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# Finnish Organ-on-Chip meeting 2025

8-9 October 2025

Tampere University, Kauppi campus, Arvo building,

Arvo Ylpön katu 34, 33520 Tampere, Finland

BOC Centre of Excellence in Body-on-Chip Research

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Centre of Excellence in Body-on-Chip Research

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HaikaLab Immuno-oncology lab

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The FIN OoC 2025 Scientific Board and Award Committee evaluates the abstracts and nominates the best presentation awards.

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# Event location and maps

## Conference Venue

Tampere University, Kauppi campus, Arvo Ylpön katu 34, 33520 Tampere

Location in Google Maps

Destination Tram Stop: **Kaupin kampus B**

Tram Line: 1 TAYS

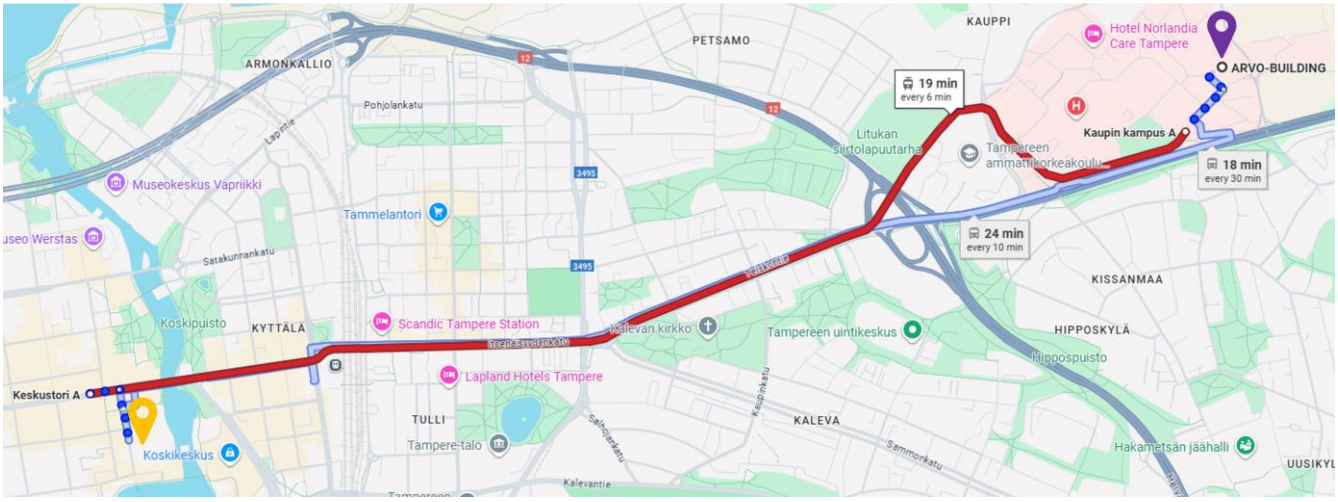
## Conference Dinner

Lounas- ja tilausravintola Koski, Kirkkokatu 10, 33200 Tampere

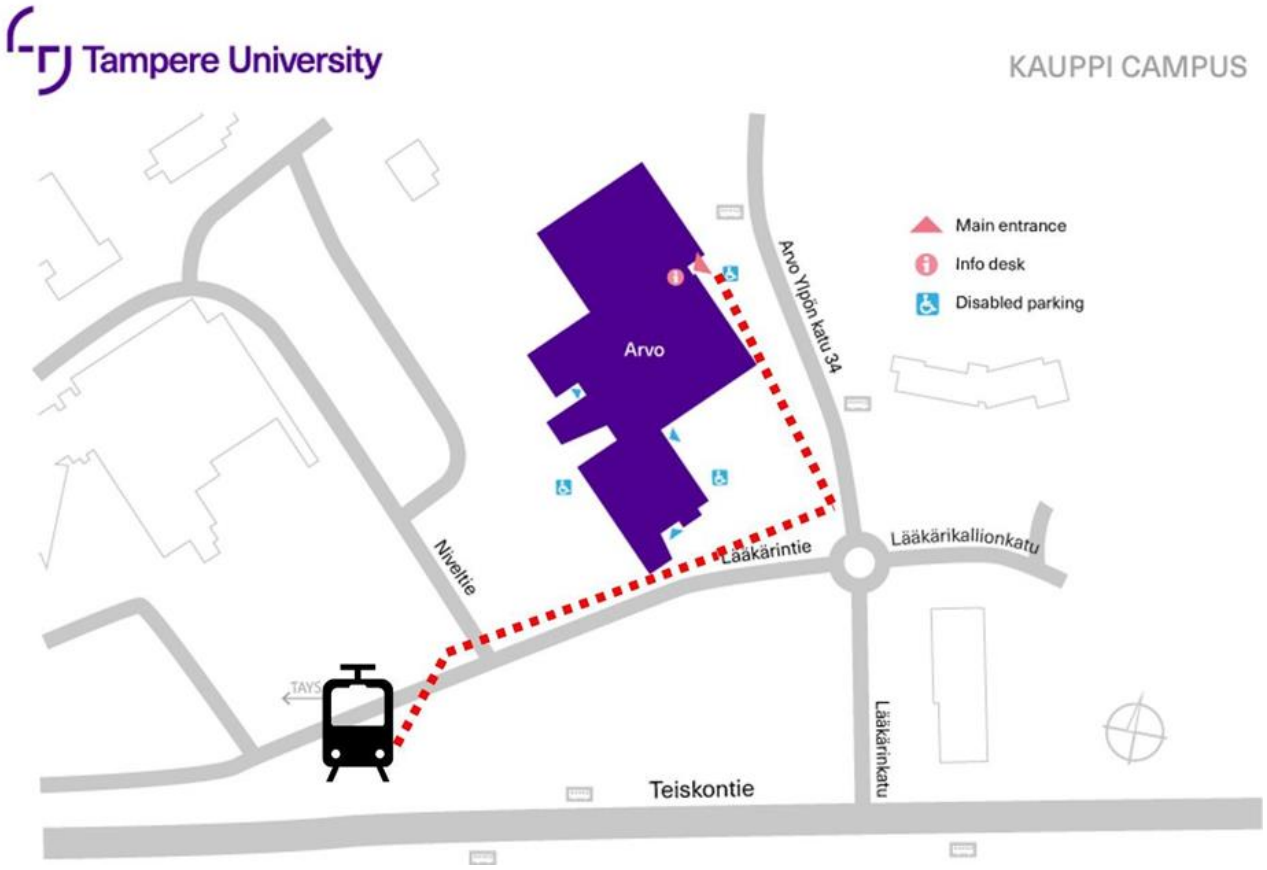
Location in Google Maps

Tram Stop: Kaupin kampus A to **Keskustori A**

Tram Line: 1 Lentävänniemi



The main entrance of Arvo is found on the eastern side of the building. If you are coming from the direction of the tram station, the main entrance is located behind the Arvo building.

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**Roam.fi**: Finnish wireless access service. Log in with your home institution's username and password. roam.fi (in Finnish)

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# Keynote speakers

## Hazel Screen

*Professor at the School of Engineering and Materials Science*
*Queen Mary University of London*

Hazel Screen is a Professor of Biomedical Engineering interested in developing organ-chip models to support both discovery science and therapeutic testing. She has a particular interest in developing models of mechanically functional tissues such as those in the musculoskeletal or cardiovascular systems, developing novel approaches to first analyse tissue structure-function in situ and then to recapitulate the physical niche environment perceived by cells within organ-chip models.

She co-directed the UK Organ-on-a-Chip Technologies Network and now co-leads the Centre for Predictive in vitro Models at Queen Mary University of London. She has recently led a successful £7M project proposal to establish an EPSRC Centre for Doctoral Training in Next Generation Organ-on-a-Chip Technology (COaCT), which will start admitting and training PhD students in October 2025.

She plays an active role in helping to shape the field and associated policy and regulation, as well as driving her own research group, funded from a range of UKRI and charity sources.

## Tarja Malm

*Professor at A.I. Virtanen Institute for Molecular Sciences,*
*Faculty of Health Sciences, University of Eastern Finland*

Tarja Malm is Professor in Molecular Neurobiology and the head of the Neuroinflammation research group at the A.I.Virtanen Institute, University of Eastern Finland. She is also the head of the “In vitro and ex vivo electrophysiology core facility” belonging to the Biocenter Kuopio and Biocenter Finland. She obtained her PhD in 2006 in Neurobiology with the focus glial cell biology and carried out her postdoctoral training at the Case Western Reserve University, USA. Her research focuses on understanding microglia-neuron signalling. Her group uses interdisciplinary approaches and develops novel, human based models to find therapeutic strategies to combat brain diseases. Her research group has pioneered development of methodologies to differentiate microglia and microglia containing cerebral organoids from human induced pluripotent stem cells. In the past years, her research group has established methodologies to evaluate neuronal circuit functionalities from cortical biopsies obtained from patients of idiopathic normal pressure hydrocephalus (iNPH) offering a novel source to study AD-related events at the molecular, functional and structural level.

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# Pasi Kallio

*Professor at the Faculty of Medicine and Health Technology*
*Tampere University, Finland*

Professor Pasi Kallio leads the Micro- and Nanosystems Research Group at the Faculty of Medicine and Health Technology, Tampere University, Finland. Since 2008, he has held a professorship in Biomedical Micro- and Nanodevices and served as Vice Dean for Research in the faculty from 2019 to 2023.

Prof. Kallio has authored more than 190 peer-reviewed publications, holds 16 patent applications, and has co-founded three spin-off companies. Prof. Kallio's research group has over 20 years of expertise in microfabrication, microfluidics, micro- and biosensors and image-based measurements, particularly in organ-on-chip applications.

The group has developed several novel concepts for advanced microphysiological systems with a strong emphasis on physioxic and hypoxic oxygen conditions in neural disorder and heart disease models. Key innovations include compartmentalized oxygen control and microfluidic perfusion as well as oxygen and electrophysiological measurements in 2D and 3D cell environments. The group has also developed mechanical stimulation platforms, including systems for stretching and compression.

# Otto Kalliokoski

*Associated Professor at Department of Veterinary and Animal Sciences, University of Copenhagen, Denmark*

Biomedical researcher – formerly an engineer, now a laboratory animal scientist – with a focus on improving pre-clinical methodology and novel methods for unbiased assessments of animal welfare. I have been teaching meta-analysis, statistics and experimental design for more than a decade at the University of Copenhagen. My current interests lie in exploring how meta-analytical investigations can be used to replace redundant animal experiments. It is my firm belief that improving animal welfare in pre-clinical medicine benefits not only the animals, but also the research itself.

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# Conference programme

**All sessions are held in Jarmo Visakorpi Auditorium**

## Day 1 Wed 8 Oct

| | | |
|---|---|---|
| 12:00-14:00 | *Registration open* | *Next to the main entrance and Arvo info desk (1st floor)* |

### 13:00 Session 1

| | | |
|---|---|---|
| 13:00 | Opening remarks | Organisers |
| 13:15 | Keynote lecture – Prof. Hazel Screen | Addressing physical niche design in organ-chip development – A musculoskeletal case study |
| 14:00 | Siiri Suominen | Physioxia-driven maturation of iPSC-derived hepatic cells |
| 14:15 | Elena Kremneva | Precision tumor-on-chip model for personalized drug efficacy and immune cell delivery assessment |
| 14:30 | Ella Lampela | Engineered 3D skeletal muscle myobundles with functional vascular networks |
| 14:45 | Curi Bio | Sponsor talk curi bio |
| 15:00 | *Coffee break and sponsor exhibition in the Yellow Hall* | |

### 15:30 Session 2

| | | |
|---|---|---|
| 15:30 | Keynote lecture – Prof. Pasi Kallio | Oxygen Matters: Replicating Physoxic and Hypoxic Conditions in Organ-on-Chip Platforms |
| 16:15 | Martina Freisa | Modeling early invasion in colorectal cancer using a microfluidic gut-on-chip system |
| 16:30 | Iván Perez-Torres | Computational Simulation of Electrical Temporal Interference Stimulation of a Myelinated and Unmyelinated Neurons |
| 16:45 | Cellbox Labs | Sponsor talk Cellbox Labs |
| 17:00 | *Poster session and sponsor exhibition in the Yellow Hall* | |
| 19:00 | *Dinner* | *Lounas- ja tilausravintola Koski (for dinner registrants only)* |

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## Day 2 Thu 9 Oct

| | | |
|---|---|---|
| 8:00-10:00 | *Registration open* | *Next to the main entrance and Arvo info desk (1st floor)* |
| 9:00 | **Session 3** | |
| 9:00 | Keynote lecture – Prof. Tarja Malm | Modeling microglia-neuron interaction using iPSC-based organoid models |
| 9:45 | Carl-Johan Hörberg | Large-Scale Topographical Control of Cultured Network of Neurons |
| 10:00 | Iisa Tujula | Human iPSC-based coculture models reveal neuroinflammatory crosstalk between microglia and astrocytes |
| 10:15 | MaxWell | Sponsor talk maxwell BIOSYSTEMS |
| 10:30 | *Coffee break, poster session and sponsor exhibition in the Yellow Hall* | |
| 11:30 | **Session 4** | |
| 11:30 | Lotta Kulmala | Miniature Engineered Heart Tissues From Human iPSC-Cardiomyocytes on a Hypoxia on-a-Chip Platform |
| 11:45 | Anna Katharina Köhler | Engineered heart tissues as a model to study exercise-induced ventricular arrhythmias in hypertrophic cardiomyopathy |
| 12:00 | Kaisla Walls | 3D imaging of engineered heart tissues using inverted selective plane illumination microscopy |
| 12:15 | Marita Meurer | Oxygenation in In Vitro Lung Models: Key to Physiological Relevance in Infection Research |
| 12:30 | *Lunch and sponsor exhibition* | |
| 13:30 | **Session 5** | |
| 13:30 | Keynote lecture – Assoc. Prof. Otto Kalliokoski | Are fraudulent studies undermining evidence synthesis in preclinical medicine? |
| 14:15 | Pauline Jeckel | Advancing Microphysiological Systems Adoption Through Targeted Education and Training Formats |
| 14:30 | Kati Rinnekari | Investigating the Role of S53P4 Bioactive Glass in Osteogenic Differentiation of 3D Bioprinted Human Bone Marrow Stem/Stromal Cells with Animal-Free Bioinks |
| 14:45 | Nithin Sadeesh | Non-destructive monitoring of inflammatory biomarker release in joint explant cultures using near-infrared spectroscopy and machine learning |
| 15:00 | Closing | Organisers |
| 15:30 | **Labtour** | Separate sign-up |

