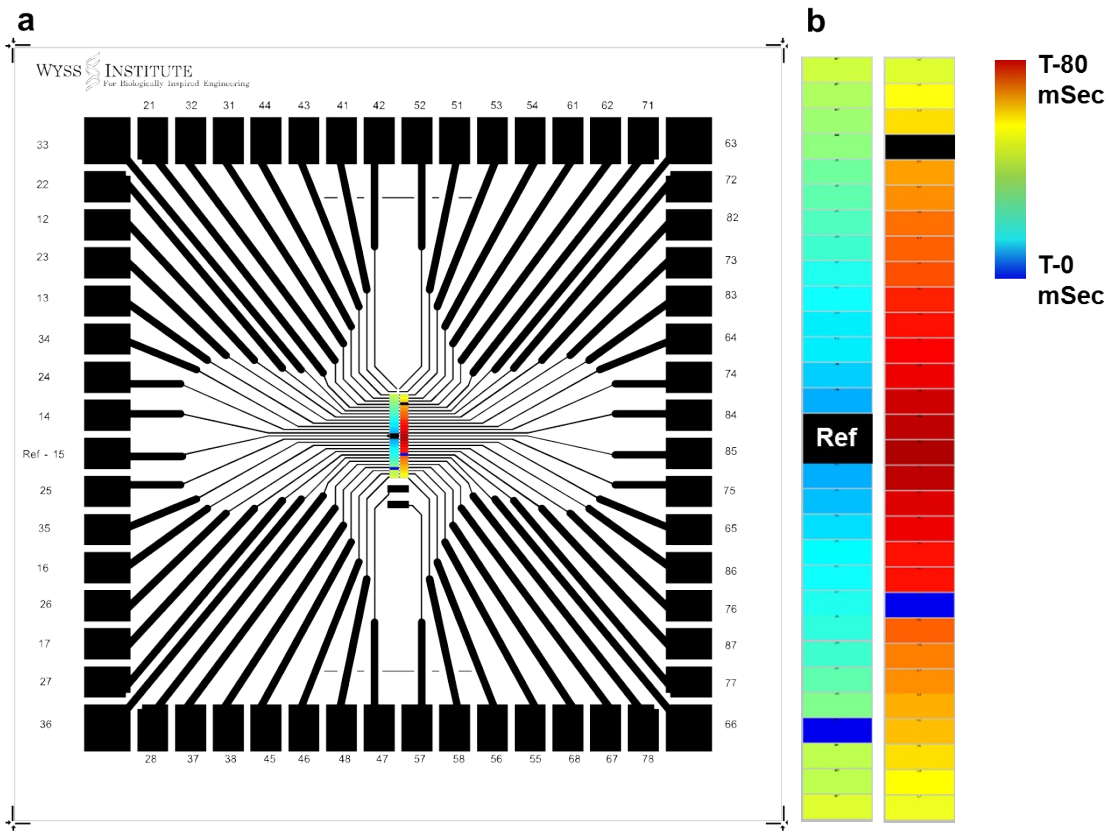
SIFig. 2 – Experimental setup – 8 TEER MEA chips were connected to a peristaltic pump. Each chip had an endothelial medium reservoir (light pink) and one cardiomyocytes medium reservoir (red).

