

# Brigitta Rita Szabó

ESR1

Supervisors

Elena Matsa  
Paul Volders



# Personal Background

**Hungary**

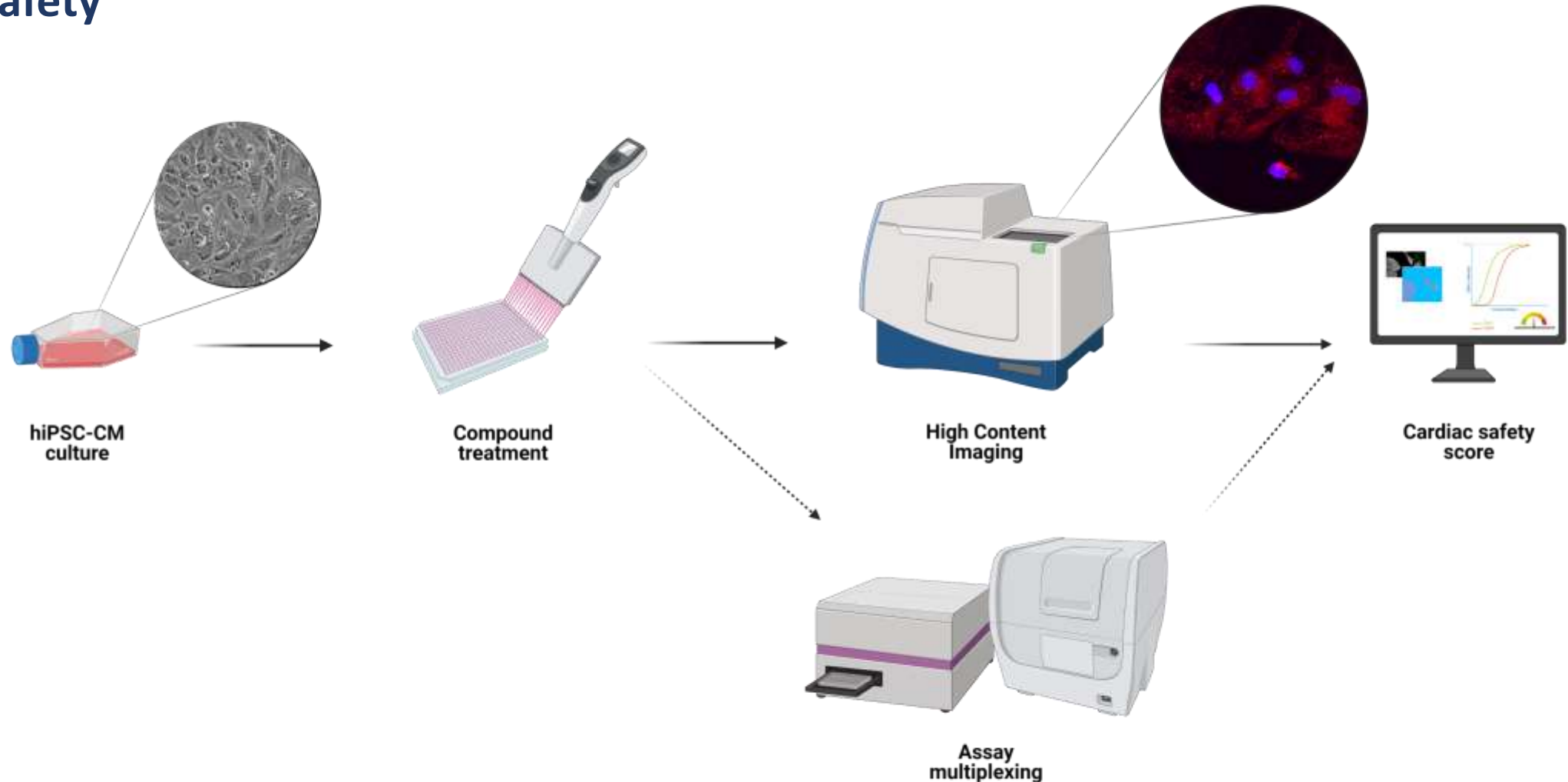


**Medicine**



# Research Project

Development and validation of improved hiPSC-CM assays to study cardiac safety



# Training & Secondments



**Maastricht University**



**Pharma**



# Thank You For Your Attention

Contact: [brigitta.szabo@ncardia.com](mailto:brigitta.szabo@ncardia.com)

# Martina Cherubin

## ESR2



Inspired by **patients**.  
Driven by **science**.



**Universiteit Antwerpen**



# Personal Background

**Master thesis**  
**«Amyloid- $\beta$  Modulation of**  
**microglia zinc homeostasis»**

**University of Reading, UK**



**MSc in Chemistry and**  
**Pharmaceutical Techniques**  
**(2014-2019)**



**Università degli Studi di  
Padova, IT**



**Born in Venice, IT**

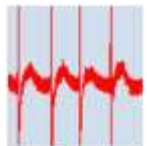


# Research Project

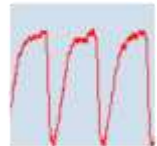
Development and validation of cardiomyocyte model as a predictive assay  
to assess functional and structural cardiac liabilities

## *In Vitro*

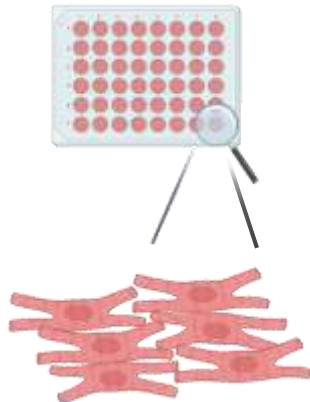
### RTCA CardioECR



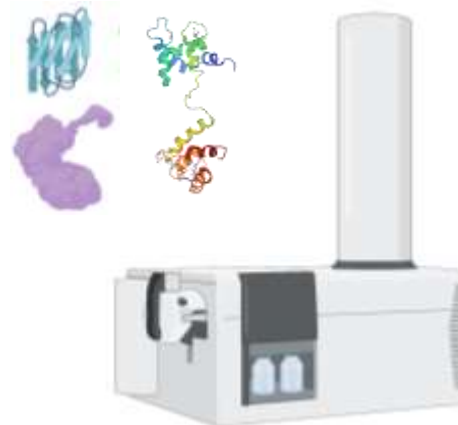
ECR



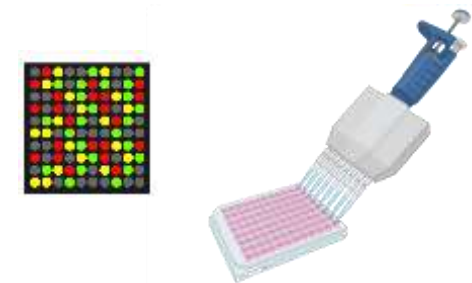
Impedence



### Biomarker Analysis



### Translatability





# Training & Secondments



Universiteit  
Antwerpen



# Thank You For Your Attention

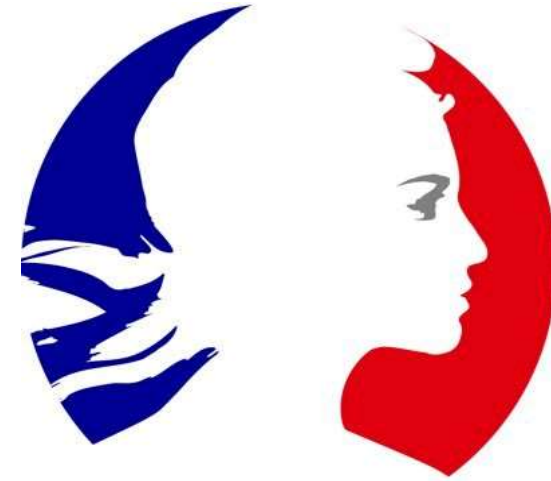
Contact: [Martina.Cherubin@ucb.com](mailto:Martina.Cherubin@ucb.com)

