



Corporate Overview

2013

TissUse: Emulating Human Biology

Company:

- *Berlin-based “human on a chip” company founded in 2010*
- *Dr. Uwe Marx, renowned bioreactor expert and serial biotech entrepreneur (VITA 34, ProBioGen)*
- *The four founders each have a 15- to 20-year track record in tissue engineering and organogenesis*
- *Engineering experience include human skin, lymph node, bone-marrow, liver, intestine, trachea, hair follicle, and microcapillaries*
- *Human-like safety and diseases models for compound testing*
- *Tissue regeneration technology for therapeutic application*

Social and commercial value

Problem: *Drugs pass preclinical, but fail in clinical development*

Innovation Need:

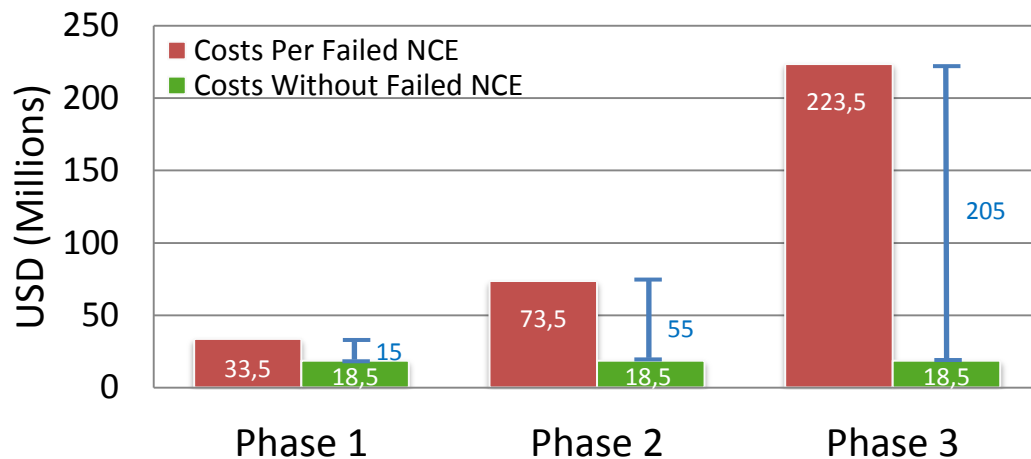
Of 100 New Chemical Entities (NCEs) progressed from preclinical to clinical development :

- *46 fail due to toxicity*
- *35 fail due to lack of efficacy*

Current Market:

- *USD 612 million estimated annual spending on preclinical efficacy testing in disease models*
- *USD 260 million estimated annual spending on preclinical ADME-Tox testing*

Cost-Savings of Eliminating Failed NCEs



By eliminating NCEs in pre-clinic, large cost savings can be attained:

- *Phase I: USD 15 million*
- *Phase II: USD 55 million*
- *Phase III: USD 205 million*

S. M. Paul et Al. How to improve R&D productivity: the pharmaceutical industry's grand challenge.

Nature Reviews Drug Discovery. 2010. (9), 205-214.

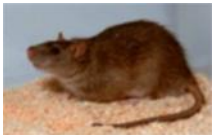
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The Substance Testing Dilemma

