micronit
microfluidics

organ-on-a-chip revolutionises cell culturing

customisable, accessible & scalable

The solution is Micronit's creative product development. Now what was the question?

Whatever challenges you face or advances you'd like to make, Micronit can help. For more than 15 years, Micronit has been a leading manufacturer of high quality microfluidic products that are delivered all over the world. We provide microfabrication services, such as micro-structuring of glass, silicon and polymer components for life sciences and medical applications.

We create large scale manufacturing solutions as well as specific, unique prototypes. With a multidisciplinary team of experts, we combine our skills and expertise to create functional and scalable industrial solutions. Designed for manufacturability, reliability and robustness.

At Micronit we believe in strong, collaborative partnerships. Few companies are better placed to offer a total tailored solution, because few offer our breadth of expertise. This brochure provides an overview of our technical capacities as well as our versatile platform for organ-on-a-chip applications.

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Organ-on-a-chip is a field that will revolutionalise our insights into the **building blocks of life**.

It will change and expedite the way we will be able to **cure diseases** and **improve our wellbeing**.

what is organ-on-a-chip?

Organ-on-a-chip empowers a newly developed multi-disciplinary field, in which human cell biology and micro-fluidics are merged on top of a lab-on-a-chip architecture that is created by advanced biomedical engineering, bioMEMS, microfabrication and micro-electronics.
It's not about recreating entire synthetically produced organs on a chip, but about mimicing human organ functionality, micro-physiology and morphology *in vitro.*

According to the pioneering founders of the Wyss Institute, organ-on-a-chip is, "a microfluidic cell culture device... inhabited by living cells arranged to simulate tissue- and organ-level physiology... These devices produce levels of tissue and organ functionality not possible with conventional 2D or 3D culture systems. They also enable high-resolution, real-time imaging and *in vitro* analysis of biochemical, genetic and metabolic activities of living cells in a functional tissue and organ context. This technology has great potential to advance the study of tissue development, organ physiology and disease etiology." *

** Source: Donald E. Ingber et.al., Nature Biotechnology vol. 32 number 8 august 2014.*

micronit's technologies offer the following 5 benefits

5-and-1

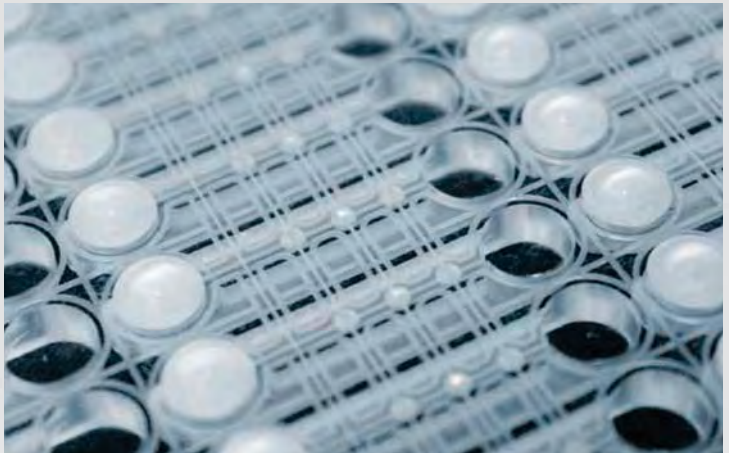
Customisable tissue culturing under dynamic microfluidic flow conditions

Access to flow chamber and bio-content whenever required

Potential reduction, replacement and refinement (3Rs) alternatives to animal testing

Easy to setup for non-microfluidic experts for research as well as screening applications

