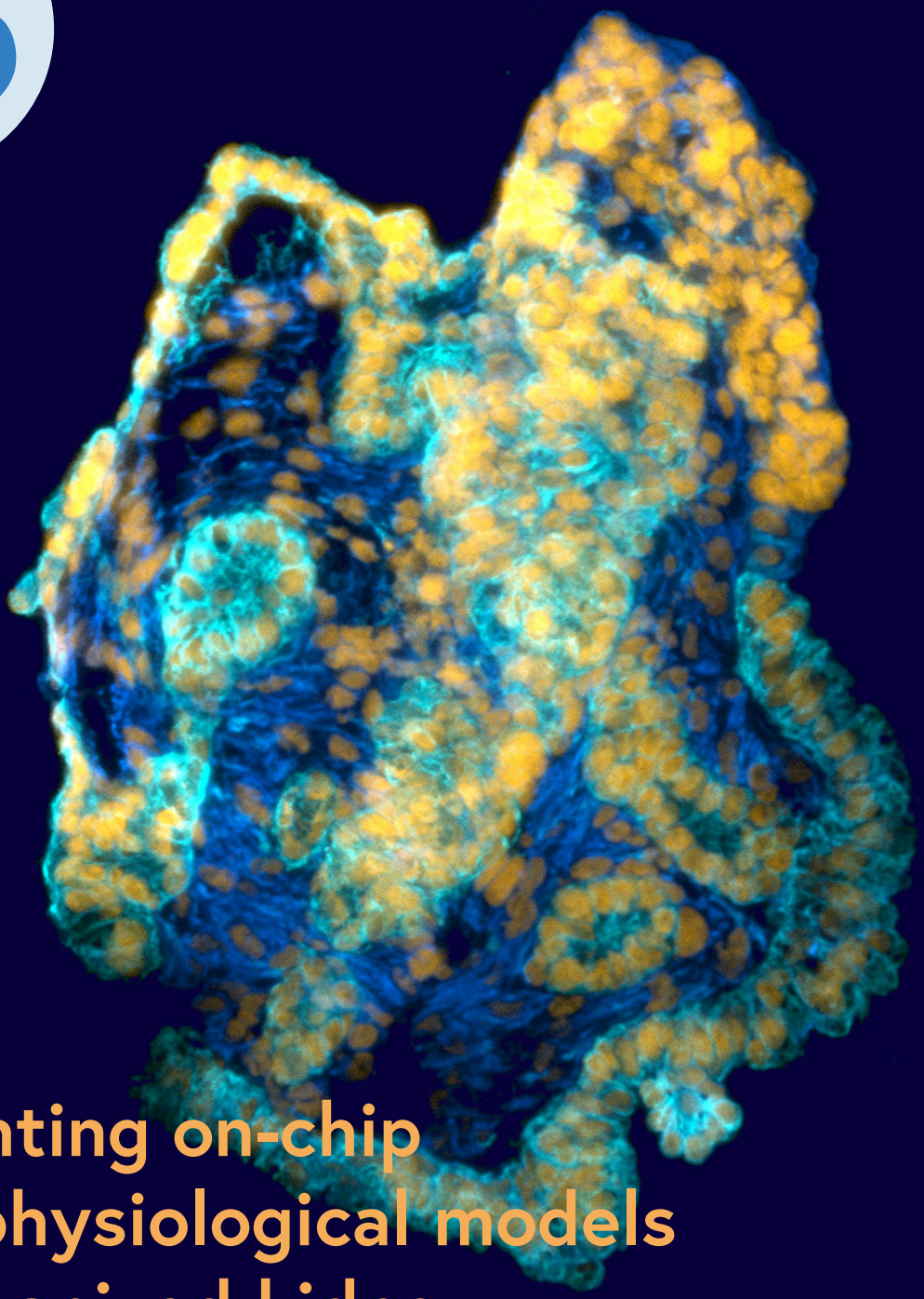
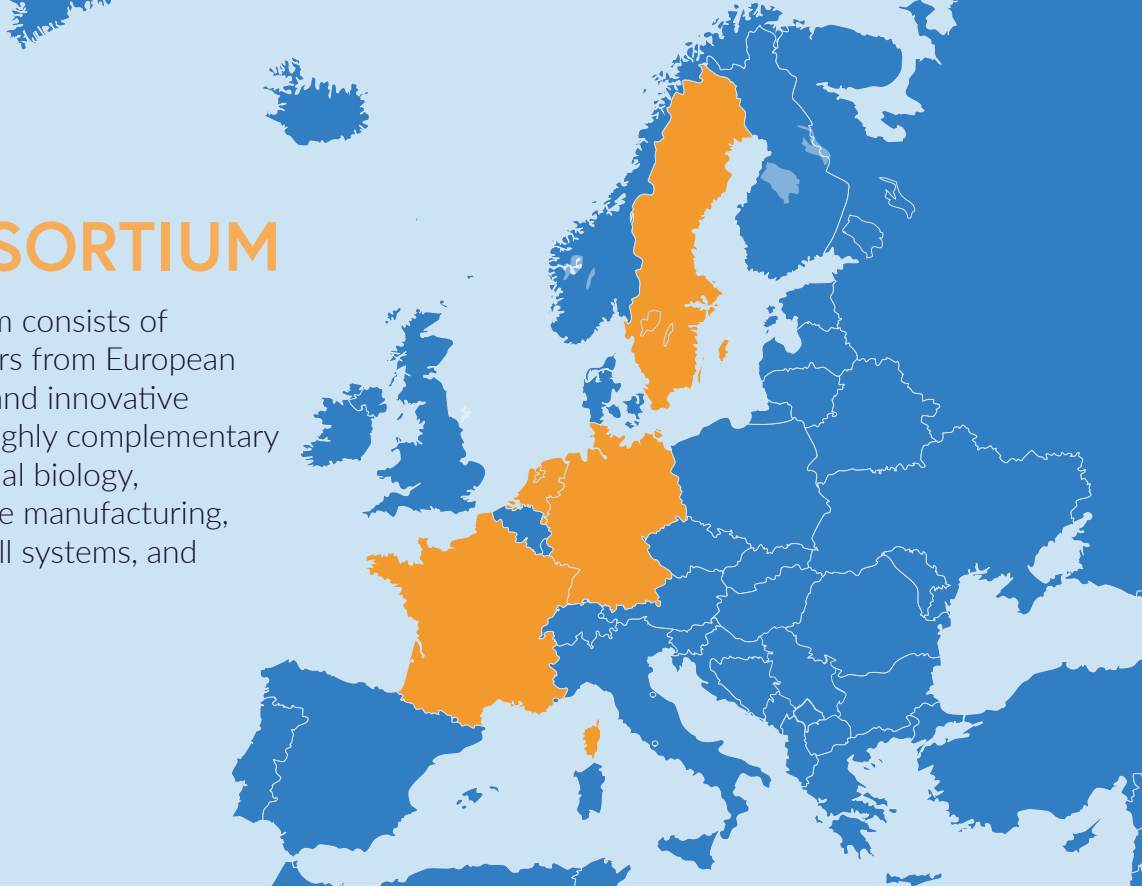