TISSUSE
Emulating Human Biology



“human on a chip”
human AND systemic



animal models
systemic but NOT human

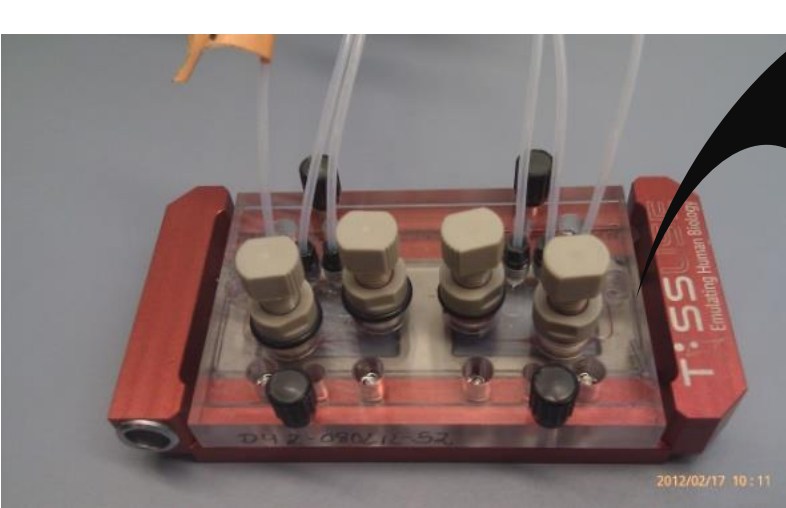


static 2D & 3D
human cell culture
human but NOT systemic

Mission

- *Establish miniaturized equivalents to human organs, physiologically combined into multi-organ arrangements to truly emulate human organismal long-term homeostasis*
- *Develop qualified on-chip assays for safety and efficacy evaluation of substances in a human organismal setting*
- *Provide automation tools for high content analysis*

The Multi-Organ Chip (MOC) Technology

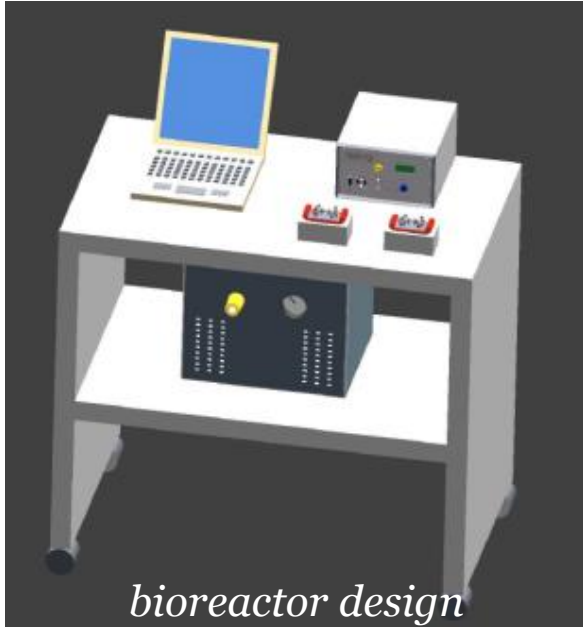


Features:

- *Chip format of a standard microscopic slide*
- *On-chip micro-pump and natural tissue to fluid ratio*
- *Variable physiological shear stresses applicable*
- *Tissue cultures 100,000-fold smaller than original organs*
- *Compatible with live tissue imaging*
- *Rapid prototyping of any relevant chip design*

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Laboratory bioreactor



bioreactor design



bioreactor in operation

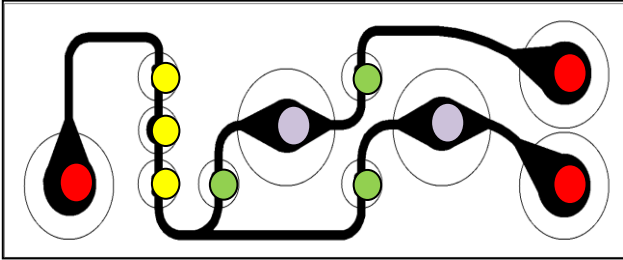
- *Controlling 12 pneumatic actors*
- *Two chips per system*
- *Adjustable temperature and fluid flow*
- *Software control (e.g. WINDOWS, LINUX, MAC)*
- *Telemonitoring*