Optional real-time monitoring and bio-sensing of 2D or 3D tissue



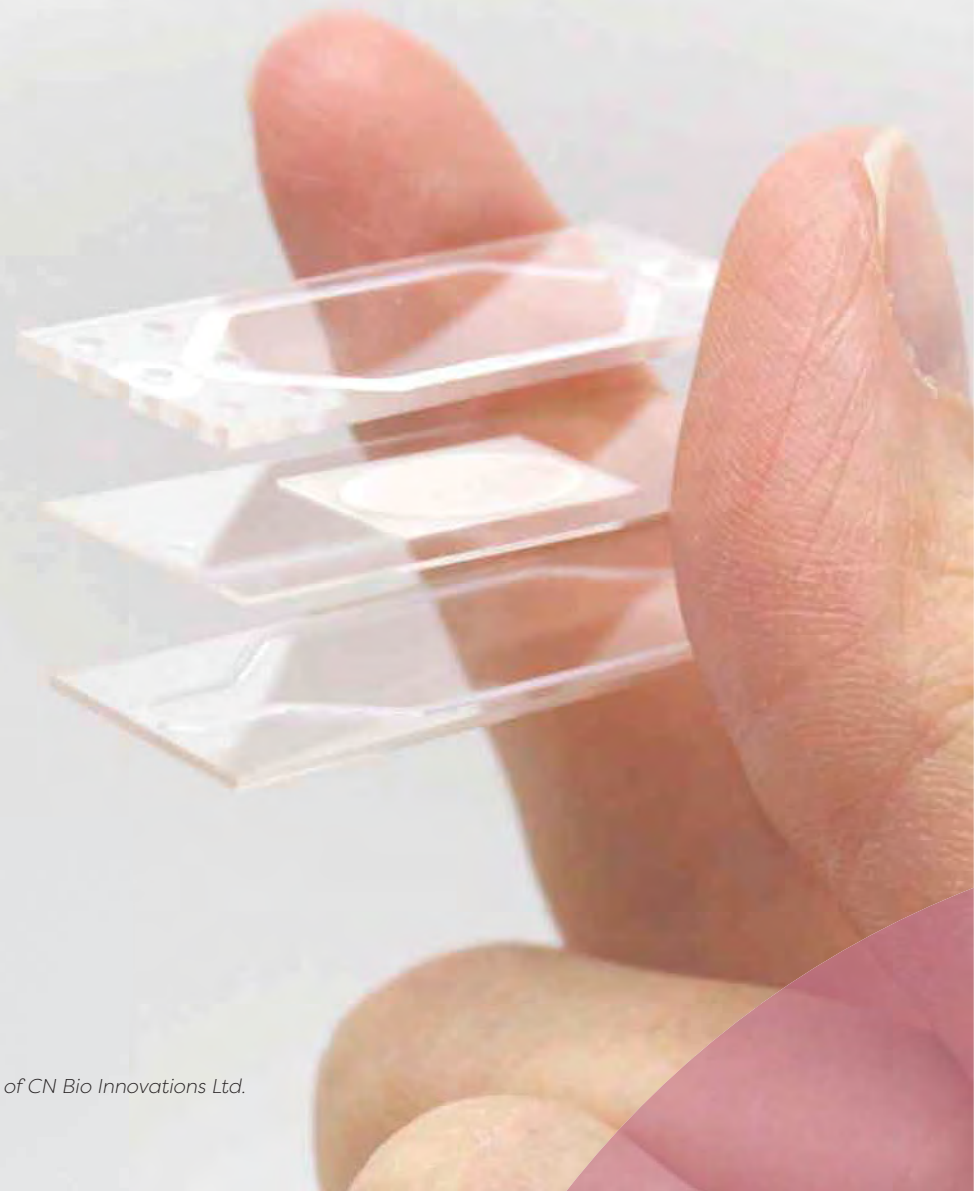
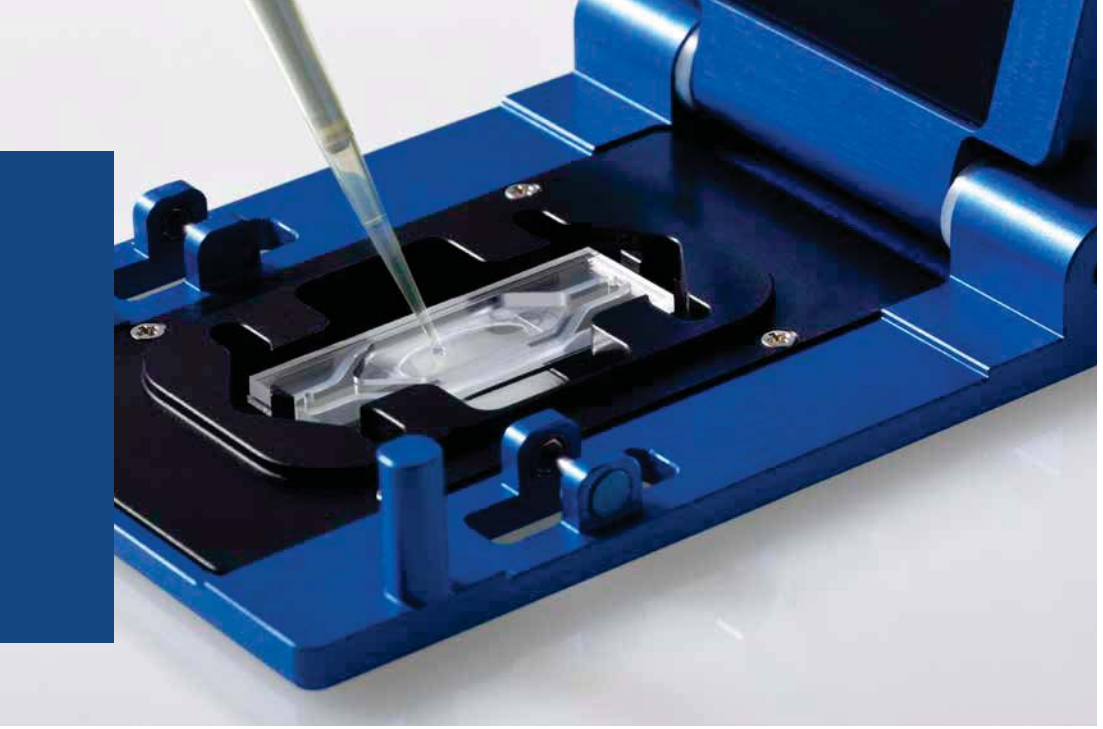


