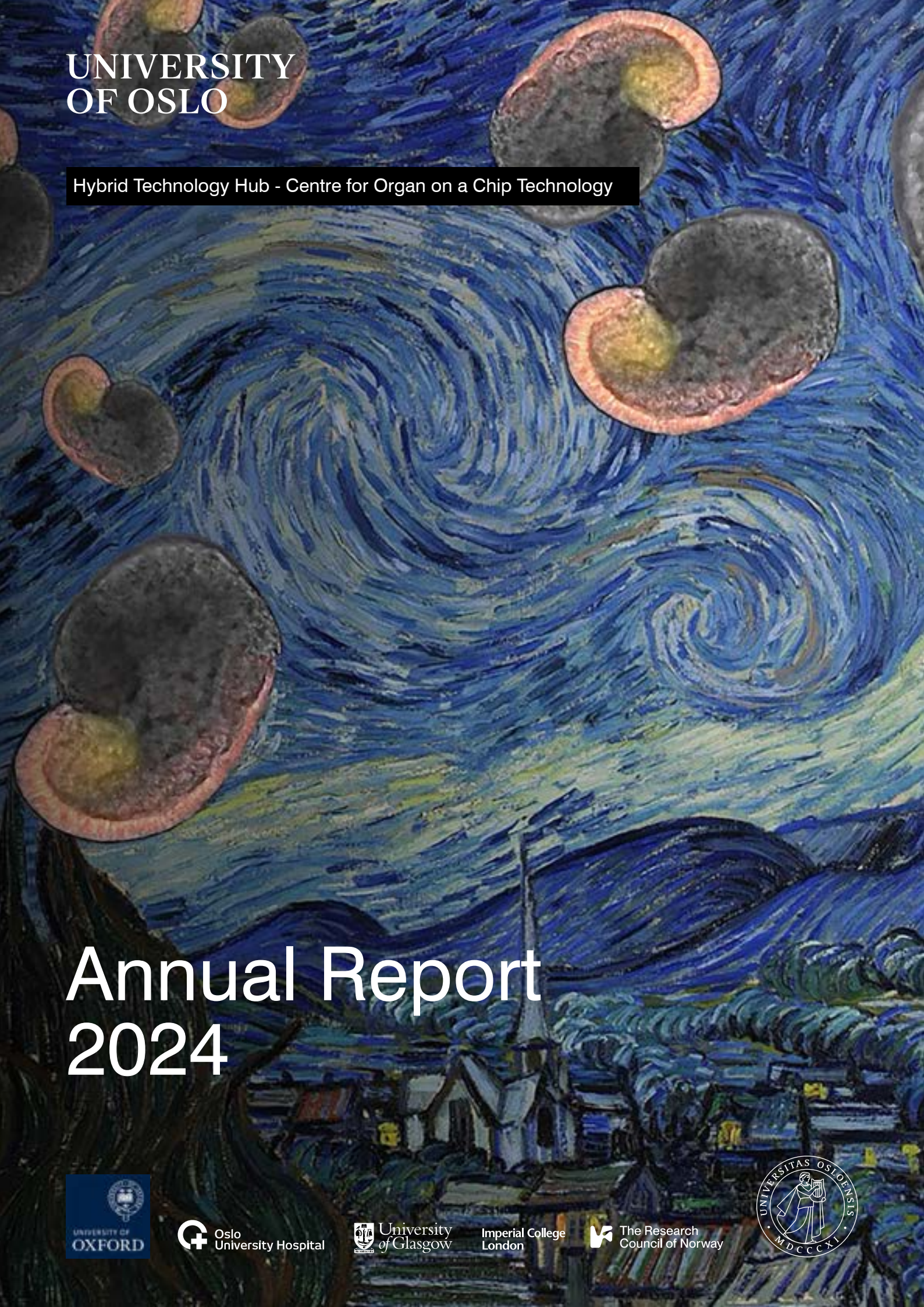


UNIVERSITY OF OSLO

Hybrid Technology Hub - Centre for Organ on a Chip Technology

Annual Report 2024

UNIVERSITY OF OXFORD

Oslo University Hospital

University of Glasgow

Imperial College London

The Research Council of Norway

UNIVERSITAS OSLOENSIS MDCCCXI

Contents

From the director

Complex in vitro models are often essential for replicating the higher-level anatomical, physiological, and pathological characteristics of tissues and organs. Organoids and organ-on-chip (OoC) technologies have emerged as advanced in vitro models.

Organoids are self-organizing, three-dimensional (3D) tissue cultures, typically derived from stem cells, that simulate organ development, composition, and function. OoC technology integrates microfabrication and in vitro cell cultivation techniques to create engineered environments that replicate in vivo-like conditions, enabling the reproduction of organotypic cellular architecture and functionality. Over the past decade, organoids and OoCs have become physiologically relevant models, offering significant advantages over traditional two-dimensional tissue cultures and animal models. As a result, these technologies are increasingly utilized for modeling organ physiology, disease conditions, and drug development, with growing support for their use in personalized medicine. The recent "FDA Modernization Act 2.0," passed by the US Senate, highlights these models as potential alternatives to animal testing. Looking ahead, these technologies also offer the potential for developing human organ representations for transplantation.

The Hybrid Technology Hub (HTH) Centre of Excellence is advancing stem cell-derived representations of organs critical for energy homeostasis. This involves a combination of supervised differentiation protocols, microfluidics, imaging, tracking technologies, integrated bioinformatics, advanced -omics (including single-cell RNA sequencing and spatial transcriptomics), and, as the technology evolves, ethical oversight.

In 2024, the Centre focused on further improving liver, bile duct, and heart organoids, while also advancing the OoC platform. Through a European Innovation Council grant, the Centre has incorporated gastruloid and placenta-on-chip models into its research portfolio. Additionally, the Centre participates in a Wellcome Leap project focused on modeling aspects of aging using microphysiological systems. These efforts contribute to ongoing research on the interaction of gender, hormones, and environmental factors on organ models. Throughout all of these initiatives, the Centre is committed to standardization, scaling, and automation, with the ultimate goal of clinical translation.

To date, the Centre has published 168 peer-reviewed scientific articles, filed five patents, and secured 351 million NOK in complementary external funding. This includes grants from the Research Council of Norway, Health Region East (HSØ), and the Norwegian Cancer Society. The Centre staff have also received three Oslo Life Science convergence environment grants and five SPARK innovation grants. Furthermore, PIs at the Centre were awarded a European Research Council (ERC) advanced grant, an EU "Science With and For Society" (SwafS) project, and grants from the European Innovation Council (EIC), Wellcome Leap, and Novo Nordisk.

In terms of innovation, the Centre has initiated a Research Council-funded collaboration with the Norwegian startup Oncosyne AS to develop and validate pancreas cancer-on-chip models. The Centre has also established partnerships with Novartis and Merck Group and deepened its collaboration with Symeres Inc.

HTH Centre Director Prof. Stefan Krauss on hiking trip in Nepal.

On the analytical front, the Centre has advanced mass spectrometry techniques for metabolic measurements from dual Organ-on-chip platforms, enabling the study of metabolic interactions between liver and islet organoids. The Centre has also established a Raman confocal spectroscopy platform in Oslo, compatible with partner laboratories at Imperial College London, which allows for direct chemometric measurements of organoids and gastruloids. Recently, the Centre added a Tomocube holotomographic system to enhance label-free live tracking of cells and organoids. Additionally, the Centre is progressing in spatial transcriptomics and single-cell RNA sequencing technologies. In bioinformatics, the Centre has completed a globally accessible distributed data-sharing (GADDS) platform, partially based on blockchain technology, to support FAIR-like data sharing.

The Centre organizes an annual Convention on micro physiological systems (NOR-MPS) and contributes to the Research School for Training the Next Generation of Micro- and Nanotechnology Researchers in Norway (TNNN) while Centre PIs, PDs and PhDs participate in a plethora of international conferences with posters, talks and keynotes.

I would like to extend my gratitude to the PIs, researchers, and staff at the Centre for their hard work and exceptional collaborative spirit—without their dedication, the Centre's progress would not be possible. I also wish to thank our host, the Institute of Basic Medical Sciences at the University of Oslo, as well as the Department of Immunology at Oslo University Hospital, the University of Glasgow, and University of Oxford for their unwavering support. We are grateful to our Scientific Advisory Board, led by Prof. Bengt Norden, for their excellent scientific guidance, and to the Centre's Board, led by Prof. Jan G. Bjålie, for their professional oversight.

Science is the most powerful tool for advancing humanity. We are proud to dedicate our efforts to developing novel knowledge, models, and technologies that improve our understanding of disease and, ultimately, contribute to better treatment options for patients.

Stefan Krauss
Centre Director

Microfluidic cell sorter.
Image credit: Thomas Combriat

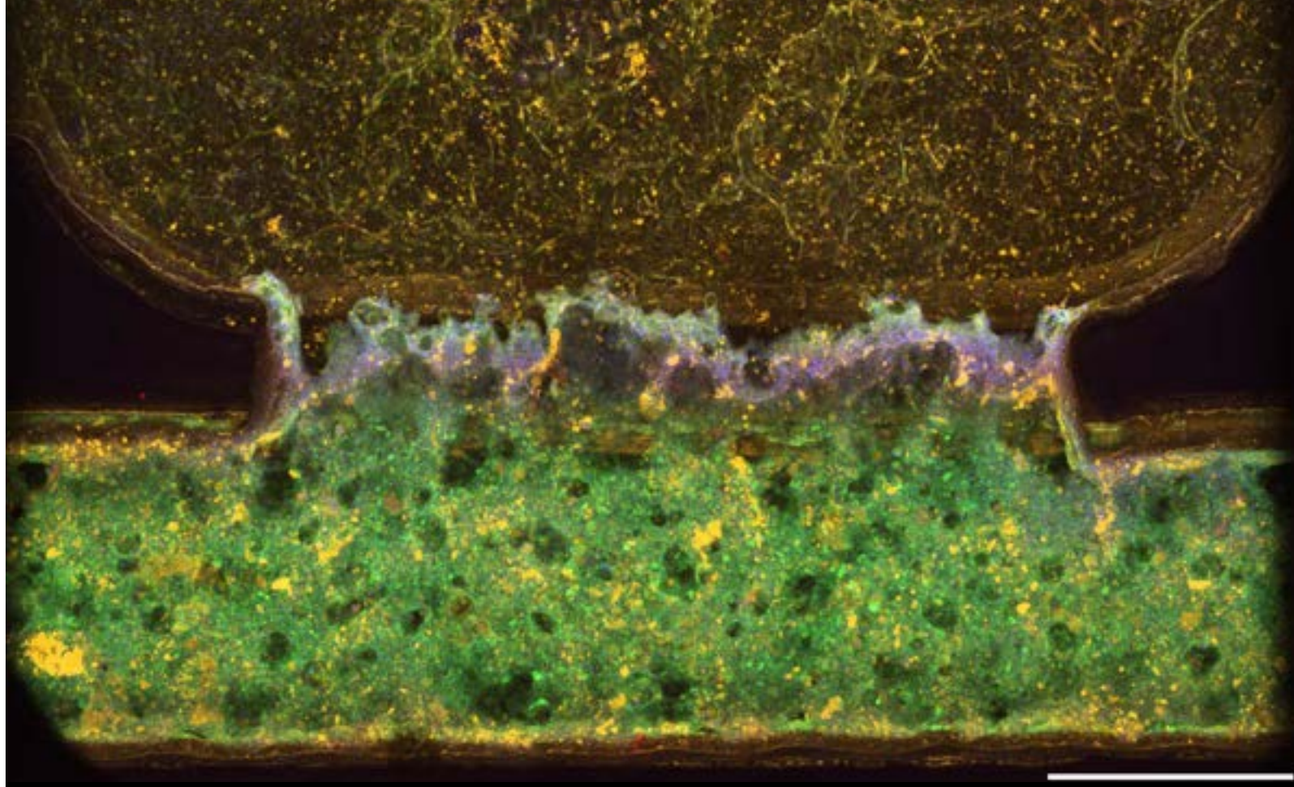
Research groups

Krauss group

Microphysiological systems and developmental pathways

Stefan Krauss
Centre Director

Coming from a developmental biology background we apply principles of self-organization to improve hiPSC derived organ representations for biomedical applications.



Implantation-chip to study vasculature remodeling. Vessels on-chip (HUVECs in yellow/red) in co-culture with trophoblasts (green/yellow). Scale bar: 1000 μm (credit: Ludivine Delon).

A novel organ-on-chip platform

We developed a novel, scalable directional flow organ-on-a-chip (rOoC) platform that creates controlled unidirectional gravity-driven flow by a combination of a 3D-tilting system and an optimized microfluidic layout. The platform allows integrating organoids with endothelialized microfluidic channels and components of the immune system. The platform is currently used for i) combining stem cell derived islets and liver organoids to reconstitute the metabolic cross talk between the two organ representations, ii) for integrating and analyzing the interactions between monocytes and healthy/diseased liver organoids and for developing a placenta-on-chip platform. Work on the rOoC platform has been published in *Advanced Healthcare Materials*: A. Aizenshtadt et al., DOI: *10.1002/adhm.202303785*, a patent is pending. In addition, we have received Wellcome Leap (Dynamic Resilience) funding to use the rOoC platform for modelling resilience upon stressors using liver spheroids, adipose tissues and immune cells “on chip”. This project is coordinated by P. Loskill (U. Tubingen) with partners at the Sanger Institute (R. Vento). We also have received funding from the Norwegian Cancer Society for exploring intravasation/extravasation in a tumor-on-chip model and have recently entered a collaboration with the Norwegian startup Oncosyne AS to develop tumor models using the rOoC platform.

Liver organoids

Coming from a developmental biology background, the laboratory works towards an improved structure and functionality of liver organoids, and hence a better physiological representation of the human liver. The liver is shaped by morphogenetic signals from the central vein and the portal triade. Identifying these signals, and applying them for directing organoid development has been a major challenge. Using hESC and hiPSC derived hepatocyte lineages, endothelial lineages and stellate cells we have achieved stable features of zonation in liver organoids and differential response to fibrotic challenges (e.g. I Wilhelmsen et al., *Stem Cell Research & Therapy* 15 (1), 223). As a next step, we have integrated liver organoids in a directional flow platform that has been developed in our laboratory. We are now working towards using the liver organoids for i) testing immune responses to drug induced liver injury, ii) for testing the toxicity of PFOS, iii) for probing the impact of nutrition and iv) for testing the age and individualized response to stressors and resiliencers (A. Aizenshtadt et al., manuscript in preparation). Collaborative (S. Wilson, M. Stevens, N. Gadegaard, D. Dyste, H. Scholz) published work on liver organoids includes S. Kogler et al., *Analytical Chemistry*, DOI: *10.1021/acs.analchem.4c02246*; P.D. Menezes et al., *Advanced Engineering Materials*, DOI: *10.1002/adem.202400276*; Wang et al., Front. Bioeng. Biotechnol., DOI: *10.3389/fbioe.2024.1392575*; T Combriat et al., *Advanced Science* DOI: *10.1002/advs.202307929*; H. Hruskova et al., *Journal of Chromatography*, DOI: *10.1016/j.chroma.2024.464669*; C Wang et al., *Transpl Int*, DOI: *10.3389/ti.2024.11900*. Collaborative work with E. Melum is ongoing to model the bile duct in a microphysiological system.

Gastruloid development

Common organoid technology is based on individual hiPSC derived lineages that are combined to 3D structures. However, despite significant progress in organoid and organ-on-chip technology, it remains challenging to achieve the high physiological and histological complexity of mature organs. A potential alley to reach higher tissue complexity is to develop organs in their naïve embryonic 3D tissue context. Towards this goal we have established a gastruloid sub-group that develops anteriorized mouse and human gastruloids with the aim of reaching organ induction. The group is supported by two Marie Skłodowska Curie fellowships and a European Innovation Council (EIC) pathfinder project “supervised morphogenesis” that is coordinated by S. Krauss and comprises partners at U. Glasgow, Imperial College, MPG Dresden and others. The projects enters the EIC portfolio “Engineered Living Materials (ELM). At current we analyze optimized gastruloids obtained by aggreegoid technology by scRNAseq and other analytical methods. Two manuscripts are in preparation.

WNT inhibitor development

The laboratory has a long track record on morphogenetic signals and chemical biology. In this context we have developed a WNT inhibitor program centered around the central tankyrase (TNKS) biotarget. For this program we are now establishing a startup with the aim of bringing the lead inhibitor in this program to IND with lung fibrosis as the primary indication. The work is a collaboration with Centre partner Jo Waaler and Symeres Inc. Two publications are in preparation.

Meta-analysis of the Tumor organoid and OoC field

In the context of mapping the Tumor organoid and OoC field we have published a comprehensive review that categorizes the field, its technologies and and geographic distribution of the research (Shoji et al., Cancers, DOI: *10.3390/cancers17010108*).

Aims: The Krauss lab. works towards advanced organoids/OoC models and on methods for interrogating them.

