## EMBL



## 3<sup>rd</sup> edition EMBL · IBEC Conference ENGINEERING MULTICELLULAR SYSTEMS

24th - 26th April 2024 · PRBB, Barcelona

ABSTRACT BOOK

Designed and produced by the Communications Office of the Institute for Bioengineering of Catalonia

### www.ibecbarcelona.eu

### Welcome to the 3er edition EMBL · IBEC Conference on ENGINEERING MULTICELLULAR SYSTEMS

Recent breakthroughs in stem cell biology, organ-on-chip assays, 3-D bioprinting, and cell mechanobiology have revolutionized our ability to design and assemble multicellular living systems, from organoids to embryos.

This biennial series of will focus on how engineering multicellular living systems is boosting our understanding of tissue and organ function, with applications in disease modelling, drug screening, and tissue engineering.

The 3rd edition conference will take place in PRBB Auditorium (Barcelona Biomedical Research Park), in Barcelona from 24-26th April 2024. We expect to bring together 150 researchers including stem cell biologists, systems biologists, physicists and engineers.





### Programme 24th April

08:30 - 09:10	Registration
09:10 - 09:30	Opening remarks
Session 1	Chair: James Sharpe
09:30 - 10:00	Human pluripotent stem cells come of age in modelling cardiovascular diseases and toxicity. Christine Mummery, Leiden University, Netherlands.
10:00 - 10:30	Modeling post-implantation human development to yolk sac blood emergence. Mo Ebrahimkhani, University of Pittsburgh, USA
10:30 - 10:45	Short Talk <b>Size control of in vitro somites.</b> Maria Costanzo, European Molecular Biology Laboratory, Spain
10:45 - 11:00	Sponsor Talk <b>A leap forward in cytoprotection.</b> Christoph Hoefer, Thermo Fisher Scientific
11:00 - 11:30	Coffee break
Session 2	Chair: Josep Samitier
11:30 - 12:00	<b>Coordination of morphogenesis and cell state by mechanical forces.</b> Sara Wickstrom, Max Planck Institute for Molecular Biomedicine, Germany.
12:00 - 12:15	Short Talk Mechanics of Human and Mouse Embryo Implantation Amélie Godeau, Institute for Bioengineering of Catalonia (IBEC)

12:15 - 12:45	Mitochondrial reprogramming regulates stem cell fate in early development. Prof. Maneesha Inamdar, Institute for Stem Cell Science and Regenerative Medicine, India
12:45 - 13:15	Flash talks
13:15 - 14:45	Lunch and Poster session
Session 3	Chair: Vikas Trivedi
14:45 - 15:15	Epithelial Folding Irreversibility is Controlled by Elastoplastic Transition via Mechanosensitive Actin Bracket Formation. Satoru Okuda, WPI Kanazawa University, Japan.
15:15 - 15:30	Short Talk Artificial extracellular matrices based on 3D hybrid hydrogels for immune cell and organoid manufacture. Judith Guasch, ICMAB-CSIC
15:30 - 16:00	Coffee break
16:00 - 16:30	Optimizing hiPSC-Derived Spinal Cord Models by Engineering Synthetic Extracellular Matrix Microenvironments. Zaida Álvarez, Institute for Bioengineering of Catalonia, Spain
16:30 – 16:45	Short Talk <b>Nematically-guided morphogenesis.</b> Pau Guillamat, Institute for Bioengineering of Catalonia, Spain
16:45 – 17:15	Modeling the menstrual cycle using endometrial organoids. Margherita Turco, Friedrich Miescher Institute for Biomedical Research
	Satellite Programme
16:45 – 17:15	Video essay "HeLa et al." Tess Marschner, Artist-in-Residence at Institute of Bioengineering of Catalonia (IBEC)

Programme 25th April

Session 4	Chair: Kristina Haase
09:00 – 9:30	Constructing and deconstructing the human nervous system to study development and disease. Sergiu Paşca, WU Tsai Neurciences Institute · Standford University, USA
9:30 – 10:00	Architected hydrogels for Engineering Aligned Tissues. Marcy Zenobi-Wong, Swiss Federal Institute for Technology, Switzerland.
10:00 - 10:15	Short Talk <b>Replicating Dynamic Immune Responses within a Microfluidic Human</b> <b>Skin Equivalent Model.</b> Sarah Hindle, Blizard Institute, Queen Mary University of London
10:15 - 10:45	Automatic inference and design of spatial regulatory mechanisms. Daniel Lobo, University of Maryland, USA
10:45 - 11:15	Coffee Break
Session 5	Chair: Miki Ebisuya
11:15 - 11:45	Organoids to model human disease. Hans Clevers, Utrecht University, Netherlands.
11:45 - 12:00	Short Talk Harnessing the rhythmic biology of early kidney formation for synthetic morphogenesis. Alex Hughes, Department of Bioengineering, University of Pennsylvania
12:00 - 12:30	Myogenic differentiation, bioprocess optimization, and tissue engineering in a Pacific salmon model: using cellular agriculture technologies for sustainable seafood production. Arye Elfenbein, Wildtype, USA

12:30 - 13:15	Flash talks
13:15 - 13:20	Group photo
13:15 - 14:30	Lunch and Poster session (even numbers)
Session 6	Chair: Núria Montserrat
14:30 – 14:50	Short Talk <b>Role of mechanotransduction in the control of interneurons migration</b> <b>in the cortex.</b> Míriam Javier Torrent, University of Liège, GIGA Neurosciences
14:50 – 15:20	Access and Affordability Paradigms for Advanced Biomedical Technologies. Ubaka Ogbogu, University of Alberta, Canada.
15:20 - 15:50	Building Organoids by learning signaling gradients. Sharad Ramanathan, Harvard University, USA
15:50 - 16:15	Coffee break
16:15 - 16:45	Stem Cell Modeling of Human Embryonic Development. Berna Sozen, Yale University, USA.
16:45 – 17:00	Short Talk SHAPE: Investigating innate immunity in real microgravity aboard the International Space Station using advanced human bone marrow organoids. Ryan Sarkar, BMLS, Goethe University Frankfurt a.M.
17:00 – 17:30	Approaches to engineering spatially organized multicellular systems. Jamie Davies, The University of Edinburgh, UK

### Programme 26th April

Session 7	Chair: Xavier Trepat
09:00 – 9:30	To brain or not to brain: Using organoids to uncover how brain cell fate is determined. Madeline Lancaster, MRC Laboratory of Molecular Biology, UK.
9:30 – 9:45	Short Talk Hormonal Regulation of Germ Layer Specification in Micropatterned Gastruloids Joana Silva, European Molecular Biology Laboratory, Spain
9:45 – 10:15	Programming intercellular communication to assemble engineered neuromuscular systems. Ritu Raman, Massachussetts Institute of Technology, USA.
10:15 – 11:15	Coffee Break and Poster session
11:45 – 12:15	Break to build: exploring the role of fracture during morphogenesis. Alejandro Torres-Sanchez, EMBL Barcelona, Spain.
12:15 - 12:30	Short Talk DNA microbeads for spatio-temporally controlled morphogen release within organoids Tobias Walther, Max Planck Institute for Medical Research
12:30 - 13:00	<b>Retinal Organoid Transplantation</b> Masayo Takahashi, Riken, Japan
13:00 - 13:15	Closing remarks and awards

# Keynote Lectures

Wednesday 24th April · 09:30

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### "Human pluripotent stem cells come of age in modelling cardiovascular diseases and toxicity"

Christine Mummery

Our lab creates models for cardiovascular disease based on pluripotent stem cells (hPSCs). We use these for understanding disease mechanisms and cardiotoxic effects of drugs. We can predict the toxic effects of test drugs with almost 80% accuracy in (immature) cardiomyocyte monolayer cultures When we require mature cells, we combine hPSC-cardiomyocytes with cardiac fibroblasts and endothelial cells in "microtissues". The cardiomyocytes develop electrical, metabolic and functional features allowing us to model postnatal onset diseases or dissect which cell types in the heart are actually responsible for the disease phenotype. We showed for example fibroblasts in the heart can contribute to abnormal heart contraction in patients with arrhythmogenic cardiomyopathy. These complex cell systems are paving the way towards better understanding of disease mechanisms and drug discovery.



#### Christine Mummery Department of Anatomy and Embryology, Leiden University Medical Centre

Christine Mummery is Professor of Developmental Biology at Leiden University Medical Center. Following a PhD in Biophysics, she moved to the Hubrecht Institute to study ion channels and later, cardiovascular diseases using pluripotent stem cells from patients, developing organ-on-chip models. This has centred on safety

pharmacology to predict toxic effects of drugs on the human heart and capturing cardiac and vascular disease phenotypes including identifying individual vulnerability and drug sensitivity. She was president of the International Society for Stem Cell Research (2020-2021) and co-founded the European Organ-on-Chip Society. She is also a member of the Royal Netherlands Academy of Science. In 2021, she was awarded the Lefoulon Delalande Prize jointly with Gordon Keller.

Wednesday 24th April · 10:00

### 3rd edition EMBL - IBEC Conference ENGINEERING MULTICELLULAR SYSTEMS

### Modeling post-implantation human development to yolk sac blood emergence Mo Ebrahimkhani

Implantation of the human embryo begins a critical developmental stage that encompasses crucial events, including the formation of the body axis and germ layers and the emergence of the hematopoietic system. However, the early post-implantation stages of human development are difficult to study due to technical and ethical challenges. We present a genetically inducible embryo model named heX-embryoids that shows self-organizing peri/post-implantation cellular programs, including the formation of the amniotic cavity and bilaminar disc as well as the generation of A/P and D/V body axis. The extra-embryonic layer in heX-embryoids displays multilineage yolk sac morphogenesis with distinct waves of blood formation. These embryoids are highly scalable and leverage self-organization from 2D to 3D to improve reproducibility and efficiency. As such, they will provide new opportunities to study early human development and to advance developmental toxicology and regenerative cell therapies.



