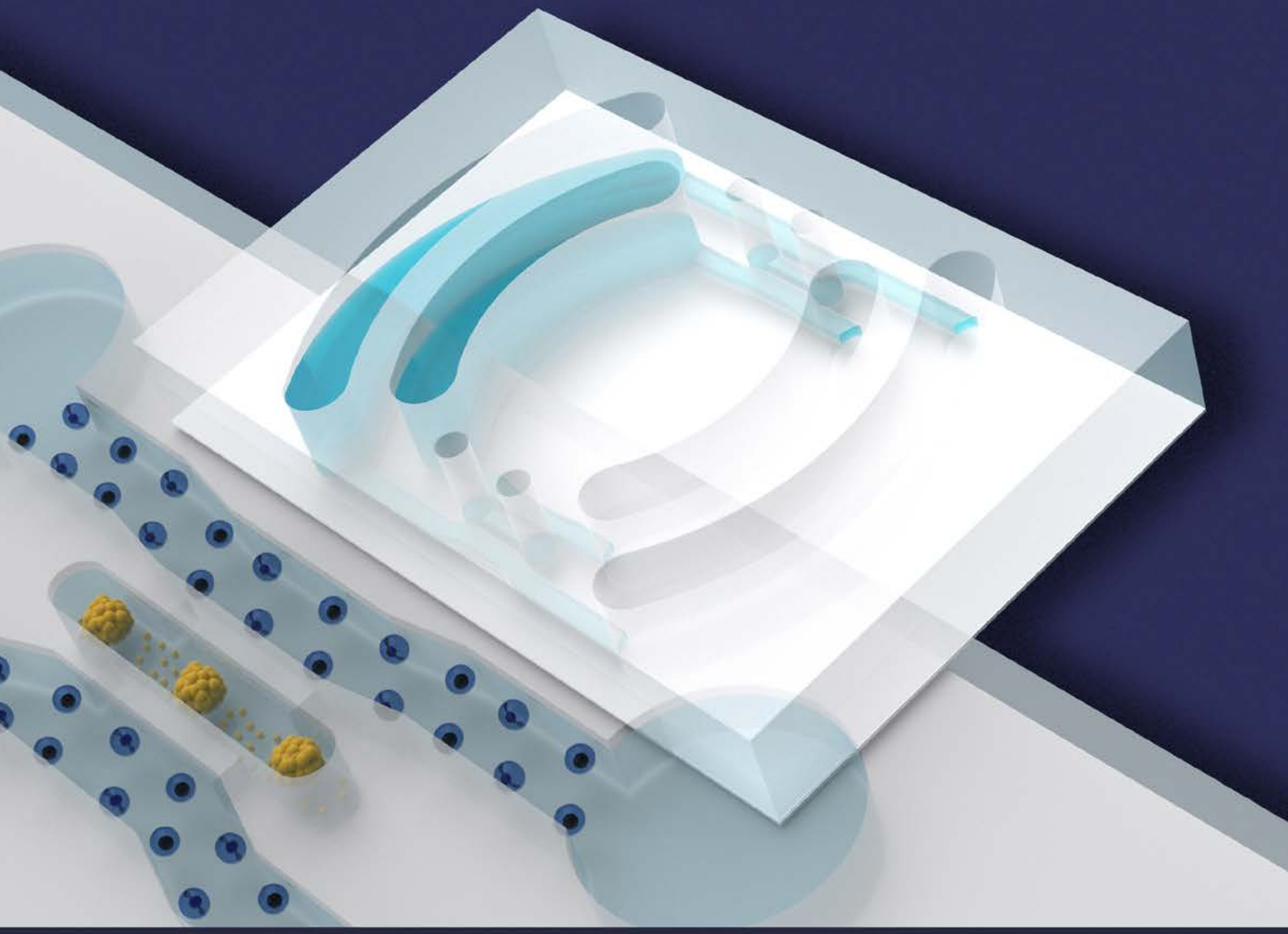
UNIVERSITY OF OSLO

Hybrid Technology Hub - Centre for Organ on a Chip Technology



Annual Report 2022

Oslo University Hospital

University of Glasgow

Imperial College London

The Research Council of Norway

Universitas Osloensis MDCCCXI

Contents

From the director

In vitro models are often needed to recapitulate higher-level anatomical, physiological or pathological aspects of tissues and organs. Organoids and organ-on-chip technology are such emerging *in vitro* models.

Organoids are defined as self-organizing, three-dimensional (3D) tissue cultures, typically grown from stem cells, that model aspects of organ development, composition and function. Organ-on-chip (OoC) technology combines microfabrication and *in vitro* cell cultivation techniques to grow cells in an engineered environment under *in vivo*-like conditions, in order to recapitulate organotypic cellular architecture and functionality. Over the past decade, organoids and OoCs have emerged as physiologically relevant model systems that are complementary, and sometimes superior, to two-dimensional tissue cultures and animal models. Accordingly, organoids and OoCs are increasingly used for modeling organ physiology and disease conditions. Moreover, they are proving valuable models for drug development and personalized medicine, evidence by the recent “FDA Modernization Act 2.0” bill passed in the US Senate that specifically mentions these models as potential replacements for animal testing. Beyond that, the technology has an outlook towards developing human organ representations for transplantations. However, current organoid technology only fragmentary represent the histology and physiology of adult organs and is hampered by inconsistent production/ characterization procedures - resulting in significant variability.

The Hybrid Technology Hub (HTH) Centre of Excellence is working towards stem cell derived representations of organs that are central in controlling energy homeostasis with a focus on liver, adipose tissue and pancreas islets. This requires an interplay of supervised differentiation protocols, microfluidics, imaging and tracking technologies, integrated bioinformatics, and – as the technology matures – ethical supervision.

In 2022 the Centre concluded its first project period and passed to the second 5 year funding period. Hitherto, the Centre published 104 peer reviewed scientific articles, filed 3 patents, was involved in establishing the Research School for Training the Next Generation of Micro- and Nanotechnology Researchers in Norway (TNNN), and raised 189 mio NOK in complementary external funding, including grants from the Research Council of Norway, from the Health Region East (HSØ) and from the Norwegian Cancer Society, three Oslo Life Science convergence environment grants, three SPARK innovation grants, a European Research Council (ERC) advanced grant, a EU “Science With and For Society” (SwafS) project, and a European Innovation Council (EIC) grant. The Centre is grateful for the substantial funding that enables us to deepen and expand our research portfolio.

Hence, in 2022, the Centre has added further capacity by inviting professor William Louch who brings world leading imaging competence to the Centre, and associated professor Hanne Rødberg-Larsen, a leading specialist in mass spectrometry. The Centre has made further process in its liver, adipose and islet organoid and started to integrate the organoids into the rOoC microfluidic platform that was developed in the Centre and that allows integrating organ representations with components of the immune system. The Centre has started to develop a bile duct-on-chip platform that draws on a significant biobank of healthy and diseased human material. Furthermore, the Centre has established a sub-group that works on gastruloid technology that should boost our understanding of early steps in organogenesis in a move towards more complex organ representation. This project received substantial funding from the European Innovation Council. The ethic aspects of this work are addressed by an EU funded program on the ethics of organoids that embraces prominent European scholars including the head of the International Society for Stem Cell Research (ISSCR) Prof. Christine Mummery.

On the analytical side, the Centre has advanced mass spectrometry to deliver metabolic measurements from a dual organ-on-chip platform, allowing measuring metabolic interactions between liver and islet organoids. The Centre has established a Raman confocal spectroscopy platform in Oslo that is compatible with the partner laboratory at Imperial, and that allows direct chemometric measurement on organoids and gastruloids. Furthermore, the Centre is advancing spatial transcriptomics and single cell RNA sequencing technologies. In the Bioinformatics program, the Centre has completed a globally accessible distributed data sharing (GADDS) platform based in parts on block-chain technology to facilitate FAIR-like data-sharing.

HTH Centre Director Prof. Stefan Krauss.

I want to thank the PIs, researchers and staff in the Centre for their hard work and unmatched collaborative spirit – without their dedication, the Centre would not be possible. I also want to thank our host, the Institute of Basic Medical Sciences at the University of Oslo, as well as the Department of Immunology at the Oslo University Hospital, the University of Glasgow and Imperial College London for their dedication and support. We are grateful to the Scientific Advisory Board headed by Prof. Bengt Norden for excellent scientific advice as well as to the board of the Centre headed by Prof. Tom Hemming Karlsson for professional supervision. Finally, I want to thank for the significant resources that we received to be able to work towards advancing biomedical science. What could be a more fulfilling task?

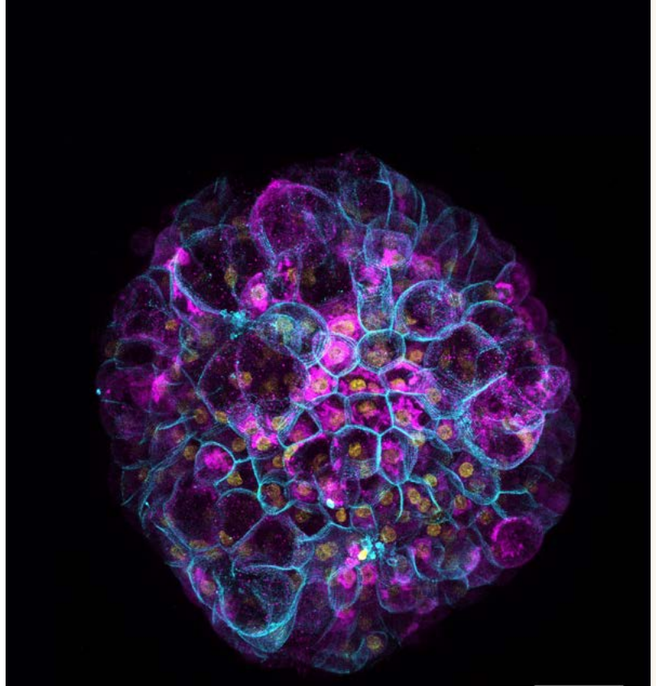
Stefan Krauss
Centre Director

Research groups

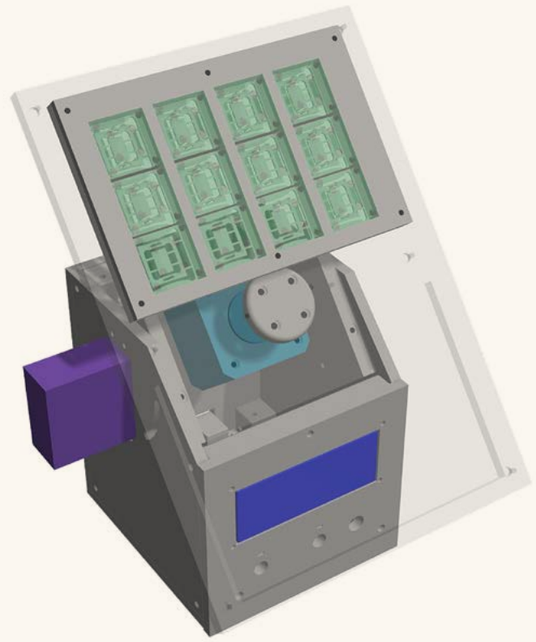
Krauss group
Developmental pathways

Stefan Krauss
Centre Director

Coming from a developmental biology background we apply principles of self-organization to improve hiPSC derived organ representations that are compatible with scalable drug interrogation.



Immunofluorescence image of liver organoid, labeled with antibodies against HNF4α (yellow), E-cadherin (cyan) and albumin (magenta). Scale bar: 50 μm. Credit: Aleksandra Aizenshtadt.



3D tilting platform holding 12 rOoC. Credit: Mathias Busek.

A novel organ-in-a-column platform

In a close collaboration with Centre partner Steven Wilson, we have contributed to the development of an organ-in-a-column platform that allows direct on-line LC-MS measurements of metabolites from liver organoids. This has been done by loading a liquid chromatography column with human induced pluripotent stem cell (hiPSC) derived liver organoids, and subsequently coupling this “organ-in-a-column” unit directly with liquid chromatography-mass spectrometry (LC-MS). The liver organoids were then interrogated “on column” with heroin, followed by on-line monitoring of the drug’s phase 1 metabolism. Enzymatic metabolites of heroin produced in the “organ-in-a-column” units were detected and monitored using a triple quadrupole MS instrument, serving as a proof-of-concept for on-line coupling of liver organoids and mass spectrometry. Taken together, the technology enables direct integration of liver organoids with LC-MS, allowing selective and automated tracking of drug metabolism over time. The work has been published in *Analytical Chemistry* *https://doi.org/10.1021/acs.analchem.2c04530*

Raman based chemometric imaging on liver organoids

Quantitative chemometric imaging tools for validating the composition of organoids, their functional maturity, disease state and response to therapeutic interventions are of significant interest in the rapidly expanding organoid arena. Raman spectral imaging (RSI) allows high-content, label-free detection of tell-tale biomolecules, but requires reliable quantification of deconvoluted spectra to unfold its full potential. Using qRamanomics, developed in the laboratory of Centre partner Molly Stevens, we first tested liver organoid maturity and variation. We then used the method to identify biomolecular response signatures to a panel of liver altering drugs, probing drug-induced compositional changes in the organoids. We also were able to follow for the first time *in situ* monitoring of drug metabolism and accumulation in liver organoids. The work is in press in *Cell Reports Methods.*

Liver organoids

Coming from a developmental biology background, the laboratory works towards an improved structure and functionality of liver organoids, and hence 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. 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 i) integrating the liver organoids with islets (developed in the laboratory of Centre partner Hanne Scholz) and ii) increasing complexity of the organoids. Manuscripts are in preparation.

A novel organ-on-chip platform

We developed a novel, pump-less directional flow recirculating organ-on-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 being scaled up in collaboration with Centre partner Nikolaj Gadegaard. The work has been published in «Lab on a Chip» (*https://doi.org/10.1039/D2LC00919F*), a patent is pending.

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 groups is supported by two Marie Skłodowska Curie fellowships and the recently awarded European Innovation Council (EIC) pathfinder project “supervised morphogenesis”.

WNT inhibitor development

The laboratory has a long track record on morphogenetic signals and chemical biology. One of our lead candidates is now being tested by an international pharma company with the aim of a license agreement. The work is a collaboration with Centre partner Jo Waaler, the Lari Lehtio laboratory and Symeres Inc.

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 works on developing new cell-based therapies to treat diabetes in a pre-clinical and clinical setting. The group's research focuses on developing islet organoids from pluripotent stem cells with properties of mature metabolic control.

Beta cell replacement therapy

by clinical allogenic islet transplantation is a minimally invasive procedure that has evolved as a safe and efficient treatment option for type 1 diabetic patients with poor glycaemic control. Islet transplantation has also recently been shown to be more efficient than intensive insulin treatment and has improved health-related quality of life for patients. The Scholz group works actively through International networks which have raised the voice to improve and broaden this therapy worldwide.