Scholz group
Islets

Hanne Scholz
Vice Director

The Scholz Group develops new cell-based therapies for diabetes in both preclinical and clinical settings. Their research focuses on generating and cultivating organoids from pluripotent stem cells and pancreatic progenitor cells, aiming for true metabolic regulation by studying their metabolism and maturation. A major highlight this year has been the successful development of functional islet cells derived from pluripotent stem cells in both in vitro and in vivo models.

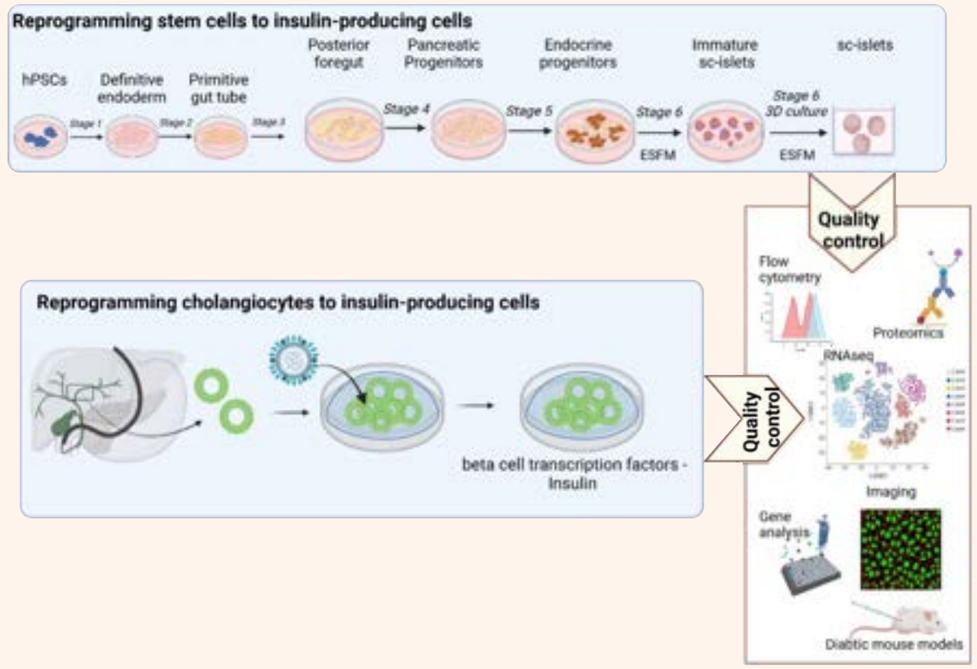


Figure: Illustration of projects on developing reprogramming in vitro protocols on differentiation of stem cell and cholangiocytes towards insulin-producing islets. Credit: Shadab Abadpour. Created with Biorender.com

Beta cell replacement therapy

Beta cell replacement therapy through clinical allogeneic islet transplantation is a minimally invasive procedure that has emerged as a safe and effective treatment for type 1 diabetes patients with poor glycemic control. Islet transplantations performed at the Department of Transplantation Medicine, OUS (H. Scholz), have recently been shown to be more effective than intensive insulin therapy and have significantly improved patients' quality of life. The Scholz Group actively collaborates with international networks (IPITA, ESOT, EPITA, NNCIT) to enhance and expand this therapy globally.

Highlights from the research projects conducted in the UiO: Life Science Convergence ABINO (led by Hanne Scholz)

On September 2, 2024, ABINO PhD candidate M.Sc. Chencheng Wang (Institute of Basic Medical Sciences, HTH - Organ-on-Chip) successfully defended his thesis, "Human pluripotent stem cell-derived islet cells for diabetes modeling and drug testing." Advances in stem cell-derived islet (SC-islet) research have transformed diabetes treatment: SC-islets not only serve as an unlimited cell source for curative therapy but also provide a physiologically relevant model for studying disease mechanisms and drug development.

In collaboration with HTH researcher Dag Kristian Dysthe and CompSci PhD candidate Franziska Schob, the team is developing deep learning-based analyses of stem cell differentiation pathways.

Generation of islet cells from pluripotent stem cells (PSCs)

Through the ABINO project, the Scholz team has established a state-of-the-art protocol for direct in vitro differentiation of human PSCs into insulin-producing cells at the HTH core facility. This project has been recognized as an innovative research initiative and has received a DOFI. These cells demonstrate functional responses to various stimuli, including glucose, both in vivo and in vitro. However, they do not fully replicate mature human islets. Studies on glucose exposure have shown beneficial effects on KATP channel activity but at the cost of mitochondrial respiration efficiency. To address this, the team is now conducting proteomics studies on these differentiated islet cells at various maturation stages, comparing them to primary human islets to identify key signaling pathways involved in pancreatic islet maturation. Their findings have been published in a scientific journal (see reference below) and featured in *forskning.no.*

In addition, primary human islets contain alpha cells, which produce glucagon and regulate blood glucose alongside insulin. The team is currently working on generating alpha cells by reprogramming stem cells in vitro and has recently received innovation research funding from *The UiO Growth House* to support this project.

Generation of insulin-producing cells from cholangiocyte organoids (CO)

In collaboration with HTH scientists E. Melum and Prof. Sampaziotis (University of Cambridge, UK), the Scholz Group aims to develop an in vitro differentiation protocol to generate pancreatic progenitor cells—and eventually insulin-producing cells—from cholangiocyte organoids (COs). Our HTH collaborators have established a method for harvesting biliary organoids from the human bile duct using brush samples obtained during Endoscopic Retrograde Cholangiopancreatography (ERCP). Using a lentiviral system expressing key beta cell transcription factors, we have recently demonstrated that these cells can produce insulin. Currently, we are refining our protocol for functional insulin-producing cells and analyzing their function and maturation using advanced techniques, including RNA sequencing, proteomics, imaging, and in vivo studies. Our goal is to validate COs as a viable source for insulin-producing cells and to identify the key signaling pathways involved in this differentiation process. In the long term, this research could lead to improved differentiation protocols for replacing dysfunctional beta cells—bringing us closer to a curative treatment for type 1 diabetes (T1D).

Rayner group
Computational Biology

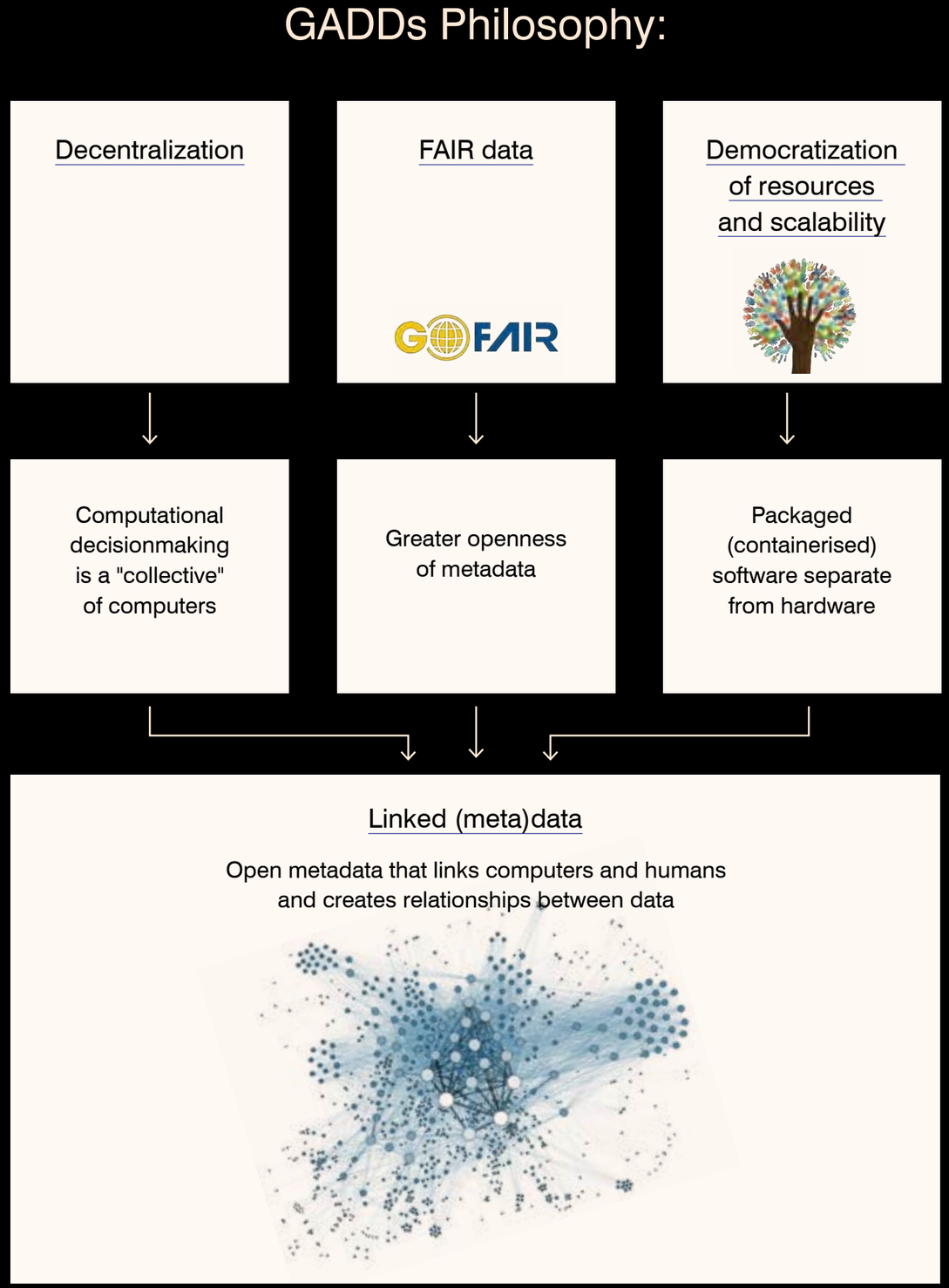
Simon Rayner
Principal Investigator

The primary research focus of the group is understanding how systems evolve in response to external influences. So, we consider ourselves a Computational Biology group rather than a Bioinformatics group – we are developing software to understand biological function rather than writing software to analyze biological data.

While we use publicly available data in this work, this doesn't always meet our needs sowe also carry out our own experimental studies. This includes standard experiments such as Next Generation Sequence to profile miRNA and mRNA expression and their associated regulatory networks, but also more advanced technologies such as Single Cell Spatial Sequencing. For example, we have been using the technique to characterize brain organoids to profile the impact of Human Cytomegaloviruses infection of brain development in newborns.

These works are relevant to the research in the HTH as we can use these tools to study organoids at the genetic level and identify differences with human organs. For example, liver organoids have been developed that exhibit core structural features and express key genes, but their regulatory profiles have not been characterized. Similarly, Single Cell sequencing yield deeper characterization of organoids to help understand how well they approximate living systems.

Another important area is in data standardization and integration. The Findable, Accessible, Interoperable and Reusable (FAIR) principles provide a framework to define the basic elements required to support effective data management but implementing the FAIR principles remains a challenge. We have developed the Globally Accessible Distributed Data Sharing (GADDS) platform to facilitate FAIR like data sharing in cross-disciplinary research collaborations. The platform consists of (i) a blockchain based metadata quality control system, (ii) a private cloud-like storage system and (iii) a version control system. GADDS uses containerized technologies, providing minimal hardware standards and easing scalability, and offers decentralized trust via transparency of metadata, facilitating data exchange and collaboration.



Stevens group

Imaging and sensor technology

Molly Stevens
Principal Investigator

We are developing advanced imaging and sensing technologies to be able to analyze organoids and biological material on-chip.

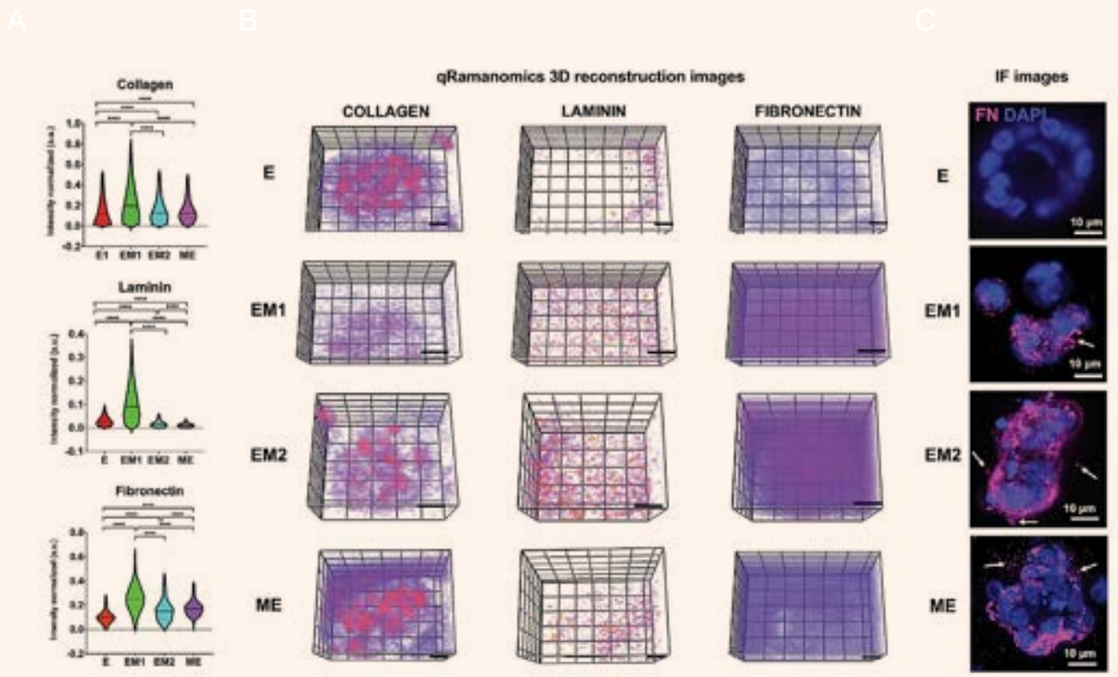
Advances in Raman Imaging

We have previously developed Quantitative Ramanomics (qRamanomics) – a transformative, label-free analytical approach for probing the biochemical complexities of cells and tissues providing high-content, subcellular spatial resolution. We have applied this technique to investigate the epithelial-to-mesenchymal transition (EMT) in 3D tumour models. qRamanomics detected significant disruptions in structure and biomolecular organization, including delocalization of collagen and laminin and increased fibronectin levels in EMT states. The method enabled detailed phenotyping of tumour-like stiffness and composition effects on EMT, amplifying our understanding of matrix-driven cellular behaviour. These findings highlight qRamanomics as a powerful tool for characterizing tumour biology, uncovering new therapeutic targets, and enhancing the fidelity of *in vitro* cancer research platforms, bridging critical gaps in EMT-focused investigations.

In other advances in Raman analysis, our team has published an open-source package, RamanSPy, that supports day-to-day tasks, integrative analyses, the development of methods and protocols, and the integration of advanced data analytics. We are, for example, applying this tool for pre-processing gastruloid Raman microspectroscopy data to better understand the developmental trajectory of organ development (work embedded in the SUMO consortium). Moreover, taking advantage of advances on machine learning methods we have developed framework for Raman hyperspectral unmixing based on autoencoder neural networks. In our recent report in PNAS we demonstrated the applicability of this method using synthetic (biomolecule solutions) and experimental (cells) benchmark databases. The framework resulted in improved accuracy, robustness, and efficiency compared to standard unmixing methods for extracting biochemical features in complex biological samples. Together these advances can enable a broad range of applications of Raman spectroscopy of relevance to the Hub.

Sensor systems

The rapid rise of diabetes underscores the need for innovative platforms to study its mechanisms and develop targeted therapies. To this end, we have developed a cutting-edge localised plasmon resonance-based (LSPR) biosensor integrated with organ-on-a-chip technology for real-time insulin monitoring, addressing the complexities of Type II diabetes (T2D). Combining experimental methods with molecular dynamics (MD) simulations, the sensor utilises engineered affibodies immobilised on citrate-coated gold nanoparticles (AuNPs) for selective insulin binding. MD simulations revealed how cysteine placement optimises affibody orientation and enhances binding affinity, guiding nanoscale biorecognition element design. Affibodies are small protein constructs designed to bind a desired target via combinatorial randomization of surface-located positions, followed by in vitro selection using phage, bacterial or ribosomal display. Affibodies lack animal derived Fc regions reducing concerns about cross-reactivity between human and animal-derived antibodies. The application of affibodies in biosensing has recently emerged proving to be viable alternatives to antibodies in ELISAs and protein microarrays. Our integrated approach is advancing in vitro modelling using T2D as a proof-of-concept by enabling precise, dynamic metabolic assessments and inter-organ communication studies. We are also using affibodies as capture and detection agents in paper based lateral flow immunoassays engineered using commercially relevant manufacture techniques and materials without reduction in performance and with proven temperature and humidity stability compared to antibodies. These findings pave the way for improved biosensor development, offering powerful tools to accelerate biosensing research.



Quantitative Ramanomics reveal differences in the quantity and spatial distribution of ECM proteins across different EMT/MET states.

