



RESEARCH  
PROGRAM  
ORGANS AND  
ORGANOIDS  
ON CHIP



Inserm

# Organs and Organoids on Chip

France 2030  
Research Program

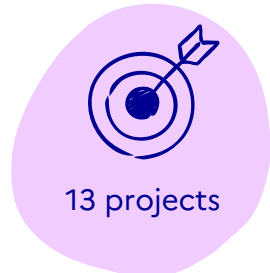
Annual Scientific Meeting  
1 and 2 June  
Institut Pasteur de Lille

anr®



## Organs and Organoids on Chip Research Program (PEPR MED-OOC)

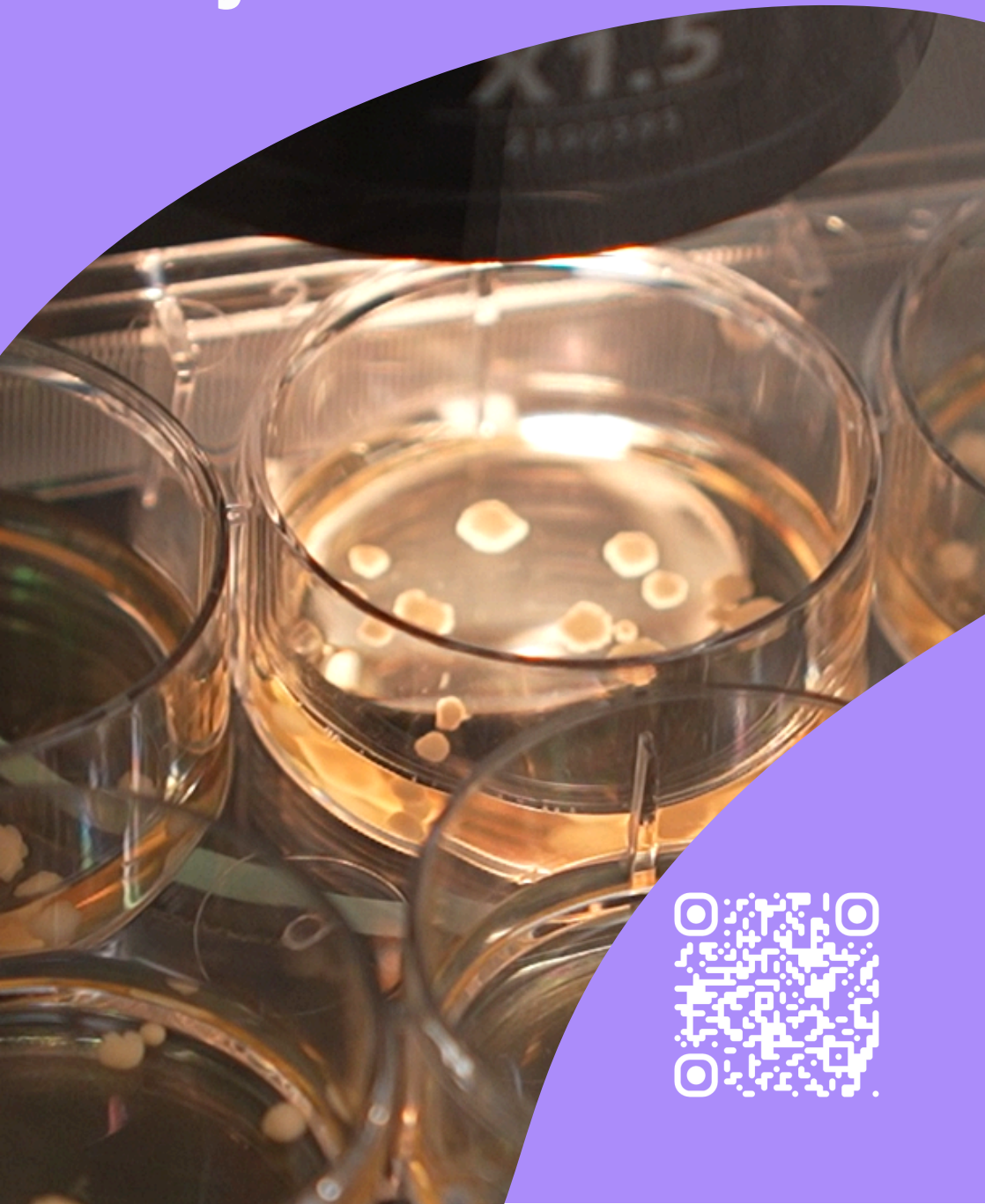
The exploratory research program Organs and organoids on chips (PEPR MED-OOC) aims to deploy a new generation of biological models in France through the development of organs and organoids on chips (O&OoC). The State has entrusted its management to the **CEA**, the **CNRS** and **Inserm**, and the scientific direction to Arnaud Millet (CEA), Stéphanie Descroix (CNRS), and Maxime Mahé (Inserm). MED-OOC is funded by **France 2030** over **6 years** and has a budget of **€48.4 million** operated by the National Research Agency (**ANR**).



MED-OOC aims to achieve scientific and technological breakthroughs via three promising thematic axes:

- **Multi-sensing O&OoCs.** Challenge: instrument O&OoCs with sensors and actuators that monitor several key parameters involved in tissue metabolism but also more “sophisticated” functions.
- **Patient-derived O&OoCs, “clinical twins” of patients for personalized medicine.** Challenge: define and implement the minimum conditions necessary to faithfully imitate the patient’s pathology on-chip.
- **Multifunctional and multi-organ O&OoCs** for new therapies. Challenge: develop these O&OoCs as preclinical models to screen and validate drugs, immuno- and biotherapies.

# Projects





## Technology for microenvironment engineering and imaging for organs-on-a-chip

Current organ-on-chip (OoC) systems lack modular, scalable devices capable of mimicking complex tissue architectures while providing real-time access to cellular and molecular events. EnVie addresses this gap by developing a standardised, modular culture technology that combines microfluidic environmental control with innovative biofabrication methods. Two complementary approaches are pursued: tissue reconstruction (demonstrated on a colon-on-a-chip) and tissue integration (demonstrated by embedding pancreatic ductal adenocarcinoma explants on a chip). The platform integrates a library of ECM-type biomaterials with tuneable mechanical properties, microfluidic perfusion circuits, embedded biosensors, and high-resolution 3D live imaging. Interconnectable EnVie modules enable inter-organ communication studies.



**Audrey Ferrand**

Group Leader I2MC, Inserm  
u1297, Toulouse University,  
**Inserm**



**Laurent Malaquin**

Research Director LAAS-CNRS,  
CNRS UPR 8001, **CNRS**

The ultimate objective is to sustain primary patient-derived tissue cultures over several weeks and screen drugs or microbiota effects, providing a validated technological foundation for personalised medicine applications across the PEPR MED-OoC program.



## MAGIC

### Type 1 Diabetes on Chip

Type 1 diabetes (T1D) affects approximately 10% of the 537 million people living with diabetes worldwide. The current gold-standard treatment, developed by Grenoble University Hospital and reimbursed in France since 2021, is transplantation of pancreatic islets which restores insulin secretion. Yet 40% of patients experience rejection or autoimmune relapse within five years. Monitoring graft function is technically challenging because islets disperse diffusely in the recipient's liver. MAGIC develops Vascularized Islets of Langerhans on a Chip (VLoC): a microfluidic device seeded with a frozen islet sample from each transplanted patient and perfused with the patient's own T cells. Real-time sensors measure insulin secretion as a surrogate of graft viability.