# Haibo Liu

NOTOCORD and Inria

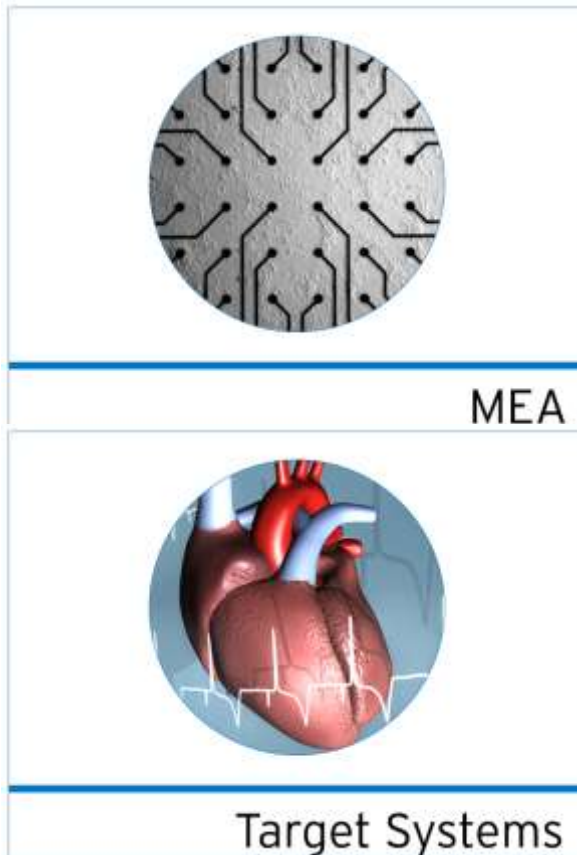


# Personal Background

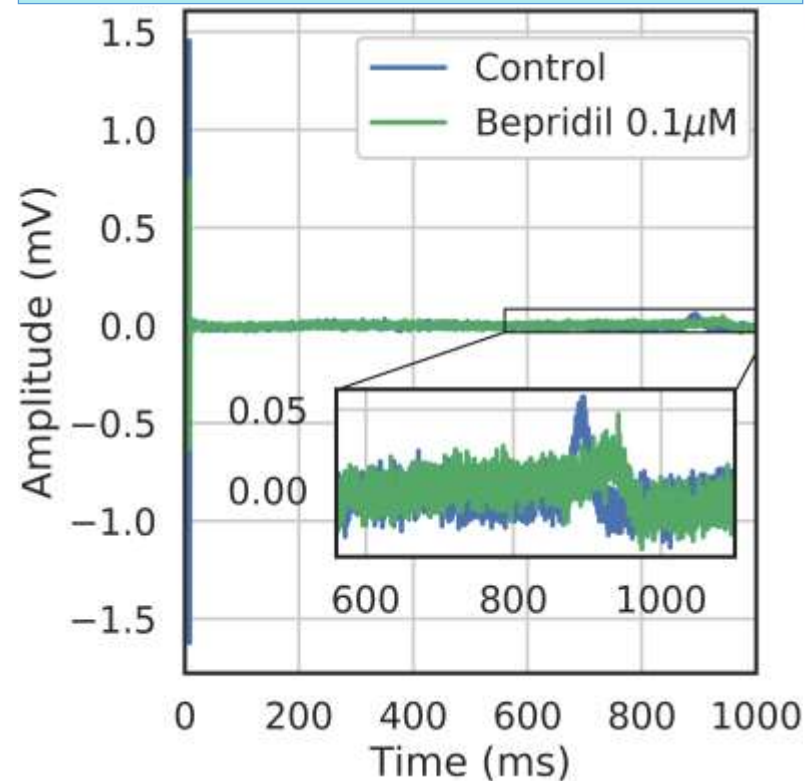


# Research Project

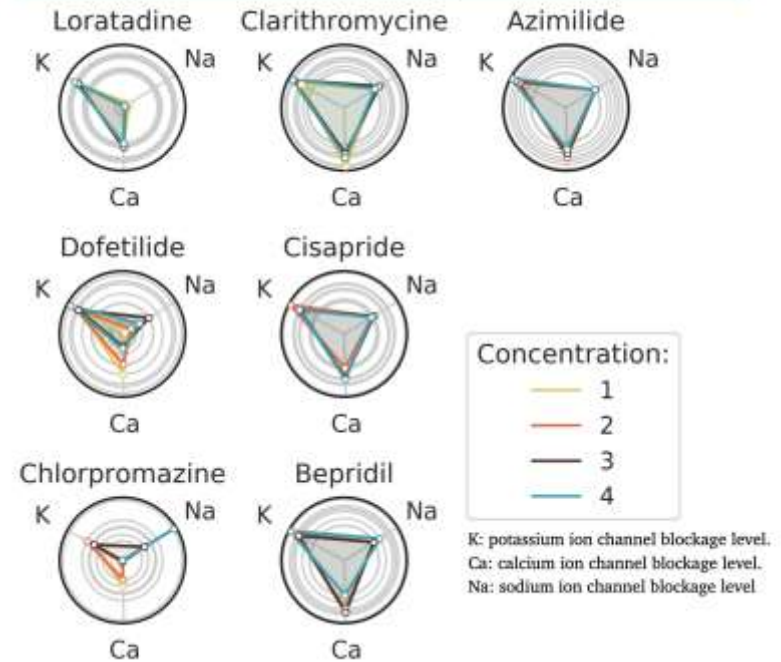
## Empowering Predictivity and Speed of hiPSC CM Assays by Machine Learning Approach



Example of experimental data for control case compared with drug Bepridil (field potential signal – extracellular recording)

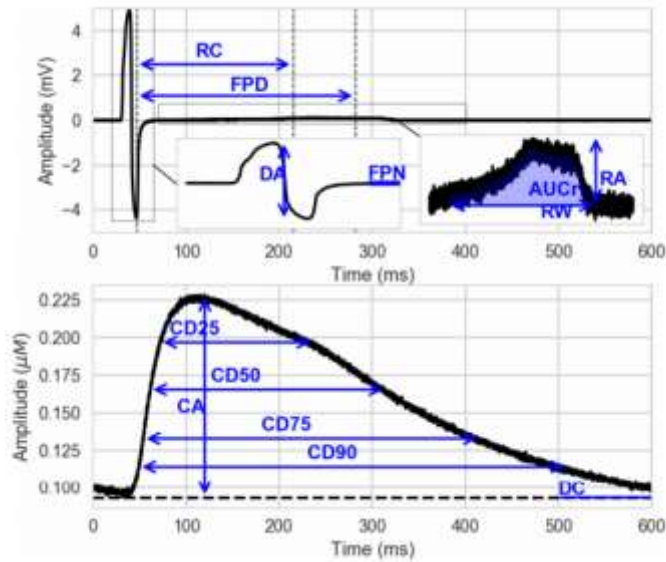


hiPSC CM Experimental Data Classification in Ternary Case for Each Drug Concentration

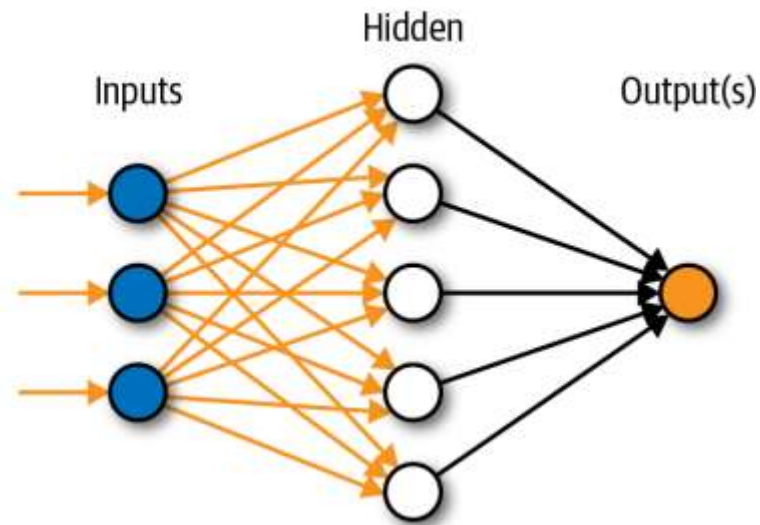




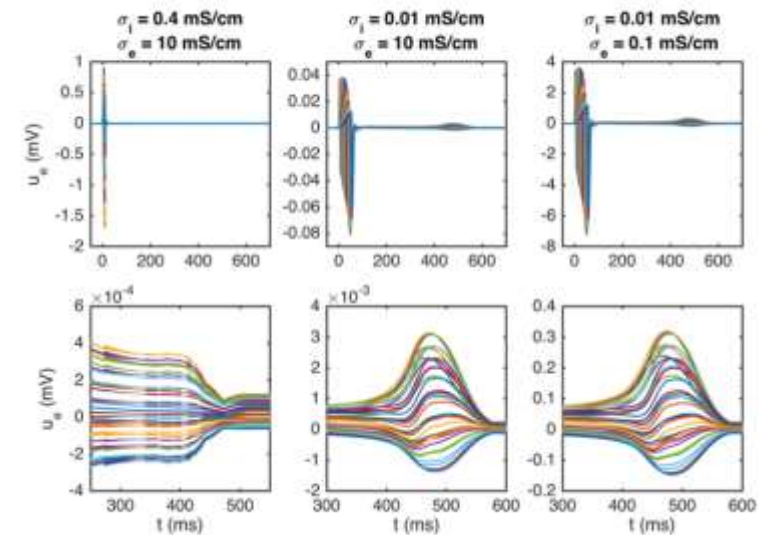
# Current Progression



## Artificial Neural Network



## B: Bidomain-base model simulations



# Training & Secondments



*Inria*



Photo by  
Gilles Scagnelli



# Thank You For Your Attention

Contact: [Haibo.liu@instem.com](mailto:Haibo.liu@instem.com)



## Reference

1. Jæger, Karoline & Wall, Sam & Charwat, Verena & Healy, Kevin & Tveito, Aslak. (2020). Identifying drug response by combining measurements of the membrane potential, the cytosolic calcium concentration, and the extracellular potential in microphysiological systems. 10.1101/2020.05.29.122747.
2. Raphel F, De Korte T, Lombardi D, Braam S, Gerbeau JF. (2020). A greedy classifier optimization strategy to assess ion channel blocking activity and pro-arrhythmia in hiPSC-cardiomyocytes. PLOS Computational Biology 16(9): e1008203. <https://doi.org/10.1371/journal.pcbi.1008203>