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# Abstracts for oral presentations

| NO. | SESSION | PRESENTER | TITLE OF THE ABSTRACT |
|---|---|---|---|
| 1. | 1 | Siiri Suominen | Physioxia-driven maturation of iPSC-derived hepatic cells |
| 2. | 1 | Elena Kremneva | Precision tumor-on-chip model for personalized drug efficacy and immune cell delivery assessment |
| 3. | 1 | Ella Lampela | Engineered 3D skeletal muscle myobundles with functional vascular networks |
| 4. | 2 | Martina Freisa | Modeling early invasion in colorectal cancer using a microfluidic gut-on-chip system |
| 5. | 2 | Ivan Perez Torres | Computational Simulation of Electrical Temporal Interference Stimulation of a Myelinated and Unmyelinated Neurons |
| 6. | 3 | Carl-Johan Hörberg | Large-Scale Topographical Control of Cultured Network of Neurons |
| 7. | 3 | Iisa Tujula | Human iPSC-based coculture models reveal neuroinflammatory crosstalk between microglia and astrocytes |
| 8. | 4 | Lotta Kulmala | Miniature Engineered Heart Tissues from Human iPSC-Cardiomyocytes on a Hypoxia on-a-Chip Platform |
| 9. | 4 | Anna Katharina Köhler | Engineered heart tissues as a model to study exercise-induced ventricular arrhythmias in hypertrophic cardiomyopathy |
| 10. | 4 | Kaisla Walls | 3D imaging of engineered heart tissues using inverted selective plane illumination microscopy |
| 11. | 4 | Marita Meurer | Oxygenation in In Vitro Lung Models: Key to Physiological Relevance in Infection Research |
| 12. | 5 | Pauline Jeckel | Advancing Microphysiological Systems Adoption Through Targeted Education and Training Formats |
| 13. | 5 | Kati Rinnekari | Investigating the Role of S53P4 Bioactive Glass in Osteogenic Differentiation of 3D Bioprinted Human Bone Marrow Stem/Stromal Cells with Animal-Free Bioinks |
| 14. | 5 | Nithin Sadeesh | Non-destructive monitoring of inflammatory biomarker release in joint explant cultures using near-infrared spectroscopy and machine learning |

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[Oral presentation 1]

# Physioxia-driven maturation of iPSC-derived hepatic cells

Siiri Suominen[1], Hannu Välimäki[2], Joose Kreutzer[2,3], Leena Viiri[2], Pasi Kallio[2] and Katriina Aalto-Setälä[1]

[1]Heart Group, Tampere University, Tampere, Finland
[2]Micro- and Nanosystems Research Group, Tampere University, Tampere, Finland
[3]BioGenium Microsystems Oy, Tampere, Finland

**Abstract**

In the human liver, hepatocytes, the main cell type of the liver, are arranged in functional units called hepatic lobules, each further divided into three metabolically distinct zones. This zonation can be attributed to the presence of various gradients, such as glucose and oxygen gradients. Notably, drug metabolism, one of the liver's most crucial functions, is mediated by cytochrome P450 enzymes, which are predominantly expressed in the least oxygenated zone of the liver lobules.

Our study highlights the often-overlooked role of physiological oxygen levels in the differentiation and culture of induced pluripotent stem cell (iPSC) derived cells. While extensive efforts are made to optimise various aspects of cell culture environments, such as media composition, oxygen levels are frequently neglected, despite their profound influence on cellular function and the stark contrast between atmospheric oxygen levels (~21%) and tissue-specific physioxia. In the liver, oxygen concentrations range from approximately 4% to 10% along the lobule axis.

To better replicate the liver's natural microenvironment, we differentiated iPSC-derived hepatocytes in 1-well culture chambers under physiologically relevant oxygen conditions. By introducing physioxia at various stages of differentiation, we observed clear improvements in cell functionality. Our analyses indicated increased secretion of liver-specific proteins such as albumin and urea, along with up-regulated expression of key hepatic genes, including members of the P450 family, even in the absence of media perfusion or 3D culture conditions.

Our findings demonstrate that adjusting a single physical parameter, such as oxygen levels, can significantly enhance the functionality of iPSC-derived hepatic cells. This simple yet impactful approach underscores the importance of mimicking physiological oxygen levels to support the liver's complex functions and offers a promising strategy for advancing liver research and developing more advanced and physiologically accurate in vitro liver models.

**Keywords**: iPSCs, hepatocytes, physioxia, hypoxia, cell microenvironment, stem cell differentiation

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[Oral presentation 2]

# Precision tumor-on-chip model for personalized drug efficacy and immune cell delivery assessment

Elena Kremneva[1], Johannes Smolander[1], Lilja Lahtinen[1], Shadi Jansouz[1], Bassel Alsaed[1], Heidi M. Haikala[1], Pauliina Junttila[2], Sebastien Mosser[2], Mikaela Grönholm[3], Tuomas Pylkkö[4], Sanna Vainionpää[5], Eva Sutinen[6], Hanna Seppänen[7] and Ilkka Ilonen[8]

[1]Immuno-oncology group, Translational Immunology research program (TRIMM), Faculty of Medicine, University of Helsinki
[2]Finnadvance Oy, Helsinki, Finland.
[3]Laboratory of Immunovirotherapy, Drug Research Program, Faculty of Pharmacy, University of Helsinki.
[4]Drug Research Program, Faculty of Pharmacy, University of Helsinki.
[5]Department of Abdominal Surgery, Helsinki University Hospital and University of Helsinki.
[6]Department of Pulmonary Medicine, Heart and Lung Center, Helsinki University Hospital & University of Helsinki.
[7]Dept of gastrointestinal surgery, Helsinki University Hospital & University of Helsinki.
[8]Department of General Thoracic and Esophageal Surgery, Heart and Lung Center, Helsinki University Hospital & University of Helsinki.

**Abstract**

Tumors generally consist of highly heterogeneous cell populations which lead to variation in responses to chemotherapy. Moreover, most cancer drugs have toxicities or induce resistance to chemotherapy, that can exceed their potential cancer-killing effects. Development of a reliable system that could predict patient drug responses and help to choose the most efficient treatment course would be highly beneficial.

We implemented microfluidics to develop a high-throughput tumor-on-chip (TOC) platform, where patient's own cells are used to reconstruct an in vivo circulatory system to recreate cancer drug and immune cell transport from the vasculature into tumor tissue. Physically separated open-top chamber and microfluidic channel allow to measure the infiltration of various compounds through an endothelial barrier built inside the chip. The predictive capabilities of the model have been tested in a retrospective co-clinical trial using patients' cancer samples. The idea of this study is to compare the responses to chemotherapy treatment received by patients in the clinic and by patient-derived organoids cultured in the chip system or in regular "static" 3D-culture conditions.

We have shown that those different cell culture conditions affect drug sensitivity of cancer samples, and variation in responses to chemotherapy treatment between different organoid models is more pronounced when they are cultured in TOC system. Furthermore, by applying single-cell RNA sequencing technique, we uncovered gene expression shifts and pathway rewiring at single-cell resolution depending on culture conditions.

In addition, we demonstrated an applicability of the TOC system to modeling immune cell migration towards cancer organoids. The efficiency of immune cell motility is cancer type dependent and can be enhanced by virus-induced inflammation.

Taken together, our findings highlight the importance of incorporating physiologically relevant systems, like fluidic culture, to better capture tumor-specific resistance and to model treatment outcomes.

**Keywords**: tumor-on-chip, organoids, cancer, microfluidics, drug resistance, scRNA-seq

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[Oral presentation 3]

# Engineered 3D skeletal muscle myobundles with functional vascular networks

Ella Lampela[1,2], Vilma Jokinen[1,2], Susanna Miettinen[1,2] and Miina Björninen[1,2]

[1]Adult Stem Cell Research Group, Faculty of Medicine and Health Technology, Tampere University, Pirkanmaa, Finland
[2]Tays Research Services, Wellbeing Services County of Pirkanmaa, Tampere University Hospital, Tampere, Finland

**Abstract**

Skeletal muscle, a key organ in glucose homeostasis, is vital for metabolic research. To complement and reduce animal testing, vascularized in vitro models with integrated vasculature are needed. Integrating vasculature enhances physiological relevance and enables the study of intercellular crosstalk between endothelial (EC) and skeletal muscle cells (SkMCs). Such existing models face challenges achieving SkMC maturation and functional vascularization due to conflicting medium requirements [1].

We aimed to develop a sequential technique for casting fibrin hydrogel for engineered 3D SkMC- and vasculature compartments, while investigating the uncertain role of adipose-derived mesenchymal stem cells (ASCs) in myogenic culture. These experiments tested coculture medium compositions for muscle and vascular development. 3D-imaging and segmentation pipelines were developed for quantifying myogenic and vascular parameters [2].

First, in ASC-C2C12 mouse myoblast cocultures, differentiation improvements were minimal compared to C2C12 monocultures. ASCs rarely fused into C2C12-myotubes. This result suggests ASCs playing a greater role in the vascular than the SkMC compartment of engineered models [3].

Our 3D formation technique enabled culturing ECs in their respective medium before introducing human SkMCs, enabling the formation of branching vessels with lumen-like endothelial structure. The surrounding muscle contained multinucleated, aligned cells expressing muscle marker dystrophin. Hydrogels with strictly human-origin cells supported robust SkMC and vascular development under various medium conditions, with or without ASCs.

In conclusion, our technique helps reconcile EC network formation with muscle maturation. While ASCs are nonessential in the SkMC compartment, their relevance in the vascular compartment is under investigation. Additionally, we established a 3D-segmentation pipeline assessing myotube fusion, providing a powerful tool for future research.

References:

1. Broer, T., et al. (2024). Acta Biomater 188, 65-78. doi:10.1016/j.actbio.2024.09.020
2. Yrjänäinen A., et al. (2024). Sci Rep 14, 22916. doi:10.1038/s41598-024-74493-3
3. Yrjänäinen, A., et al. (2022). Front Bioeng Biotechnol 10. doi:10.3389/fbioe.2022.764237

**Keywords**: skeletal muscle, myogenic cell culture, tissue engineering, 3D models

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[Oral presentation 4]

# Modeling early invasion in colorectal cancer using a microfluidic gut-on-chip system

Martina Freisa[1], Viviana Salvatore[1], Alessandro Lucini Paioni[1], Ambra Dondi[1], Marco Rasponi[2], Simona Rodighiero[1] and Luigi Nezi[1]

[1]Department of Experimental Oncology, Istituto Europeo di Oncologia – IRCCS (IEO), Milan, Italy.
[2]Department of Electronics, Information and Bioengineering, Politecnico di Milano, Milan, Italy.

**Abstract**

Most cancer-related deaths are caused by metastases [1], a process that involves the spreading of cancer cells from the primary site to distant organs. Thus, understanding the mechanisms regulating early steps of this stepwise process is crucial to develop more effective therapeutics [2].

Here, we present a microfluidic based gut-on-chip model to investigate early events of colorectal cancer metastatization. Our system replicates the main structural and functional features of the intestinal epithelium [3] and employs the connection to a mechanical actuator to generate peristalsis-like mechanical forces. As proof of principle, we co-culture Caco-2 and HT29MTX human cell lines to model the intestinal epithelium, while SW480 human cell line is seeded to model resident and migrating colon cancer. This experimental setting allows both epithelial maturation and analysis of early metastatic invasion into the adjacent collagen based extracellular matrix (ECM) over 9 days of observation.
Indeed, we confirmed the pro-invasive behavior of SW480 cells as they migrated through and modify the ECM. Notably, the controlled application of mechanical forces enhanced this invasive activity compared to the static counterpart, enabling future investigation of mechano -sensing and -signaling molecular pathways involved in the metastatization process.

Overall, we set up a novel experimental system for direct visualization of tumor–epithelial interactions and invasive dynamics within a biologically relevant microenvironment and demonstrate that it is suitable to investigate early pro-metastatic events.

References:
[1] Mani, K. et al. Nat. Commun. 15, 1–9 (2024)
[2] Brooks, A. et al. Adv. Healthc. Mater. 13, (2024)
[3] Ballerini, M. et al. Nat. Biomed. Eng. 9, 967–984 (2025)

**Keywords**: Gut-on-chip, microfluidic, colorectal cancer, metastases, tumor progression

Tampere University

[Oral presentation 5]

# Computational Simulation of Electrical Temporal Interference Stimulation of a Myelinated and Unmyelinated Neurons

Iván Perez-Torres[1], Annika Ahtiainen[1], Jarno M. A. Tanskanen[1] and Jari A. K. Hyttinen[1]

[1]CBIG, Tampere University

**Abstract**

Temporal Interference Stimulation (TIS) is a novel non-invasive brain electrical stimulation technique that offers the possibility of reaching deep brain structures. TIS uses two or more high-frequency electric fields with slightly different frequencies that interfere to generate a low-frequency electric field envelope, potentially allowing targeted stimulation of specific brain regions. Initial studies have demonstrated efficacy both in vivo [1] and in vitro [2]. While promising, the mechanisms of these neuronal responses are not completely understood.

In this study, we employed computational simulations using modified Blue Brain Project Hodgkin–Huxley multicompartment neuron models. The models incorporated realistic neuronal morphologies and ion channel dynamics, adapted to represent both myelinated and unmyelinated axons. Uniform electric fields with amplitude envelopes derived from high-frequency interference were applied, and neuronal activation thresholds were quantified across varying field strengths and orientations.

Our results show that pyramidal neurons with myelinated axons exhibit significantly lower activation thresholds under TIS compared to their unmyelinated counterparts. This finding suggests that axonal myelination plays a relevant role in neuronal responsiveness to TIS. These insights are relevant given that deep brain regions consist of both myelinated and unmyelinated neuronal populations.

In conclusion, the study shows that myelination influences neuronal excitability under TIS, useful for optimizing stimulation parameters and improving selectivity in clinical applications. Future work should extend these simulations to different neuronal types and network-level models to better understand the implications of TIS.

References

[1] N. Grossman, et al., “Non-invasive deep brain stimulation via temporally interfering electric fields,” Cell, vol. 169, no. 6, pp. 1029– 1041, June 2017.
[2] A. Ahtiainen, et al., “Electric field temporal interference stimulation of neurons in vitro,” Lab Chip, vol. 24, no. 19, pp. 3945–3957, July 2024.

**Keywords**: Neuroscience, Bioinformatics and Computational Biology, Temporal Interference Stimulation, Cell and Tissue Models

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[Oral presentation 6]

# Large-Scale Topographical Control of Cultured Network of Neurons

Carl-Johan Hörberg[1], Jason Beech[2], David O'Carroll[1] and Per Fredrik Johansson[1]

[1]Department of Biology - Lund University
[2]Solid State Physics - Lund University

**Abstract**

Technological advancements has recently enabled human neuronal in vitro models with unprecedented sophistication. However, virtually all in vitro neuronal systems exhibit similar activity patterns of periodic hypersynchronous "burst" events, which are not seen in healthy tissue. The presence of unhealthy neuronal activity raises the concern that these systems are not suitable as models for the brain. It is possible that the cause of the hypersynchronous behavior is due to a combination of unstructured growth, and the absence of sensory input and neuromodulation that often occurs in cultured neurons. To circumvent these issues, and to provide structure for cultured neurons, we used microfabricated elastomere channels which could produce highly specific neuronal growth patterns. By using an array of microwells coupled to the microfabricated channels, we could achieve control of the entire neuronal network topography, and thus circumventing a common issue otherwise faced when using similar fabrication techniques. To investigate how the neuronal activity was influenced by topographical control, we applied the microfabricated device to microelectrode arrays, and cultured human iPSC-derived neurons and astrocytes on it. The neuronal activity was still characterized by pervasive hypersynchronous burst events, but exhibited several key differences. Notably, bursts were intermixed with more desynchronous activity, and propagated through the network in accordance with the growth that the microfabricated channels supported. To investigate the role of sensory deprivation in hypersynchronous activity, we stimulated the neurons with electrical impulses aimed at recreating sensory input. Following stimulation, we observed lasting suppression of hypersynchronous activity, and also some indication of short-term plasticity during stimulation. Together, these results point to the utility of a novel microfabrication design which achieves large-scale control of neuronal networks in vitro.