**Fabrice Navarro**  
Department manager  
« Microsystems for life  
interaction » CEA Leti, **CEA**



**Sandrine Lablanche**  
Head of the Endocrinology,  
Diabetology and Nutrition  
Department,  
**CHU Grenoble Alpes**

A low-risk clinical study with at least ten transplanted patients will validate this approach. In parallel, the VLoC will serve as a drug-testing tool for new immunosuppressants and explore overexpression of PD-L1 in iPSC-derived islets as a path toward autologous cell therapy requiring fewer immunosuppressive agents.



## MSY-OOC

### Multi-organ coupling on a chip for metabolic syndrome monitoring

Metabolic-associated fatty liver disease (MAFLD) affects 25% of European adults and can progress to cirrhosis or hepatocellular carcinoma. It is tightly linked to metabolic syndrome (MSy), encompassing type 2 diabetes, obesity, and cardiovascular disease, which affects up to 36% of the European population. Animal models fail to reproduce human hepatic metabolism, and existing liver-on-chips do not fully recapitulate the perfused human liver. MSY-OOC builds on 20 years of consortium expertise in hepatic engineering and microphysiological systems to develop a next-generation liver-on-chip that reproduces cellular interactions, ECM properties, and lipotoxic conditions of MAFLD. A multi-organ demonstrator will couple the liver, adipose tissue, and vascular wall using the patented CCDIM Box platform. Biomarkers validated against patient cohort data will be identified, and innovative therapies evaluated, supporting risk stratification and personalised treatment development.



**Jean-Charles Duclos-Vallée**  
PUPH in gastroenterology and hepatology at the Centre Hépatobiliaire of Hôpital Paul-Brousse APHP, Inserm, Paris Saclay U, **Inserm**



**Eric Leclerc**  
Research Director  
IRL 2820 LIMMS  
CNRS/Tokyo U  
**CNRS**



**Cécile Legallais**  
Research Director  
UMR BMBI CNRS and  
UTC, **CNRS**

# TME ON CHIP

## Tumor-on-a-Chip to Improve Patient Care

Cancer is the leading cause of premature death in France, with approximately 3.8 million people currently living with the disease. Response to treatment, including immunotherapy, is strongly shaped by the tumour microenvironment (TME), yet reliable patient-derived in vitro predictive models are lacking. TME On Chip develops patient-derived Tumour-on-Chip (ToC) devices that faithfully reproduce breast cancer TME complexity, integrating tumour cells, cancer-associated fibroblasts (CAFs), immune cells, and an endothelial vessel within a 3D matrix. The project focuses on triple-negative breast cancer (TNBC) and advanced cancers.



**Stéphanie Descroix**  
Researcher Director  
Cell Physics and Cancer Unit  
(UMR 168) Institut Curie, CNRS,  
PSL U, Sorbonne U, **CNRS**



**Luc Cabel**  
Medical Oncologist,  
**Institut Curie**

Two clinical studies will be conducted at Institut Curie: an observational study (~80 patients per stage) assessing predictive concordance between ToC and patient response, followed by an interventional trial using ToC-based 'tumorigrams' to guide treatment selection, with a target response rate of at least 25% versus 10–15% with conventional chemotherapy.

**AUGMENT****Advanced Gut on a Chip to Decipher Gamma-delta T Cells Mediated Immune Response to a Viral or Fungal Infection**

Conventional gut-on-chip models rely on oversimplified epithelial monolayers that ignore immune and stromal components, limiting their relevance for host-pathogen interaction studies. AUGMENT designs and validates a next-generation gut-on-chip (GoC) platform that incorporates the intestinal stromal microenvironment, including fibroblasts and  $\gamma\delta$  T cells, to investigate host responses to *Candida albicans* and Cytomegalovirus (CMV) infections.  $\gamma\delta$  T cells, abundant in the gut and occupying a unique interface between innate and adaptive immunity, are a particular focus. The chip architecture is optimised for live imaging and integrates photopatterned hydrogels mimicking ECM properties, full-field optical coherence tomography (FF-OCT), and an Incubascope for real-time label-free monitoring of cell dynamics.



**Julie Déchanet-Merville**  
Research Director  
**CNRS**

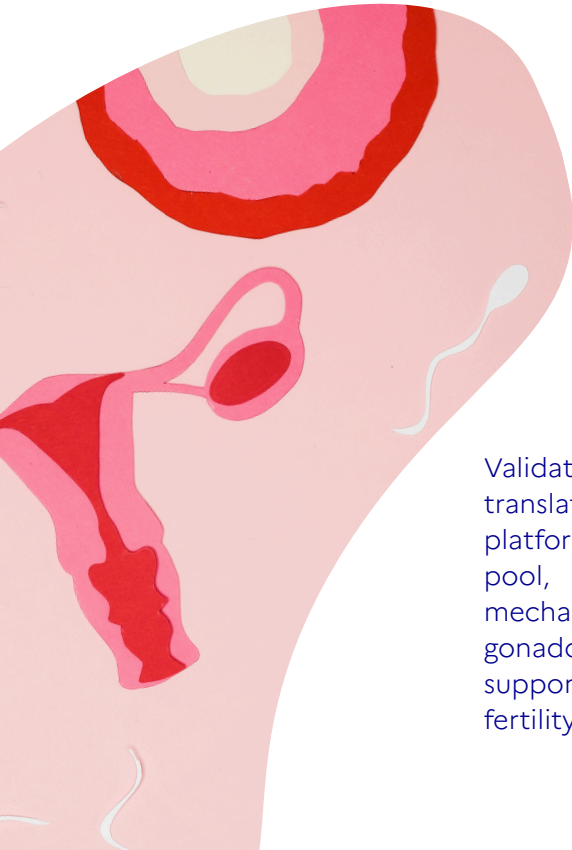
Primary cells from a donor biobank established with Bordeaux University Hospital will be compared against cell lines via multiplex imaging and single-cell RNA sequencing, providing mechanistic insights into immune regulation and identifying new therapeutic targets.



## FERTILOOC

### Testis organ-on-chip: an asset to study spermatogonial stem cell fate and develop biotherapies of infertility

Infertility affects one in six couples worldwide, with male factors responsible for approximately half of cases. For patients undergoing gonadotoxic therapies, particularly prepubertal boys who cannot yet bank sperm, cryopreserved testicular biopsies represent the only fertility-preservation option, yet the molecular mechanisms governing spermatogonial stem cell (SSC) self-renewal and differentiation remain poorly understood. FERTILOOC develops testicular organ-on-chips designed to recapitulate in vitro the microenvironment required for SSC maintenance and induction of spermatogenesis in prepubertal tissue. A key innovation is a parallelised, live-imaging OoC system capable of analysing multiple chips simultaneously under oscillatory fluidic patterns that mimic systemic hormonal regulation.



**Pierre Fouchet**  
Research Director  
**CEA**

Validated first in murine models then translated to human biopsies, the platform will delineate the human SSC pool, reveal niche interaction mechanisms, enable screening of gonadotoxic agents, and ultimately support cell-therapy strategies for fertility preservation in cancer patients.