Bioprinting on-chip microphysiological models of humanized kidney tubulointerstitium

BIRDIE Annual report 2022

THE CONSORTIUM

The BIRDIE consortium consists of experienced researchers from European academic institutions and innovative SMEs. The team has highly complementary expertise in translational biology, bioprinting and additive manufacturing, microfluidics, single-cell systems, and organ-on-chip models.



Maastricht University

Maastricht University (MU) is the youngest and most international university in the Netherlands. Ranked 7 in QS "Top 50 under 50", the university has more than 16.500 students, 4.000 staff and 55.000 alumni, with over 70% foreign PhD students from more than 100 student nationalities. MU is part of the Maastricht health campus and the constant interaction with hospital physicians ensures the proper environment for the development of clinically and physiological relevant models.

Nantes Université

Nantes Université (NU) has approximately 38,000 students enrolled each year, one doctoral college with eight post-graduate schools and 3,200 research staff working in 75 accredited labs. NU has research agreements with industry and shares its discoveries with the society at large. As a multidisciplinary university, programs in most fields of knowledge and academic paths are offered.

TissUse Emulating Human Biology

TissUse is a Berlin, Germany-based, biotech company who has developed a unique "Multi-Organ-Chip" platform to accelerate the development of pharmaceutical, chemical, cosmetic, and personalized medical products. Therewith, TissUse's Multi-Organ-Chips provide preclinical insight on a systemic level using human tissue and enable the direct prediction of effects of substances and their metabolism on near real-life models.

