From self-organization to biofabrication – a report on the EMBO | EMBL Symposium 'Organoids: modelling organ development and disease in 3D'

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Abstract: For the fifth time, the EMBO | EMBL Symposium 'Organoids: modelling organ development and disease in 3D' brought together leading experts in the fields of organoid research and biofabrication in Heidelberg. Over the course of four days, a multitude of organ models and disease modelling techniques was presented, ranging from pioneer work in neural organoid research, gastroenterology and developmental biology to complex platforms designed for studying tumorgenesis, viral infections and other disease mechanisms. This report gives an overview over the event by means of a comprehensive summary of the individual sessions, keynote lectures and talks. It concludes with final remarks on ethical issues that were touched upon during the conference and underscore the interdisciplinary relevance of the symposium.

Keywords: Organoids, biofabrication, organ development, disease modelling, bioethics

1. Introduction

Started in 2016 by Jürgen Knoblich (Institute of Molecular Biotechnology, Austria), Mina Bissell (Lawrence Berkeley National Laboratory, USA) and Esther Schnapp (EMBO Press, Germany), the biannual EMBO | EMBL Symposium 'Organoids: modelling organ development and disease in 3D' has quickly become a vital and flourishing meeting place for the world-wide organoid research community. And so, it must have come to nobody's surprise that more than 600 participants (440 on site, 179 virtually) gathered for this year's meeting (the 5th of the conference series) that took place from 22 – 25 October 2025 at EMBL Heidelberg. Those who attended were presented with a carefully orchestrated program curated by the scientific organizers Meritxell Huch (Max Planck Institute of Molecular Cell Biology and Genetics, Germany), Karl Koehler (Boston Children's Hospital/Harvard Medical School, USA), Madeline Lancaster (MRC Laboratory of Molecular Biology, UK) and – for the fifth and final time – Esther Schnapp. Over the course of four days, forty main talks, numerous flash talks, and over 200 posters were presented, alongside ample opportunities to meet speakers, socialize, and network.

Due to spatial constraints – a concept probably woefully familiar to many organoid researchers – this article cannot cover the entire program of this year's symposium. Instead, it aims to provide a succinct report on the major topics and research developments that were discussed during the main talks, by summarizing the keynote lectures and individual talks from each session.[i] Wherever possible, reference is made to recent publications by the speakers on the topic presented. Since the author of this event report is not a life scientist, but a researcher specialized in the ethics of emerging biotechnologies, the article concludes with a few stray observations and reflections on socio-ethical issues related to organoid research that deserve interdisciplinary attention.

2. Concepts from development (Wednesday, 22 October)

In their highly anticipated keynote lecture “Passage of time in brain organoids: the journey to understand human brain development” that kicked off the first session, Paola Arlotta (Harvard University, USA) presented human cortical organoids that were cultured for unprecedented lengths of time ranging from 6 months to over 5 years in vitro, and could be shown to develop and mature while in culture for these extended periods as confirmed by methylation profiling. Notably, they could further report that human brain organoids are capable of "recording and recalling" developmental time in a certain sense as demonstrated by the ability of "old" progenitors to rapidly produce late progeny when exposed to inductive developmental signals. Adding a third achievement to their already impressive talk, Arlotta also introduced chimeroids of differentially patterned neural progenitors that were shown to produce multi-regional organoids following endogenous principles of brain self-organization. (Antón-Bolaños *et al,* 2024; Faravelli *et al,* 2025)

Conceptually, Magdalena Sutcliffe’s (MRC Laboratory of Molecular Biology, UK) talk served as a link between Arlotta's keynote and the presentations on (extra-)embryonic lineages that made up the majority of the remaining talks on Day 1. Not only were they able to show that aberrant transcriptional and chromatin states are responsible for the incompetence of some human PSC lines to differentiate into cerebral organoids. Impressively, they were also successful in resetting these states thereby re-establishing a fully pluripotent and uncommitted regional epiblast identity. (Sutcliffe *et al,* 2024)