## HITOC

### Development of a neurocompetent multi segment intestinal OoC based on hiPSC for studying intestinal infectious diseases

Existing intestinal OoC models are restricted to single segments and lack the enteric nervous system (ENS), critically limiting their ability to capture spatially resolved host-pathogen interactions and gut-brain axis communication. HITOC builds a next-generation intestinal tract-on-chip from human induced pluripotent stem cells (hiPSCs) that recapitulates rostrocaudal gut segmentation (duodenum, jejunum, ileum, colon) and integrates a functional ENS derived from vagal neural crest cells. Spatially controlled morphogen gradients guide segment-specific differentiation on chip. Transparent 3D microelectrode arrays (MEAs) enable simultaneous electrophysiological recording of ENS activity, calcium imaging, and impedance-based epithelial barrier monitoring in real time.



**Alexandre Grassart**  
Assistant Professor  
**Inserm**

As a proof of concept, the platform will model infection by human-restricted pathogens (Shigella, Norovirus) known to target distinct gut regions, and will explore how microbiota-derived short-chain fatty acids modulate ENS neuronal circuits, providing new insights into gut-brain communication and neurogastrointestinal disorders.



## MICROCOSM

### A modular multi-organ-on-chip for personalized medicine in chronic obstructive pulmonary disease (COPD)

COPD is the third leading cause of death worldwide, yet treatment personalisation remains limited due to patient heterogeneity and a lack of predictive models. While the recent FDA approval of dupilumab for eosinophilic COPD represents progress, its benefit is restricted to a subset of patients, and identifying responders to biologics targeting epithelial alarmins (TSLP, IL-33) remains a major challenge. In addition, systemic effects of biologics remain to be determined, such as effects on skeletal muscles. Indeed, sarcopenia further increases mortality risk in COPD, highlighting the need for improved therapeutic strategies, but the lack of predictive models further hampers personalized treatment approaches.



**Isabelle Dupin**

Professor

**Université de Bordeaux**

MICROCOSM develops a modular multi-organ-on-chip integrating lung (airway and alveolar) and skeletal muscle cells derived from COPD patient progenitors. This model will allow to better mimic human physiology, and pave the way for personalized immunotherapy in COPD, improving patient outcomes and therapeutic success rates.

**MOHICAN****Microassays Of Immune Cells Functional Analysis for Routine Personalized Clinical Oncology**

Functional immunological assays are essential for guiding immunotherapy but are too complex, slow, and costly for routine clinical use. MOHICAN develops new microfluidic medical devices that integrate subcellular-scale molecular micropatterns to recreate structures mimicking secondary and tertiary lymphoid tissues. These devices enable real-time, single-cell, multiparametric kinetic analysis of T lymphocytes, CAR-T cells, and NK cells, including sorting, positioning, spatiotemporal activation, and detection of surface markers and cytokine secretion. Clinical applications focus on haematological cancers in collaboration with AP-HM and the Paoli-Calmettes Institute: patient stratification for monoclonal antibody therapies, predictive profiling of CAR-T cell products before administration, and post-treatment monitoring.



**Olivier Theodoly**  
Research Director  
**CNRS**

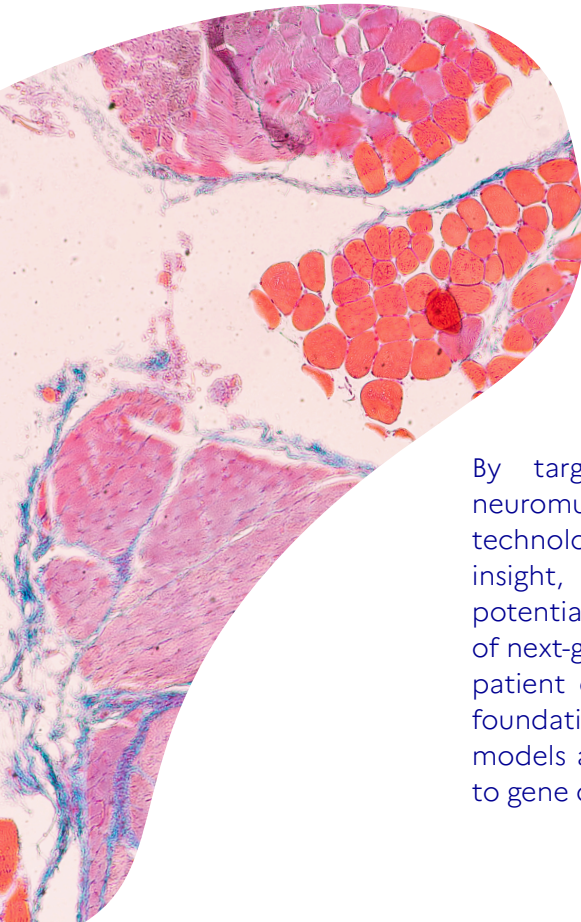


The chip fabrication process will be fully automated for high-throughput production. A complete technological pipeline from blood sampling to multiparametric immune readout will be integrated into routine hospital workflows, constituting a central companion diagnostic device for personalised immunotherapy.

## MUSCLOR-OC

### The Skeletal Muscle Complexity Recapitulated on a Chip to Model Neuromuscular Diseases and Predict Treatment Efficacy

Skeletal muscle is the most abundant tissue in the human body and is critically compromised in neuromuscular disorders (NMDs) such as Duchenne Muscular Dystrophy (DMD) and Spinal Muscular Atrophy (SMA), as well as in sarcopenia and chronic disease. Current in vitro models fail to reproduce native muscle's spatial organisation, cellular complexity, and domain-specific functionality. MUSCLOR-oC engineers a next-generation human skeletal muscle-on-chip that, uniquely, integrates both neuromuscular junctions (NMJs) and myotendinous junctions (MTJs) within a single construct.



**Frédéric Relaix**  
University Professor and  
Hospital Partitioner  
**Inserm**

By targeting key unmet needs in neuromuscular research and integrating technological innovation with logical insight, MUSCLOR-oC holds strong potential to accelerate the development of next-generation therapies and improve patient outcomes. It will also provide a foundation for building clinical twin models and stratifying patient responses to gene or drug therapies.

## NEMOCHIP

### Integrated Human Neuromuscular-on-Chip and Virtual Replica Platform for Diagnosis, Disease Modelling, and Drug Evaluation

Neuromuscular diseases (NMDs) are primarily genetic, often progressive and incurable, affecting millions worldwide. Diagnostic delays are common due to restricted access to patient-derived tissue and the limited human relevance of animal models - particularly at the neuromuscular junction (NMJ), the critical site of nerve-muscle communication. NeMOCHIP creates standardised, patient-derived hPSC-based neuromuscular platforms that incorporate spinal motor neurons, skeletal muscle, and self-organising NMJs in OoC systems enabling real-time non-invasive functional assessment.

A comprehensive NMJ atlas combining RNA-seq, spatial transcriptomics, imaging, and biosensor data is integrated into a virtual replica (digital twin) for personalised diagnostics and treatment planning.