Team successes

We have moved to the University of Oxford in April 2024 and are now based at the Kavli Institute for Nanoscience Discovery. This transition enables a stronger focus on translating our scientific work into applicable and commercializable technologies that can make a tangible impact in the real world. Prof Stevens was appointed Dame Commander of the Most Excellent Order of the British Empire (DBE) for services to medicine, featured in the Clarivate Analytics Highly Cited Researcher list and received the ESC Paul Hugenholtz Lecture in Innovation, Royal Society Armourers & Brasiers' Company Prize and the UK Society for Biomaterials President's Award.

Related papers

P. Barros da Silva, Z. Zhao, S. J. Bidarra, D. S. Nascimento, V. Lalone, B. N. Lourenco, J. Paredes, M. M. Stevens, C. C. Barrias. "Tunable hybrid hydrogels of alginate and cell-derived dECM to study impact of matrix alterations on epithelial-to-mesenchymal transition." Advanced Healthcare Materials. DOI: 10.1002/adhm.202401032.

K. A. Giraldo, O. Bibikova, A. Kamboukos, C. Echalier, C. J. Sadler, A. Creamer, J. Nilvebrant, K. A. Giang, M. Busek, A. Aizenshtadt, N. Todorova, P. Charchar, S. Krauss, P.-A. Nygren, I. Yarovsky, M. M. Stevens. "Selection of engineered biorecognition elements for in situ insulin sensing." *In preparation*.

Gadegaard group

Chip design

Nikolaj Gadegaard
Principal Investigator

The Biomedical Interfaces at Glasgow (BIG) focuses on the design, simulation and scalable fabrication of microfluidic and organ-on-chip (OoC) technology.

Microfluidic and OoC research is, to this day, primarily performed on polydimethylsiloxane (PDMS) substrates. Despite the many advantages that justified the leading role of this material for the past two decades in research, PDMS provides critical drawback. These include small molecule absorption and incompatibility with high-volume manufacturing procedures. For this reason, research is turning to thermoplastic materials, and at BIG, a novel procedure based on fabricating microfluidic rapid tooling (RT) for injection moulding using 3D printing, has been developed and published [1]. This manufacturing protocol takes advantage of the unique ability of 3D printing to rapid prototype microfluidic devices with exceptional geometric complexity, and provides a pathway to mass scale the respective designs by converting them into tools for injection moulding. The published work goes further in investigating the relevant control parameters and defining the production of microfluidic devices with an optical transparency close to that of a glass substrate, and a feature resolution of <50 µm. More so, it was also shown that the fabricated microfluidic tooling was capable of withstanding small batch production, > 500 injection moulded parts, and therefore demonstrate the scalability of the developed procedure. More importantly, the respective RT procedure was proven to provide a turnaround production time, from computer-aided design (CAD) to a fully functional microfluidic device, just under 3 h, and from CAD to 500 replicas, of approximately 8.5 h. Additionally ultrasonic welding was studied as a complementary procedure for the integration of porous membranes in individual microfluidic compartments, providing quick and reliable seals, and enabling the stretching of the membrane's surface as a function of welding parameters.

FEM is a powerful tool with extensive application in the simulation and optimization of microfluidic systems. At BIG, FEM has been extensively employed not only to investigate real systems with unique fluidic and transport properties, but also, to provide detailed guidelines on the design and optimization of complex microfluidic environments integrating porous membranes for tissue culture and controlled permeability. As a result of the work with FEM, three major projects were completed, two of which resulted last year in published material. The first project consisted of predicting shear stress as a function of flow rate and design parameters, to sustain the experimental results obtained *in vitro* for a human placental barrier model developed by the group at HTH in Oslo. The second project [2] was based on characterizing the unique kinetics of mass transport originating from the pulsatile and asymmetrical fluidic profile characteristic to the novel pumpless, recirculating OoC (rOoC) platform developed at HTH. The numerical data produced helped explaining the transport directional bias existing in the respective platform, and support experimental data modelling the metabolic crosstalk between islet and liver organoids. Finally, the third project [3] consisted of establishing an in-depth study characterizing the relevant control parameters defining the kinetics of flow and transport in microfluidic devices with integrated porous membranes. Not only did this work provide extensive design guidelines uncovering non-linear relationships between fluidic patterns and the resulting dynamics of transport, but also, it demonstrated the biological relevance of the numerical data by validating the obtained results with *on chip* permeability data.

References

1. Menezes, P.D., et al., *Scalable, Transparent, and Micro: 3D-Printed Rapid Tooling for Injection Molded Microfluidics.* Advanced Engineering Materials, 2024. **26**(20): p. 2400276.

2. Aizenshtadt, A., et al., *Pump-Less, Recirculating Organ-on-Chip (rOoC) Platform to Model the Metabolic Crosstalk between Islets and Liver.* Advanced Healthcare Materials, 2024. **13**(13): p. 2303785.

3. Menezes, P.D., et al., *A membrane's blueprint: In silico investigation of fluid flow and molecular transport as a function of membrane design parameters in organ-on-a-chip.* Chemical Engineering Journal, 2024. **481**: p. 148189.

Figure 1: →

a) Scalable fabrication of polystyrene microfluidic droplet generator devices enabled by the developed RT protocol.

b) Droplet generation within the respective devices.

c) A multi-layered device with an integrated porous membrane and two separate, parallel channels, coloured in blue and red.

d) A membrane-chip device manufactured for pumpless, recirculating flow, with 3D rocking.

e) Scanning electron microscopy (SEM) images of a porous membrane ultrasonic welded to the microfluidic devices.

f) Membrane waviness as a function of welding energy, respectively equivalent to 20 Ws, top image, and 160 Ws, bottom image.

g) Membrane waviness plotted along the membrane diameter as a function of welding energy, in blue for 20 Ws and yellow for 160 Ws.

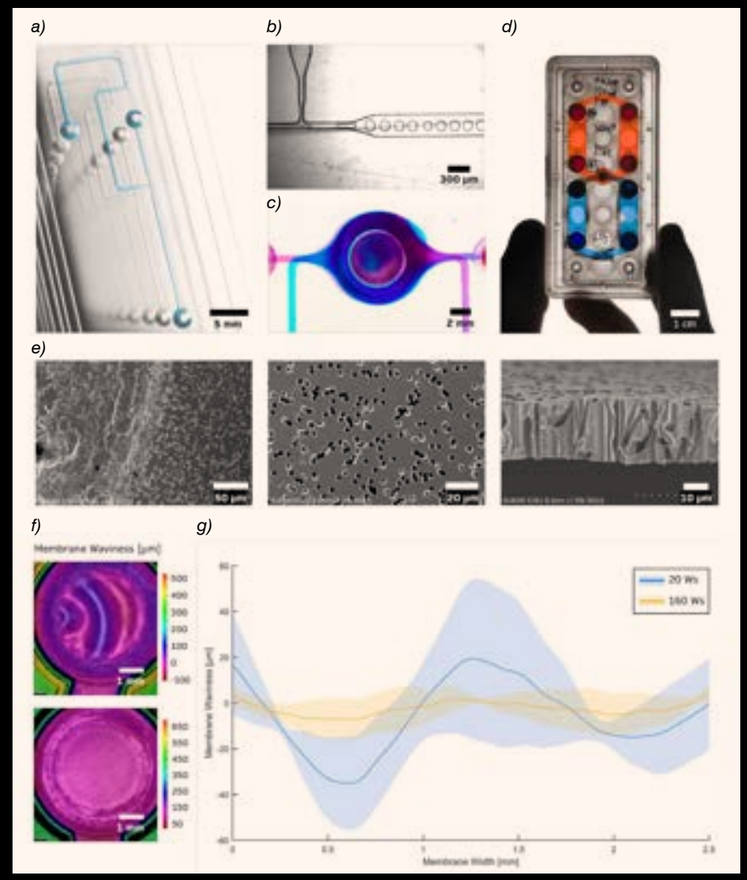


Figure 2: →

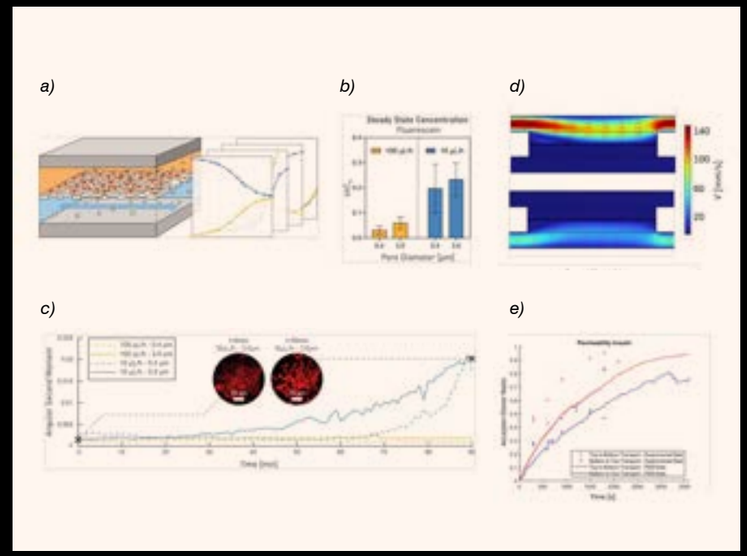
a) On the left, illustration of a bilayer microfluidic device with an integrated porous membrane and cells cultured on the top surface, and on the right, numerical data describing the relationships between control parameters and the variables describing the kinetics of flow and transport.

b) Permeability of porous membranes measured experimentally with fluorescein, corroborating the numerical data.

c) The biological relevance of membrane design parameters, as demonstrated by the effect of porous transport of cytochalasin D on a culture of MDCK cells.

d) Membrane model evidencing the pulsatile, recirculating, asymmetrical flow of the rOoC platform.

e) Permeability of Insulin, as measured numerically and experimentally in the rOoC platform, evidencing good affinity between the in silico and in vitro data.



Louch group
Cardiomyocyte function

William Edward Louch
Principal Investigator

Employing stem-cell derived cardiomyocytes to investigate cellular structure and function in health and disease.

The heartbeat is triggered by the coordinated contraction and relaxation of muscle cells called cardiomyocytes. This process is initiated by the subcellular release of calcium from the Sarcoplasmic Reticulum (SR) at specialized sites. Here, membrane invaginations (t-tubules) and their contained proteins closely interact with release channels (Ryanodine Receptors, RyR) in the SR (Figure 1). However, despite several decades of investigation, the precise positioning of these proteins and their interactions remain unclear. Indeed, the cleft between the two membranes measures only approximately 9 nm, making examination of these structures difficult.

To address this challenge, and understand the basic mechanisms by which the heartbeat is triggered, we employ emerging techniques for super-resolution microscopy. These approaches allow us to carefully localize calcium-handling proteins such as the L-type calcium channel (LTCC), sodium-calcium exchanger (NCX), and RyRs in their respective membranes, as well as structural proteins such as BIN1 and junctophilin-2 (Figure 1). Furthermore, with live-cell imaging, these techniques can allow us to directly link these nanoscale arrangements to calcium release itself (Hou et al., *Nat Cardiovasc Res*, 2023).

How are these structures put together in the developing heart? Our recent work in sheep indicates that the calcium signaling apparatus is carefully assembled starting *in utero*, and that this process is completed after birth (Figure 1). Importantly, we observed that this assembly is highly dependent on the gradually increasing workload that the fetal heart experiences. These conditions drive the growth of the t-tubules and the placement of their component proteins, strengthening the heartbeat of the growing fetus.

But does a similar process occur in the development of human cardiomyocytes? The emergence of human, induced pluripotent stem cell (iPSC)-derived cardiomyocytes has provided fresh insight. Through collaborative efforts with the Hybrid Technology Hub, we have observed that these developing cells also exhibit a well-ordered assembly of t-tubules and their associated proteins (Figure 2). As in the developing sheep heart, we have observed that the mechanical workload that the iPSC-derived cardiomyocytes experience is critical. This can be manipulated by altering culture conditions, including contact points between neighbouring cells and the stiffness of the growth medium.

Continued improvement of the maturation of our iPSC-derived cardiomyocytes is making these cells ever-more appropriate for pharmaceutical testing. However, we ultimately aim to transplant iPSC-derived cells into diseased human hearts. In conditions like heart failure, we have observed that the workload that the heart muscle experiences is excessive. Unlike the situation in the developing heart (Figure 1), our new data have demonstrated that this mechanical overload has opposite effects, causing degradation of t-tubule structure and weakening of the heartbeat (Figure 3). With the help of iPSC-derived cardiomyocytes, we currently aim to understand the workload conditions that support optimal calcium signaling and powerful cardiomyocyte contraction. This will allow us to fine-tune the application of load-reducing medications for the benefit of patients.

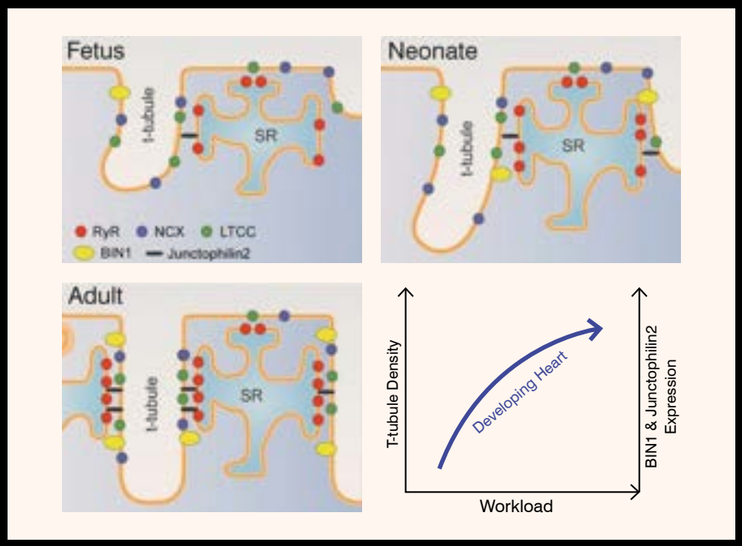


Figure 1: Assembly of the calcium signaling apparatus in the developing cardiomyocyte. From Manfra *et al., J Physiol*, 2024.

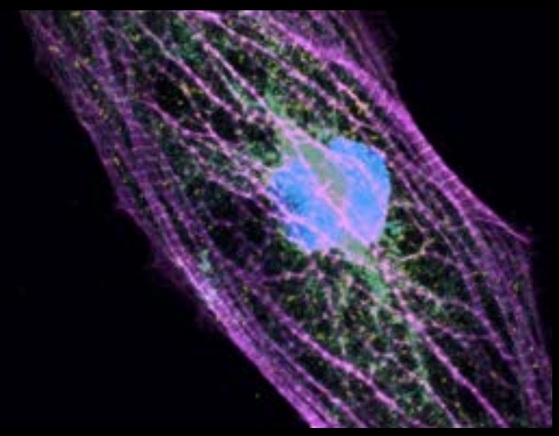


Figure 2: T-tubule growth in an iPSC-derived cardiomyocyte. Labelled are LTCCs (yellow), BIN1 (cyan), and F-actin (purple). Courtesy of Pugal Erusappan.

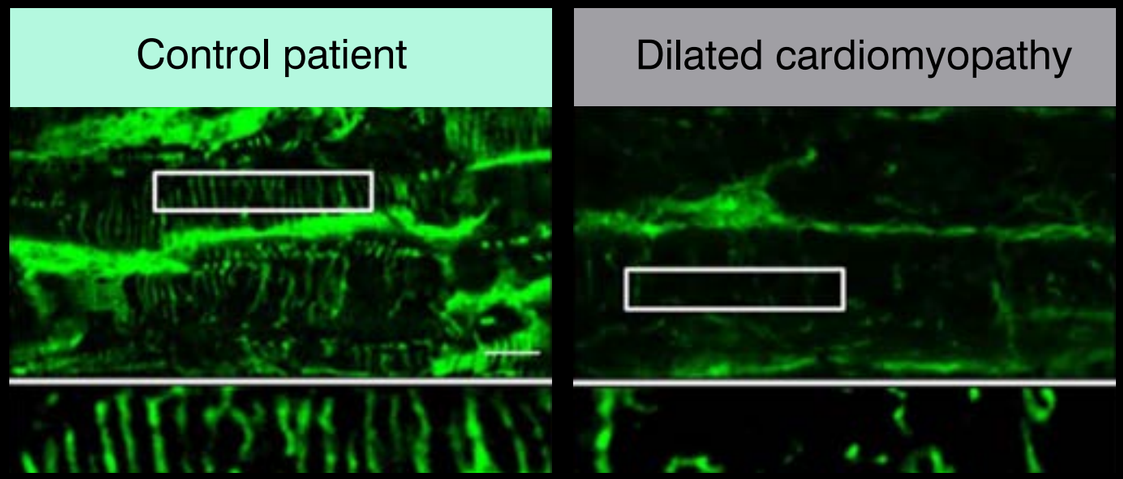


Figure 3: Biopsies from explanted human hearts reveal marked degradation of t-tubule structure in patients with dilated cardiomyopathy (heart failure). Boxed regions shown enlarged below. From Ruud *et al., J Physiol*, 2024.

Solbakk group
Ethic of organoids

Jan Helge Solbakk
Principal Investigator

The ethics group focuses on the law and ethics of organoids. In 2024, this included contributions to three EU funded projects.