### Mo Ebrahimkhani University of Pittsburgh

Mo Ebrahimkhani is an Associate Professor of Pathology and Bioengineering at the University of Pittsburgh. He performed his postdoctoral training in synthetic morphogenesis and organoids at MIT Biological Engineering. His lab has developed a novel human embryoid that shows the intricate process of the first blood formation in the yolk sac. His team integrates human stem cells and synthetic biology to understand

tissue development and build regenerative technologies, focusing on early postimplantation events, the development of hematopoietic systems, and the liver. Wednesday 24th April • 11:30

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### Coordination of morphogenesis and cell states by mechanical forces

Sara A. Wickström

The structure of tissues is tightly linked to their function. During formation of functional organs, large-scale changes in tissue elongation, stretching, compression, folding/buckling, and budding impact the shape, position, packing, and contractility state of cells. Conversely, changes in single cell contractility, shape and position locally alter tissue organization and mechanics. Thus, forces function as important ques that are transmitted to the nucleus to coordinate gene expression programs to control cell states. On the other hand, excessive mechanical stresses have the potential to damage cells and tissues. In my presentation I will discuss our recent research on how cells use the nucleus and the nuclear envelope/chromatin interface to sense mechanical forces and how these mechanosignals are integrated with biochemical inputs to alter cell states and to generate and maintain tissue architecture.



### Sara A. Wickström Max Planck Institute for Molecular Biomedicine, Muenster, Germany

Sara Wickström received her MD in 2001 and PhD in 2004 from the University of Helsinki, Finland. After postdoctoral training at the Max Planck Institute (MPI) for Biochemistry she became Group Leader at the MPI for Biology of Ageing in 2010. In 2018 her laboratory moved to the University of Helsinki where she was professor of Cell and Developmental Biology.

In 2022 Wickström was appointed as Director of the MPI for Molecular Biomedicine in Münster.

Research in the Wickström lab aims to understand how mammalian epithelial tissues are generated and maintained, and in particular how mechanical forces and cellular interactions integrate single cell behaviors to pattern these structurally extremely robust yet dynamic tissues. Wednesday 24th April • 12:15

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### Mitochondrial reprogramming regulates stem cell fate in early development.

Aishwarya Prakash, Kajal Kamat, Maneesha S Inamdar\*

Generation of functional multicellular systems in vitro requires controlled expansion of stem cells and their self-assembling structures. The inherent molecular heterogeneity in stem cell pools gives rise to transient cellular sub-states, which makes it difficult to predict and control their output. For example, human pluripotent stem cells exist in a continuum of developmental sub-states with diverging potencies. Similarly, immunophenotypically defined hematopoietic stem cells are heterogenous in molecular and functional characteristics, which can impact their cell fate and lineage bias. Understanding how these discrete cellular states arise and subsequently transition to a differentiated state is fundamental for designing robust in vitro differentiation strategies. Mitochondrial activity plays pivotal roles in dictating stem cell fate. Increased insights into mechanisms that integrate mitochondrial function with stem cell differentiation are required to tune, trap and expand stem cell states in vitro. Using a multiplexed approach, in mouse embryogenesis and human pluripotent stem cell-derived models, we show a correlation between stem cell fate and mitochondrial activity across different stages of early development. Pharmacological and genetic modulation of mitochondrial activity altered the distribution of early stem cell subsets, which affects their differentiation output. We propose that differential mitochondrial activity during early development manifests as gene regulatory changes, that affect their fate and function



#### Maneesha Inamdar Director, (inStem) (Institute for Stem Cell Science and Regenerative Medicine)

Professor Maneesha Inamdar is a stem cell and developmental biologist conducting research at Bangalore, India. Her group studies cardiovascular and blood development, using stem cells and animal models. A key approach is to genetically modify human stem cells to understand development and disease. This research has

application in prevention of congenital defects as well as for regenerative therapies.

Dr. Inamdar pioneered human embryonic stem cell derivation and use in India, providing stem cells that represent the Indian genetic diversity, are eligible for use globally and have been distributed worldwide. She has national and international projects, including recently from the Bill and Melinda Gates Foundation.

Dr. Inamdar was a member of the World Health Organization (WHO) Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome editing. She is a member of the International Society for Stem Cell Research (ISSCR) Task Force to develop standards for stem cell research; the steering group of the International Stem Cell Banking Initiative (ISCBI); Scientific Advisory Board, human pluripotent stem cell Registry, Europe and was part of the International Stem Cell Initiative (ISCI) projects.

Prof. Inamdar heads or serves on several scientific review, funding and ethics committees. While furthering discovery, she is deeply involved in research training, developing international guidance and policy, science outreach, education and public engagement at multiple levels and in varied formats. Her recent article in the journal Nature was highlighted for its call to bring equity and accessibility through global research standards.

Prof. Inamdar did her PhD at the Tata Institute of Fundamental Research (TIFR), Mumbai; Postdoctoral research at the University of North Carolina, Chapel Hill, USA. She was Professor and Chairperson (Molecular Biology and Genetics Unit), JNCASR; Dean (Fellowships and Extension Programmes), JNCASR; Adjunct Professor, inStem and Visiting Professor, Tata Institute for Genetics and Society Centre at inStem. She is presently Director of inStem, India's first stem cell institute.

She has several awards, including the National Bioscience Award, the Dr. Kalpana Chawla Award, the C.N.R. Rao Oration award. She is an elected fellow of the Indian Academy of Sciences and the Indian National Science Academy, and a J C Bose National Fellow. Wednesday 24th April • 14:45

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### Epithelial Folding Irreversibility is Controlled by Elastoplastic Transition via Mechanosensitive Actin Bracket Formation Satoru Okuda

During morphogenesis, epithelial sheets undergo sequential folding to form threedimensional organ structures. The resulting folds are irreversible, ensuring that morphogenesis progresses in one direction. However, the mechanism establishing the irreversibility of folding remains unclear. Here, we report a novel mechanical property of epithelia that is responsible for folding irreversibility. Using a newly developed mechanical indentation assay, we demonstrate that short-term or low-amount folding induces an elastic, shape-restoring response. In contrast, combined long-term, high-amount folding results in plastic, irreversible deformation. This elastic-to-plastic transition occurs in a switch-like manner, with critical thresholds for the folding amount and duration. Specific cells at the fold initiate this transition, sensing the amount and duration of folding on their apical side via mechanosensitive signaling pathways, including transient receptor potential canonical (TRPC) 3/6-mediated calcium influx and ligand-independent epidermal growth factor receptor activation. These pathways induce F-actin accumulation into a bracket-like structure across the fold, establishing the transition. The duration threshold is determined and tunable by the actin polymerization rate. These results demonstrate that cells control the irreversibility of epithelial folding by detecting folding characteristics and adaptively switching between elastic and plastic responses. This finding resolves a long-standing question about the directionality of morphogenesis.



#### Satoru Okuda Nano Life Science Institute of Kanazawa University

Satoru Okuda is an Associate Professor at the Nano Life Science Institute of Kanazawa University, specializing in mechanical engineering and developmental biology. He holds a Doctorate in Engineering from Kyoto University and has trained at RIKEN CDB. His research focuses on understanding the mechanical and biological principles underlying multicellular self-organization.

Okuda has contributed to the field through his work on the development of 3D vertex models and the understanding of epithelial morphogenesis.

### Optimizing hiPSC-Derived Spinal Cord Models by Engineering Synthetic Extracellular Matrix Microenvironments

Zaida Álvarez

Spinal motor neurons (MNs) can be effectively differentiated from pluripotent stem cells using established protocols based on small molecule signaling or, more recently, by overexpression of key transcription factors. When grown as an adherent 2D monolayer, these stem cell-derived MNs form a uniform cell population. This setup is ideal for high-throughput biochemical studies, in-depth molecular mechanism experiments, and drug screening initiatives due to the high degree of control over external factors. However, this approach has significant limitations, including insufficient levels of functional maturation and reduced long-term viability. In addition, the tendency of these cells to aggregate limits their accessibility, thereby reducing their utility. Transcriptional analysis also reveals that these in vitro-grown, stem cellderived MNs resemble neurons from late embryonic to early postnatal stages. This similarity poses a challenge in the study of late neurodevelopmental processes and adult-onset neurodegenerative diseases that occur later in life. Currently, extracellular matrix (ECM) methods for adherent in vitro culture of iPSC-derived neurons involve the use of purified or recombinant proteins, such as laminin and fibronectin, applied to glass or plastic-coated surfaces. While these components are abundant in the ECM of most tissues and their use is biologically logical, they are insufficient to promote advanced neuronal maturation. Our study aims to improve iPSC neuronal model systems by providing CNS-specific and developmentally appropriate ECM cues. We focused on analyzing the composition and remodeling of the mammalian spinal cord matrisome in vivo to design, characterize, and establish new ECM mimetic matrices that can recapitulate the architecture and modulatory activity of specific components of the physiological matrisome. These matrices are designed to integrate biological signals that promote cell adhesion, migration, proliferation, and support maturation and aging of stem cell-derived human neuron models in vitro. With their unique combination of order and dynamics, these systems show great promise as artificial ECMs. These synthetic ECM materials may facilitate the development of additional ECM mimetic platforms relevant to the study of human neuronal development, function and dysfunction.



#### Zaida Álvarez Institute of Bioengineering of Catalonia (IBEC).

Dr. Zaida Alvarez currently leads the Biomaterials for Neural Regeneration group as a Ramon y Cajal Junior Group Leader at the Institute of Bioengineering of Catalonia (IBEC) in Spain. She completed her Ph.D. in Biomedical Engineering at the Polytechnic University of Catalonia in 2014. In 2015, she joined the laboratory of Professor Samuel Stupp at Northwestern University in

Chicago as a self-funded postdoctoral fellow to work on peptide amphiphiles for neural regeneration. In 2019, she was appointed Assistant Professor in the Department of Medicine at the Feinberg Medical School at Northwestern University, where she continued her research on supramolecular biomaterials for in vitro modeling of human IPS-derived neurons in injury and disease. Since 2019, she has also served as a consulting engineer for various technology firms in the US, contributing her expertise to four active patents related to innovative biomaterials for neural repair. Throughout her career, she has received numerous awards including the Young Baxter investigator award in 2019 and the Rafael Hervada award in 2021. Her current research with the IBEC group focuses on understanding the molecular dynamics of regenerative failure in the central nervous system and leveraging this insight to devise biomaterial-based strategies aimed at overcoming paralysis.

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### Modeling the menstrual cycle using endometrial organoids

Margherita Yayoi Turco

Proper function of the endometrium, the mucosal lining of the uterus, is essential for women's health and to fulfil its ultimate role in the establishment and maintenance of pregnancy. In humans, it undergoes monthly shedding, regeneration and differentiation under the control of ovarian hormones. Dysregulation in these processes manifest themselves through a number of common clinical conditions including infertility, endometriosis, hyperplasia, and adenocarcinoma. There are major gaps in our understanding of the fundamental biology of this tissue because of the challenges in modeling the dramatic and cyclical changes the human endometrium undergoes. We have derived endometrial organoids that can be cultured long-term, retain the morphology, function, and gene signature of the tissue in vivo. We are using this multicellular system to model the changes occurring during the menstrual cycle to investigate the mechanisms that regulate regeneration and differentiation of the endometrial epithelium as well as understanding how its function may differ in women who have fertility issues.