**Cécile Martinat**  
Directrice de  
recherche  
**Inserm**



Translational applications include standardised functional assays for myasthenic syndromes, disease-specific models for myotonic dystrophy type 1 (DM1) and facioscapulohumeral dystrophy (FSHD), and tools for therapeutic screening and patient stratification. All resources - cell lines, atlases, and analytical tools - will be made openly accessible, supporting the French National Plan for Rare Diseases (PNMR4).



**ON-CHIP****Optic Nerve-on-Chip: A 3D iPSC-Based Platform for Vision Repair and Drug Discovery**

Glaucoma - particularly primary open-angle glaucoma (POAG) - causes progressive and irreversible degeneration of retinal ganglion cells (RGCs), whose axons form the optic nerve. No existing OoC model integrates the multiple interacting components of this disease. ON-CHIP develops a human Optic Nerve-on-a-Chip by unidirectionally connecting iPSC-derived retinal organoids to cerebral assembloids through a 3D microfluidic channel that enables RGC axon growth and fasciculation - reconstituting a three-dimensional optic nerve for the first time in vitro. The platform incorporates glial cells, microglia, and inflammatory monocytes to reproduce neuroinflammation, and allows controlled channel deformation to mimic elevated intraocular pressure.



**Xavier  
Guillonnet**  
Chargé de  
recherche  
**Inserm**

Retinal organoids may be genetically modified to introduce patient-specific POAG risk variants. Genetically encoded sensors provide dynamic real-time monitoring of RGC homeostasis. The system will be used for pharmacological screening, gene therapy validation, and evaluation of iPSC-derived cell transplantation strategies to overcome the limited survival and integration of grafted cells in the altered glaucomatous environment.

**SOFTER**

**SOFT Tumour On Chip Mimicking Endometrial Tumour Microenvironment to Predict Therapeutic Efficacy**

Endometrial cancer (EC) is projected to become the third most common cancer and fourth leading cause of cancer deaths in women by 2030. While immunotherapy benefits patients with microsatellite instability (MSI), the majority (75%) of EC cases are microsatellite stable (MSS) and respond poorly. Advanced preclinical models that predict individual treatment responses are urgently needed. SOFTER develops a Soft-Tumour-on-Chip (Soft-ToC) that recapitulates key EC tumour microenvironment (TME) features: hypoxia, tuneable ECM stiffness, endothelialized vascular channels, and resident immune cells. By combining multiplexing, automation readiness, and physiological relevance, the platform aims to meet the reproducibility and scalability standards required for translational research and preclinical drug testing.



**Charlotte Rivière**  
Professeure des Universités  
**Université Claude Bernard Lyon 1**



Predictive performance for standard chemotherapies and immunotherapeutics will be benchmarked against tumoroids and validated through correlation with patient outcome data. Deep Learning approaches will be used to correlate multi-parametric readouts with clinical outcomes and identify robust biomarker signatures, supporting personalised therapeutic decision-making.

# Annual Scientific Meeting



program, abstracts and speakers



## PROGRAM - DAY 1

### Monday 1 June

9:30	Welcome coffee
10:00	Opening words from MED-OOC's co-directors - Arnaud Millet (CEA), Stéphanie Descroix (CNRS), Maxime Mahé (Inserm)
10:05	<b>Madalena Cipriano</b> (University of Tuebingen) Drug and Energy Metabolism in Cardiometabolic Organ-on-Chip Models: Combining Functional Readouts with Non-Invasive Online Sensing
10:35	<b>Adrien Bottacci</b> (Aix-Marseille Université) French Regulatory Procedures for Cell Procurement: Where We Stand and Where We Are Headed
11:05	<b>Anna Labernadie</b> (Valencia Biomedical Research Foundation) Micro Immune Response On-chip (MIRO): a model of tumour-stroma interface for immunotherapy testing
11:35	<b>Short talks</b> - Lucas Chassatte (Institut Curie)   Stephen Adonai Leon Icaza (University of Cambridge)
12:05	Lunch break
13:30	<b>Franck Lebrin</b> (Leiden University Medical Center) Modeling Hereditary Hemorrhagic Telangiectasia using stem cell-based systems: challenges and opportunities
14:00	<b>Eugenio Martinelli</b> (University of Rome) Real-Time Multiplexed Biosensing in Organ-on-Chip Platforms
14:30	<b>Olivier Guenat</b> (University of Bern) Microengineered Lung Parenchyma: Alveolar and Vascular-on-Chip Models
15:00	<b>Alessandro Furlan</b> (University of Lille) Investigating DMG microenvironment importance in response to therapies, with DMG-on-chips
15:30	<b>Short talks</b> - Céline Cougoule (CNRS, Université de Toulouse)   Isy Petit (Inserm, Université de Limoges)
16:00	Coffee & Posters
17:00	AUGMENT - Julie Dechanet-Merville
17:15	FERTILOoC - Pierre Fouchet
17:30	HITOC - Alexandre Grassart
17:45	MICROCOSM - Isabelle Dupin
18:00	MOHICAN - Olivier Théodoly
18:30	Cocktail

**Session 1**  
Clinical twins for a personalized medicine

Presentation of the selected projects from the ANR call

Tuesday 2 June

8:30	Welcome coffee	
9:00	<b>Kristina Haase</b> (European Molecular Biology Laboratory) Engineering Vascular Models for Human-Relevant Translational Research	<b>Session 2</b> Multi-functional & multi-organ O&OoC
9:30	<b>Danijela Vignjevic</b> (Institut Curie) Organoid models to study colorectal cancer progression and therapy resistance	
10:00	<b>Short talks</b> - Emmanuelle Rota Graziosi (Ecole Normale Supérieure, PSL)   Elise Delannoy (Institut Pasteur de Lille)	
10:30	Coffee & Posters	
11:30	MUSCLOR-oC - Frédéric Relaix	Presentation of the selected projects from the ANR call
11:45	NeMOCHIP - Cécile Martinat	
12:00	ON-CHIP - Xavier Guillonneau	
12:15	SOFTER - Charlotte Rivière	
12:30	Lunch break	
14:00	<b>Lourdes Basabe Desmots</b> (Lascary Research Center) CellStudio: A Modular 2.3D Biosensing Platform for Spatially Resolved Secretomics and Solid-Phase Stimulation	<b>Session 3</b> Sensing and actuating O&OoC
14:30	<b>Róisín Owens</b> (University of Cambridge) In vitro models of the microbiome-gut-brain axis with integrated monitoring	
15:00	Closing remarks and awards ceremony for best poster and best short talk	
15:15	Mandatory for MED-OOC members - in french Mots sur le fonctionnement du PEPR	
15:30	End of the event	



### Madalena Cipriano

Madalena Cipriano is Group Leader for Drug and Energy Metabolism at  $\mu$ OrganoLab. She earned her PharmD and later her PhD in Pharmacy (Toxicology) from the Universidade de Lisboa, where her research focused on 3D hepatic models for drug toxicology, including a research stay at BCRT, Charité Berlin. She subsequently worked at EURL-ECVAM, contributing to European guidance on the use of in vitro methods for chemical classification and labelling. Since joining the Organ-on-a-Chip field in 2018, her work has centred on advancing OoC models for pharmaceutical research, from ocular systems to cardiometabolic platforms. Her current research focuses on developing and applying liver-, pancreas-, heart-, and white adipose tissue-chip models, including multi-organ combinations, for drug testing, insulin production, and metabolic response studies using advanced sensing technologies.