# Christian Klein

**TSE systems, Germany**

Wageningen University and Research, the Netherlands



# Personal Background



## Wageningen University & Research



**BSc in Nutrition & Health**

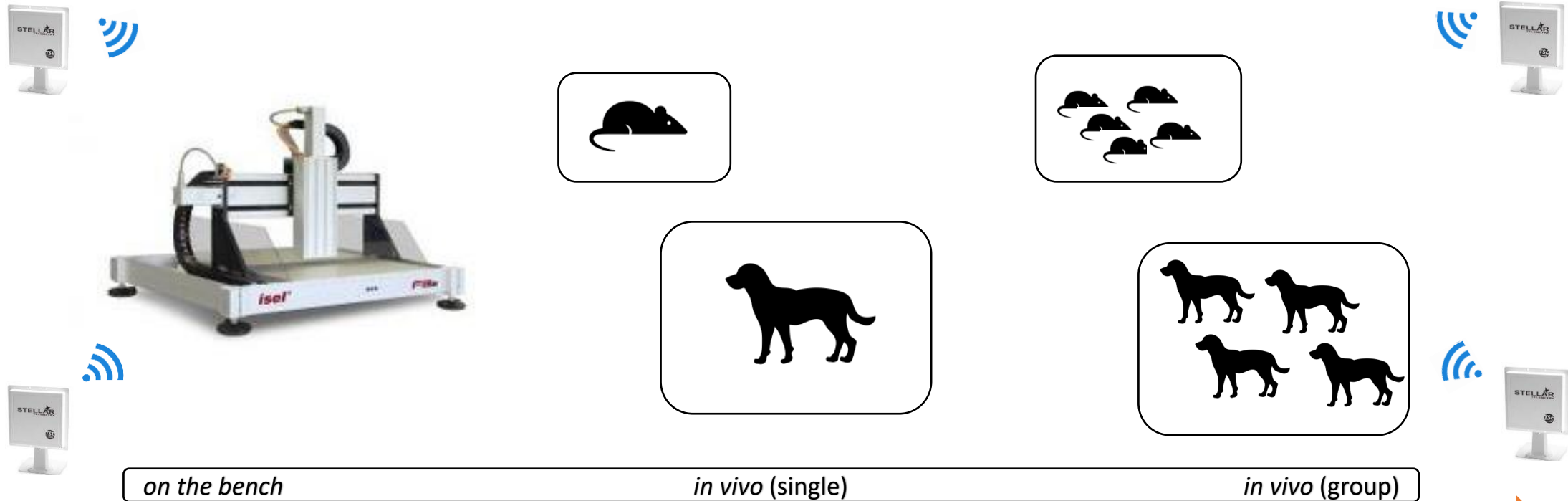
➔ Innovation & Entrepreneurship

**MSc in Nutrition & Health**

➔ Nutritional Physiology

# Research Project

**Development and scientific validation of novel telemetry implants  
with added 3D micro-GPS functionality**



# Training & Secondments



Boehringer  
Ingelheim



מכון ויצמן למדע  
WEIZMANN INSTITUTE OF SCIENCE



WAGENINGEN  
UNIVERSITY & RESEARCH

# Thank You

Contact: [Chris.Klein@tse-systems.com](mailto:Chris.Klein@tse-systems.com)

# Tommaso Biagini

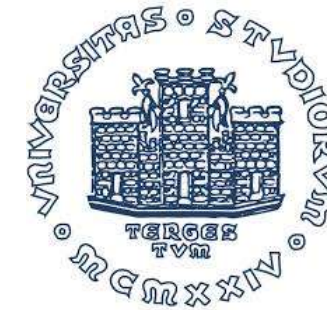
Weizmann Institute of Science

# Personal Background

## Italy



Bachelor Degree in  
Biotechnologies

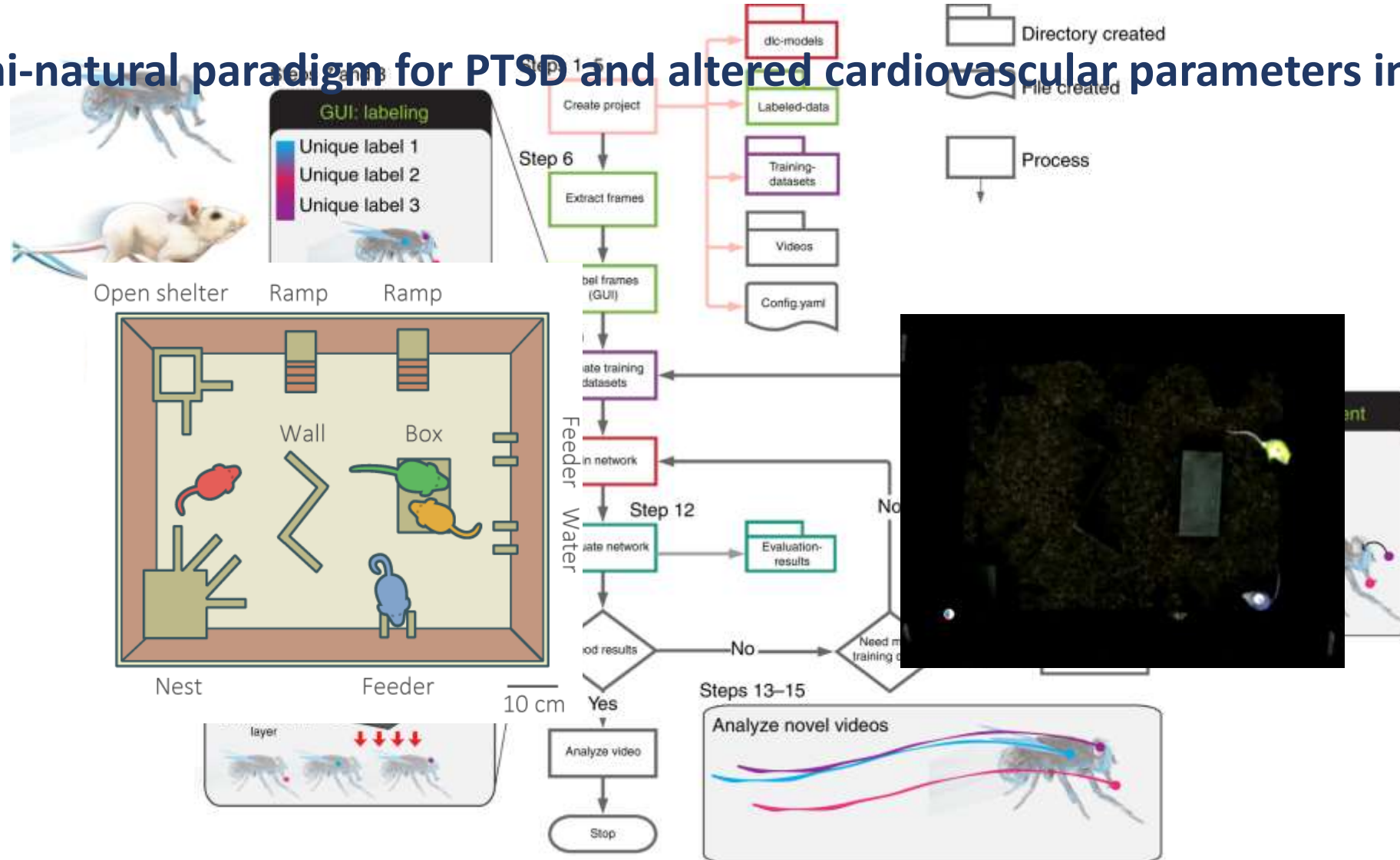


International  
Master Degree in  
Neuroscience



# Research Project

A semi-natural paradigm for PTSD and altered cardiovascular parameters in mice



# Training & Secondments



1 month

TSE  
Technical & Scientific  
Equipment GmbH



3 months



# Thank you for the attention!

Contact: [tommaso.biagini19@gmail.com](mailto:tommaso.biagini19@gmail.com)

# Elham Ataei Alizadeh

Boehringer Ingelheim



# Personal Background

**Iran**



**Italy**



**Spain**



# Research Project

## Validation and use of novel telemetry implants with 3D micro-GPS functionality for integrated neuro-cardiovascular assessment

- ☒ Validate new methods to analyze and interpret the variability of existed cardiovascular data.
  - Optimize future experiments
  - Direct connection to databases
- ☐ Using Micro-**GPS** telemetry system to explore cardiovascular data in group housing of laboratory animals.
  - Group housing
  - Increase number of gathered parameters
  - Animal refinement (3R)
- ☐ Evaluating laboratory animal behavior using video capturing in cardiovascular experiments.
  - Group housing
  - Identification of effective factors in each experiment
  - Combination of cardiovascular and CNS experiments (3R)

# Training & Secondments



# Thank You For Your Attention

**Contact:**

[Elham.Ataei\\_Alizadeh@boehringer-ingenlheim.com](mailto:Elham.Ataei_Alizadeh@boehringer-ingenlheim.com)

[Elham.AtaeiAlizadeh@student.uantwerpen.be](mailto:Elham.AtaeiAlizadeh@student.uantwerpen.be)



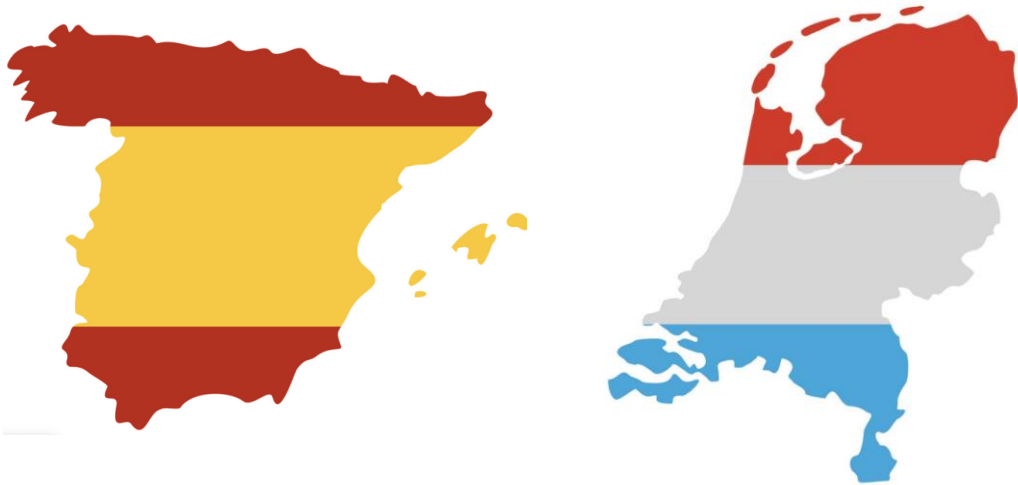
# Sara Costa Faya

*Institut National de Recherche en Informatique et en  
Automatique (INRIA)*



# Personal Background

**BSc in Physics:  
Spain & The Netherlands**

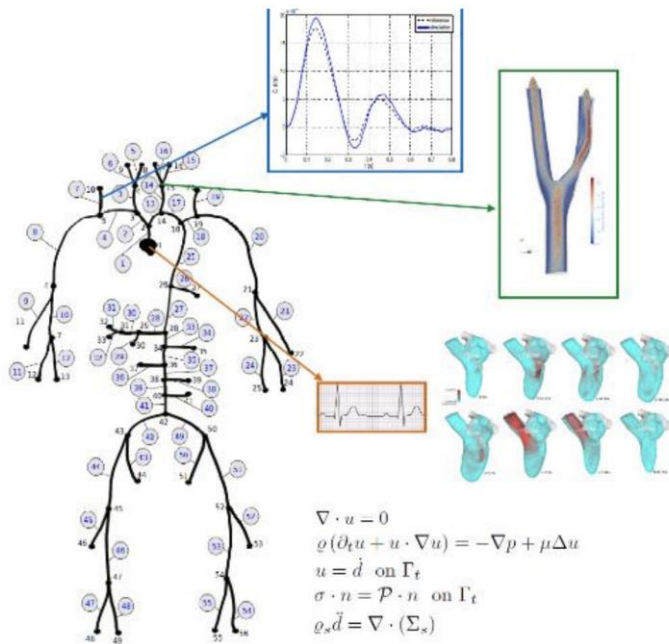


**MSc in Industrial  
Mathematics: Spain**



# Research Project

## Modelling and numerical simulation applied to the prediction of the effect of drugs in our cardiovascular system



Develop novel *in silico* models to describe the effect of drugs on the cardiovascular function (changes in pressure, flow, arteries stiffness)