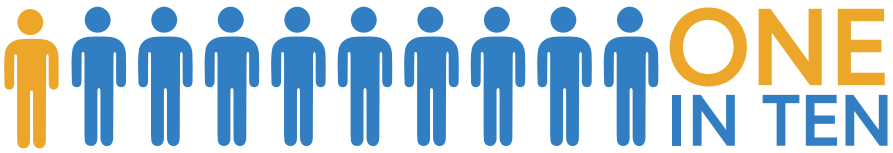
fluicell®

Fluicell AB is a Sweden-based, publicly traded, biotech company with a commercialized product portfolio for biomedical research. The company is a world leader and pioneer in open-volume microfluidics for the life sciences and holds a strong IP and patent position with five different patent families in the estate. By zooming into the level of individual cells, the company redefines the approach to cell biology with its unique microfluidic technologies.

THE BURDEN OF CHRONIC KIDNEY DISEASE

Chronic Kidney Disease (CKD) is predicted to become the 5th leading cause of death world wide*. Among the risk factors for he development of CKD, drugs, and in general nephrotoxicants, and viral infection (BK Virus) play a major role. Moreover, therapeutic options offered to patients are still limited to renal replacement therapies such as dialysis or, in extreme cases, transplantation.

*C. P. Kovesdy, Epidemiology of chronic kidney disease: an update 2022. *KI Supplements*. **14**, 7-11 (2022).



843.6 Million affected globally (2017)*

Building a foundation for future therapies through state of the art biomedical technology

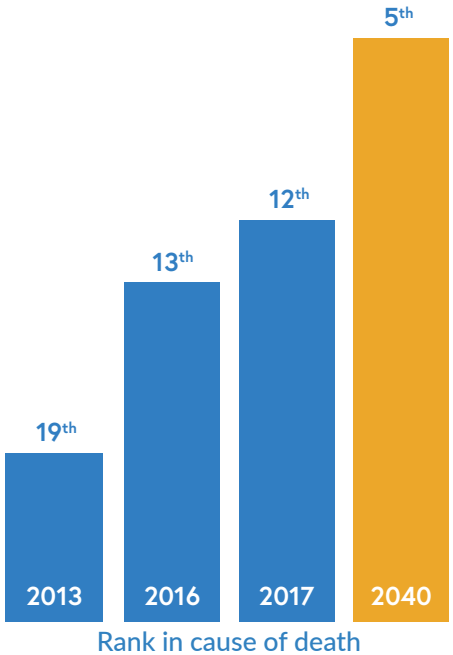
The BIRDIE project was formulated with an emphasis of bringing broad societal impact from the development of state-of-the-art biomedical technology. Our vision is that the humanized kidney in vitro models developed within the BIRDIE project will allow further understanding of kidney disease while supporting future therapies for patients. Furthermore, the aimed in vitro models will be essential to test new therapies administered to patients (e.g. during drug development) or ultimately being able to generate patient-specific in vitro models (derived for iPSCs generated from patient cells) allowing personalized medicine approaches.

Microphysiological Model
Leader: Nantes Université

Organ-on-Chip
Leader: TissUse GmbH

iPSC-based models
Leader: Maastricht University

Bioprinting
Leader: Fluicell AB



Rank in cause of death

+41.5 % Death rate increase 1990-2017*

THE BIRDIE APPROACH

Microphysiological model

During BIRDIE project we are looking to set up long-term microphysiological models of human renal proximal cells cultured under physiological and disease states. The optimized model will be challenged with both BK virus infection and nephrotoxic drugs, and transcriptomics will be used as a guidance system to constantly assess the proximity of our models compared to healthy or diseased native renal sorted cells and tissues.

Organ-on-Chip

Organ-on-a-chip systems enable a co-culture of physiologically relevant tissue models in a closed microfluidic circuit emulating the blood perfusion. During the BIRDIE project a novel chip enabling a dual perfusion of a kidney model by overlapping a blood and a urinary microfluidic circuit will be developed by TissUse GmbH. This chip will harbor the 3D bioprinted models developed within the other work packages.

IPSC-based models

Induced pluripotent stem cells (iPSCs) allow the generation of renal progenitors and organoids relevant for kidney in vitro models. IPSCs-derived organoids will be generated and combined with bioprinting and microfluidics for nephrotoxicity and viral infection screenings.