Image courtesy of CN Bio Innovations Ltd.

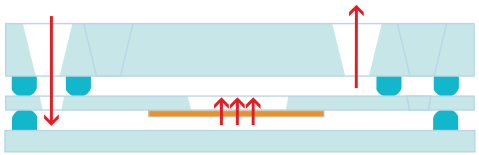
organ-on-a-chip key technical capabilities and technologies

For an at-a-glance overview of key technologies, please consult the table below. We always listen to your requirements first, and then recommend the appropriate processes.

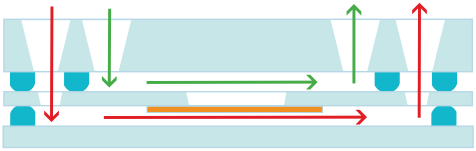
FLOW CONTROL	Dynamic and continuous	Parallel-, serial- and counter flow		Re-circulation	Mixing
	Interfacing - connecting components	Valves		Sampling	
SENSOR INTEGRATION	Culture monitoring	Flow rate sensor		Gas sensors	Temperature sensor
	Electrical sensing	Electrochemical Impedance Spectroscopy			
HYBRID INTEGRATION	Porous membranes & thin films	Polycarbonate (PC)	Polyethylene terephthalate (PET)	Cyclic Olefin Copolymer (COC)	Polystyrene (PS)
	Bioarchitectures	Explant-, organoid-, spheroid-, culture cavities and moieties		Pillar arrays	
OPTICAL INTEGRATION		Top & bottom optical access		Low autofluorescence	Real-time imaging
SURFACE MODIFICATION	Structuring	Nano- / microstructuring		Embossing	
	Functionalisation	Wet coating		Plasma activation	Plasma modification



single flow



cross flow



parrallel flow

counter flow

recirculate

Membrane *Elastomer gasket* *Flow direction 1* *Flow direction 2*

configurable & versatile platform technology

- Re-sealable glass slides with integrated cell culture membrane
- Two separate flow chambers
- Dynamic microfluidic flow

various configuration options

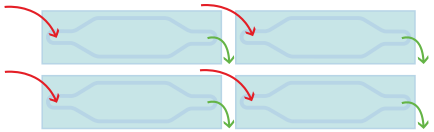
> Independent perfusion for each compartment in each flow cell (8 configurable flow rates)

> Parallel perfusion from common source through four different flow cells (up to 2 configurable flow rates)

> Serial perfusion from one flow cell to another, enabling Multi Organ Culture (up to 2 configurable flow rates)