Adipose-derived stromal cells preserve pancreatic islet function in a 3D bioprinted scaffold

Mesenchymal stromal cells (MSCs) are known for their beneficial impacts on islet viability and function. However, there is a lack of a method that allows the generation of a composite graft of islets and MSCs. We have developed a method that uses adipose-derived stromal cells (ASCs) to promote islet graft viability and function in a transplantable scaffold using 3D bioprinting. We first show that we could engineer a bioprinted double-layered cell delivery scaffold based on hydrogel bioink. Next, we show that ASCs preserve pancreatic islet function in a transplantable 3D bioprinted scaffold. We believe that this could allow for transplantation to another site than the liver and that there is a possible role of ASCs on improving the islet micro-environment for implementation into *in vitro* models such as islet organoids on chip.

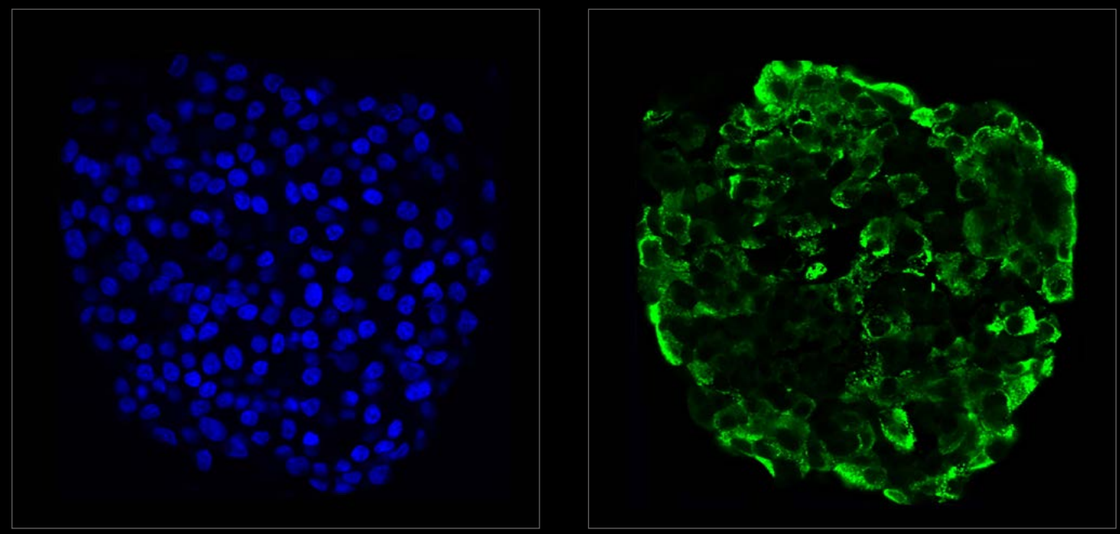
Generation of beta cells from human induced pluripotent stem cells (hiPSCs)

Through the ABINO project and in collaboration with Prof. Helge Ræder at UiB we have established state of art protocol for direct *in vitro* differentiation of human hiPSCs to insulin-producing cells at the HTH core facility. However, differentiated cells do not fully recapitulate the defining feature of mature human islets. We study the influence of high versus low glucose concentrations on hiPSCs differentiation. We found a beneficial effect on the K_{ATP} activity, but on the cost of the mitochondrial respiration ability. To follow up, we now do a systematic study on the different nutrients that control insulin secretion in these stem cell-derived islets.

Determination of insulin secretion from islet organoids

HiPSC can generate islet organoids that can be used for drug screening and regenerative medicine. In a joint project with Steven R. Wilson's group, we successfully developed a method for quantifying insulin production from islet organoids based on reverse-phase liquid chromatography-tandem mass spectrometry (RPLC-MS/MS). The next step is to allow for the simultaneous detection of the islet's specific hormones; insulin, glucagon, and somatostatin.

The group also collaborates within HTH with Espen Melum group on cholangiocyte organoids, Stefan Krauss group on developing the metabolism on chip, Molly Stevens group on imaging and sensor development, and Simon Rayner Group on bioinformatics.



Immunostining staing of stem cell derived islets. Representative immunostainings of C-peptide (green, labeling beta cells) and Glucagon (red, labeling alpha cells) in 10-μm cryosections from a stem cell-derived islet. Nuclei were stained with Hoechst 33342 (blue). Credit: Chencheng Wang.

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. Using computational biology we develop software to understand biological function.

The most obvious example of evolution in a biological system is when a pathogen, such as a coronavirus, mutates to evade a vaccine. However, such evolutionary mechanisms are present in other systems too. For example, there is clear evidence the human genome has evolved in response to environment, with specific populations showing distinct genetic traits associated with geographical location. A third example is how scientific publications are influenced by measures such as Impact Factor. For example, researchers can publish research that will be rated higher if they focus on viruses such as HIV or influenza, rather than neglected pathogens which tend to be published in lower impact factor journals. We are investigating each of these systems by developing a suite of software tools and algorithms and defining metrics to identify and quantify changes.

For our studies of the evolution of human genome, we are focusing on the non-coding regions of the genome and investigating how genetic and epigenetic changes impact regulatory control. One of our specific interests is the regulatory role of microRNAs (miRNAs). These are short RNA segments that regulate gene expression by binding to the 3'UTR of their gene targets. However, rather than performing standard miRNA studies which identify single miRNAs associated with a specific condition (such as cancer), we are interested in the role of miRNAs in providing stability in biological systems.

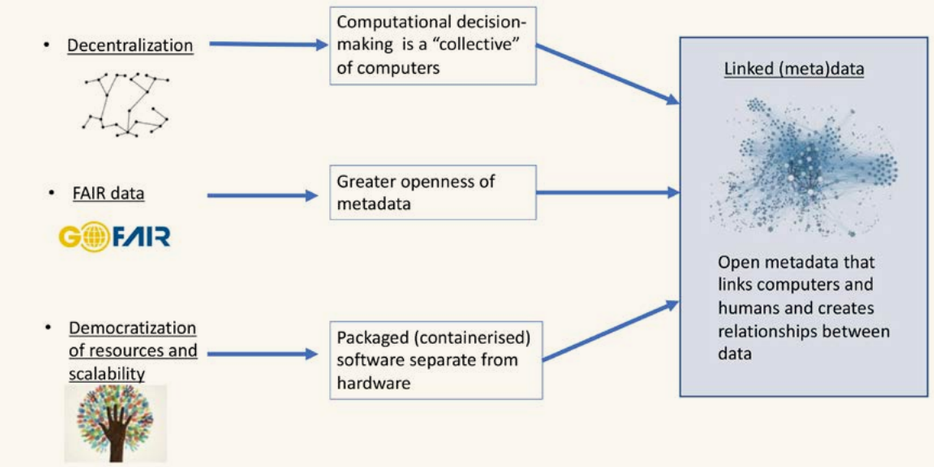
While we use publicly available data in this work, this doesn't always meet our needs and we also carry out our own experimental studies. This includes standard experiments such as Next Generation Sequence to profile miRNA and mRNA expression and their associated regulatory networks, but also more advanced 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.

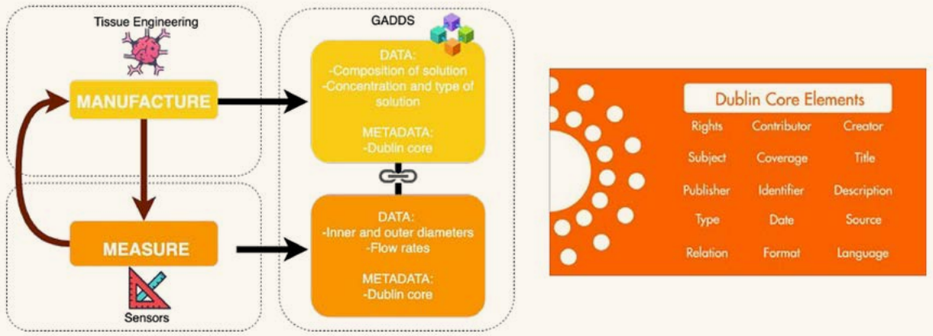
These works are particularly relevant to the research that is carried out in the HTH as we can use these tools to study organoids at the genetic level and identify differences with human organs. For example, liver organoids have been developed that exhibit core structural features and express key genes, 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 area where we contribute to the HTH 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.

We are working with all groups in the HTH to integrate the different generated data types (for example microscopy data, sequencing data and metadata for experimental protocols) to allow the application of advanced statistical learning approaches to analyze the data.





↑
Schematic showing how data collection and storage is handling in the GADDS platform in the context of a tissue engineering study.

Left: Manufacture and Measurement occurs in an iterative manner where the changes to manufacturing protocols are characterized by experimental measurement of generated tissue.

Middle: Meta(data) is uploaded to GADDS, where it is verified and stored in the ledger, and the corresponding experimental data is stored in the cloud. Metadata and data are linked by a unique Data ID (DID). In this case, Metdata is stored using elements defined according the Dublin Core standard.

Stevens group
Imaging and sensor technology

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

Molly Stevens
Principal Investigator

Accomplishments
Quantitative Ramanomics

The Stevens group has developed a quantitative chemometric imaging tool, Quantitative Ramanomics (qRamanomics), which is able to quantitatively chemotype the biomolecular spatial distribution in organoids. Collaborative work with the Krauss group resulted in a manuscript recently accepted in Cell Reports Methods, applying the method to liver organoids. The Stevens Group is now utilizing this Raman strategy to analyse the development of brain organoids. This method has helped us identify some essential extracellular matrix (ECM) proteins secreted by the cells during brain organoids development.

Sensor systems

We have been working on the development of a Localized Surface Plasmon Resonance (LSPR) insulin sensor to explore the fundamental biology of insulin secretion and organoid response to drug treatment. We optimised an LSPR chip design and build it on biocompatible plastic to be able to embed it to the organ-on-chip microfluidic system. The pumping system of the LSPR sensor is based on a microfluidic approach that improved the chip mechanical properties. There are tailor-made affinity proteins based on the insulin receptor-binding domain. We evaluated the performance of the optimised LSPR sensor on insulin solutions and we will further validate the sensor on the secretion from pancreatic islets and in-real time embedded in the organ-on-chip system.

SERS sensing

We are establishing a method for the online detection and quantitative assay of parental drugs and associated metabolites in physiologically relevant concentrations in liver organoids and supernatant medium to develop a high-throughput drug screening platform to investigate the influence of hepatotoxic drugs. We are using Surface-enhanced Raman Spectroscopy (SERS) platforms for measuring the complex secretome of liver organoids, incubated with Neratinib, Amiodarone and other drugs to extract quantifiable SERS signals. Further, real-time monitoring of the supernatants of the drug-applied liver organoids will be established and demonstrated to study the dynamic effects of the drugs on the liver. The next step of the project will be focused on combining the sensor with organ-on-chip systems.

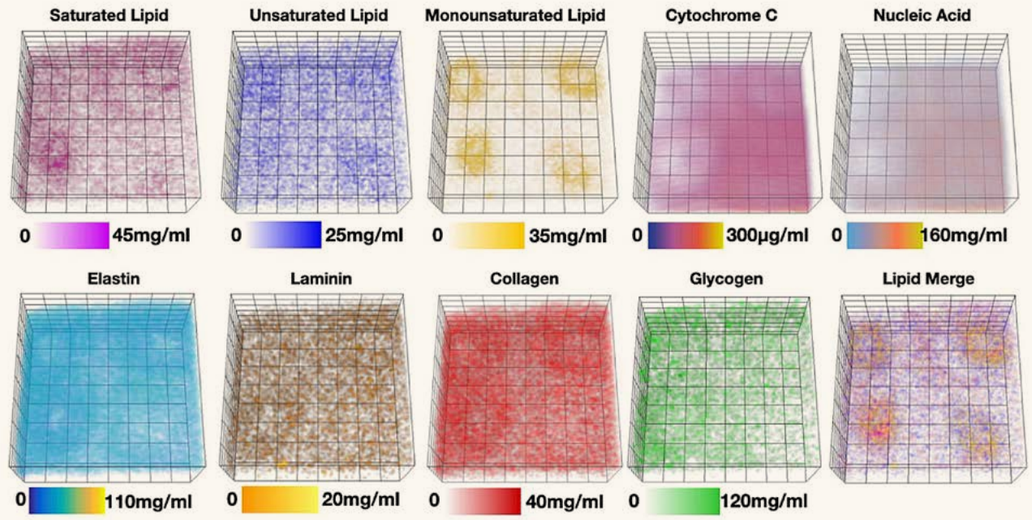
Optogenetics

We have been working on the optogenetic stimulation of human induced pluripotent stem cells (hiPSC) derived cells and organoids for their spatiotemporal control. An hiPSCs line with light-sensitive ion channels has been established using lentiviral transduction, and it has been confirmed that optogenetic hiPSCs-derived cardiomyocytes could be manipulated by light. This work was published in Advanced Science. Following up on this work, we developed an additional hiPSCs line including both excitatory and inhibitory optogenetic channels to provide enhanced spaciotemporal control of their activity. This was confirmed again using hiPSCs-derived cardiomyocytes that could be stimulated or inhibited used different light wavelengths.

SPARTA®

We have made many improvements to the SPARTA® platform for the investigation of extracellular vesicles (EVs). The SPARTA® platform is now in its third core physical iteration in a fully enclosed benchtop instrument at TRL 6. This new platform has been dubbed the SPARTA-Alpha system, which brings core improvements to the sensitivity and throughput of the system, as well as being safer and more user-friendly to use. In addition, we have made a dedicated software package that strongly improves the user experience and ease of data acquisition.

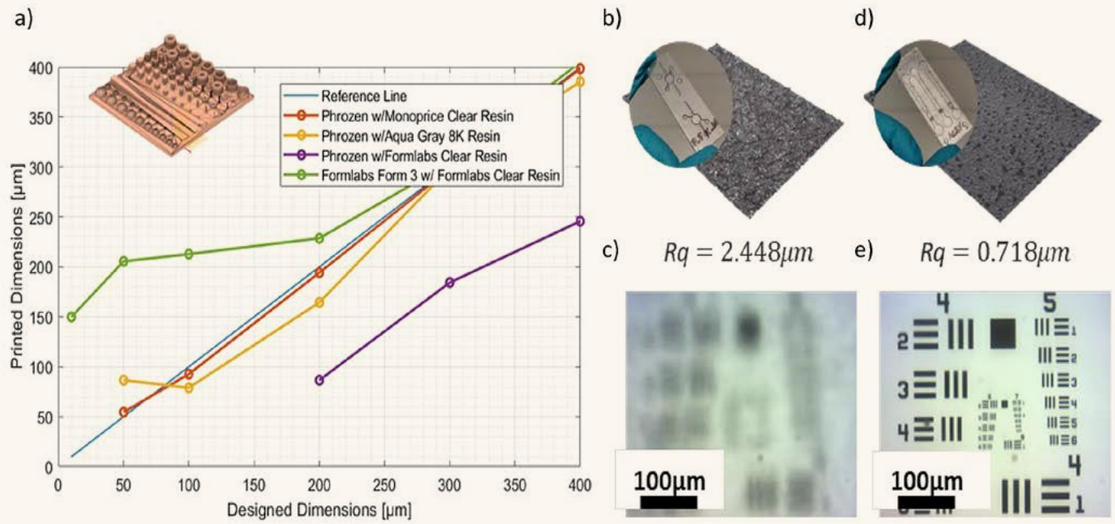
With regards to EV analysis, we have had a strong focus on expanding our previous work of breast cancer derived EVs. Major efforts were geared to improve the purification of EVs, which is a major challenge in the field. Using a combination of standard techniques (blotting, flow cytometry) in supplement with SPARTA® we have shown excellent separation between EVs and contaminant lipoprotein particles by density gradient and size exclusion chromatography separation techniques.