The Horizon 2020 Science with and for Society funded HYBRIDA project (Embedding a comprehensive ethical dimension to organoïd-based research and resulting technologies) with Heidi Beate Bentzen and Maxence Gaillard as two of the researchers, and Stefan Krauss as a member of the Advisory Board, was finalized in July 2024. All were present at a HYBRIDA consortium meeting in Oslo in January. Stefan Krauss gave a presentation and Heidi Beate Bentzen chaired a panel in the final HYBRIDA event in Brussels in May 2024. The final event was also streamed.

The European Innovation Council Pathfinder Challenges funded SUMO project (Supervised morphogenesis in gastruloids) coordinated by HTH with Stefan Krauss as PI, started in November 2022 at which time Heidi Beate Bentzen came onboard to address the ethics requirements and conduct tasks related to creating best practice guidelines for the gastruloid research field, a role she continued throughout 2024. An embedded ethics approach is used, where the ethics is interwoven with the science and best ethics practices are developed in tandem with the scientific advancements. To achieve this, quarterly ethics review meetings chaired by Bentzen are attended by the entire consortium, and ethics issues are discussed collaboratively. In 2024, Maxence Gaillard also joined the project as an ethics researcher. Professor Rosario Isasi joined Megan Munsie as a member of the SUMO Ethics Advisory Board. A consortium meeting in Oxford was attended in December 2024, and Bentzen conducted an ethics lab visit to Oxford in October. Two Engineered Living Material Portfolio meetings were also attended, one by Krauss and Bentzen in Brussels in January, and one by Krauss in Saarbrücken in September 2024.

The Marie Skłodowska-Curie Actions Doctoral Network funded TOP-GUT project (Training for Organoids modelling Physiology and Pathology in the human gastrointestinal tract), which started in November 2023, continued through 2024 and include 11 PhD Candidates. The PhD Candidate to be based in Oslo, started in May 2024, and is supervised by Heidi Beate Bentzen. Stefan Krauss is on the TOP-GUT Advisory Board, and both Krauss and Bentzen attended the project kick-off meeting in Berlin in May 2024 where Krauss also delivered the keynote presentation.

Additional networking in the field was achieved by Krauss and Bentzen giving presentations during a lunch meeting organized by the Norwegian Biotechnology Advisory Board on stem-cell derived human embryo models in Oslo in May, and Bentzen being invited to give a presentation to the Norwegian Biotechnology Advisory Board in Bergen in June in preparation for the Board's discussion on the legal regulation of human embryo models. Bentzen further participated in a COST Action CA21151 Generation of hiPSCs from haplo-selected cord blood samples meeting in Amsterdam in May and one in Hamburg in July 2024.

Bentzen sole-authored a book chapter related to HYBRIDA and SUMO on the legal aspects of human organoids; *Human organoids: things or data?* In: Confidentiality, Privacy, and Data Protection in Biomedicine International Concepts and Issues. Routledge (2024), 293-314 (*https://www.taylorfrancis.com/chapters/edit/10.4324/9781003394518-15/human-organoids-heidi-beate-bentzen*.) Bentzen furthermore published a paper with colleagues related to HYBRIDA and SUMO on dynamic consent in stem cell research; Isasi R, Bentzen HB, Fabbri M, Fuhr A, Glover JC, Mah N et al. *Dynamic Governance: A new era for consent for stem cell research*. Stem Cell Reports (2024), doi: *10.1016/j.stemcr.2024.07.006*

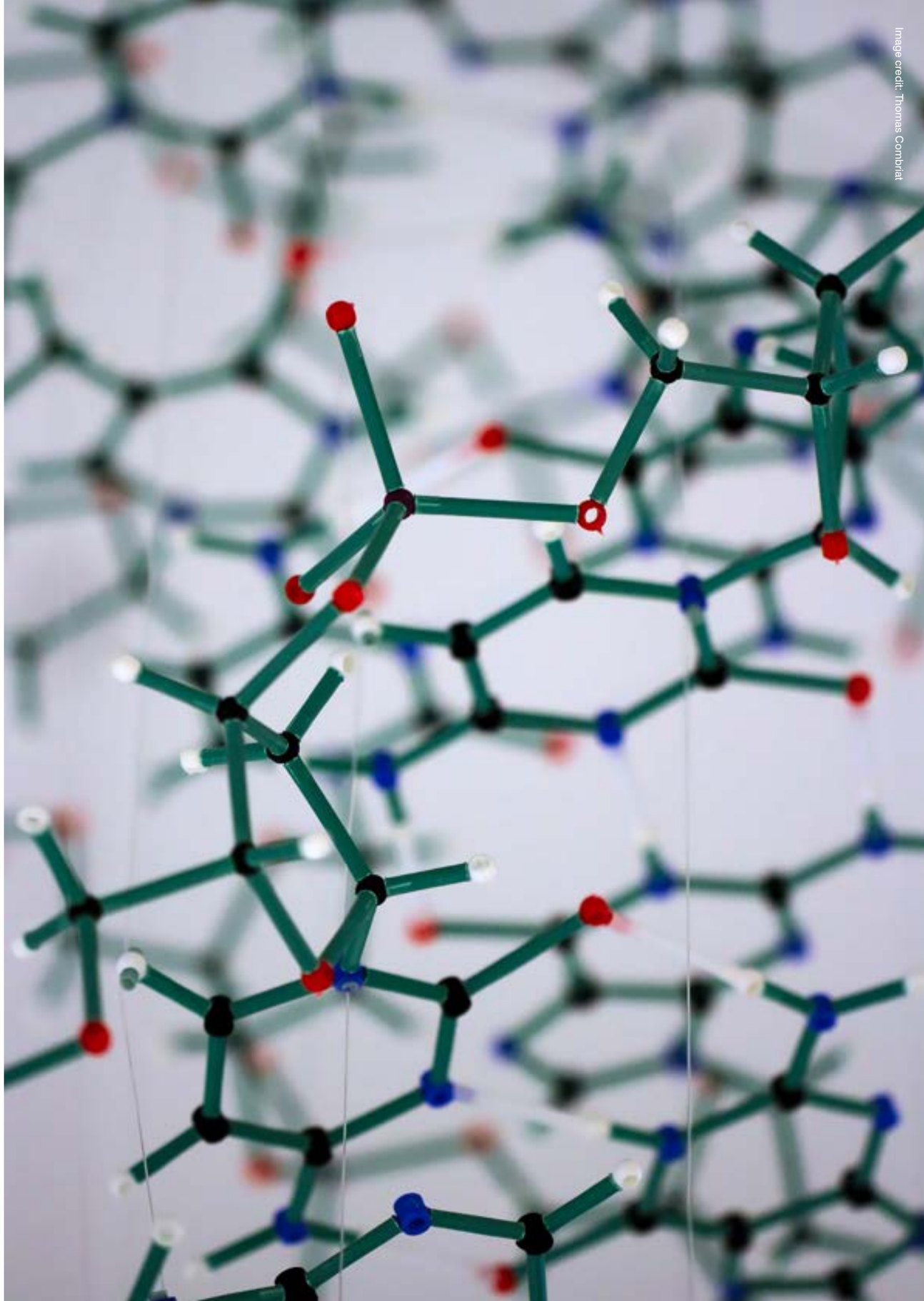


Image credit: Thomas Combriat

Bioanalytical chemistry team

Steven Wilson
Principal Investigator

Hanne Røberg-Larsen
Associated Parter

The bioanalytical chemistry team specializes in employing mass spectrometry for analyzing organoids and organ-on-a-chip systems.

The Bioanalytical Chemistry group consists of two permanent scientific staff members, Steven Ray Wilson (PI, HTH) and Hanne Røberg-Larsen (group leader, associated member HTH). The group also includes 5 PhDs and 1 post doctorate fellow. This team supervises around 15 master students. The activity of the group can roughly be divided into three parts:

1. Novel approaches to sample preparation and analysis of organoids and OoCs

Two main approaches are being explored. The first is “AFFL-LC-MS”, which allows for biosamples to be analyzed with minimal sample preparation, skipping steps such as protein precipitation and off-line extraction steps. The AFFL approach allows for cell culture media, packed with salts, nutrients and proteins to be directly injected onto a mass spectrometry system, for e.g. drug metabolism studies. The system was validated according to FDA guidelines, and was shown to be remarkably robust, allowing thousand-scale injections of unprepared samples without any maintenance. The approach was reported in *Analytical Chemistry* (*https://doi.org/10.1021/acs.analchem.4c02246*) and was supported by funding obtained in 2024 through the Norwegian Research Council and Dyrevernsalliansen, and a collaboration with Merck Life Science.

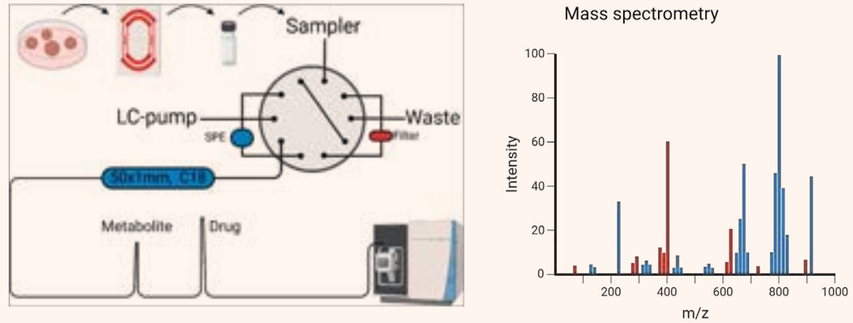
A second approach is being explored, namely electromembrane extraction (EME). The team, in collaboration with SINTEF and others, have received funding from SPARK Norway and Novo Nordisk to develop chip variants of EME. EME is essentially an electrophoresis across an oil membrane, allowing for exhaustive clean-up of biosamples for measuring small molecule drugs and metabolites. The team is currently designing and manufacturing chips and is focusing on commercialization possibilities. A manuscript on describing their recent efforts in under review.

2. Studying the effect of PFAS on organoids

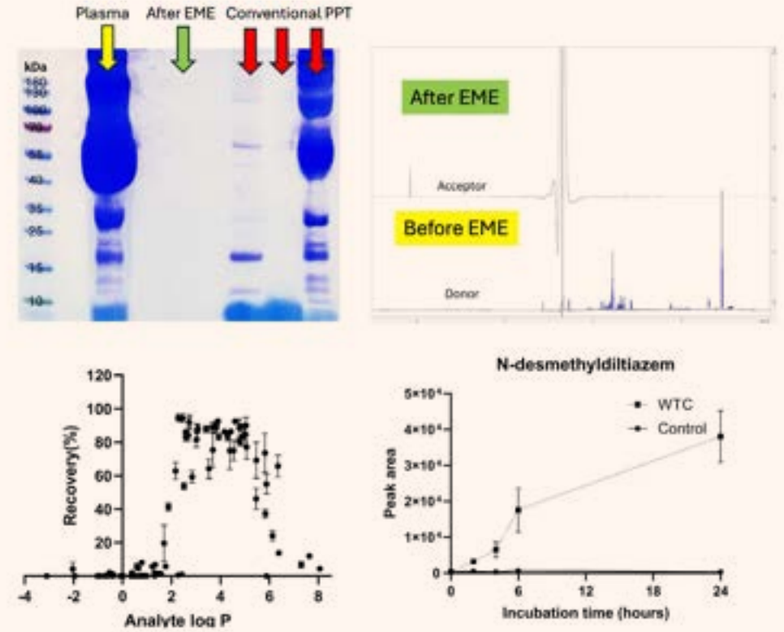
PFAS (per- and polyfluoroalkyl substances) are a group of synthetic chemicals used in a broad range of products and are potentially problematic because they persist in the environment, accumulate in living organisms, and have been linked to adverse health effects, including hormonal disruptions and increased cancer risk. BACH is developing analytical methods to studying the effect of PFAS, using organoids and models. The project is supported by a FRIPRO grant. In 2024, BACH has developed methods for measuring selected PFAS in liver organoids using the aforementioned AFFL system, and also for measuring potential biomarkers of liver disease and hormonal peturbances, e.g. sterols and pancreatic hormones. The project undertaked in close collaboration with the Norwegian Public Health Institute (folkehelseinstituttet). Several manuscripts are in preparation and will be submitted in 2025.

3. Chemical analysis of gastruloids

BACH is also developing approaches to studying gastruloids, employing LC-MS for sterolomics and proteomics, but also mass spectrometry imaging (MSI) for mapping the spatial distribution of analytes. Also in this project, PFAS is being studied with MSI, in collaboration with Waters. Several manuscripts are expected to be submitted in the first half of 2025.



↑
A self-cleaning LC-MS system. Cell culture medium containing drugs and organoid-generated metabolites are injected directly onto the "AFFL" system, allowing for fully automated sample preparation and detection. The system removes proteins and salts before entering the LC-MS system, allowing for sensitive and robust detection. The system was fully validated in accordance with FDA guidelines for bioanalysis.



↑
Electromembrane extraction for monitoring drug metabolism in orgnaoids. Top left: EME allows for unprecedented removal of proteins in biosamples, here exemplified with human plasma (first two SDS-PAGE lanes). In contrast, common sample preparation approaches (protein precipitation) used for clinical samples suffer from incomplete protein removal (last three lanes), thus not optimal for in-line analysis and small samples. Top right: EME also removes small molecule nutrients in cell medium, as these compounds are typically polar and/or uncharged, and are hence not extracted. Bottom left: the EME can be tuned to extract small molecules with given logP values and charge. Here, an NPOE oil is employed, that extracts drugs with logP range 3-5 (tested with 90 drug panel). Bottom right: Extracted samples are readily analyzed with LC-MS (here demonstrated with a CYP3A4 metabolite of the calcium channel blocker diltiazem) or even simple UV detectors, due to clean extraction and hence minimal interfering compounds.

Melum group
Experimental liver research

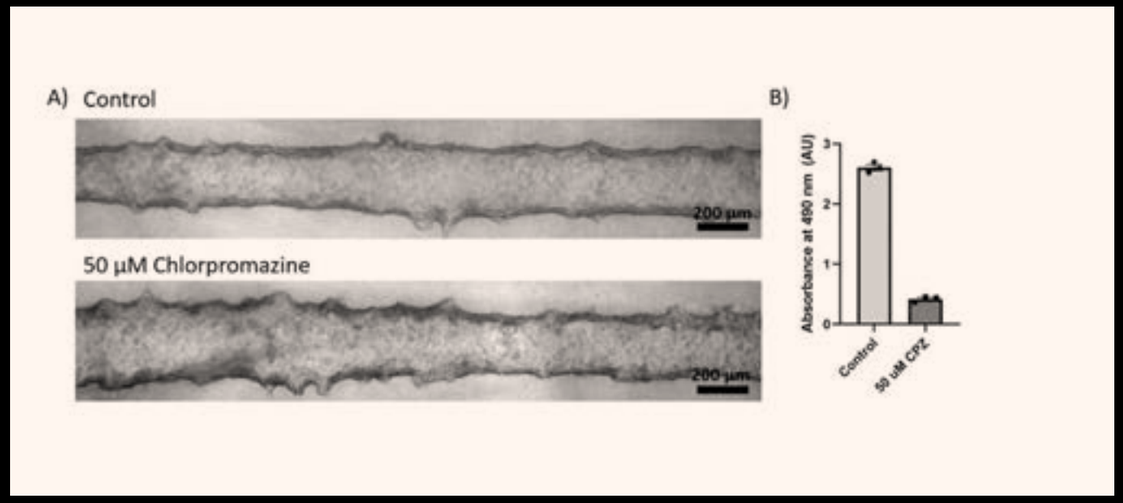
Espen Melum
Principal Investigator

The group's primary focus is understanding the mechanisms behind cholangitis, with an emphasis on immunology, the immune system's interaction with the microbiome, and the role of cholangiocytes in inflammatory processes.

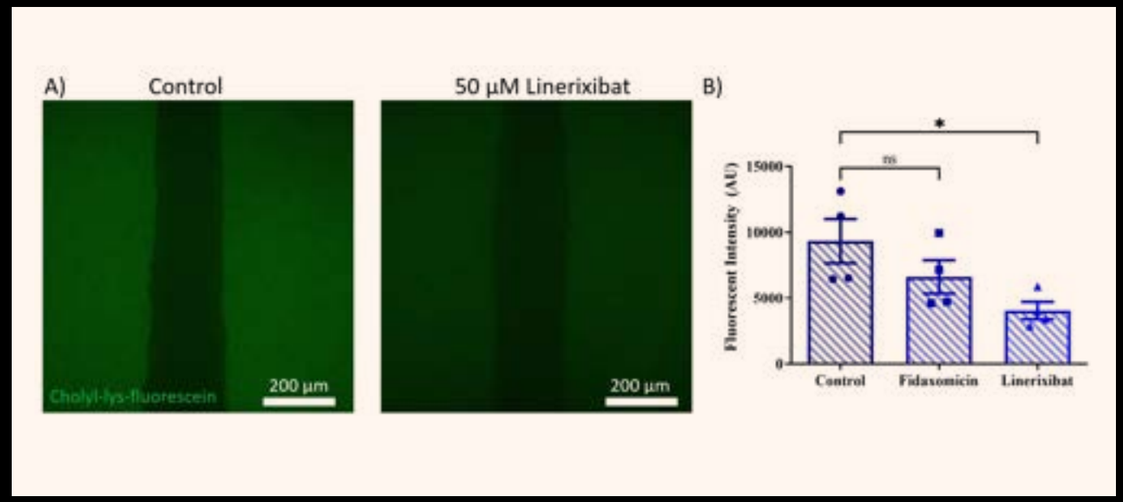
The experimental liver research group focuses on understanding bile duct inflammation and is part of the Norwegian PSC research center (NoPSC). Our laboratory activities take place at both the Research Institute of Internal Medicine and the Hybrid Technology Hub (HTH). In 2024 the group consisted of the group leader, four senior researchers, four postdocs, four PhD students, the lab manager, one researcher and two technicians. The overarching topic in the group is to understand mechanisms regulating cholangitis with a clear focus on immunology and the interaction of the immune system with the microbiome and what role the cholangiocytes play in propagation of inflammatory processes. Together with HTH we are addressing these questions using organoid and bile-duct-on-a-chip technology.