SIFig. 3



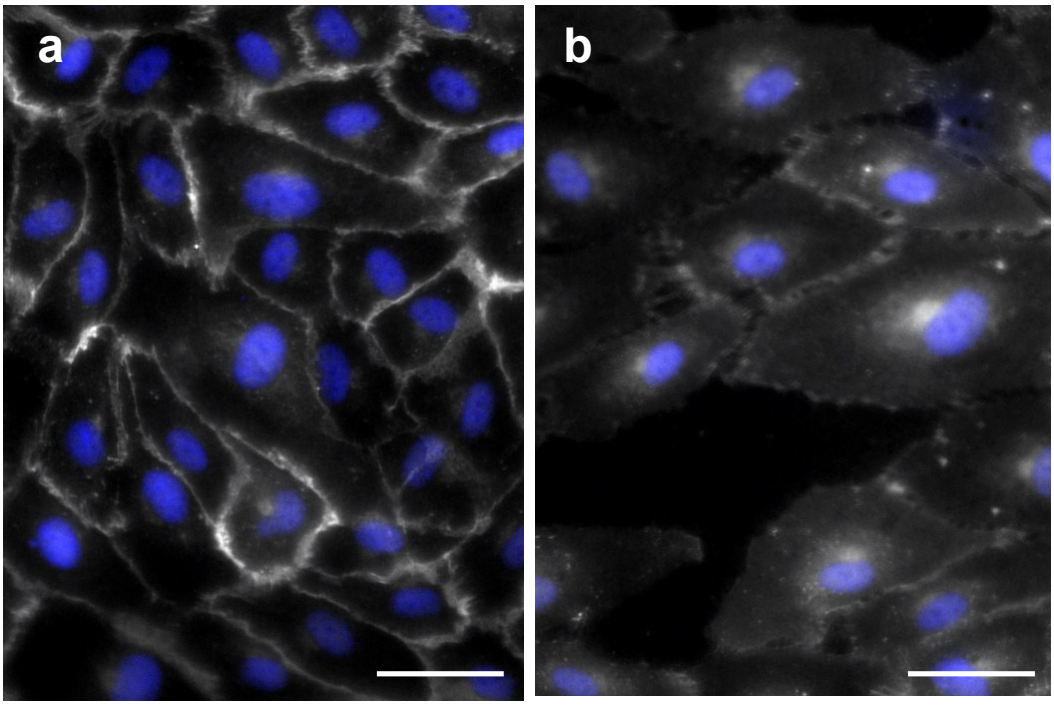
SIFig. 3 Layer formation - DIC image of the endothelial layer on top of the PET membrane 24 hours after seeding. The black horizontal elongated shadows are the MEAs from the bottom layer. b. Cardiomyocytes forming a myocardial tissue on the MEA (black). Scale bar 20µm.

SIFig 4



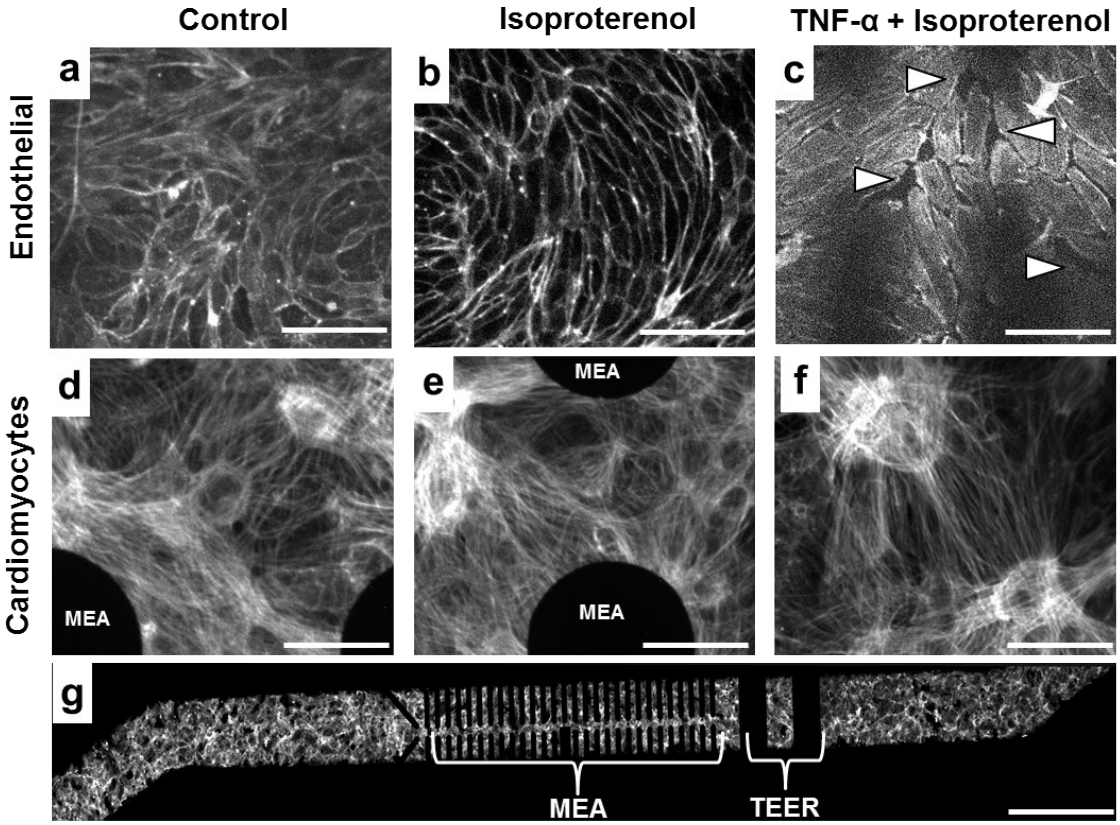
SIFig 4 – Spatial analysis of conduction velocity. a. electrode map. b. spatial analysis of the conduction velocity. Trigger analysis identified the first electrode, which sensed FP signal (T0-mSec, blue) and assigned each electrode by the time electrical signal was detected relative to the first electrode (T-80mSec, Red). Each electrode represents an average of >200 spikes, detected over 2 minutes as recorded in a chip.

