
UNIVERSITY OF TWENTE. | TECHMED CENTRE
THE TECHMED EVENT | SHAPING A HEALTHY FUTURE
[14.04h] | [On generating spin-off activities in the Organ-on-Chip field] | [Carla Cofiño Fabrés & Marcelo C. Ribeiro]

On generating spin-off activities in the Organ-on-Chip field

Dr. CARLA COFIÑO FABRÉS – UNIVERSITY OF TWENTE
Dr. MARCELO CATARINO RIBEIRO – RIVER BIOMEDICS

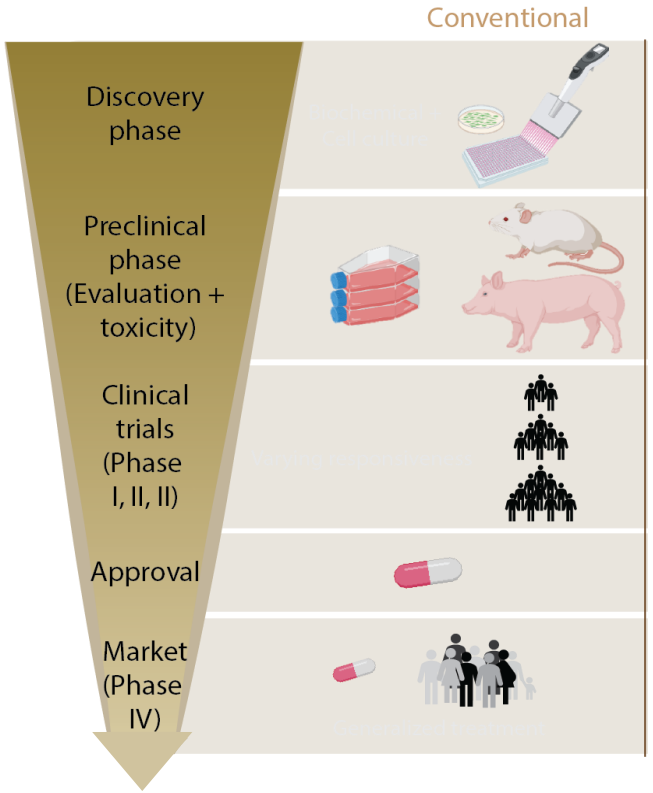
DISCLOSURE SLIDE

Carla Cofiño Fabrés does not have any financial interest concerning information presented
Marcelo Ribeiro is co-founder of River BioMedics B.V.

HPSC-BASED MODELS CAN *SPEED UP* DRUG DISCOVERY

- Low efficacy and toxicity evaluation in conventional, ***animal-based*** drug discovery pipelines.
  - >10 years;
  - Low success
  - ~$2.7billion

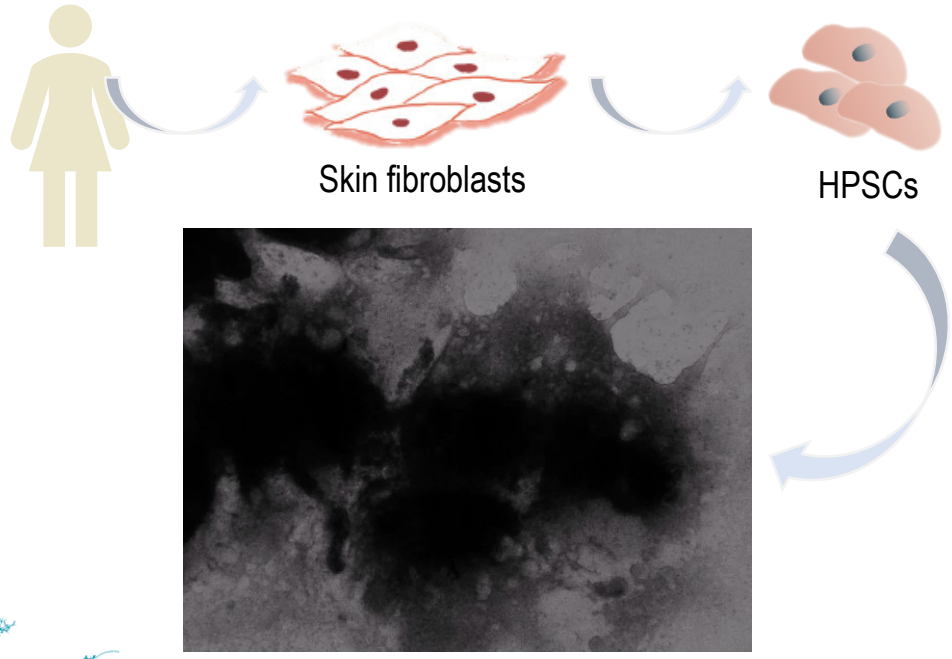
- Human pluripotent stem cell ***(hPSC)-based models***:
  - Human physiology
  - Patient stratification