The subsequent talk by José Polo (University of Adelaide, Australia) recapitulated their ground-breaking research into the molecular mechanisms of stem cell reversion that led to the derivation of induced Trophoblast Stem Cells (iTSCs) and novel trophoblast organoids as well as so-called iBlastoids – a self-organized combination of cells with characteristics similar to those of the embryonic trophectoderm, hypoblast and epiblast. (Liu & Polo, 2024) Polo was followed by Borzo Gharibi (The Francis Crick Institute, UK), who introduced post-gastrulation amnioids (PGAs) – an embryonic stem cell-derived 3D model of the post-gastrulation amnion, that faithfully recapitulates extra-embryonic development up to 4 weeks post-fertilization, closely mimicking the functional traits of the human amniotic sac and making accessible embryo-amnion interactions beyond gastrulation. (Gharibi *et al,* 2025)

Gharibi, in turn, handed over to Nicolas Rivron (Institute of Molecular Biotechnology, Austrian Academy of Sciences, Austria), who outlined a compelling theory concerning the evolution of Great apes – including humans – based on his blastoid research according to which Old World Monkeys acquired a viral sequence that led to a change in cell fate progression and contributed to defining the temporal window of blastocyst implantation and depth of embedding that enabled the development of metabolically-demanding foetuses with larger brains. In their talk, Luca Schwarz (MRC Laboratory of Molecular Biology, UK) emphasized the lasting importance of research on human embryos for the study of placental pathophysiology as they presented (aneuploid) trophoblast organoids generated from human blastocysts with extraembryonic mesoderm cells in the same culture conditions that recapitulate the cell type composition, morphology and functionality of the in vivo trophoblast. (Schwarz *et al,* 2025) The insightful first day was rounded off by Prisca Liberali (Friedrich Mischer Institute for Biomedical Research, Switzerland), whose quantitative description of the phenotypic landscape of intestinal organoids and mapping of genetic

interactions uncovering mechanisms that orchestrate both organoid formation and the regeneration of intestinal tissue, was received with great interest. (Xue *et al,* 2025)

3. Building organoid complexity (Thursday, October 23rd)

The main talks on Day 2 were divided into two sessions. However, since both of them were devoted to showcasing research into advanced, versatile models of different tissues, organs, and body systems, they are presented *en bloc* in this report.

Jesse Veenvliet (Max Planck Institute of Molecular Cell Biology and Genetics, Germany) focused on non-genetic developmental principles, showing that typical mammalian embryo architecture missing in current gastruloids can be created by precisely timed addition of an extracellular matrix, thus emphasizing the importance of physiology in stem cell research. (Maroudas-Sacks *et al,* 2025; Trani-Bustos *et al,* 2025) In the same vein, Ryan Harrison (University of Warwick / The Francis Crick Institute, UK) later in the day highlighted the role of mechanical forces, alongside signaling cues, in shaping early human structures by introducing a micropatterned organoid system that models the caudal end of the embryo during late gastrulation and early neurulation, capturing key features of axis elongation. (Loo *et al,* 2025)

Before that, however, Jonathan Brassard (University of Cincinnati, USA) described a novel human pancreatic organoid system that combines pluripotent stem cell-derived mesenchyme with posterior foregut cells and recapitulates many critical aspects of pancreatic development. They were able to show that after two months in culture, organoids had formed that contained all the relevant cell types observed in the fetal pancreas, were cellularly organized in ways that reflect complex in vivo architecture, and continued to mature even if transplanted under the kidney capsule of a mouse. (Brassard *et al,* 2025) Building on a model first described in 2021, Jiyoon Lee (Boston Children's Hospital / Harvard Medical School, USA) presented "sensing skin organoids" (senSkOs), a novel platform that models how human skin and sensory neurons derived from hPSC develop and interact with each other when they are brought together as floating assembloids or co-cultures on a chip. In both systems successful innervation and functional neural integration were achieved, while Capsaicin treatment and mechanical deflection led to promising results regarding the functional activation of nociceptors and mechanoreceptors, respectively. (Lee & Koehler, 2021)

