Organoid derivation: application in intestinal transplants

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Objectives

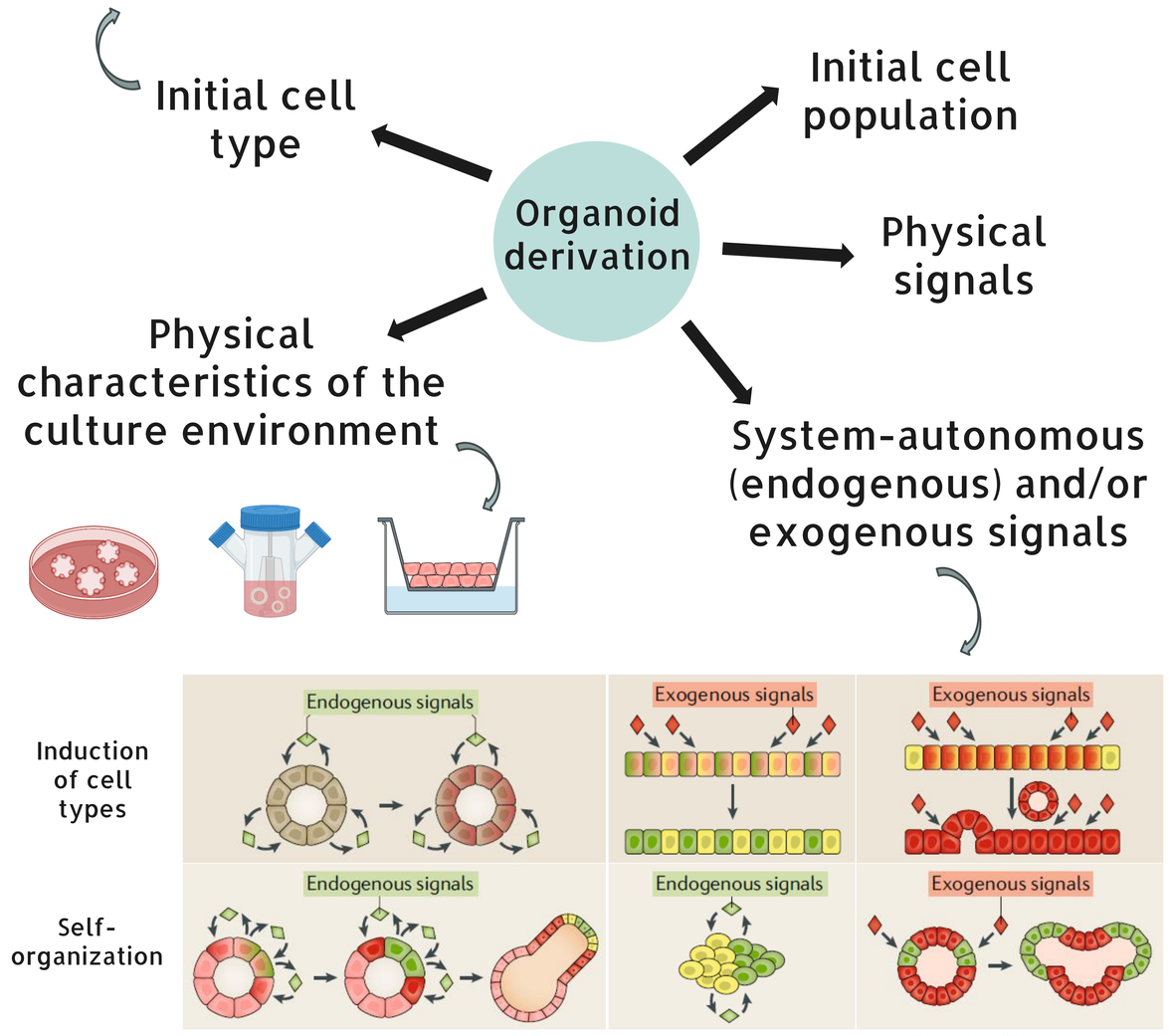
- Analyse and understand how organoids are generated.
- Examine the various applications of organoids in the field of veterinary research.
- Analyze the current state of research on intestinal organoid transplants in domestic animals, exploring their advancements and associated challenges.