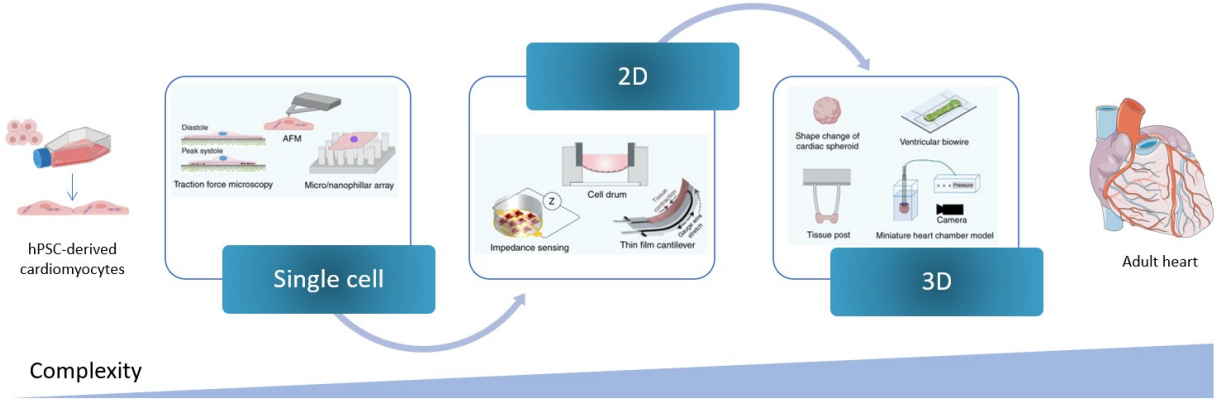
CARDIOVASCULAR DISEASE

NEED OF ADVANCED *HEART-ON-CHIP* MODELS

- Successful generation of *hPSC-cardiomyocytes in vitro*

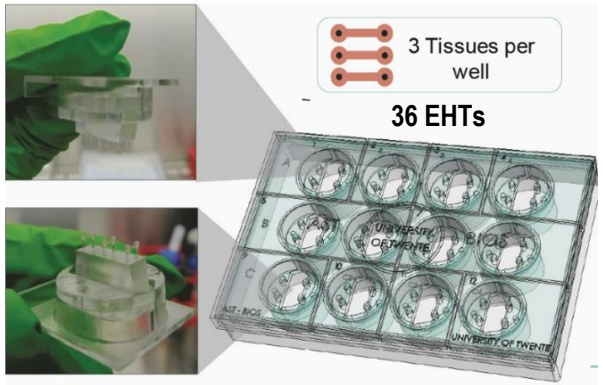


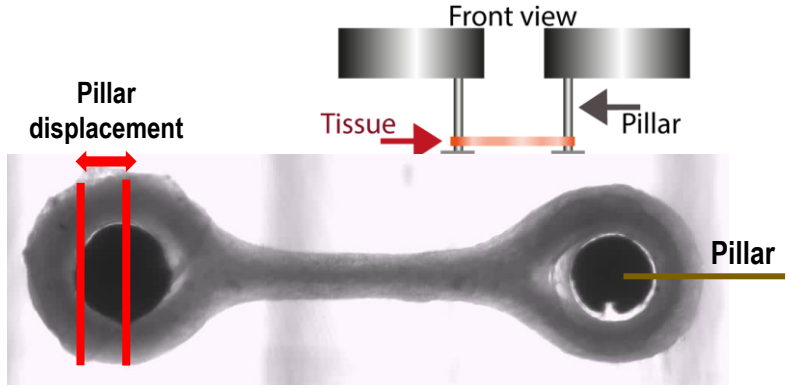
- Lack of the human heart *complexity*



ENGINEERED HEART TISSUES

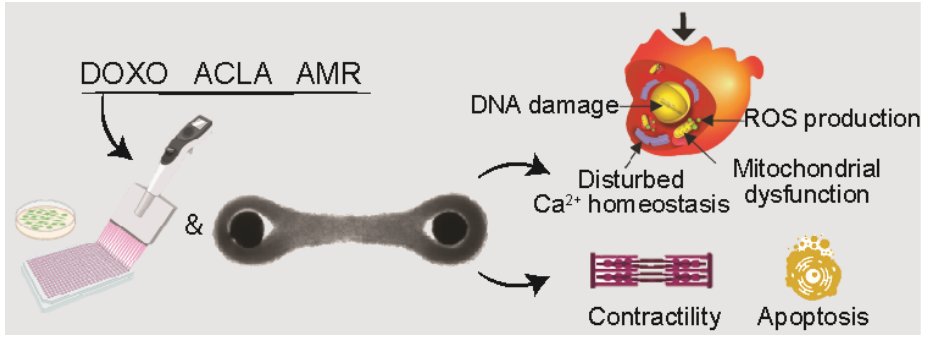
TOWARDS ADVANCED *HEART-ON-CHIP* MODELS

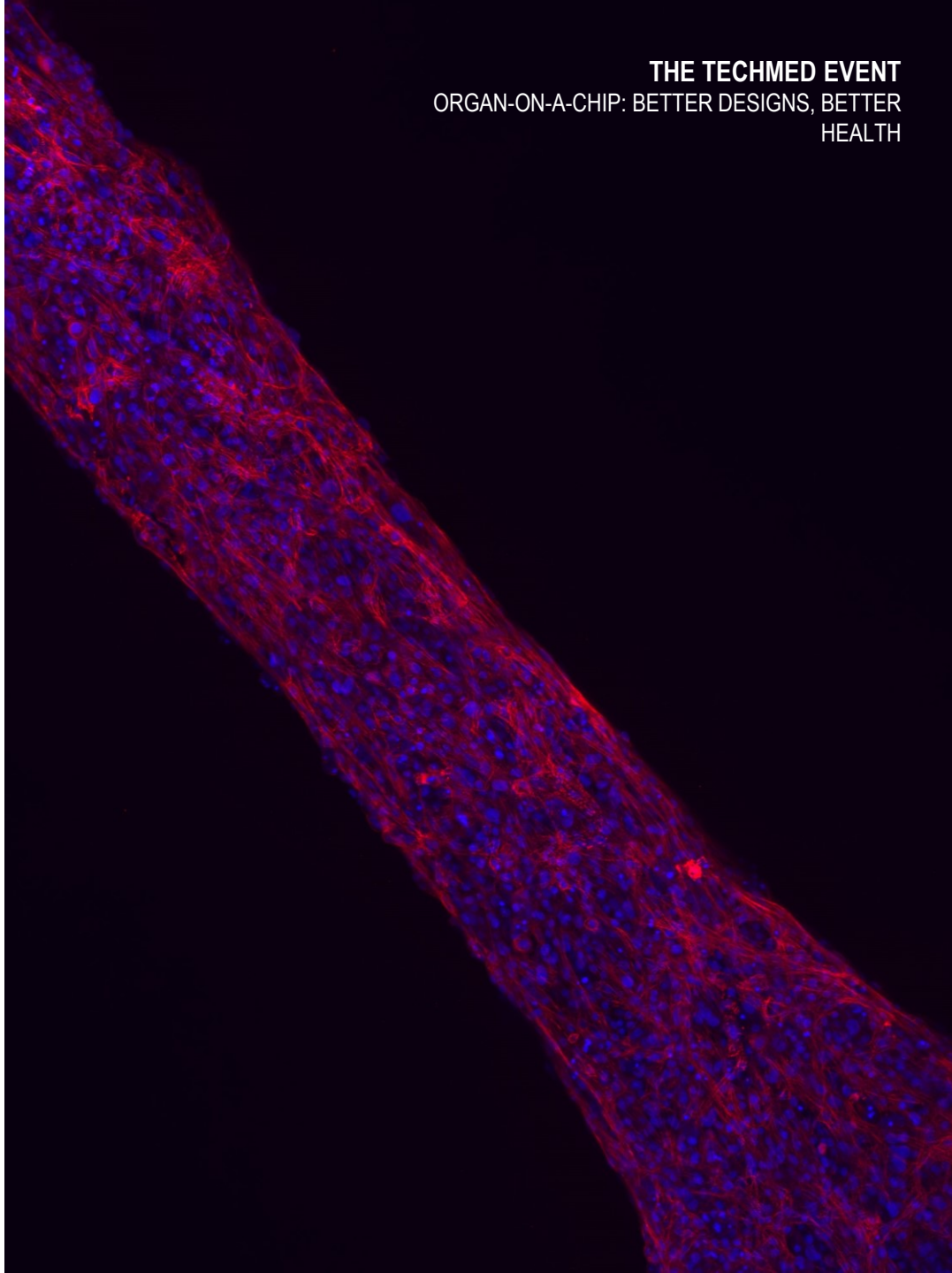




Ribeiro, M. C., Rivera-Arbeláez, J.M., & Cofiño-Fabres, C. et al. A New Versatile Platform for Assessment of Improved Cardiac Performance in Human-Engineered Heart Tissues. J. Pers. Med. 2022, Vol. 12, Page 214 12, 214 (2022).