SIFig 5



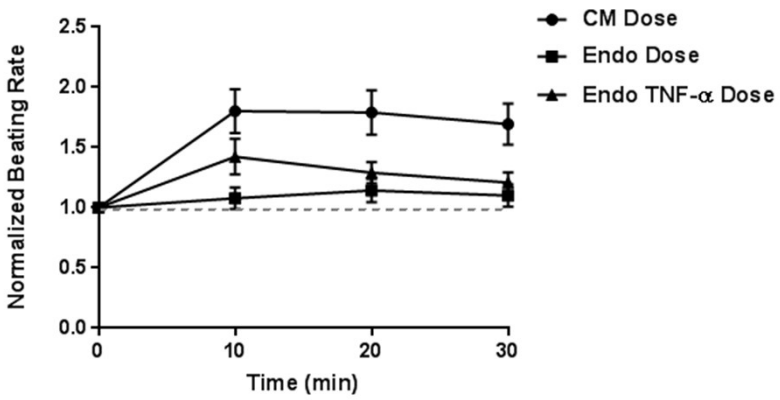
SIFig 5 – TNF-α does not cause apoptotic nuclei a-b. Immunocytochemistry of the confluent endothelial layer, Phalloidin (white) was used to stain f-actin and Hoechst (blue) stained the nuclei a. the non-treated control reveals a confluent endothelial layer, b. TNF-α treatment, the barrier was damaged and holes can be observed to decrease in the TEER values. Scale bar 40µm.

SIFig 6



SIFig 6 – Endothelial monolayer and myocardium in the device a-c. Immunocytochemistry of the confluent endothelial layer, Phalloidin was used to stain f-actin. Note, this is the same view as Fig4 but with Phalloidin stain instead of VE-cadherin. a. the non-treated control reveals a confluent endothelial layer, b. isoproterenol treatment did not show any change in the integrity of the barrier (supported with the TEER data), c. TNF-α challenge, the barrier was damaged and holes can be observed to decrease in the TEER values, (scale bar 10μm). d-f. Immunocytochemistry of myocardial tissue on the MEA (Phalloidin). The cardiomyocytes did not show major changes between the control samples and drug addition. (scale bar 10μm) g. Overview of the myocardial tissue that was formed in the lower channel of the chip (MEA layer). The TEER and MEA electrodes can be seen in black (scale bar 5.0mm).

SIFig 7



SIFig 7 – Time Course of Drug Effects in the TEER –MEA chip. Isoproterenol infusion will have different dynamics and magnitude of effect, depending on whether or not the drug must past through an endothelial barrier to reach the cardiomyocytes. When Isoproterenol was introduced either directly into the myocardial channel or into the vascular channel of chips that were treated with TNF-α to disrupt endothelial junctions, the cardiomyocytes exhibited larger and more rapid increases in beating rate (peaking at 10 min) than when the drug was perfused through the vascular channel lined by an intact endothelium, which peaked at 20 min.

SI Movie 1 – Spontaneous contractility of the myocardial tissue on the MEA before the addition of Isoproterenol

SI Movie 2 – Spontaneous contractility of the myocardial tissue on the MEA 10 min after the addition of Isoproterenol. The beat rate is higher and the FP amplitude stronger.