An **organoid** is a three-dimensional structure derived from stem cells that self-organizes and has the capacity for self-renewal and differentiation to give rise to the different morphotypes constitutive of the tissue it aims to mimic and reproduce at least some of its physiological functions.

Organoid derivation

Table 1. Comparison of different types of stem cells and their derived organoids.

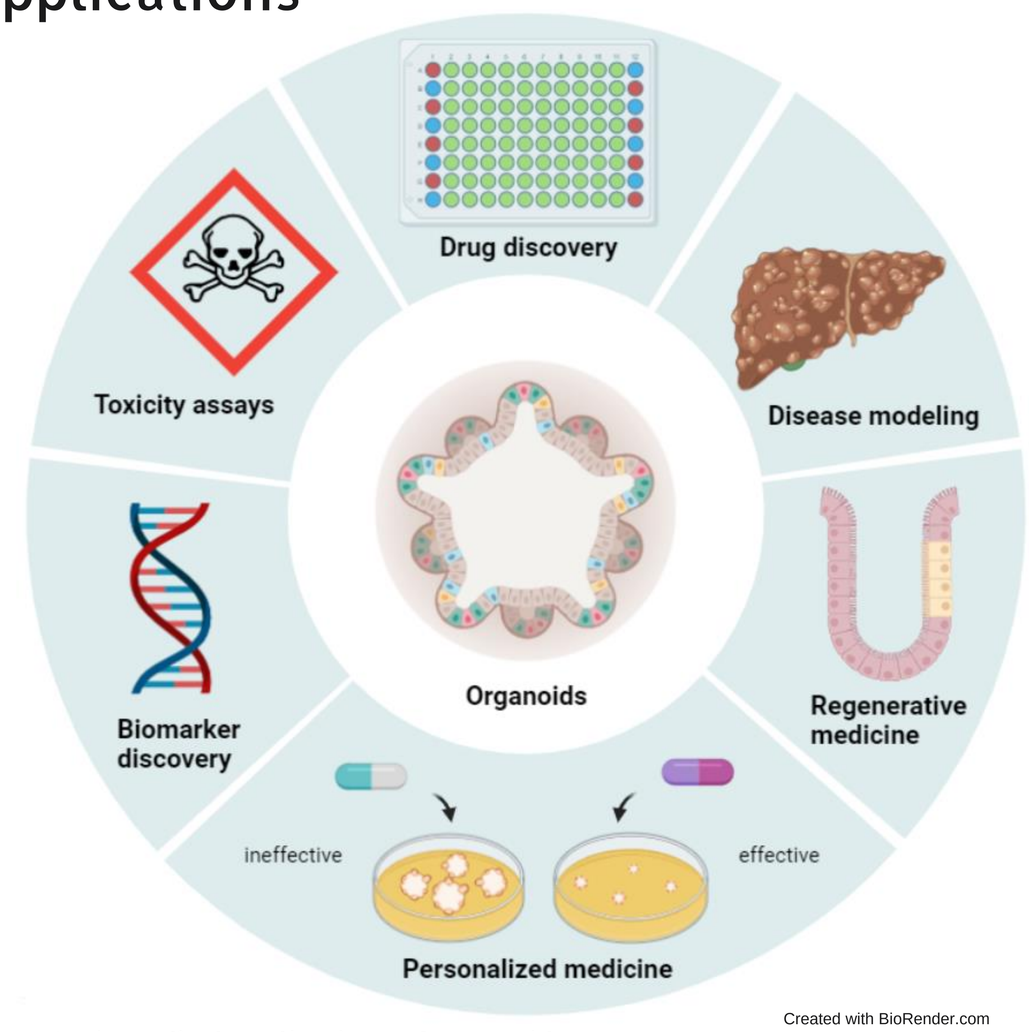
	PLURIPOTENT STEM CELLS	ADULT STEM CELLS	INDUCED PLURIPOTENT STEM CELLS
ORIGIN	Early embryos (blastocyst)	Multipotent cells (embryonic and adult tissues)	Reprogramming of somatic cells
PROPERTIES	Unique self-renewal and differentiation properties, along with high cellular plasticity, allowing differentiation into a wide range of cell types	Self-renewal and differentiation properties, with more limited plasticity compared to CMPs. Capable of generating all specialized cell types found in the specific tissue or organ from which they were isolated	Similar properties to CMPs, but without the ethical issues associated with embryo usage
DERIVED ORGANOIDS	Derived from self-organization during *in vitro* differentiation. Can accurately mimic complex tissue structures	Generated from self-organization and differentiation into three-dimensional structures representing cellular morphology of the tissue of origin. Require specific protocols for organoid generation from each tissue.	Derived from self-organization and differentiation of reprogrammed cells into three-dimensional structures mimicking the morphology and function of the original tissues.