- Enhancement of hPSC-cardiomyocyte maturation
- Enabled the evaluation of cardiotoxic drugs



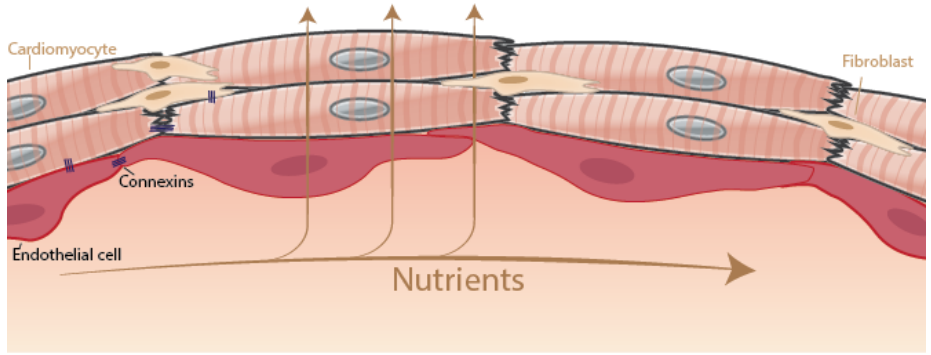


MICRO ENGINEERED HEART TISSUES

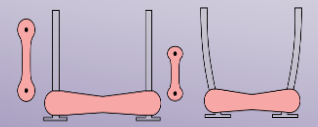
TOWARDS ADVANCED *HEART-ON-CHIP* MODELS

In vivo:

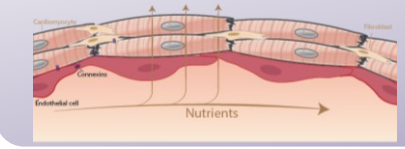
- Endothelial cells play a role in nutrient transport and waste removal
- CM-NonCM direct contact: evidence of improved CM maturation



OOC-based =
Microfluidic system



EHT format =
functional readouts

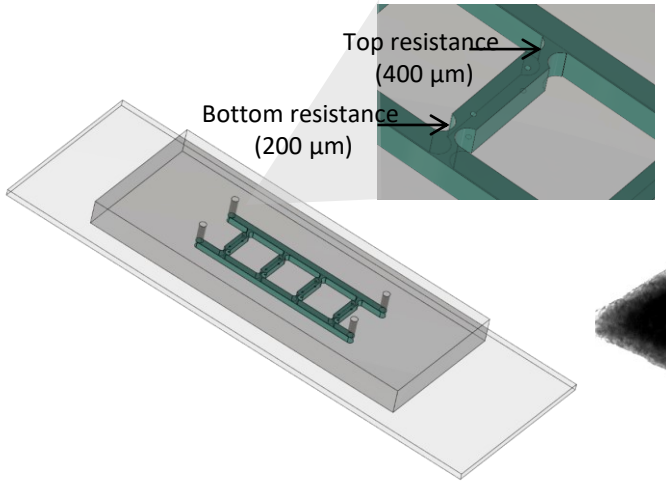


In vivo-like
Cell organization

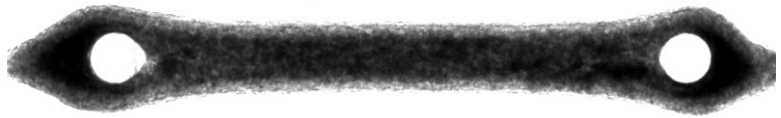
Marcelo C. Ribeiro
Carla Cofino Fabres
Tom Boonen