3D reconstructed Raman images of brain organoids.
Size of each 3D image: 400 x 400 x 200 μm.

Gadegaard group
Chip design

Nikolaj Gadegaard
Principal Investigator



a) Feature resolution in the xy plane for several tested photopolymer resins;
b) and **d)** demonstrate injection moulded samples and their respective topography, whereas **c)** and **e)**, demonstrate their resulting optical transparency. The samples presented in **d)** and **e)** are injection moulded with DLP 3D printed moulds, and respectively demonstrate superior quality in terms of surface roughness, Rq, and optical transparency, when compared to other moulds.

We work towards novel functionalities for the organ-on-chip platform.

Accomplishments

The past year of 2022 saw the Biomedical Interfaces at Glasgow (BIG) Research Group consolidating its scalable, low-cost, manufacturing procedure for Organ-on-chip (OoC) technology, and further expanding it with the incorporation of new fluidic designs, barrier components and hierarchical features. The following technical progresses were achieved: 1) manufacture of multi-layered, high complexity OoC devices, via DLP 3D printing, injection moulding and ultrasonic welding; 2) integration of porous membranes with controlled surface deflection, by using ultrasonic welding; and 3), incorporation of hierarchical features onto 3D printed moulds, by replica moulding with optical adhesives. Via collaborations in both Glasgow and Oslo, the technological component was followed by experimental testing, where biology was incorporated to culture gastruloids, simulate the placental barrier, and investigate osteoarthritis.

Manufacturing Process

OoC technology currently faces the challenge of bridging the gap between academic research and the pharmaceutical industry. Manufacturing scalability is key in overcoming this aspect, given that current methods are notoriously low-throughput and incompatible with automation. It is then proposed an alternative procedure, based on 3D printing, injection moulding and ultrasonic welding, defining an industrial scale, very high speed, and extremely low-cost method, enabling the development of hundreds of identical devices within less than a single working day – from CAD design to injection moulded parts. Following previous work achieved in the lab, Duarte Menezes (PhD Student, University of Glasgow) has successfully consolidated the respective technology to allow the development of multi-layered, high complexity OoC designs. The dimensions and geometry of 3D printed features have been studied to obtain injection moulded through holes, and enable the manufacture of devices with interconnected, multi-layered channels. Further, the use of DLP 3D printing has been investigated to increase the properties of moulds, and ultimately, the quality of injection moulded parts. Several photopolymer resins have been researched regarding the feature resolution and surface roughness provided by their respective 3D printed moulds. It was not only possible to achieve feature resolution under 100 μm, but also, a sub-micron surface roughness, the latter being critical in ensuring high optical clarity of the resulting injection moulded channels.

Membrane Integration

The tight and robust integration of porous membranes into non-PDMS microfluidic systems requires complex fabrication procedures and poses a widely acknowledged challenge. Aiming to overcome this issue, the group has investigated the integration of polymeric membranes via ultrasonic welding. Sealing is ensured by the welding of narrow structures, known as energy directors, which after localized high-frequency vibration and pressure, establish bonding between the membrane and the polymeric substrate. Results demonstrated that, not only does this method provide a reliable sealing of the membrane, where a physical barrier is established between adjacent microfluidic channels, but also, that its porous network is kept intact, meaning that the membrane's permeability properties are conserved. Given that the whole procedure is achieved in less than a few seconds, this protocol too, is characterized with high scalability. Finally, the amount of energy transferred during the ultrasonic welding procedure, was studied as a parameter capable of regulating the deflection of the membrane. By applying a higher energy rate, the membrane can be stretched to present a deflection of less than 20 μm. Ultimately, a flat membrane will not only benefit cell culture but also microscopy, therefore establishing a platform with greater potential for biological research.

Louch group
Cardiomyocyte function

William Edward Louch
Principal Investigator

Analyzing subcellular structures in stem cell derived cardiomyocytes is central for understanding their function and maturity, and for developing predictive *in vitro* models.

Our group's interests are specifically focused on the subcellular structure of cardiac muscle cells (cardiomyocytes) and the role that these structures play in generating the heartbeat. Contraction of each cell is initiated as calcium is released at tiny elements called "dyads", where invaginations of the cell membrane called t-tubules are in close apposition to the sarcoplasmic reticulum calcium store. Our group has observed that dyads are assembled gradually in the developing heart, allowing progressive strengthening of the heartbeat (**Figure 1**; Lipsett et al., J Physiol, 2019). However, these structures are unfortunately disassembled during the progression of diseases such as heart failure (Frisk et al., J Am College Cardiol, 2021). This re-emergence of a fetal phenotype during disease has highlighted the critical importance of understanding the mechanisms controlling dyadic formation and stability, as these structures may serve as key therapeutic targets for cardiac patients.

In our field, like many others, animal models have served an important role over the past decades. However, in recent years, our investigations of human cardiac tissue have indicated that dyadic structure/function are considerably different than in model species, particularly in comparison with rodents (Frisk et al., J Am Coll Cardiol, 2021). Access to healthy human tissue is limited, especially in the developing heart where we are most eager to understand the signals responsible for cardiomyocyte assembly. Fortunately, with the advent of human induced pluripotent stem cell (hiPSC)-derived cardiomyocytes and cardiac organoids, our group has been able to garner new insights into these processes in human cells (Parikh et al., Circ Res, 2017; Foo et al., Mol Therapy, 2021). Nevertheless, through collaboration with Hybrid Technology Hub members, we have observed that differentiation of these cardiomyocytes remains far from complete.

To improve upon the differentiation of cardiomyocytes from iPSCs and within organoids, our group has recently investigated the role of various proteins involved in assembling cellular substructure. Postdoc Harmonie Perdreau-Dahl has observed that the membrane-bending protein BIN1 is particularly critical, as overexpression of this protein in iPSCs promotes t-tubule formation (**Figure 2**, in revision at *Circulation Research*). Her work has additionally shown that BIN1 accomplishes this role through collaboration with partner proteins myotubularin and dynamin-2. However, it is not only the position of the dyadic membranes which is critical, as we have observed that the nanoscale arrangement of calcium-handling proteins within dyads determines their function (Kolstad et al., eLife, 2018; Shen et al., eLife, 2022). Importantly, BIN1 is capable of recruiting L-type calcium channels (LTCCs) and calcium release channels called Ryanodine Receptors (RyRs) to newly grown membranes (Figure 2), thus allowing effective cellular calcium transport. In the year ahead, we look forward to an expanded collaboration with HTH staff as we continue to identify the critical signals that control cardiomyocyte assembly, with the eventual aim of bioengineering mature myocardium.

References:

Foo et al., Mol Therapy, 2021
https://doi.org/10.1016/j.ymthe.2020.11.015

Frisk et al., J Am Coll Cardiol, 2021
https://doi.org/10.1016/j.jacc.2020.11.044

Kolstad et al., eLife, 2018
https://doi.org/10.7554/eLife.39427

Lipsett et al., J Physiol, 2019
https://doi.org/10.1113/JP277273

Parikh et al., Circ Res, 2017
https://doi.org/10.1161/CIRCRESAHA.117.311920

Shen et al., eLife, 2022
https://doi.org/10.7554/eLife.77725

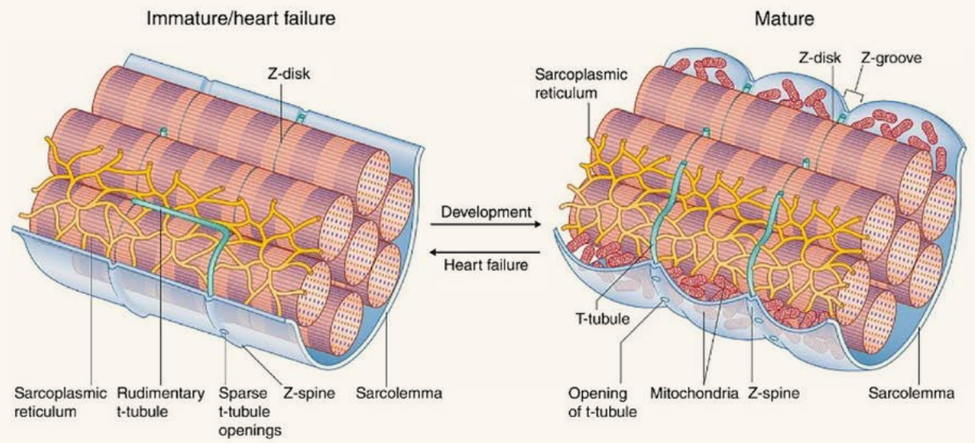


Figure 1.

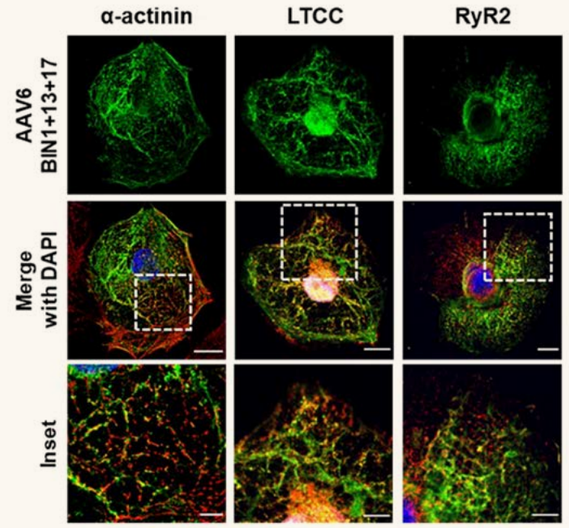


Figure 2.

Solbakk group
Ethic of organoids

Jan Helge Solbakk
Principal Investigator

The rapidly expanding organoid filed goes hand in hand with ethical implications that require careful clarifications.

The most important result in work package (WP) 6 has become the HYBRIDA project, which seeks to embed a comprehensive ethical dimension to organoid-based research and related technologies. See hybrida-project.eu. HYBRIDA is a multi-million Euro and prestigious European Commision SWAF (Science With and For Society) project. HYBRIDA is to a large a extent a project that is the child of WP6. The proposal was drafted by PI Jan Helge and Stefan Krauss together with other collaborators outside the project. Funding for HYBRIDA, and, in particular work package 2 in that project, meant that more money and work could be spent on the questions in WP6 as they are highly overlapping. In practice, the work in WP6 has now merged with work on WP2 in HYBRIDA.

The WP 6 has until recently consisted of one 65% PD position (Henrik Vogt) under the supervision of PI Jan Helge Solbakk. In March 2022 however, Vogt was appointed work package leader for WP2 in HYBRIDA. Throughout the year he has led work on an amended and comprehensive health technology assessment of organoids and organ-on-chip technology for personalized medicine. This work is in practice synergistic with, and an extension of, the work that has been ongoing in WP6. The first result here was the development of a method for an amended HTA of organoids and OoC as emerging technologies, which was submitted to the EU as a report in August 2022. He also oversaw the final work with a mapping of the organoids and organ-on-chip fields that were submitted at the same time by Hybrid Tecbnology Hub members Junya Shoji and Stefan Krauss and colleagues as part of the same HYBRIDA work package. A publication based on this work is forthcoming. Vogt is now leading a team which will apply the method of health technology assessment to deliver a comprehensive HTA of organoids and organ-on-chip technology this Spring (2023). This work will among other questions answer the key aim in WP6: How do we know if organoid and organ-on-chip technologies work in the context of precision medicine where the number of people with a condition may be so small that commonly used methods such as randomized controlled trials (RCTs) may not work. A publication based on this work with an amended HTA is planned.

This publication is a continuation of previous work in this work package on the vision of precision medicine in the organoid and organ-on-chip field(s) together with assistant professor Sara Green from The University of Copenhagen. This paper will map and critically examine the scientific and theoretical underpinnings of this vision: What are its promises, what are the underlying assumptions and is the vision credible and responsible. This is a form of vision assessment, looking at technologies that are mostly in the future and not yet realized. Organoids and organs-on-chip are to a large extent such technologies, at least when it comes to direct clinical applications on patients. The WP6 is in this regard performing cutting edge health technology assessment.

In October 2023, Vogt moved to a new position as associate professor at the Institute for Health and Society, University of Oslo. While continuing to work in HYBRIDA, and ascribing coming publications from this work also to the Hybrid Technology Hub and NRC funding, his position as PD was terminated at that point. The opportunity was then taken to employ PhD Maxence Gaillard in a 15% position in WP6 using the remaining funding from Vogt´s PD. Gaillard will work on the other key goal of WP6: A typology of organoids and organ-on-chip technologies (hybrid technologies). In this Gaillard will draw on his previous work on the topic in HYBRIDA underscoring the synergy that has become possible due to HYBRIDA springing out of WP6.

The ethics group is working on the philosophy of precision medicine in relation to organ-on-chip technology.

Wilson group
Mass Spectrometry

Steven Wilson
Principal Investigator

We explore the potential of combining organoid and organ-on-chip technology on-line with mass spectrometry.

The Wilson team focuses on studying organoids and organ-on-chip systems with mass spectrometry. Other important ingredients are applying various approaches in separation science and sample preparation, often coupled to mass spectrometry in an automated format.

In 2022, Wilson and co-workers at the Department of Chemistry have been developing and applying methods for testing drug metabolism and various omics approaches, including lipidomics and proteomics, for studying liver and islet organoids.

For example, Wilson et al. published a first direct coupling of organ-on-chip and mass spectrometry, using a chip featuring electromembrane extraction (EME), which allows drugs and metabolite to be selectively extracted from organoids to mass spectrometry (Skottvoll et al, Analysis and Sensing, 2022).

The team has also explored alternative variants of coupling liver organoids and mass spectrometry, e.g. filling organoids in chromatography columns and coupling directly to the mass spectrometer (Kogler et al, Analytical Chemistry, 2022).

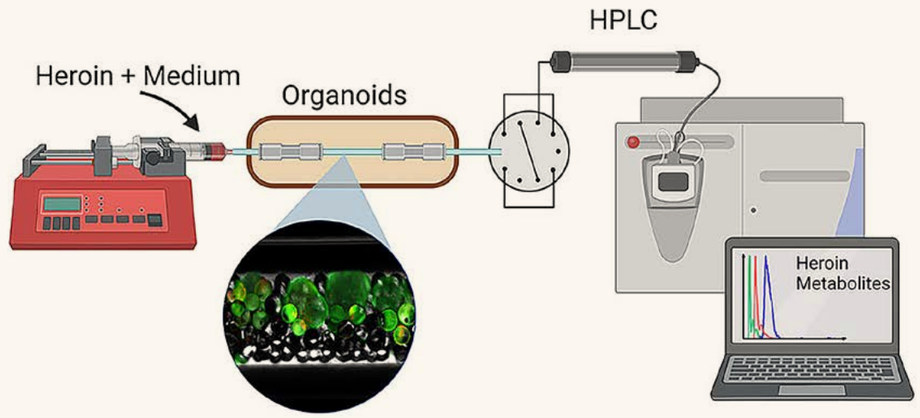
Associated member Hanne Røberg-Larsen (group leader at bioanalytical chemistry, Dep. Chemistry) has developed a method for biomarker discovery in models of non-alcoholic fatty liver disease (NAFLD), focusing on sterol analysis. The manuscript will be published in 2023 (Kømurcu et al.)