In another fascinating talk, Minoru Takasato (RIKEN Center for Biosystems Dynamics Research, Japan) explained how they guided hPSC differentiation stepwise into hindgut, cloaca, and then bladder organoids with structural and functional characteristics specific for the bladder that matured further when they were cultured with surrounding mesenchyme. They also reported on their on-going efforts to co-culture bladder and kidney organoids, ideally connected by a ureter and supported by urothelium to improve vascularization and morphogenesis that would ultimately lead to majorly improved models of urinary tract development, functionality and disease. Following Ryan Harrison's talk, Giorgia Quadrato (University of Southern California, USA) picked up where the earlier talks on day one left off, and presented a novel human cerebellar organoid (hCerO) system that recapitulates the cellular diversity and distinct functional features of the fetal cerebellum. A particularly impressive aspect of their presentation was the successful long-term

culture and maturation of Purkinje cells exhibiting molecular and electrophysiological characteristics of their in vivo counterparts. (Atamian *et al,* 2024)

Chrysanthi-Maria Moysidou (Max Delbrück Center for Molecular Medicine, Germany) gave insights into a strategy for enhancing the maturation status of human neuromuscular organoids (NMOs) through long-term Electrical Pulse Stimulation (EPS) training. At the end of the training period described by them (60 days), NMOs exhibited significantly more frequent and stronger spontaneous contractions, compared to NMOs not subjected to training, while such enhanced contractile activity was sustained for at least two weeks post-EPS training. (Moysidou *et al,* 2025) Yuan Lei's talk (Max Planck Institute of Molecular Cell Biology and Genetics, Germany) focused on the promises of human periportal liver assembloids generated by combining hepatocyte organoids, cholangiocyte organoids, and primary portal mesenchyme, all from the same patient. They expressed confidence that these assembloids can provide a robust, patient-specific platform for modeling liver disease and screening antifibrotic compounds as they recapitulate the histological architecture, cellular composition, and spatial organization of the human periportal liver zone. (Huch *et al,* 2025)

The already impressive repertoire of models of embryos, pancreases, skin, urinary tract, cerebellum, neuromuscular system, and liver was then expanded by Joo-Hyeon Lee (Memorial Sloan Kettering Cancer Center, USA) to include patient-derived lung organoids and large-scale organoid models to uncover compounds that reverse pro-fibrotic states and promote alveolar differentiation during early tumorgenesis and fibrosis. Maximiliano Arce (Uppsala University, Sweden), on the other hand, drew the audience's attention to the topic of vascularization. By their report, IPSCs were generated from patients with cerebral cavernous malformations and vascularization organoids created from these cells that showed an abnormal vascular network and developed macrostructural abnormalities. In addition, the prospect of co-culturing brain and vascularized organoids to recapitulate neurovascular interactions and study environmental-related disease mechanisms was raised. (Arce *et al,* 2025)

Originally, Melissa Little (Murdoch Children's Research Institute, USA) was not scheduled as speaker for this year's symposium. However, they graciously accepted to stand in for a speaker who was unable to attend at short notice, and provided valuable insight into their recent research efforts demonstrating that glomeruli derived from kidney organoids can accurately model podocyte disease and potential therapeutic applications. (Zylberberg *et al,* 2025) The final word of the day went to Calvin Kuo (Stanford University, USA), who introduced novel human organoid systems of diverse human tissues that encompass both epithelial cells together with their associated stroma and immune cells, making them potentially useful for modeling complex immune-epithelial interactions related to a variety of health issues like cancer, autoimmunity or infectious disease.