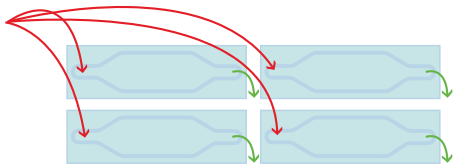
1

Independent control of
> flow rates
> culture medium composition



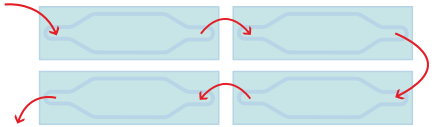
2

Same source
> parallel configuration



3

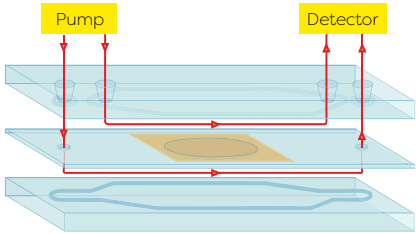
Outlet-to-inlet
> serial configuration



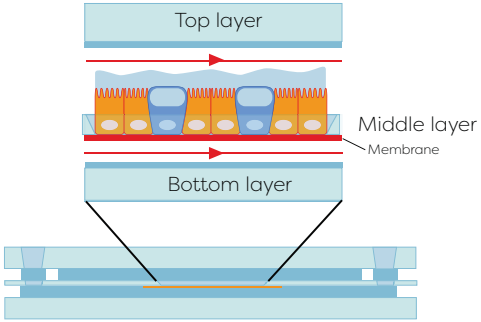
human gut-on-a-chip platform as a model for bioavailability and biotransformation studies

> Results from integrated gut model based on Caco-2 cells in a microfluidic flow cell system indicate enhanced cell proliferation and possibly differentiation

> Faster and more extensive 3D tissue growth

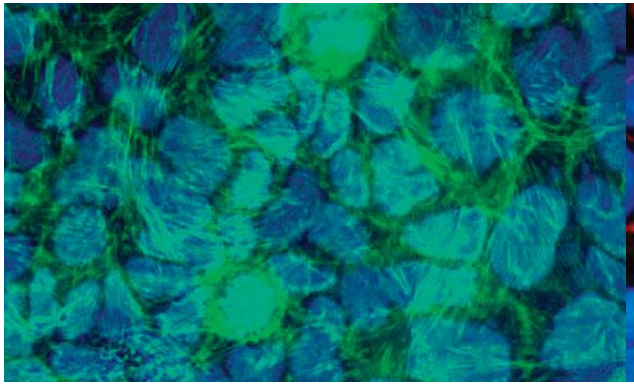


Resealable flow cell

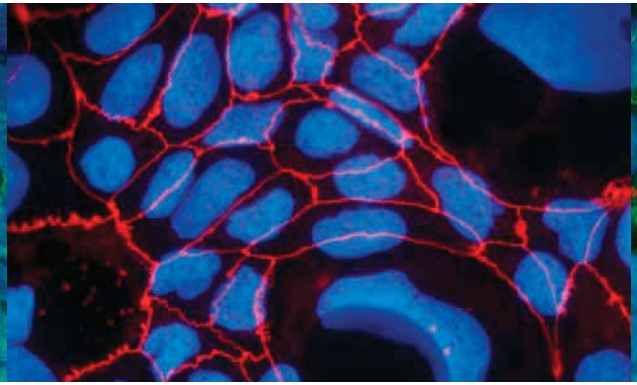


Model concept

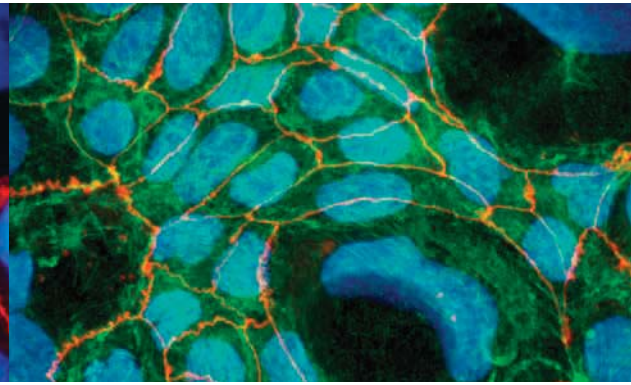
Confocal microscopy images after Caco-2 cell culturing in a resealable flow cell



Cytoskeleton staining (green) and nucleus staining (blue)



Tight junctions staining (red) and nucleus staining (blue)



Cytoskeletonstaining (green), nucleus staining (blue) and tight junctions staining (red)

Images courtesy of RIKILT-WUR

gut-on-a-chip setup

The setup of integrated gut-on-a-chip solution, including four organ-on-a-chip systems with 8-channel microfluidic pumping module and medium reservoirs.

This integrated solution fits easily into any generic incubator.