#### Margherita Yayoi Turco Friedrich Miescher Institute for Biomedical Research

Margherita Yayoi Turco is a Group Leader at the Friedrich Miescher Institute for Biomedical Research in Basel, Switzerland. The research focus of her lab is to understand how the human placenta develops and how this process is influenced by the maternal uterine environment. Her interest in cell fate decisions and embryonic development began during her studies in

Biotechnology at the University of Bologna (Italy), where she investigated the role of endogenous cannabinoid signalling in pre-implantation embryos. During her PhD in Molecular Medicine at the University of Milano and European Institute of Oncology (Italy), she continued to explore the role of adaptor molecules in development and cancer using several stem cell models. Margherita then joined the Centre for Trophoblast Research at the University of Cambridge (UK) as a postdoctoral fellow under the supervision of Prof. Graham Burton, Dr. Myriam Hemberger and Prof. Ashley Moffett to establish tissue-derived organoid systems of human trophoblast and endometrium. She was awarded the Intra-European Marie-Curie and Royal Society Dorothy Hodgkin fellowships and L'Oreal Women in Science Award during her time in Cambridge followed by the ERC Starting Grant to start her own lab. Her team is now using trophoblast and endometrial culture systems combined with imaging, gene editing, single cell technologies and bioengineering approaches to address the key questions on the maternal-fetal interactions critical for a successful pregnancy. Thursday 25th April • 09:00

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# Constructing and deconstructing the human nervous system to study development and disease

Sergiu Pasca

A critical challenge in understanding the programs underlying development, assembly and disease of the human brain is the lack of direct access to intact, functioning human neural tissue for detailed investigation and manipulation. In my talk, I will first describe how my laboratory has been leveraging instructive signals to develop, starting from human pluripotent stem cells, self-organizing neural organoids resembling specific domains of the nervous system. I will next introduce a novel self-organizing cellular preparation named an assembloid that we created to model cell migration and circuit in the developing human nervous system. Lastly, I will illustrate how organoids and assembloids can be used to study development, evolution and to model genetic neuropsychiatric disease.



### Sergiu Pasca Stanford University

Sergiu P. Pasca, MD, holds the Kenneth T. Norris, Jr. Endowed Professorship in Psychiatry and Behavioral Sciences at Stanford University, where he also serves as the Uytengsu Family Founding Director of the Stanford Brain Organogenesis Program. Prof. Pasca's work focuses on deciphering the principles of human brain assembly and disease mechanisms. He was born and raised in Romania where he trained as a medical

doctor where his early work combined biochemistry and genetics to study autism. He continued his training in electrophysiology at the Max Planck Institute, and then as postdoctoral fellow at Stanford where he developed some of the initial models of neuropsychiatric disorder studies using stem cells.

In his lab, he introduced the use of instructive signals for reproducibly deriving selforganizing organoids that resemble regions of the human nervous system; he then pioneered assembloids to study migration and neural circuit formation and developed integrated human circuits in living animals following transplantation. Through these models, Prof. Pasca has advanced understanding of human physiology, evolution, and disease, and proposed new therapeutic strategies. He also played a pivotal role in supporting global research communities through educational courses, leading international conferences, and collaborative efforts to standardize nomenclature and quality controls in this new field.

Pasca was named a Visionary in Medicine and Science by the New York Times. He is a Knight of the Order of Merit and a Doctor Honoris Causa. He was featured as a physician-scientist by Nature Medicine and a TED 2022 Speaker. He is the recipient of the Vilcek Award for Creative Biomedical Promise (2018), NIMH BRAINS Award (2015), MQ Award for Transforming Mental Health (2014), A.E. Bennett Award in Biological Psychiatry (2018), Folch-Pi Neurochemistry Award (2017), Günter Blobel Award for Cell Biology (2018), Daniel E. Efron Award in Neuropsychopharmacology (2018), a Breakthrough in Life Sciences Prize (2020) from Falling Walls, International Schizophrenia Prize (2021), Joseph Altman Award in Developmental Neuroscience (2021), Theodore Reich Award (2021), Judson Daland Prize from the American Philosophical Society (2021), 13th IBRO-Kemali Neuroscience Award (2022), CINP Sumitomo/Sunovion Award (2023), and ISSCR Momentum Award (2024). Thursday 25th April • 09:30

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### Architected hydrogels for Engineering Aligned Tissues

Marcy Zenobi-Wong

The development of functional engineered tissues can be greatly enhanced through the use of scaffolds which contain cell-instructive cues. Materials which are composed of individual microgels are bettered positioned to provide these important cell signals compared to bulk materials. Microgels can promote biological processes such as cell migration, cell viability, and cell proliferation due to the increased diffusional properties afforded by the natural void spaces. Microgels can also direct the spatial deposition of extracellular matrix and cell and nuclear morphology. I will discuss how microgels can be incorporated into different strategies such as extrusion bioprinting and filamented light (FLight) biofabrication.



### Marcy Zenobi-Wong ETH Zürich, Switzerland

Dr. Marcy Zenobi-Wong is a full Professor of Tissue Engineering and Biofabrication at ETH Zürich, Switzerland. She obtained her PhD from Stanford University and then did a post-doctoral fellowship in the Orthopaedic Research Laboratories, University of Michigan. In 2012, she moved to the Department of Health Sciences & Technology at ETH Zürich. The Zenobi-Wong research group is

focused on the development of advanced biomaterials for tissue regeneration using biofabrication technologies including bioprinting, two-photon polymerization, casting and electrospinning. Dr. Zenobi-Wong is the author of over 120 peer-reviewed publications and co-inventor on four licensed patents. She has held leadership roles at the Swiss Society for Biomaterials and Regenerative Medicine, the International Society of Biofabrication (ISBF) and is past director of the Institute for Biomechanics, ETH Zürich. She serves on the editorial board for Biofabrication and Advanced Healthcare Materials. Thursday 25th April • 10:15

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# Automatic inference and design of spatial regulatory mechanisms

Multicellular organisms dynamically develop target patterns, shapes, and forms as a result of cell differentiation, proliferation, and migration. The regulatory mechanisms controlling these target phenotypes involve the interaction of molecular signals, mechanical forces, and metabolic pathways that form complex, non-linear feedback loops. In this talk I will present our automated approach based on evolutionary computation combined with mathematical and molecular methods to calibrate, infer, and design de novo mechanistic regulatory networks from dynamic, spatial phenotypes. We have successfully applied this methodology to understand how planarian flatworms can regulate their whole-body shape during growth, degrowth, and regeneration as well as to automatically design synthetic gene regulatory mechanistic insights into the dynamic regulation of whole-body shapes as well as an automated method to design biological circuits for pattern formation towards a wide range of biomedical and biotechnological applications.



### Daniel Lobo University of Maryland

Dr. Daniel Lobo is an Associate Professor in the Department of Biological Sciences at the University of Maryland, Baltimore County and Member of the Greenebaum Comprehensive Cancer Center and the Center for Stem Cell Biology & Regenerative Medicine at the University of Maryland, School of Medicine. Dr. Lobo received his Ph.D. from the University of Malaga in Spain before completing his postdoctoral

training at Tufts University in Massachusetts. Dr. Lobo's lab in Systems Biology aims to understand, control, and design the dynamic regulatory mechanisms governing biological growth and form. To this end, his group combines molecular methods with computational approaches towards the reverse-engineering of mechanistic models from biological data and the automatic design of regulatory networks for specific functions. They seek to discover the mechanisms of development and regeneration, find therapies for cancer and other diseases, and streamline the application of systems and synthetic biology. Dr. Lobo has received several awards for his research, including the NIH Outstanding Investigator Award, the PhRMA Foundation Research Starter Award, and the UMBC Early Career Faculty Excellence Award. His work on Systems Biology has attracted widespread media coverage including PBS, Wired, TechRadar, and Popular Mechanics. Thursday 25th April • 11:15

### 3rd edition EMBL - IBEC Conference ENGINEERING MULTICELLULAR SYSTEMS

### Organoids to model human disease

Hans Clevers, M.D., Ph.D.

The intestinal epithelium is the most rapidly self-renewing tissue in adult mammals. We originally found that Lgr5+ve crypt base columnar cells (CBC) generated all epithelial lineages throughout life, implying that they represent the stem cell of the small intestine and colon. Lgr5 was subsequently found by us to represent an exquisitely specific, yet 'generic' marker for active epithelial stem cells, including in hair follicles, kidney, liver, mammary gland, inner ear, tongue and stomach epithelium.

Single sorted Lgr5+ve stem cells can initiate ever-expanding organoids in the lab. These organoids recapitulate key aspects of the organ from which the stem cells were taken. 3D organoids have been developed for the Lgr5+ve stem cells of human stomach, liver, pancreas, prostate, kidney, breast and many others. Using CRISPR/ Cas9 technology, genes can be efficiently modified in these organoids . Organoid technology opens avenues for the study of development, physiology and disease, for drug development and for personalized medicine. In the long run, cultured miniorgans may replace transplant organs from donors and hold promise in gene therapy.



Hans Clevers Head of Pharma Research & Early Development

Hans Clevers has been the Head of Pharma Research and Early Development (pRED) at Roche since 2022. In this role, he is responsible for the strategy, development and management of all aspects of early research and discovery at pRED, from lead identification to

target progression to late stage development. In 2023, he oversaw the successful establishment of the Institute of Human Biology, a key long-term investment to bridge the gap between academic and pharmaceutical research in Basel, Switzerland. In addition, he is a member of the expanded Corporate Executive Committee for Roche.

Hans Clevers is world-renowned for his work in the fields of cell biology, molecular signaling and stem cells. His research groups' discoveries include the detailed characterization of the molecular effectors and integrators of the "Wnt" pathway, which play crucial roles in health and disease, including colon cancer. His group provided important insights into the roles of the LGR5 protein in stem cell regeneration. The Clevers's group pioneered "organoids", 3-dimensional in vitro structures that behave anatomically and molecularly like the organ from which they are derived. Organoid biology has revolutionized the way we understand and approach human biology and medicine. (https://www.hubrecht.eu/research-groups/clevers-group/)

Hans Clevers obtained his MD and PhD degrees from the University Utrecht, the Netherlands. He holds a professorship in Molecular Genetics from the University Utrecht. He previously held directorship/President positions at the Hubrecht Institute, the Royal Netherlands Academy of Arts and Sciences and the Princess Maxima Center for pediatric oncology.

