NANOTOX CHIP
Development of a cytotoxicity chip for screening of toxicity of multiple-size nanoparticles on multiple cell types in parallel

Dr. Andries D. van der Meer
Assistant Professor Applied Stem Cell Technologies
Coordinator Strategic Research Orientation ‘Organs-on-Chips’
Living **microsystems** that emulate human **physiology** in the lab

Picture: Martin Straver
Atherosclerosis-on-a-Chip – Collaboration with Maastricht University and Baker IDI Heart & Diabetes Institute

Vascular tissue

Inflammation

Fluid dynamics

Q = 0.5 ml/hr
v = 9 mm/s

Wall shear rate (s⁻¹)

1000 4000 8000

§ 52 µm

§ 300 µm

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http://dx.doi.org/10.1073/pnas.1209905110
Atherosclerosis-on-a-Chip – Collaboration with Maastricht University and Baker IDI Heart & Diabetes Institute

http://dx.doi.org/10.1073/pnas.1209905110

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Precision Medicine

- The average patient doesn’t exist
- Finding the ‘blue’ patient: precision medicine

http://dx.doi.org/10.1038/520609a
Precision Medicine

- Health data
  - Genomics, transcriptomics, metabolomics, microbiomics
  - Blood pressure, heart rate
  - Exercise, diet
  - Health, disease, prevention and treatment, outcome

“The Precision Medicine Initiative will leverage advances in genomics, emerging methods for managing and analyzing large data sets while protecting privacy, and health information technology to accelerate biomedical discoveries. The Initiative will also engage a million or more Americans to volunteer to contribute their health data.”

Mandel Ngan/AFP/Getty
Precision Medicine

- Health data
  - Genomics, transcriptomics, metabolomics, microbiomics
  - Blood pressure, heart rate
  - Exercise, diet
  - Health, disease, prevention and treatment, outcome
- Analyze and find trends
Data for Precision Medicine

Biometric data

...data analysis...
...genomics, transcriptomics, metabolomics, microbiomics, blood pressure, heart rate, exercise, diet...

Outcome data

...data analysis...
...health, disease, prevention response, treatment response...

Precision Medicine

...personalized treatment options, lifestyle advice...
Data for Precision Medicine

Organs-on-Chips

Biometric data

Precision Medicine

Outcome data
Platelet inhibitors (aspirin, clopidogrel, etc.) reduce the chance of new infarctions, stroke, or death

- Identify non-responders
  - Change dose
  - Change drug

- Organs-on-Chips for Outcome Data: Thrombosis

- Platelet inhibitors (aspirin, clopidogrel, etc.) reduce the chance of new infarctions, stroke, or death
- Identify non-responders
  - Change dose
  - Change drug

http://dx.doi.org/10.1136/bmj.324.7329.71
Thrombosis-on-a-Chip – Collaboration with

- Microfluidic channel – 400 µm x 100 µm x 2 cm
- Endothelium – inflamed or healthy
- Human whole blood – labeled platelets, 30 µl/minute, 750 s⁻¹
Thrombosis-on-a-Chip – Collaboration with WYSS INSTITUTE and emulate

Blue, nuclei  Green, fibrin  Red, platelets

100 µm

[Image of a micrograph with labeled colors: Blue for nuclei, Green for fibrin, Red for platelets with a scale bar of 100 µm]

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Abhishek Jain, Andries van der Meer, Don Ingber, Unpublished
Thrombosis-on-a-Chip – Collaboration with

Platelet Coverage

100 ng/ml TNF-α
Endothelium

5 ng/ml TNF-α
Endothelium

Control Endothelium

Abhishek Jain, Andries van der Meer, Don Ingber, Unpublished
Thrombosis-on-a-Chip – Collaboration with

- Drug efficacy analysis
  - Patients on aspirin and/or clopidogrel
  - Normal control blood
  - Analyze platelet aggregation on 5 ng/ml TNF-α inflamed endothelium

- Future research
  - Is the non-responder also a non-responder in follow-up patient studies?
  - Can we use stem cell technology to engineer patient-specific channels?
Organs-on-Chips and Data for Precision Medicine

“An organ-on-a-chip is like an avatar of a patient.”
-Clive Svendsen

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Engineering the Avatar: 3D Biofabrication

Human cerebral endothelial cells, human astrocytes.
Green: VE-Cadherin, Blue: Nuclei, Red: F-actin

100 µm
Technology Development

- Biomaterials
- Microfluidics
- Sensors
- Stem cell technology
- Actuators
- Imaging and image analysis
- Automation and mechanical engineering
- User interface design
- Control systems engineering

"If we don’t know what the final product will look like, we should design it through agile engineering."

-Daniel Levner
THANK YOU!