In 2024 our bile-duct-on-a-chip was ready for being used in large scale experiments and we could establish the relevant use cases, probe bile duct function and ensure that bile duct identity was maintained in the system. After these initial characterizations the system has been used to test the effect of various drugs and exogenous challenges on bile duct function and integrity. An important milestone was the integration of human bile which further increased the relevance for human disease. Seeding of cholangiocytes organoids in the chip is a central element of the system. These organoids are generated from brushings of the bile ducts during endoscopic retrograde cholangiopancreatography (ERCP), a method used for diagnostic and therapeutic approaches in the bile ducts. In 2024 we published a paper where we used single-cell sequencing to compare organoids generated from brushes from PSC patients and controls demonstrating important similarities in the transcriptomic profiles. The bile-duct-on-a-chip system was in 2023 accepted into the University of Oslo's SPARK program for commercialization an effort that has been led by Dr. Henry W. Hoyle and Dr. Anne Frank from the group. In 2024 a patent was filed together with Inven2, the technology transfer office of the University of Oslo and Oslo university hospital which will form the basis for a start-up company focusing on contract research using the bile duct chip. Since the bile duct disorders PSC and PBC that affect the bile ducts are believed to be driven by immune mechanisms it is crucial to include the immune system to properly evaluate effects of interventions in the chip. In October 2024 Dr. Wen Jie (Jeremy) Yeoh started as a postdoc in the group and will take on the task of integrating the immune system both in terms of a separate channel in the chip as well as in a static setting.

In addition to the chip-based project, that is an integrated project within HTH, the experimental hepatology group also has large projects related to single-cell sequencing and spatial transcriptomics using both human and murine material. These studies aim to uncover driving mechanism for bile duct disorders of high relevance for the chip system as well as being of methodological relevance for other projects at HTH. Two large projects related to this agenda were wrapped up and submitted for publication at the end of the year. Together with other researchers at HTH we are also using these technologies to gain an increased understanding of developmental biology using gastruloids.



Results from treatment of the DUCT chip with 50 μM chlorpromazine (CPZ). A) Microscopy images show significant branching of the duct into the surrounding ECM with 24 hours of treatment as well as abnormal cell morphology. B) the MTS assay demonstrates a significantly reduced viability of the channel after CPZ treatment.



Transport of cholyl-lys-fluorescein from the interior of the duct to the surrounding gel. A) Fluorescence images of the channels shows a reduction in CLF in the surrounding gel after treatment with the ASBT inhibitor Linerixibat. B) Plate reader quantification of the fluorescence intensity in the basal medium after treatment with fidaxomicin and linerixibat.

Corthay group
Tumor immunology

Alexandre Corthay
Principal Investigator

Tumor on chip technology allows us to develop novel immunotherapies for cancer *in vitro* by modulating a complex tumor microenvironment.

Recreating an immunocompetent tumor microenvironment on a chip

Solid tumors consist of clusters of cancer cells embedded in a stroma made of extracellular matrix and non-malignant cells such as fibroblasts, endothelial cells, and multiple types of immune cells. To better understand how the immune system fights cancer and to strengthen this process, our group is working on recreating a complex tumor microenvironment *in vitro* on a chip. It allows us to dissect the complex cellular and molecular interactions that take place in human tumors with the goal of developing novel immunotherapies for cancer. We have been able so far to recreate a basic tumor microenvironment that includes cancer cells, tumor-specific T cells, dendritic cells, and tumor-associated macrophages, in microfluidic devices (chips) as 3D co-cultures in biomimetic hydrogel. Cell interactions and key processes such as cell division and cell death are being visualized over several days by high-content video-microscopy.

High production of interleukin-12 by human dendritic cells

The cytokine interleukin-12 (IL-12) is crucial for T helper 1 T-cell polarization and the generation of type 1 immunity that is required to fight cancer. Therefore, strategies to optimize the production of IL-12 by human dendritic cells (DCs) may significantly improve the efficacy of vaccines and immunotherapies against cancer. To uncover the rules governing the production of IL-12, we stimulated pattern recognition receptors (PRRs) representing five families of PRRs, to evaluate their ability to elicit high production of IL-12 by monocyte-derived DCs. We used ten well-characterized agonists and stimulated DCs *in vitro* with either single agonists or 27 different combinations. We identified six different combinations of PRR agonists that could synergize to elicit high production of IL-12 by human DCs, and thereby represent strong adjuvant candidates, in particular for therapeutic cancer vaccines.

The potential of fungal polysaccharides for macrophage-targeted cancer immunotherapy

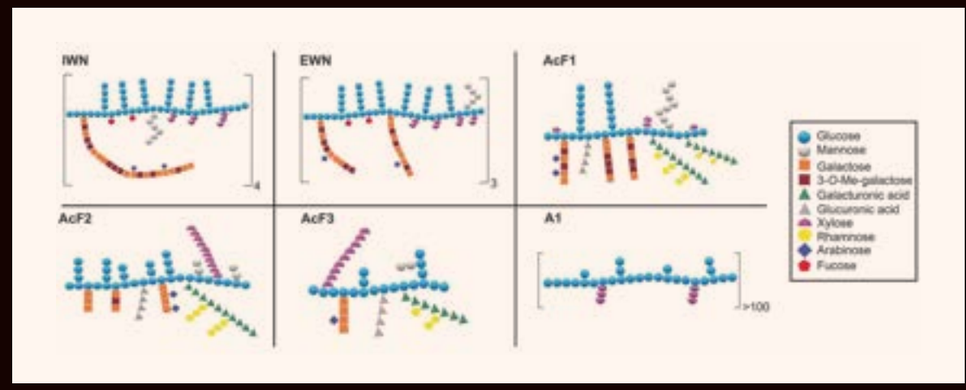
Previous work in our lab has revealed that a type of immune cells called macrophages may be very efficient at eliminating cancer cells, and we are therefore working on developing a novel cancer immunotherapy based on the optimized activation of tumor-associated macrophages. Tumor on a chip technology is a central tool to help clarify the cellular and molecular mechanisms how to make human macrophages kill cancer cells. We have established a microscopy-based, live imaging assay to visualize *in vitro* the killing of cancer cells by activated human macrophages. Fungal polysaccharides can exert immunomodulating activity by triggering pattern recognition receptors (PRRs) on innate immune cells such as macrophages. We tested six polysaccharides isolated from the medicinal fungus *Inonotus obliquus* for their ability to activate mouse and human macrophages. We identified two water-soluble polysaccharides, AcF1 and AcF3, being able to trigger several critical antitumor functions of macrophages. Combined with the cytokine interferon-γ, the fungal polysaccharides were shown to trigger high production of IL-12, a central cytokine for antitumor immunity, and to induce macrophage-mediated inhibition of cancer cell growth *in vitro* and *in vivo*. Thus, the water-soluble polysaccharides AcF1 and AcF3 from *I. obliquus* have a strong potential for cancer immunotherapy by triggering multiple PRRs and by inducing potent anti-cancer activity of macrophages.

Related papers

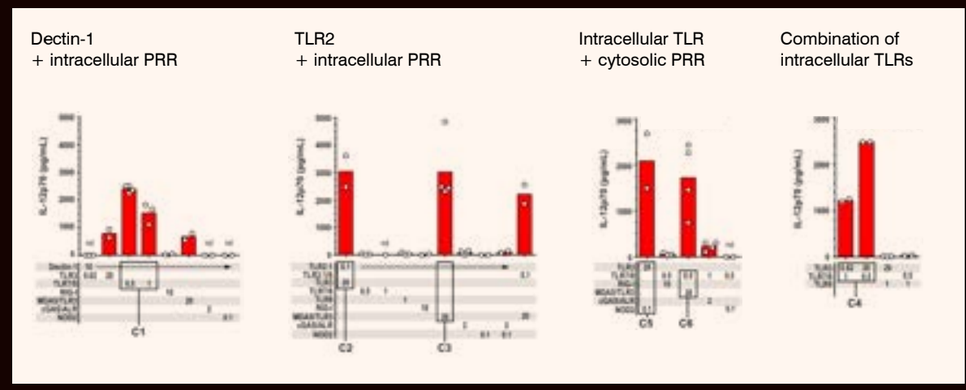
B. C. Gilmour, A. Corthay, I. Øynebråten. High production of IL-12 by human dendritic cells stimulated with combinations of pattern-recognition receptor agonists. *NPJ Vaccines*. 2024.

C. W. Wold, P. F. Christopoulos, M. A. Arias, D. E. Dzovor, I. Øynebråten, A. Corthay, K. T. Inngjerdingen. Fungal polysaccharides from Inonotus obliquus are agonists for Toll-like receptors and induce macrophage anti-cancer activity. *Communications Biology*. 2024.

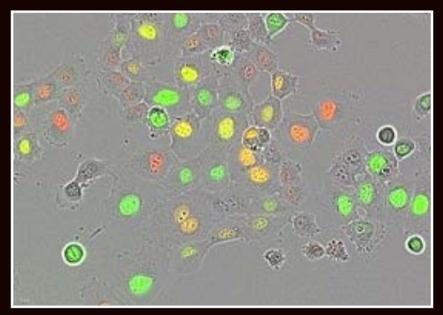
A. Bioactive polysaccharides from *Inonotus obliquus*



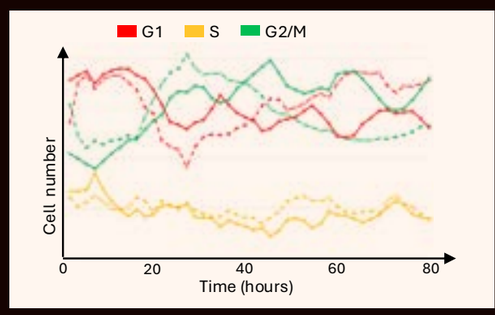
B. Activation of dendritic cells with agonists of pattern recognition receptors (PRR)



C. Melanoma cells



D.



A. Tentative structures of polysaccharides isolated from the fungus *Inonotus obliquus*. AcF1 and AcF3 are potent activators of macrophages. Wold *et al.* 2024. *Communications Biology.* B. Dendritic cells secrete IL-12p70 (a cytokine critical for polarization of T helper 1 cells) in response to combinations of pattern recognition receptor (PRR) agonists. Gilmour *et al.* 2024. *npj Vaccines.* C. Visualization of the cell cycle (G1, red; S, yellow; and G2/M, green) in a cancer cell line (melanoma). D. Real time measurements of the effect of macrophages on the cell cycle of melanoma cells.

Associated groups

Confocal Raman microscope.
Image credit: Thomas Combriat

Waaler group

Cell Signaling and Drug Discovery

Jo Waaler
Associated partner

The research group's objective is to apply its extensive experience in cell signaling pathways and drug discovery to contribute to disease modelling.

Cell Signaling and Drug Development

The group specializes in studying tankyrase 1 and tankyrase 2 (TNKS1/2), enzymes from the PARP family that regulate protein activity, interactions, and degradation through mono- or poly-ADP-ribosylation and downstream cell signaling. These proteins play essential roles in WNT/β-catenin and Hippo signaling pathways, which are closely linked to diseases such as cancer, immune evasion, and fibrosis. As a result, significant efforts have been directed toward developing selective inhibitors of TNKS1/2.

Oslo University Hospital has become a leading center for chemical biology, spearheading a small-molecule TNKS inhibitor program. These inhibitors target proteins like AXIN1 and AXIN2 within the β-catenin destruction complex to inhibit WNT/β-catenin signaling and AMOT proteins within the Hippo signaling pathway to suppress YAP signaling. The group's expertise lies in molecular and mechanistic studies of these central developmental and cancer-promoting pathways, focusing on how WNT/β-catenin and YAP signaling influence tumor progression, tumor-immune cell interactions, and immunotherapy sensitivity.

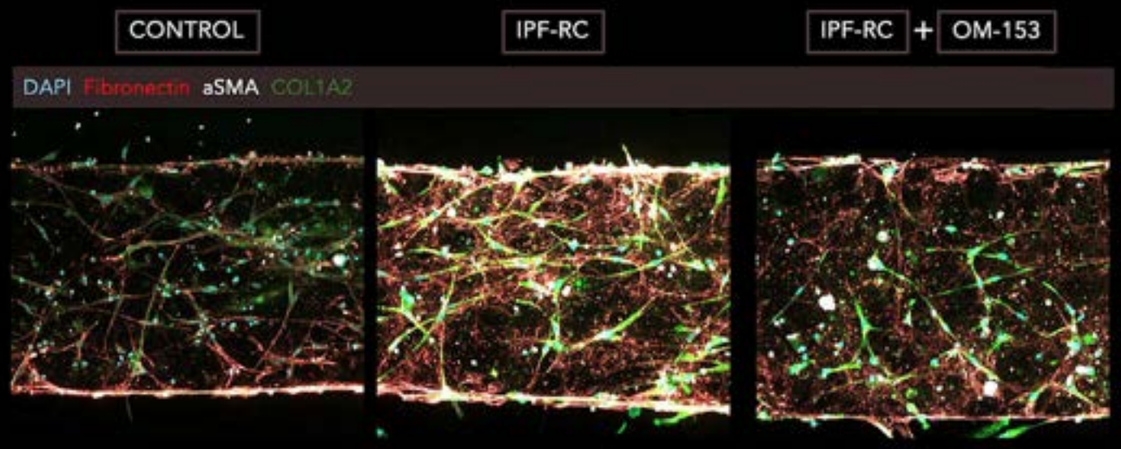
TNKS inhibitor drug discovery

Although dysregulation of WNT/β-catenin and YAP signaling is a hallmark in many cancers and other diseases, including fibrosis, therapies targeting these pathways are not yet available in clinical practice. Since 2006, Jo Waaler and Stefan Krauss have led a drug development initiative identifying TNKS1 and TNKS2 as key, previously unaddressed therapeutic targets. This initiative collaborates with Symeres Inc., a Dutch chemistry company, and Inven2, the technology transfer office for Oslo University Hospital. Substantial funding from the Norwegian Research Council, UiO Innovation, and SPARK Norway supports the program, which is considered a leader in the field of therapeutic TNKS-WNT/β-catenin-YAP signaling inhibitors.

In 2021 and 2022, the group published two key studies. The first, featured in the *Journal of Medicinal Chemistry*, detailed the development of OM-153, a novel TNKS inhibitor. OM-153 demonstrated picomolar potency in a WNT/β-catenin signaling assay (IC50 of 630 pM), exhibited no off-target liabilities, and displayed favorable pharmacokinetics and ADME properties. The second study, published in *Cancer Research Communications*, explored the biological properties of OM-153, showing robust anti-tumor effects in colon carcinoma and immune-oncology models with a significant therapeutic window (0.33 mg/kg to ≥10 mg/kg, dosed twice daily). These findings are especially notable, as concerns about intestinal toxicity associated with TNKS inhibitors have persisted since 2013. Building on this success, Odin Therapeutics was established in December 2023 by Stefan Krauss and collaborators, aiming to develop a clinical portfolio of TNKS inhibitors.

Tankyrase inhibitor treatment (OM-153) of cytokine cocktail–induced (IPF-RC) fibrogenesis in experimental lung-on-chip model

(collaboration with Politecnico di Milano and BiomimX Srl – Italy)



Ongoing Projects

The ongoing research aims to identify TNKS-dependent diseases with high unmet medical needs, assess the therapeutic potential of TNKS inhibitors, and investigate their mechanisms of action. The team is focused on advancing preclinical drug candidates toward clinical trials in collaboration with Odin Therapeutics. Current projects include evaluating the effects and mechanisms of TNKS inhibitors as monotherapies and in combination therapies for cancer and other diseases. This involves using cell cultures, ex vivo systems, and rodent models, as well as testing drugs on Organ-on-Chip platforms.

A significant aspect of the research is understanding the effects of TNKS inhibitors combined with immune checkpoint inhibitors in melanoma treatment, examining the roles of the adaptive and innate immune systems through isogenic mouse models. Another critical objective is to evaluate TNKS inhibitors as potential therapies for pulmonary fibrosis, including idiopathic pulmonary fibrosis (IPF), a condition with an urgent need for effective treatments. This comprehensive approach underscores the group's commitment to translating innovative research into impactful clinical applications.