Validation of the model with experimental data:

- Regional flow rate (ESR11)
- Artery Wall displacements (ESR10)
- Local blood pressure simultaneously assessed by intravascular catheters



Develop markers by using mathematical modelling. Perform classification tasks and estimate quantities of interest given the experimental measurements.



Relate measurements with the predictions using machine learning algorithms and data assimilation techniques



Practical tool through a web application

# Training & Secondments



Universiteit  
Antwerpen



# Thank You For Your Attention

Contact: [sara.costa-faya@inria.fr](mailto:sara.costa-faya@inria.fr)

# Charles Van Assche

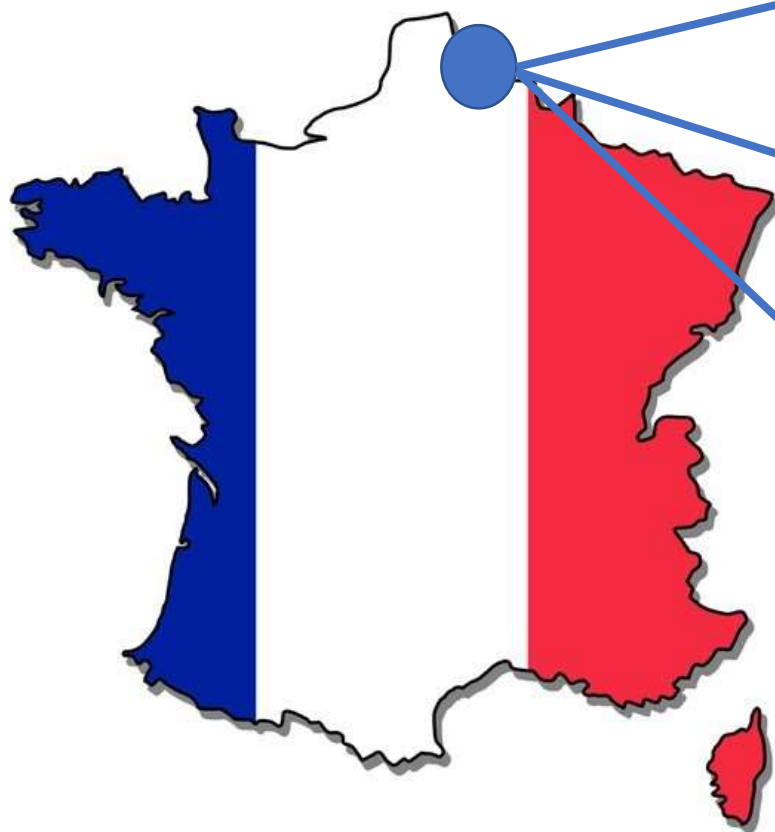
Maastricht University

M4i platform



# Personal Background

France



Université  
de Lille

MSc Bio-analytical chemistry

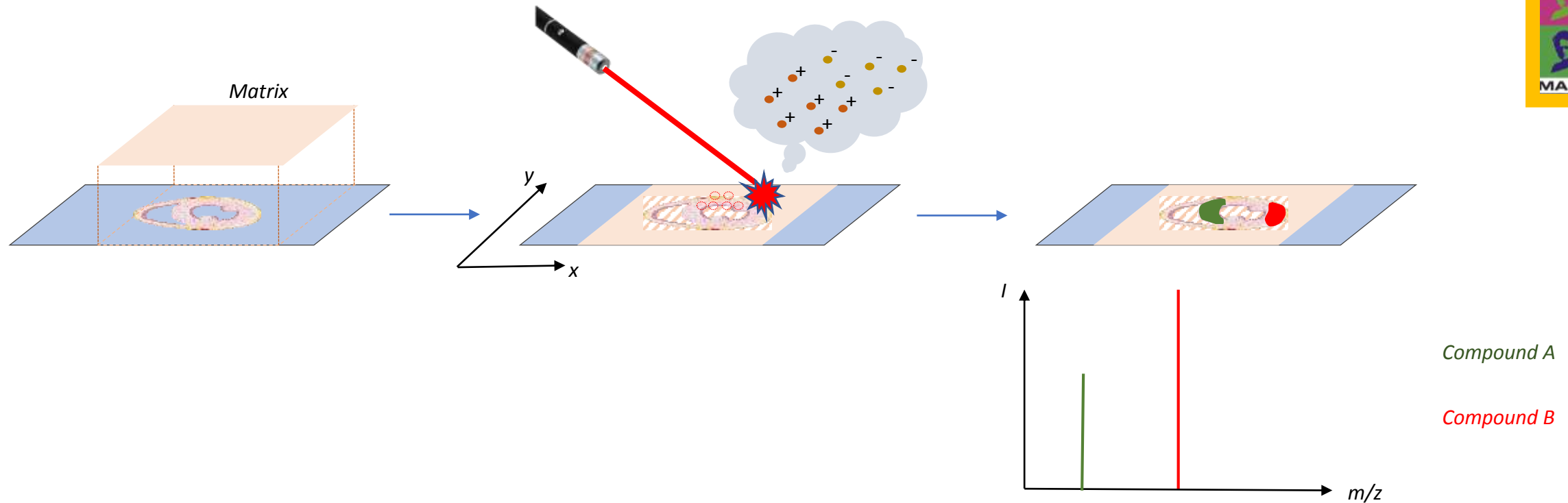


**imabiotech**  
accelerating discovery, driving innovation



# Research Project

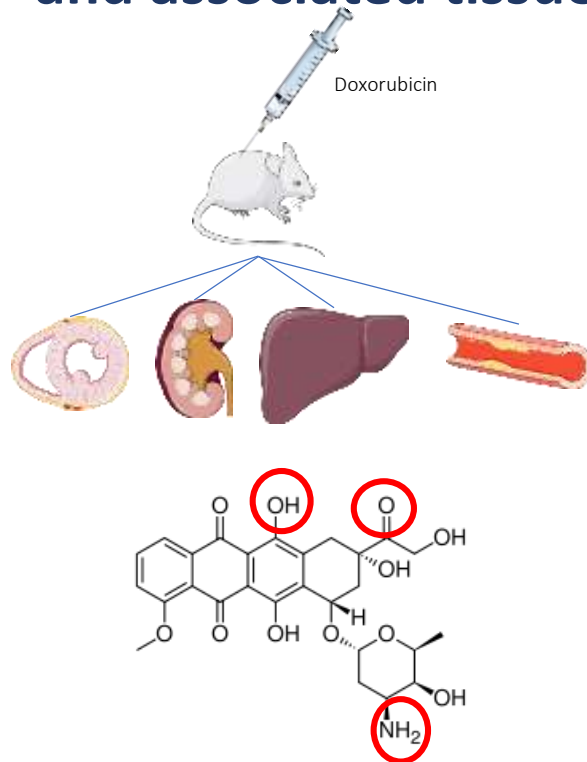
## Principle of Mass Spectrometry Imaging





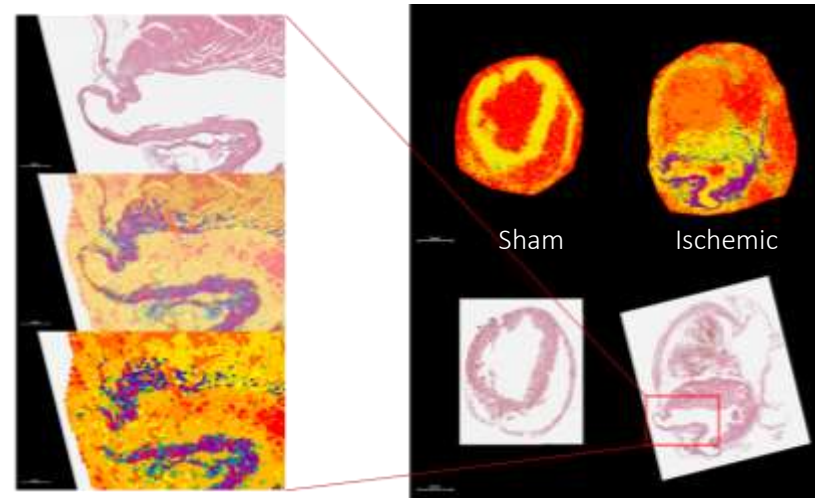
# Research Project

## Development of mass spectrometry imaging tools to study drug distribution and associated tissue-specific effect



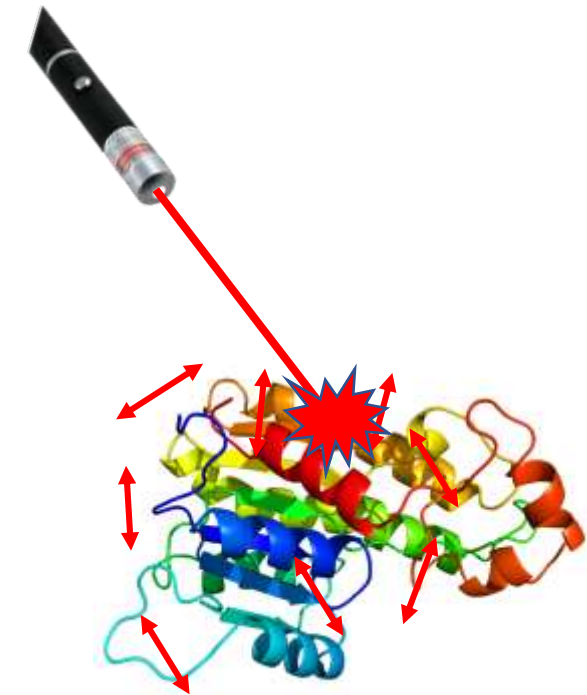
- 1) Derivatization strategies to enhance detection of Doxorubicin in dosed tissues