*He is the recipient of multiple international scientific awards, including the Breakthrough Prize in Life Science.* 

Hans Clevers is a member of the Royal Netherlands Academy of Arts and Sciences (NL), the National Academy of Sciences (USA), the Royal Society (UK) and the Academie des Sciences (France). He is also Chevalier de la Légion d'Honneur and Knight in the Order of the Netherlands Lion, among many other international accolades.

### Myogenic differentiation, bioprocess optimization, and tissue engineering in a Pacific salmon model: using cellular agriculture technologies for sustainable seafood production.

### Aryé Elfenbein

World seafood consumption has been expected to double between 2015 and 2050, leading the United Nations FAO and others to predict increasing shortfalls as supplies struggle to keep up with demand. The deleterious environmental effects of industrial fishing are also highlighted by recent reports about practices such as deep sea trawling, which by itself releases as much carbon per year as the combined global aviation industry. Finally, numerous reports describe the increasing contamination of conventional seafood supplies, including heavy metals and pharmaceutical agents.

Cellular agriculture, or ex vivo food production, represents a new source of meat and seafood. Rather than growing an entire animal to subsequently harvest cuts of meat or seafood, cellular agriculture technologies enable the efficient creation of contaminant-free meat and seafood directly from animal cells. In this session, we report discoveries involving myogenic differentiation, bioprocess optimization, and tissue engineering in the unique context of Pacific salmon. We will also describe current challenges faced by the industry, including the transition from bench-scale to large-scale production.



### Aryé Elfenbein Kyoto University

Aryé earned an MD and PhD at Dartmouth and Kyoto University, and subsequently completed his clinical training in Internal Medicine and Cardiology at Yale. He was a research fellow in cardiovascular regenerative medicine at The Gladstone Institutes / UCSF before co-founding Wildtype, a startup in San Francisco developing cellular agriculture technologies for a clean and accessible seafood future. He currently oversees

the company's scientific research programs, including cell and molecular biology, tissue engineering, bioprocess development, food science, and media development. He continues to practice medicine in the critical care setting. Thursday 25th April • 14:50

3rd edition EMBL - IBEC Conference ENGINEERING MULTICELLULAR SYSTEMS

### Access and Affordability Paradigms for Advanced Biomedical Technologies Ubaka Ogbogu

In recent years, several approved advanced therapies (encompassing cell, gene and tissue-engineered therapies) have been withdrawn from the market for reasons linke

tissue-engineered therapies) have been withdrawn from the market for reasons linked mainly or in part to steep pricing and consequently, failure to attract willing payers. These therapies, along with others that remain on the market, almost exclusively target healthcare payers and patients in high-resource settings, thus limiting access for patients in low-resource settings. In this presentation, I argue that both trends create affordability and access "valleys of death" for advanced therapies that *will*, in turn, undermine clinical translation of promising preclinical research and deepen existing challenges that academic researchers face with pushing innovation across the biomedical valley of death. I also argue that overcoming these upstream translational research challenges requires interventions that both attenuate cost and access barriers and transform the imperatives driving biomedical research.



### Ubaka Ogbogu University of Alberta, Canada.

Ubaka Ogbogu is a Professor and the Associate Dean Research in the Faculty of Law. He is a Member of the Royal Society of Canada's College of New Scholars, Artists and Scientists (2023 Cohort) and the Chair of the University of Alberta Research Ethics Board 2. Dr. Ogbogu is a recipient of the Confederation of Alberta Faculty Associations Distinguished Academic Early Career Award. He holds a doctorate in law from the

University of Toronto, a Master of Laws degree from the University of Alberta and undergraduate degrees in law from the University of Benin, Nigeria and the Nigerian Law School. Ogbogu's scholarly work is focused broadly on the ethical, legal and societal implications of novel and emerging biotechnologies and associated research. His publications have explored a diverse range of issues in this field, including the ethical and legal issues associated with stem cell research, gene and engineered cell therapies, biobanks, germline gene editing and assisted reproductive technologies. As a multidisciplinary scholar, his teaching and research activities explore and cut across various fields, including health law, bioethics, science policy, science and technology studies, public health, legal history and legal philosophy. He has led or been involved in many prominent national and international biotechnology policymaking activities and writes and comments frequently in the popular press on matters relating to the impacts of biotechnology and science on society. Ogbogu has served on numerous boards and councils, including the Health Quality Council of Alberta, Council of Canadian Academies Expert Panel on Somatic Gene and Engineered Cell Therapies. the Council of Canadian Academies Expert Panel on Medical Assistance in Dying, the Canadian Institutes of Health Research (CIHR) Stem Cell Oversight Committee, the Canadian Institutes of Health Research Governing Council's Standing Committee on Ethics, and the International Society for Stem Cell Research Task Force on Guidelines for Stem Cell Research and Clinical Translation.

Thursday 25th April • 15:20

### 3rd edition EMBL - IBEC Conference ENGINEERING MULTICELLULAR SYSTEMS

## Building Organoids by learning signaling gradients

Sharad Ramanathan

I will present recent results from our work on learning appropriate spatial gradients of signals to achieve the desired patterning of organoids. The methods include a combination of bioengineering and statistical learning.

Using these methods I will demonstrate our successes in robustly patterning the posterior neural tube and flanking mesodermal tissues. I will also present recent results on patterning the anterior neural tube. Finally I will present some methods to exploit these in vitro systems to uncover the mechanisms underlying cell fate decision and morphogenesis.


#### Sharad Ramanathan Harvard University, USA.

Sharad Ramanathan was trained as a theoretical physicist and was a member of technical staff in the theoretical physics department at Bell labs. He is currently the Lllura and Gordon Gund Professor of Neurosciences and of Molecular and Cellular Biology, as well as a professor of Applied Physics and of Stem Cell and Regenerative Biology. His recent work has focused on developing robust models for human

development and uncovering cell types and developmental mechanisms that are unique to humans.

Thursday 25th April • 16:15

### 3rd edition EMBL - IBEC Conference ENGINEERING MULTICELLULAR SYSTEMS

# Stem Cell Modeling of Human Embryonic Development

#### Berna Sozen

The foundation of the human body plan is laid during early embryogenesis. However, our understanding of early human development is significantly constrained by current ethical and technical limitations. In recent years, considerable effort has been devoted to overcoming these barriers through the development of advanced in vitro engineering approaches, leveraging the self-organizing properties of stem cells derived from embryos. Our study introduces a new strategy that illustrates how human pluripotent stem cells can be prompted to autonomously organize into threedimensional structures. These structures recapitulate key spatiotemporal events of early human post-implantation embryonic development. This system consistently captures the spontaneous differentiation and co-development of embryonic epiblastlike and extra-embryonic hypoblast-like lineages, establishes crucial signaling hubs with secreted modulators, and undergoes events reminiscent of symmetry breaking. A comprehensive understanding of the interconnected cellular events in this system is essential for advancing our knowledge of developmental and reproductive health, offering a unique opportunity to unravel the cellular and molecular mechanisms underlying early miscarriage and congenital pathologies.



#### Berna Sozen Yale University, USA.

Berna Sozen is an Assistant Professor at Yale University Department of Genetics and secondary faculty at the Department of Ob/Gyn & Reproductive Sciences. Originally trained as a Reproductive Biologist, Berna later pursued studies in Developmental Stem Cell Biology at the University of Cambridge and CalTech. Her research group currently integrates in vivo embryos and in vitro stem cell systems to investigate key

mechanisms shaping both local and global embryonic structures and how metabolic signals coordinate cellular functions in mouse and human development, with a long-term aim to understand the origins of developmental disease.

Thursday 25th April • 17:00

### 3rd edition EMBL - IBEC Conference ENGINEERING MULTICELLULAR SYSTEMS

# Approaches to engineering spatially organized multicellular systems.

Jamie Davies

This talk will present 3 approaches to making spatially-organized multicellular systems. The approaches lie on a spectrum of how much control comes from outside, and how much lies within cells themselves. An example of control coming mostly from outside is provided by engineering cells with optogenetic systems, and using light, directed at specific times and places, to control cell behaviour relatively directly. At the other end of the spectrum is the approach of working with the natural agency of wild-type cells. Local sources of natural signalling factors can, for example, be used to impose spatial control on the development of wild-type organoids to improve their anatomies. Unusual environments can surface novel behaviours from even wild-type cells, as in self-reproducing Xenobots. Between these is the approach of engineering new behaviours into cells, so that in the right environment they have the agency to produce desired patterns and structures for themselves. Each has its advantages and disadvantages, in terms of scaleability, safety and precision. These will be explored in the talk.



#### Jamie Davies University of Edinburgh, Scotland.

Jamie Davies is Professor of Experimental Anatomy at the University of Edinburgh, Scotland. He is a scientistengineer with an interest in how simple things become complicated. His lab studies organ development, by 'wetlab' techniques and computer modelling, and applies knowledge gained to the problem of engineering realistic tissues and organs from stem cells. This is coupled to an

interest in engineering completely novel forms of development using the techniques of synthetic biology. The lab also hosts the main drug database of the International Union of Basic and Clinical Pharmacology. He has published over 200 research papers and 11 books on these topics.

Friday 26th April • 09:00

### 3rd edition EMBL - IBEC Conference ENGINEERING MULTICELLULAR SYSTEMS

### To brain or not to brain: Using organoids to uncover how brain cell fate is determined Madeline Lancaster

The human brain sets us apart as a species, yet how it develops and functions differently to that of other mammals is still largely unclear. This also makes it difficult to understand how disorders of the brain such as neurodevelopmental defects and neurological disorders arise, and therefore how to treat them. In an effort to better understand the events that give rise to the complex human brain, we use a model system in a dish called cerebral organoids, or brain organoids. These 3D tissues are generated from pluripotent stem cells through neural differentiation and a supportive 3D microenvironment to generate organoids with the same tissue architecture as the early human fetal brain. Such organoids are allowing us to tackle questions previously impossible with more traditional approaches. Indeed, our recent findings provide insight into how the human brain becomes so large, and how external stimuli can influence brain development.

