

Human Intestinal Organoids for Regenerative Medicine and Translational Applications

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Abstract

Human intestinal organoids provide a renewable source of tissue-specific cells with the capacity for long-term expansion, differentiation, and epithelial regeneration. We have developed human pluripotent stem cell-derived intestinal organoid systems and organoid-derived intestinal stem/progenitor cell platforms for regenerative applications, with a particular focus on controlling cell state, improving manufacturability, and enhancing transplantation potential.

Our previous studies demonstrated that intestinal organoid maturation can be regulated by defined niche signals and that expandable intestinal stem/progenitor populations can be generated from human intestinal organoids while retaining multilineage epithelial differentiation and regenerative potential. More recently, we have focused on optimizing the cellular and culture environments required to maintain regenerative capacity during expansion and transplantation. These studies support the development of intestinal organoids and organoid-derived cells as regenerative products for the reconstruction of damaged intestinal epithelium.

For clinical translation, reproducible manufacturing and delivery are also important considerations. We are developing chemically defined and xenogeneic-free culture systems that support scalable expansion while maintaining intestinal identity and regenerative properties. In parallel, culture and delivery strategies are being optimized to improve the suitability of organoid-derived products for transplantation. Studies using intestinal injury models further support the potential of these approaches for mucosal repair and provide a basis for continued development toward intestinal regenerative therapy.

In addition to regenerative applications, we have used gastrointestinal organoids as human-relevant platforms for microbiome research. Intestinal and gastric organoid models have been applied to microbial screening and functional evaluation, including the assessment of epithelial maturation, barrier protection, host-microbe interactions, and tissue-protective effects. These platforms provide an experimental link between microbial screening and functional validation in human gastrointestinal tissues.

As organoid technologies expand into regenerative medicine, microbiome research, and pharmaceutical applications, reproducibility and standardization are becoming increasingly important. We are therefore participating in international standardization efforts, including ISO-related activities, to establish common terminology, quality attributes, and performance criteria for organoid technologies.

In this presentation, I will discuss our progress in human intestinal organoid-based regenerative therapy and its broader application to microbiome evaluation and international standardization.