Localization of doxorubicin in heart, aorta and muscle & metabolism products



- 2) Peptides imaging in ischemic hearts

Spatially resolved biological effects (glycans and proteins)



- 3) Proteomics combined with MSI on dosed tissue

# Training & Secondments



Proteomics

(source: Bruker.com)



Laser-capture  
Microdissection

(source: Leica.com)



Cardiomyocytes culture



Instruments training

Tutorials & teaching  
activities



Mass Spec summer school



# Thank You For Your Attention

Contact: [c.vanassche@maastrichtuniversity.nl](mailto:c.vanassche@maastrichtuniversity.nl)

# Callan Wesley

University of Antwerp

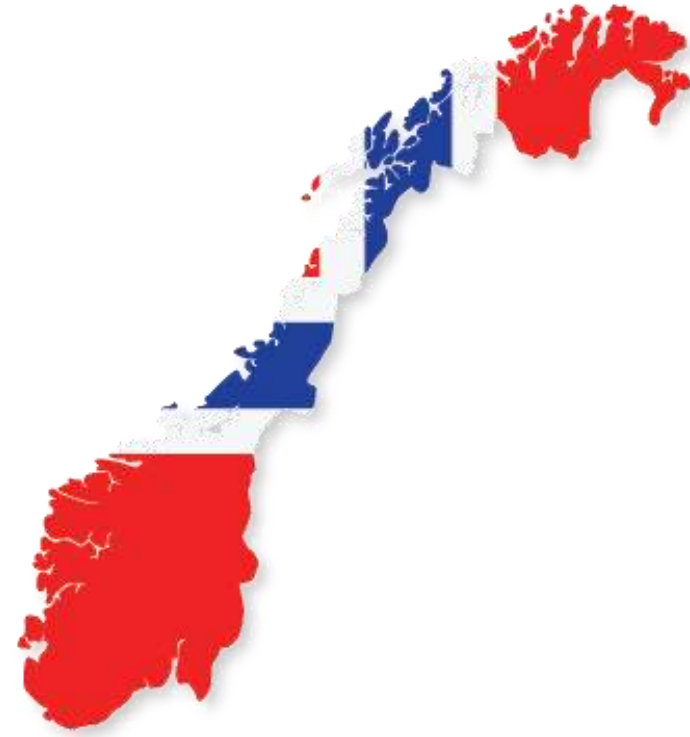


# Personal Background

## South Africa



## Norway

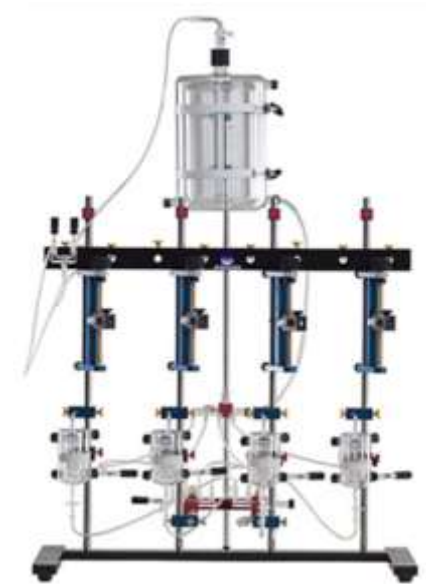
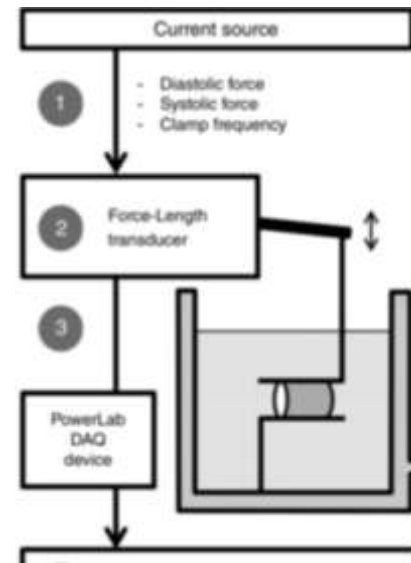


# Research Project

Measuring arterial stiffness at different scales: a new toolbox for safety pharmacology



*In Vivo*



*Ex Vivo*

# Training & Secondments



*Inria*





# Thank You For Your Attention

Contact: [Callan.Wesley@uantwerpen.be](mailto:Callan.Wesley@uantwerpen.be)

# Marieke Van Daele

University of Nottingham

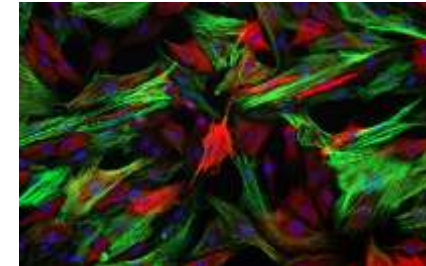


The University of  
**Nottingham**

UNITED KINGDOM • CHINA • MALAYSIA



# Personal Background

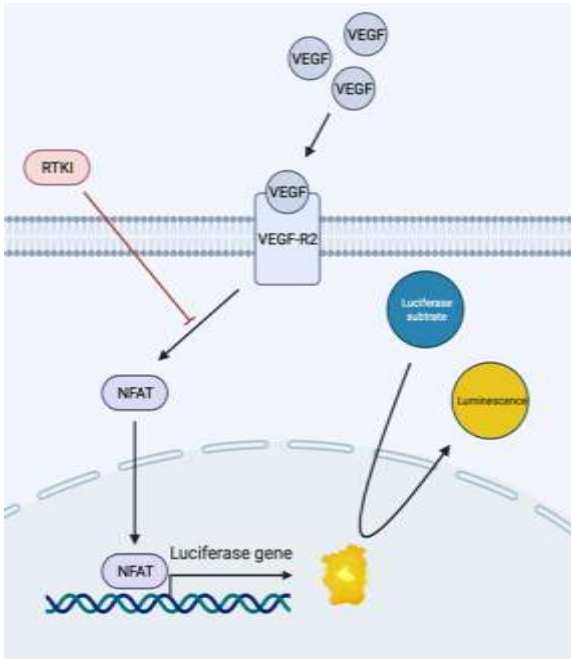


# Research Project

New preclinical screens in safety pharmacology assessment: detection of cardiovascular effects in “failed” NCE.

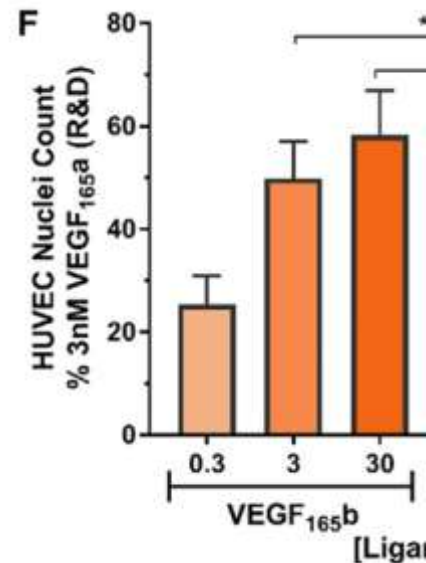
## *In vitro*

*Luciferase NFAT  
reporter gene assay*



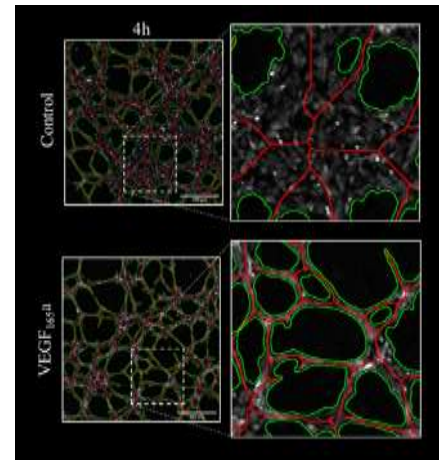
Created with BioRender.com

*HUVEC proliferation  
assay*



Peach CJ *et al.*, *Cell  
Chemical Biology* (2019)

*Livecyte cytometer*



Mignone VW *et al.* unpublished.

## *Ex vivo*

*Pressure myography*



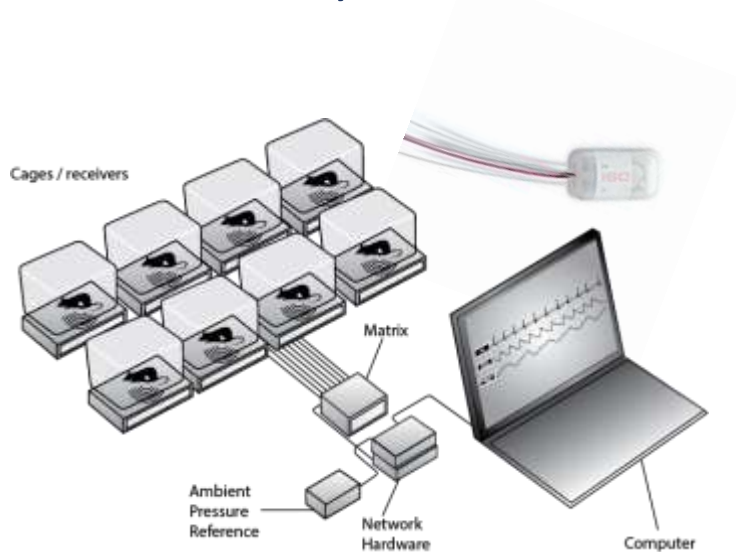
Image from InsideScientific.com

# Research Project

New preclinical screens in safety pharmacology assessment: detection of cardiovascular effects in “failed” NCE.

