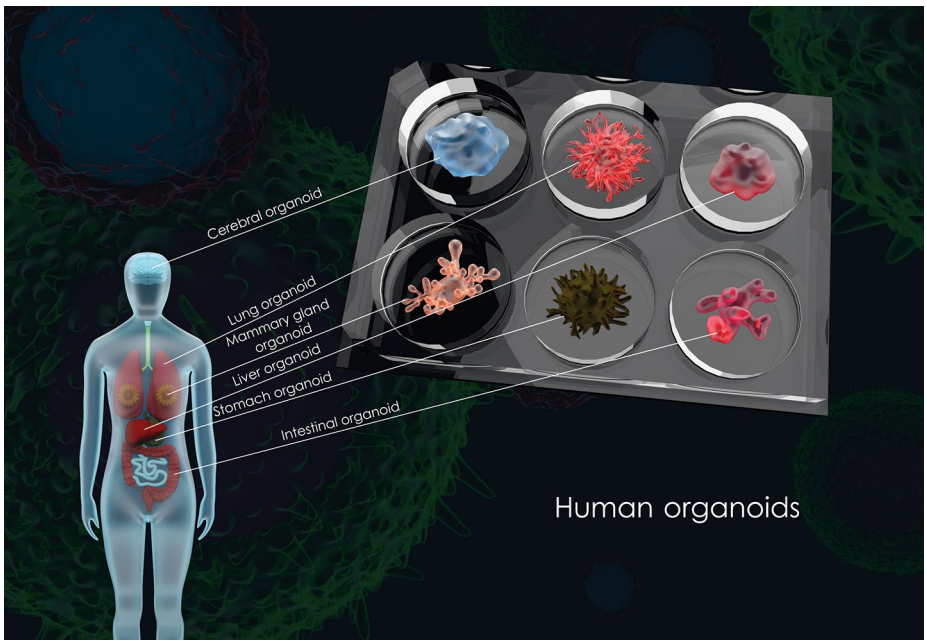
The promise of organoids and embryoids

Over the last few years, there has been a shift towards the use of three-dimensional multicellular structures that more closely recapitulate native tissues and organs as tools to understand development, physiology and pathology.

Organoids and embryoids are multicellular structures that contain organ-specific or embryonic cell types having the ability to self-organize similarly to the process that occurs in vivo[1,2]. They are generally developed from adult, embryonic and induced-pluripotent stem cells that can generate differentiated progeny and exhibit structural, morphogenetic and functional properties that resemble those of their in vivo counterparts. Organoids have been widely employed in basic and translational research, in part due to the enormous potential for manipulation of specific niche components and extensive morphogenetic patterning. To date, there are a wide range of organoids that have been generated as model systems to understand organogenesis and disease progression. Indeed, nearly every organ in the human body has been explored, from the brain to intestine[3]. As an emerging field, embryoids have been successfully developed to model mammalian development, from pre-implantation to early organogenesis. Importantly, artificial matrices have been crucial in facilitating the self-organization of organoids and embryoids and materials science has played a significant role in generating natural and synthetic hydrogels that mimic the native extracellular matrix.



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In this Focus issue, we highlight studies that demonstrate the promise of organoids and embryoids. In their Article, Eileen Gentleman, Joana Neves and colleagues investigated the role of a rare cell type present in inflamed intestinal tissue, type-1 innate lymphoid cells (ILC1). Using a polyethylene glycol hydrogel as an artificial extracellular matrix, they found that these cells regulate the extracellular matrix by balancing matrix deposition and the expression of matrix-degrading enzymes. Such bioengineering approaches are instrumental in understanding the interaction of immune cells with their microenvironment, as suggested in an accompanying News & Views by Bauer LeSavage and Sarah Heilshorn. In another example where bioengineering tools have been pivotal, Melissa Little and colleagues demonstrate in their Article how they can generate bioprinted kidney organoids in a highly reproducible manner. They created cell bioinks from cultures of induced pluripotent stem cells and subsequently printed them using an automated extrusion-based process that could produce organoids that spontaneously form features native to kidneys. This study has been summarized in a News & Views by Benjamin Humphreys that indicates how such an approach can aid in reducing variability in organoid research.

We also invited experts to review the progress made in the techniques for the generation of organoids and embryoids as well as their multiple uses. Nuria Montserrat and colleagues highlight in their Review Article how tools such as micropatterning and microfluidic systems can be employed to facilitate the self-organization as well as to enhance the complexity of organoids. In another Review Article, Masayuki Fujii and Toshiro Sato highlight how organoids can be generated from patient-derived pathological tissue or engineered using genetic tools such as CRISPR–Cas9 and employed as prototypes of human tissue to understand disease progression. Jianping Fu and colleagues highlight in a Review Article how stem cell-derived embryoids can be powerful platforms to understand various aspects of mouse and human development. This is particularly significant due to the ethical limitations of carrying out research with human embryo specimens.

Indeed, an important requirement within the fields of organoid and embryoid research is thorough ethical integrity. The ethical and legal status of these model systems and the guidelines on their culture need to be thoroughly defined to facilitate research whilst also deterring their objectionable use[2]. In addition, policies regarding informed consent should be at the fore of responsible research, particularly with biobanking of patient-derived tissues. In this regard, the International Society for Stem Cell Research has been actively facilitating discourse among researchers and has continuously provided recommendations on the isolation, culture and safe use of stem cell-derived constructs[4].

Ultimately, it is clear that organoids and embryoids offer great promise as first line tools that can complement or even be utilized as proxies for some of the very basic studies carried out with animals such as in the fight against COVID-19 (ref. [5]). ❐

Published online: 27 January 2021
https://doi.org/10.1038/s41563-021-00926-3

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