4. Organoids in regenerative medicine and disease modeling (Friday, October 24th)

The first session on the third day was kicked off with a concise talk by Hans Clevers (F. Hoffmann-La Roche Ltd / Hubrecht Institute, The Netherlands), who promoted the use of Invasin as a fully defined, affordable, versatile, and animal-free complement to Matrigel/BME. (Wijnakker *et al,* 2025) Clevers' convincing pitch was followed by Robin Journot (Institut Curie, France), who

identified tissue architecture as a decisive factor in the embryonic development of mice by studying how molecular cues guide stem cells to differentiate within precise spatial arrangements using in vitro organoids, ex vivo embryonic tissue explants, and single-cell quantitative imaging. (Journot *et al,* 2025) Next was Laura Pellegrini (King's College London, UK), who gave an account of human choroid plexus organoids generated to recapitulate fundamental functions like cerebrospinal fluid secretion and the formation of a tight, selectively permeable epithelial barrier by introducing a combination of signaling molecules that are physiologically present during the stages of development of this tissue. (Zhao *et al,* 2025) And Margherita Yayoi Turco (Friedrich Miescher Institute for Biomedical Research, Switzerland) explained their use of trophoblast organoids derived from first-trimester placental tissues to model villous and extravillous differentiation pathways in vitro and to systematically dissect the signaling pathways controlling trophoblast proliferation and differentiation. Their exciting and ambitious goal: Revealing how intrinsic trophoblast programs and extrinsic uterine signals cooperate to drive placental growth and function. (Bondarenko & Turco, 2025)

The final three talks of the first session consisted of a beautiful presentation by Guo-li Ming (University of Pennsylvania, USA) sandwiched by two talks about research conducted at the Georg-Speyer-Haus, Institute for Tumor Biology and Experimental Therapy in Germany. The first half was presented by Maria Correia Melo, who introduced colorectal cancer assembloids created through a combination of patient-derived organoids, cancer-associated fibroblasts, and primary endothelial cells that help to recapitulate the cellular and spatial complexity of tumor microenvironments. Then, Henner Farin demonstrated why organoid platforms like this can also be useful to assess the efficacy of therapeutics by modeling processes like CAR T cell infiltration and cytotoxicity. (Ndreshkjana & Kress, 2025) Meanwhile, Ming showcased single rosette (cortical) organoids derived from patients suffering from subcortical band heterotopia that were used to research the molecular and cellular mechanisms underlying this neurodevelopmental malformation, which includes genetic mutation resulting in a defective stem cell migration and localization in the cortical plate.

Juergen Knoblich opened the second session with a magnificent talk that summarized recent developments in brain organoid research and demonstrated how advanced cerebral organoids matured for more than a year can be used to model processes that can lead to post-natal neuro-developmental disorders, when disrupted. (Pașca *et al,* 2025; Wong *et al,* 2025; Li & Knoblich, 2025) Ruolan Tang (Westlake University, China) reported performing lineage tracing and oncogenic modeling to dissect the tumor initiation potential of two spatially distinct mammary stem cell populations identified in vivo by utilizing a 3D mammary mini-gland culture system that recapitulates epithelial organization and stem cell dynamics in vitro. They found that stem cell fate commitment dictates tumor onset, spatial distribution, and subtype-specific aggressiveness. (Lin *et al,* 2025) In their subsequent report, Bonis Evangelos (ETH Zurich, Switzerland) identified Kupffer cells as primary niche cells in liver micro-metastases by use of a novel niche labeling system based on receptor-mediated uptake of locally produced fluorophores enabling detection and analysis of niches at the micro-metastatic state.

Complementing the earlier talks by Melo and Farin, Eduard Batlle (Barcelona Institute of Science and Technology, Spain) demonstrated the importance of phenotypic plasticity – the ability of

cancer cells to adopt different transcriptional states without underlying heritable (epi)genetic alterations – for the metastatic progression of colorectal cancer as well as the central role inhibition of the oncogene KRAS plays in governing this plasticity. (Cañellas-Socias *et al,* 2024; Centonze *et al,* 2025) Amal Fahmi (University of Bern, Switzerland), on the other hand, took things in a unique and completely new direction. They employed human neural organoids to evaluate the neurodevelopmental impact of orthoflavivirus infections like Zika, Dengue and West Nile Virus and found that Zika and West Nile – but not Dengue – were causing toxicity and abnormal neurodevelopment in the models, suggesting a potential risk of fetal brain injury stemming from virus infections.