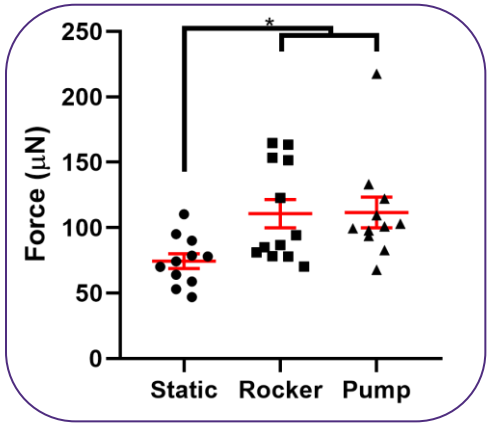
MICRO ENGINEERED HEART TISSUES

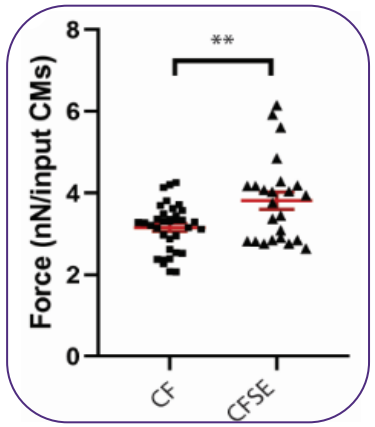
TOWARDS ADVANCED *HEART-ON-CHIP* MODELS

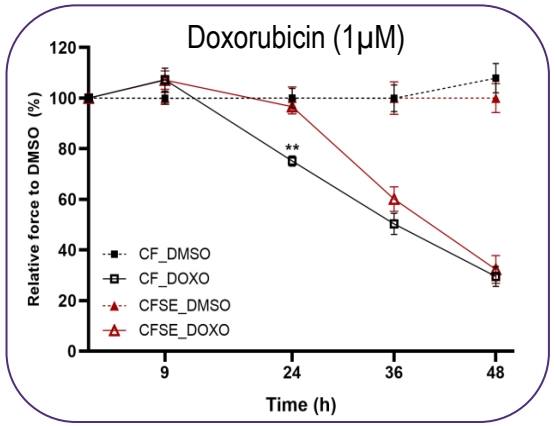


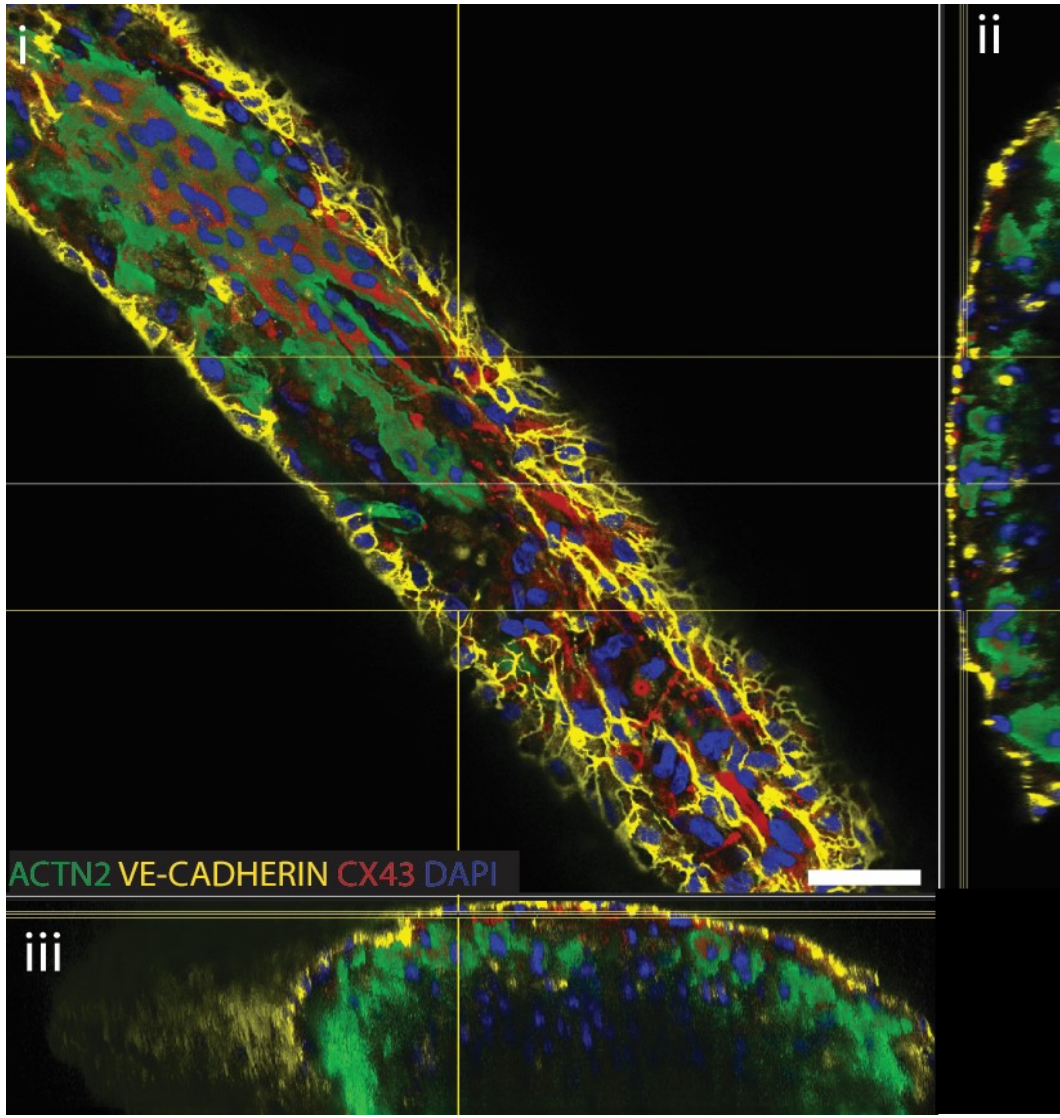
- ✓ EHT technology
- ✓ 50,000 cells/µEHT
- ✓ Microfluidic culture









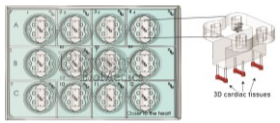


Cofiño-Fabrés, C. et al. (in revision)

River Biomedics a cardiovascular drug discovery company

2018

3D Cardiac Strip technology platform developed by Dr. Marcelo Ribeiro at Passier Lab



2020

River BioMedics spun-out of University of Twente, by Prof. Passier, Dr. Marcelo Ribeiro and Dr. Lisanne Blauw

UNIVERSITY OF TWENTE.