**Keywords**: iPSC, In Vitro, Microfluidics, Microelectrode Arrays, Neurons

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[Oral presentation 7]

# Human iPSC-based coculture models reveal neuroinflammatory crosstalk between microglia and astrocytes

Iisa Tujula[1], Tanja Hyvärinen[1], Johanna Tilvis[1], Julia Rogal[2,3,4], Dimitrios Voulgaris[2,3,4], Lassi Sukki[5], Kaisa Tornberg[5], Katri Korpela[1], Henna Jäntti[6], Tarja Malm[6], Anna Herland[2,3,4], Pasi Kallio[5], Susanna Narkilahti[7] and Sanna Hagman[1]

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[2]Science for Life Laboratory, Division of Nanobiotechnology, Department of Protein Science, Royal Institute of Technology (KTH), 171 65 Solna, Sweden
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[6]Neuroinflammation research group, Faculty of Health Sciences, A.I. Virtanen Institute for Molecular Sciences, University of Eastern Finland, Kuopio, Finland
[7]NeuroGroup, Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland

**Abstract**

Increasing evidence is indicating a role of microglia and astrocytes as central mediators of neuroinflammatory processes in neurodegenerative diseases. However, their intricate bidirectional communication and contribution to pathogenesis remain largely unclear. Novel in vitro approaches are therefore needed for investigating glial functions in neuroinflammation. Here, the aim was to develop advanced human-based glial coculture models to investigate the inflammatory responses and crosstalk of microglia and astrocytes in vitro.

Human induced pluripotent stem cell (iPSC)-derived microglia and astrocytes were cocultured both in conventional culture dishes and in a microfluidic coculture platform featuring separate compartments for both cell types. The compartmentalized design of the platform enables the establishment of distinct microenvironments, while allowing spontaneous microglial migration toward astrocytes through interconnecting microtunnels. Inflammatory activation of glial cultures was stimulated with lipopolysaccharide (LPS), a combination of tumor necrosis factor-α (TNF-α) and interleukin-1β (IL-1β) or interferon-γ (IFN-γ). The following inflammatory responses and glial crosstalk were analyzed with immunocytochemistry and by measuring the secretion of inflammatory mediators and quantifying microglial migration.

Glial cocultures were successfully generated in both conventional culture dishes and the microfluidic coculture platform. Microglia and astrocytes responded to LPS and TNF-α/IL-1β stimuli in a cell type-specific manner and markedly altered their responses under coculture conditions, revealing glial crosstalk. Microfluidic coculture platform demonstrated efficient microglial migration toward astrocytes and successfully recapitulated glial responses and crosstalk within the inflammatory microenvironments. Furthermore, inflammatory crosstalk between microglia and astrocytes resulted in enhanced secretion of complement component C3, highlighting its role in the interplay between inflammatory microglia and astrocytes. To conclude, our results demonstrate an intricate molecular conversation between microglia and astrocytes during neuroinflammation. Our microfluidic coculture platform provides a more functional and controllable setup for investigating inflammatory glial interactions in vitro.

Tujula, I et al. (2025). Cell Communication and Signaling 23, 298.

**Keywords**: astrocyte, human induced pluripotent stem cell, in vitro model, microglia, neuroinflammation

Tampere University

[Oral presentation 8]

# Miniature Engineered Heart Tissues from Human iPSC-Cardiomyocytes on a Hypoxia on-a-Chip Platform

Lotta Kulmala[1], Kreutzer Joose[2], Katila Henri[1], Walls Kaisla[3], Belay Birhanu[3], Pekkanen-Mattila Mari[1], Hyttinen Jari[3] and Aalto-Setälä Katriina[1,4]

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**Abstract**

Ischemic heart disease (IHD) is the leading cause of death globally. In IHD, the blood flow to the myocardium is reduced, leading to oxygen deprivation and tissue damage. The primary treatment is reperfusion to restore blood flow, and antiarrhythmic medication to prevent arrhythmias. Reperfusion, however, can lead to worsening of the tissue injury. Previous animal experiments have provided promising results for medical interventions, but have failed in human clinical trials, indicating the need for human based models. Understanding the pathophysiology on a cellular lever, promotes the development of more effective treatments.

Human induced pluripotent stem cell derived cardiomyocytes (hiPSC-CMs) have been used to study IHD, but the experiments have been conducted mostly with 2D cell models. To better mimic physiological environments, in-vitro disease models are being shifted from 2D to more complex 3D systems.
Here, we present a novel 3D hypoxia platform, combining engineered heart tissue (EHT) with a system enabling precise control over oxygen concentrations on the chip. The base of the platform is an OxyGenie mini-incubator (BioGenium Microsystems, Finland) combined with field stimulation electrodes and an EHT-insert. Miniature EHT s are constructed on the EHT-insert lid by embedding 300 000 hiPSC-CMs within fibrinogen. The hypoxia-on-a-chip platform allows electrical stimulation on the tissue, and a real time analysis of cardiac functionality during hypoxic periods, including assessment of the beating rate, emerging arrythmias and contractile force.

Here we present that with our hypoxia-on-a-chip platform, iPSC-CMs and EHT technology can be effectively utilized to study cardiac tissue function under hypoxia. The miniature EHTs start beating spontaneously within the first week of culture and respond to the electrical stimulation. The chip design enables advanced imaging and precise control over temperature and oxygen concentration for real-time monitoring of the oxygen dynamics. Our preliminary results show strong potential for use in IHD modeling.

**Keywords**: iPSC cardiomyocytes, Cardiac Ischemia, Engineered Heart Tissues

Tampere University

[Oral presentation 9]

# Engineered heart tissues as a model to study exercise-induced ventricular arrhythmias in hypertrophic cardiomyopathy

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**Abstract**

Background: Sudden cardiac death by ventricular arrhythmias is one of the leading causes of death in hypertrophic cardiomyopathy (HCM) patients and physical activity a classical trigger. Catecholamine release is an obvious culprit, but other physiological parameters such as temperature and potassium concentrations also increase markedly in sporting individuals. The aim of this project is to evaluate the contribution of these conditions in human induced pluripotent stem cell-derived engineered heart tissue (hiPSC-EHT).

Material and Methods: EHTs from a healthy control hiPSC line (n=33, four differentiation batches) were exposed to a multi-step stress protocol and action potentials (AP) were measured via sharp microelectrode technique. EHTs were challenged by the following interventions: pH was decreased (7.4 to 7.0), temperature was raised from 37 °C to 40 °C, extracellular potassium levels were increased from 5.4 mM to 10 mM and 10 µM norepinephrine was administered.

Results: EHTs from a healthy proband tolerated all interventions without developing arrhythmias. While AP-parameters did not change in time-matched controls (30 min), the rise in temperature and concomitant drop of pH reduced AP duration at 90% repolarization (APD90) from 296 ± 21 to 246 ± 15 ms, n=8, $p<0.05$, but did not alter any other AP-parameter. Norepinephrine decreased cycle length (CL) from 1.2 ± 0.2 to 0.9 ± 0.1 s (n=7, $p<0.05$) and shortened APD90 from 311 ± 21 to 268 ± 12 ms (n = 7, $p <0.05$), but rate-corrected APD90 remained unaffected. High potassium did not change neither CL nor APD90. When norepinephrine and potassium were applied together at 40,0 °C and pH 7,0, APD90 dropped significantly from 257 ± 15 to 188 ± 8 ms (n=10, $p<0.05$). No afterdepolarizations were observed and beat-to-beat-variability did not increase.

Conclusion: EHT from a healthy proband tolerate all four interventions without obvious signs of electrical instability.

**Keywords**: Electrophysiology, Hypertrophic Cardiomyopathy, engineered heart tissue, sharp microelectrode, sport, potassium, pH, temperature, norepinephrine

Tampere University

[Oral presentation 10]

# 3D imaging of engineered heart tissues using inverted selective plane illumination microscopy

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**Abstract**

The leading cause of mortality globally being cardiovascular diseases, there is an urgent need for advanced heart tissue models that replicate native cardiac structure and function. Engineered heart tissues (EHTs) provide aligned cardiac contractions in 3D, support more mature tissue models, and allow straightforward force measurements. However, imaging EHTs at cellular and subcellular levels presents significant challenges due to photobleaching and limited imaging depth of currently used techniques. To address these challenges, we developed an optimized inverted selective plane illumination microscopy (iSPIM) system for high-resolution, volumetric imaging of EHTs.

The iSPIM system, equipped with a 10x/0.3 numerical aperture (NA) water immersion objective for excitation and a 20x/0.5 NA water immersion objective for detection, was used to acquire optical Z-stacks of fixed EHTs. Three lasers (488 nm, 561 nm, and 638 nm) were used for imaging fluorescence from connexin 43, troponin T, and nuclei, respectively. The resolution of the iSPIM was measured at 1 µm laterally and 9.6 µm axially, and neural networks were implemented for enhancing the axial resolution. Optimized deskewing and deconvolution were performed using Python and Huygens Essential software.

Using the iSPIM system, we achieved high-resolution visualization of key components within EHTs. This system enabled rapid imaging across the entire tissue thickness and, through segmentation, provided detailed insights into cell alignment. Our optimized iSPIM system is a powerful tool for analyzing EHTs, demonstrating its versatility for imaging complex 3D tissue structures. Future adaptations will allow extended imaging periods of live EHTs, enabling high-speed imaging of tissue dynamics.

**Keywords**: biomedical imaging, cardiovascular, image processing, high speed 3D imaging, iSPIM, engineered heart tissue

[Oral presentation 11]

# Oxygenation in In Vitro Lung Models: Key to Physiological Relevance in Infection Research

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**Abstract**

The development of physiologically relevant in vitro models for lung infection research necessitates careful consideration of culture complexity and oxygenation. Localized hypoxia, a hallmark of lung tissue infection, is often overlooked in standard in vitro systems. Our study characterizes classical air-liquid interface (cALI) and liquid-liquid interface (LLI) cultures of permanent bronchial epithelial (Calu-3) cells under hypoxic and normoxic conditions, alongside primary human bronchial epithelial cell (hBEC) cALI cultures, to evaluate the impact of oxygen availability on epithelial responses.

Trans epithelial electrical resistance (TEER) measurements revealed the formation of epithelial barriers with high integrity across all models, with maturation-dependent changes in permeability observed during cultivation. Histological analysis demonstrated distinct morphological features for each 3D model, with the hBEC cALI model exhibiting the greatest similarity to in vivo conditions. Under hypoxia, extracellular oxygen depletion was complete within 6-7 hours for all models, with no discernible differences in depletion patterns. In contrast, normoxic conditions yielded unique oxygen depletion profiles for each model, resulting in varied oxygenation statuses post-incubation.

The observed variations in oxygen depletion rates among Calu-3 LLI, Calu-3 cALI, and hBEC cALI models suggest that cellular oxygen consumption is influenced by both cell type and culture format. These findings highlight the utility of the presented models for in vitro lung research, underscore the importance of model selection in experimental design, and provide valuable insights for the development of microfluidic systems to study the human lung epithelium under flow conditions. This work emphasizes the need for precise control of oxygenation even in chip-based platforms to mimic physiological and pathological lung environments accurately. By incorporating oxygen sensors and simulating natural airflow and medium circulation, this model will provide novel insights into lung pathologies.

**Keywords**: physiological oxygen conditions, lung model, ALI, TEER, transwell, infection

Tampere University

[Oral presentation 12]

# Advancing Microphysiological Systems Adoption Through Targeted Education and Training Formats

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**Abstract**

Microphysiological systems (MPS), including organoids and Organ-on-Chip (OoC) technologies, are cutting-edge tools that closely replicate human physiology. They are increasingly used in biomedical, pharmaceutical, and basic research due to their clear advantages over traditional animal models. Yet, despite their potential, widespread adoption remains limited. Sustainable replacement of animal testing requires more than innovation—it demands a shift in mindset. We need visionary model developers creating reliable platforms, and equally, well-trained researchers who understand and apply non-animal methods with confidence.

The 3R-Center Tübingen is deeply committed to education and training. By equipping scientists early in their careers with solid knowledge, we enable informed decisions and foster a transition toward more ethical, human-relevant research. To address these challenges, the 3R-Center Tübingen conducted a study to identify the specific training needs of diverse stakeholder groups. Based on the findings, tailored education programs were developed for audiences ranging from children and students to researchers, regulators, and policymakers. Formats are adapted to different age groups, expertise levels, and professional backgrounds and include an OoC Summer School, a Master's-level module at the University of Tübingen, science days for children, student and researcher internships, and a monthly webinar series.

In addition to academic and public sector stakeholders, industry also shows a clear need for training, as small and medium-sized enterprises (SMEs) in particular face notable challenges in adopting Novel Approach Methodologies (NAMs). As part of the EU-funded STEP4NAMs project, the 3R-Center Tübingen supports SMEs in adopting human-relevant NAMs, with a focus on OoC systems. Planned activities include for example a free online course, on-site training courses to build practical skills, and a 1:1 consulting of SMEs.

Equipping current and future stakeholders with knowledge and skills in MPS technology is key to raising awareness, building expertise and trust, and enabling the adoption of these technologies. Ultimately, these efforts aim to drive progress in 3R-aligned research.

**Keywords**: 3R-Center, Education,Training, MPS, Organ-on-Chip, Replace, Reduce

Tampere University

[Oral presentation 13]

# Investigating the Role of S53P4 Bioactive Glass in Osteogenic Differentiation of 3D Bioprinted Human Bone Marrow Stem/Stromal Cells with Animal-Free Bioinks

Kati Rinnekari[1,2], Roope Ohlsbom[1,2], Kartikeya Dixit[1,2], Karoliina Hopia[3], Paula Puistola[3], Anni Mörö[3], Jonathan Massera[4], Janne T. Koivisto[5] and Susanna Miettinen[1,2]

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**Abstract**

There is a growing demand in biomedicine for tissue models that closely replicate native tissues for studying tissue development, disease mechanisms, and therapeutic innovations. Bone tissue models are essential for investigating conditions such as bone defects and fractures, osteoporosis, and cancer metastases to bone. Bioactive glass (BAG), known for its biocompatibility and bone-stimulating properties, has shown promise in orthopedic and dental applications. Nanofibrillated cellulose (NFC), a biodegradable and biocompatible material derived from wood, has demonstrated potential in improving bioinks for tissue engineering.

This study investigated the effects of S53P4 BAG extract on 3D bioprinted human bone marrow stem/stromal cells using two animal-free bioinks containing modified hyaluronic acid, collagen type I, and either unmodified hyaluronic acid or NFC. The 3D bioprinted constructs were cultured in osteogenic medium with or without BAG extract. Cell viability, functions, proliferation, and osteogenic differentiation were assessed using Live/Dead assays, immunocytochemistry, CyQuant assay, quantitative reverse transcription polymerase chain reaction (RT-qPCR), and ALP activity assays. Mineralization and mechanical properties were evaluated via micro-computed tomography (μCT), and compression testing.