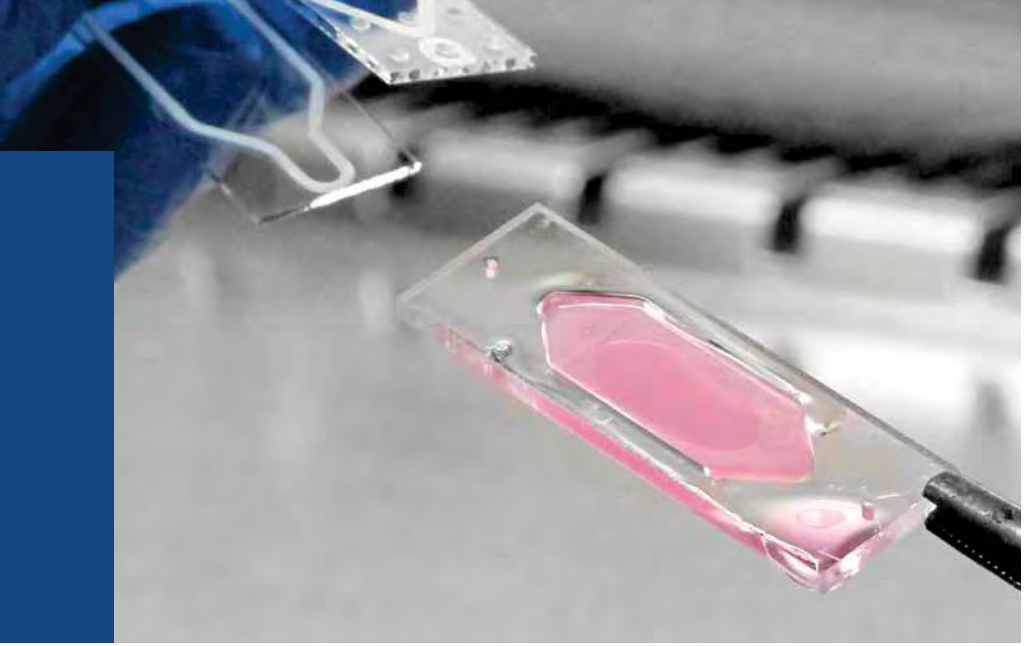
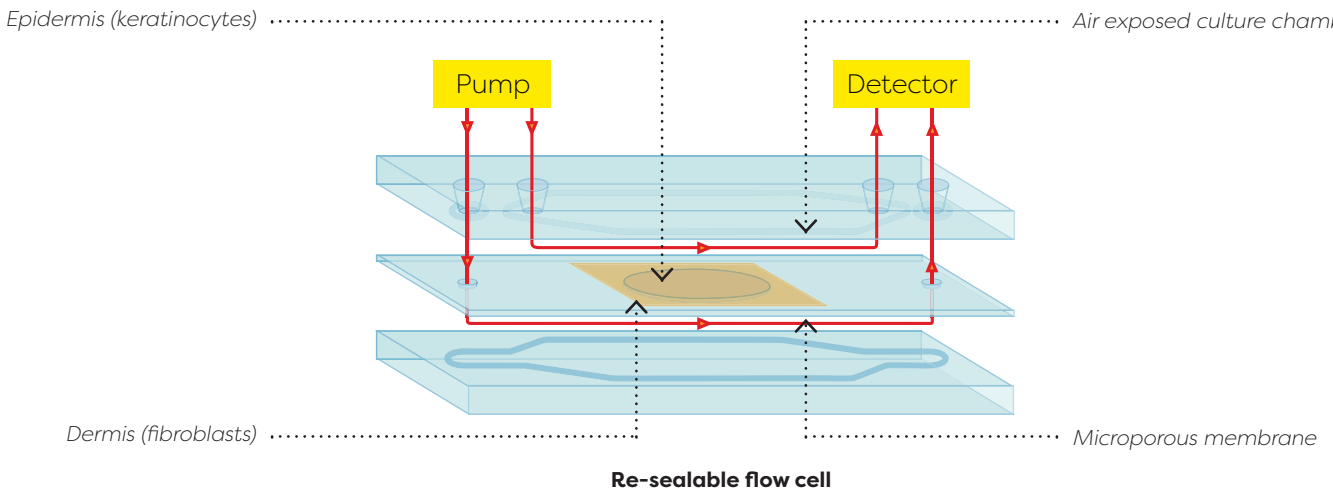


Image courtesy of VuMC

human skin-on-a-chip platform as a physiologically relevant model for skin studies

- Integrated skin model based on primary skin cells
- Middle layer customisation to accommodate tissue-engineered skin equivalents



Re-sealable flow cell

scalable multi-well organ-on-a-chip dynamic flow plates

benefits

- Dynamic microfluidic flow mimics *in vivo* physiology
- Cost reduction
  - parallel testing options with multiple wells
  - decreased liquid volumes
- Facilitates increased throughput, using robotic liquid handling platforms compliant to the Society for Biological Screening (SBS) Standard

Picture of a novel platform in development for in vitro dynamic flow tissue culturing, to enable and accelerate the development of regenerative and personal medicine therapies. Courtesy of CN Bio Innovations Ltd.

partnerships, examples for offering integrated solutions

Micronit collaborates with various industrial system and service providers, including Fluigent S.A. for microfluidic pumping systems (top), Optics11 B.V. for integration of fiber optics (middle) and OxSyBio Ltd. for 3D bio printing (bottom).