Organoids can also be generated from patient-derived cells and are therefore providing new insight into how human conditions arise and even uncovering new drugs that can be used to treat these conditions. But the use of various starting cell lines brings with it certain issues related to reproducibility, as cell line variability can be a major hurdle for organoids and in vitro models in general. We have begun exploring why certain cell lines succeed at generating brain organoids and others do not, which has revealed a specific epigenetic footprint associated with suboptimal performing cell lines that can be reversed using a cocktail of small molecules. Not only can this technique open the door to more reliable disease modelling and therapeutics discovery, it is also revealing insight into the earliest stages of pluripotent stem cell fate determination.



#### Dr Madeline Lancaster Group Leader Human brain development in cerebral organoids

Dr Madeline Lancaster is a Group Leader in the Cell Biology Division of the Medical Research Council Laboratory of Molecular Biology (LMB), part of the Cambridge Biomedical Campus in Cambridge, UK. Madeline joined the LMB in 2015, after completing a postdoctoral fellowship at the Institute of Molecular Biotechnology of the Austrian

Academy of Sciences (IMBA) in Vienna, where she developed brain organoids.

Research in the Lancaster lab focuses on human brain development using stem cells to generate brain organoids that allow modelling of human brain development in vitro. The laboratory studies the most fundamental differences between human brain development and that of other mammalian species. The lab also studies cellular mechanisms underlying neurodevelopmental disorders such as autism and intellectual disability.

Madeline was awarded the 3Rs Prize by the National Centre for Replacement, Refinement and Reduction of Animals in Research (NC3Rs) in 2015 for her development of brain organoids, and was chosen as an EMBO Young Investigator in 2019. She was awarded the International Society for Stem Cell Research (ISSCR) Dr Susan Lim Award for Outstanding Young Investigator and a Vallee Scholarship in 2021. Madeline was honoured as the Laureate for Life Sciences in the Blavatnik Award for Young Scientists in the UK and was elected an EMBO member in 2022. Friday 26th April • 09:45

3rd edition EMBL - IBEC Conference ENGINEERING MULTICELLULAR SYSTEMS

## Programming intercellular communication to assemble engineered neuromuscular systems Ritu Raman

Human beings and other biological creatures navigate unpredictable and dynamic environments by leveraging the motor control system, which integrates the compliant actuation of skeletal muscle with neural control and sensory feedback. Our lab is focused on assembling hierarchical neuromuscular tissues in vitro, with the goal of mapping and modulating intercellular communication in this complex multicellular system. This talk will focus on decoupling mechanical and biochemical signaling within tissues to program muscle-nerve crosstalk in physiological and pathological states. We will cover applications of our technologies in human disease as well as in next-generation soft robotics.



#### Ritu Raman Massachussetts Institute of Technology, USA.

Ritu Raman, PhD is the d'Arbeloff Career Development Assistant Professor of Mechanical Engineering at MIT. Prof. Raman has received several recognitions for scientific innovation, including the NSF CAREER Award, the Army Research Office YIP Award, the Office of Naval Research YIP Award, and being named a Kavli

Fellow by the National Academy of Sciences. She has also been named to the Forbes 30 Under 30 and MIT Technology Review 35 Innovators Under 35 lists, and is the author of the MIT Press book Biofabrication. She is passionate about increasing diversity in STEM and has championed many initiatives to empower women in science, including being named a AAAS IF/ THEN ambassador and founding the Women in Innovation and STEM Database at MIT (WISDM). Prof. Raman received her BS from Cornell University and her PhD as an NSF Graduate Research Fellow at the University of Illinois at Urbana-Champaign. She completed her postdoctoral research with Prof. Robert Langer at MIT, funded by a L'Oréal USA For Women in Science Fellowship and a Ford Foundation Fellowship from the National Academies of Sciences, Engineering, and Medicine. Friday 26th April  $\cdot$  11:45

3rd edition EMBL - IBEC Conference ENGINEERING MULTICELLULAR SYSTEMS

# Break to build: exploring the role of fracture during morphogenesis

Alejando Torres-Sánchez

"Although one might intuitively think that biological tissues have evolved to resist mechanical fracture, it is becoming apparent that tissues undergo fracture routinely as part of their biological function, especially during development. Here I will discuss the role of fracture in two different morphogenetic processes. First, I will examine the role of hydraulic fracture and coarsening during lumen formation, using a combination of *in vitro* and computational models. I will also discuss how fracture of the extracellular matrix due to mechanical stretch during heart development in zebrafish acts an essential patterning mechanism for trabeculation. I will show that a mechanical model of the extracellular matrix incorporating mechanical deformation and damage explains the patterning of fractures *in vivo*."



#### Alejando Torres-Sánchez EMBL Barcelona, Spain.

Alejandro Torres-Sánchez leads a research group at the European Molecular Biology Laboratory (EMBL) in Barcelona. He earned his PhD in Applied Mathematics from the Polytechnic University of Catalonia in 2017. Following postdoctoral work at the Francis Crick Institute and the Institute for Bioengineering of Catalonia, Alejandro established his own group at EMBL-

Barcelona in 2022. His group integrates methods from theoretical physics and computational engineering to develop mathematical models and computer simulations of cells and tissues. In collaboration with experimentalists, his group applies these methods to understand the physical principles that underpin tissue self-organisation and shape generation. Some of their current interests are the role of mechanical fracture during morphogenesis, the multiscale properties of tissue rheology, and the generation of large-scale tissue flows and deformations during embryogenesis. Friday 26th April • 12:30

### 3rd edition EMBL - IBEC Conference ENGINEERING MULTICELLULAR SYSTEMS

# Retinal Organoid Transplantation

Masayo Takahashi MD. PhD.<sup>1,2,3</sup>

1) Vision Care Inc.
2) Kobe Eye Center

3) Ritsumeikan Univ.

We started the first in man application of iPSC in 2013 as retinal pigment epithelial cell transplantation. Since then, we improved the formulation to achieve the most effect.

The next challenge is photoreceptor replacement. iPSC-retinal organoid transplantation is a promising treatment to restore visual function to degenerated retinas. We proved that grafted photoreceptor cells formed synapses only when they were transplanted in the form of organoids. They showed the functional recovery in the completely photoreceptor degenerated blind mice after transplantation. With those findings as POC, we performed clinical study using retinal organoid for retinitis pigmentosa.

The presence of secondary neurons restrains photoreceptors from making contact with the host secondary neurons in some area. For this, as a next generation we prepared a bipolar differentiation factor islet-1 gene KO iPSC line with a similar in vitro retinal differentiation potency to wildtype cell lines. After transplantation, KO iPSC-retinas readily integrated to the host, with an apparently improved contact judging by the overall proximity of graft photoreceptor cells and host bipolar cells.



#### Masayo Takahashi Riken, Japan.

Masayo Takahashi is a Japanese ophthalmologist and stem cell researcher. She received her MD, PhD from Kyoto University and worked as a retinal surgeon at the Kyoto University Hospital (finally as an Associate Professor). She became a visiting researcher in the Salk Institute in the USA and started the stem cell research in 1995. She joined the RIKEN Center for Developmental Biology in

Kobe, Japan in 2006, where she began to focus on developing new therapies for retinal diseases using stem cells.

Takahashi is known for leading the world's first clinical study of induced pluripotent stem cell-based therapy in 2013. The trial involved transplanting retinal cells differentiated from autologous iPSCs into the patient's eye with age-related macular degeneration (AMD). The initial trial was successful, and a larger clinical study using HLA matched allogeneic iPSCs was launched in 2017 to test the therapy's safety and efficacy.

Takahashi has received numerous awards and honors for her work, including the Commendation for Science and Technology by the Japan Minister of Education, Culture, Sports, Science and Technology, one of the country's most prestigious scientific awards. She is also a board member of the Japanese Society for Regenerative Medicine, and Japanese Retina and Vitreous Society.

In addition to her work on stem cell therapies for retinal diseases, Takahashi's team has also been involved and leading the low vision care field through NPO called 'NEXT VISION'. Her contributions to the field of regenerative medicine using iPSCs and patients care have been significant, and she continues to be a leader in the field of ophthalmology and stem cell research.

# Short talks

Institu

Wednesday 24th April · 10:30

### 3rd edition EMBL - IBEC Conference ENGINEERING MULTICELLULAR SYSTEMS

# Size control of in vitro somites

Costanzo M., Sanaki-Matsumiya M., Gritti N., Trivedi V., Ebisuya M.

Somites, the precursors of our body vertebrae, ribs, and skeletal muscles, emerge as repetitive structures lining either side of the neural tube during the post-gastrulating embryo development. Different models have been proposed so far to explain somite size determination, with classical ones pointing to patterning and global positional information as a possible answer (e.g. the clock and wavefront model), and more recent ones emphasizing the role of local cell-cell interactions in self-organizing the somite unit. Recently, a 3D in vitro model of human somitogenesis has been established in our lab, starting from human induced pluripotent stem cells (iPSCs): the somitoids. Interestingly, when we increase the number of cells to aggregate to make the somitoids, the size of the somites remains constant despite the overall size of the organoid getting bigger. This non-scaling behavior of somites makes human somitoids a suitable model to investigate which factors control somite size in vitro. Quantifying the tissue proportions in somitoids of different sizes, we found out that another tissue displays similar behavior as the somites: the presomitic mesoderm, which is the source of somites themselves. We hypothesize that the size of in vitro somites is controlled because a size control mechanism is acting upstream, on the presomitic mesoderm. Our current focus is therefore trying to understand how the size of presomitic mesoderm is controlled and how the regulation of this tissue proportion can change during somitoids development.

## Mechanics of Human and Mouse Embryo Implantation

**Amélie L. Godeau**<sup>1</sup>, Anna Seriola<sup>1</sup>, Oren Tchaicheeyan<sup>2</sup>, Marc Casals<sup>1</sup>, Denitza Denkova<sup>1</sup>, Ester Aroca<sup>1</sup>, Albert Parra<sup>1</sup>, Maria Demestre<sup>1</sup>, Anna Ferrer-Vaquer<sup>1</sup>, Shahar Goren<sup>2</sup>, Anna Veiga<sup>4</sup>, Miquel Solé5, Montse Boada<sup>5</sup>, Jordi Comelles<sup>1,6</sup>, Elena Martínez<sup>1,6,7</sup>, Julien Colombelli<sup>8</sup>, Ayelet Lesman<sup>2,3</sup>, Samuel Ojosnegros<sup>1</sup>

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<sup>2</sup> School of Mechanical Engineering, Faculty of Engineering, Tel-Aviv University, Tel-Aviv, 55 Chaim Levanon St., Ramat Aviv 69978, Israel.