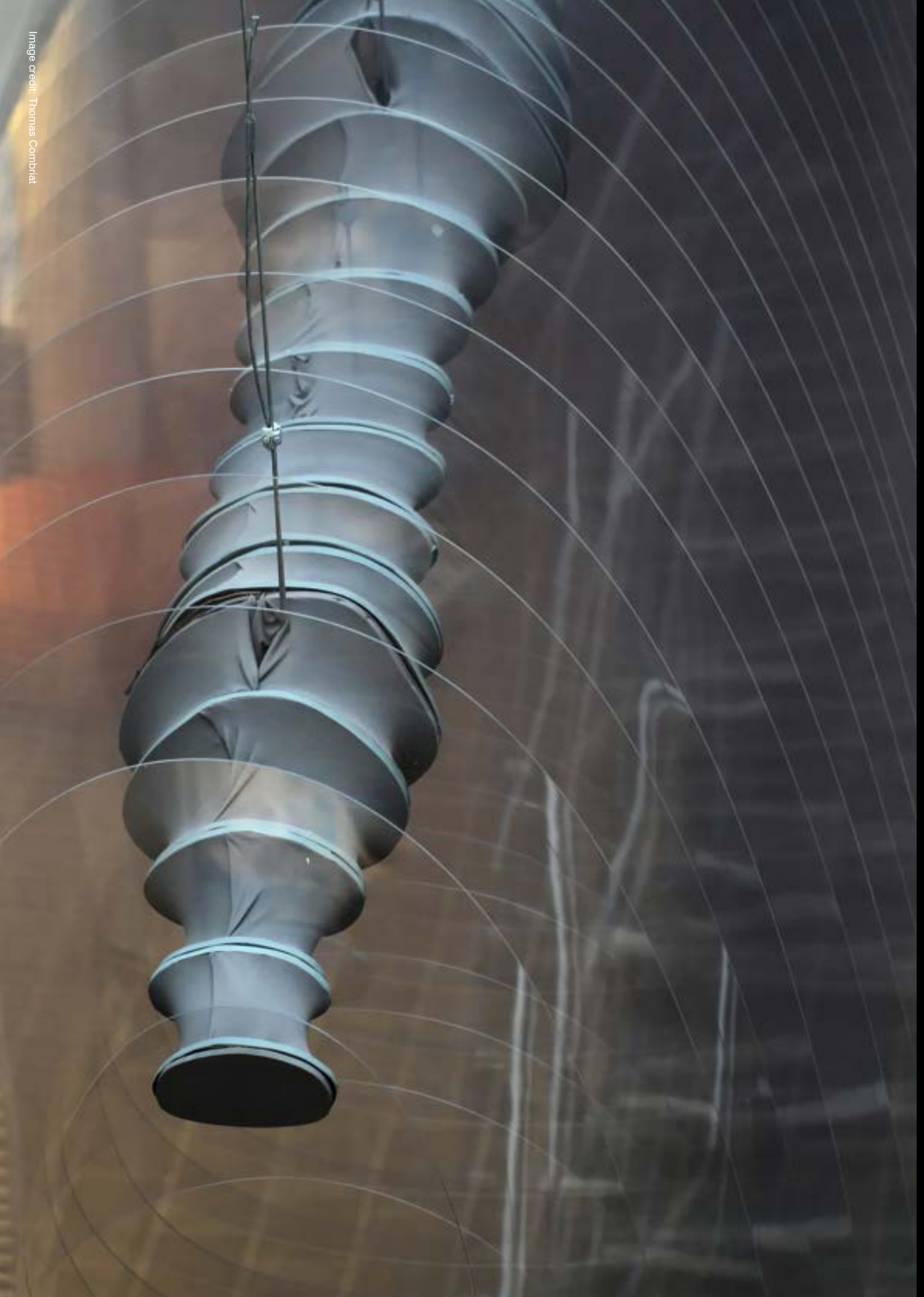


Image credit: Thomas Combriat

HTH associated research projects

ITOM

Integrated technologies for tracking organoid morphogenesis (2022–2026)

About the project

There is a significant need for developing reliable human organ representations (termed organoids) for drug development, personalized drug testing, and on the longer run for organ transplantations. The advent of human induced pluripotent cell (hiPSC) technology has allowed developing *in vitro* human organoids that show features of the organs they represent, but are significantly less structured and less mature than their human counterparts. The field therefore requires high-content tracking tools and algorithms to guide organoid development. Developing such technologies will represent a leap towards reliable personalized organoids with organ-like histology and functionality.

In this project we will work on three technological platforms to track organoid morphology.

1. Confocal Raman microscopy that allows label-free visualization of Raman active molecules in fixed and living specimens.
2. High-resolution spatial transcriptomics and desorption electrospray ionization-mass spectrometry (DESI-MS).
3. Lightsheet microscopy for fast and slow time-lapse imaging of cells in the organoids.

Based on the imaging data, we will develop statistical physics models for organ/organoid pattern formation *in vitro*. The information will be used to tailor statistical models to improve organoid formation *in vitro*.

PROJECT LEADER

Prof. Stefan Krauss
Hybrid Technology Hub – Centre of Excellence, Institute of Basic Medical Sciences, University of Oslo (UiO) and Oslo University Hospital

PARTICIPANTS

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Department of Chemistry, UiO

Dr. Richard David Jun-Geet Ho
NJORD Physics - Centre for Studies of the Physics of the Earth, UiO.

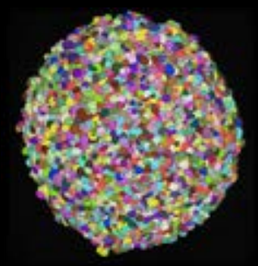
Dr. Joachim Mossige
RITMO Centre for Interdisciplinary Studies in Rhythm, Time and Motion, UiO.

FUNDING

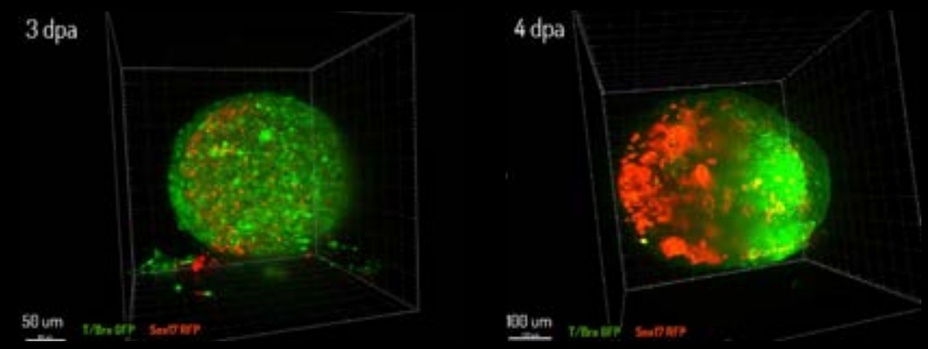
The 4 year project is funded by the UiO: Life Science convergence environment program with 16,9 million NOK

FURTHER INFORMATION

https://www.uio.no/english/research/strategic-research-areas/life-science/research/convergence-environments/itom/



→
The image shows 3D data of segmented cell nuclei for a 3-day-old mouse gastruloid derived from the MP1 mESC cell line and stained with DAPI stain to make the cell nuclei visible. The sample was imaged with a light-sheet microscope, and the cell nuclei were segmented using a machine learning algorithm. Diameter of sample: 300 micrometer (credit: Sunny Dai and Jana Harizanova at the Core Facility for Integrated Microscopy at the University of Copenhagen)



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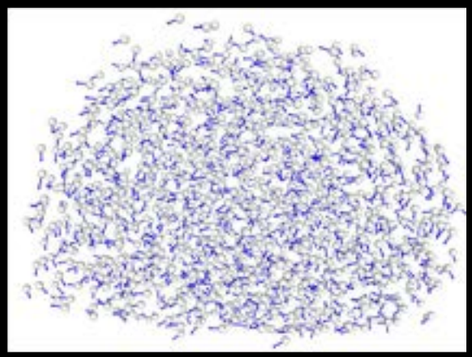
3D images (maximum intensity projections) showing how an early mouse model embryo (gastruloid) elongates and how cells self-organize between day 3 (left) and day 4 (right) after aggregation. The gastruloids were prepared by Sergei Ponomartcev using mouse embryonic stem cells from the MP1 mESC dual reporter cell line with Sox17 RFP (red: endoderm) and T/Bra GFP (green: mesoderm) reporters. Imaged by Joachim Mossige (UiO) using a home-built light-sheet microscope and rendered in 3D by Xian Hu.



↑
Left image shows an optical section of cell nuclei in a cleared mouse gastruloid at 2 days post aggregation. The image displays the MP1 mESC cell line stained with DAPI to visualise the cell nuclei (credit: Sunny Dai and Jana Harizanova at the Core Facility for Integrated Microscopy at the University of Copenhagen). The right image shows the principal directions of the cell nuclei, which is used as a proxy of the cell orientation. The cell orientation data were compared to 3D simulations by Richard Ho (UiO).

SUMO

Supervised morphogenesis in gastruloids (2022–2027)

About the project

The lack of realistic *in vitro* organ models that can faithfully represent *in vivo* physiological processes is a major obstacle affecting the biological and medical sciences. The emergence of stem cell engineered organ models called organoids represents a viable alternative to animal research. However, current organoid technology has yet to produce larger histological and physiological faithful organ models. Specifically, current organoids are too small, not vascularized and lack the 3-dimensional organization found *in vivo*. In this interdisciplinary project we aim to challenge all these limitations by using the emerging gastruloid technology guided by cutting edge bioengineering and artificial intelligence.

The work of the consortium focuses on:

1. Developing mouse gastruloid technology to achieve reproducible heart and gut development.
2. Vascularization of gastruloids to produce 1 cm^3 ELM.
3. Advancing human gastruloid technology within ethical boundaries
4. Developing correlative live imaging technologies and Raman spectroscopy as a benchmarking and tracking tool for gastruloids.
5. Developing machine learning (ML) based tracking algorithms in 3D.
6. Establishing a standardized close-loop system and DBTL platform for upscaling.
7. Implementing a DBTL platform to establish a PoC environmental toxicology pipeline.
8. Providing an ethical, safety and regulatory framework for advanced human gastruloid technology.
9. Engageing in a social dialogue with the public advanced human gastruloid technology.
10. Strengthening gastruloid/organoid community; Disseminate technology to the European biotech industry.

The SUMO project enters a thematic “Engineered Living Matter” portfolio that comprises 7 projects.

PROJECT LEADER

Prof. Stefan Krauss
Hybrid Technology Hub – Centre of Excellence, Institute of Basic Medical Sciences, University of Oslo (UiO) and Oslo University Hospital

PARTICIPANTS

Prof. Jan Helge Solbakk
Centre for Medical Ethics, Institute of Health and Society, University of Oslo

Prof. Molly Stevens
Imperial College of Science, Technolgy and Medicine, London

Prof. Nikolaj Gadegaard
University of Glasgow

Dr. Jesse Veenvliet
Max-Planck-Gesellschaft Dresden

Dr. Jens v Kries
Forschungsverbund Berlin

Dr. Iftach Nachmann
Tel Aviv University

FUNDING

The 5 year project is funded by the EU program: HORIZON.3.1 – The European Innovation Council (EIC) with 4,95 million Euro

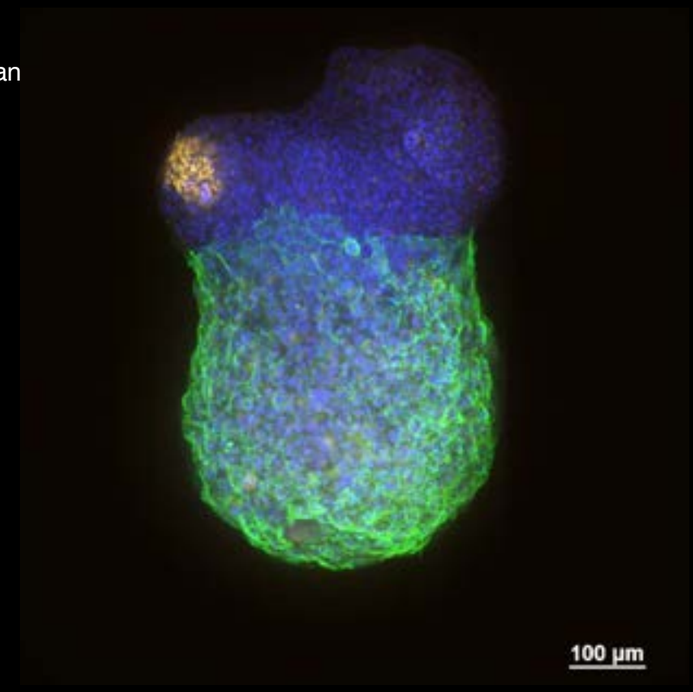
FURTHER INFORMATION

https://cordis.europa.eu/project/id/101071203

https://supervised-morphogenesis.eu

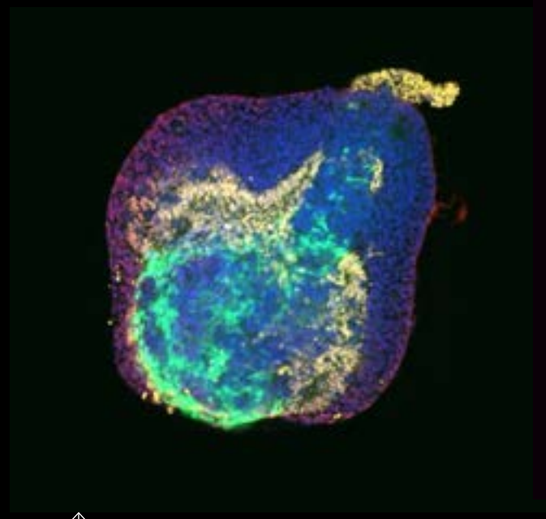
https://cordis.europa.eu/programme/id/HORIZON_HORIZON-EIC-2021-PATHFINDERCHALLENGES-01-05

Integration and support of human in vitro embryo model

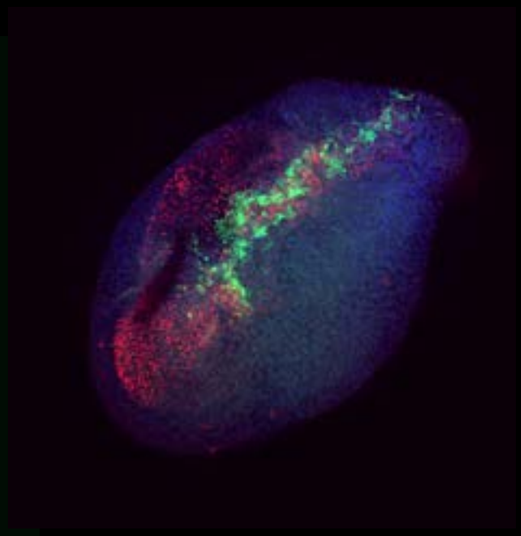


→
“Aggregoid” of a human gastruloid (blue and yellow) with a human trophoblast spheroid (green) (Credit: Ludivine Delon).

Mouse gastruloids co-aggregated with Visceral Endoderm-like cells form the structure resembling Anterior Primitive Streak (APS) and notochord



↑
DAPI (blue), T/BRA (green), SOX17 (yellow) FOXC1 (red) (Credit: Natalia Smirnova and Sergei Ponomartcev).



↑
DAPI (blue), T/BRA (green), FOXA2 (red) (Credit: Natalia Smirnova and Sergei Ponomartcev).

HYBRIDA

Embedding a comprehensive ethical dimension to organoid-based research and related technologies (2021-2024)

About the project

The main objective of the project is to develop a comprehensive regulatory framework for organoid research and organoid-related technologies. The work in the consortium focuses on:

1. Identify different forms of conceptual uncertainty by exploring the ontological, moral and legal status of organoids present in different cultures and knowledge traditions.
2. Reducing epistemological uncertainty in organoid research and produce improvements in impact assessment of organoïd-related technologies.
3. Exploring regulatory uncertainty prevalent in existing normative and ethical frameworks pertaining to technologies similar to organoid-related technologies.
4. Understanding the worries, fears and expectations of the general public, vulnerable groups, patients, donors and civil society organisations with respect to organoids.
5. Engaging relevant stakeholders, in order to co-create and validate the 4 main products of HYBRIDA.
6. Producing a set of operational guidelines for the field of organoid research.
7. Producing a Code of responsible conduct for organoid researchers and, if needed, suggest a supplement to the ECoC.
8. Enhancing existing ethics and normative frameworks with a focus on organoid research and organoid-related technologies.