### Drug and Energy Metabolism in Cardiometabolic Organ-on-Chip Models: Combining Functional Readouts with Non-Invasive Online Sensing

Organ-on-Chip (OoC) systems are emerging as powerful tools for safety assessment in cardiometabolic drug development. Over the last decade, we developed a panel of tailored OoC models that combine high tissue density, vasculature-like perfusion, and integrated non-invasive sensing. These platforms enable functional and metabolic characterization of organ-specific responses under controlled culture conditions. Across the different systems (e.g. liver, heart, pancreas, white adipose tissue), optical oxygen sensing supports continuous monitoring of tissue activity and treatment effects, while platform-specific readouts capture key physiological functions. Together, these cardiometabolic OoC models provide a versatile approach for mechanistic safety studies and long-term evaluation of therapeutic effects.



### Adrien Bottacci

Adrien Bottacci is a PhD candidate in public law from Aix-Marseille Université, France (UMR 7268 ADES, CDSA Health Law Centre and UMR 7318 DICE CERIC International, Comparative and European Laws). His research focuses on the regulation of stem cell research and more particularly on ethically sensitive models such as neural organoids, stem cell-based embryo models and chimeras. He is part of the French ANR project "Organact" which takes an interdisciplinary approach combining sociology, anthropology and law to examine human organoids and the issues raised by their production, circulation and use.

### French Regulatory Procedures for Cell Procurement: Where We Stand and Where We Are Headed

This talk aims to present and clarify France's complex regulatory framework for human cell procurement underpinning research into organoids and organ-on-chip technologies. Several legal frameworks might apply and overlap depending on the source of the cells, the purpose of their use and the data associated with them. While France's regulatory landscape is complex, it is grounded in a strong ethical stance. Yet, various stakeholders call for clearer regulations to strike a better balance between ethics and the competitiveness of the research environment. As we approach the new revision of the Bioethics Laws, this talk also invites interested stakeholders to partake in public and policy discussions to share their perspectives on how regulations could evolve.



#### Anna Labernadie

Dr. Anna Labernadie heads the Cell Behaviour and Tissue Bioengineering group at the Príncipe Felipe Research Center (CIPF) in Valencia. Her work centers on mechano-oncology, with a particular focus on how mechanosensing shapes tumor dissemination and modulates immune responses in cancer. To investigate these processes, her team integrates biophysical methods, cellular co-culture systems, and organ-on-chip technologies, aiming to replicate the physical constraints, cell-cell interactions, and spatial organization characteristic of tissues and tumors. She earned her PhD in Cell Biology from the University of Toulouse in 2012, and then conducted postdoctoral research in the laboratory of Xavier Trepats at IBEC (Barcelona), where she studied the physical interplay between tumor cells and stromal fibroblasts during cancer progression. In 2022, she was awarded a Ramón y Cajal Fellowship, enabling her to establish her independent research group at the CIPF.

### Micro Immune Response On-chip (MIRO): a model of tumour-stroma interface for immunotherapy testing

Immunotherapies represent a major advance in cancer treatment, yet only 20–40% of patients derive benefit. To improve treatment prediction, models that accurately reflect tumour architecture and the interplay between cancer cells and the microenvironment are essential. In this study, we introduce Micro Immune Response On-chip (MIRO), an *ex vivo* platform that generates 3D barriers built by cancer-associated fibroblasts (CAFs) and their secreted extracellular matrix, which enclose cancer cell clusters. We applied MIRO to study resistance to antibody-dependent cellular cytotoxicity (ADCC) under targeted therapies. Our results indicate that stromal barriers are associated with immune exclusion and reduced ADCC efficacy. We further show that IL2 stimulation enhances immune cell velocity, counteracting stromal immunosuppression. This restoration of immune activity demonstrates the ability of IL2 to overcome stroma-mediated resistance. Overall, MIRO emerges as a translational platform for drug testing and for evaluating novel immunotherapeutic strategies.



### Franck Lebrin

Franck Lebrin, PhD, is a vascular biologist and Director of an international Inserm JointLab at Leiden University Medical Center (LUMC, Department of Internal Medicine), and a member of Inserm Abroad. His research focuses on microvascular disorders, particularly Hereditary Hemorrhagic Telangiectasia (HHT), with an emphasis on endothelial-pericyte interactions. He develops advanced human hiPSC- and mouse-based models, combined with ultrasound imaging, to investigate disease mechanisms and support translational research. His work has contributed to the development of AKT inhibitors currently in Phase I and III clinical trials, as well as small molecules promoting vessel stability and integrity for HHT and pericyte-related diseases affecting the brain, eye, and kidney. He is Vice-Chair of Cure HHT International and founder of RougeTX, a spin-off developing pericyte-focused therapies.

### Modeling Hereditary Hemorrhagic Telangiectasia using stem cell-based systems: challenges and opportunities

Hereditary Hemorrhagic Telangiectasia (HHT) is a genetic vascular disorder characterized by marked inter- and intra-familial variability, shaped by genetic modifiers. hiPSCs provide a powerful platform to capture this diversity in patient-specific models, although identifying reproducible disease phenotypes remains difficult. A key objective is to define phenotypes linked to relevant endothelial cell states. The choice of experimental system, 2D, 3D, or microfluidic, profoundly impacts signaling and functional readouts, highlighting the role of endothelial cell states and their environment. HHT has attracted growing interest from biotech and pharmaceutical sectors, underscoring the need to improve translational strategies. In this context, aligning data across species under comparable conditions offers a valuable bridge. This integration will help connect in vitro results to in vivo outcomes and improve the predictive value of preclinical models.



### Eugenio Martinelli

Eugenio Martinelli is a Full Professor at the University of Rome Tor Vergata, specializing in electronic engineering and artificial olfaction. His research spans sensor systems, machine learning, lab-on-chip, and organ-on-chip technologies for medical, industrial, and space applications. He has authored over 280 publications, with more than 8000 citations and an H-index of 45, along with seven patents. He has led major national and international projects, including experiments aboard the International Space Station (IENOS, STS-134 mission).

He has coordinated and contributed to EU, NIH, and Italian-funded projects on diagnostics, sensing systems, and biomedical platforms. He is currently leader of the BEE group and co-director of the interdisciplinary center on organ-on-chip and lab-on-chip technologies. He has received prestigious awards, including the Eurosensors Fellowship Award and Vebleo Fellow Award. He actively collaborates with leading international institutions across Europe and the USA in sensing and biomedical engineering. He is founder and vice-president of SIOOC, Italian Society of Organ on chip. He serves as editor, reviewer, and scientific committee member in major journals and conferences in sensors and computational intelligence.

### Real-Time Multiplexed Biosensing in Organ-on-Chip Platforms

Organ-on-chip technologies have emerged as powerful platforms for replicating key aspects of human physiology in controlled microscale environments. While these systems enable increasingly sophisticated biological models, a fundamental bottleneck remains: how to effectively access and measure all the information they generate. In particular, integrating sensing capabilities without compromising the biological and structural integrity of the device, and enabling real-time, multiplexed measurements, are still open challenges.

