TISSUSE

Emulating Human Biology

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*

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Social and commercial value

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

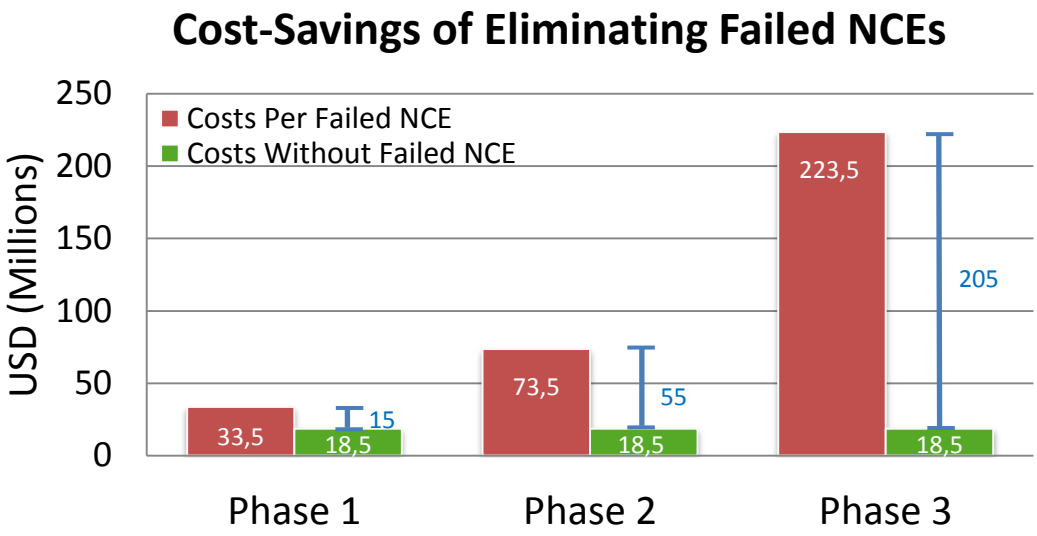
Innovation Need:

Of 100 New Chemical Entities (NCEs) progressed form 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*



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

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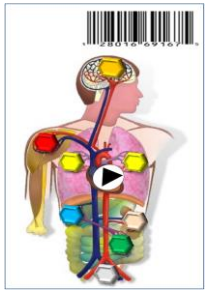
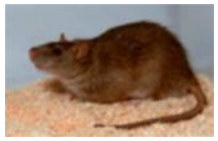


"human on a chip"

human AND systemic



animal models

systemic but NOT human

static 2D & 3D
human cell culture

human but NOT systemic

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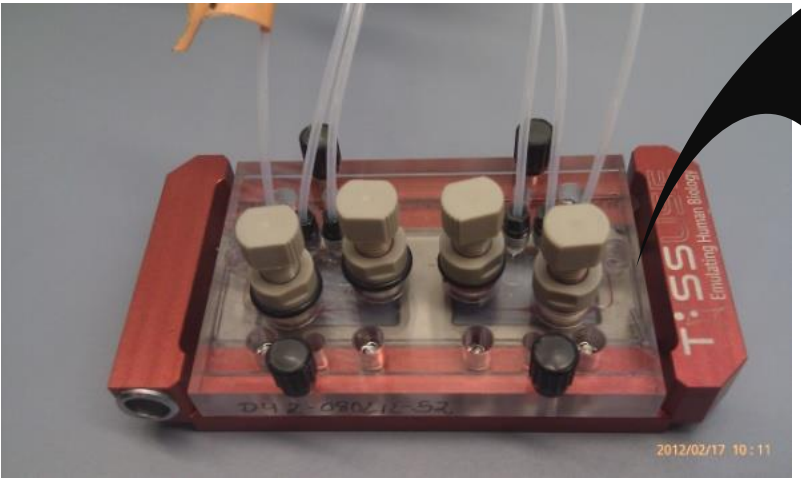
Mission

- *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 life tissue imaging*
- *Rapid prototyping of any relevant chip design*