PROJECT LEADER

Søren Holm
Department of Law, School of Social Sciences, University of Manchester / University of Oslo

PARTICIPANTS

The University of Manchester;
Universite Catholique de Louvain;
Aarhus University;
University Leiden;
Technical University Athens;
Insubria University
University of Oslo

FUNDING

The 3 year project is funded by the EU program: H2020-EU.5. – SCIENCE WITH AND FOR SOCIETY with 26,5 million NOK

FURTHER INFORMATION

https://hybrida-project.eu

https://cordis.europa.eu/project/id/101006012

Image credit: Thomas Combriat

Wellcome LEAP

Female resilience on-chip: Monitoring dynamic resilience using Multi-Organ-Chips linking metabolic state and immune response in pre- and postmenopausal women (2023–2026)

About the project

Current research on dynamic resilience has been limited to observational clinical settings and simplified *in vitro* assays. However, in order to investigate the mechanisms that control and alter resilience and to identify associated biomarkers, advanced *in vitro* models that can be subjected to stressors in defined ways are urgently needed. Organ-on-Chip (OoC) technology has the potential to address these limitations by enabling the connection of multiple tissue models and the integration of immune components, allowing for studies on human physiological processes with a granularity that current models do not provide.

In this project we unite experts in OoC platform design, organoid development, immunology, genomics, bioinformatics/ artificial intelligence, and clinical research to create a resilience-on-chip platform. We believe that metabolic changes during aging contribute to an inflammatory environment, impacting resilience and having immune metabolic effects. We hypothesize that dynamic resilience mechanisms are centrally impacted by metabolic changes during aging that create an overall inflammatory environment which leads to loss of resilience and hence are of immune metabolic nature.

To explore this hypothesis with high granularity, we propose:

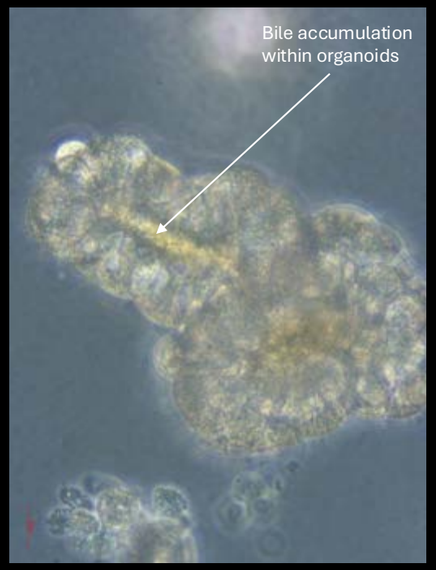
1. Leveraging a three-organ Multi-Organ-Chip (MOoC) connecting hormone, metabolic and immune sensitive organs (WAT, liver and lymphoid tissue).

2. Applying a series of readouts that allow the dynamic monitoring of immune metabolic changes in an integrated approach.

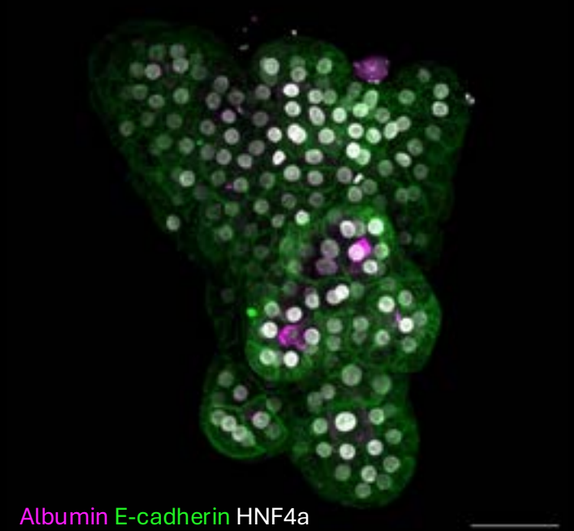
3. Interrogating the platform with a battery of stressors.

4. Benchmarking the in vitro data set with the human in vivo situation on a patient-specific level.

Liver organoids generated from human hepatic progenitors, isolated from donor liver tissue (Credit: Alexandra Aizenshtadt).



↑
Bright field imaging of liver organoid in extracellular matrix, showing morphology and accumulation of bile (yellow color). Scale bar 50 um.



↑
Confocal imaging of human tissue-derived liver organoid, expressing E-cadherin (green), albumin (magenta) and HNF4a (white). Scale bar 50 um.

PROJECT LEADER

Prof. Peter Loskill
Natural and Medical Sciences Institute at the University of Tübingen (NMI), Germany.

PARTICIPANTS

NMI-μOrgano team
Prof. Dr. Peter Loskill
Dr. Claudia Teufel
Dr. Madalena Cipriano

NMI-MIA team
Dr. Nicole Schneiderhan-Marra
Dr. Alex Dulovic NMA

Wellcome Sanger Institute team
Dr. Roser VentoTormo

University of Oslo team
Prof. Stefan Krauss
Prof. Dr. Espen Melum
Dr. Aleksandra Aizenshtadt
Dr. Mathias Busek

Clinical and Regulatory Advisory Board
Prof. Dr. Sara Y. Brucker, EKUT University Women's Hospital, Tubingen.

Prof. Dr. Espen Melum, Research Institute of Internal Medicine (RIIM), UiO.

Dr. Heidi Beate Berntzen, UiO.

FUNDING

The 3-year project is funded by the Wellcome Leap Dynamic Resilience program with 6,3 million USD.

FURTHER INFORMATION

https://wellcomeleap.org/dr/program/

Research and engagement

Innovation

SPARK teams

SPARK is a two-year UiO:Life Science innovation program to further develop ideas within health-related life sciences for the benefit of patients and society.

rOoC (revolving Organ-on-chip platform)

Project leader

Dr. Aleksandra Aizenshtadt, HTH, UiO.

Team members

Dr. Shadab Abadpour, Dr. Mathias Busek, Chencheng Wang, Prof. Steven Ray Haakon Wilson, Prof. Stefan Krauss, Dr. Hanne Scholz.

Tankyrase inhibition for therapy of fibrotic diseases

Project leader

Shoshy Alam Brinch, Hybrid Technology Hub, UiO and Department of Immunology and Transfusion Medicine, Oslo University Hospital.

Team members

Jo Waaler (OUS/UiO) and Stefan Krauss (UiO/OUS)

DUCT chip – An artificial bile duct on a chip recapitulating immune functions

Project leader

Henry Hoyle, Division of Surgery, Inflammatory Diseases and Transplantation, OUS.

Team members

Anna Katharina Frank, Espen Melum, Stefan Krauss, Mathias Busek, Aleksandra Aizenshtadt and Kayoko Shoji

Patents

Krauss S, Nazare M, Lehtio L, Waaler J, Wegert A, Leenders R.G.G "compounds". Application submitted 19. June 2018 IPO patent application number 1810071.9. Published 29.12.2019 WO2019/243822

Krauss S, Waler J, Lehtio L, Leenders R.G.G. Wegert A. “compounds” application submitted 6. July 2020 IPO patent application number 2010359.4

Krauss S, Aizhenshtadt A, Mikel Martinez, Busek M “Cell Culture Device”. Application submitted 19 July 2021 UK patent application (Appl. 2110366.8)

DOFI

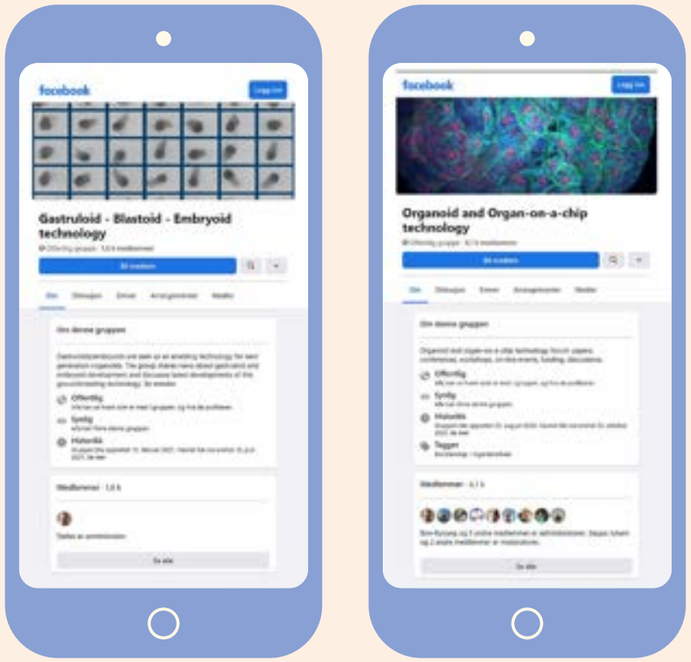
14/09/2020 DUCT chip – An artificial bile duct on a chip recapitulating immune functions; Espen Melum, Anna Frank, Stefan Krauss

13/08/2021 Human iPS derived zone specific hepatocytes; Aleksandra Aizenshtadt and Stefan Krauss

10/01/2023 Devise for analytical Electromembrane Extraction from 3D cell culture, Organoids and organ-on-a-chip platforms; Frøydis Sved Skottvoll, Steven Ray Wilson, Stig Pedersen Bjergaard, Jörg P. Kutter, Michal Mielnik, Aleksandra Aizenshtadt, Stefan Krauss

Outreach

Media / Social media



Facebook

HTH manages two public Facebook groups focused on gastruloids and organoids, with 1700 and 4300 followers, respectively.

https://www.facebook.com/groups/143900280909369

https://www.facebook.com/groups/304082784189295

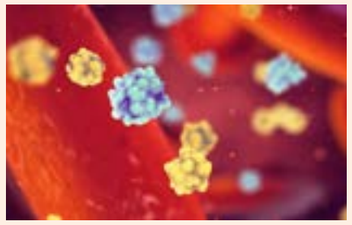
Linkedin

HTH managed group

https://www.linkedin.com/groups/12584551/

1700 + 4300
followers

Popular science presentations / Articles in media



Diabetiker lager sitt eget insulin etter å ha fått satt inn dyrkede celler

HTH Vice director Hanne Scholz comments on new diabetes treatment in Forskning.no

https://www.forskning.no/diabetes/diabetiker-lager-sitt-eget-insulin-etter-a-ha-fatt-satt-inn-dyrkede-celler/2414692

Education

TNNN – Research School for Training the Next Generation of Micro- and Nanotechnology Researchers in Norway

About the project

The Hybrid Technology Hub CoE participates in the Research School for Training the Next Generation of Micro- and Nanotechnology Researchers in Norway (TNNN). Micro and Nano Science and Technology is a highly cross disciplinary field that covers many areas of science including physics, chemistry, material technology, biology and medicine. It is the driving force behind a large part of modern science and technology, with numerous applications that span photovoltaics, batteries, fuel cells, opto-electronics, sensors, medical diagnostics, biomedical research, quantum computing and many others.

The Research School for Training the Next Generation of Micro- and Nanotechnology Researchers in Norway (TNNN) will address current gaps in PhD-level education in this field. In particular, it will establish a vibrant national network of junior scientists working in this area of science and technology development, provide training in transferable skills and facilitate collaboration with industry.

The Research School focuses on:

1. National Junior Scientist Research Conference: This conference will be organized every year and will include plenary and invited talks from leaders in various areas of nanotechnology, contributed talks from PhD candidates and postdoctoral researchers, presentations from industry, workshops and networking events
2. Workshops in generic/transferable skills
3. Problem solving workshops organized together with partners from the Norwegian industry
4. Innovation, entrepreneurship and commercialization courses and workshops

The TNNN research school held its 3rd annual national conference at the UiO Campus Blindern, Oslo 6 – 8 of June 2024. The conference was a part of Oslo Science Week, which also included the Nordic Nanolab User's Meeting (3–4 of June) and Sintef's Sensor Decade (5–6 of June).

HTH contact point

Dr. Hanne Scholz, Hybrid Technology Hub – Centre of Excellence, Institute of Basic Medical Sciences, University of Oslo (UiO) and Oslo University Hospital.

Further information

Research School for Training the Next Generation of Micro- and Nanotechnology Researchers in Norway (TNNN) – NTNU.

https://www.ntnu.edu/tnnn

Education

NOR-MPS symposium- microphysiological systems, organoids and organ-on-chip technology

HTH organized the one-day symposium on February 14, 2024. The NOR-MPS symposium brought together Norwegian and international experts to present their research and discuss the latest advancements in microphysiological systems, organoids, and organ-on-chip technology.

Held as a side event to the Norway Life Science Conference, the symposium featured keynote talks by senior scientists, short project presentations by postdocs and PhD students, a poster session, and roundtable discussions on cutting-edge developments and ethical considerations on research using stem cells and organoids.

The event was highly successful, with over 100 participants and a fully booked program.

HTH PhD student Ingrid Wilhelmsen presenting at the PD/ PhD pitching session.

Graduated PhD students

On September 2, 2024, Chencheng Wang successfully defended his dissertation titled "Human Pluripotent Stem Cell-Derived Islet Cells for Diabetes Modelling and Drug Testing." The title of his trial lecture was "Can Organ-on-Chip Technology Replace Animal Experiments?"