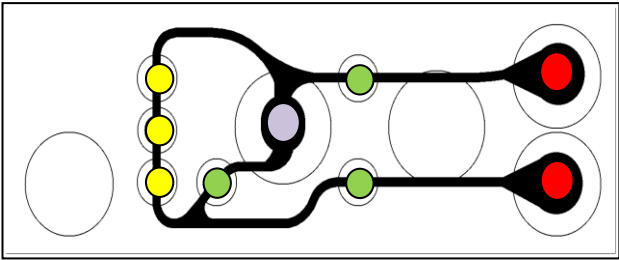
Robust manufacturing background



single “organ” perfusion chip



single “organ” circulation chip

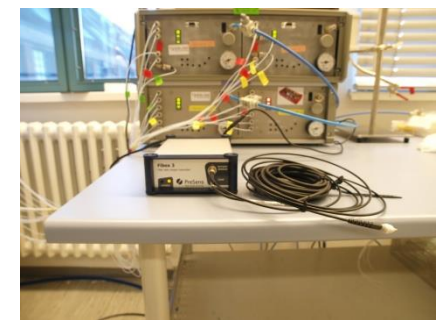
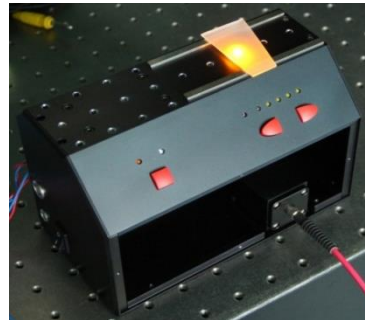


Sensors / In-process-controls

<i>parameter</i>	<i>flow velocity</i>	<i>organ viability</i>	<i>organ functionality</i>	<i>pH & pO₂</i>	<i>t°</i>
<i>approach</i>					
<i>principle</i>	<i>particle imaging velocimetry</i>	<i>fluorescence spectroscopy</i>	<i>surface plasmon resonance for secreted proteins</i>	<i>fluorescence lifetime</i>	<i>PT1000 temperature detector</i>
<i>features</i>	<i>non invasive different spots biological particles</i>	<i>cell tracker live imaging double staining possible</i>	<i>multiple proteins (46 per micro sensor 10 mm x 0.8 mm)</i>	<i>fibre coupled external calibration</i>	<i>long-term robustness</i>

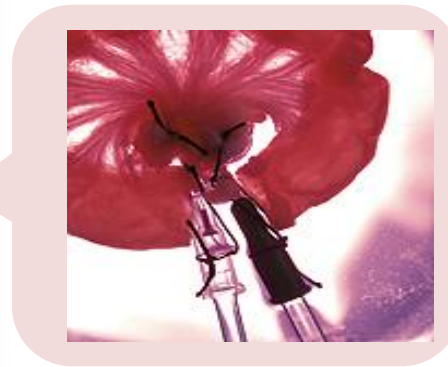
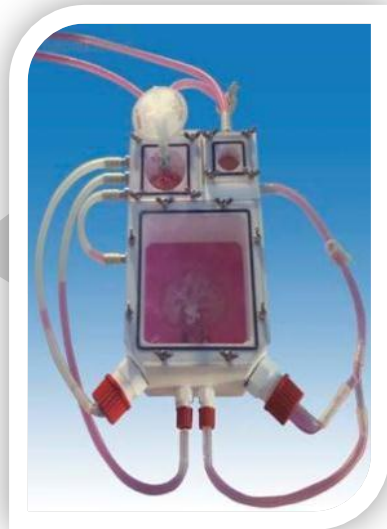
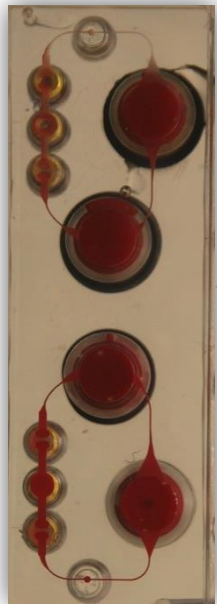


