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1 *Assembly of Organ-on-a-Chip system.*

MICROPHYSIOLOGICAL ORGAN-ON-A-CHIP SYSTEMS

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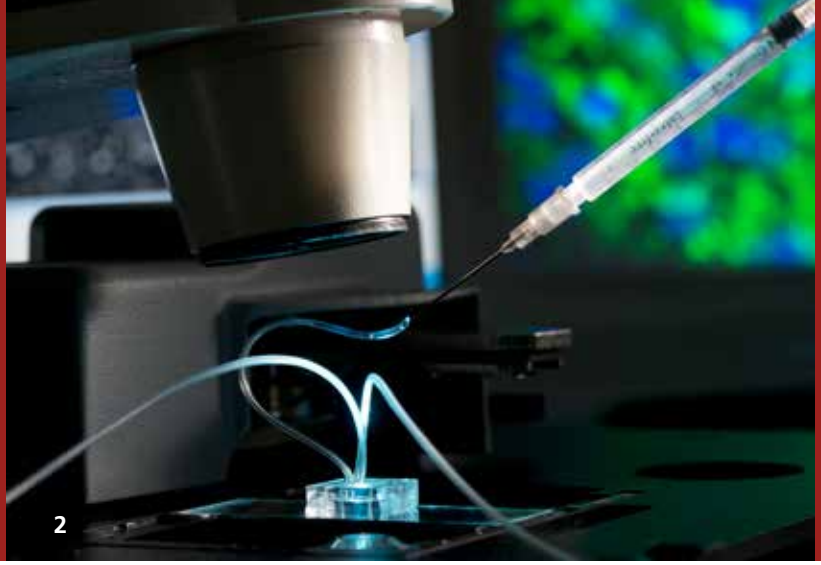
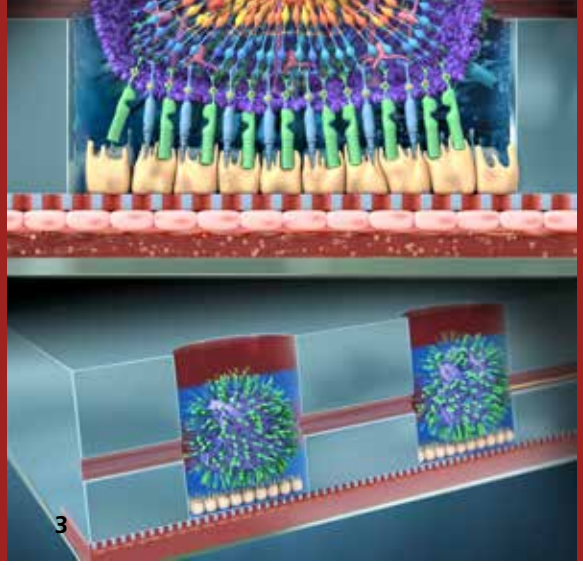
Limitations of current models

The drug discovery pipeline to date is characterized by ever-increasing costs and time durations to bring a single drug to the market. Current research in drug discovery and development is inhibited by two major barriers: the unacceptable risks of experimental *in vivo* interventions in people as well as the limited comparability of non-human animal models and conventional cell assays to human physiology. Animal models and cell assays, moreover, do not only play a key role in pharmaceutical research but also in the cosmetics and chemical industries, as well as in academic research. However, even highly developed animal models are not able to replicate the complex human body, particularly human disease, and are additionally ethically questionable. Cell assays, on the other hand, are often of cancerous tissue origin and are cultured in two dimensional monocultures in a static bath of media. The physiological relevance of these cultures compared to human tissue is thereby very limited and obtained results often do not correctly predict a drug's effect in humans.

Organ-on-a-Chip – Ushering a new era of drug discovery and development

In the Fraunhofer Attract Group of Jun.-Prof. Dr. Peter Loskill microphysiological Organ-on-a-Chip (OoC) platforms are being developed and utilized. OoCs recapitulate *in vitro* the *in vivo* structure and functionalities of human organs and tissues by integrating 3D cell constructs into a perfused physiological microenvironment. Drawing from microfabrication, biomaterial, and induced pluripotent stem cell (iPSC) technologies, the systems combine the unique features of classical cell assays (human genetic background) and of animal





models (complex physiology). They provide the potential to improve the predictive value of preclinical results and thus make the entire development process more cost-effective, safer and faster.

Services

- **Development, characterization, and fabrication of tissue- and application-specific Organ-on-a-Chip systems**
  based on microfluidic modules consisting of (combinations of) various elastomeric or thermoplastic materials, which can be further functionalized with specific surface modification
- **Development of enabling technologies**
  for scale-up, automation as well as multi-organ integration
- **Testing and validation of compounds as well as disease modeling**
  making use of our already established OoC platforms (Box 1) including for instance:
  I) Retina-on-a-Chip systems, comprising all essential cell types (derived from iPSCs) as well as the complex stratified structure of the human retina. Suited for applications related to retinal diseases such as age-related macular degeneration, retinitis pigmentosa and diabetic retinopathy.
  II) White adipose tissue (WAT)-on-a-Chip systems, integrating human primary adipocytes in a 3D vascularized environment with tissue-specific extracellular matrix.
  III) Heart-on-a-Chip, representing a physiological relevant *in vitro* model for studying cardiovascular disease based on a functional 3D cardiac microtissue derived from human iPSCs.

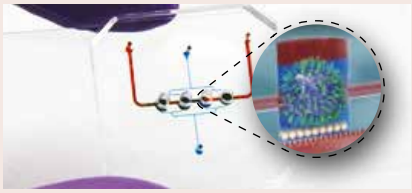
Expertise

- Many years of experience in the design, fabrication, and testing of Organ-on-a-Chip systems
- Experts from various disciplines (biology, physics, engineering, chemistry) experienced in tackling interdisciplinary challenges
- Goal-driven and application oriented development of entirely new approaches
- Directed differentiation of induced pluripotent stem cells
- Isolation of a variety of human cell types and access to patient material
- Integration of biofunctional materials into OoC systems

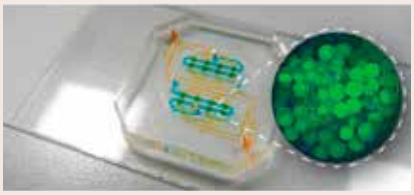
2 *Organ-on-a-Chip system during analysis.*

3 *Retina-on-a-Chip.*

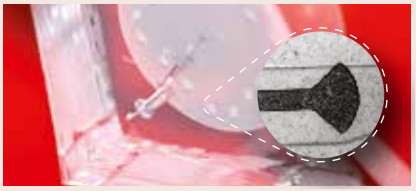
Examples of Organ-on-a-Chip systems



Retina-on-a-Chip
Recapitulation of the complex stratified multi-cellular structure of the human retina enabling the study of physiological mechanisms and intra-tissue interactions, so far not achievable *in vitro*.



WAT-on-a-Chip
Recapitulation of human white adipose tissue in a 3D perfused environment important for research on PK/PD, ADMET as well as metabolic diseases.



Heart-on-a-Chip
Recapitulation of human myocardial tissue in a strongly anisotropic 3D structure featuring physiological beating and suitable for cardiotoxicity evaluations.