Islet organoids have been studied using liquid chromatography-mass spectrometry (LC-MS) with regards to hormones such as insulin (Olsen et al, Sep. Sci. Plus, 2022 and Olsen et al, J. Chromotogr. B, accepted 2022). The work has paved the way for selective multi-analyte studies of islet hormones and is now currently being explored for multi-organ chip systems as well.

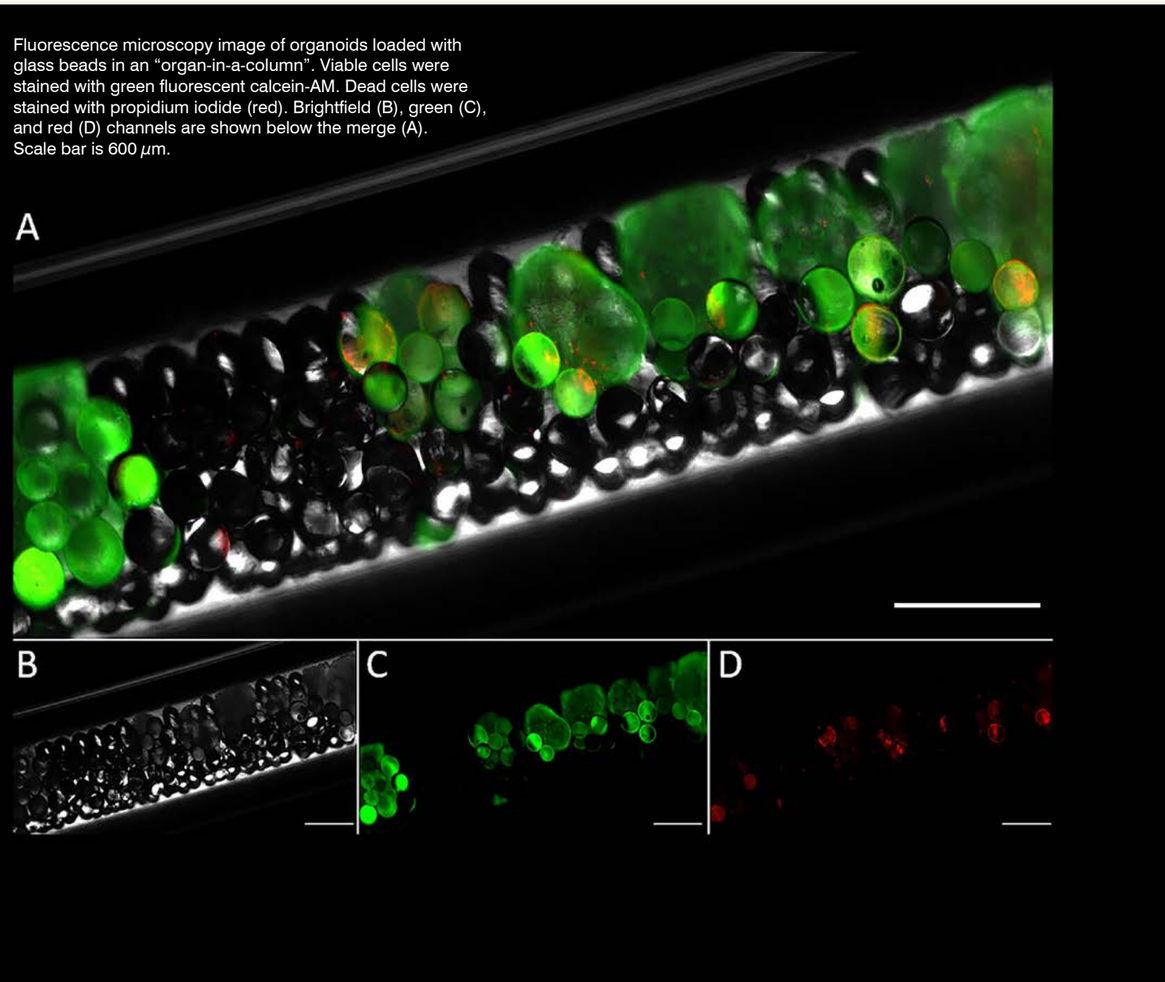
The team has also been expanded with a new PhD, Malgorzata Zawadzka, who will expand the analytical portfolio to include MS-imaging, which can be used for organoids and gastruloids.

Wilson and co-workers have also been communicating their results in a number of national and international conferences, through e.g. invited lectures and keynotes. They have also communicated their work to hundreds of high school students that have visited the Department of Chemistry, in efforts to recruit young students to science studies.

For his efforts in teaching and communicating chemistry, Wilson was awarded the Thalouw award, as the 8th recipient since it was established in 1874.



Schematic of the ”organ-in-a-column” coupled with liquid chromatography and mass spectrometry (from Kogler et al., 2022).



Fluorescence microscopy image of organoids loaded with glass beads in an “organ-in-a-column”. Viable cells were stained with green fluorescent calcein-AM. Dead cells were stained with propidium iodide (red). Brightfield (B), green (C), and red (D) channels are shown below the merge (A). Scale bar is 600 μm.

Melum group
Experimental liver research

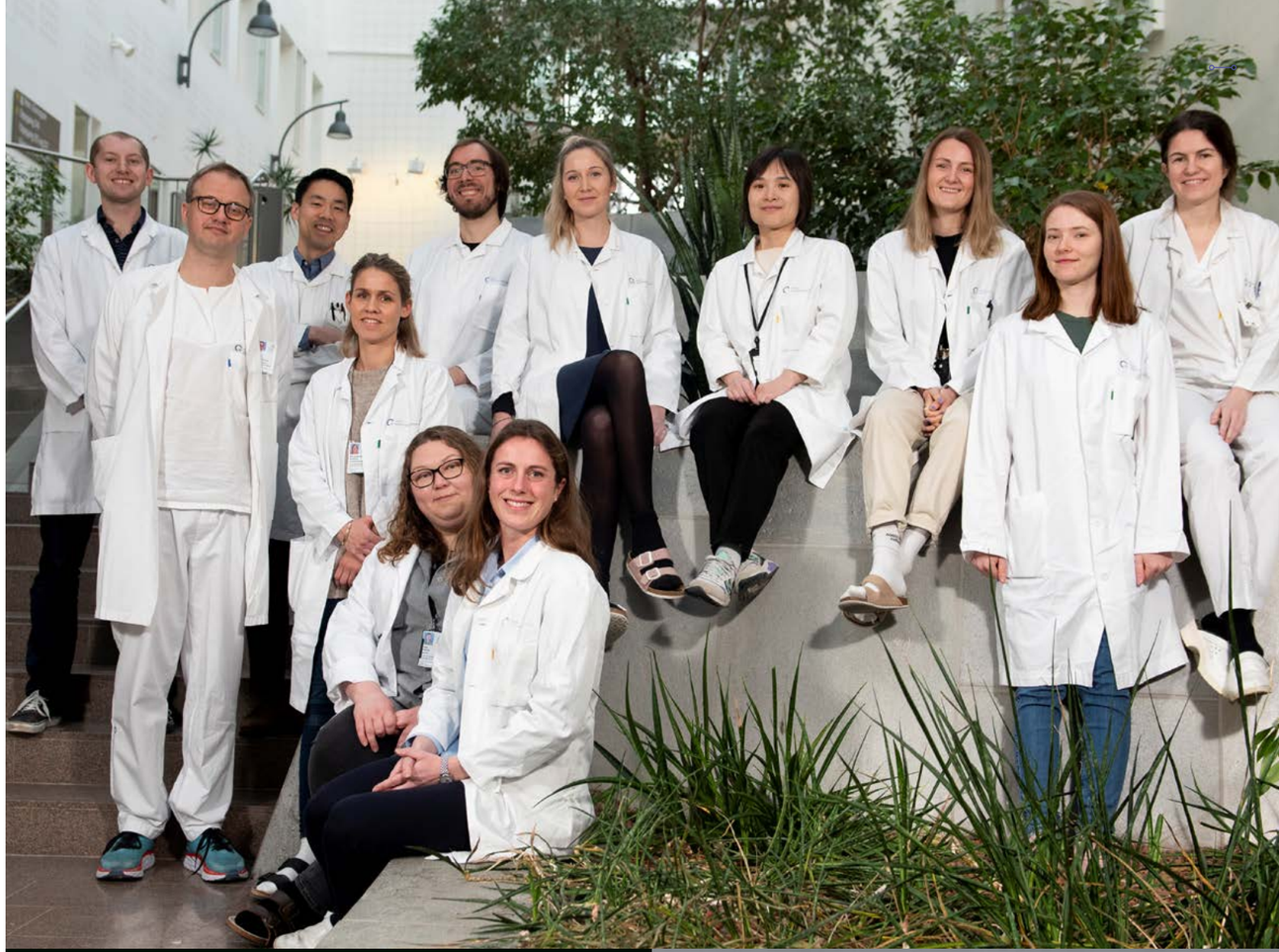
Espen Melum
Principal Investigator

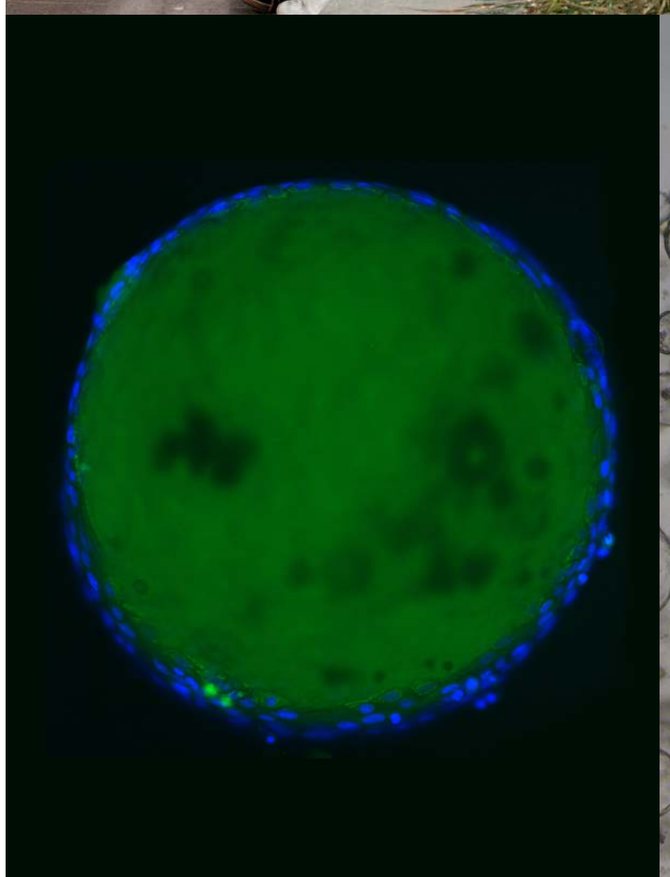
Colangiocytes are central for the understanding of liver development and diseases.

The experimental liver research group is focusing on experimental and translational studies related to primary sclerosing cholangitis (PSC) and is part of the Norwegian PSC research center (NoPSC) and HTH-CoE. Our laboratory activities take place at the Research institute of Internal Medicine. In 2022 the group consisted of the group leader, two senior researchers, four postdocs, five PhD students, the lab manager, one researcher and two technicians. The overall main aim of our research 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 the inflammatory process.

Our strong collaboration with the Hybrid Technology Hub on establishing a bile-bile-duct-on-chip was in 2022 strengthened by the recruitment of Henry W. Hoyle who joined the group in June. Henry has an ideal background for the project with a combination of molecular biology and physics. He defended his PhD thesis at the University of Durham before joining NoPSC. His main responsibility will be to improve the chip design and its integration with cholangiocyte organoids and immune cells. The organoid and bile-duct-on-chip projects were also strengthened in 2022 by Yuliia Boichuk who contacted us through the Science of Ukraine initiative where NoPSC offered to help Ukrainian scientists. Yuliia was one of the two Ukrainian colleagues that joined NoPSC. She has a solid background in molecular biology and long experience with advanced cell culture and was therefore an ideal fit for the ongoing work on organoids and chip-based technologies. At the end of the year her position was prolonged by a grant from “Fondsstiftelsen” at Oslo university hospital.

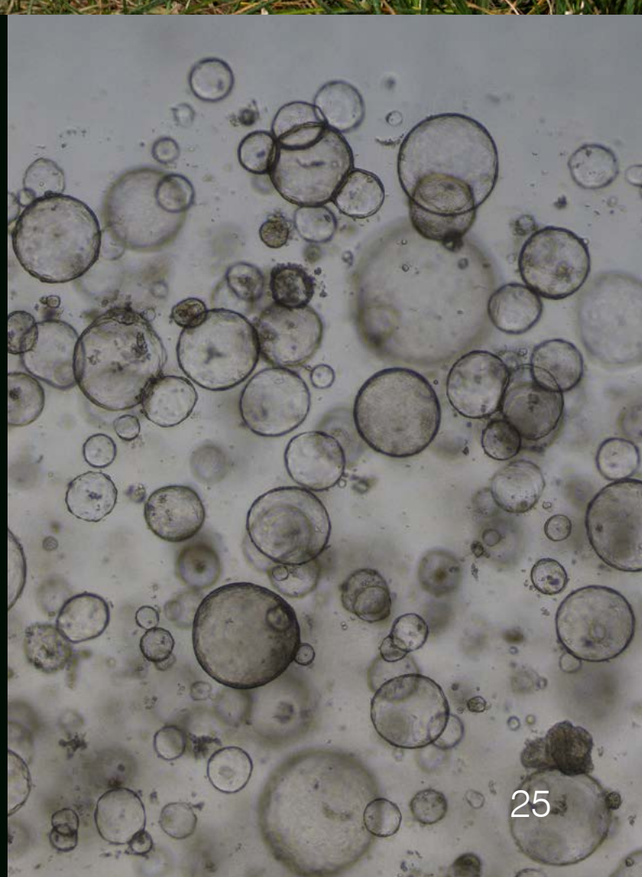
We have expanded our work on using 10x technology to examine the single cells and spatial transcriptomics in two different mouse models that we have used for many years in the group; NOD.c3c4 mice with spontaneous bile duct inflammation and induced bile duct inflammation following direct injection of oxazolone in the bile ducts. These two projects will be part of the PhD work of Markus Jördens and will accompany studies using the same methodologies in a large panel of PSC patients.





→
Left: A cholangiocyte organoid after treatment with rhodamine 123 (green), demonstrating directional transport of the compound into the center of the organoid. Co-staining (blue) was carried out with Hoechst 33342 to stain the cell nuclei. Credit: Henry W. Hoyle.

→ →
Right: A brightfield microscope image of a culture of human patient-derived cholangiocyte organoids after 5 days in culture. Credit: Henry W. Hoyle.