<sup>3</sup> Center for Physics and Chemistry of Living Systems, Tel Aviv University, Tel-Aviv, 55 Chaim Levanon St., Ramat Aviv 69978, Israel.

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<sup>5</sup> Reproductive Medicine Unit, Department of Obstetrics, Gynaecology and Reproduction, Dexeus Mujer, Hospital Universitari Dexeus, Gran Vía Carles III, 71-75, 08028, Barcelona, Spain

<sup>6</sup> Department of Electronics and Biomedical Engineering, University of Barcelona (UB), c/Martí i Franquès 1-11, 08028 Barcelona, Spain

<sup>7</sup> Centro de Investigación Biomédica en Red (CIBER), Av. Monforte de Lemos 3-5, Pabellón 11, Planta 0, 28029 Madrid, Spain

<sup>8</sup> Institute for Research in Biomedicine (IRB Barcelona), The Barcelona Institute of Science and Technology, Barcelona 08028, Spain

During implantation, the mammalian embryo establishes attachment to the endometrium, the lining of the maternal uterus, followed by invasion into the underlying tissue. To understand how embryos penetrate the collagen-rich endometrial stroma, we have developed an innovative hydrogel-based ex-vivo platform supporting traction force microscopy. We reveal the forces applied by human and mouse embryos and recapitulate implantation specificities of both species in our platform. Mouse embryos exhibit limited penetration depth whereas human embryos integrate into the matrix. Nevertheless, both types of embryos apply forces during implantation resulting in the remodelling of the collagen matrix. Interestingly, the applied forces lead to distinct displacement patterns: Isotropic radial displacement for human and anisotropic with main displacement axes for mouse embryos.

Blocking force transmission through integrins, specifically  $\beta$ 5 and  $\beta$ 3 integrins with a cyclic pentapeptide or Src kinase with dasatinib, reduces the size of mouse embryos and their matrix displacement. Notably, when placed pairwise, embryos form tension-bearing mechanical bridges between them, leading to collagen densification and directed matrix displacement along the connecting axis.

Furthermore, both human and mouse embryos exhibit mechanosensitive responses to an external mechanical stimulus: The mouse embryo either orients its growth direction or aligns its axis relative to the external force cue. The human embryo recruits phosphorylated myosin basally and forms a cellular protrusion towards the external force cue.

In conclusion, our findings highlight the intricate mechanical interactions between embryos and their environments and mechanosensitive capacity of embryos during implantation. We suggest that mechanical forces may play an important role in guiding the invasion of the extracellular matrix during implantation.

## Artificial extracellular matrices based on 3D hybrid hydrogels for immune cell and organoid manufacture

Miquel Castellote-Borrell <sup>1,2</sup>, Francesca Merlina<sup>1,2,</sup> Adrián Rodriguez<sup>1,2</sup>, Fabião Santos<sup>1,3</sup>, Eduardo Pérez del Río<sup>1,3</sup>, **Judith Guasch**<sup>1,2,3</sup>

<sup>1</sup> Institute of Materials Science of Barcelona (ICMAB-CSIC), Campus UAB, 08193 Bellaterra, Spain

<sup>2</sup> Dynamic Biomaterials for Cancer Immunotherapy, Max Planck Partner Group (ICMAB- CSIC), Campus UAB, 08193 Bellaterra, Spain

<sup>3</sup> Centro de Investigación Biomédica en Red de Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), Instituto de Salud Carlos III, Campus UAB, 08193 Bellaterra, Spain

Artificial extracellular matrices (ECM) based on 3D hydrogels consisting of covalently crosslinked polyethylene(glycol) and heparin have been developed, which can easily be loaded with positively charged biomolecules through electrostatic interactions.<sup>1</sup> To finely control both the structural and mechanical properties of these 3D hydrogels, we have used different manufacturing procedures, such us the inverse opal technique or 3D printing.<sup>2</sup>

These PEG-heparin hydrogels were designed to mimic the ECM of healthy secondary lymphoid organs, in particular the lymph nodes, with the objective of improving the current T cell expansion technologies. In particular, our goal was to obtain in vivo persistent CAR T cells; a current limitation of the adoptive cell (immuno)therapies. Indeed, we have been able to increase the proliferation of primary human CD4+ T cells, when compared with state-of-the- art expansion systems, while maintaining therapeutically desired phenotypes.1-2 Additionally, we tailored our 3D hydrogels to mimic the ECM of malignant tissues with the aim of creating well-controlled and reproducible patient-derived tumoroids.

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Wednesday 24th April · 16:30

### 3rd edition EMBL - IBEC Conference ENGINEERING MULTICELLULAR SYSTEMS

# Nematically-guided morphogenesis

#### **Pau Guillamat**<sup>1</sup>, Waleed Mirza<sup>2</sup>, Pradeep K. Bal<sup>3</sup>, Manuel Gómez-González<sup>1</sup>, Marino Arroyo<sup>3</sup>, Xavier Trepat<sup>1</sup>

<sup>1</sup> Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute for Science and Technology (BIST), Barcelona, Catalunya.

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<sup>3</sup> LaCàN, Universitat Politècnica de Catalunya (UPC) – BarcelonaTech, Barcelona, Catalunya

Tissue morphogenesis relies on the orchestration of subcellular contractility into supracellular force patterns by multicellular assemblies, governed by an interplay of chemical and physical cues<sup>1</sup>. Despite the numerous scientific opportunities associated with the creation of synthetic tissues, both in fundamental and applied contexts, the precise control of tissue reshaping in vitro continues to pose a significant challenge<sup>2</sup>. To address this, it is crucial to develop experimental systems that leverage the inherent self-organization mechanisms of living tissues to promote force patterns leading to specific morphogenetic transformations. For instance, in tissues composed of elongated cells, force organization is dominated by the orientation of cells in nematically-ordered domains and the presence of topological defects, regions where the order is lost<sup>3</sup>. Here, we harness these characteristics, known to provide unique mechanical cues crucial for tissue remodelling<sup>4-7</sup>, to induce pre-defined tissue deformations. In particular, by directly controlling cellular orientation and topological defects, we obtain cellular monolayers that feature nematically-guided tension patterns, which can be released via out- of-plane deformations into reproducible three-dimensional tissue shapes. By enabling the mapping of morphogenetic events within living tissues, this strategy has the potential to open doors to applications across diverse fields, ranging from tissue engineering to soft robotics.

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## Replicating Dynamic Immune Responses within a Microfluidic Human Skin Equivalent Model

**Sarah Hindle**, Dr. Liisa Blowes, Dr. Bhumika Singh, Dr. Matthew Caley and Prof. John Connelly

Blizard Institute, Department of Cell Biology and Cutaneous Research, Barts and the London School of Medicine and Dentistry, Queen Mary University of London.

Dynamic communication between tissue resident cells and circulating immune cells, including monocytes, orchestrates the skin's responses to infection and plays a role in tissue repair and regeneration. However, the factors that drive monocyte recruitment into human skin during inflammatory events and the signals that direct monocyte fate are poorly understood. Current 3D in vitro models recapitulate the structure of skin by fabricating dermal and epidermal-like layers. However, only a limited number of in vitro skin models have incorporated immune cells, and these do not effectively model the complex and dynamic interactions between the tissue and immune system. This research aimed to gain new insights into human-specific inflammatory responses within skin, through the development of a novel immune-responsive in vitro model, using 3D bioprinting technology. A microfluidic human skin equivalent (HSE) was constructed by 3D printing a sacrificial gelatin microchannel template within a fibroblast embedded fibrin hydrogel. The microchannel template was then selectively removed by melting the gelatin at 37∞C. The hollow microchannel was then lined with human endothelial cells, mimicking a vascularised dermis. Human keratinocytes were cultured on the surface of the construct to create mimic the epidermis.

Dynamic immune responses in the HSE were investigated by exposing the epidermal layer to lipopolysaccharide and nigericin, activating the inflammasome and inducing the secretion of cytokines, including IL-1 $\beta$  and IL-18. The vascular microchannel was then employed as a conduit for the delivery of primary CD14+ monocytes, and monocyte trafficking into the tissue was investigated by live confocal microscopy. Monocyte fate within the microfluidic HSE was first investigated using whole mount immunofluorescence staining for tissue resident macrophages. CD68+ and CD163+ cells could be identified within the dermal and epidermal compartments in both control and treated day 1 and day 6 conditions, with significantly increased numbers (2-3 fold) of recruited cells in the treated conditions, compared to controls.

Single cell transcriptomic analysis (10X Genomics) of the microfluidic HSE revealed dynamic transcriptional responses activated by inflammation in the resident skin cell populations and monocytes. Monocyte-derived cells displayed early inflammatory and migratory gene signatures at day 1, which resolved by day 6. Three distinct monocyte-derived clusters were identified in the day 6 samples, and results demonstrated the plasticity and differential potential of recruited monocytes within the in vitro model.

Additionally, the gene signatures of these populations closely aligned with the profiles of resident myeloid cells in existing in vivo human skin datasets. Further analysis of putative inter-cellular signalling networks (CellPhoneDB) identified not only expected chemokine and cytokine interactions in the inflamed conditions, but also integrin, semaphorin, Wnt and Notch signalling between resident cell populations and monocytes. Furthermore, potentially novel nectin-nectin interactions were identified between keratinocytes and monocyte-derived cells.

Overall, the microfluidic HSE developed here accurately modelled dynamic immune responses in human skin and could be a powerful tool in drug development and discovery research.

#### Harnessing the rhythmic biology of early kidney formation for synthetic morphogenesis Viola, J.M., Liu, J., Grindel, S.H., Davis, S., Prahl, L.S., Huang, A., Chan, T.J., Hayward-Lara, G., Porter, C.M., Zhang, J. and **Hughes, A.J.**<sup>1-6</sup>

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<sup>5</sup> Center for Soft and Living Matter, University of Pennsylvania, Philadelphia, 19104, PA, USA.

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In this work we discover rhythmic mechanical and differentiation 'pace-making' in nephron-forming kidney niches using live imaging, packing theory, organoids, and spatial sequencing. We apply these new rhythmic biology principles to human kidney organoid engineering for regenerative medicine.