Frank Sonntag

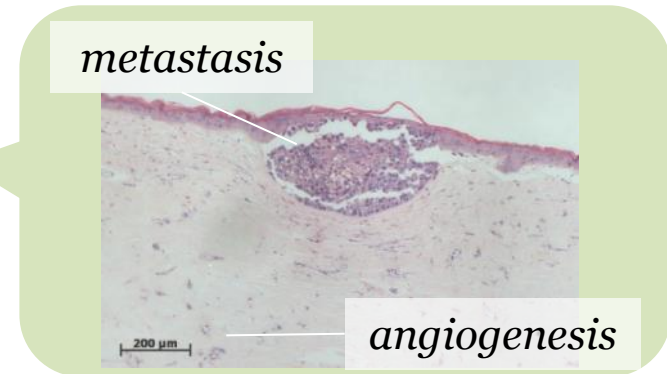


A Pipeline of Customizable Disease Models

Example: Organoid Disease Modeling - Melanoma



Jejunum vasculature scaffold

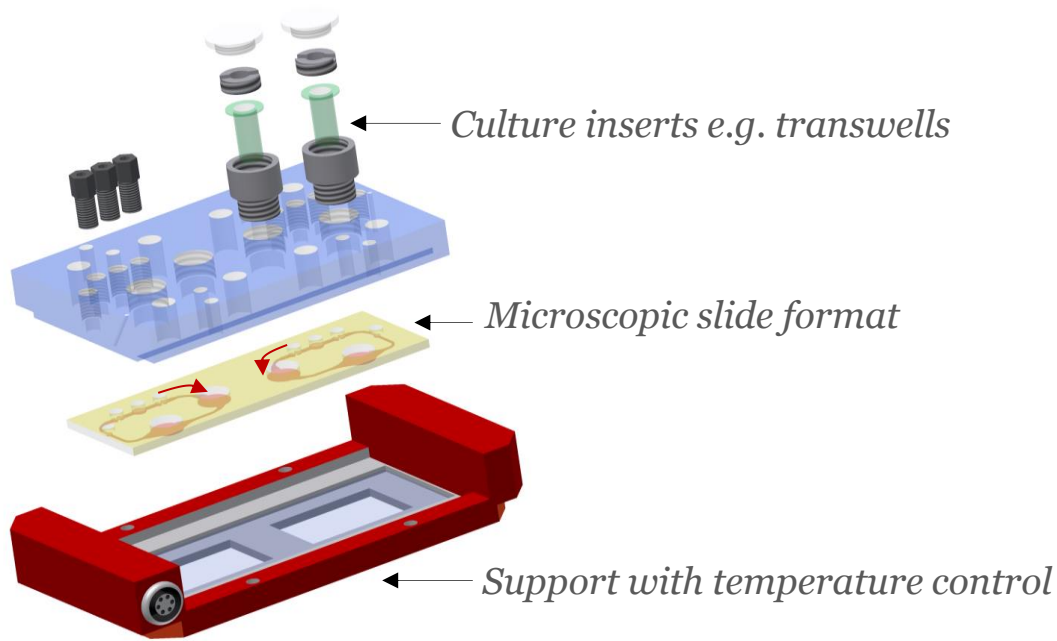


Advanced skin cancer model

Goal: Candidate evaluation – generate human-like data in preclinical

More to come: liver disease, infectious disease, cancer, auto-immune

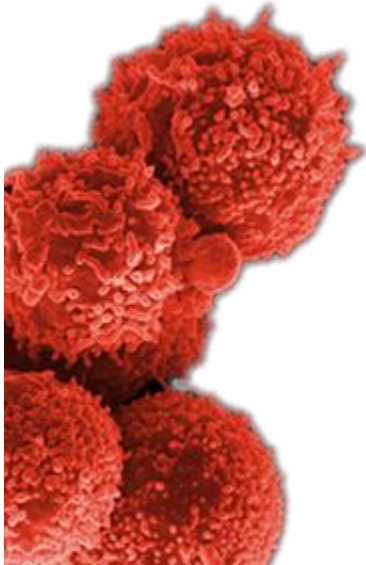
The human liver + “one” chip



Duration + „organ“	Short-term (<48h)	Long-term (<28d)	Homeostasis (90d, 1y...)
skin	✓	✓	in progress
vasculature	✓	✓	in progress
intestine	✓	in progress	in progress
lymph node	in progress	in progress	-

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