2021

Drug discovery efforts initiated led by Dr. Nicky Cooper

€1.8M seed financing raised

FIRST BGV KIKK CAPITAL oost nl

2022

Target 1[1] small molecule drug discovery initiated via partnership with Sygnature Discovery

Development of HTS initiated funded by €1.5M EIC transition grant[2]

SYGNATURE DISCOVERY

2023

Hit Strategy In place for Target 1 for HFpEF

€2M additional financing attracting new investor **Libertatis Ergo Holding B.V. (LEH)**

FIRST BGV KIKK CAPITAL oost nl

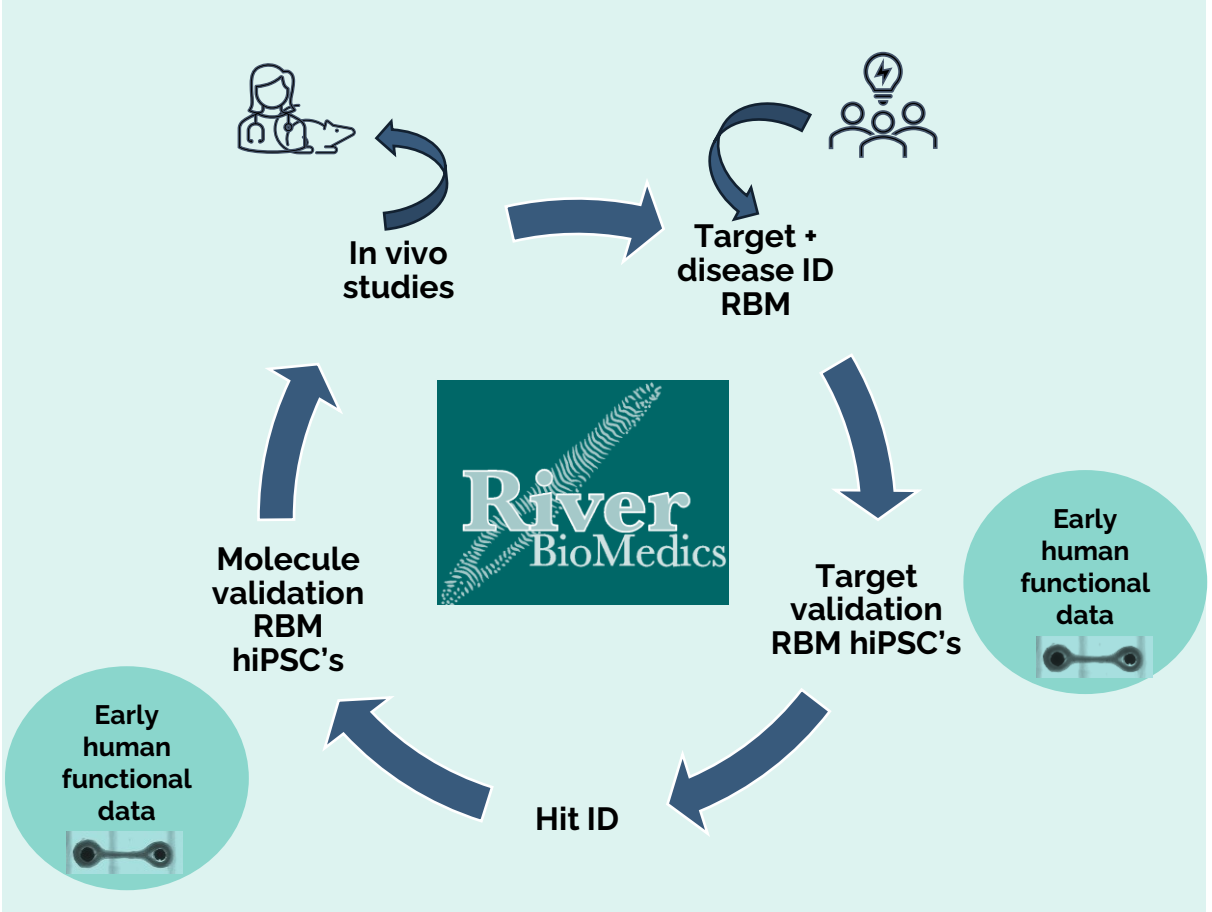
LEH LIBERTATIS ERGO HOLDING | Universiteit Leiden The Netherlands

Future milestones

- Secure Series A fundraise
- Progress small molecule inhibitors of Target 1 to PoC animal data
- Development of HTS human 3D cardiac strip platform – *establish pharma partnership*
- Further pipeline expansion

1. **Target 1** GWAS association to HF with PoC animal data, 2. Additional 1 million non-dilutive funding EIC Pathfinder grant – Mini-heart project also raised

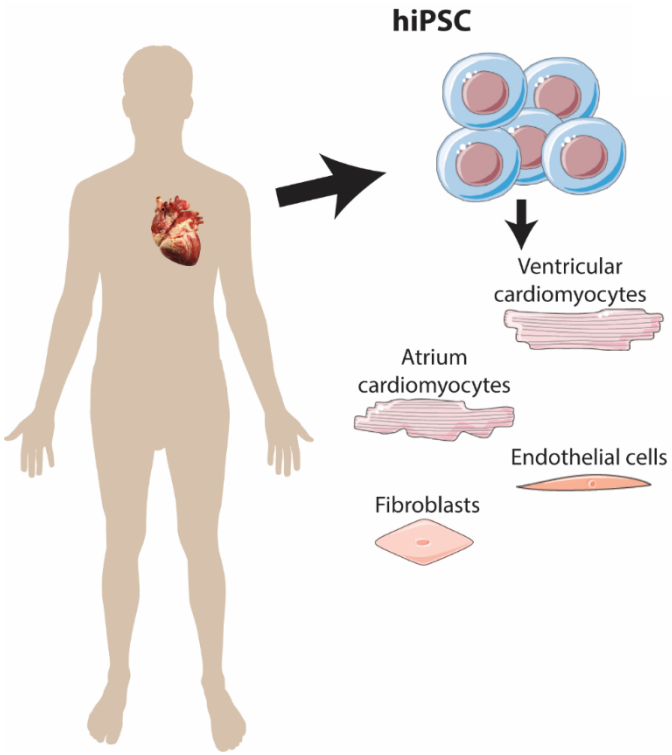
River BM drug discovery process utilizes proprietary technology to support target progression



Target progression utilizing RBM's platform provides functional, human cardiomyocyte data at a very early stage in drug discovery for target and molecule validation