In this talk, we discuss general strategies for incorporating sensing capabilities into organ-on-chip devices, with an emphasis on scalable and minimally invasive approaches. We also highlight the role of data-driven methods in handling complex, multi-signal outputs. Advancing these aspects is essential for developing more informative and autonomous platforms, with broad implications for biological research, drug development, and disease modeling.



### Olivier Guenat

Olivier T. Guenat is Professor in Biomedical Engineering at the University of Bern in Switzerland and Head of the Organs-on-Chip Technologies Group at the ARTORG Center. He is associated with the Pulmonary Medicine and the Thoracic Surgery Divisions of the University Hospital of Bern. His research focuses on the development of organs-on-chip, in particular lung-on-chip models that mimic the healthy and diseased in-vivo cellular microenvironments of the lung parenchyma. Prior to his position at the University of Bern, he worked at the Swiss Centre for Electronics and Microelectronics (CSEM), was an assistant professor at Ecole Polytechnique de Montréal (QC, Canada), and did postdoctoral work at Harvard Medical School in Boston and at the University of Neuchâtel in Switzerland. He is the founder of AlveoliX and co-founder of Vitronco, two biotech start-ups that spun out of his lab.

### Microengineered Lung Parenchyma: Alveolar and Vascular-on-Chip Models

Our group has spent 15 years developing lung-on-chip systems that closely mimic human lung parenchyma. Early breathing-motion platforms, now commercialized by AlveoliX, revealed how airborne toxicants synergize with mechanical strain and the air-liquid interface to disrupt the alveolar barrier. These models evolved into second-generation chips with collagen-elastin membranes shaped into alveoli-sized compartments. An idiopathic pulmonary fibrosis model showed how cyclic strain drives tissue remodeling and alters responses to nintedanib. We also developed vasculature-on-chip systems formed by vasculogenesis to study how mechanical cues, drugs, and circulating cancer cell phenotypes influence microvascular function and extravasation. Together, these integrated alveolar-vascular platforms enable physiologically relevant studies of lung physiology, disease, and therapeutic responses.



#### Alessandro Furlan

Alessandro Furlan is an Assistant Professor at the University of Lille. Passionate about the tumour microenvironment and its importance in tumour progression and resistance to therapies, he has investigated this concept in several cancer models throughout his career. To this end, he has developed various 3D (co-)culture systems to recapitulate the adequate matrix architecture and cell interactions found in tumour ecosystems, and has used fluorescence microscopy tools to decipher the cellular and molecular mechanisms at play. He has ultimately focused his research on paediatric Diffuse Midline Gliomas, implementing interdisciplinary approaches to tackle this fatal disease.

### Investigating DMG microenvironment importance in response to therapies, with DMG-on-chips

Despite significant efforts, Diffuse Midline Gliomas (DMGs) remain incurable. By integrating elements of the biophysical tumor microenvironment known to regulate the response to therapies, we developed a new preclinical tool to better evaluate the efficacy of antitumoral strategies. This novel DMG-on-Chip (DoC) is engineered with a 3D dense tumor disk embedded in an extracellular matrix, accessible for real-time monitoring using wide-field phase contrast or confocal fluorescence microscopy. By driving the oxygen supply within the chip in a radial manner, a hypoxia gradient is established that can be associated with changes in DMG cell phenotype and proliferation.

Finally, we used this DoC to evidence a spatial heterogeneity of response of DMG cell lines and patient-derived 3D cultures to radiotherapy. This proof-of-concept validates this new tool as an interesting healthcare solution to understand how cell responses are modulated by biophysical or biochemical cues in the tumor microenvironment.



### Kristina Haase

Kristina Haase is a bioengineer and Group Leader at EMBL Barcelona, where she leads an interdisciplinary team developing vascularized human organ-on-chip models for biomedical research and drug discovery. Her group leverages advanced tissue engineering approaches to uncover how microvessel dysfunction drives disease. Her work focuses on tissue-specific models including placenta, lung, and cardiovascular systems, with an emphasis on sex differences and translational applications in drug development.

## Engineering Vascular Models for Human-Relevant Translational Research

The vascular system plays a central, yet often underrepresented, role in shaping tissue function, disease progression, and drug response. This talk will highlight several of our human vascularized models - the placenta, heart, and lung - which are used to study inflammation-driven tissue responses in a controlled environment. In our cardiac microvascular model, we show that sex hormones modulate endothelial dysfunction, revealing protective effects relevant to cardiovascular disease. In a lung infection model, we capture key features of inflammation induced by the cytokine storm and viral exposure and explore potential intervention strategies. And finally, a placenta-on-chip enables assessment of drug transport and toxicity. Across these systems, we identify how tissue-specific vasculature regulates barrier function in response to exposures (infection, inflammation, drugs). These models collectively demonstrate the value of engineered vasculature for linking human biology with translational applications in drug development and disease modeling.



### Danijela Vignjevic

Danijela Matic Vignjevic was trained as a molecular biologist at the University of Belgrade, Serbia and the University of Wisconsin-Madison, US. She did her PhD in cell biology, working on the actin cytoskeleton during cell migration at Northwestern University, Chicago, US. She then did a post-doc at Institut Curie, working on mouse models for colon cancer metastasis as an HFSP fellow and later as an Inserm researcher. She started her independent team at Institut Curie in 2013 when she got interested in how epithelial cells interact with their microenvironment in homeostasis, wound repair, and cancer invasion. Her research strategy combines cell biology and mechanobiology techniques with live-cell imaging using different model systems such as 2D and 3D in vitro cell cultures; tissue slices cultured ex vivo; and different transgenic mouse models. She is a recipient of ERC starting and consolidator grants. She is currently Research director (DR1) at Inserm, team leader and deputy director of UMR144/CNRS department at Institut Curie

### Organoid models to study colorectal cancer progression and therapy resistance

Colorectal cancer progression is shaped by both intrinsic tumor dynamics and interactions with the tumor microenvironment. Using organoid-based and bioengineered models, we investigate how mechanical and cellular cues regulate tumor heterogeneity, invasion, and therapy response. Mouse tumor organoid monolayers reveal that tumors can spontaneously organize distinct cell states through intrinsic mechanochemical feedback: growth-induced crowding generates central compression that promotes stemness and ultimately leads to mitotic arrest and apoptotic core formation. In parallel, a 3D co-culture system shows that cancer-associated fibroblasts (CAFs) compress tumor spheroids through Myosin-II-dependent contractility, promoting chemotherapy resistance. Finally, using a colon-on-chip model, we demonstrate that physiological mechanical stimuli such as peristaltic stretching cooperate with CAFs to stimulate cancer cell invasion. Together, these systems reveal how mechanical forces emerging from tumor growth, stromal contractility, and tissue-level dynamics shape colorectal cancer plasticity and progression.



### Lourdes Basabe Desmots

Lourdes Basabe is an Ikerbasque Research Professor and the founding Director of the Microfluidics & BIOMICs Cluster at the University of the Basque Country (UPV/EHU). She earned her PhD at the MESA+ Institute (Twente, The Netherlands) and spent six years at Dublin City University (Ireland) developing microsystems for biomedical diagnostics. Her early career was recognized with the prestigious UK & Ireland L'OREAL-UNESCO Women in Science Fellowship. Nowadays her research focuses on multidisciplinary systems for chemical and cellular monitoring, integrating microfluidics, functional materials, and surface engineering. She has published over 90 peer-reviewed articles (90% in Q1) and led more than 20 national and EU-funded projects. Very involved in technology transfer, she holds 20 patent applications and has contributed to build up startups to commercialize microfluidics solutions. Prof. Basabe holds international roles as Chair of MicroTAS 2026 and Member of Board of Directors of the Chemical and Biological Microsystems Society (CBMS). She is also Founder and Secretary of the Spanish Society of Organ-on-Chip (SESMOOC).