Fahmi's presentation was followed by an eagerly awaited talk of Toshiro Sato (Keio University School of Medicine, Japan), in which they pointed out that the preservation of the stem-cell niche in the context of gastrointestinal organoid transplantation markedly improves transplantation efficiency leading them to the general concluding recommendation: "Don't destroy the niche!" The audience's final attention, however, belonged to Clément Morival's (Nantes Université, France) successful cultivation of mature retinal organoids with proper organization and discernible photoreceptors in their on-going attempts to model the visual cycle and its deregulation in Stargardt disease – an autosomal recessive genetic disorder that leads to a juvenile form of severe macular dystrophy.

5. Organoids and engineering (Saturday, October 25th)

The honor of opening the fourth and final day of the symposium fell to Bon-Kyoung Koo (Center for Genome Engineering, Republic of Korea Building on their collection of diverse bat organoids, (Kim *et al,* 2025) they announced the establishment of a cross-species "organoid zoo" – a platform of adult stem cell–derived intestinal organoids from 26 vertebrate species (spanning rodents, bats, avians, minipigs, and primates amongst others) that can be robustly maintained in a unified, commercially available medium, enabling systematic cross-species analysis. No less impressive was Holly M Poling (University of Cincinnati, USA), who presented a confined culture system that enables a faster and denser generation of larger small intestinal, colonic, and gastric organoids that co-develop a functional de novo enteric nervous system and exhibit neuromuscular coordination with isometric force contractions comparable to that of native human tissue. (Poling *et al,* 2025)

Vincenzo Corbo (University of Verona, Italy) was only the second speaker at the conference who talked about organoid pancreas models. The project they gave insights into used whole-genome sequencing and in situ single-cell analyses across a large cohort of organoids derived from pancreatic cancer patients to study extrachromosomal DNA dynamics that amplify oncogenic expression and affect cell fitness. (Xu *et al,* 2025a) Drawing from research on rhesus macaque brain organoids, Tor Rasmus Memhave (German Primate Center, Germany) added to the symposium from an unexpected interdisciplinary perspective. The computational chemist and neuroscientist specialized in Magnetic Resonance Imaging and Spectroscopy (MRI/S) presented these tools as useful complementary approaches for the non-invasive and longitudinal study of maturation processes in neural organoid models.

Memhave's unique contribution was followed by Miki Ebisuya-Matsuda (TU Dresden, Germany), whose exemplary research uncovered transient fluidization that occurs exclusively in the basal region of human neuroepithelia, by quantitatively characterizing tissue dynamics and mechanics with oil microdroplets in cerebral organoids derived from humans, gorillas, and mice. (Xu *et al,* 2025b) In the penultimate talk of the symposium, Luigi Aloia (AstraZeneca, UK) demonstrated how human patient-derived organoids that were gene-edited and drug perturbed can be used to increase target efficacy and identify novel combination strategies in the discovery of cancer therapeutics, if screened properly with the help of advanced imaging and measurement systems.

The second keynote lecture "Engineering organoids – Deconstructing and reconstructing intestinal morphogenesis through biofabrication" by Matthias Lütolf (Roche Institute of Human Biology, Switzerland) brought the fifth EMBO | EMBL Symposium 'Organoids' to a fitting close. Drawing on their many high-profile collaborations with other expert organoid researchers, Lütolf presented their exemplary efforts in developing intestinal organoids assembled by guiding cell-intrinsic self-patterning through engineered stem cell microenvironments. Among the more recent kinds of model Lütolf showcased, were also the following three: intestinal organoids used to test the theory that intestinal cell extrusion is regulated by intercellular force transmission arising from crowding or other mechanical interactions; gastric, small-intestinal, caecal and colonic epithelial models that faithfully reproduce their respective tissue geometries and that exhibited stem cell regionalization and transcriptional resemblance to in vivo epitheliam; and a patterned homeostatic human gastric organoid-on-a-chip system with bilateral access that is capable of modeling H. pylori niche establishment and persistent colonization of the gastric epithelium. Together, these biofabricated systems contribute to the reconstruction of intestinal morphogenesis, the illumination of failure modes in disease, and the development of next-generation therapeutics. (Hofer *et al,* 2025a; Hofer *et al,* 2025b; Krueger *et al,* 2025)