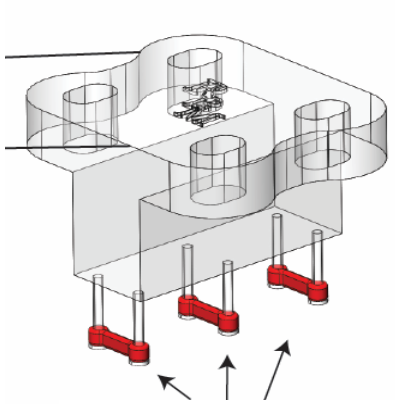
hiPSC derived 3D cardiac strip

hiPSC derived cardiomyocytes



Cardiomyocytes cultured as 3D tissues around flexible poles

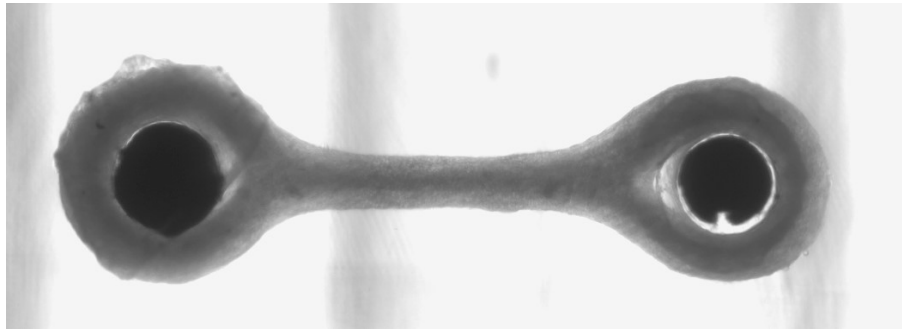
Human3D cardiac strip technology



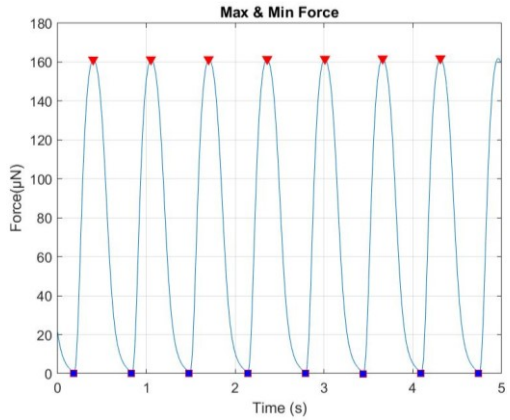
3D Cardiac tissues around flexible poles