Corthay group
Tumor immunology

Alexandre Corthay
Principal Investigator

Tumor-on-chip technology has a significant potential for exploring the complex interactions between immune cells and cancer cells in a tumor microenvironment as a basis for the development of novel immunotherapies for cancer.

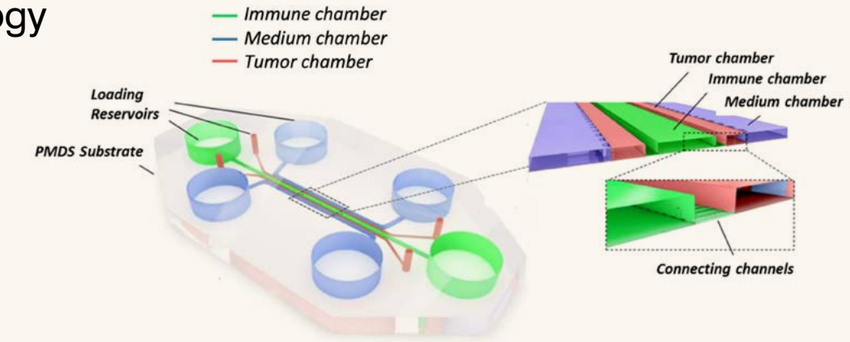
Tumor on a chip

In an ongoing collaboration between the Corthay and Krauss group, we pursed our efforts to recreate an immunocompetent tumor microenvironment on a chip. It allows us to investigate *in vitro* the complex cellular and molecular interactions that take place in either mouse or human tumors with the goal of developing novel immunotherapies for cancer. In 2022, we have been able to recreate a basic tumor microenvironment that includes cancer cells, tumor-specific T cells, and tumor-associated macrophages, in microfluidic devices (chips) as 3D co-cultures in biomimetic hydrogel. Macrophages were generated *in vitro* either from human monocytes or mouse bone marrow. Cell interactions and key processes such as cell division and death are being visualized over several days by high-content video-microscopy. In 2022, we have established a live imaging assay to observe the recruitment of T cells into a tumor, which is considered to represent a key and limiting step for the success of T cell-based cancer immunotherapy. This work is supported by our key international collaborators Luca Businaro (Rome, Italy), and Nadège Bercovici (Paris, France).

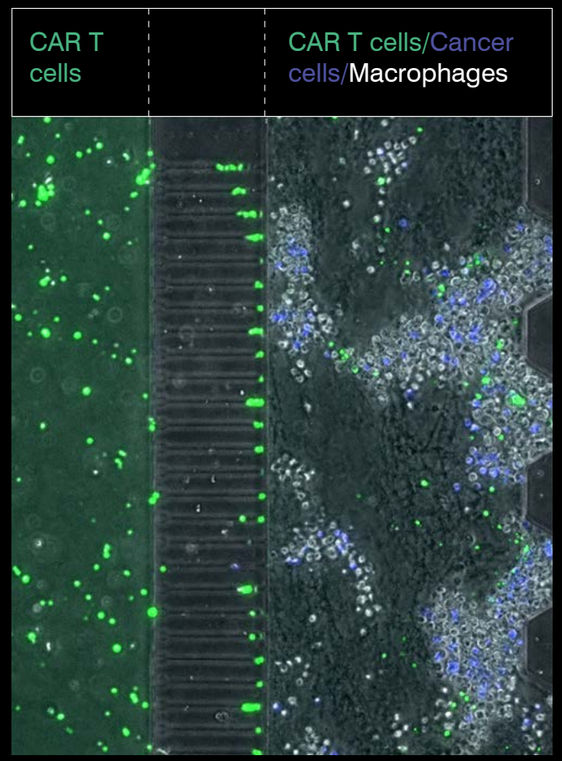
Towards macrophage-based cancer immunotherapy

The Corthay group is working on developing a novel strategy for cancer immunotherapy based on the optimized activation of tumor-associated macrophages. Tumor on a chip technology is a central tool for this endeavor. Activated macrophages can inhibit cancer cell growth *in vitro* and tumor development *in vivo*, but the mechanisms of macrophage-mediated cancer cell elimination remain poorly characterized. In 2022, we have made great progress in establishing a microscopy-based, live imaging assay to visualize *in vitro* the killing of cancer cells by activated mouse macrophages. This assay will allow us to test *in vitro* various conditions and delivery techniques to optimize the induction of cytotoxic activity of tumor-associated macrophages towards cancer cells in situ in tumors.

Immune-oncology chip

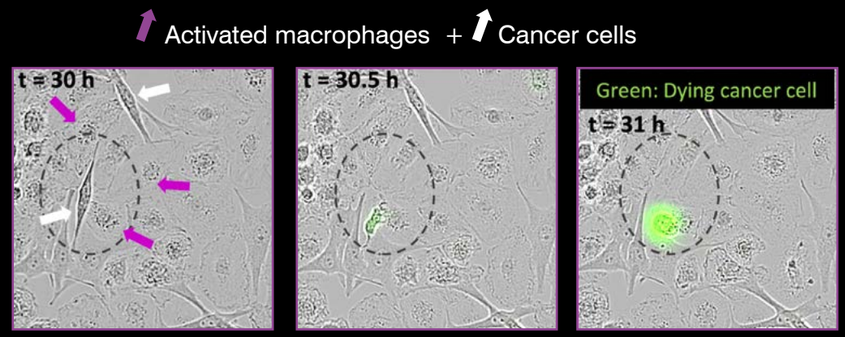


A microfluidic device is used to recreate physiological microenvironments in 3D.



Tumor specific CAR T cells (green) in the left chamber migrate to the right chamber via micro-channels (center).

In the right chamber, a basic human tumor micro-environment is recreated in a 3D collagen gel. Upon migration CAR T cells make contacts with clusters of cancer cells (blue) and macrophages (white).



Activated macrophages kill a cancer cell, visualized with a dying cell-sensitive probe (green).

Associated groups

Waaler group
Cell Signaling and Drug Discovery

Jo Waaler
Associated partner

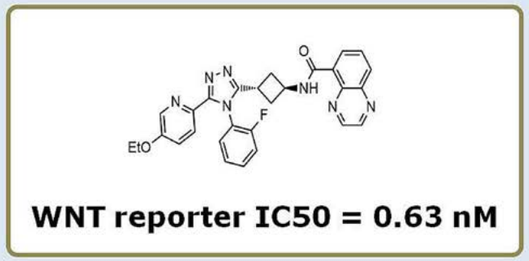
The objective for the research group is to translate the experience from work with cell signaling pathways and drug discovery to the work in the Centre. The work is a collaboration with the Krauss lab.

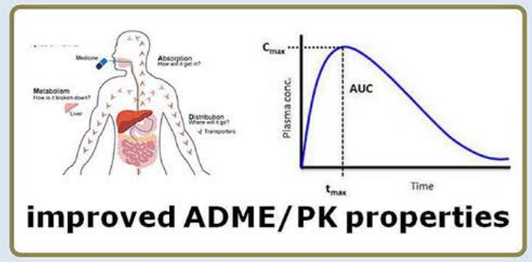
Cell Signaling and Drug Development

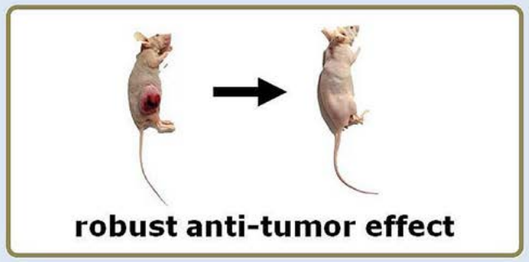
The key scientific expertise of the research group is within molecular and mechanistic studies of central developmental and cancer-promoting cell signaling pathways. The research in particular focus on detailed molecular and mechanistic studies of WNT/β-catenin and YAP signaling pathways in control of tumor development/progression and microenvironment tumor-immune cell interplay, as well as sensitivity to immunotherapy.

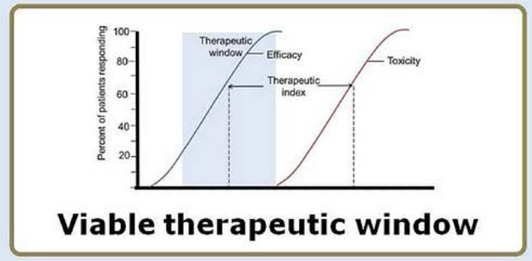
Drug development

Although dysregulation of WNT/β-catenin and YAP signaling are hallmarks in a major fraction of cancers and diseases including fibrosis, therapy targeting these pathways is currently not available in clinical practice. Since 2006, Jo Waaler and Stefan Krauss have been central in a drug development program that has identified TNKS1 and 2 as key targets controling these pathways that have hitherto not been therapeutically addressed. Our program aiming towards clinical studies is executed together with Symeres Inc., an acknowledged Dutch chemistry company acting as our close scientific and business partner as well as Inven2, the TTO for Oslo University Hospital. The project has obtained extensive innovation funding in the recent years and at current we are supported by the Norwegian Research Council, UiO innovation and SPARK Norway. To our knowledge, our drug development program is leading the field for the biotarget and for a therapeutic TNKS-WNT/β-catenin-YAP signaling inhibitor. We aim for a preclinical investment in the form of a license, partnering or joint venture in 2023/2024.









Identification of the novel TNKS inhibitor OM-153

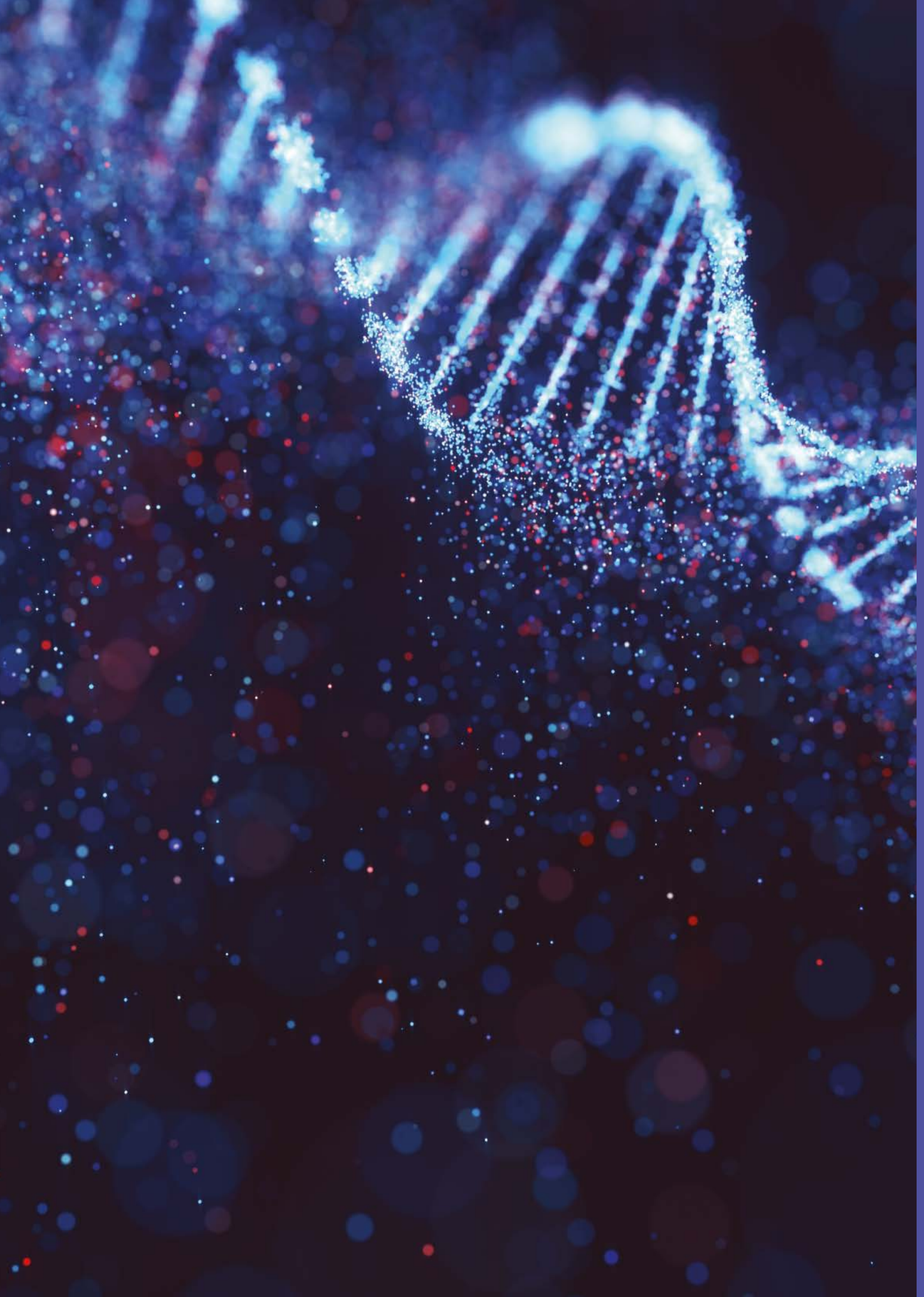
In 2021 and 2022 we published two closely related papers. The first paper (Journal of Medicinal Chemistry), described the development of the novel TNKS inhibitor OM-153. OM-153 showed picomolar IC50 inhibition in a cellular WNT/β-catenin signaling reporter assay (630 pM), no off-target liabilities, overall favorable absorption, distribution, metabolism, and excretion (ADME) properties, and an improved pharmacokinetic profile in mice. In the paper further addressing the biological properties of OM-153 (Cancer Research Communications, new AACR journal), we could show a robust anti-tumor effect in a colon carcinoma and immune oncology model, and importantly, with a significant therapeutic window (0.33 mg/kg - ≥10 mg/kg, dosed twice daily). This is remarkable, since the field was restricted by worries regarding intestinal toxicity mediated by TNKS inhibitors since 2013 (see figure).

Ongoing Projects

A current objective is to evaluate the effect and mechanism of action for TNKS inhibitor monotherapy and combination therapies in the regulation of signaling pathways in cancer and disease using cell culture and mouse models. The objective also includes testing of drugs in Organ-on-chip-based platforms and models.

WNT/β-catenin signaling can play a central regulatory role in immune cell homeostasis, development and function as well as in peripheral T cell activation, differentiation and tumor cell -immune cell interplay. Another objective for the research group is to assess the effect of and mechanism of action behind TNKS/immune checkpoint inhibitor anti-cancer combination therapy against melanoma, as well as the involvement of the adaptive and innate immune system using isogenic mouse models.

↑ The tankyrase inhibitor OM-153 demonstrates anti-tumor efficacy and a therapeutic window in mouse models.



HTH associated research projects

ABINO

Artificial Biomimetic systems – the Niche of Islet Organoid 2019–2023

About the project

The convergence environment works towards developing future models for diabetes research by amending protocols for stem cell differentiation. Diabetes is a global chronic disease, impacting daily life and can have long term severe consequences for patients such as blindness, kidney failure, stroke, leading to premature death. Restoring the body insulin by introducing functional healthy insulin producing islets to patients is an effective solution, but donor material is extremely limited and accessing the pancreas tissue from deceased donors is a complex and lengthy process. The convergence environment integrates our knowledge of islet biology and differentiation pathways, together with expertise in matrices and mechanical stimuli to improve differentiation protocols to achieve human stem cell derived islets.