The kidney develops through branching of ureteric bud epithelial tubules (the future urinary collecting ducts), stroma, and nephron progenitors in the cap mesenchyme that surrounds each tubule tip. Dynamic interactions between these tissues set nephron numbers for life, impacting adult disease. How then are the rates of nephron formation and ureteric tubule branching balanced? Here we study the consequences of tubule tip packing at the embryonic kidney surface for tip organization and nephron formation. Over developmental time, kidney curvature reduces and 'tip domains' pack more closely, creating a semicrystalline tip geometry at the kidney surface. This causes a rigidity transition to more solid-like tissue properties at later developmental stages, confirmed by micromechanical measurements. We then define a tip 'life- cycle' between branching events, and find that nephrogenesis rate varies over this life-cycle. We show that tip domains experience a cyclical mechanical transient over each life-cycle. We then hypothesized that tip duplication periodically creates a mechanical microenvironment permissive to nephrogenesis. Indeed, mimicking a mechanical transient in human iPSC-derived nephron progenitor organoids increased Wnt-driven commitment to early nephron cell aggregates. The data suggest that temporal waves of mechanical stress within nephron progenitor populations could constitute a clock that synchronizes nephron formation and ureteric tubule duplication. We went on to find that the avalanche-like commitment of nephron progenitors to early nephrons reflects rhythmic transcriptional priming associated with the ureteric bud branch life-cycle using spatial sequencing. This acts to peg nephron formation rate to the ureteric bud branching rate. This rhythm shares features with the somitogenesis clock, an intriguing observation for future study. We next observe significant changes in renewal vs. differentiation and subsequent nephron segmentation upon mimicking rhythmic YAP and retinoic acid signaling in nephron progenitor organoids. This new rhythmic biology principle presents the opportunity to create self-sustaining nephrogenic niches in vitro by mimicking cycles of alternating differentiation and renewal cues. Ongoing work will clarify variation in nephron endowment between kidneys and advance engineered replacement kidney tissues for regenerative medicine.

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# Role of mechanotransduction in the control of interneurons migration in the cortex

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Cortical interneurons (cINs) are born in the ganglionic eminences (GE) and enter into multiple tangential routes to reach the cortex. While migrating, cINs are subjected to mechanical forces arising from cellular interactions and the extracellular matrix. Here we aim to understand how mechanotransduction events may shape cINs behaviour during cortical development. By combining atomic force microscopy (AFM) with time-lapse recordings we found that the intermediate zone gets stiffer at E16.5 as compared to E13.5, which also correlates with cINs migrating slower and with a reduced nuclear translocation frequency. These migration differences were also seen between E13.5 and E16.5 cINs cultured within a viscous 3D environment. Using heterochronic organotypic slices, we showed that the migration of E16.5 cINs within heterochronic cortex (i.e. E13.5) induced an increase of speed and frequency as compared to the controls. By performing single cell AFM we found that E16.5 cINs exhibit softer somas and display higher nuclear deformations while migrating. Finally, transcriptomic data from cINs at both stages indicated differences in expression of key nuclear and mechanotransduction genes during development. Our findings suggest that while migrating, E16.5 cINs might be more sensitive to environmental changes in part due to their viscoelastic properties which would allow them to integrate shifts of substrate stiffness and adapt their migratory behavior.

# SHAPE: Investigating innate immunity in real microgravity aboard the International Space Station using advanced human bone marrow organoids.

#### Ryan Sarkar, Louise Breideband, Francesco Pampaloni<sup>1</sup>

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In 2025, NASA through their Artemis program aims to send humans beyond Low-Earth Orbit for the first time since 1972. As focus on space exploration shifts from the International Space Station (ISS) to targets farther away, the impact of longduration space travel on the human body and the ability to withstand these effects are becoming the primary factors precluding further expansion of humanity's reach into space. The space environment poses numerous unique challenges to astronauts, with typical examples including immune dysfunction and the loss of bone density.

Advanced bone marrow organoids comprised of primary human mesenchymal and hematopoietic stem cells were developed to investigate links between those two phenomena in real microgravity aboard the ISS. The unique spatial requirements necessitated development of a novel system, termed Hydrowells, to facilitate the long-term culture and subsequent fixation of many organoids in a small volume, remotely. Validating Hydrowells as a suitable system for 3D *in vitro* experiments in space allows for future experiments with diverse model systems.

The SHAPE project flew over 2,000 organoids to the ISS to investigate innate immunity in vitro in real microgravity. Morphological analysis demonstrated compact organoids with a hematopoietic stem cell niche under earth gravity while space led to looser cell aggregates. The ISS data will be compared to samples cultured in simulated microgravity, centrifuge controls, and earth gravity. Furthermore, MACE-sequencing (Massive Analysis of cDNA Ends) is currently underway to provide insight into the effects of different gravitational conditions on gene expression regarding innate immunity.

Technical insight from SHAPE and the Hydrowells facilitates future 3D *in vitro* experiments in real microgravity with culture systems as diverse as gastruloids. The results from SHAPE will increase understanding of the interplay between innate immunity and bone morphology in space, enabling the mitigation of health risks to astronauts and freeing humanity to explore our galaxy further.

Friday 26th April • 09:30

#### 3rd edition EMBL - IBEC Conference ENGINEERING MULTICELLULAR SYSTEMS

## Hormonal Regulation of Germ Layer Specification in Micropatterned Gastruloids Joana Silva<sup>1</sup>, Vikas Trivedi<sup>1</sup>, Kristina Haase<sup>1</sup>

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Hormones play a crucial role in successful embryo implantation and pregnancy outcomes, and have been identified as key players in early differentiation processes. For instance, progesterone stimulation has increased the number of somites in mouse embryos and human chorionic gonadotropin induced neural rosettes in embryoid bodies. However, the direct impact of hormones on early embryonic development remains poorly understood given the limited knowledge of the underlying cellular mechanisms and difficulty to study them from both technical and ethical perspectives in vivo. To bridge this gap in knowledge, we employ an in vitro technique using human pluripotent stem cell (hPSC) micropatterns to investigate the role of progesterone, estrogen, and human chorionic gonadotropin during a gastrulation-like process.

Receptors for estrogen and progesterone are highly expressed in hPSC micropatterns during pluripotency. Thus, we hypothesised hormones may regulate differentiation and the formation of germ layers. Surprisingly, exogenous hormonal stimulation did not disrupt the differentiation of micropatterned gastruloids into ectoderm, mesoderm, endoderm, or the extra-embryonic trophectoderm. Inhibiting estrogen signalling, at the aromatase or receptor levels, suppresses mesendoderm emergence, resulting in the absence of Brachyury and Sox17 expression. Rescue with exogenous estrogen was not successful; however, WNT/Nodal activation reestablishes mesendoderm formation.

Overall, germ layer formation progresses normally in hPSC micropatterns in the presence of pregnancy-related hormones, yet, disrupting estrogen signalling suppresses mesendoderm emergence. These findings highlight a possible interaction between WNT/Nodal and estrogen in germ layer formation during early development. We are also exploring whether impaired hormone signalling in mouse 3D gastruloids similarly affects germ layer specification, which may have wide-implications for the role of hormones in early developing mammals.

# DNA microbeads for spatio-temporally controlled morphogen release within organoids

Tobias Walther, Cassian Afting, Joachim Wittbrodt, Kerstin Göpfrich

Max Planck Institute for Medical Research

Organoids have proven to be powerful in vitro model systems that mimic features of the corresponding tissue in vivo. However, across tissue types and species, organoids still often fail to reach full maturity and function, because biochemical cues cannot be provided from within the organoid to guide their development. The establishment of such tools has been identified as a major goal of the field. Here, we introduce DNA microbeads as a novel tool for implementing spatio-temporally controlled morphogen gradients inside of organoids at any point in their life cycle. The DNA microbeads are formed in a simple one-pot process, they can be stored for a year and their viscoelastic behavior and surface modification is tunable to mimic the corresponding tissue. Employing medaka retinal organoids and early embryos, we show that DNA microbeads can be integrated into embryos and organoids by microinjection and erased in a non-invasive manner with light. Coupling a recombinant surrogate Wht to the DNA microbeads we demonstrate the spatio-temporally controlled release of the morphogen from the microinjection site, which leads to the formation of retinal pigmented epithelium while maintaining neuroretinal ganglion cells. We were thus able to bioengineer retinal organoids to more closely mirror the cell type diversity of in vivo retinas. The DNA microbead technology can easily be adapted to other organoid applications for improved tissue mimicry.

# Posters

5

Posters

N	Name	Affiliation	Title
1	Aina Abad	Institute for Bioengineering of Catalonia (IBEC)	Long-range organization of primary intestinal fibroblasts guides in vitro epithelial migration through the secretion of aligned extracellular matrix proteins
2	Juan Francisco Abenza Martínez	Institute for Bioengineering of Catalonia (IBEC)	Mechanical control of the mammalian circadian clock via YAP/TAZ
3	Gaia Amato	Institute for Bioengineering of Catalonia (IBEC)	Developing Human Organoids To Model Genetic And Systemic Conditions During Congenital Anomalies Of The Kidney And Urinary Tract.
4	Maria José Antunes Sintra	EMBL	In vitro recapitulation of heterochrony during vertebrate anterior?posterior axis development
5	Katia Barrett	IBDM	Epithelial-mesenchymal coupling drives axis elongation in Xenopus explants
6	Nataliya Basalova	Lomonosov Moscow State University	Dynamics of fibrotic foci formation during bleomycin-induced pulmonary fibrosis in mice
7	Alina Batzilla	EMBL Barcelona	The contribution of the innate immune response to blood-brain barrier breakdown in Cerebral Malaria
8	Dirk Benzinger	The Francis Crick Institute	Optogenetic engineering of morphogen gradients recapitulates dynamic neural tube patterning
9	Valentin Bonnet	Institut Pasteur / Ecole Polytechnique	Deciphering the impact of the APC mutation on CAR T cells cytotoxicity using mouse and patient-derived 3D models in microfluidics.