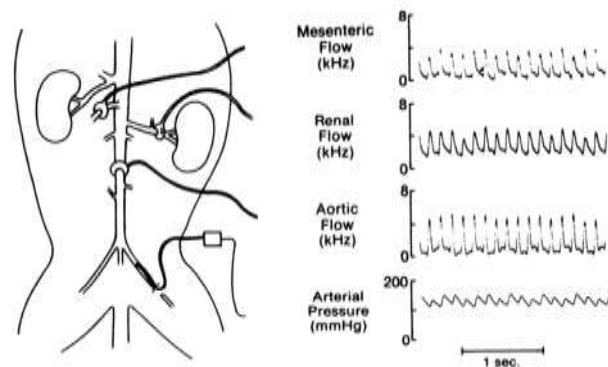
*In vivo*

*Radiotelemetry*



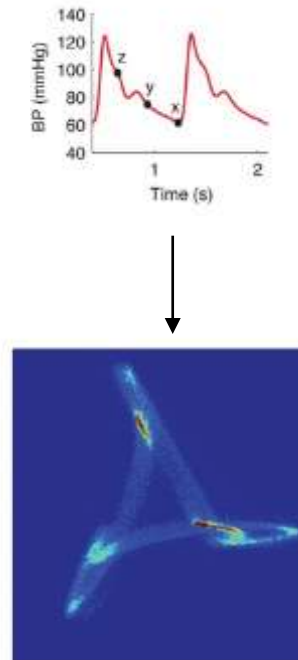
Images from Datasci.com

*Doppler flow model*



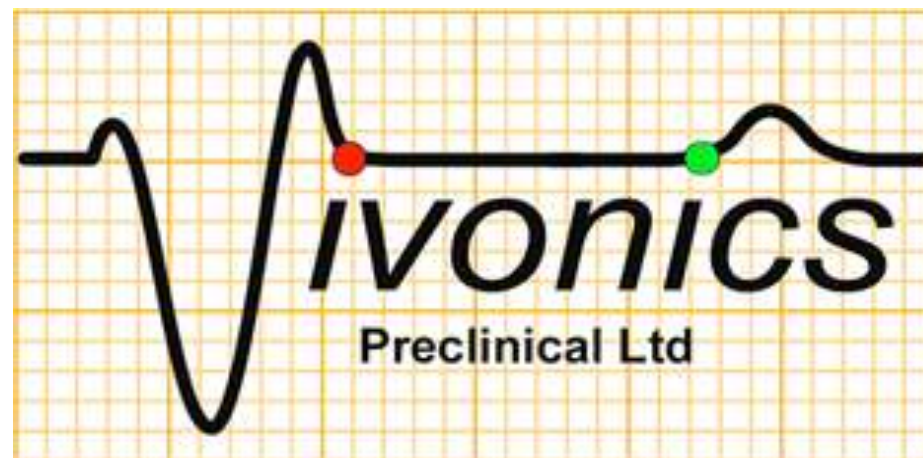
Haywood, J. R. *et al.*  
*C. Am. J. Physiol. - Hear. Circ. Physiol.* (1981)

*Attractor reconstruction*



Nandi, M. & Aston, P. J. *Exp. Physiol.* (2020)

# Training & Secondments





# Thank You For Your Attention

Contact: [marieke.vandaele@nottingham.ac.uk](mailto:marieke.vandaele@nottingham.ac.uk)