In the project we will work on several technological platforms:

1. Morphogen and metabolite driven differentiation of stem cells to functional betacells
2. Exploration of the impact of mechanical (acoustic) signals on differentiation
3. Exploration of variation of acoustic signals on differentiation

By applying deep learning and modeling approaches, we optimize current protocols to improve differentiation efficiency and functionality of betacells and islets. Beta cells/islets with improved functionality are an important step towards therapeutic transplantations and towards achieving models for drug testing and development. Finally, in spite of the central role in development, stem cells remain a controversial and often misunderstood concept. We will therefore encapsulate collected knowledge into an education platform in an endeavour to foster better communication related to this topic.

PROJECT LEADER

Dr. Hanne Scholz
Faculty of Medicine, Institute of Basic Medical Sciences (IMB), UiO and Division of Surgery, Inflammatory medicine, and Transplantation, OUS

PARTICIPANTS

Prof. Anne Danielsen
Department of Musicology and CoE-RITMO

Prof. Alexander Refsum Jensenius
Department of Musicology and CoE-RITMO

Prof. Anders Malthe-Sørenssen
Department of Physics and CoE-CCSE

Prof. Simon Rayner
Department of Medical Genetics OUS and CoE-HTH

Prof. Stefan Krauss
Institute of Basic Medical Sciences and CoE-HTH

Prof. Dag Kristian Dysthe
Department of Physics, UiO

Dr. Petter Angell Olsen
Researcher, CoE-HTH

Dr. Thomas Combriat
Post-doctoral fellow, CoE-CCSE

Chencheng Wang
Doctoral research fellow, CoE-HTH

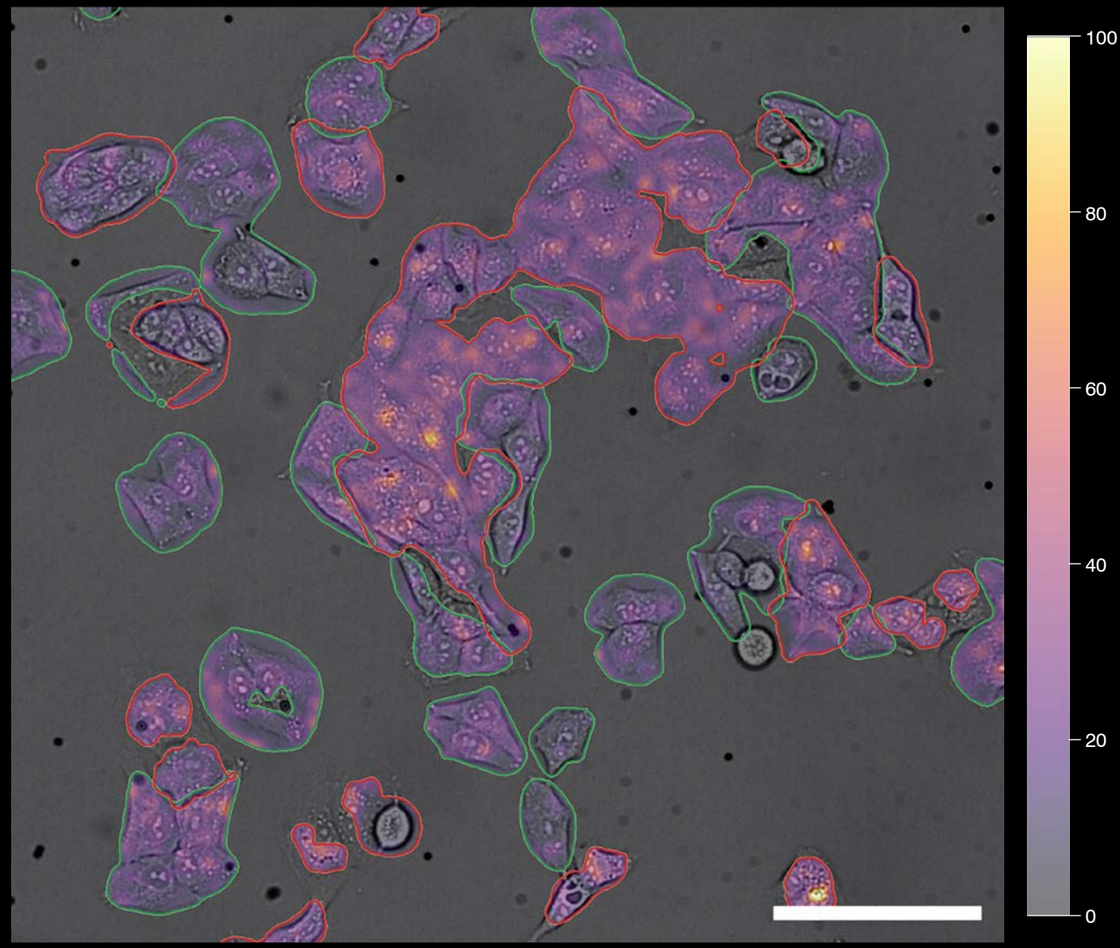
Dongho Daniel Kwak
Doctoral research fellow, CoE-RITMO

FUNDING

The 4 year project is funded by the UiO: Life Science convergence environment program with 3 positions

FURTHER INFORMATION

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



By analyzing the movement of a mixed population of meljuso (green outline) and MDCK (red outline) cells under ultrasonic stress at a frequency of 45 kHz, the dynamic modulus was quantified. The absolute dynamic modulus is represented by a color gradient. Scale bar is 100 microns.
Credit: Thomas Combriat.

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

Prof. Luiza Angheluta-Bauer
Department of Physics, UiO

Prof. Dag Kristian Dysthe
Department of Physics, UiO

Prof. Steven Ray Haakon Wilson
Department of Chemistry, UiO

Prof. Alexander Refsum Jensenius
Department of Musicology, UiO and CoE-RITMO

Prof. Molly Stevens
Imperial College London, UK

Prof. Joachim Mathiesen
Niels Bohr Institute, University of Copenhagen, DK.

Dr. Hanne Røberg-Larsen
Department of Chemistry, UiO

Dr. Håkon Høgset
Institute of Basic Medical Sciences, 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/

SUMO

Supervised morphogenesis in gastruloids

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, Technology 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

Immunofluorescence image of a human gastruloid 5 days post aggregation showing N-cadherin in magenta and Brachyury-T in green. Credit: Håkon Høgset.

Raman spectroscopic imaging highlighting nuclear (cyan) and cytosolic (orange) components of the tail region on a mouse gastruloid at 5 days after aggregation. Credit: Håkon Høgset.

HYBRIDA

Embedding a comprehensive ethical dimension to organoid-based research and related technologies

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

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

PARTICIPANTS

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

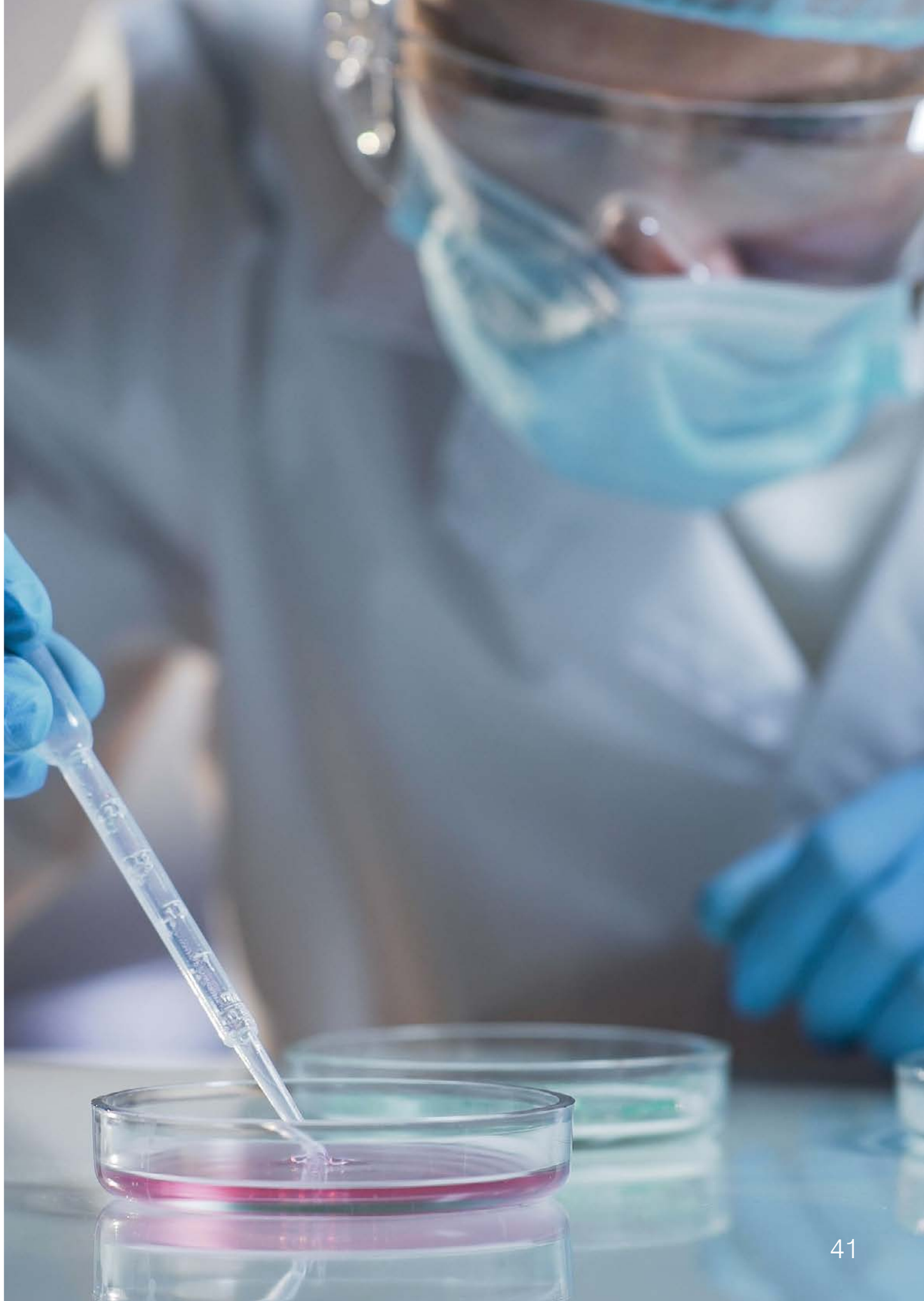
FUNDING

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



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.

Metabolism-on-chip

Project leader

Dr. Shadab Abadpour, Dept. of Transplantation and Institute for Surgical Research, OUS / Hybrid Technology Hub–Centre of Excellence, UiO

Team members

Dr. Aleksandra Aizenshtadt, 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, Waaler J, Lehtio L, Leenders R.G.G. Wegert A. “compounds” application submitted 6. July 2020 IPO patent application number 2010359.4 PCT application 6. July 2021 submission number 1200413344; PCT application number PCT/GB2021/051714

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

DOFI

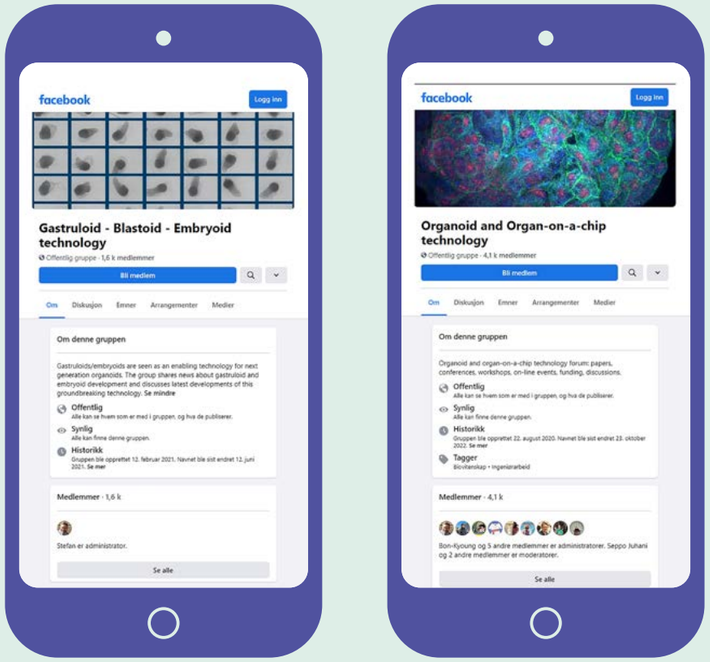
14/09/2020 DUCT chip – An artificial bile duct on a chip recapitulating immune functions; Espen Melum, Anna Frank, Stefan Krauss

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 1600 and 4100 followers, respectively.

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

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

1600+
4100
followers

NRK radio

Hanne Scholz was a guest on the Abels Forgård radioshow and podcast talking about 3D printing of organs.

https://radio.nrk.no/podkast/abels_taarn/sesong/202203/l_1e994fa7-9813-4a47-994f-a798138a478e

Education

RESEARCH SCHOOL FOR TRAINING THE NEXT GENERATION OF MICRO- AND NANO-TECHNOLOGY RESEARCHERS IN NORWAY

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, optoelectronics, 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 research school held its 1st National Junior Scientist Research Conference in Nanoscience and Nanotechnology in Trondheim 30 November-2 December 2022.