Bioprinting

The combination of multiple bioprinting techniques is of paramount importance to achieve a broader range of complexity and mimicry in kidney models. Within BIRDIE we will use multiple bioprinting techniques to produce macro-size features and Fluicell's unique single cell bioprinting to fine-tune cellular compositions within the kidney tubulointerstitium space.

THE BIRDIE IMPACT

STAKEHOLDER ENGAGEMENT

Stakeholder meeting: The Future of *In Vitro* Models

On June 16th 2022, the BIRDIE consortium organized a stakeholder meeting where Opinion Leaders, Experts and Regulatory Authorities met with researchers and discussed current developments of *in vitro* models.

The invited stakeholders were **Prof. Luc Frimat** (SFNDT/SAB), **Dr. Jasper Boomker** (Dutch Kidney foundation, program manager technological innovation), **Prof. Claire Rigothier** (SFNDT/SAB), **Dr. Alexandre Ribeiro** (Hovione, previous FDA), **Dr. Monica Piergiovanni** (Joint Research Centre, Chemical Safety & Alternative Methods), **Dr. Udo Kraushaar** (Natural and Medical Sciences Institute) and **Dr. Lucile Figueres** (Nantes Université).

During the workshop, the challenges that the field of bioengineering still needs to face, such as the need for a complex in vitro physiological system.

The discussion was focus on kidney (organ of interest of BIRDIE project) which is not a simple organ; therefore, as mentioned by the stakeholders, the in vitro model cannot be simple. Organ on-chip represents a promising tool to model kidney physiology and study its pathophysiology. These can be used to model multi-organ pathophysiology, drug screening, and personalized screening platforms.

- Watch the workshop **ONLINE**

What are the key advantages of on-chip in vitro models?

Organ-on-chip **technology** could answer very specific questions, such as chronic pathology.

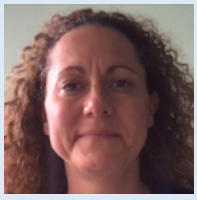
Dr. Jasper Boomker
Dutch Kidney Foundation

These models will enable patient-specific research and **personalized medicine**.

Prof Luc Frimat
SFNDT / SAB

Advanced models mimicking genetic or rare diseases will allow further learning of **kidney pathophysiology**.

Dr. Lucile Figueres
Nantes Université



These tools can facilitate the **translation** between research and clinics.

Prof. Claire Rigothier
SFNDT / SAB

Depending on the context of use, organ-on-chips can be developed to be more **predictive** than 2D cell culture assays.

Dr. Alexandre Ribeiro
Hovione

It is essential to work together with **regulatory agencies** and **industry** to bring these technologies to the clinics.

Dr. Udo Kraushaar
Natural and Medical Sciences Institute

One of the main challenges of this model remains the lack of **standardization**.

Dr. Monica Piergiovanni
Joint Research Centre, Chemical Safety & Alternative Methods

THE CONSORTIUM LEADERS

Project Coordinator

Dr. Carlos Mota

Assistant Professor,
Department of Complex Tissue Regeneration
MERLN Institute for Technology-inspired Regenerative Medicine.
Maastricht University, Netherlands

Research Team Leaders

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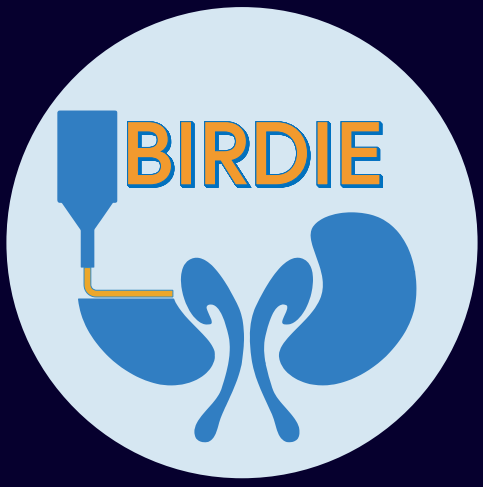
Head of Research and Development.
TissUse GMBH, Germany.

Dr. Franck Halary

NSERM Research Associate in the Center for Research in Transplantation and Translational Immunology (CR2TI)
Nantes Université, France.

Dr. Gavin Jeffries

Chief Technology Officer
Fluicell AB, Sweden.



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