# Benji van Berlo

University of Antwerp





# Personal Background



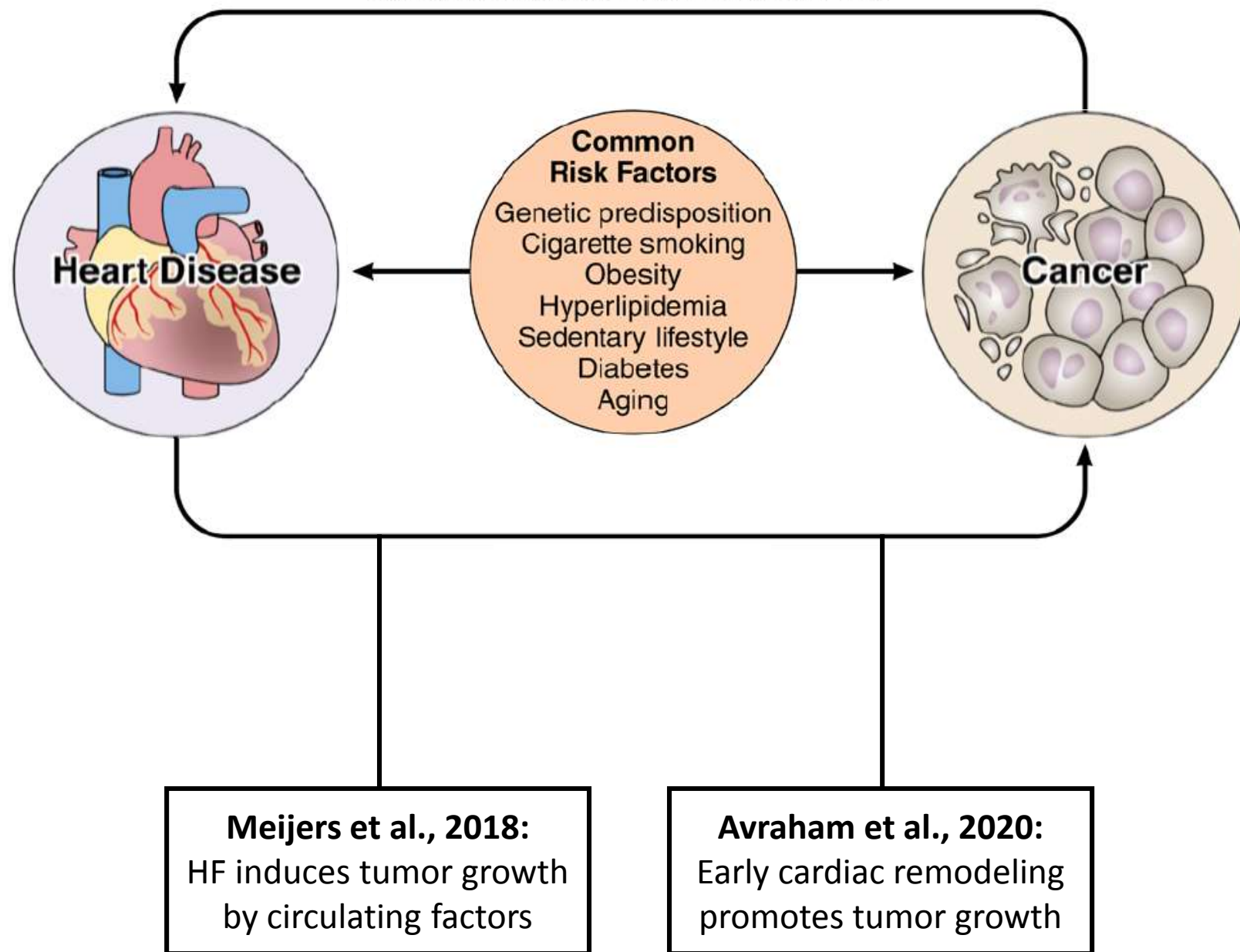
# Research Project



**Investigating the link between heart failure and cancer:  
The role of endothelial neuregulin-1 in cancer promotion**

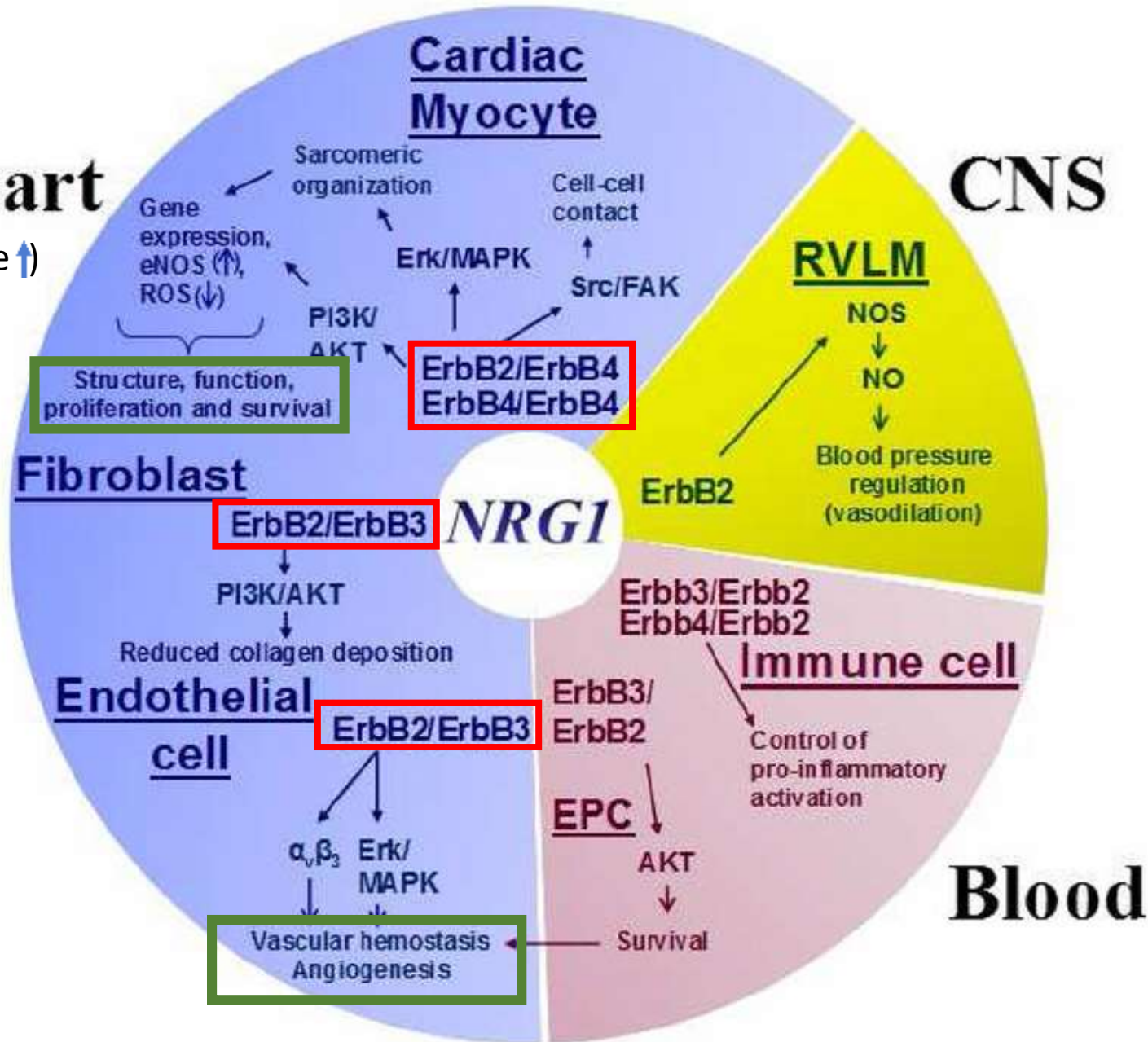


## Cancer and cancer treatment toxicities



**Heart**  
(failure ↑)

**CNS**





**CVD**

**NRG-1?**

**CANCER**



# Training & Secondments



# Thank You For Your Attention

Contact: [Benji.vanBerlo@uantwerpen.be](mailto:Benji.vanBerlo@uantwerpen.be)



# Dustin Krüger

University of Antwerp





# About me



ulm university universität  
**uulm**

- Cell biology and genetics



Universitätsklinikum  
Hamburg-Eppendorf

- Cardiology, tissue engineering, synthetic cell biology



# Research Project

Investigation of cardiotoxic effects during and after cancer treatment (*in/ex vivo*).



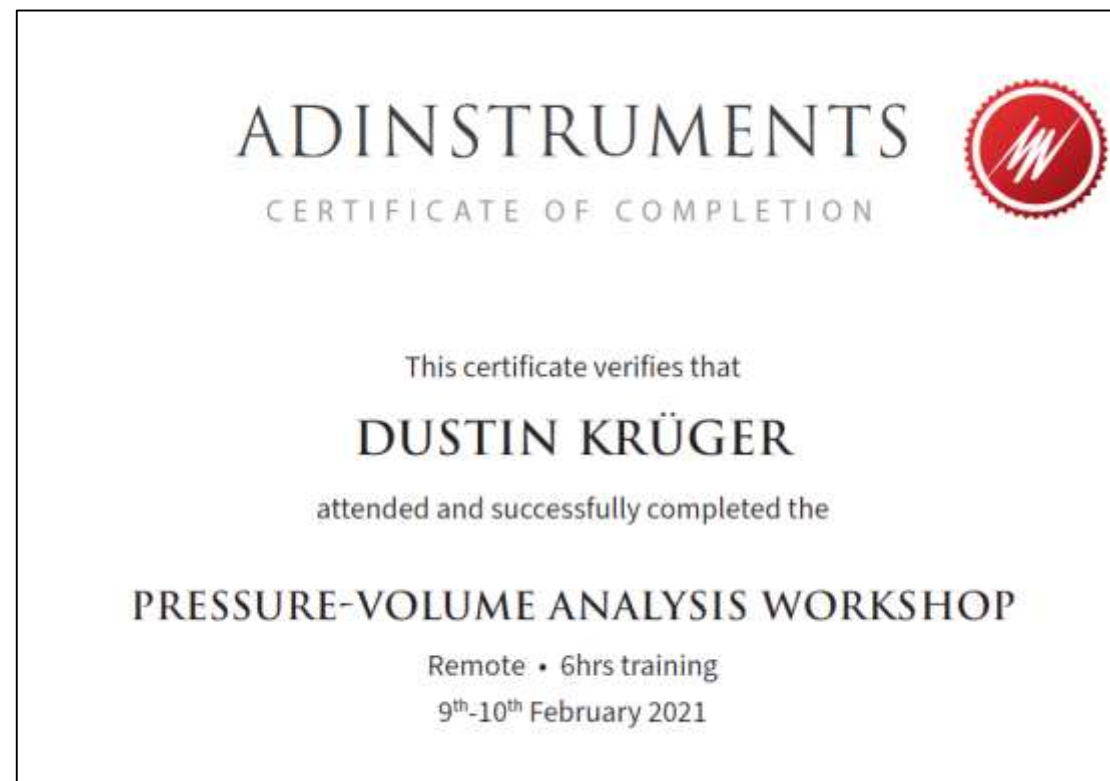
# Research Project

Investigation of cardiotoxic effects during and after cancer treatment (*in/ex vivo*).





# Training & Secondments



# Thank You For Your Attention

Contact: [Dustin.Kruger@uantwerpen.be](mailto:Dustin.Kruger@uantwerpen.be)



## Personalized safety pharmacology against drug-evoked proarrhythmia

Early Stage Researcher 15: Anna Savchenko

Supervisor: Prof. Paul Volders



# My academic background: Undergrad (2013 – 2017)

University

Moscow State  
University

Majoring in

Microbiology



- ✓ Yeast metabolism study using HPLC and molecular biology methods (cloning, PCR)

# My academic background: Master's (2018 – 2020)

University

The University of  
Tokyo

Majoring in

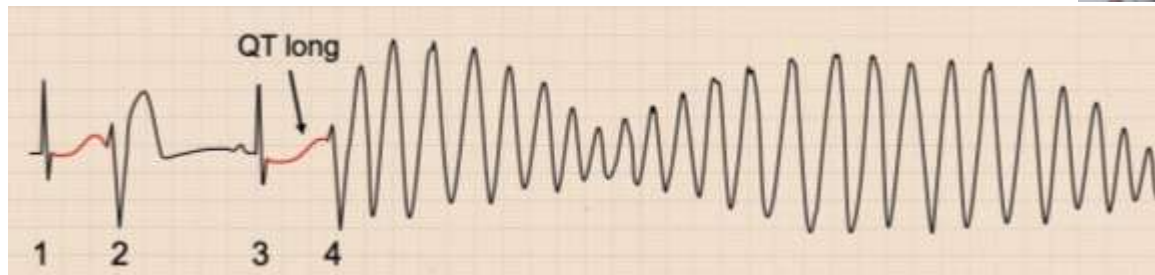
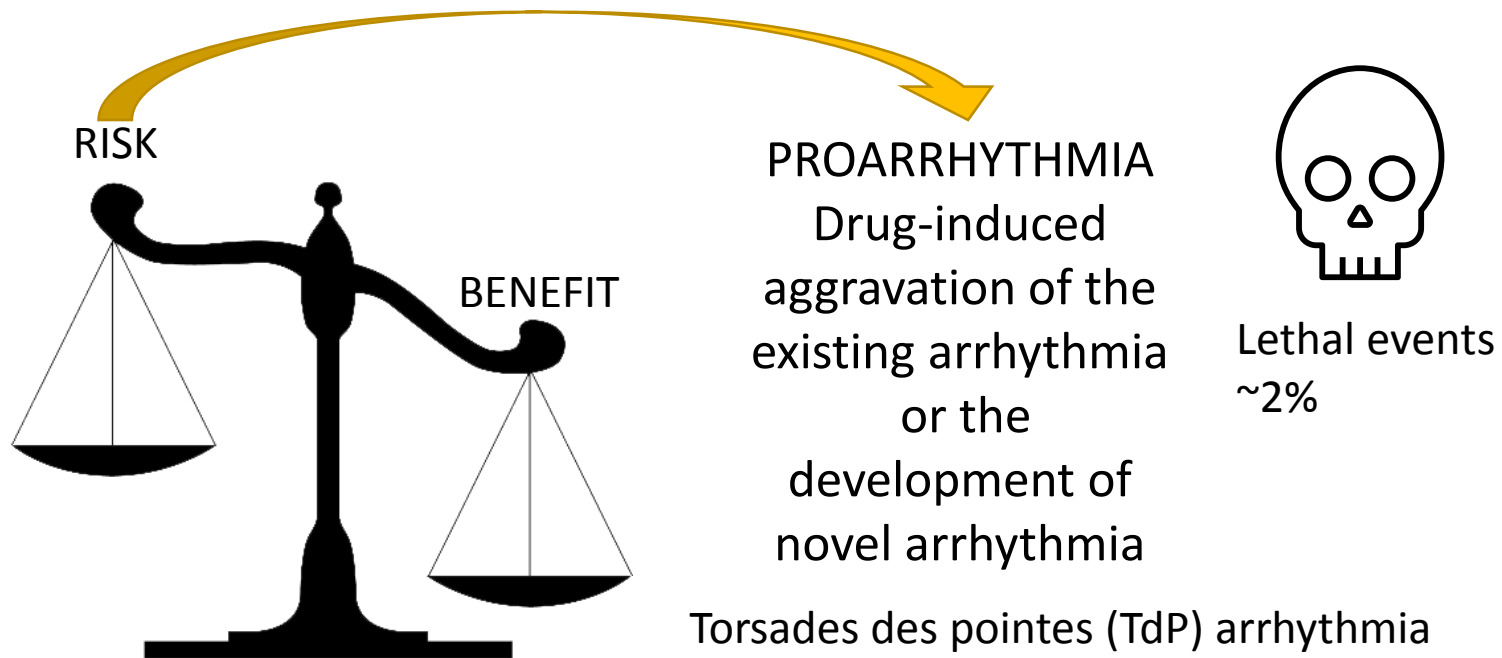
Molecular  
biology