Real-time readout – contraction and relaxation

For human cardiomyocyte-based drug discovery

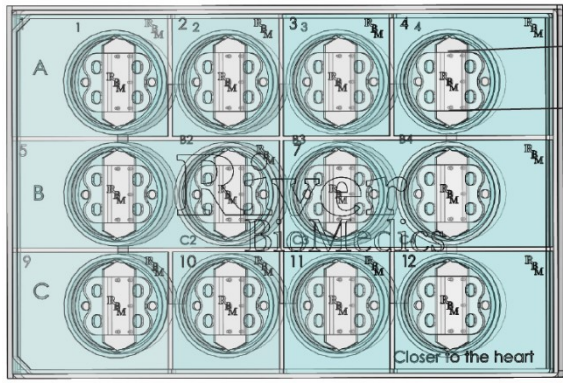


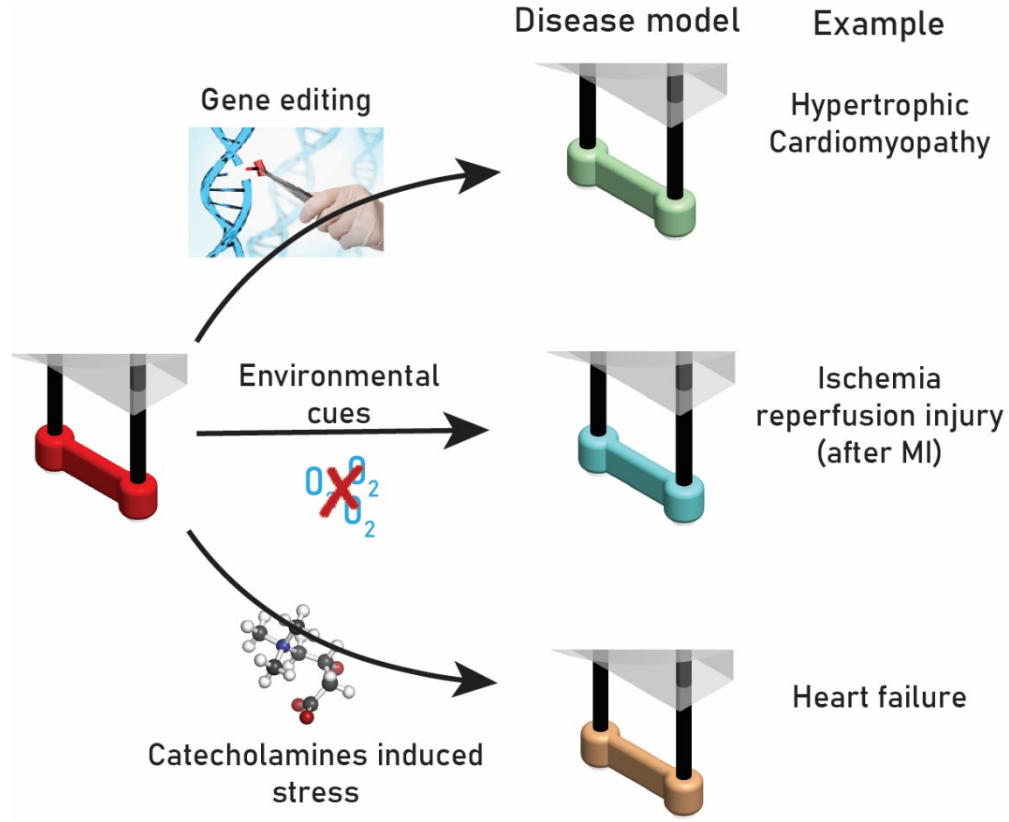
Data Readout



Combining our technology and biology know-how

3D cardiac strip technology	Biology know-how	Drug discovery





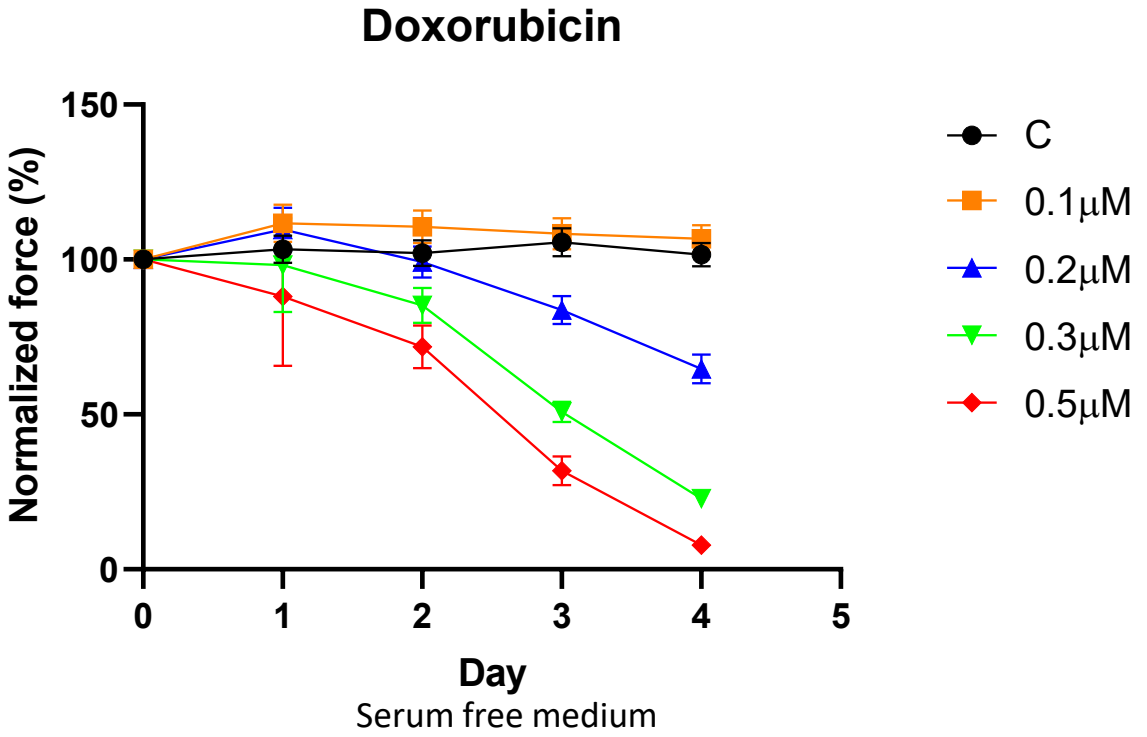
- **Target discovery**
- **Target validation**
- **Compound screens**

Doxorubicin induced heart failure

3D cardiac strips under cardiotoxicity stress

- Doxorubicin is an anthracycline chemotherapy drug
- Doxorubicin causes dose dependent cardiotoxicity including heart failure

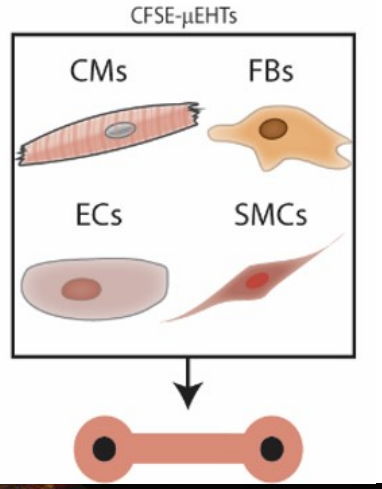
Doxorubicin treatment reduces contraction force in 3D cardiac strips, in a concentration dependent manner