### CellStudio: A Modular 2.3D Biosensing Platform for Spatially Resolved Secretomics and Solid-Phase Stimulation

Traditional cell culture methods lack spatial and temporal precision to monitor cell secretions, relying on bulk analyses that poorly mimic tissue interactions. To address this, we present CellStudio, a modular biosensing platform integrating high-resolution protein monitoring within the culture environment. It combines 2D protein patterns with a 3D microbead network to organize hundreds of cell clusters, each surrounded by functionalized beads acting as carriers and biosensors.

CellStudio introduces a “present-and-measure” approach where microbeads deliver stimuli (e.g., FGF-2) while capturing responses in situ. Localized FGF-2 stimulation of h-HF-MSCs showed increased VEGF secretion by 735%, demonstrating the platform’s ability to uncover complex cellular interactions and its potential in regenerative medicine, drug discovery, and high-resolution secretomics.



### Róisín M. Owens

Róisín M. Owens is Professor of Bioelectronics at the Dept. of Chemical Engineering and Biotechnology in the University of Cambridge and a Fellow of Newnham College. She received her BA in Natural Sciences at Trinity College Dublin, and her PhD in Biochemistry and Molecular Biology at Southampton University. She carried out two postdoc fellowships at Cornell University, on host-pathogen interactions. She is a 2019 laureate of the Suffrage Science award and the 2024 AstraZeneca Biochemical Society Award. She has been awarded ERC Starting, Consolidator and Advanced awards. She serves as Scientific Editor for Materials Horizons (RSC). She is author of 150+ publications and 3 patents and her work has been cited more than 13000 times.

### **In vitro models of the microbiome-gut-brain axis with integrated monitoring**

The microbiome-gut-brain axis (MGBA), has emerged as an incredibly important, but complex, part of human physiology. Dysregulation or disruption of the MGBA is implicated in a host of pathologies that affect brain and gut (e.g. Autism Spectrum disorder, Crohn’s disease) but also whole body disorders where inflammation and metabolism are affected (e.g. diabetes). Physiologically relevant in vitro human models, as well as advanced tools to study in vivo animal models, are urgently required to elucidate mechanisms in MGBA. Until recently, the majority of studies that seek to explore the mechanisms underlying the microbiome-gut-brain axis relied almost exclusively on animal models. Despite the great progress made with these models, various limitations, including ethical considerations and interspecies differences that limit the translatability of data to human systems, pushed researchers to seek for alternatives. In this talk I’ll discuss a new generation of electronic tools, based on conducting polymers, for understanding the gut-brain-microbiome axis. First, I’ll discuss our progress towards generating a complete platform of the human microbiota-gut-brain axis with integrated monitoring and sensing capabilities. Bringing together principles of materials science, tissue engineering, 3D cell biology and bioelectronics, we are building advanced models of the GI, with integrated real-time and label-free electronic monitoring, aiming to elucidate the role of microbiota in the gut-brain axis communication. Recent integration of patient derived microbiome and gut biopsy derived epithelial organoids makes the models more human relevant. Second, I’ll discuss conformable electronic devices we’ve developed for both ex-situ measurements of GI tissue from rats in organ baths as well as validation in vivo experiments in live rats. Integration of fluidics is an ongoing concern. Our device platforms ultimately aim to allow highly sensitive monitoring of impedance of the tissue (as an indicator of gut health) as well as the enteric nervous system.

Lucas Chassatte (CNRS - Institut Curie)

### **Developing a 3D dynamic colorectal cancer-on-chip to decipher the role of mechanical forces in tumor growth and invasion**

Colorectal cancer is the second leading cause of cancer mortality worldwide, largely due to metastatic dissemination. Cancer invasion is modulated by stromal cells such as cancer-associated fibroblasts (CAFs), which actively generate and transmit mechanical forces. In the colon, cancer cells are additionally exposed to peristalsis-driven mechanical stretching, yet the contribution of this physiological force to cancer progression and invasion remains poorly understood.

In my PhD project, I developed a colorectal cancer-on-chip model that recapitulates colonic crypt architecture, incorporates colorectal cancer cells and CAFs, and enables precise control of mechanical stress mimicking peristalsis. Using this system, we showed that cyclic stretching significantly enhances cancer cell invasion and that this effect depends strictly on the presence of CAFs. Increased invasion is not driven by cancer cell overcrowding or direct CAF-cancer cell contact, suggesting a role for paracrine signaling and extracellular matrix remodeling.

Stephen Adonai, Leon Icaza (University of Cambridge)

### **Organoid Models for Assessment of Novel Therapeutics Against Bk Polyomavirus**

BK polyomavirus (BKPyV) poses a significant threat to kidney transplant recipients, leading to graft loss in approximately 50% of polyomavirus-associated nephropathy cases. With no effective antivirals available, there is an urgent need for host-directed strategies.

We established advanced 3D human kidney organoid models to study BKPyV infection, including adult stem cell-derived kidney tubuloids (KTs) and KT<sub>s</sub>-on-a-chip, which recapitulate renal epithelial complexity. BKPyV efficiently infected and spread across nephron epithelial cells in both systems.

Using a genome-wide CRISPR/Cas9 knockout screen in renal proximal tubule epithelial cells, we identified Methionine Adenosyltransferase 2A (MAT2A) as a potential proviral factor. Pharmacological inhibition of MAT2A significantly reduced BKPyV replication in our 3D models, delaying early (LTag) and late (VP1) viral protein expression and impairing viral production. Moreover, combining MAT2A inhibitors with the CFTR inhibitor glibenclamide, which blocks viral entry, showed a synergistic antiviral effect.

Together, our findings identify MAT2A as a promising host target for therapeutic intervention against BKPyV.

Céline Cougoule (CNRS - Université de Toulouse)

### **Development of a Human Lung-Liver-Lymph Node on a Chip Platform for Tuberculosis Modelling & Vaccine Evaluation**

Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (Mtb), remains one of the leading infectious causes of death worldwide. The significant limitations of existing animal models for TB vaccine pre-clinical testing prompt us to develop a TB modelling platform. Here, we describe an in vitro autologous human iPSC-derived lung-liver-lymph node co-culture system on a chip, containing circulating PBMC, based on the HUMIMIC chip technology.

The lung compartment, the primary site of Mtb infection, replicated critical protective mechanisms, such as an intact barrier function and pulmonary surfactant production. Alveolar macrophage-like cells, the cellular niche for Mtb replication, showed abilities to phagocytose Mtb, and support its proliferation, associated with an elevated pro-inflammatory response. The chips were benchmarked with the reference BCG vaccine and demonstrated an effective adaptive immune response in the lymph node and lung compartments.

By mimicking key elements of TB infection and immune response, this cutting-edge human co-culture system offers a promising platform for pre-clinical acceleration of TB vaccine candidate development towards clinical testing.