Results showed that cells remained viable and exhibited elongated morphology, indicating good cell attachment. The cells expressed osteogenic markers like osteocalcin and collagen I, and showed varying ALP activity. BAG extract enhanced cells' elongated morphology and osteocalcin expression. Both BAG and NFC improved mineral deposition and the mechanical strength of the constructs.

These findings support the use of BAG and NFC in bioinks for bone tissue engineering and highlight the need for further research into their specific roles and mechanisms.

**Keywords**: Bone tissue engineering, Nanofibrillated cellulose, 3D Bioprinting, Bioactive glass

Tampere University

[Oral presentation 14]

# Non-destructive monitoring of inflammatory biomarker release in joint explant cultures using near-infrared spectroscopy and machine learning

Nithin Sadeesh[1], Fatemeh Safari[2], Zhen Li[2], Arjen Gebraad[1,3], Ervin Nippolainen[1], Susanna Miettinen[3], Sybille Grad[2] and Isaac O. Afara[1]

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**Abstract**

Chronic joint disorders like osteoarthritis (OA) are degenerative diseases marked by inflammation and complex interactions within joint structures (1). Despite progress, many aspects of OA pathophysiology remain unclear. Inflammatory biomarkers such as glycosaminoglycan (GAG) and nitric oxide (NO) are commonly studied using explant degeneration models (2). Traditional methods like ELISA and mass spectrometry are accurate but costly and time-consuming. This study explores near-infrared spectroscopy (NIRS) combined with machine learning (ML) as a novel optical approach for rapid and non-destructive monitoring the release of key biomarkers, such as GAG and NO (3, 4).

Bovine osteochondral explants and synovium (n=24) were co-cultured in high glucose (HG) and low glucose (LG) DMEM media, with and without TNF and IL1B. GAG and NO release were measured daily over 14 days using dimethyl-methylene blue and Griess assays. NIR spectral data were acquired in transflection mode using a fiber optic probe and spectrometer (900–1700 nm, StellarNet, USA). Data analysis was conducted in QUASAR-Orange (3, 4), where ML algorithms (Random Forest, Adaptive Boosting, Support Vector Machine, Gradient Boosting) were used to classify the spectral data into four classes based on medium composition.

GAG and NO production were significantly affected by glucose concentration and inflammatory stimuli. Preliminary findings show that NIRS combined with ML can reliably classify media conditions and enable estimation of key biomarker concentration in situ. Early results suggest that NIRS can detect low concentrations of GAG and NO, highlighting the potential of NIRS as a non-invasive tool for assessing release of OA biomarkers. Ongoing work aims to quantify these biomarkers to further validate the utility of NIRS in bioprocess monitoring.

References

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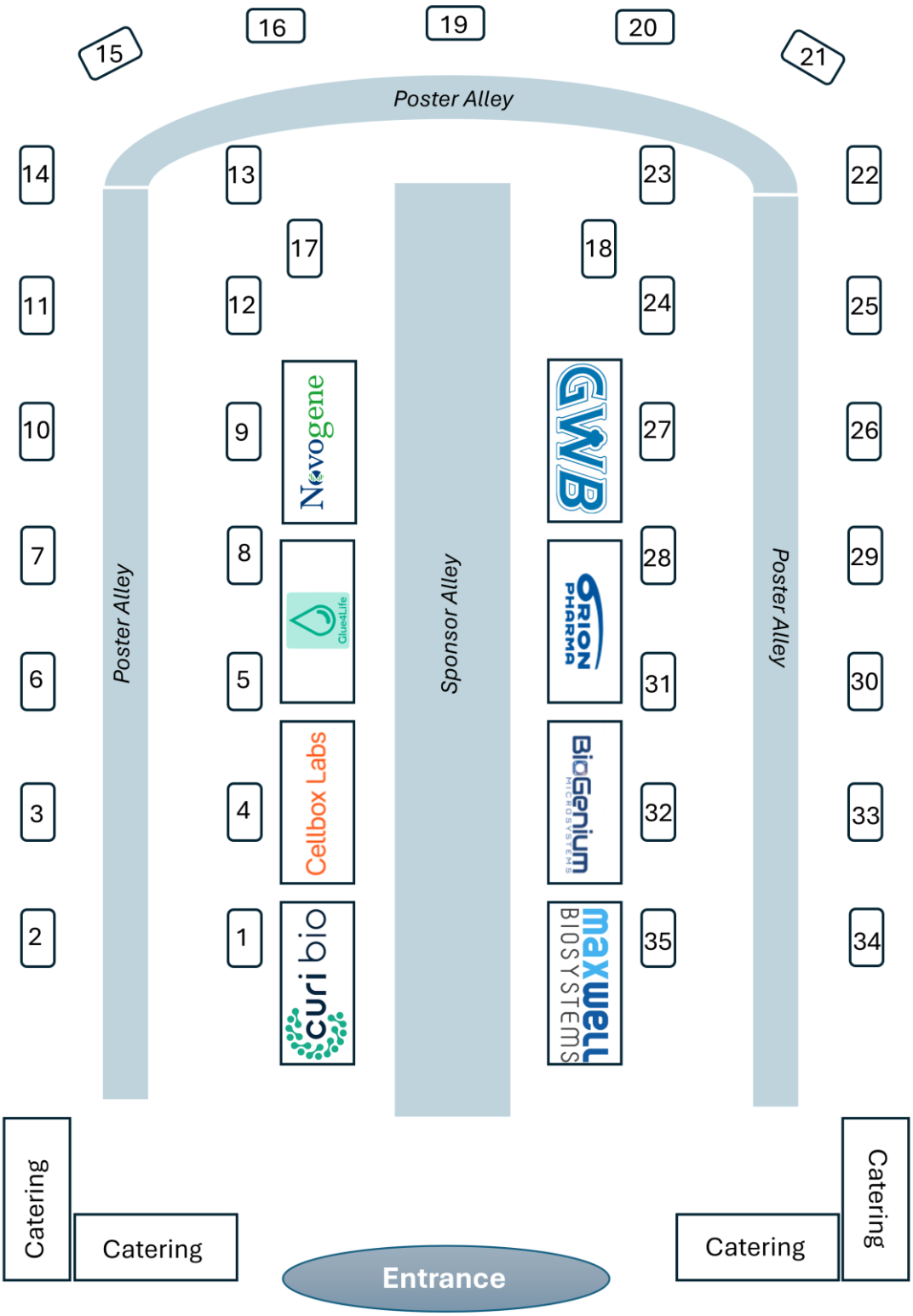
**Keywords**: Osteoarthritis, Optical monitoring approach, NIR spectroscopy, Biomarkers, Culture medium

Tampere University

# Poster presentations

**Posters are displayed in the Yellow Hall alongside the sponsor exhibition**



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# Abstracts for poster presentations

| POSTERS | PRESENTATION TIME |
|---|---|
| ODD-NUMBERED POSTERS | WEDNESDAY 8 OCTOBER 17:00-18:15 |
| EVEN-NUMBERED POSTERS | THURSDAY 9 OCTOBER 10:30-11:30 |

We recommend that authors be present at their posters during their designated poster sessions. Posters should be set up at the beginning of the event and remain on display for its entire duration.

| NO | PRESENTER | TITLE OF THE ABSTRACT |
|---|---|---|
| 1. | Emma Pesu | Human cardiac innervation-on-a-chip platform for disease modeling |
| 2. | Martta Häkli | Modeling hypertrophic cardiomyopathy with human heart organoids |
| 3. | Henna Lappi | Severe genetic arrhythmia (CPVT) studied with iPSC-cardiac model derived from pediatric patients |
| 4. | Anni Marjomaa | Generation of Cardiac Organoids for Hypertrophic Cardiomyopathy (HCM) Modeling |
| 5. | Shambhavee Annurakshita | Photocrosslinkable Graphene-Enhanced Biomaterial Inks for Improved Printability and Structural Fidelity |
| 6. | Anastasiia Mykuliak | A novel blue light crosslinking fibrin-hyaluronan hydrogel for vascular tissue engineering |
| 7. | Tuulia Taipale | 3D Microrheology for Microstructural Analysis of Extracellular Matrix Based 3D Hydrogels |
| 8. | Moe Awashra | Superhydrophobic Cell-Repellent Microstructures |
| 9. | Heidi Vänskä | Thiol–ene click chemistry enables low-temperature gelation of norbornene-functionalized gelatin and PEG-thiol hydrogel |
| 10. | Tasneem Un Nissa | Development of porous scaffolds for bone tissue engineering by incorporating polysaccharide gums |
| 11. | Vilhelmiina Hännikäinen | Graphene field-effect transistors as measurement devices for in vitro neuronal activity |
| 12. | Valtteri Vuolanto | Software for Multifaceted Analysis of Microelectrode Array Data |
| 13. | Hanna Vuorenpää | Driving 3R´s with industrial adoption of Microphysiological Systems as Novel Approach Methodologies in Replacing animal experiments |
| 14. | Hamed Ghazizadeh | Innervation Induces a Distinct Force–Frequency Phenotype in 3D Human Neuromuscular Junction Tissues |
| 15. | Lotta Isosaari | Exploring multicellular interactions between glioblastoma and the brain: a 3D open-top microfluidic chip model with integrated neurovascular networks |
| 16. | Anastasiia Tourbier | Next-generation electrophysiology for functional characterization of human neural organoids and assembloids |
| 17. | Fulya Ersoy | Characterization of electrophysiological activity in neurospheres using a novel NeuroMPS with integrated micro electrodes |

| | | |
|---|---|---|
| **18.** | Fikret Emre Kapucu | Tripartite Human Neuronal Network for Modeling Pathological Propagation and Functional Dynamics in Neurological Disorders |
| **19.** | Siiri Sihvonen | Suppressing neuronal seizure-like activity in vitro |
| **20.** | Oskari Kulta | Distinct functional properties of human iPSC-derived sympathetic neurons in vitro |
| **21.** | Venla Harju | Modelling ischemic stroke in vitro with human induced pluripotent stem cell derived neurons |
| **22.** | Tanja Hyvärinen | Human-specific model to study foamy microglia in multiple sclerosis |
| **23.** | Austin Donnelly Evans | Modular Plug and Play Recombinant 3D hydrogel system for studying cancer invasion |
| **24.** | Arun Teotia | Cell microenvironment engineered organ-on-chip microphysiological system with 3D spatiotemporal presentation of physical and biochemical cues |
| **25.** | Ilona van der Weij | Donor characteristics of hASC-derived adipocytes and oxygen environment affecting steatosis induction in hiPSC-derived hepatocytes. |
| **26.** | Claudio Costantini | Modeling secondary hyperoxaluria in a microphysiological system and testing of microbial metabolites as potential protective agents |
| **27.** | Uzma Hasan | Investigating subtype-specific migration of patient-derived glioma cells in 3D matrix models |
| **28.** | Emilia Piki | Modeling the metastatic ovarian cancer microenvironment in vitro using xeno-free hydrogel and patient-derived matrix |
| **29.** | Lassi Sukki | PDMS - epoxy hybrid microfluidic device with compartmentalised hypoxia for neuronal studies |
| **30.** | Katariina Taipalus | Developing a Border Zone-on-chip |
| **31.** | Emon Hossain | Thermoplastic elastomer hot embossing in fabrication of microfluidic cell culture devices |
| **32.** | Harini Karunarathna | Monitoring Early-Stage Osteoarthritis in a Tissue-Engineered In Vitro Model Using Near-Infrared Spectroscopy |
| **33.** | Sini Saarimaa | Comparison of platforms for 3D cocultures of neurons and adipocytes |
| **34.** | Igor Shevkunov | Noninvasive time-lapse Cell Imaging with Quantitative Phase Retrieval via Lensless Microscope |

Tampere University

[Poster presentation 1]

# Human cardiac innervation-on-a-chip platform for disease modeling

Emma Pesu[1], Elias Kuusela[1], Anna-Mari Moilanen[2], Andrey Vinogradov[2], Kaisa Tornberg[3], Henna Lappi[1], Lassi Sukki[3], Tomi Ryynänen[3], Timo Salpavaara[3], Fikret Emre Kapucu[3], Pasi Kallio[3], Katriina Aalto-Setälä[1], Susanna Narkilahti[2]

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**Abstract**

The cardiac autonomic nervous system (cANS) regulates cardiac function through innervation. Dysfunction of neuronal and cardiovascular crosstalk has been linked to various pathologies. Completely human cell-based in vitro models for studying brain-heart interactions with the central nervous system (CNS), peripheral nervous system (PNS), and cardiac tissue are lacking in the field. Our aim is to model the function of cANS in vitro by combining CNS type neurons (CNs), PNS type neurons (PNs) and cardiomyocytes (CMs) derived from human induced pluripotent stem cells (hiPSC) in a compartmentalized microfluidic device called a 3D3C chip. The structure of the 3D3C chip allows for the culturing of each cell type separately while allowing axonal connections to form via microtunnels to the adjacent cell compartment. Integrated in-house produced microelectrode arrays (MEAs) enable repeatable measurements of cellular activity in the multiculture and investigation of cell-specific electrophysiological functionality development and responses. By stimulating neural activity in the neuronal compartments, axon-mediated functional responses between the cell types can be investigated. Here, hiPSC-derived CNs, PNs and CMs were successfully multicultured in the 3D3C chip for up to three weeks, allowing physical axonal connections to form via microtunnels from CNs to PNs and from PNs to CMs. All cell types developed cell-specific electrophysiological functionality in the platform over time and axonal connections were confirmed to be functional with pharmacological excitation of neuronal activity, indicating of successful innervation. This advanced, completely human cell-based cardiac innervation-on-a-chip provides a powerful platform for examining disease-related mechanisms in which the brain-heart axis is involved.

**Keywords**: cardiomyocytes, central nervous system, cortical neurons, electrophysiology, human induced pluripotent stem cells, microelectrode array, microphysiological systems, peripheral nervous system, sympathetic neurons

Tampere University

[Poster presentation 2]

# Modeling hypertrophic cardiomyopathy with human heart organoids

Martta Häkli[1], Katriina Aalto-Setälä[1,2]

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**Abstract**

Cardiovascular diseases are the most common cause of death worldwide. Hypertrophic cardiomyopathy (HCM) is the most common genetic cardiovascular disease caused by several known mutations, mostly in sarcomeric genes. However, it can also be caused by non-sacromeric genes, such as the less studied heterozygous Finnish founder mutation c.482C>A, p.(Thr161Lys) in junctophilin-2 (JPH2). The mutation carriers suffer from significant septal thickening and have a high prevalence of arrhythmias. JPH2 is a structural protein connecting cell membrane to sarcoendoplasmic reticulum and has a crucial role in efficient calcium handling and contraction of cardiomyocytes (CM).