HTH contact point

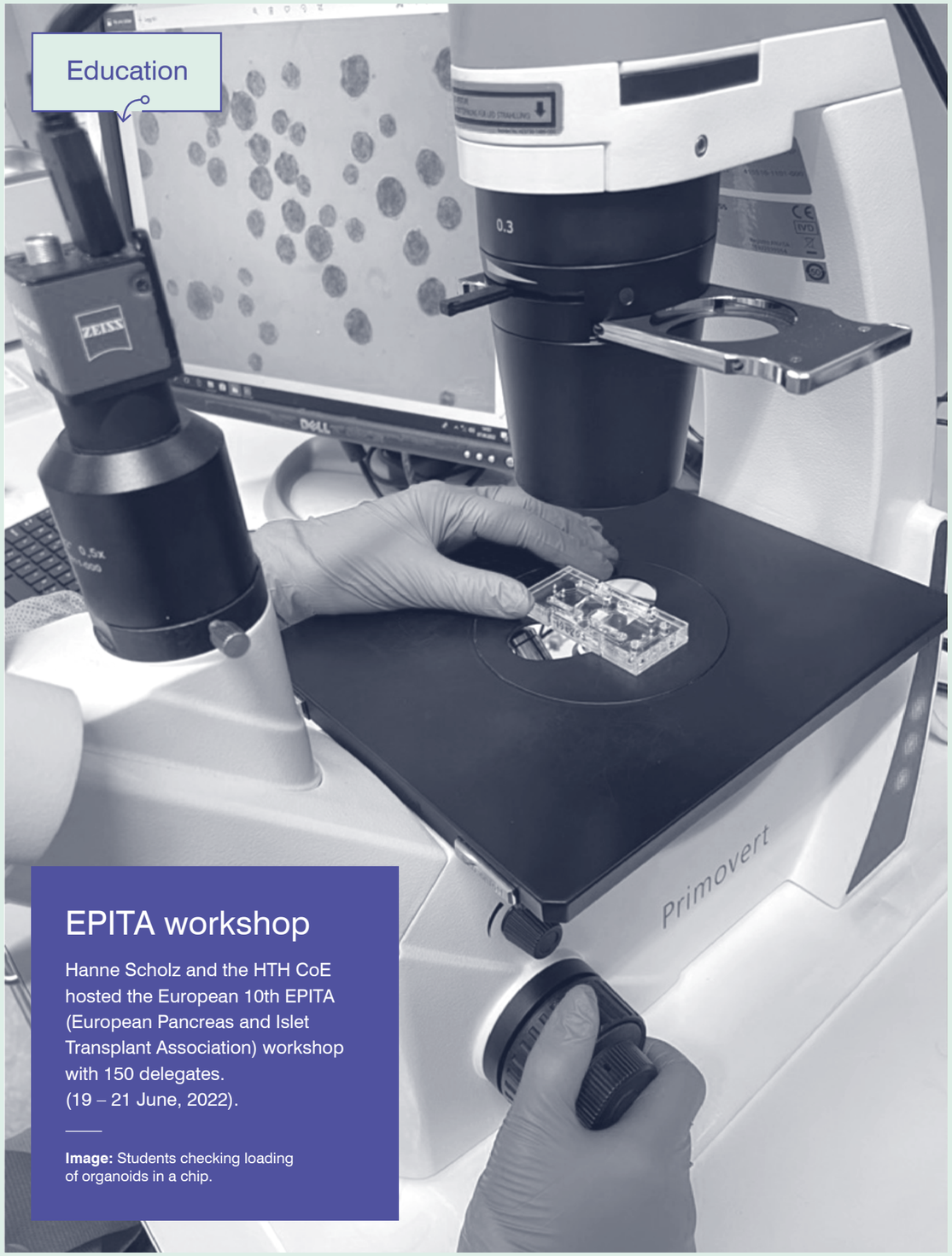
Dr. Hanne Scholz, Hybrid Technology Hub – Centre of Excellence, Institute of Basic Medical Sciences, University of Oslo (UiO) and Oslo University Hospital.

Further information

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

https://www.ntnu.edu/tnnn

Education



EPITA workshop

Hanne Scholz and the HTH CoE hosted the European 10th EPITA (European Pancreas and Islet Transplant Association) workshop with 150 delegates.
(19 – 21 June, 2022).

Image: Students checking loading of organoids in a chip.

The NoOC (The Nordic organ-on-chip Network) networking event

27 October

The NoOC networking event took place as a virtual meeting, featuring keynote speeches from experienced researchers and presentations by PhD and postdoctoral students from across the Nordic region.

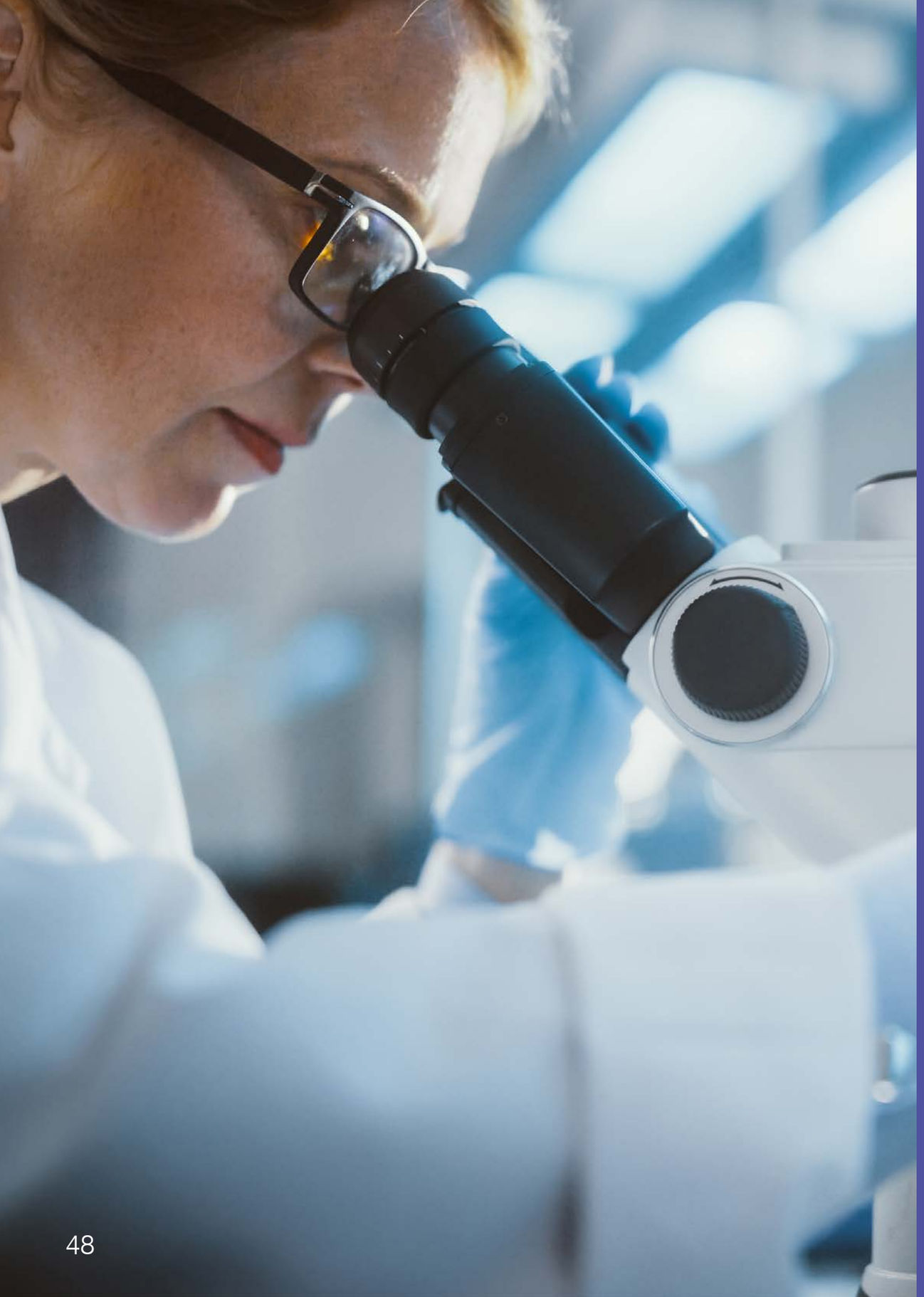
NoOC web site:
https://nordic-organ-on-a-chip.eu

Graduated PhD students

Frøydis Skottvoll, Thesis: "Liver organoids, mass spectrometry and separation science".

→

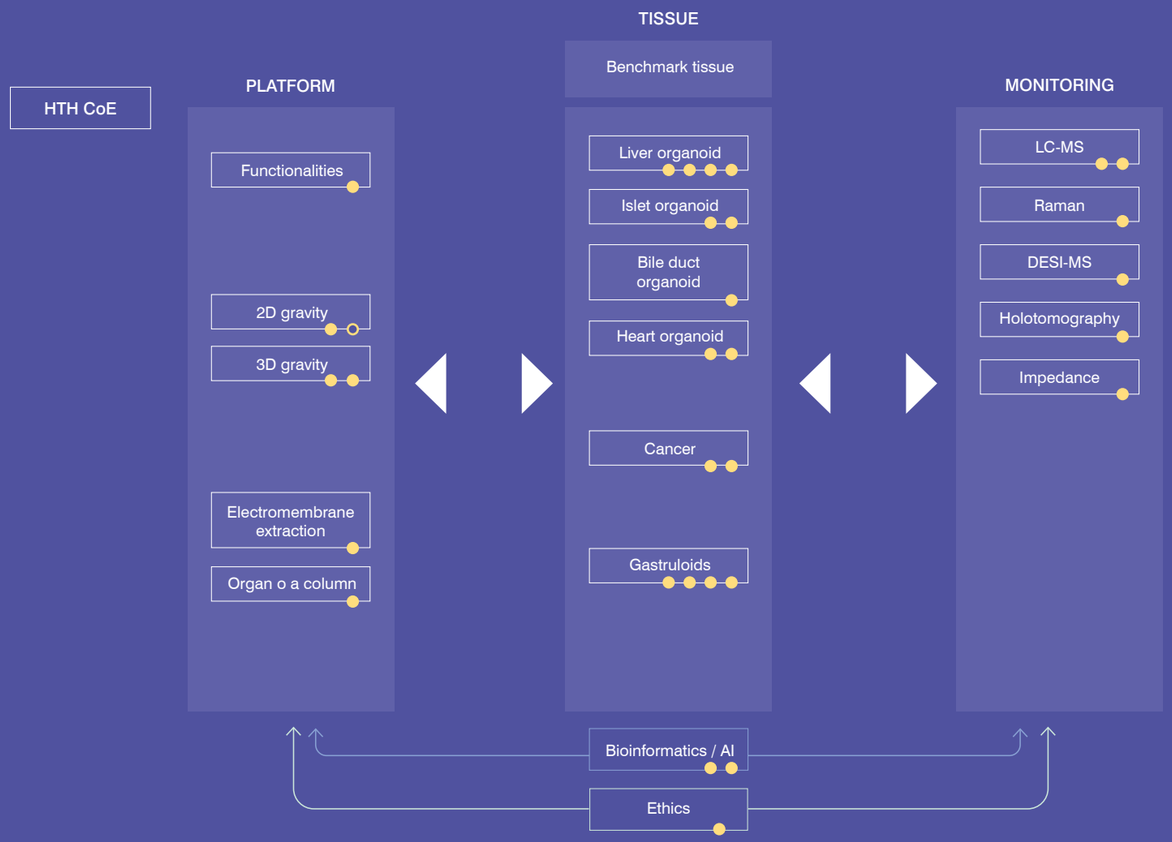
Dr. Frøydis Skottvoll with her newly obtained PhD diploma at the conferral ceremony.



About the centre

Organizational chart

- 1 man-year
- 1/2 man-year



Team members 2022

Centre leadership

Stefan Krauss
Centre Director

Hanne Scholz
Vice Director

Petter Angell Olsen
Facility manager and
Administrative coordinator

Haakon Berg Johnsen
Administrative coordinator
(until August 2022)

Principal investigators

Nikolaj Gadegaard

Molly Stevens

Simon Rayner

Steven Wilson

Jan Helge Solbakk

William Edward Louch

Espen Melum

Alexandre Corthay

Associated Partner

Jo Waaler

Team members 2022

Postdoctoral fellows and researchers


Alexandra Aizenshtadt
Lab. manager


Anna Frank


Henrik Vogt


Hyemin Kim


Håkon Høgset


Igor Meszka


Jelle Penders


Junya Shoji


Kayoko Shoji


Ludivine Delon


Mathias Busek


Olga Bibikova


Pavel Vazquez


Sean Harrison


Sergei Ponomartcev


Shadab Abadpour


Thomas Combriat


Vernon LaLone

PhD candidates


Chencheng Wang


Dongho Daniel Kwak


Duarte Menezes


Essi Niemi


Franziska Schoeb


Frøydis Sved Skottvoll


Henry Hole


Ingrid Wilhelmsen


Malgorzata Elzbieta Zawadzka


Mikel Amirola Martinez


Neil Convery


Saphira Felicitas Baumgarten


Shoshy Mahmuda


Steffen Nøvik


Stian Kogler

Principal engineer


Justyna Stokowiec

Technicians


Alexey Golovin


Ida Johnsen


Lydia Busek

Board 2022

Professor
Tom Hemming Karlsen
Head of Research, Division of Surgery, Inflammatory diseases and Transplantation, Oslo University Hospital

Chairman of the board

Board members

Professor
Lars Eide
Institute of Clinical Medicine, University of Oslo

Professor
Lene Frost Andersen
Head of department, Institute of Basic Medical Sciences, 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) 2022

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 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
- 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
- CVMD iMed Bioscience
- Symeres Inc

About the centre

Retreats

Flakstad, Lofoten.
Credit: Petter Angell Olsen

Centre Director Stefan Krauss together with PI's Nikolaj Gadegaard and Molly Stevens at the top of Reinebringen.

12–15 September

Midterm planning retreat

Attendees: Molly Stevens, Nikolaj Gadegaard, Steven Wilson, Espen Melum, Alexandre Corthay, Petter Angell Olsen, Stefan Krauss, and guest speaker Dag Dysthe. The scientific discussions were livestreamed via Zoom for HTH PIs who were unable to be present physically.

This year, the HTH PIs organized a planning retreat in Reine, Lofoten, which included a combination of scientific advancements and strategic planning. Additionally, the retreat featured social activities such as hiking to Reinebringen and a boat excursion to Bunes beach.

17 November

HTH annual retreat

The yearly HTH retreat of this year took place at the Lysebu hotel and had a total of 50 attendees. The schedule featured 2 motivational talks from invited speakers, 5-minute flash talks by the centre's PhD students and postdoctoral researchers, and culminated in a dinner and awards ceremony.

Ingrid Wilhelmsen is presented with the award for the best presentation by co-director Hanne Scholz at the Lysebu retreat.
Credit: Stefan Krauss.

Group photo from the Lysebu retreat.

Publications

Adrian Eek Mariampillai, Sissel Hauge, Inger Øynebråten, Gro Elise Rødland, Alexandre Corthay, Randi G Syljuåsen

Caspase activation counteracts interferon signaling after G2 checkpoint abrogation by ATR inhibition in irradiated human cancer cells

Front Oncol. 2022 Oct 28;12:981332. doi: 10.3389/fonc.2022.981332.

Adrian Najer, Alexis Belessiotis-Richards, Hyemin Kim, Catherine Saunders, Federico Fenaroli, Christopher Adrianus, Junyi Che, Renée L Tonkin, Håkon Høgset, Samuel Lörcher, Matthew Penna, Stuart G Higgins, Wolfgang Meier, Irene Yarovsky, Molly M Stevens

Block Length-Dependent Protein Fouling on Poly(2-oxazoline)-Based Polymersomes: Influence on Macrophage Association and Circulation Behavior

Small. 2022 Jul;18(27):e2201993. doi: 10.1002/smll.202201993.

Alexandre Corthay, Tibor Bakacs, Govindarajan Thangavelu, Colin C Anderson

Tackling cancer cell dormancy: Insights from immune models, and transplantation

Semin Cancer Biol. 2022 Jan;78:5-16. doi: 10.1016/j.semcancer.2021.02.002.

Anbin Chen, Cecilie Katrin Kristiansen, Lena Elise Høyland, Mathias Ziegler, Jian Wang, Gareth John Sullivan, Xingang Li, Laurence A Bindoff, Kristina Xiao Liang

POLG mutations lead to abnormal mitochondrial remodeling during neural differentiation of human pluripotent stem cells via SIRT3/AMPK pathway inhibition

Cell Cycle. 2022 Jun;21(11):1178-1193. doi: 10.1080/15384101.2022.2044136.