Making a difference together – development through strategic customer partnerships – We are partnering with world-class experts in centres of excellence, to develop organ-on-a-chip applications in an iterative manner. This creates improved and enhanced solutions based on pragmatic and real life experiences. We initially focus on barrier functions, such as gut-on-a-chip and skin-on-a-chip, but other organ-on-a-chip application areas and concurrent partnerships are under development. We are always open to and keen for additional and new strategic collaborations with partners that can bring synergy with complementary businesses.

Micronit is committed to co-developing solutions that help our customers improve their products and research, contributing to quality of life.

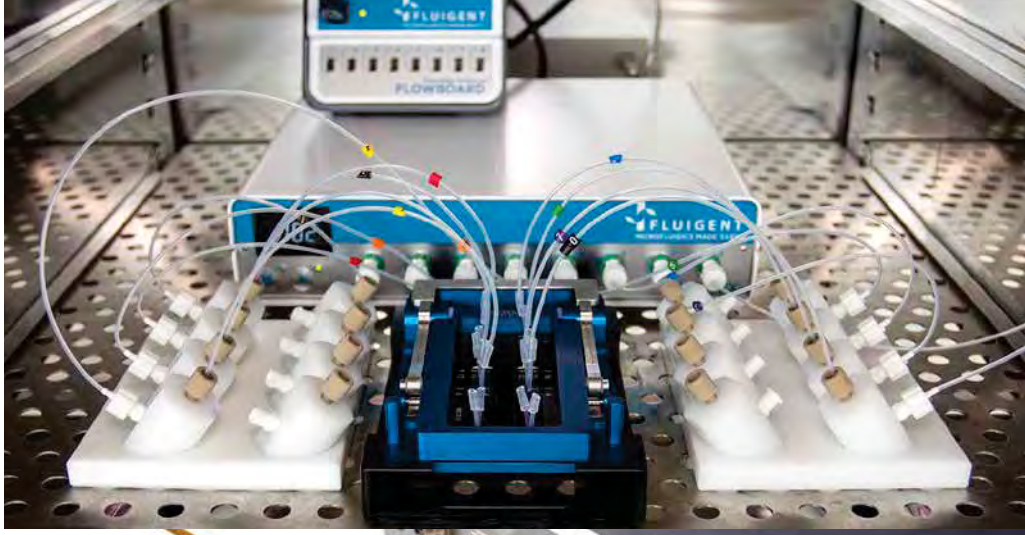


Image of 3D printed cells on Micronit's flow cell middle layer

Image courtesy of OxSyBio Ltd.

organ-on-a-chip empowers a new developing multi-disciplinary field

At Micronit, we synchronise expertise of engineers and biologists to develop cutting edge technologies that enable our customers to excel in their field of expertise. We are committed to help overcoming these challenges together with our customers and partners.

next generation co-development perspectives

- Surface functionalised supports and cell-adhesive membranes for cell grafting and -guidance
- Real-time, bio-sensing of cell culture conditions
- Bio-assay development
- Integration of electrical interfaces for cell tissue characterisation
- Multi Electrode Array (MEA) sensors, Transepithelial Electrical Resistance (TEER)
- Big data mining based on metabolite profiling
- Interfacing to instrumental analysis platforms (NMR, LC-MS, GC-MS, ICP-MS, etc.)
- Optimisation of 3D biomatrices, to better mimic *in vitro* physiology
- Co-culturing solutions for Multi-Organ-Culturing
- Understanding microbiome-, pathogen-cell/-organ Interactions

Micronit, your partner in organ-on-a-chip design, prototyping, product development and manufacturing.

find out more

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If you have any queries...
Simply send us an email to get full, informative answers.

If you'd like more in-depth information...
We can send you extensive documentation that covers every aspect of our services.

If you'd prefer a consultation...
We're more than happy to organise an on-site meeting.

And to check specific possibilities...
Our feasibility study offers you clear, coherent insight.

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