This study aims to model HCM caused by the JPH2 mutation in human heart organoids (hHOs) to elucidate HCM disease phenotype, progression and mechanisms. Human heart organoids can be generated from induced pluripotent stem cells (hiPSCs), which will self-assemble into heart organoids and differentiate into several cardiac cell types, including CMs, cardiac fibroblasts (CF), endothelial cells (EC), epicardial cells (EPI) and vascular smooth muscle cells (VSMC). Especially CFs have a key role in development of fibrosis in HCM, which is one of the key features of the disease, making the hHO model consisting of multiple cell types relevant for studying the disease phenotype and mechanisms.

In this study, three hiPSC lines are used to generate hHOs. The cell lines include a wild type hiPSC line derived from a healthy control, hiPSC line derived from an HCM patient carrying the JPH2 mutation, as well as a hiPSC line with isogenic correction of the mutation. The hHOs will be cultured for 2-6 weeks, and the disease progression and phenotype will be evaluated using video microscopy and calcium imaging to assess the contractility and arrhythmogenicity, as well as immunocytochemical staining and RT-qPCR to assess the cellular composition of the hHOs, as well as CM hypertrophy and fibrosis.

**Keywords**: human induced pluripotent stem cell, cardiomyocyte, human heart organoid, hypertrophic cardiomyopathy

Tampere University

[Poster presentation 3]

# Severe genetic arrhythmia (CPVT) studied with iPSC-cardiac model derived from pediatric patients

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**Abstract**

Catecholaminergic polymorphic ventricular tachycardia (CPVT) is a genetic cardiac condition causing severe risk for sudden cardiac death. Structure of a patient's heart is normal, and no arrhythmias are detected at rest. When the heart rate increases due to emotional stress or exercise severe arrhythmias occur causing symptoms like loss of consciousness, and even sudden death. Approximately 30% of the patients receive symptoms before age of 10 and prognosis of death before age of 30 is 30-35%.

We have derived iPSC lines from the blood samples of six patients from 10 to 18 years old carrying severe form of the CPVT. These iPSC lines are differentiated into cardiomyocytes and their electrical properties are measured with calcium imaging method. We have now studied calcium release from the calcium storages which are essential for beating of the cardiomyocytes. As the severe clinical phenotype of the patients predicts, there are also challenges in a cell model when the beat rate increases. Previously we have studied cardiomyocytes derived from adult CPVT patients in 3D bioprinted cardiac structures which showed normal functionality, Ca2+ handling properties and disease phenotypic response to adrenaline treatment. This cardiac iPSC model could be used to determine why the clinical phenotype, especially with these patients, is so life threatening and in addition to test drugs to treat arrhythmias caused by increased beat rate.

**Keywords**: iPSC, cardiomyocytes, disease modelling, calcium imaging, CPVT

Tampere University

[Poster presentation 4]

# Generation of Cardiac Organoids for Hypertrophic Cardiomyopathy (HCM) Modeling

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**Abstract**

Hypertrophic cardiomyopathy (HCM) is a hereditary cardiac disease characterized by abnormal thickening of the heart, particularly left-ventricular myocardium, primarily due to cardiomyocyte hypertrophy and myocardial fibrosis, which leads to altered cardiac function and an increased risk of arrhythmias and sudden cardiac death. HCM is estimated to occur in one in 500 people and is a leading cause of sudden cardiac death (SCD) in young people, particularly athletes. Despite its clinical importance, understanding the molecular and cellular mechanisms of HCM remains limited, due to the lack of physiologically relevant human models. Current in vitro models, mainly 2D cultures of human pluripotent stem cell (hPSC)-derived cardiomyocytes fail to replicate the multicellular interactions that contribute to disease progression.

The aim of this project is to establish and optimize a 3D cardiac organoid platform to model HCM in vitro more accurately than existing models. Using patient-derived induced pluripotent stem cells (hiPSCs) harboring junctophilin-2 (JPH2) mutation, cardiomyocytes (CM) and epicardial cells (EPI) are first differentiated and then combined to generate organoids. Within these organoids, epicardial cells further differentiate into cardiac fibroblasts and smooth muscle cells. The main advantage of this model is its ability to better recapitulate disease mechanisms, particularly its capacity to model cardiac fibrosis.

Phenotypic characterization will include immunostaining, functional assays and gene expression analysis. We aim to establish a cardiac organoid model that provides a physiologically relevant platform that more accurately mimics in vivo cardiac function found in human hearts to model HCM.

**Keywords**: Cardiac organoids, Hypertrophic cardiomyopathy (HCM), Human induced pluripotent stem cells (hiPSCs)

Tampere University

[Poster presentation 5]

# Photocrosslinkable Graphene-Enhanced Biomaterial Inks for Improved Printability and Structural Fidelity

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**Abstract**

Background: Multimaterial bioinks combine complementary properties for tunable functionality. Graphene provides electrical and mechanical strength, while gellan gum ensures structural support and biocompatibility. Their integration into a photocrosslinkable system enables stable, high-precision constructs, offering a promising platform for next-generation biofabrication technologies.

Material and methods: Gellan gum (GG) was methacrylated under basic conditions to produce GGMA, with modification confirmed by 1H-NMR. Bioinks were prepared by dissolving 1.5% w/v GGMA in 0.5% w/v Irgacure and adding 0.25%, 0.50%, or 1.00% w/w graphene. Rheological measurements assessed flow behavior and viscoelasticity, and inks were printed using extrusion-based bioprinting. For cell-laden formulations, human dermal fibroblasts ($5 \times 10^6$ cells/mL) were mixed into the precursors.

Results and Discussion: The methacrylation was obtained at pH 8-9 and degree of modification was ~30%. The hydrogel precursors were obtained by dissolving GGMA 1.5% w/v in 0.5% irgacure solution followed by the addition of 0.25%, 0.5% and 1.0% w/w graphene solution. The flow behavior of inks formulations was characterized by rheological measurements. The biomaterial ink formulations exhibited excellent printability, viscoelastic properties, and high shape fidelity. The rheological analysis demonstrates that the modified hydrogel formulations possess optimal shear-thinning properties, ensuring smooth extrusion while maintaining printability. This is critical for achieving high-resolution constructs with precise geometry, as observed in the printed scaffold. All inks were printed in grids and cylinder structures with high resolutions and stackability (10 layers grids were printed). However, 0.5 % graphene exhibited better shape fidelity and higher stability. The viability of cell-laden bioprinted constructs was assessed at Days 1, 3, and 7. The cells were uniformly distributed and exhibited elongated morphologies, indicative of good attachment and viability after printing.

The developed photocrosslinkable multimaterial bioinks showed excellent rheology, printability, and structural stability, with 0.5% graphene performing best, effectively overcoming single-material limitations and enabling high-resolution, stable constructs for advanced biofabrication.

**Keywords**: Multimaterial-Bioink, Graphene, Bioprinting, Photocrosslinking

Tampere University

[Poster presentation 6]

# A novel blue light crosslinking fibrin-hyaluronan hydrogel for vascular tissue engineering

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**Abstract**

Fibrin is widely utilized in tissue engineering and microphysiological systems due to its excellent biocompatibility and user-friendly handling . Its intrinsic pro-angiogenic properties are critical for the development of vascularized tissue constructs, facilitating nutrient and oxygen delivery and enhancing physiological relevance. However, the limited mechanical strength of fibrin often results in rapid hydrogel contraction and degradation. In this study, we investigate a novel blue light-crosslinked fibrin-hyaluronan hydrogel as an effective strategy to enhance the long-term stability of fibrin hydrogel and evaluate its potential for vascular tissue engineering applications.

Microvascular networks were formed by human umbilical vein endothelial cells and bone-marrow derived mesenchymal stem/stromal cells within hydrogels composed of fibrin and gallic acid-functionalized hyaluronic acid (HAGA; 1, 2, 5, and 10 mg/ml final concentration). Hydrogel compaction, encapsulated cell viability and proliferation were monitored for three weeks and compared to pure fibrin hydrogel. Microvascular network parameters, including vasculature area coverage and total vasculature length, as well as extracellular matrix protein expression, were assessed after one week of culture. Additionally, microvascular networks were established within AimBiotech microfluidic chips, and vasculature perfusability was evaluated.

Fibrin-HAGA hydrogels supported cell viability and proliferation in all tested groups and maintained hydrogel integrity during extended culture period (5, 10 mg/ml HAGA). Hydrogels with low to moderate HAGA concentration supported 3D vascular network development while hydrogel with 10 mg/ml HAGA caused poor vasculature formation. Fibrin-HAGA hydrogels supported formation of microvascular networks-on-a-chip. Overall, formulations containing 2 and 5 mg/ml HAGA demonstrated optimal performance, supporting vascular network formation while significantly reducing construct shrinkage.

In conclusion, a novel blue-light crosslinking fibrin-HAGA hydrogel is a promising candidate for long-term vascularized tissue engineering and organ-on-a-chip applications. Fine-tuning hydrogel stiffness by adjusting fibrin to HAGA content and optimizing initial cell seeding densities are important to achieve the desired vascularization outcomes.

**Keywords**: Fibrin hydrogel, hyaluronic acid, vascular networks, tissue engineering

Tampere University

[Poster presentation 7]

# 3D Microrheology for Microstructural Analysis of Extracellular Matrix Based 3D Hydrogels

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**Abstract**

Spatial mapping of hydrogel microstructure enables discoveries on the formation of complex biomaterials and cell-hydrogel interactions. Passive microrheology with multiple particle tracking (MPT) using tracer particles enables hydrogel characterization in high spatial resolution and in 3D, enabling analysis of viscoelastic micromechanics and porosity. In MPT, a hydrogel is filled with fluorescence particles and imaged as time series, from which Brownian motion of the particles is tracked. These motion patterns reveal rigid, viscoelastic, and fluid-like areas in the hydrogel. When a specific location is imaged on consecutive days, biodegradation of the hydrogel by enzymes or hydrolysis can be seen at the specific location.

We used Nikon Eclipse Ti2 microscope, to image hydrogels filled with 200 nm diameter fluorescent particles (Bangs Laboratories). In our proof-of-concept research, we used GeltrexTM and collagen type I from rat-tail, with human fibroblasts in 3D. For data analysis and visualization, we developed MuRheo software with Unreal Engine 5. MuRheo uses methods for particle detection and tracking based on optimized nearest neighbour algorithm. When 3D data is used, different levels are processed in parallel for faster computations. Hydrogel composition is visualized with Voronoi diagram based on mean squared displacement (MSD) of particles. From amounts of similarly moving particles, we get a statistical overview of hydrogel microstructure. From 3D mapping we can detect and study more closely areas where particles move freely, viscoelastic areas, and rigid areas, defined by adjustable MSD thresholds. Our data shows that fibroblasts modify their environment for example by degrading material, and pore volume can increase even 20% from total volume during 4-day culture in same locations. We have also observed that pore volumes of Geltrex:tm: samples can be over 10% higher than in collagen 1 samples at d0. The presented approach for 3D microrheology analysis can be used for any transparent hydrogels.

**Keywords**: Hydrogel, micromechanics, methods development, 3D imaging

Tampere University

[Poster presentation 8]

# Superhydrophobic Cell-Repellent Microstructures

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**Abstract**

Controlling cell adhesion is critical for biomedical devices, biosensors, and antifouling surfaces. We investigated how surface wettability and topography, ranging from superhydrophilic to superhydrophobic and including smooth, nanostructured, and micropillar geometries, affect the adhesion of A549 epithelial cells. Our silicon-based superhydrophobic micropillar arrays facilitate stable air retention (plastron) at the solid–liquid interface, which serves as a physical barrier that substantially reduces cell-surface contact.

Notably, a geometry with 5 μm micropillars and a 7.4% solid–liquid contact fraction reduced cell density by ≈83% compared to hydrophobic controls and by ≈95% compared to hydrophilic surfaces after 4 hours, with similar reductions (≈90% and ≈93%) sustained at 24 hours, equating to an approximate 10-fold decrease in adhesion. These micropillar arrays consistently outperformed nanostructures, thanks to air gaps exceeding 10 μm that physically obstruct cell attachment.

We observed a trade-off: low solid-fraction structures showed pronounced short-term repellency but compromised plastron stability over time, leading to delayed fouling. In contrast, higher solid-fraction designs maintained the air layer beyond 72 h but exhibited less initial repellency due to increased contact area. Our findings establish that optimized microscale superhydrophobic textures can deliver time-dependent, highly effective bio-repellency. This work offers a rational, geometry-based strategy for designing non-fouling materials.

Ref: M. Awashra and V. Jokinen, “ Superhydrophobic Cell-Repellent Microstructures: Plastron-Mediated Inhibition of A549 Epithelial Cell Adhesion.” Small (2025): e06022. https://doi.org/10.1002/smll.202506022

**Keywords**: air plastron; biointerfaces; cell adhesion; microstructures; superhydrophobic

Tampere University

[Poster presentation 9]

# Thiol–ene click chemistry enables low-temperature gelation of norbornene-functionalized gelatin and PEG-thiol hydrogel

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**Abstract**

Radical crosslinking of a hydrogel typically requires complex setup or lifted temperatures. The radical crosslinking is initiated using radical initiators which form high numbers of radicals. [1] However, thiol-ene click reaction is a highly efficient reaction requiring much lower radical concentration than typical radical crosslinking. [2] Thiol-ene reaction is also known as being highly specific, bioorthogonal, and it is not affected by for example oxygen molecules in solution liquid. [2] Herein we discovered a dynamic double network hydrogel that crosslinks at room-temperature via very low concentration of ammoniumpersulfate.

In this study gelatin type A was functionalized with norbornene using EDC coupling reaction in aqueous medium. Modification was quantified with 1H-NMR and TNBS assay with UV-spectroscopy being 44%. Low-temperature gelation of a hybrid hydrogel was initiated using a low amount of 0.5 w% of ammoniumpersulfate initiator to utilize thiol-ene click reaction for hydrogel formation. Hydrogel polymer concentration of 5 w% was used in 1:1 conversion of gelatin-norbornene and polyethylene-glycol (PEG)-thiol which were mixed together and pipetted into a mold. After pipetting the hydrogel its gelation began spontaneously at room temperature in 25 to 30 minutes forming a clear and stable hydrogel. Gelation time was determined using rotational rheometry and tube tilt test. With higher temperature or initiator concentration the gelation was accelerated. Viscoelastic properties of the hydrogel were characterized with rotational rheometry showing linear behaviour with storage modulus of 1000 Pa at 1 Hz frequency in lower strains until 16 % strain. A swelling study was conducted in alpha MEM cell culturing medium showing low swelling of the hydrogel.

This thiol-ene click chemistry offers a safe and easy hydrogel gelation mechanism at room temperature with a gelation time window suitable for applications such as cell encapsulation.

[1] Lin et al., 2024
[2] Muñoz et al., 2014

**Keywords**: biomaterial, hydrogel, thiol-ene click chemistry, low-temperature gelation, gelatin-norbornene, PEG-thiol, rheology

Tampere University

[Poster presentation 10]

# Development of porous scaffolds for bone tissue engineering by incorporating polysaccharide gums

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**Abstract**

Introduction: Porous scaffolds are essential in bone tissue engineering, as they mimic the extracellular matrix, facilitate nutrient transport, and support cellular adhesion, proliferation, and migration. Emulsion polymerization offers a promising route to fabricate scaffolds with highly interconnected pores and tunable properties, addressing limitations of conventional methods like electrospinning and freeze drying [1]. This study aims on synthesis and characterization of emulsion polymerised scaffolds fabricated via a medium internal phase emulsion (PolyMIPE) method. The base formulation comprised of poly (ethylene glycol) diacrylate (PEGDA), as a monomer with incorporating two variants of polysaccharide gums, gellan gum (GG) and gum arabic (GA) for comparative analysis to evaluate their contribution in developing the pore morphology and overall scaffold properties.