Rossi *et al.* (2018) *Nature Reviews*

Figure 1. Exogenous vs. endogenous signals in organoid derivation.

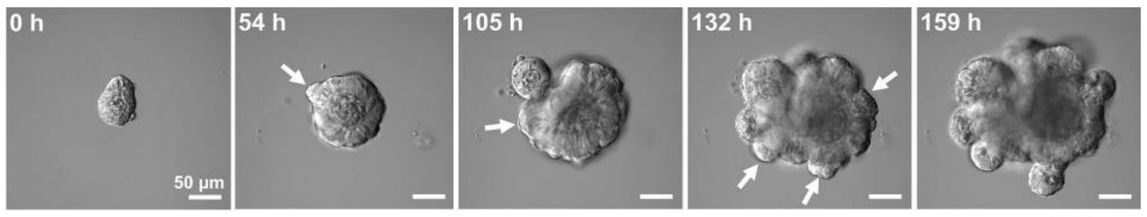
Applications



Created with BioRender.com

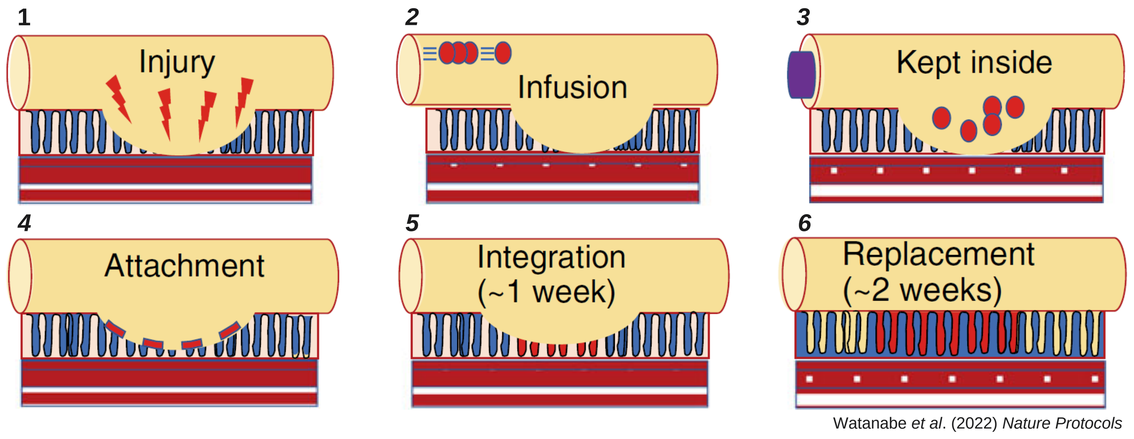
Figure 2. Biomedical applications of organoids.

Intestinal transplants



Takase *et al.* (2023) *JoVE*

Figure 3. Sequential images of the generation of a mouse intestinal organoid. The white arrows indicate crypt budding.



Watanabe *et al.* (2022) *Nature Protocols*

Figure 4. Schematic showing the process of engraftment of intestinal organoids into the colonic lumen.

Limitations
- Vascularization
- Tissue integration
- Cell viability
- Immune rejection

Conclusions

- The diversity of techniques and variables in organoid generation offers opportunities to adapt protocols according to experimental and clinical needs.
- Improvements in technology could enable the creation of functional, transplantable organoids in the near future.
- The vascularization, integration, viability and immune rejection are the major limitations of organoid transplantation.
- The applications of this technology are in early research stages and need further exploration across animal species and clinical contexts.