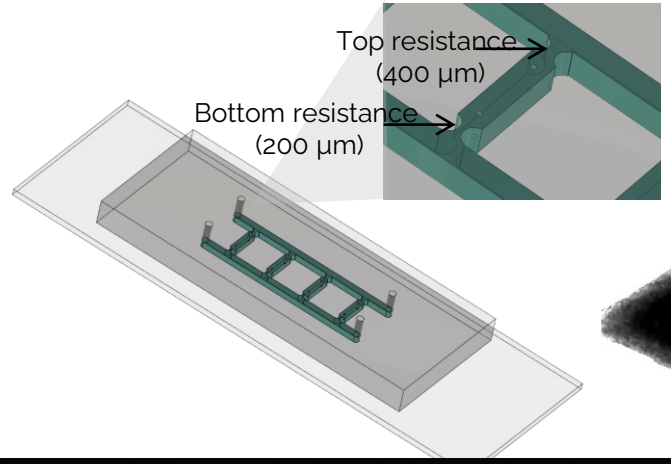


Micro Engineered cardiac tissues to improve heart modeling *in vitro*

Carla Cofino Fabres
Tom Boonen
Marcelo C. Ribeiro

TOWARDS ADVANCED *HEART-ON-CHIP* MODELS





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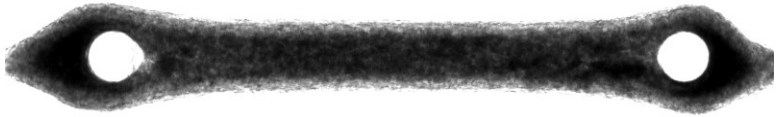
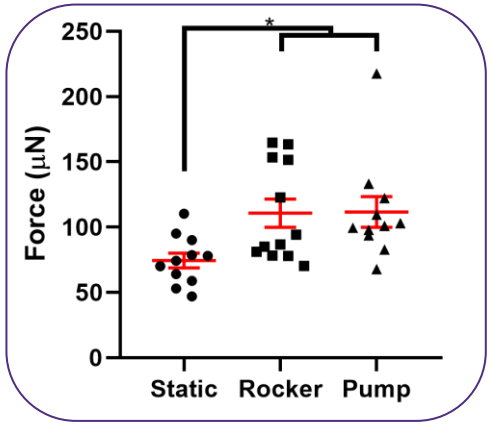
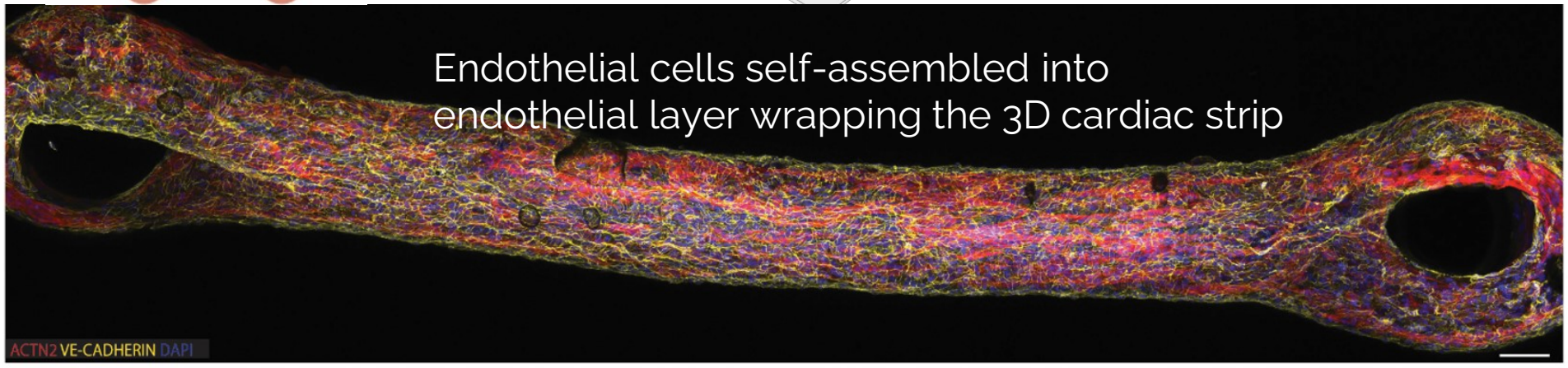
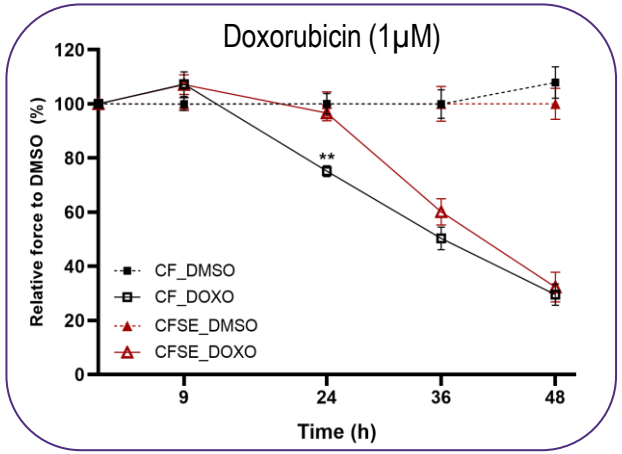


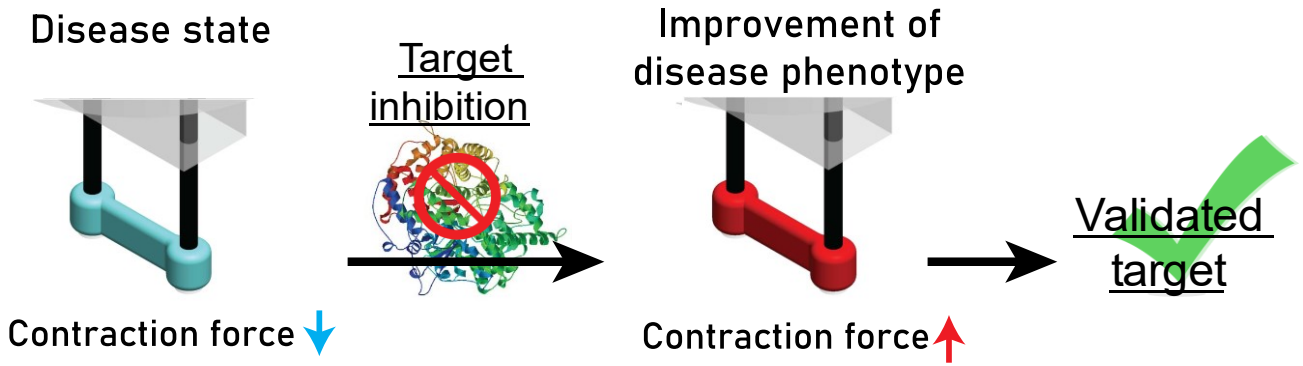




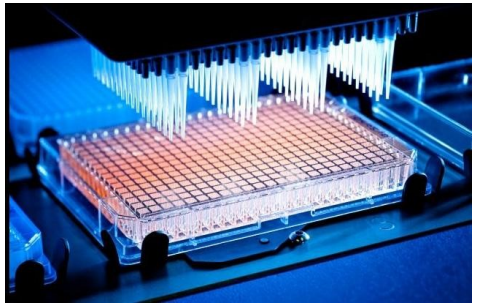


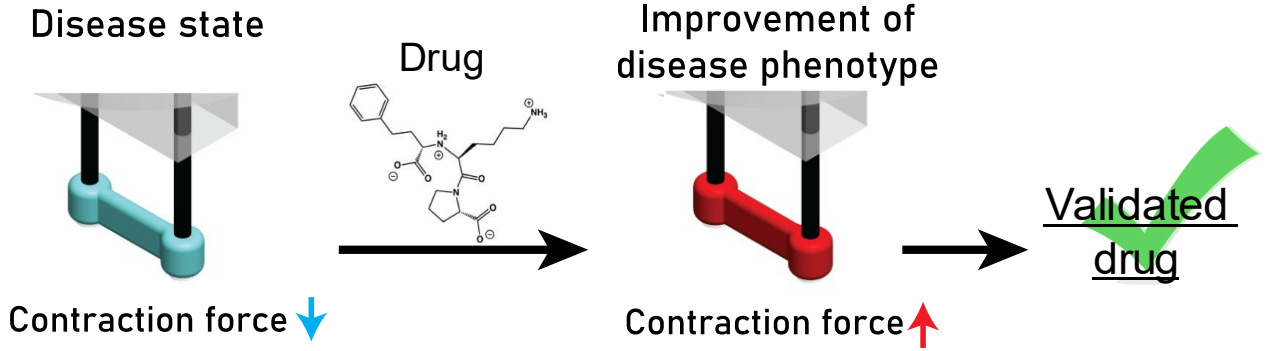
Cofiño-Fabrés, C. et al. (in revision)

Leveraging our novel 3D Cardiac tissues to start drug discovery



High throughput screen



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