Materials and Methods: Scaffolds were synthesized using a medium internal phase emulsion (PolyMIPE) method with PEGDA as the base polymer. Two variants were prepared by incorporating GG and GA at three different concentrations (0.1%, 0.5%, and 1%). Degradation was assessed under enzymatic (lysozyme, pH 4), alkaline (NaOH, pH 9), and hydrolytic (PBS, pH 7.4) conditions. Swelling behaviour was evaluated in PBS at pH 4, 7.4, and 9 over six weeks.

Results: The scaffolds exhibit good porosity, as observed through visual examination. PEG Basic scaffolds showed minimal degradation and retained the highest mass over time. GG and GA variants exhibited concentration dependent degradation, with higher concentrations degrading less. Swelling was most pronounced at pH 4, particularly in PEG GG 0.5% and PEG GA 1%. PEG GG 0.1% demonstrated consistent swelling across all pH levels, indicating reduced pH sensitivity. All scaffolds exhibited highly porous and interconnected structures.

Discussion and Conclusions: The incorporation of polysaccharides significantly influenced both degradation and swelling behaviour, suggesting potential for application specific scaffold tuning. PEGDA based PolyMIPE scaffolds incorporated with GG and GA offer a versatile platform for osteochondral tissue regeneration. Their tunable properties and high interconnectivity make them potential material for further biological evaluation and clinical translation and other applications such as sensors. Future work will include advanced characterization techniques such as FTIR to better understand morphological studies.

References:

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**Keywords**: PolyMIPE, Gellan gum, Gum arabic, Porosity, Scaffold

Tampere University

[Poster presentation 11]

# Graphene field-effect transistors as measurement devices for in vitro neuronal activity

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**Abstract**

Novel cell sensor platforms are actively being researched to enable the development of increasingly miniaturized and precise biosensing technologies. Among these, field-effect transistor (FET)-based devices have garnered significant interest due to their ability to scale down to subcellular dimensions. Graphene FETs (GFETs) are particularly promising, owing to graphene's exceptional electrical conductivity, mechanical flexibility, and optical transparency. These properties allow for the fabrication of highly sensitive biosensors capable of capturing subtle electrophysiological signals, thereby enhancing the relevance and resolution of cellular activity measurements.

In this study, the cytocompatibility and functionality of GFETs were evaluated using human induced pluripotent stem cell (hiPSC)-derived cortical and peripheral neurons. Cultures were maintained on GFETA surfaces for four weeks to assess long-term viability, and morphological and electrophysiological maturation of neuronal networks. Cell morphology was monitored through phase contrast imaging during the culture period and by immunocytochemical staining post-culture. The functionality of the GFET platform was assessed by performing electrical recordings at regular intervals, with tetrodotoxin (TTX) planned for use in on-going experiment with peripheral neurons to distinguish biologically derived signals from background noise.

Neurons cultured on GFETA surfaces exhibited healthy morphology and maturing neuronal networks, with uniform attachment of somas and neurites across the platform, including the transistor gates. Long-term viability assays confirmed the biocompatibility of both graphene and SU-8 materials used as insulator. Electrophysiological recordings revealed neuron-like activity with high amplitudes and developmental patterns consistent with network maturation in both type of neuronal cultures, indicating the potential of GFETs for advanced neurophysiological applications.

**Keywords:** Human Pluripotent Stem Cell Derived Neuron, Graphene Field-effect transistor, Sensor Functionality, Cytocompatibility, In Vitro Testing

Tampere University

[Poster presentation 12]

# Software for Multifaceted Analysis of Microelectrode Array Data

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**Abstract**

Multielectrode arrays (MEAs) are widely used for the functional characterization of electrically active cells. Many different MEA platforms and experimental setups are used as well as being developed. Furthermore, there is growing interest in developing physiologically relevant in vitro models. Human induced pluripotent stem cell (hiPSC) based experiments have been a large advancement towards human relevant research. As such, hiPSC derived cortical and peripheral neurons as well as other cell types are now frequently used to study pathologies of the nervous system, and its interaction with other physiological systems with coculture models. Robust data analysis pipelines that aid the investigation of these models are needed. For these reasons, we have been developing a MATLAB-based MEA data analysis pipeline which considers different experimental setups and data types, while producing the crucial statistics of neuronal function. This is accomplished by combining previously validated algorithms for neuronal spike and burst detection into a cohesive computer program. The application also has further high-level analysis capabilities detecting network bursts and detecting network connectivity with a spike- or a burst-based algorithm as needed. In this research, the analyses help elucidate the function of cortical and peripheral neurons and their interplay in a compartmentalized coculture even with other cell types like cardiomyocytes. The developed easy-to-use application is validated with a large dataset of MEA data from hiPSC -derived cortical and peripheral neurons. In this way, we can also discover crucial information on the possible differences of the activity of the neuron types.

**Keywords:** MEA, Software Development, Data Analysis, Signal Processing, Neuron Activity

Tampere University

[Poster presentation 13]

# Driving 3R´s with industrial adoption of Microphysiological Systems as Novel Approach Methodologies in Replacing animal experiments

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**Abstract**

Microphysiological systems (MPS), including organoid and Organ-on-Chip technologies, are complex in vitro test systems that enable improved mimicry of human physiology. MPS gain increasing attention in biomedical research, pharmaceutical industry, and in medical device technology. Widespread adoption of MPS has been struggling with limited expertise and funding, lack of knowledge and awareness, and low regulatory readiness level of the test systems. While several research institutions provide well-established infrastructure and training for animal experimentation, corresponding institutional support for MPS is lacking.

To address this gap, the 3R-Center Tübingen is establishing the first of its kind MPS Core Facility. This facility aims to provide researchers with low-threshold access to MPS and drive the integration of MPS as alternatives or complements to animal models. To demonstrate the concept, three research groups were recruited as pilot users with each project focusing on distinct organ system with established, commercially available Organ-on-Chip. Each project included a planning step involving the selection of appropriate MPS and cell sources suitable for their specific research question. In the implementation phase, non-expert users are trained on MPS, supported in establishing the test system and conducting experiments.

Recently, as part of European Union co-funded initiative Step up the use of novel approach methodologies to replace animal testing, STEP4NAMs, the 3R-Center Tübingen provides targeted support for small and medium-sized companies in adopting NAMs. We coordinate a multi-site pre-validation of Organ-on-Chips with industry partners to build confidence in the technology. Pre-validation studies will include assessment of stability, reproducibility, and predictive capacity of target MPS.

At the 3R-Center Tübingen, we are convinced that in order to replace the use of animals in research and in industry, it is essential to establish new training platforms, provide an easy access to the cutting-edge technology and facilitate validation of MPS with the industry.

**Keywords**: 3R´s, Replacement, new approach methodolodies, industry

[Poster presentation 14]

# Innervation Induces a Distinct Force–Frequency Phenotype in 3D Human Neuromuscular Junction Tissues

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**Abstract**

Neuromuscular junction (NMJ) dysfunction underlies many devastating neuromuscular diseases, highlighting the need for clinically relevant human NMJ models. While embedding motor neurons within 3D skeletal muscle (SkM) models improves biochemical and contractile properties in primary cell-derived models, comparable benefits in induced pluripotent stem cell (iPSC)-derived systems remain unexplored. Here, we present an iPSC-derived 3D NMJ model showing an advanced contractile phenotype not observed in the absence of motor neurons.

We generated SkM-only and NMJ 3D tissues from iPSC-derived myoblasts and motor neurons using the commercially available Mantarray platform in two independent experiments (n=3 per group per experiment). On Day −1, myoblasts and stromal cells were cast into SkM tissues. On Day 11, SkM tissues were combined with iPSC-derived neurospheres via a collagen/matrigel hydrogel to generate NMJs or treated with the hydrogel alone to create SkM-only controls. Contractility was assessed every 2-3 days from Day 17 through Day 31 using electrically stimulated twitch and force–vs-frequency (FVF) protocols.

While twitch and tetanus forces were comparable between groups, NMJ tissues exhibited a distinct FVF plateau above 50 Hz, a phenotype absent from SkM-only controls. By Day 31, NMJs had a 72% reduction in Freq50 (the frequency required to elicit 50% of maximal tetanic force) and a 42% decrease in tetanus-to-twitch ratio. Both differences were statistically significant between groups (t-test; $p<.001$).

This study demonstrates a robust phenotypic difference in the FVF response between SkM-only tissues and NMJs, which has not been previously reported. We hypothesize that this differential FVF response may be due to a shift in myosin isoform and ion channel expression, and our ongoing work will characterize the transcriptomic profiles of SkM-only and NMJ tissues through RNA-seq analysis. This work advances in vitro models of the NMJ for high-throughput therapeutic screening, potency testing, and neuromuscular disease modeling.

**Keywords**: Neuromuscular Junction, Engineered Muscle, Contractility, Contraction Kinetics

Tampere University

[Poster presentation 15]

# Exploring multicellular interactions between glioblastoma and the brain: a 3D open-top microfluidic chip model with integrated neurovascular networks

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**Abstract**

Glioblastoma (GB) is the most common malignant primary brain cancer and has a median patient survival time of only 14 months. A key factor driving this poor outcome is cancer cell infiltration into healthy brain tissue, which makes complete surgical removal impossible. Infiltration also destroys normal brain structures and functions, causing several comorbidities. The interactions of GB cells with both neurons and vasculature in the tumor microenvironment (TME) can promote tumor progression but still require more detailed comprehension. [1] Better understanding these interactions offers a window to study GB infiltration and identify new therapeutic targets.

Here, we established a 3D Brain-GB-on-chip model using a novel open-top microfluidic chip [2] that integrates GB spheres into pre-existing neuronal and vascular networks [3], mimicking the in vivo conditions. The functionality of the neurovascular networks was assessed in the model by perfusing the blood vessels with fluorescent particles and monitoring neuronal activity with calcium imaging. Cellular interactions within the chip-TME were examined with confocal imaging. To validate the model, we assessed the effects of the standard chemotherapy drug temozolomide, demonstrating the ability of the platform to differentiate between safe and harmful drug concentrations in relation to the functionality of the nonmalignant host cells.

The Brain-GB-on-chip model offers valuable insights into neurovascular interactions with GBs and contributes to the understanding of GB progression. The model can be utilized as a novel platform for drug screening and personalized medicine applications, providing a tool for evaluating therapeutic efficacy and safety.

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**Keywords**: Calcium imaging, Cellular interactions, Drug testing, Hydrogel, Perfusion, Tumor microenvironment

Tampere University

[Poster presentation 16]

# NEXT-GENERATION ELECTROPHYSIOLOGY FOR FUNCTIONAL CHARACTERIZATION OF HUMAN NEURAL ORGANOIDS AND ASSEMBLOIDS

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**Abstract**

Three-dimensional neural systems derived from human-induced pluripotent stem cells (hiPSCs), including organoids and assembloids, have emerged as powerful model systems for mimicking crucial aspects of human brain development. These models are increasingly applied to study neurological disorders such as Alzheimer's and Parkinson's disease. To investigate the intricate dynamics of the neuronal networks in these self-organizing in vitro models, methods that allow for real-time and label-free measurement of electrical activity are required. High-density microelectrode arrays (HD-MEAs) offer such an approach, enabling non-invasive, high-content activity recordings from a variety of electrogenic samples, such as neural organoids, assembloids, and retinal or brain tissue explants. Here, we employed the MaxOne and MaxTwo HD-MEA platforms, each incorporating 26,400 electrodes per well, to record extracellular action potentials from a range of 3D neural models. Recordings spanned multiple scales, from network-level dynamics to single-cell and subcellular activity. The ability to flexibly select recording electrodes was shown to increase the reproducibility and statistical power of recorded data. Key parameters, including firing rate, spike amplitude, and network burst profiles, were extracted and analyzed. Furthermore, we applied the AxonTracking Assay to trace action potential propagation along axonal branches, yielding detailed information on axonal architecture and function, including conduction velocity and latency, axonal length, and branching patterns. This breakthrough assay allows for high-resolution investigation of disease models targeting axon initial segments, axonal development and conduction. The capability of targeted electrode selection improves the HD-MEA platforms' data consistency while supporting more comprehensive statistical analyses. Together with the automated data visualization and parameter extraction, these platforms establish a versatile, accessible and user-friendly technology for in-vitro disease modeling and drug testing in both acute and longitudinal studies.

**Keywords**: neural organoids, electrophysiology, HD-MEA, extracellular recording, label-free, non-invasive, functional phenotyping, disease modeling, pharmacology

Tampere University

[Poster presentation 17]

# Characterization of electrophysiological activity in neurospheres using a novel NeuroMPS with integrated micro electrodes

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**Abstract**

The increasing prevalence of neurological disorders calls for advanced human in vitro platforms capable of capturing the cellular and functional mechanisms underlying neurodegeneration and neuroinflammation. Although iPSC-derived organoids have improved structural modeling, systems reliably reproducing electrophysiological function remain limited. To fill this gap, we developed a neuro-microphysiological system (NeuroMPS) that combines iPSC-derived neurospheres with custom microelectrode arrays, enabling non-invasive, high-resolution interrogation of neuronal network dynamics and functional maturation in vitro.

iPSC-derived neurospheres containing neurons and glial cells exhibited synchronous network activity after six weeks of differentiation. To investigate this functionality, we employed the NeuroMPS, which comprises two key elements: a custom microelectrode array with capped electrodes for neurite-level signal acquisition and a glass microwell module that provides structural confinement and optical transparency. This platform enabled time-resolved monitoring of neurosphere electrophysiology while remaining fully compatible with high-resolution imaging modalities. Platform sensitivity was validated with multiple compounds (bicuculline, CNQX, 4-AP) and a neurotoxin (rotenone), with effects assessed via electrophysiological recordings, morphological analyses, and effluent profiling. Notably, alterations in network activity were detected within minutes at the lowest concentrations, whereas corresponding morphological and metabolic changes emerged only at higher doses and later time points. These findings highlight the superior sensitivity of electrophysiological readouts in three-dimensional neuronal cultures, confirming their value for predicting drug responses. The NeuroMPS represents a physiologically relevant, non-invasive, and scalable platform that advances the functional assessment of human neural networks, providing a robust foundation for next-generation in vitro models in neuropharmacology and neurotoxicology.

**Keywords**: Neuromicrophysiological systems, Neurospheres, electrophysiology

Tampere University

[Poster presentation 18]

# Tripartite Human Neuronal Network for Modeling Pathological Propagation and Functional Dynamics in Neurological Disorders

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**Abstract**

Neurological diseases disrupt functional dynamics across interconnected brain regions, and such alterations can often be detected before overt pathological progression. To investigate these spatiotemporal dynamics in vitro, we developed a circular tripartite human neuronal network that enables the study of both pathological propagation and functional changes within defined, interconnected compartments. This network is implemented using a microfluidic device integrated with microelectrode arrays (MEAs), allowing simultaneous monitoring of activity in spatially separated yet synaptically connected neuronal populations [1].