10	Miquel Bosch Padrós	Institute for Bioengineering of Catalonia (IBEC)	Mechanics of apical constriction: an optogenetic approach
11	Louise Breideband	BMLS, Goethe University Frankfurt a.M.	Upgrading a Consumer Stereolithographic 3D Printer to Produce Physiologically Relevant Cancer Models
12	Joan Casamitjana	UB / IDIBELL	A single-cell atlas of the murine pancreatic ductal tree identifies novel cell populations with potential implications in pancreas regeneration and exocrine pathogenesis.
13	Maria Costanzo	EMBL Barcelona	Size control of in vitro somites
14	Ibrahim Halilullah Erbay	University of Galway/ IBEC	Integrated Computational-Experimental Analysis of Shear Impact on Intestinal Crypt Dynamics and Mucus Mechanics
15	Hiromune Eto	Hubrecht Institute	Microfluidic control of Notch signalling reveals a dynamic communication code for cell fate determination during intestinal homeostasis
16	Laura Faure	Institute for Bioengineering of Catalonia (IBEC)	3D micropatterned traction force microscopy : a new technique revels that single epithelial cells can exert pushing forces on their environment
17	Ainhoa Ferret Miñana	Institute for Bioengineering of Catalonia (IBEC)	3D bioengineered liver for the study of acute and chronic hepatic damage
18	Daniel Garcia- Gonzalez	Universidad Carlos III de Madrid	Mechanical and Functional Responses in Astrocytes under Alternating Deformation Modes Using Magneto-active Substrates
19	Amélie Godeau	Institute for Bioengineering of Catalonia (IBEC)	Mechanics of Human and Mouse Embryo Implantation
20	Jordi Gonzalez Molina	Karolinska Institutet	Adipose Prototissues: biomaterial-based synthetic tissues to investigate cancer metastasis
21	Matt Govendir	EMBL Barcelona	Biomechanics of blood brain barrier disruption in cerebral malaria
22	Olga Grigorieva	Lomonosov Moscow State University	Reconstitution of the cellular microenvironment using decellularized extracellular matrix activates cell differentiation in vitro

23	Alice Gros	IBDM/Aix Marseille Uni/CNRS/Turing Centre for Living Systems	3D quantitative analysis of gastruloid symmetry breaking
24	Judith Guasch	ICMAB-CSIC	Artificial extracellular matrices based on 3D hybrid hydrogels for immune cell and organoid manufacture
25	Pedro Enrique Guerrero	Universidad de Zaragoza	Targeting hypersialylation in pancreatic ductal adenocarcinoma models generated with microfluidic devices reverses its malignant phenotype
26	Paula Guerrero López	Aragon Institute of Engineering Research (I3A)	Unravelling the relationship between nutrient availability in tumor microenvironment and cancer progression
27	Pau Guillamat	Institute for Bioengineering of Catalonia (IBEC)	Nematically-guided morphogenesis
28	Levin Hafa	BMLS - Uni Frankfurt	Laser patterning bioprinting using a light sheet- based system equipped with light sheet imaging produces long-term viable full- thickness skin constructs
29	Masaya Hagiwara	RIKEN BDR	Engineering In-vitro Microenvironments to Replicate Complex In Vivo Conditions for Organoid Architecture
30	Elisa Hahn	EMBL Barcelona	Cellular Mechanics and Self-Organization during Axes Formation in Mouse Gastruloids
31	Soraya Hernández	University of Zaragoza	Engineering of a simplified 3D microfluidic in vitro model for tumour-stroma dynamics of pancreatic ductal adenocarcinoma microenvironment
32	Sarah Hindle	Blizard Institute, Queen Mary University of London	Replicating Dynamic Immune Responses within a Microfluidic Human Skin Equivalent Model
33	Christine Ho	University of Southern California	Synthetically guided development of mobile embryoid bodies based on cardiac contractions Biomechanics of the progression of hypermethylated colorectal carcinomas
34	Alex Hughes	Department of Bioengineering, University of Pennsylvania	Harnessing the rhythmic biology of early kidney formation for synthetic morphogenesis
35	Viola Introini	EMBL Barcelona	Effect of febrile temperatures on cerebral malaria in a 3D in vitro microvascular model

36	Míriam Javier Torrent	University of Liège, GIGA Neurosciences	Role of mechanotransduction in the control of interneurons migration in the cortex
37	Marsel Khaliullin	Alabuga International School	Généra ? a Tissue Engineering Machine
38	Hiedi Klumpe	Boston University	Engineering adhesion to identify design principles for robust cell-cell aggregation
39	Sebastian Kühn	Leibniz-Institut für Polymerforschung Dresden e.V.	μGUIDe ? A precision microgel platform to direct development in vitro
40	Jorge Lázaro Farré	EMBL	A stem cell zoo to study interspecies differences in developmental tempo
41	Jia Le Lim	EMBL Barcelona	The gastrulating zebrafish under cold spells.
42	Valentina Magno	Leibniz Institute for Polymer Research	Sulfated glycosaminoglycan-based microgels for programming VEGF gradients in human kidney organoids
43	Marina Marchenko	Physics of Life TU Dresden / EMBL Barcelona	Influence of apical constriction on tissue morphology and cell fate in brain organoids
44	Nick Marschlich	EMBL	Influence of geometry on self-organisation in early zebrafish development
45	Guillermo Martínez-Ara	Institute for bioengineering of Catalonia (IBEC)	An optogenetic toolset to understand and control epithelial mechanical balance
46	Marija Matejcic	Institute for bioengineering of Catalonia (IBEC)	Mechanics of cell extrusion in intestinal organoids
47	Antoni Matyjaszkiewicz	EMBL Barcelona	LimbNET: modelling and simulation of limb developmental patterning in an online platform
48	Matthias Merkel	Turing Center for Living Systems, Center for Theoretical Physics, CNRS, Aix-Marseille University	Robustness of oriented tissue deformation

49	Laura Morato Concejero	Universidad de Sevilla	From morphology patterns to epithelial morphogenesis: exploring topology and natural variation
50	Jose Muñoz	Universitat Politècnica de Catalunya	Computation of growth distribution in organogenesis
51	Tomas Noordzij	Hubrecht Institute	Uncovering the maternal-fetal crosstalk during implantation by live-imaging
52	David Oriola	Polytechnic University of Catalonia	A positive feedback loop controls the onset of gastruloid symmetry-breaking
53	Mallica Pandya	University College London	Engineering Shape Changing Tissues to Understand Morphogenesis
54	Francesco Pasqualini	University of Pavia	Mechanobiology and Morphogenesis: New (Vertically Integrated) Tools for an Old Problem
55	Marion Raich	Technical University of Munich (TUM), Department of Bioscience	Multi-cellular rosette formation guides cellular rearrangement initiating lumen opening in PDAC organoids
56	Fabian Reinisch	Goethe University Frankfurt	Exploring Embryonic Development in Simulated Microgravity: Insights from Gastruloid Cultures
57	Marc Rico Pastó	Institute for bioengineering of Catalonia (IBEC)	Circulation-on-a-Chip: Cell Survival Under Pro- Apoptotic Mechanical Cues in Metastasis
58	Tosca Roncada	Trinity College Dublin	Biofabrication of Structurally Organised Cartilage Through the Integration of Melt Electrowriting and Photocrosslinkable Decellularized ECM Hydrogels
59	Tamara Rossy	Massachusetts Institute of Technology	Investigating the role of exercise on neuromuscular health and disease in a multi- tissue in vitro model
60	Ayse Tugce Sahin	Helmholtz Munich- Helmholtz Pioneer Campus	Structure-Function Relationships of Mucociliary Clearance in the Human Airways as Benchmark for Organotypic Lung Tissue Engineering
61	Ryan Sarkar	BMLS, Goethe University Frankfurt a.M.	SHAPE: Investigating innate immunity in real microgravity aboard the International Space Station using advanced human bone marrow organoids

62	Sebastien Sart	Institut Pasteur	Microfluidic Droplets for Mapping and Regulating Self-Organization of Organoids
63	Joana Silva	EMBL Barcelona	Hormonal Regulation of Germ Layer Specification in Micropatterned Gastruloids
64	Bart Smeets	KU Leuven	Active foam behavior of tissue coalescence in biofabrication
65	Kristina Stapornwongkul	EMBL Barcelona	Metabolic control of germ layer proportions through regulation of Nodal and Wnt signalling
66	Meenakshi Suku	Ms	Engineering innate immunology in a humanized, functional, in vitro model of healthy myocardium
67	Hanna Szafranska	Laboratory of Molecular Biology	Scaled-up temporally resolved transcriptomics to uncover species-specific neurodevelopmental regulation
68	Wim Thiels	KU Leuven	Using mechanical simulation to study early gastrulation movements in C. elegans.
69	Casper van Bavel	KU Leuven	A Minimal Model for Early C. elegans Embryogenesis
70	Michiel Vanslambrouck	KU Leuven	Image-based force inference by biomechanical simulation
71	Virgile Viasnoff	CNRS	Bioengineering Intrahepatic bile duct tubulogenesis from hIPSC using ligand-bound colloidal scaffolds
72	Isabel Villaoslada	Instituto de Investigación Sanitaria de Aragón	PDXO-on-chip: a novel approach for studying mechanical properties on pancreatic ductal adenocarcinoma.
73	Srivatsava Viswanadha Venkata Naga Sai	Institute for bioengineering of Catalonia (IBEC)	Cell-matrix force transmission regulates the transition between naïve and primed pluripotency.
74	Kaja Nicole Wächtershäuser	BMLS, Goethe University Frankfurt a.M.	Modulating ubiquitin signaling to control (non) immunogenic cell death, necroinflammation, and tumor development in patient-derived human mammary organoids

75	Tobias Walther	Max Planck Institute for Medical Research	DNA microbeads for spatio-temporally controlled morphogen release within organoids
76	Thomas Wilson	Institute for bioengineering of Catalonia (IBEC)	Unveiling the 3D Mechanics of Tubular Epithelial Structures for Biohybrid Devices
77	Shafaq Zahra	Universitat Politècnica de Catalunya	Inference of cytoskeleton and cell stress from TFM
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## **ENERGY**

- Turn off lab equipment and switch off computers/screens and light.
- Shut the Sash of the fume hood.
- Reduce the frequency and duration of opening the doors in freezer/ultrafreezers.
- Keep the freezer organized so you can find your samples quickly.
- Throw away all the frozen samples that you are not going to use anymore
- Avoid using air conditioning or heat.

#### WATER

- Limit the use of distilled and deionized water.
- Reduce single-pass cooling.
- Use auto service autoclaves efficiently.
- Use tap water strainers
- Report leaks promptly.

# **REDUCE, REUSE AND RECYCLE WASTE**

- Label and dispose hazardous waste according to PCB guidelines.
- Reduce the use of disposable plastics by considering the use of glassware.
- Reduce the volume of disposable plastic purchased.
- Find ways to treat and reuse some disposable plastics items.
- Reduce the use of paper. Be conscious of printing practices.

• Separate clean plastic and paper and take them to the yellow and blue containers respectively to recycle.

### PURCHASING

· Consolidate orders.

 Reduce the quantities of purchased chemicals.

• Purchase green.

## TRAVEL AND COMMUTING

- Commute to work in a sustainable way.
- Reduce flight frequency: travel by train if possible.