Casey Ward, Jon S Odorico, Michael R Rickels, Thierry Berney, George W Burke 3rd, Thomas W H Kay, Olivier Thaunat, Pablo D Uva, Eelco J P de Koning, Helmut Arbogast, Hanne Scholz, Mark S Cattral, Robert J Stratta, Peter G Stock

International Pancreas and Islet Transplant Association Beta-Cell Replacement Therapy Monitoring Task Force. International Survey of Clinical Monitoring Practices in Pancreas and Islet Transplantation

Transplantation. 2022 Aug 1;106(8): 1647-1655. doi: 10.1097/TP.0000000000004058.

Cathrine R Carlson, Jan Magnus Aronsen, Anna Bergan-Dahl, Marie Christine Moutty, Marianne Lunde, Per Kristian Lunde, Hilde Jarstadmarken, Pimthanya Wanichawan, Laetitia Pereira, Terje R S Kolstad, Bjørn Dalhus, Hariharan Subramanian, Susanne Hille, Geir Christensen, Oliver J Müller, Viacheslav Nikolaev, Donald M Bers, Ivar Sjaastad, Xin Shen, William E Louch, Enno Klussmann, Ole M Sejersted

AKAP18δ Anchors and Regulates CaMKII Activity at Phospholamban-SERCA2 and RYR

Circ Res. 2022 Jan 7;130(1):27-44. doi: 10.1161/CIRCRESAHA.120.317976.

Cecilie Katrin Kristiansen, Anbin Chen, Lena Elise Høyland, Mathias Ziegler, Gareth John Sullivan, Laurence A Bindoff, Kristina Xiao Liang

Comparing the mitochondrial signatures in ESCs 1 and iPSCs and their neural derivations

Cell Cycle. 2022 Oct;21(20):2206-2221. doi: 10.1080/15384101.2022.2092185.

Chloe Rixon, Kristine Andreassen, Xin Shen, Pugazendi Murugan Erusappan, Vibeke Marie Almaas, Sheryl Palmero, Christen P Dahl, Ivar Sjaastad, William E Louch, Mathis K Stokke, Theis Tønnessen, Geir Christensen, Ida G Lunde

Lumican accumulates with fibrillar collagen in fibrosis in hypertrophic cardiomyopathy

ESC Heart Fail. 2022 Nov 29. doi: 10.1002/ehf2.14234.

Christine Olsen, Chencheng Wang, Shadab Abadpour, Elsa Lundanes, Audun Skau Hansen, Frøydis Sved Skottvoll, Hanne Scholz, Steven Ray Wilson

Determination of insulin secretion from stem cell-derived islet organoids with liquid chromatography-tandem mass spectrometry

J Chromatogr B Analyt Technol Biomed Life Sci. 2023 Jan 15;1215:123577. doi: 10.1016/j.jchromb.2022.123577.

Christine Olsen, Elisa Wiborg, Elsa Lundanes, Shadab Abadpour, Hanne Scholz, Steven Ray Wilson

On-line reduction of insulin disulfide bonds with photoinduced radical reactions, upstream to nano liquid chromatography-mass spectrometry

SSC Plus. 2022 April 7. doi: 10.1002/sscp.202200022

Dongho Kwak, Thomas Combriat, Chencheng Wang, Hanne Scholz, Anne Danielsen, Alexander Refsum Jensenius

Music for Cells? A Systematic Review of Studies Investigating the Effects of Audible Sound Played Through Speaker-Based Systems on Cell Cultures

Music & Science. 2022 March 4. doi: 10.1177/20592043221080965

Erwin De Genst, Kylie S Foo, Yao Xiao, Eduarde Rohner, Emma de Vries, Jesper Sohlmér, Nevin Witman, Alejandro Hidalgo, Terje R S Kolstad, William E Louch, Susanne Pehrsson, Andrew Park, Yasuhiro Ikeda, Xidan Li, Lorenz M Mayr, Kate Wickson, Karin Jennbacken, Kenny Hansson, Regina Fritsche-Danielson, James Hunt, Kenneth R Chien

Blocking phospholamban with VHH intrabodies enhances contractility and relaxation in heart failure

Nat Commun. 2022 May 31;13(1):3018. doi: 10.1038/s41467-022-29703-9.

Hyemin Kim, Jonathan Yeow, Adrian Najer, Worrapong Kit-Anan, Richard Wang, Omar Rifaie-Graham, Chalaisorn Thanapongpibul, Molly M Stevens

Microliter Scale Synthesis of Luciferase-Encapsulated Polymersomes as Artificial Organelles for Optogenetic Modulation of Cardiomyocyte Beating

Adv Sci (Weinh). 2022 Sep;9(27):e2200239. doi: 10.1002/advs.202200239.

Karoline B Rypdal, A Olav Melleby, Emma L Robinson, Jia Li, Sheryl Palmero, Deborah E Seifert, Daniel Martin, Catelyn Clark, Begoña López, Kristine Andreassen, Christen P Dahl, Ivar Sjaastad, Theis Tønnessen, Mathis K Stokke, William E Louch, Arantxa González, Stephane Heymans, Geir Christensen, Suneel S Apte, Ida G Lunde

ADAMTSL3 knock-out mice develop cardiac dysfunction and dilatation with increased TGFβ signalling after pressure overload

Commun Biol. 2022 Dec 20;5(1):1392. doi: 10.1038/s42003-022-04361-1.

Katharine M Dibb, William E Louch, Andrew W Trafford

Cardiac Transverse Tubules in Physiology and Heart Failure

Annu Rev Physiol. 2022 Feb 10;84:229-255. doi: 10.1146/annurev-physiol-061121-040148.

Leandro M Sommese, María Florencia Racioppi, Xin Shen, Alejandro Orlowski, Carlos A Valverde, William E Louch, Martín Vila Petroff, Luis A Gonano

Discordant Ca2+ release in cardiac myocytes: characterization and susceptibility to pharmacological RyR2 modulation

Pflugers Arch. 2022 Jun;474(6):625-636. doi: 10.1007/s00424-022-02678-8.

Luiza Ghila, Kenichiro Furuyama, Shane T Grey, Hanne Scholz, Simona Chera

Editorial: Beta-Cell Fate: From Gene Circuits to Disease Mechanisms

Front Genet. 2022 Feb 25;13:822440. doi: 10.3389/fgene.2022.822440.

Manuel Carrasco, Chencheng Wang, Anne M Søviknes, Yngvild Bjørlykke, Shadab Abadpour, Joao A Paulo, Erling Tjora, Pål Njølstad, Jonas Ghabayen, Ingrid Nermoen, Valeriya Lyssenko, Simona Chera, Luiza M Ghila, Marc Vaudel, Hanne Scholz, Helge Ræder

Spatial Environment Affects HNF4A Mutation-Specific Proteome Signatures and Cellular Morphology in hiPSC-Derived β-Like Cells Diabetes

Diabetes. 2022 Apr 1;71(4):862-869. doi: 10.2337/db20-1279.

Maria Bogdanova, Arsenii Zabirnyk, Anna Malashicheva, Daria Semenova, John-Peder Escobar Kvitting, Mari-Liis Kaljusto, Maria Del Mar Perez, Anna Kostareva, Kåre-Olav Stensløkken, Gareth J Sullivan, Arkady Rutkovskiy, Jarle Vaage

Models And Techniques To Study Aortic Valve Calcification In Vitro, Ex Vivo, And In Vivo. An Overview

Front Pharmacol. 2022 Jun 2;13:835825. doi: 10.3389/fphar.2022.835825.

María Hernández Mesa, Jonas van den Brink, William E Louch, Kimberly J McCabe, Padmini Rangamani

Nanoscale organization of ryanodine receptor distribution and phosphorylation pattern determines the dynamics of calcium sparks

PLoS Comput Biol. 2022 Jun 6;18(6):e1010126. doi: 10.1371/journal.pcbi.1010126.

Marta Broto, Michael M Kaminski, Christopher Adrianus, Nayoung Kim, Robert Greensmith, Schan Dissanayake-Perera, Alexander J Schubert, Xiao Tan, Hyemin Kim, Anand S Dighe, James J Collins, Molly M Stevens

Nanozyme-catalysed CRISPR assay for preamplification-free detection of non-coding RNAs

Nat Nanotechnol. 2022 Oct;17(10):1120-1126. doi: 10.1038/s41565-022-01179-0.

Mathias Busek, Aleksandra Aizenshtadt, Mikel Amirola Martinez, Ludivine Delon, Stefan Krauss

Academic User View: Organ-on-a-Chip Technology

Biosensors (Basel). 2022 Feb 16;12(2):126. doi: 10.3390/bios12020126.

Mathias Busek, Aleksandra Aizenshtadt, Timo Koch, Anna Frank, Ludivine Delon, Mikel Amirola Martinez, Alexey Golovin, Clotilde Dumas, Justyna Stokowiec, Stefan Gruenzner, Espen Melum, Stefan Krauss

Pump-less, recirculating organ-on-a-chip (rOoC) platform

Lab Chip . 2023 Jan 19. doi: 10.1039/d2lc00919f.

Michael Frisk, Per Andreas Norseng, Emil Knut Stenersen Espe, William E Louch

Tubulator: An automated approach to analysis of t-tubule and dyadic organization in cardiomyocytes

Philos Trans R Soc Lond B Biol Sci. 2022 Nov 21;377(1864):20210468. doi: 10.1098/rstb.2021.0468.

Pavel Vazquez, Kayoko Hirayama-Shoji, Steffen Novik, Stefan Krauss, Simon Rayner

Globally Accessible Distributed Data Sharing (GADDS): a decentralized FAIR platform to facilitate data sharing in the life sciences

Bioinformatics. 2022 Aug 2;38(15): 3812-3817. doi: 10.1093/bioinformatics/btac362.

Sanna Sämfors, Essi M. Niemi, Kristin Oskarsdotter, Claudia Villar Egea, Andreas Mark, Hanne Scholz, Paul Gatenholm

Design and biofabrication of a leaf-inspired vascularized cell-delivery device

Bioprinting. 2022 June. Volume 26, e00199. doi: 10.1016/j.bprint.2022.e00199.

Shoshy A Brinch, Enya Amundsen-Isaksen, Sandra Espada, Clara Hammarström, Aleksandra Aizenshtadt, Petter A Olsen, Lone Holmen, Merete Høyem, Hanne Scholz, Gunnveig Grødeland, Sven T Sowa, Albert Galera-Prat, Lari Lehtiö, Ilonka ATM Meerts, Ruben GG Leenders, Anita Wegert, Stefan Krauss*, Jo Waaler* (shared last authorship)

The Tankyrase Inhibitor OM-153 Demonstrates Antitumor Efficacy and a Therapeutic Window in Mouse Models

Cancer Res Commun. 2022 2 (4), 233-245. doi: 10.1158/2767-9764.CRC-22-0027

Steffen Novik, Magnus Flo Drageseth, Magnus Borresen Grondalen, Ola Nilsen, Stefan Johannes Karl Krauss, Orjan Grottem Martinsen, Philipp Dominik Hafliger

A CMOS Multi-Electrode Array for Four Electrode Bioimpedance Measurements

IEEE Trans Biomed Circuits Syst. 2022 Oct 13;PP. doi: 10.1109/TBCAS.2022.3214243.

Stian Kogler, Aleksandra Aizenshtadt, Sean Harrison, Frøydis Sved Skottvoll, Henriette Engen Berg, Shadab Abadpour, Hanne Scholz, Gareth Sullivan, Bernd Thiede, Elsa Lundanes, Inger Lise Bogen, Stefan Krauss, Hanne Røberg-Larsen, Steven Ray Wilson

"Organ-in-a-Column" Coupled On-line with Liquid Chromatography-Mass Spectrometry

Anal Chem. 2022 Dec 20;94(50):17677-17684. doi: 10.1021/acs.analchem.2c04530

Thea Parsberg Støle, Marianne Lunde, Xin Shen, Marita Martinsen, Per Kristian Lunde, Jia Li, Francesca Lockwood, Ivar Sjaastad, William Edward Louch, Jan Magnus Aronsen, Geir Christensen, Cathrine Rein Carlson

The female syndecan-4-/- heart has smaller cardiomyocytes, augmented insulin/pSer473-Akt/pSer9-GSK-3β signaling, and lowered SCOP, pThr308-Akt/Akt and GLUT4 levels

Front Cell Dev Biol. 2022 Aug 25;10:908126. doi: 10.3389/fcell.2022.908126.

Thierry Berney, Axel Andres, Melena D Bellin, Eelco J P de Koning, Paul R V Johnson, Thomas W H Kay, Torbjörn Lundgren, Michael R Rickels, Hanne Scholz, Peter G Stock, Steve White; International Islet Transplant Centers, on behalf of the European Islet and Pancreas Transplant Association (EPITA) and the International Islet and Pancreas Transplant Association (IPITA)

A Worldwide Survey of Activities and Practices in Clinical Islet of Langerhans Transplantation

Transpl Int. 2022 Aug 11;35:10507. doi: 10.3389/ti.2022.10507.

William E Louch

A TRP to the emergency room: Understanding arrhythmia in the ageing heart

Cardiovasc Res. 2022 Mar 16;118(4): 932-933. doi: 10.1093/cvr/cvac017.

William E Louch, Harmonie Perdreau-Dahl, Andrew G Edwards

Image-Driven Modeling of Nanoscopic Cardiac Function: Where Have We Come From, and Where Are We Going?

Front Physiol. 2022 Mar 8;13:834211. doi: 10.3389/fphys.2022.834211.

William E Louch, Nina D Ullrich, Manuel F Navedo, Niall Macquaide

Editorial: Nanodomain regulation of muscle physiology and alterations in disease

Front Physiol. 2022 Nov 29;13:1092304. doi: 10.3389/fphys.2022.1092304.

Xianwei Zhang, Charlotte E R Smith, Stefano Morotti, Andrew G Edwards, Daisuke Sato, William E Louch, Haibo Ni, Eleonora Grandi

Mechanisms of spontaneous Ca2+ release-mediated arrhythmia in a novel 3D human atrial myocyte model: II. Ca2+-handling protein variation

J Physiol. 2022 Sep 16. doi: 10.1113/JP283602.

Xin Shen, Jonas van den Brink, Anna Bergan-Dahl, Terje R Kolstad, Einar S Norden, Yufeng Hou, Martin Laasmaa, Yuriana Aguilar-Sanchez, Ann P Quick, Emil K S Espe, Ivar Sjaastad, Xander H T Wehrens, Andrew G Edwards, Christian Soeller, William E Louch

Prolonged β-adrenergic stimulation disperses ryanodine receptor clusters in cardiomyocytes and has implications for heart failure

Elife. 2022 Aug 1;11:e77725. doi: 10.7554/eLife.77725.

Funding 2022

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/ 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
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
INTERNATIONAL				
Hybrida – Ethics of Organoids	EU H2020 – SwafS	Jan Helge Solbakk	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

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

Visiting adress
Domus Medica, Gaustad
Sognsvannsveien 9
0372 OSLO
Norway

Mail adress
Institute of Basic Medical Sciences
P.O. Box 1110 Blindern
0317 OSLO
Norway

www
https://www.med.uio.no/hth/english/

Email
contact@hth.uio.no

Layout
Anagram Design

Cover image
Illustration of the HTH developed recirculating organ-on-chip (rOoC) platform that operates without a pump. The rOoC includes separated organoid compartments each with its own perfusion channels to provide independent support. Credit: Mathias Busek