We demonstrate the utility of this tripartite network in two disease models. In the first, Parkinson's disease–related prion-like protein propagation is modeled by exposing α-synuclein (α-s) preformed fibrils (PFFs) to a proximal compartment [2]. Over 13 days, we tracked axonal spread of α-s aggregation to distal compartments alongside evolving alterations in neuronal activity, enabling separation of early- and late-stage functional dynamics not captured in traditional cultures by conventional MEAs. In the second model, seizure-like perturbations were induced with kainic acid (KA) in a single compartment [3]. Here, we developed advanced analysis tools to quantify different levels of synchronization and functional connectivity, revealing distinct network dynamics reflecting the local, intermediate and global impacts of KA-induced disruptions.

In summary, the tripartite neuronal network, coupled with tailored analytical approaches, provides a powerful platform to dissect the progression of neurological disorders. By capturing localized pathological events and their network-wide functional consequences, this system offers new opportunities to study disease mechanisms and to evaluate potential therapeutic strategies.

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**Keywords**: MEMO, organ-on-chip, Parkinson's Disease, Seizures, Neuronal Network Analysis, Tripartite Neuronal Networks, hiPSC

Tampere University

[Poster presentation 19]

# Suppressing neuronal seizure-like activity in vitro

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**Abstract**

Epilepsy is one of the most common neurological diseases globally affecting 60 million people [1]. Anti-epileptic drugs (AEDs) are ineffective in one third of the patients and can cause adverse drug reactions (ADR) [2]. PRIME project aims to establish a software design tool for preventing epileptic seizures [1]

This research uses commercially available human induced pluripotent stem cell (hiPSC, AICS0012 TUBA1B) derived cortical neurons to study glial cell line-derived neurotrophic factor's (GDNF) effects on suppressing seizure-like activity in vitro. The seizure -like activity is induced with kainic acid (KA, 30 µM) and the activity changes are studied with microelectrode array (MEA) measurements. For treatment, ARPE-19 epithelial cells engineered to secrete GDNF are embedded into polyethersulfone (PES) tubes on top of transwell membranes. GDNF secretion is measured from media with ELISA assay. Neuron's ability to response to GDNF is validated with gene expression analysis of GFRα1 express in neurons with qPCR.

The MEA data exhibits robust network bursting activity in cortical neuron networks. KA exposure is performed at three-week time point on neurons on MEA, followed by acute and long-term follow-ups. ARPE-19 tubes are administrated to neurons immediately after KA exposure. KA introduces typical activity alterations in neuronal network however, GDNF does not alleviate these changes. Previously, GDNF was shown to reduce seizures in vivo [3], although the mechanisms of actions are unknown. This highlights the relevance to studying further the GDNF's effects on seizure-like activities in vitro.

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**Keywords**: Epilepsy, Glial cell line-derived factor, Human-derived cortical neurons, Kainic acid, Microelectrode array

Tampere University

[Poster presentation 20]

# Distinct functional properties of human iPSC-derived sympathetic neurons in vitro

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**Abstract**

The peripheral nervous system (PNS) influences the function of nearly all tissues in the body by regulating various physiological processes [1, 2]. When compared to the central nervous system (CNS) neurons, an equivalent understanding of the functional properties of human PNS neurons is lacking in vitro [1, 3]. Generating subtypes of human PNS neurons opens possibilities for Organ-on-Chip (OoC) models with innervation to study both natural organ development and function in disease stages.

Here, we modified an existing differentiation protocol for human induced pluripotent stem cell (hiPSC)-derived sympathetic neurons [1] to enable their use in OoC models. Expression of specific neuronal markers was studied with immunocytochemistry, gene expression with qPCR, and neurotransmitter secretion with ELISA. Functional characterization was performed with multielectrode array (MEA) measurements combined with pharmacological treatments. Neuronal development was followed over time with various functional parameters.

Sympathetic neurons expressed type-specific markers at gene and protein levels. Synaptic structures formed alongside cholinergic acetylcholine receptor expression, consistent with sympathetic neuron identity. Neurons exhibited robust spontaneous activity on MEAs, with distinct electrophysiological features compared with hiPSC-derived cortical neurons, including high peak activity during maturation. Neurons also responded to excitatory and inhibitory pharmacology specific for sympathetic neurons, and secretion of acetylcholine, norepinephrine, and dopamine further confirmed the maturation.

This study provides knowledge on functional properties of human sympathetic neurons and supports the establishment of physiologically relevant innervated in vitro models. Moreover, these sympathetic neurons have already been successfully integrated into multiple 3D models such as bioprinted structures and neuro-cardio, neuro-adipose and neuro-vascular cocultures.

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**Keywords**: human induced pluripotent stem cell, multielectrode array, organ-on-chip, sympathetic neurons

Tampere University

[Poster presentation 21]

# Modelling ischemic stroke in vitro with human induced pluripotent stem cell derived neurons

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**Abstract**

Brain stroke is one of the leading causes of death and disability worldwide. However, the current treatments have limited time window and regeneration potential. During ischemic stroke, neurons in the hypoxic core region are dying, but the ones in penumbra area have potential to recover opening therapeutic opportunities for supporting their survival. Extracellular vesicles (EVs) are potential treatment for stroke, as they can cross the blood-brain-barrier, and carry many molecules related to angio- and neurogenesis (Burnouf et al. 2023).

Here, we differentiated human induced pluripotent stem cells into neurons and used them to study the effects of hypoxia on the neurons. We studied neuronal morphology with immunocytochemical staining and neuronal functionality with microelectrode array. After 24 h in 1% oxygen, neurons had less neuronal activity than controls; both neuronal spiking and bursting were decreased. However, the activity was reverted after three days of reperfusion. Besides studying the effects of hypoxia, we tested human platelet derived EVs as both pre- and post-treatment for in vitro hypoxia. Neuronal uptake of Carboxyfluorescein succinimidyl ester (CFSE)-labeled EVs was confirmed with confocal imaging and analysis with Imaris software. With our study we have optimized in vitro model to study stroke and showed that neurons can uptake platelet derived EVs. Together, our findings are advancing the in vitro research of human brain stroke.

Burnouf, T. et al. Expanding applications of allogeneic platelets, platelet lysates, and platelet extracellular vesicles in cell therapy, regenerative medicine, and targeted drug delivery. J Biomed Sci 30, 79 (2023). https://doi.org/10.1186/s12929-023-00972-w

**Keywords**: extracellular vesicles, hipsc, hypoxia, neuron, stroke

Tampere University

[Poster presentation 22]

# Human-specific model to study foamy microglia in multiple sclerosis

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**Abstract**

Multiple sclerosis (MS) is an inflammatory demyelinating disease of the central nervous system. MS pathology is known to involve microglia – brain-resident immune cells that play a key role in disease progression. Microglia can become overloaded with lipids when clearing damaged myelin, forming "foamy" microglia. The phenotype of these dysfunctional cells and mechanisms by which they may amplify inflammation and contribute to disease progression remain unknown.

The aim of this study is to model the effect of myelin overload on microglia using human induced pluripotent stem cell-derived microglia-like cells (iMGLs). Differentiated iMGLs (n = 4 cell lines) were stimulated with myelin and the cytokine interferon-gamma (IFN-γ) to mimic the inflammatory environment of MS. Microglia phenotype was analyzed using RNA-sequencing, myelin phagocytosis assay, immunocytochemical staining and secretion of inflammatory mediators was studied with multiplex assay.

The results show that all iMGL lines phagocytosed myelin resulting in foamy appearance. Transcriptomic analysis confirmed increased activity in lipid metabolism and foam cell formation. Notably, we found substantial overlap in the gene expression profile between IFN-γ and myelin treatment groups suggesting shared molecular pathways in both inflammation and myelin processing. The myelin-induced expression of inflammatory genes was confirmed by increased levels of inflammatory factors in the culture medium. Overall, iMGLs exposed to myelin exhibit features of foam cells and show an altered inflammatory profile providing in vitro model of MS disease-associated microglia that can be used for disease modeling and drug testing.

**Keywords**: disease modeling, human induced pluripotent stem cells, microglia, myelin, inflammation

Tampere University

[Poster presentation 23]

# Modular Plug and Play Recombinant 3D hydrogel system for studying cancer invasion

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**Abstract**

Background
Cancer invasion is strongly influenced by the dynamic viscoelastic properties and remodeling capacity of the tumor microenvironment, which current in vitro 3D models and hydrogel materials fail to replicate accurately. To address this problem, we developed a patent pending plug and play recombinant hydrogel platform with genetically encoded mechanics, bioactivity, and customizable polymer composition. We further created a library of recombinant human extracellular matrix (ECM) protein adapters to employ in our hydrogel system.

Materials and Methods
Isopeptide adapter proteins and genetically fused isopeptide bioactive ECM crosslinkers were produced via large batch E. coli fermentation and purified via Histag isolation. Dextran (Dex) and hyaluronic acid (HA) polymers were functionalized with isopeptide modules via click chemistry. Hydrogels were formed spontaneously by mixing solutions of isopeptide conjugated polymer with a solution of isopeptide crosslinkers. Rheological properties were assessed using a Discovery HR 2 rheometer under cell culture conditions. HCT116 colorectal carcinoma cells were encapsulated at 1 million cells/mL, and their viability and morphology were monitored via live cell imaging, Calcein AM/ethidium bromide staining, and PRESTO Blue assays.

Results
The hydrogels demonstrated tunable viscoelasticity, gelation kinetics, bioactivity, and high optical transparency, supporting robust cell viability and proliferation. A double-layer 3D dome setup was used to study cancer invasion, comparing HA- and Dex-based gels. In HA gels, HCT116 cells exhibited epithelial-to-mesenchymal transition (EMT)-like behavior, spreading into single cells, breaking down gel barriers and invading throughout the gel. In Dex gels, cells maintained spheroid integrity and did not invade into surrounding gels. These findings suggest that matrix composition significantly influences cancer cell behavior and invasion characteristics.

Conclusion
Our modular hydrogel system allows precise control over mechanical and biochemical cues by altering adapter protein composition, polysaccharide backbones, and genetically encoded crosslinking chemistry. Its recombinant nature offers broad adaptability for cancer research and on chip applications.

**Keywords**: Cancer Invasion, Recombinant Hydrogels, 3D cancer models, plug and play

Tampere University

[Poster presentation 24]

# Cell microenvironment engineered organ-on-chip microphysiological system with 3D spatiotemporal presentation of physical and biochemical cues

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**Abstract**

Stem cells (SCs) are the crucial for developing viable organoids or even completely functional organs. However, for this culture and proliferation of isolated or IPSCs outside the body is indispensable. Combining the principles of microfabrication, microfluidics, cell biology, and tissue engineering we are developing platforms to precisely control the physical and chemical environment of the SCs. We use specifically designed photoactive polymers and advanced soft photolithographic and two-photon polymerization approaches to develop geometries mimicking SC niche. Employing advanced soft lithographic and orthogonal click chemistry approaches, these materials can present extracellular matrix molecules in highly controlled spatiotemporal manner to the cells on 3D matrices. We are employing these geometrically accurate and organized platforms for real time monitoring of intestinal SC cell behaviour such as division, differentiation, metabolism, tissue-specific functions and organogenesis.

**Keywords**: Intestinal stem cells, organ-on-chip, photopolymers, click chemistry, microfabrication, microphysiological systems.

Tampere University

[Poster presentation 25]

# Donor characteristics of hASC-derived adipocytes and oxygen environment affecting steatosis induction in hiPSC-derived hepatocytes

Ilona van der Weij[1], Siiri Suominen[1], Seeri Raatikainen[2], Miia Juntunen[2], Susanna Miettinen[2], Katriina Aalto-Setälä[1]

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**Abstract**

Lipid accumulation in hepatocytes predisposes the liver to metabolic dysfunction-associated steatotic liver disease (MASLD), formerly known as nonalcoholic fatty liver disease (NAFLD). It affects nearly 40% of global adult population with little treatments available and with the possibility to progress into metabolic-dysfunction associated steatohepatitis (MASH), causing cirrhosis, carcinoma and death (1). There's a critical need for more accurate models of MASLD to enable the development of new treatments.

Here, we compare the capability of hASC-derived adipocytes to induce hepatic steatosis based on their donor characteristics (normal weight/obese donor). Hepatocyte-like cells (HLCs) are cultured in both co-cultures with adipose spheroids and as mono-cultures with conditioned media from adipose spheroid cultures. HLCs are differentiated from induced pluripotent stem cells (iPSCs) in both physioxic (5% oxygen) and normoxic (21% oxygen) environments. 5% oxygen mimics the natural oxygen environment of hepatocytes in vivo improving the maturation of iPSC-HLCs in vitro (2). Lipid accumulation, lipid metabolism, oxidative stress, insulin resistance and inflammation in hepatocytes were analyzed by quantified Bodipy fluorescence, quantitative PCR and IL-6 ELISA.

Our preliminary results indicate an increase in lipid accumulation under physioxia compared to normoxia, as demonstrated by Bodipy staining and increased PLIN2 expression. Additionally, in normoxia, co-culture with adipose spheroids from obese donors resulted in higher lipid accumulation compared to co-culture with spheroids from normal weight donors.

This study demonstrates how the obese origin of adipocytes, as well as physioxia, can induce lipid accumulation and influence metabolic routes related to it, making them important factors to consider when developing models of MASLD. In the future we aim to repeat these studies to increase the reliability of results, using additional cell lines, and to further explore the relationship between hASC donors, oxygen environment and hepatic steatosis.

1. Z. Younossi et al. doi: 10.3350/cmh.2024.0431
2. S. Suominen et al. Manuscript in preparation

**Keywords**: Physioxia, MASLD, Hepatic steatosis, Hepatocyte-like cells, Adipose-derived stem cells

Tampere University

[Poster presentation 26]

# Modeling secondary hyperoxaluria in a microphysiological system and testing of microbial metabolites as potential protective agents

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**Abstract**

Hyperoxaluria is a clinical condition characterized by high levels of oxalate in the urine, ultimately resulting in calcium oxalate deposition in the kidneys and, in the more severe forms, systemically. Hyperoxaluria may be either primary (PH), i.e. occurring as a consequence of a genetic defect in the hepatic metabolism of glyoxylate, the precursor of oxalate, or secondary (SH) to other pathologies usually characterized by fat malabsorption and increased oxalate uptake [1]. While the understanding of the pathogenesis of PH has considerably moved forward in the recent years, the variety of pathological conditions underlying SH has hampered therapeutic advances. The possibility to model SH in a microphysiological system would allow to better understand disease pathogenesis and pave the way for novel therapeutic strategies.

