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## **Organoids for Liver Replacement Therapy**

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Organoids are three-dimensional structures that self-organize from human pluripotent stem cells or primary tissue, potentially serving as a traceable and manipulatable platform to facilitate our understanding of organogenesis. Despite the ongoing advancement in generating organoids of diverse systems, biological applications of in vitro generated organoids remain as a major challenge in part due to a substantial lack of intricate complexity. The studies of development and regeneration enumerate the essential roles of highly diversified non-epithelial populations such as mesenchyme and endothelium in directing fate specification, morphogenesis, and maturation. Such human organoids allow for the study of direct and indirect inter-organ crosstalk recapitulating what is seen in health and disease. For example, we show in vitro modeling of the inter-coordinated specification and invagination of the human hepato-biliary-pancreatic (multi-organ) system in 3D stem cell culture, paving a way for the study of inter-organ connectivity failure such as biliary atresia. I herein summarize the evolving organoid technology at the cell-, tissue-, system-level complexity with a main emphasis on liver derivatives and discuss its pathway to tissue replacement therapy.

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