Chencheng Wang

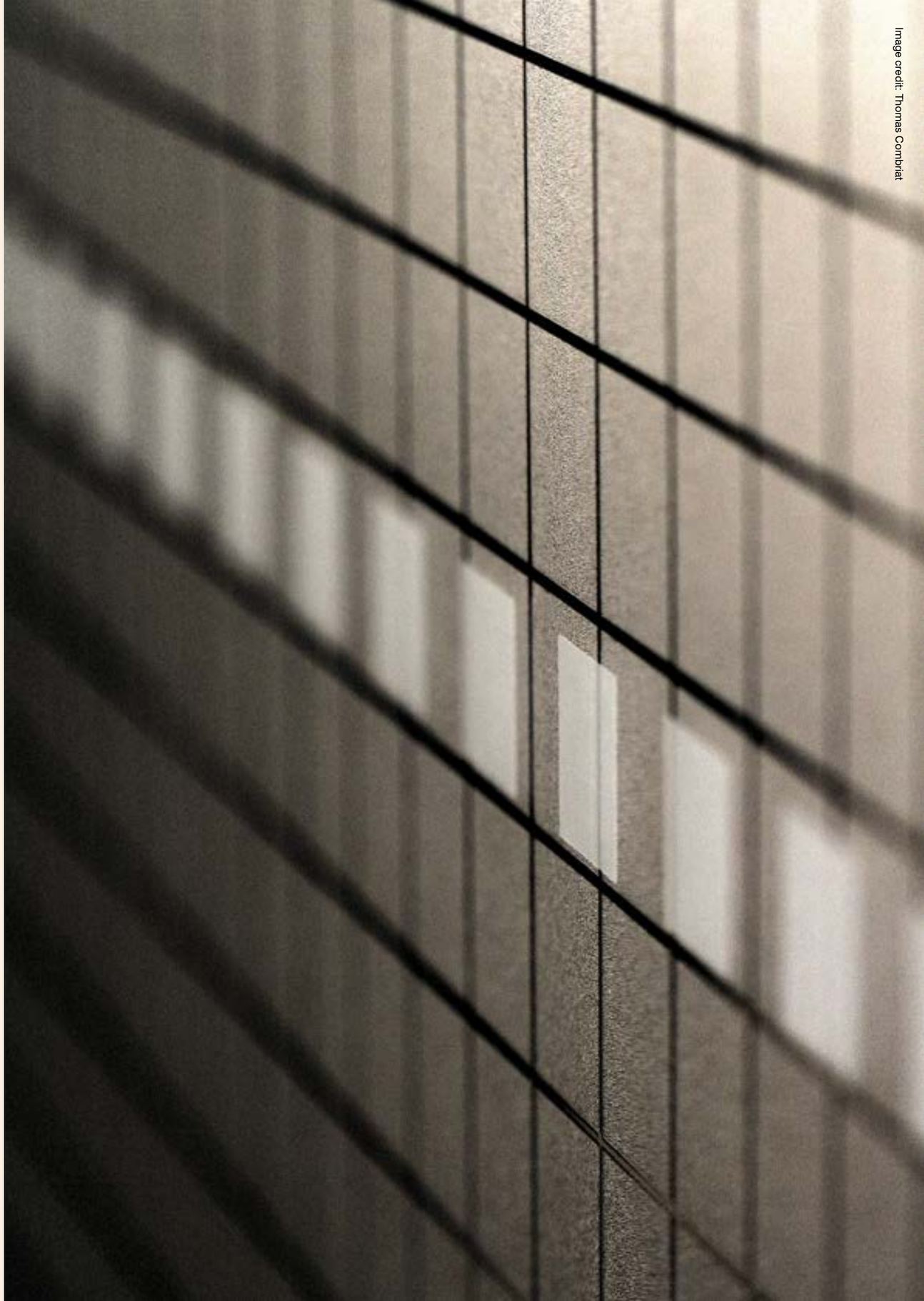


Image credit: Thomas Combriat

Image credit: Thomas Combriat

About the centre

Organizational chart

1 man-year

1/2 man-year

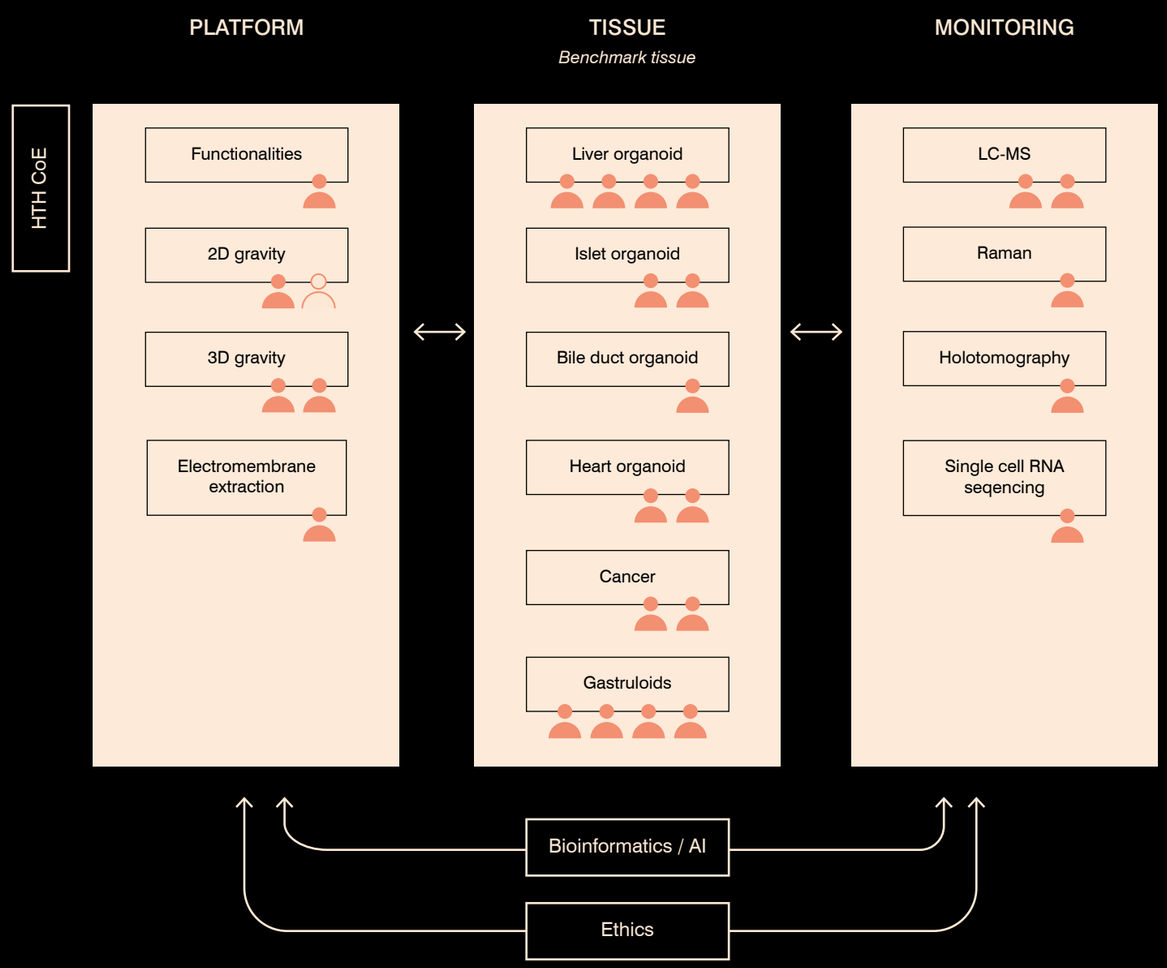


Image credit: Thomas Combriat

About the centre

Team members 2024

Management

Stefan Krauss
Centre Director

Hanne Scholz
Vice Director

Petter Angell Olsen
Administrative coordinator
and Facility manager

Principal investigators

Nikolaj Gadegaard

Molly Stevens

Simon Rayner

Steven Wilson

Jan Helge Solbakk

Stefan Krauss

Hanne Scholz

William Edward Louch

Espen Melum

Alexandre Corthay

Associated Partners

Jo Waaler

Hanne Røberg-Larsen

Team members 2024

Postdoctoral fellows and researchers


Alexandra Aizenshtadt
Lab. manager


Anna Frank


Shadab Abadpour


Mathias Busek


Thomas Combriat


Olga Bibikova


Ludivine Delon


Sergei Ponomartcev


Igor Meszka


Inger Øybråten


Andrea Dalmao-Fernandez


Jonas Aakre Wik


Henry Hoyle


Jia Li


Endalkachew Alemu


Helena Hruskova


Heidi Beate Bentzen

Head engineer


Justyna Stokowiec

PhD candidates


Almira Ibragimova


Chencheng Wang


Stian Kogler


Shoshy Alam Brinch


Ingrid Wilhelmsen


Malgorzata Elzbieta Zawadzka


Franziska Schoeb


Duarte Menezes


Natalia Smirnova


Magnhild Sekse

Technicians


Ida Johnsen


Lydia Busek


Alexey Golovin


Yuliia Boichuk


Emilie Gasparini


Dilara Lal, Lal


Jeanette Konstanse Steen


Yuchuan Li


Thea Josefine Christensen


Katharina Ferencevic


Karen Irion


Enya Amundsen-Isaksen

Oline Hovland

Jule Bekkhus

Board 2024

Professor
Jan G. Bjålie
Pro-Dean for Research and Innovation
Faculty of Medicine, University of Oslo

Chairman of the board

Board members

Professor
Lene Frost Andersen
Head of department, Institute of Basic Medical Sciences, University of Oslo

Professor
Lars Eide
Institute of Clinical Medicine, University of Oslo

Professor
Steve Beaumont
University of Glasgow

Professor Raoul Charles Coombes
Imperial College, London

Professor
Stefan Krauss
Centre Director, Hybrid Technology Hub, University of Oslo

Scientific Advisory Board (SAB) 2024

Professor
Bengt Norden
Chalmers University of Technology, Sweden

Professor
Anna Herland
KTH Royal Institute of Technology, Sweden

Professor
Peter Loskill
Fraunhofer Institute for Interfacial Engineering and Biotechnology IGB, Germany

Professor
Thomas Laurell
Department of Biomedical Engineering, Lund University

About the centre

International collaborations

ACADEMIC COLLABORATIONS

- Aarhus University
- Armauer Hansen Research Institute
- Chalmers University of Technology
- Chinese Academy of Sciences-Max Planck Gesellschaft Partner Institute for Computational Biology
- Forschungsverbund Berlin
- Harvard Medical School
- Institut Cochin
- Italian National Research Council
- Juntendo University School of Medicine
- Karolinska Institutet
- KTH Royal Institute of Technology
- Leiden University Medical Center
- Maastricht University
- Max-Planck-Gesellschaft zur Förderung der Wissenschaften
- RMIT University
- Technical University of Denmark
- Tel Aviv University
- The University of Texas Medical Branch
- Université d'Artois
- University of Arizona
- University of Bergen
- University of California
- University of Cambridge
- University of Copenhagen
- University of Glascow
- University of Helsinki
- University of Illinois at Urbana-Champaign
- University of Natural Resources and Life Sciences
- University of Oulu
- University of Turku
- Univesity of Oslo / Oslo university hospital
- University of Oxford
- Uppsala University Hospital
- Wuhan Institute of Virology
- Wyss Institute at Harvard University
- Yale School of Medicine / Yale Stem Cell Center

INDUSTRIAL COLLABORATIONS

- AstraZeneca R&D
- BiomimX S.r.l.
- CVMD iMed Bioscience
- Labcorp Drug Development Laboratories Limited
- NOVARTIS
- Symeres Inc
- TPP plc
- Waters

The 2024 HTH Annual Retreat took place on the Color Magic cruise ship.

Retreats

HTH annual retreat

December 2nd–4th 2024

The 2024 HTH annual retreat was held aboard the Color Magic cruise ship, sailing the Oslo-Kiel-Oslo route, with 40 participants from the centre. Over the course of two days, the retreat featured virtual presentations from four esteemed international speakers: Laura de Rooij, Alexander Mosig, Jesse Veenvliet, and Michael Riegler. Additionally, Vivienne Lumayag from UiO gave an insightful talk on career development. To enhance collaboration and teamwork, the schedule included group work sessions and team-building activities, concluding with a festive “Christmas table”.

Engaging discussions in one of the group work sessions.

Winner images from the “Light and Shadow” Photo Contest at the HTH Annual retreat. Left column: Best Photo category winners: “Horizons” by Thomas Combriat and “Xmas Spirit” by Aleksandra Aizenshtadt. Right column: Funniest Photo category winners: “Little Scientist Around the World” by Andrea Dalmao Fernandez and “The Light and Dark Side of Henry” by Oline Hovland.

Publications 2024

Aizenshtadt, Aleksandra, Wang, Chencheng, Abadpour, Shadab, Menezes, Pedro Duarte, Wilhelmsen, Ingrid, Dalmao-Fernandez, Andrea, Stokowiec, Justyna, Golovin, Alexey, Johnsen, Mads, Combriat, Thomas M. D., Røberg-Larsen, Hanne, Gadegaard, Nikolaj, Scholz, Hanne, Busek, Mathias & Krauss, Stefan J. K.

Pump-Less, Recirculating Organ-on-Chip (rOoC) Platform to Model the Metabolic Crosstalk between Islets and Liver.

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Enhancing Supercapacitor Electrochemical Performance with 3D Printed Cellular PEEK/MWCNT Electrodes Coated with PEDOT: PSS.

ACS Omega 2024, 9, 31, 33998–34007, 23 July 2024

https://doi.org/10.1021/acsomega.4c04576

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https://doi.org/10.1002/smll.202404536

Christian Winther Wold, Panagiotis F Christopoulos, Maykel A Arias, Deborah Elikplim Dzovor, Inger Øynebråten, Alexandre Corthay, Kari Tvete Inngjerdingen.

Fungal polysaccharides from Inonotus obliquus are agonists for Toll-like receptors and induce macrophage anti-cancer activity.

Communications biology vol. 7,1 222. 23 Feb. 2024

https://doi.org/10.1038/s42003-024-05853-y

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Acoustic Wave-Induced Stroboscopic Optical Mechanotyping of Adherent Cells.

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Cunha, André B., Schuelke, Christin, Mesri, Alireza, Ruud, Simen K., Aizenshtadt, Aleksandra, Ferrari, Giorgi, Heiskanen, Arto, Asif, Afia, Keller, Stephan S., Ramos-Moreno, Tania, Kalvøy, Håvard, Martínez-Serrano, Alberto, Krauss, Stefan, Emnéus, Jenny, Sampietro, Marco, & Martinsen, Ørjan G.

Development of a Smart Wireless Multisensor Platform for an Optogenetic Brain Implant.

Sensors 2024, 24(2), 575, 16 January 2024

https://doi.org/10.3390/s24020575

Gilmour, Brian C., Corthay, Alexandre, & Øynebråten, Inger.

High production of IL-12 by human dendritic cells stimulated with combinations of pattern-recognition receptor agonists.

npj Vaccines, Volume 9, Article number: 83 (2024), 3 May 2024

https://doi.org/10.1038/s41541-024-00869-1

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Expert Revision of Key Elements for Clinical-Grade Production and Qualification of Perinatal Derivatives.

Stem Cells Translational Medicine, Volume 13, Issue 1, Pages 14–29, January 2024, First published: 10 December 2023

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Hrušková, Helena, Olsen, Christine, Řemínek, Roman, Wang, Chencheng, Aizenshtadt, Aleksandra, Krauss, Stefan, Scholz, Hanne, Røberg-Larsen, Hanne, Foret, František, & Wilson, Steven Ray.

Preparative agarose gel electrophoresis for reducing matrix interferences of organoid cell medium prior to LC-MS analysis of insulin.

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Kogler, Stian, Pedersen, Gustav Mathings-dal, Martínez-Ramírez, Felipe, Aizenshtadt, Aleksandra, Busek, Mathias, Krauss, Stefan J. K., Wilson, Steven Ray, & Røberg-Larsen, Hanne.

An FDA-Validated, Self-Cleaning Liquid Chromatography–Mass Spectrometry System for Determining Small-Molecule Drugs and Metabolites in Organoid/Organ-on-Chip Medium.

Analytical Chemistry. Vol 96/Issue 29, 12129-12138, 10 July 2024

https://doi.org/10.1021/acs.analchem.4c02246

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Funding

Project name	Funding scheme	Project leader	Sum	Period
NATIONAL				
Tankyrase Inhibition in Cancer Immunotherapy	HSØ – Forskerstipend	Jo Waaler	4.4 M NOK	2019–2022
Scalable directional pump-less perfusion (dpp) organ-on-a-chip platform	FORNY20–2020	Stefan Krauss	0.5 M NOK	2021–2022
Scientia Fellows II	H2020-MSCA-COFUND	Stefan Krauss and Espen Melum	1.6 M NOK	2021–2022
Virus induced Acute Respiratory Distress Syndrome (ARDS): testing WNT inhibition as a novel therapeutic principle on a Lung-on–a-Chip platform	HSØ – Åpen prosjektstøtte	Stefan Krauss	9 M NOK	2021–2023
Tankyrase Inhibition in Cancer Immunotherapy	HSØ – Karrierestipend	Jo Waaler	9 M NOK	2021–2024
DUCT chip – Immune studies using a bile duct on a chip	NFR – FRIMED2-FRIPRO	Espen Melum	12 M NOK	2021–2027
Tankyrase inhibition as a therapeutic principle in idiopathic lung fibrosis	NFR – FORNY20	Stefan Krauss	5 M NOK	2022–2023
Unleashing the full antitumor potential of macrophages for next-generation cancer immunotherapy	HSØ – Åpen prosjektstøtte	Alexandre Corthay	9 M NOK	2022–2025
Integrated technologies for tracking organoid morphogenesis (ITOM)	UiO:Lifescience-Convergence	Stefan Krauss	16.9 M NOK	2022–2026
Pharmacokinetics-on-chip	NFR – FORNY20	Steven Wilson	0.5 M NOK	2023–2024
KVAL: A neural network-based image denoising software	NFR – FORNY20	Hao Wu (Louch Group)	0.5 M NOK	2023
New hope for heart failure with preserved ejection fraction (HFpEF)	HSØ – Postdoktorstipend	William E. Louch	2.6 M NOK	2023–2025
Pump-less recirculation Organ-on-Chip platform	NFR – FORNY20	Mathias Busek (Krauss group)	5.0 M NOK	2023 - 2025
TumorChip – development of a tumor-on-a-chip platform for testing WNT signaling inhibition as an enabling factor in melanoma immune oncology”	DNK	Stefan Krauss	8.0 M NOK	2023–2025
Total analytical solution for enabling robust mass spectrometric analysis of organoids and organ-on-chip samples.	FORNY20-FORNY2020	Steven Ray Wilson (Aina H. Rengmark)	0.5 M NOK	2024
Pump-less recirculation Organ-on-Chip platform	FORNY20-FORNY2020	Mathias Busek	3.9 M NOK	2023-2025
Clinical feasibility of in vitro diagnostic drug testing for pancreatic cancer.	BIA-Brukerstyrt innovasjonsarena	Jarle Bruun (CEO Oncosyne)	3.2 M NOK	2024-2028

Project name	Funding scheme	Project leader	Sum	Period
PRIVATE				
PSC Studies using a Bile-Duct-on-a-Chip	PSC partners	Tom H. Karlsen/Anna Frank/Stefan Krauss	0.6 M NOK	2021–2022
Generation of insulin-producing cells from bile duct cells (cholangiocyte organoids)	Novo Nordisk Foundation	Hanne Scholz	1.3 M NOK	2021–2023
Endocrinology & Metabolism 2022	Novo Nordisk Foundation	Hanne Scholz	1.3 M NOK	2022–2023
EMGUT: Energy Materials for the Gut	Novo Nordisk Foundation	Anja Boisen DTU/Nikolaj Gadegaard	5.5 M NOK	2022–2027
Testing av legemidler med lab-dyrkede organer, som alternativ til dyreforsøk	Dyrevernsalliansen	Steven Wilson and Stian Kogler	0.1 M NOK	2023
Wellcome LEAP: Female resilience on-chip: Monitoring dynamic resilience using Multi-Organ-Chips linking metabolic state and immune response in pre- and post-meno-pausal women.	Wellcome Trust	Peter Loskill (Co-PI: Stefan Krauss)	9.6 M NOK	2023–2027
Pharmacokinetics-on-chip.	Novo Nordisk Foundation	Steven Ray Wilson	1.6 M NOK	2024
INTERNATIONAL				
Hybrida – Ethics of Organoids	EU H2020 – SwafS	Søren Holm (HTH participants: Jan H. Solbakk, Stefan Krauss, Heidi B. Bentzen)	26.5 M NOK	2021–2024
Moral residue – epistemological ramifications, ethical implications, and didactic opportunities (MORE)	ERC Advanced Grants	Jan Helge Solbakk	27.4 M NOK	2022–2027
Supervised morphogenesis in gastruloids (SUMO)	EIC Pathfinder	Stefan Krauss	51.3 M NOK	2022–2027
EUropean network to tackle METAbolic alterations in HEART failure” (EU-METAHEART)	EU COST action	Christoph Maack (HTH participant: William E. Louch)	5.6 M NOK	2023–2027

Hybrid Technology Hub
– Centre for Organ-on-chip Technology

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Layout
Anagram Design

Cover image
A blend of Van Gogh's *Starry Night* with our lab's innovative human gastruloids, symbolizing the fusion of creativity and discovery—core values of the Hybrid Technology Hub CoE.
Credit: Igor Meszka