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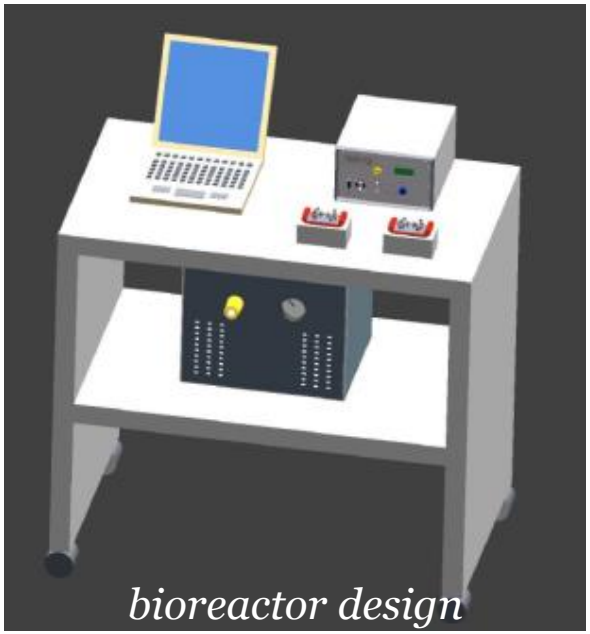
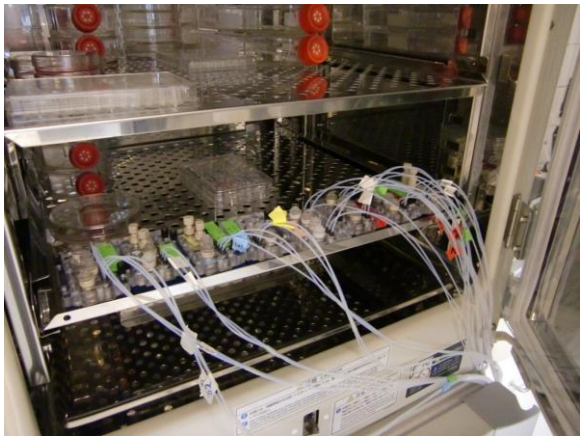
Laboratory bioreactor



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*



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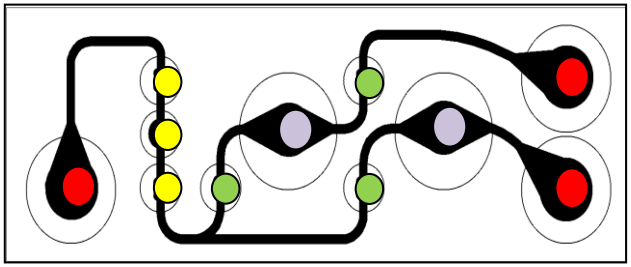
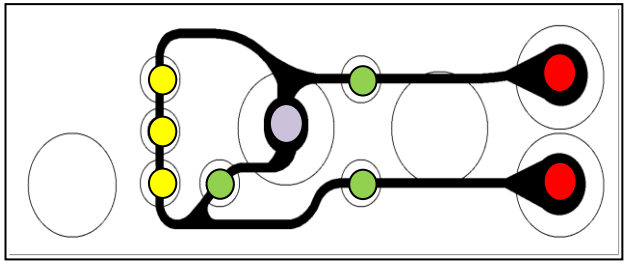
Robust manufacturing background

single "organ" perfusion chip



single "organ" circulation chip



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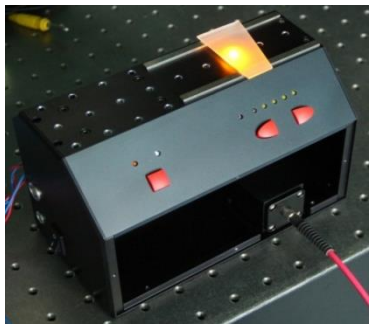
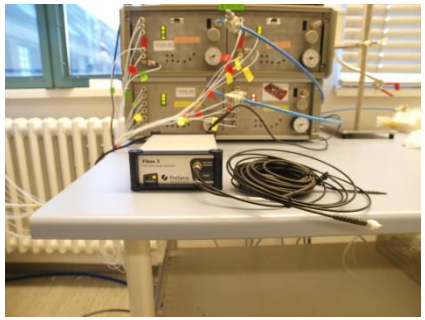
Sensors / In-process-controls

parameter / approach	flow velocity	organ viability	organ functionality	pH & pO_2	t°
principle	*particle imaging velocimetry*	*fluorescence spectroscopy*	*surface plasmon resonance for secreted proteins*	*fluorescence lifetime*	*PT1000 temperature detector*
features	*non invasive different spots biological particles*	*cell tracker live imaging double staining possible*	*multiple proteins (46 per micro sensor 10 mm x 0.8 mm)*	*fibre coupled external calibration*	*long-term robustness*