In this work, we modeled SH in a commercial microphysiological system (TissUse GmbH, Berlin, Germany) that contains two different circuits, i.e. a surrogate blood circuit and a urine circuit, and interconnects up to five different organs [2]. Human kidney-derived podocytes cell line PODO/TERT256 and human renal proximal tubular epithelial cell line RPTEC/TERT1 (Evercyte, Vienna, Austria) were seeded in the glomerular and tubular compartments, respectively, while Caco2 cells were cultured in a transwell system to mimic the intestinal barrier. Oxalate administration in the intestinal compartment resulted in absorption and excretion in the urine, an effect that was enhanced by treatment with Dextran Sodium Sulfate, a chemical commonly used to model inflammatory bowel disease. On the other hand, selected microbial metabolites could reduce the renal inflammatory response. Further development with the addition of the liver compartment would allow to recapitulate the whole-organism oxalate handling in the perspective of developing therapeutic strategies to modulate oxalate homeostasis.

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**Keywords**: Hyperoxaluria, gut-kidney axis, microbial metabolites

Tampere University

[Poster presentation 27]

# Investigating subtype-specific migration of patient-derived glioma cells in 3D matrix models

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**Abstract**

Glioblastoma (GB) and gliosarcoma (GS) are aggressive brain tumors, with GS considered a rarer subtype that contains both glial and sarcomatous components. Despite clear histological differences, both subtypes are clinically managed in the same way. However, their invasive behavior in physiologically relevant 3D environments remains poorly understood. There is a growing need for in vitro models that reflect such differences and support more subtype-specific research.

This study aims to compare the invasion and migration patterns of patient-derived GB and GS spheroids using a brain-mimicking 3D hydrogel platform.

Spheroids derived from one GB and two GS cell lines were embedded in collagen I hydrogels and monitored over seven days, with six spheroids used per line. After culture, samples were fixed and stained for glioma-associated markers Nestin, β-Tubulin III, and GFAP. Imaging and analysis focused on invasion distances and dispersal patterns within the matrix.

GB spheroids showed rapid invasion, whereas GS spheroids retained compact cores and expanded slowly and in a limited manner. Both subtypes expressed high levels of Nestin and β-Tubulin III, consistent with aggressive tumor phenotypes. GFAP expression was more prominent in GS compared to GB, reinforcing their histological differences.

Although collagen I supports 3D culture, its undefined composition and limited mechanical tunability restrict its utility. Future work will employ Glue4Life, a synthetic hyaluronic-acid-based hydrogel, to improve physiological relevance.

This platform reveals subtype-specific differences in glioma invasion and offers a valuable tool for studying tumor heterogeneity. Future versions will include neurons and vascular cells to better mimic the brain microenvironment.

**Keywords**: Glioblastoma, Gliosarcoma, spheroid, 3D hydrogel, Tumor invasion

Tampere University

[Poster presentation 28]

# Modeling the metastatic ovarian cancer microenvironment in vitro using xeno-free hydrogel and patient-derived matrix

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[4]Tampere University Hospital and Faculty of Medicine and Health Technology, Tampere University.

**Abstract**

Background

High-grade serous ovarian cancer (HGSOC) is the most lethal subtype of epithelial ovarian cancer due to late diagnosis, metastasis and treatment resistance. The omentum, a fatty peritoneal layer that lines the abdominal cavity, is the preferred metastatic site and provides a supportive tumor microenvironment where cancer cells interact with fibroblasts and other components. Understanding the effects and interplay of these interactions is essential to combat omental metastasis and treatment resistance in HGSOC.

Materials and methods

HGSOC cell lines and two hTERT-immortalized human ovarian surface epithelium lines (HOSE1C and HOSE2C) were cultured as a 2D monolayer and under 3D conditions in ultra-low attachment plates or embedded in xeno-free hydrogel VitroGel:registered:. Single-cell RNA sequencing was performed to profile transcriptional changes across conditions. To model metastatic niche exposure, conditioned media from HGSOC cultures was applied to HOSE cells, and co-cultures with long-term drug-resistant (adavosertib, paclitaxel) cells were established to further assess tumor-epithelial interactions. Finally, we used VitroGel and OmGel, a patient-derived matrix from omentum to mimic ovarian metastatic tumors and to evaluate the impact on 3D growth.

Results

Our findings reveal that the two primary HOSE1C/2C cells exhibit distinct stromal transcriptomic and morphological profiles, which can be used to model HGSOC tumor microenvironment. Accordingly, HOSE2C cells that show a fibroblast-like phenotype can promote spheroid condensation and compensate for growth disadvantages of long-term adavosertib-resistant HGSOC, highlighting the microenvironment's role in shaping tumor morphology and growth. Furthermore, in VitroGel models, OmGel increased 3D growth of several HGSOC cell lines but not HOSE1C/2C, supporting xeno-free hydrogels with omentum matrix as clinically relevant in vitro model for HGSOC microenvironment. Future outlooks involve increasing complexity by co-culturing cells in 3D with OmGel and VitroGel.

**Keywords**: Ovarian cancer, HGSOC, metastasis, in vitro model, hydrogel, VitroGel, OmGel, tumor microenvironment

Tampere University

[Poster presentation 29]

# PDMS - epoxy hybrid microfluidic device with compartmentalised hypoxia for neuronal studies

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**Abstract**

Traditionally microfluidic organ-on-a-chip devices have been fabricated by moulding, using moulds fabricated with photolithography. This approach allows fabrication of accurate micro-scale features, but limits complexity and height of the features that can be fabricated. Recent developments in 3D-printing have led research groups to experiment with it to fabricate more complex cell culture devices. Typically, this is limited to fabricating cell culture devices entirely by 3D-printing, or by 3D-printing mould or hybrid mould combining lithography with 3D-printing [1,2]. In this work we present a PDMS – 3D-printed epoxy hybrid device that combines advantages of both materials. The cell layer is composed of a thin PDMS sheet, fabricated using a lithography mould. The layer can be bonded either reversibly or permanently into glass slides or MEAs, and it contains microtunnels used to control cell growth. A 3D-printed medium compartment layer is attached on top of the cell layer. Finally, the system is sealed with 3D-printed cap-structure containing an immersed gas exchange system for controlling the oxygen level in each compartment. The low oxygen diffusion constant of epoxy facilitates highly compartmentalized oxygen control. By 2D oxygen imaging, we demonstrate how the geometry of the immersed oxygen exchange system impacts the efficiency and time constant of the oxygen control. The device has a great potential in modelling ischemic neuronal diseases, such as epilepsy and stroke.

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**Keywords**: Organ-on-a-chip, hypoxia, microfluidics, 3D-printing

Tampere University

[Poster presentation 30]

# Developing a Border Zone-on-chip

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**Abstract**

Cardiovascular diseases are among the leading causes of death worldwide, with most of the fatalities linked to cardiac ischemia, specifically sudden cardiac death caused by reperfusion induced arrhythmias. In cardiac ischemia, restricted blood flow causes localized hypoxia. Ischemia border zone (BZ), a steep oxygen gradient between the healthy and ischemic myocardium, has been recognized as arrhythmia sensitive substrate. BZ is a promising therapeutic target as it comprises both healthy and ischemic cardiomyocytes (CMs). Existing in vitro ischemia research lacks knowledge, and platforms for the study of the cellular and molecular effects of the BZ. This work aims to advance knowledge of the BZ on CM morphology and functionality. In this work, a novel in house developed BZ-on-chip is used to evaluate the effects of an oxygen gradient and reperfusion on CM morphology and functionality. The chip is validated through ratiometric oxygen measurement, and imaging of a live cell hypoxia-responsive fluorescent dye. Immunocytochemistry is used to assess the expression of cardiac specific sarcomere proteins, nuclei size, and connexin 43 localization. Functionality of the CMs is evaluated by phase contrast imaging CM beating, which is analyzed via a novel trajectory analysis. Our results demonstrate formation of an oxygen gradient, reperfusion-induced sarcomere disruption in the region subjected to hypoxia during gradient induction, and differences in beating pattern across the oxygen gradient. We managed to create an oxygen gradient platform to model BZ-on-chip, and a non-perturbative functional analysis, which displayed functional differences in CMs across the oxygen gradient.

**Keywords**: cell and tissue models, cardiac ischemia, oxygen gradient

Tampere University

[Poster presentation 31]

# THERMOPLASTIC ELASTOMER HOT EMBOSSING IN FABRICATION OF MICROFLUIDIC CELL CULTURE DEVICES

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**Abstract**

In recent years, there has been growing interest in exploring elastomer materials beyond polydimethylsiloxane (PDMS) for microfluidic and organ-on-chip devices, as PDMS presents well-known limitations in scalability and chemical compatibility [1,2]. Soft thermoplastic elastomers (sTPE) are a promising option because they combine the elasticity and transparency of PDMS with the production scalability of thermoplastics [3]. In this work, we present a fabrication method for TPE-based microfluidic devices using hot embossing with epoxy molds. We describe a fabrication route comprising (i) casting a PDMS intermediate mold from an SU-8 master, (ii) producing a durable epoxy mold from the PDMS replica, and (iii) plate-to-plate hot embossing of soft TPE sheets to achieve rapid, repeatable replication of microscale features. We thoroughly investigated resin-to-hardener formulations to maximize epoxy-mold lifetime and optimized embossing pressure and temperature to replicate the original microstructures. We evaluated the replicated microfluidic chips by profilometry for dimensional accuracy, optical inspection for defect rates and microstructure replications. We measured contact -angles to verify hydrophilicity after oxygen-plasma treatment and polyvinylpyrrolidone (PVP) coating and compared the results against similar PDMS chips. We found near design microfeature dimensions replication by optical microscope inspection, low defect rates with almost accurate height replication by profilometry analysis.

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**Keywords**: microfluidics, organ-on-chip, soft thermoplastic elastomer, hot embossing, epoxy molds, surface modification, oxygen-plasma, polyvinylpyrrolidone.

Tampere University

[Poster presentation 32]

# Monitoring Early-Stage Osteoarthritis in a Tissue-Engineered In Vitro Model Using Near-Infrared Spectroscopy

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**Abstract**

Osteoarthritis (OA) is a chronic degenerative joint disease affecting approximately 600 million people worldwide. The prevalence of OA is increasing due to an aging and increasingly obese population. Currently, there is no cure for OA due to limited understanding of OA pathophysiology. As animal models fail to accurately replicate the human condition, we aim to develop a human stem cell-based model of early-stage OA using tissue engineering (TE). This approach will yield a platform for personalized OA drug screening.

In our previous work, we developed a near-infrared (NIR) spectroscopy-based setup for monitoring TE constructs without interfering with the culture process [1]. In the current study, we aim to develop spectral data analysis pipelines capable of estimating OA disease state.

In this study, TE constructs were prepared by embedding human bone marrow-derived mesenchymal stem/stromal cells in gellan gum hydrogels. The constructs were cultured for up to 21 days in serum free chondrogenic differentiation medium to promote cartilage formation. After 14 days of culture, OA was induced using pro-inflammatory cytokines (human recombinant TNF-α, IL-6 and IL-1). NIR spectra were obtained every 24h using our custom setup.

Our preliminary analyses show that NIR spectra from constructs treated with pro-inflammatory cytokines and especially its conditioned medium were distinct from control constructs. A support vector machines model classified in situ spectra and conditioned medium with high accuracy as coming from OA-induced or control constructs. We also observed a progressive increase in secreted hyaluronan concentration in conditioned medium after OA was induced.

Overall, our results are promising and would be utilized for the development of a machine learning model for monitoring early-stage OA using NIR spectroscopy.

Reference
1. Karunarathna, H, Sadeesh, N, et al. (2025). ‘’Adaptation of Near Infrared Spectroscopy for in situ Monitoring of Tissue Engineered Cartilage and Culture Media”, Unpublished.

**Keywords**: Osteoarthritis, Tissue Engineering, Near Infrared Spectroscopy

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[Poster presentation 33]

# Comparison of platforms for 3D cocultures of neurons and adipocytes

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**Abstract**

Obesity, a global health issue, has increased the need to study human adipose tissue biology; however, the innervation of human adipose tissue remains understudied. Most existing studies use animal models, which do not fully replicate human innervated adipose tissue. To understand and model the effects of obesity, realistic in vitro models of human adipose tissue are needed. Our aim was to evaluate multiple platforms to establish a 3D neuro-adipose in vitro model using human-derived cells, providing a basis for future studies.

We cocultured human adipose stromal/stem cells (ASCs) or mature human adipocytes (ACs) with human induced pluripotent stem cells-derived peripheral neurons in a 3D environment using three different commercial platforms; static well plate, and two microfluidic open-top chips. A fibrin-collagen type I hydrogel was used in all platforms, and hydrogel shrinkage was monitored during the 21-day culture period. Formation of connections between cell types, adipogenic differentiation of ASCs and the presence of neuronal processes were confirmed using immunocytochemistry and confocal imaging. Cellular functionality was assessed by protein secretion, fatty acid uptake and lipolysis assays.

Established cocultures behaved differently depending on the culture platform, but all supported long-term cultures, the formation of connections and cellular functionality. Differences appeared in hydrogel consumption, shrinkage and fluid flow between static and microfluidic cultures; static culture lacked flow and exhibited most hydrogel shrinkage during culturing. Coculture conditions enhanced fatty acid uptake but diminished lipolysis of ASCs. Adipogenic differentiation of ASCs was robust, whereas mature ACs presented challenges across all platforms, with respect to cell viability, interstitial flow and fitting inside the chips. Since each platform has its own strengths and limitations, the platform should be chosen based on the research question. This study compared potential platforms to establish a novel human cell-based 3D in vitro model for studying adipose tissue innervation and obesity in future.

**Keywords**: 3D, Adipogenesis, Coculture, Innervation, In vitro model, Microphysiological systems

Tampere University

[Poster presentation 34]

# Noninvasive time-lapse Cell Imaging with Quantitative Phase Retrieval via Lensless Microscope

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**Abstract**

High-resolution, long-duration imaging of living cells is crucial for studying dynamic cellular phenomena, including proliferation, migration, and morphological changes. However, traditional microscopy techniques often face limitations in stability, field of view, and system size, particularly when continuous monitoring is required. We present a novel approach employing a compact lensless microscope based on a phase retrieval algorithm tailored for prolonged cell observation in a cell incubator environment.

Our system design eliminates conventional lenses, reducing complexity and enabling a minimal-footprint platform suitable for extended live-cell studies. The device records diffraction patterns of cultured cells over extended durations, which are subsequently reconstructed using an iterative phase retrieval algorithm optimized for low-light, time-lapse acquisition. This combined methodology yields high-contrast, quantitative phase images, facilitating detailed visualization of morphological transitions over time.

We validated the setup by observing LN229 cancer glioblastoma cells for 50 hours in the incubator environment under hypoxic conditions. The results demonstrate that our compact lensless system effectively tracks cell dynamics, achieving spatial and temporal resolutions comparable to conventional optical microscopes while offering enhanced stability and portability.

This work underscores the potential of lensless imaging as a scalable, cost-effective alternative for long-term cell studies, opening possibilities for integrated in situ and organ-on-chip applications. Future work will focus on integrating automated analysis pipelines and expanding imaging modalities to support multi-parameter biological investigations.

Our findings will be of interest to researchers in organ-on-chip technology, long-term cellular monitoring, and quantitative imaging, offering a lightweight and robust tool for dynamic cell biology research.

**Keywords**: microscopy, lensless microscopy, quantitative phase imaging, time-lapse imaging, live-cell imaging, non-invasive cell observation

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# Finnish Organ-on-Chip meeting 2025

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