6. The ethics of organoid research – closing observations

The ethical, social, and legal implications of stem cell research were certainly not among the main topics of the symposium. Nevertheless, there were a few aspects that stood out, of which three deserve to be explicitly mentioned:

During the Q&A session following their presentation, Paola Arlotta was asked whether their brain organoids exhibited consciousness. This was remarkable in several respects: Firstly, because a question based on the (flawed) assumption that neural organoids might actually be something like "mini brains" would have been expected in a non-specialist context, but not necessarily at a conference of stem cell researchers. Secondly, because the questioner naturally assumed that the consciousness of Arlotta's organoids would have been a clearly recognizable property that could be identified using life science methods. Thirdly, because Arlotta took the inquiry as a potential ethical criticism and responded by pointing to their constant dialogue with ethicists and philosophers as evidence of a keen awareness of any boundary issues concerning brain organoids that might come up. And fourthly, because there were no further questions of this kind during the entire rest of the conference, not even concerning groups working with mammalian gastruloids or nociceptive skin organoids.

Based on this interaction, one might therefore assume that the ontological or moral status of (human) brain organoids is quite unique even among other organoids and that research on them becomes problematic when consciousness (with or without sensitivity) comes into play. However, why this should be the case is far from self-evident and it would be interesting to hear or read how such a position would be consistently defended. Now, the 'Organoids' symposium may not be the right forum for such a discussion. But there will certainly be extensive interdisciplinary exchange about how advanced neural organoids should be assessed in terms of life sciences, law, and ethics over the course of the next years.

Another topic that played at least a marginal role during the four days was the relationship between animal research and organoid research: On the one hand, it is a widely held belief that organoids may play an important role in the development of New Approach Methodologies (NAM) that reduce or replace certain kinds of animal testing. On the other hand, there are branches of research that deal, for example, with the growth, integration, or vascularization of organoids and lead to the development of novel types of animal experiments as well as the creation of chimeric organoid entities. In addition, research into organoids generates vast amounts of knowledge about rodents, other mammals, birds, and fish – either directly, as in the case of Bon-Kyoung Koo's "Organoid Zoo," or as a byproduct of research into human development and pathogenesis.

This complex situation calls ethics into play as a reflective and critical discipline: Accordingly, instead of simply declaring the abolition of animal experiments to be good and the emergence of new animal experiments to be bad in all instances, ethicists should be expected to present a fair and nuanced picture of the diverse implications of organoid research for the scientific use of animals as research subjects. At the same time, there is something to be expected of organoid researchers in this regard, as well – namely, to be transparent and honest about the limitations of their research as well as its potentials and to acknowledge that organoids will not render most or even all animal experiments unnecessary any time soon.

The third aspect that stood out, was this: Even if only a fraction of what this year's symposium speakers hope to achieve with their models comes to fruition, it is clear that organoid research represents a tremendous asset to disease modeling and global healthcare. Naturally, there are still discussions to be had about how to use the knowledge and skills gained through this research in ways that are socially responsible, fair and equitable at global and individual levels. There are also legitimate concerns regarding, for example, the origin of certain stem cell types, the developmental potential of embryonic and other advanced organoid models or the socio-cultural consequences of editing and engineering human biology that have to be taken seriously at the least. However, none of the above changes the fact that organoid research is, first and foremost, a great technological, heuristic, diagnostic, and therapeutic advancement pursued by dedicated researchers with good intentions and deserving of ethical recognition. The 2025 edition of the EMBO | EMBL Symposium 'Organoids: modelling organ development and disease in 3D 'may be in the books, but scientifically as well as ethically there is much to look forward to for 2027 and many years to come.

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[i] To enhance and ensure accuracy, scientific abstracts provided by the speakers prior to the symposium were used in the creation of the summaries.