Frank Sonntag

Fraunhofer IWS





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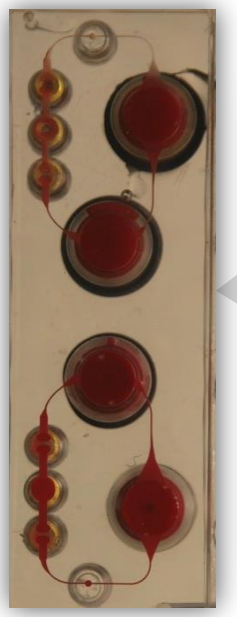
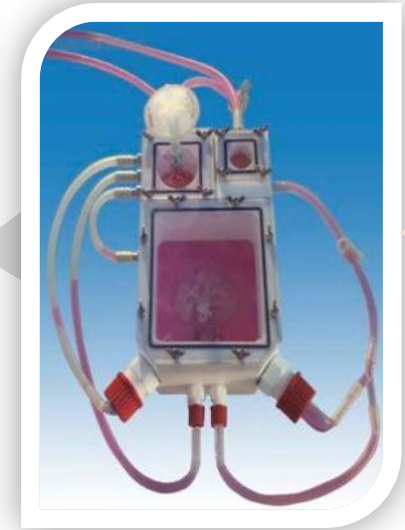
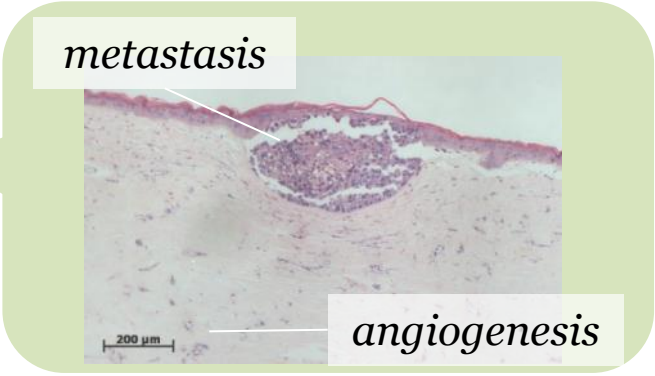
A Pipeline of Customizable Disease Models

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

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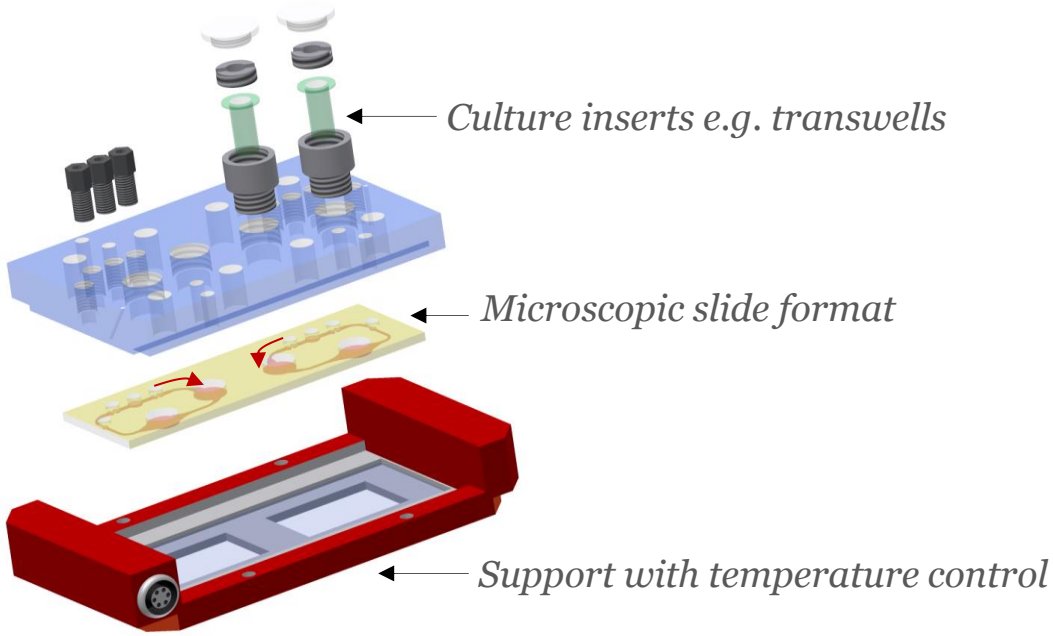
The human liver + “one” chip



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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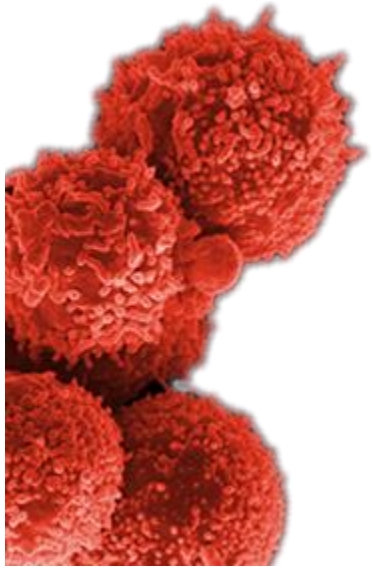
Contact



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