Isy Petit (Université de Limoges)

### **Dissecting liver–kidney crosstalk in drug disposition using a dual organ-on-chip**

Drug-induced effects often extend beyond their primary site of action, leading to systemic responses that are difficult to predict. Increasing evidence identifies circulating endogenous metabolites as key mediators of inter-organ communication through the activation of xenobiotic-sensitive transcription factors, that regulate drug transporters and metabolizing enzymes.

To investigate these mechanisms, we developed a dual organ-on-chip platform integrating human renal proximal tubule and hepatic models under continuous microfluidic flow. The renal compartment recapitulates key physiological features, including fluid shear stress influencing epithelial polarization and transporter activity, while the hepatic model supports drug metabolism. Their coupling enables bidirectional metabolite exchange, mimicking liver-kidney crosstalk.

Using clinically relevant compounds, transcriptomic and metabolomic analyses revealed distinct, compound-specific responses compared to single-organ systems.

These results demonstrate that inter-organ communication reshapes drug responses and highlight the value of multi-organ systems to better predict drug disposition.

Emmanuelle Rota Graziosi (Ecole Normale Supérieure - PSL)

### **An angiogenesis-based vascular interface for perfusion of microphysiological tissues**

Microphysiological systems and organ-on-chip models are promising tools to reproduce human tissues *in vitro*, but their relevance is often limited by the lack of functional microvascularization. Here, we present a microfabricated porous support designed as a vascular interface to generate perfusable capillary networks through angiogenesis. The device creates a controlled 2D-to-3D interface, enabling an endothelial monolayer on one side and a 3D tissue construct on the other. Endothelial cells (EC) migrate through defined pores, sprout into the tissue compartment, and self-organize into interconnected capillary-like networks. Using ECs expressing distinct fluorescent reporters on each side, we further show direct anastomosis between monolayer-derived sprouts and embedded vascular structures, resulting in a connected 3D network. Functional perfusion was demonstrated by lectin circulation through the vasculature. The modular design makes the support compatible with a wide range of engineered tissues and biomimetic constructs and enables integration into a microfluidic chip for sustained culture under flow. This plug-and-play strategy provides a versatile solution to vascularize tissue-on-chip platforms and organoid-based models.

Elise Delannoy (Institut Pasteur de Lille)

### **3DP- $\mu$ Gut: An Accessible Gut-on-Chip Platform Enabling Advanced Host-Microbe Studies**

We developed an accessible gut-on-chip platform (3DP- $\mu$ Gut) enabling physiologically relevant modeling of host-microbiota interactions. Using consumer-grade stereolithography, we produced 3D printed molds and PDMS microdevices with high reproducibility, compatible with perfusion and high-resolution imaging.

The system supports the formation of polarized intestinal epithelial monolayers that self-organize into 3D architectures closely resembling the *in vivo* barrier. It enables stable co-culture with commensal (*Lactiplantibacillus plantarum*) and pathogenic (*Shigella flexneri*) bacteria, allowing investigation of adhesion, colonization, and infection dynamics in a controlled human-relevant environment. (1)

In parallel, we developed a mechanically active model incorporating cyclic deformation mimicking intestinal segmentation, providing a novel framework to study how biomechanical forces influence epithelial function and microbial behavior.

These results establish 3DP- $\mu$ Gut as a robust and physiologically relevant platform for studying intestinal biology and host-microbiota interactions, with strong potential for disease modeling and therapeutic screening.

(1) Delannoy, E et al. (2025). *Lab. Chip* 25, 4396–4409.

**1 - François Berger (Braintech Lab Inserm UGA U1205)**

A spatial nanoporous tumoroid platform for standardized bedside precision oncology

**2 - Ghislain Banos (Inserm U955)**

Engineered 3D skeletal muscles imitating early muscle defects of Duchenne Muscular Dystrophy uncover transcriptomic signatures predictive of treatment efficacy

**3 - Quentin Faucher (Utrecht Institute for Pharmaceutical Sciences - Division of Pharmacology)**

Development of a hollow fiber membrane-based blood-brain barrier-on-chip model to study the kidney-brain axis

**4 - Nathalie Deboosere, Yoel Dagan (Univ. Lille, CNRS, Inserm, CHU Lille, Institut Pasteur de Lille, U1019 - UMR 9017 - CIIL)**

Development of a cost-effective Alveolus-on-Chip for studying Mycobacterium tuberculosis infection.

**5 - Daniel Alcaide Martin (LAAS-CNRS)**

Hybrid TEER-hydraulic platform for cell monolayer integrity assays

**6 - Elysa Capelle (INRAE, BioEcoAgro (UMRT 1158), Université de Lille; IEMN (UMR CNRS 8520), Université de Lille; Ingredia, Arras)**

Development of a dynamic gut-on-chip model to study digestion and intestinal absorption of dairy proteins

**7 - Polina Malahov (Institute de la Vision (IDV), Sorbonne Univeristy)**

Optic Nerve-on-a-Chip Platform to Model Neuroinflammation in Glaucoma

**8 - Corentin Scholaert (CNRS - IEMN)**

Facile Fabrication of Transparent PEDOT:PSS-based Microelectrode Arrays for Multimodal Monitoring

**9 - Thomas Boudou (Univ. Grenoble Alpes, CNRS, LIPhy)**

Tissue gauges for easy access to 3D microtissue contractility

**10 - Remco den Dulk (CEA-Leti)**

A modular microfluidic platform for automated organoid-on-chip experiments

11 - Ibtihal Hezili (ONCOLille, CRCLille, PERSTIM Lab, Univ. Lille, U1366 Inserm, CHU Lille, UMR9020 CNRS, Inst. Pasteur Lille, Lille, France // CNRS, IRL2820, LIMMS/IIS, University of Tokyo)

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13 - Juliette Jin (Institut Curie)

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14 - Léna Domalain & Ana Vazquez (Institut Curie)

Tumor-on-Chip as a Personalised Platform for Rapid Drug-Testing in Breast Cancer

15 - Rabia Onbas (École Centrale de Lyon)

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16 - Bruno Estebe (Institut Imagine, Inserm)

Kidney Organoids for Modeling and Therapeutic Screening in Hereditary Kidney Diseases

17 - Hasti Honari (CNRS UMR168, Laboratoire Physique des Cellules et Cancer, Institut Curie, PSL Research University)

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19 - Muriel Quaranta (University of Toulouse, Inserm, I2MC)

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**29 - Marie Hut (LAAS-CNRS)**

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**30 - Julie Foncy (LAAS-CNRS)**

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A pancreatic duct-on-chip to study KRASG12D effect on early carcinogenesis of pancreatic ductal adenocarcinoma (PDAC)

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**35 - Caio César Barbosa Bomfim (Institut de Pharmacologie et Biologie Structurale - IPBS)**

Modeling Tuberculosis in a Dual Human Lung Microenvironment: A Physiologically Relevant Platform for Drug Discovery Applications

**36 - Lilas Courtot (Comité scientifique Pro Anima)**

Pro Anima Scientific Committee, a national and transdisciplinary hub for NAMs

**37 - Catia Cerqueira (LGC Standards)**

Clinical, molecular, and functional characterization of a diverse collection of patient-derived colorectal cancer organoids from the Human Cancer Models Initiative

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