- ✓ Construction and imaging of yeast mutants of MAPK pathway (plasmid and strain construction)



# What are the safety concerns for safety pharmacology?

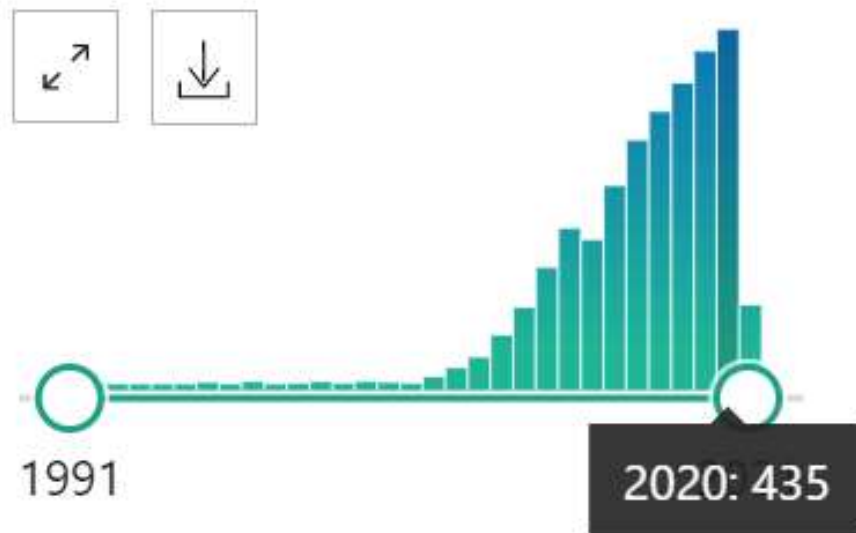


# Patient-derived iPSC-CMs is a modern revolutionary tool?

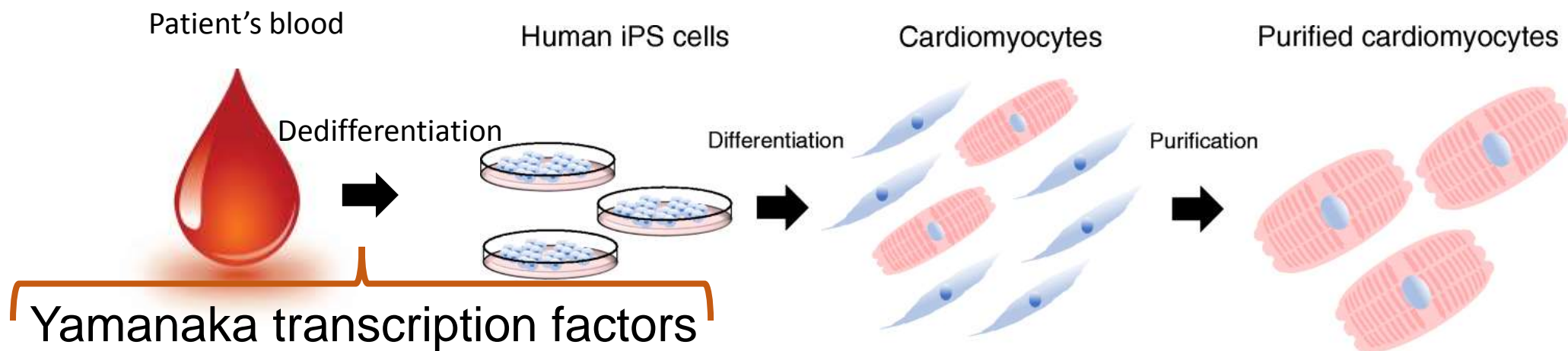
- Ethically approved
- No immune rejection
- Similar tissue
- Same genetic background

Aim of the project:  
identifying cellular  
mechanisms of a  
number of  
arrhythmogenic drugs  
and genetic factors  
predisposing to drug-  
induced  
proarrhythmias

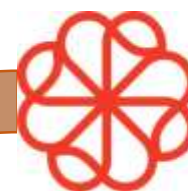
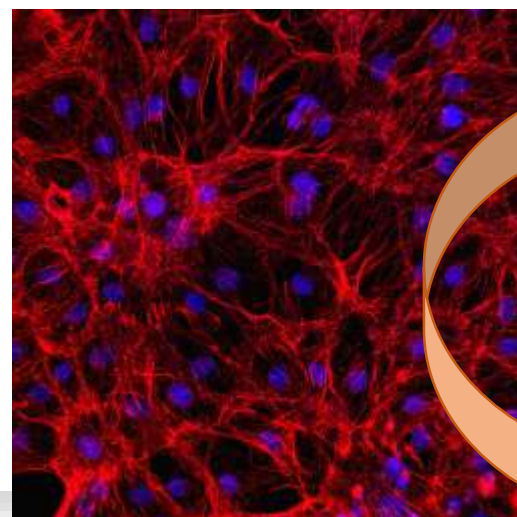
RESULTS BY YEAR



# How to establish iPSC-CMs?



Yamanaka transcription factors  
Oct3/4, Sox2, Klf4, c-Myc



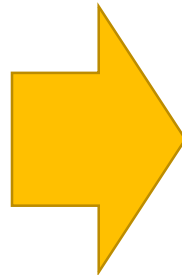
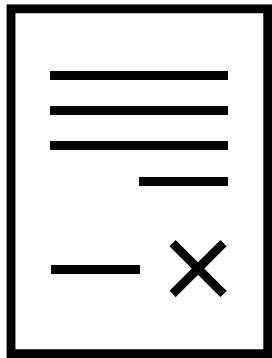
**Ncardia**  
Stem cell experts



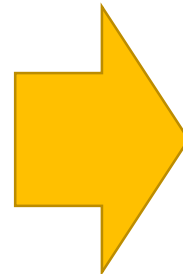
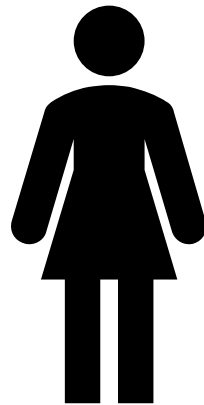
**Maastricht UMC+**

# What has been already done?

✓ Informed consent



✓ Blood drawn



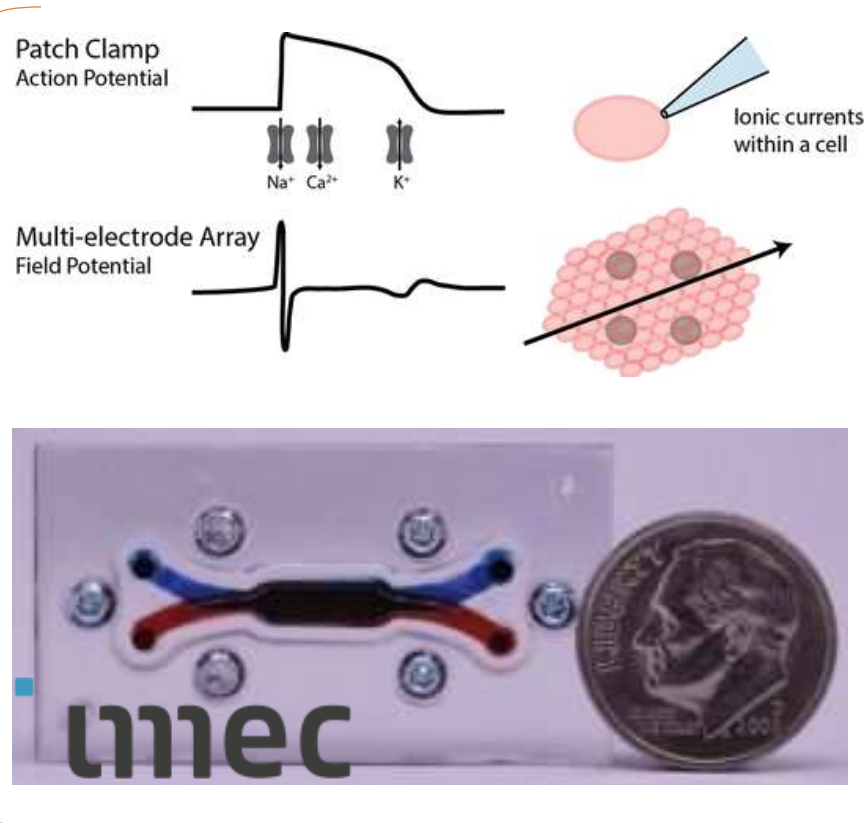
✓ Peripheral blood mononuclear cells (PBMC)



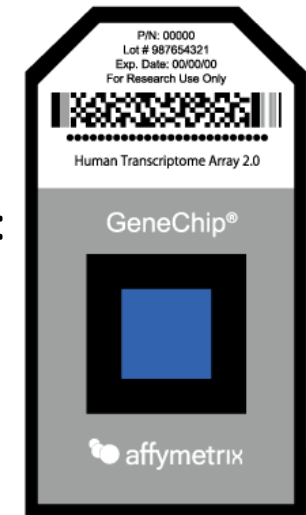


# What are the follow-up experiments on iPSC-CM to get readable output?

Electrophysiology



Transcriptome profiling:  
microarray/RNAseq



Anna Savchenko  
M.Sc. in Molecular biology  
ESR15  
Prof. Paul Volders' lab member  
[a.savchenko@maastrichtuniversity.nl](mailto:a.savchenko@maastrichtuniversity.nl)

