Organoids: The Next Frontier in Food Innovation

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Introduction

An organoid is a self-organized 3D tissue that is typically derived from stem cells (pluripotent, fetal or adult), and which mimics the key functional, structural and biological complexity of an organ (Huch and Koo, 2015). These *In-vitro,* miniaturized organ models are especially useful for studying complex multicellular structures, such as the brain, retina, kidneys, and lungs. They are now widely utilized to investigate organ development, toxicity, dosage effects, and diseases.

In contrast to traditional cultured cells and spheroids, organoids exhibit a closer anatomical and functional resemblance to the organs found in living organisms. Spheroids are primarily generated through cell-to-cell adhesion, resulting in cell aggregates. These structures can be derived from immortalized cell lines, primary cells, or sections of human tissue. In contrast, the formation of organoids is driven by the inherent self-organizing properties of stem cells, which possess the ability to self-renew and differentiate. This process leads to the development of three-dimensional structures that encompass multiple differentiated and physiologically functional cell lineages. Consequently, organoids demonstrate greater physiological relevance and are considered a more suitable option for in vitro studies.

History

In 1907, Henry Van Peters Wilson made a significant discovery when he found that mechanically dissociated sponge cells had the ability to reaggregate and self-organize into new, functionally normal sponge organisms. This foundational work paved the way for advancements in the field of cell biology. In subsequent decades, the isolation and establishment of pluripotent stem cells (PSCs) were achieved for the first time from mouse embryos in 1981. The creation of human-induced pluripotent stem cells (iPSCs) in 2006, through the reprogramming of mouse and human fibroblasts, marked a transformative milestone for stem cell and organoid research. Further advancements were made in 2010 with the production of renal organoids derived from kidney stem cells sourced from murine fetuses. *In vitro* generation of gut organoids from human PSCs followed, demonstrating the potential for organoid technology. More recently, in 2020, organoids from snake venom glands were successfully generated (Corrò *et al.*, 2020). These developments continue to underline the innovative progress in the field of regenerative medicine.

Components and formation of organoid

Organoid development relies on multiple essential components. Cell sources include tissue-derived organoids obtained from biopsy samples and iPSC-derived organoids cultured in vitro. Soluble factors such as growth factors and small molecules regulate growth. Matrices like Matrigel, collagen, and synthetic hydrogels provide structural support. Integrating cues help mimic physiological features, with bioprinting enabling tissue formation. Additionally, physical cues offer extracellular matrix support and simulate nutrient and waste diffusion similar to natural basement membranes (Zhao *et al.*, 2022).

Organoid generation begins with cell sourcing, followed by washing and purification. The purified cells are then seeded and expanded under controlled in vitro conditions. Subsequently, cells are guided through differentiation into the three germ layers—ectoderm, mesoderm, and endoderm—using specific growth factors and culture conditions. This process leads to the formation of organ-specific organoids such as brain, retina, kidney, stomach, intestine, liver, and lung. The overall proc

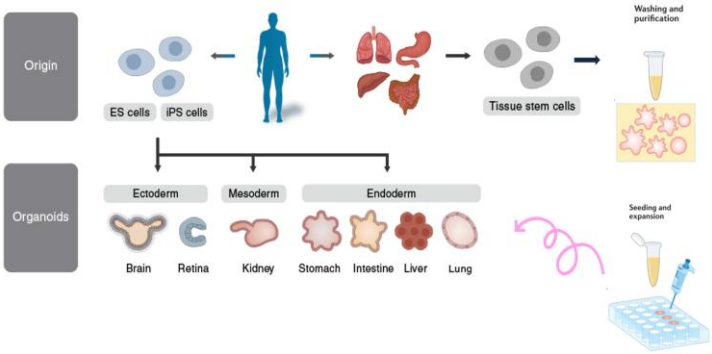

Fig. 1. General flowchart for generation of organoid (Zhao *et al.*, 2022)

Applications of organoid

Organoids are used in drug testing and also in the development of new drugs. Although organoids cannot completely replace the animal model but it may help in understanding drug behaviour on the targeted cells and organs. Organoids are successfully used in screening of drugs. Organoids have also been utilized in transplantation studies to evaluate regenerative capacity in addition to in vitro applications. Predicting patient response to therapy is another potential application of organoid technology. Organoids provide a unique insight into the individual patient's disease

and show potential for personalized therapies. OMICs, gene editing, phytogenic studies and host-microbe interactions are the current interesting research areas in the 21st organoid research.

Application in food research

Few research papers published related to organoids in food research, mainly to see the effects of nutraceutical food and food additives. The researchers focused on nutritional absorption, metabolism, and impacts of cellular responses such as pro- and anti-inflammatory effects on various cells throughout the gut. Organoids are mainly used for toxicological studies, allergen studies, interaction of microbiota with gut, etc. Food constituents such as caffeic acid, chlorogenic acid, L-Glutamic acid, monosodium salt hydrate (MSG), vitamin C, curcumin, and m-hydroxyphenylpropionic acid (mHPP) have been previously investigated in murine intestinal organoids to determine their effects on growth rate and patterns (Cai *et al*., 2018).

Freire et al. (2019) generated organoids from duodenal biopsies of both celiac (CD) and non-celiac donors. When CD organoid monolayers were exposed to gliadin, they showed increased permeability and enhanced pro-inflammatory cytokine secretion compared to non-celiac controls. Kong *et al.* (2019) cultured small intestinal organoids with 2 µg/ml sunset yellow (SY) for two generations and found that SY inhibited organoid growth by suppressing proliferation and disturbing differentiation of intestinal epithelial cells.

Advantages of organoids

Organoids retain key organ-like characteristics, closely mimicking the structure and function of real tissues. They enable realistic intercellular and cell–matrix interactions, providing better physiological relevance. Organoids offer species-specific models, reducing reliance on animal testing, and allow personalized studies at an individual level. Additionally, they support high-throughput, efficient preclinical research and are compatible with advanced genetic engineering tools.

Disadvantages of organoids

Organoids face limitations such as lack of standardized protocols, leading to variability in results. They do not fully replicate in vivo systems due to absence of vascularization, immune components, and microbiome. Their application in infection studies is limited, and high costs associated with development and maintenance restrict widespread use.

Conclusion

In conclusion, organoid research is evolving rapidly. It opens a new area of research, particularly where it is essential to perform experiments directly on human tissues or to gain good access to a multicellular complex system for imaging. Compared to animal model, organoids are low-cost and they give sufficient information for a study. However, organoids are not completely realistic and always lack some of aspect of their *in vitro* counterparts.

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