Organoid-guided Precision Hepatology

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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 and personalized drug development. Despite ongoing advancements in generating organoids of digestive systems, their applications in medicine remain challenging, partly due to a substantial lack of biological complexity. Developmental organogenesis studies underscore 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 inter-organ crosstalk, recapitulating health and disease states. For instance, we demonstrate in vitro modeling of inter-coordinated specification and invagination of the human hepato-biliary-pancreatic system in 3D stem cell culture, paving the way for studying connectivity failure, such as biliary atresia. Furthermore, by integrating polygenic risk scores and massively mosaic organoid panels, these platforms offer unprecedented opportunities for personalized drug development, enabling predictive assessments of therapeutic efficacy and toxicity across diverse genetic and environmental crosstalk. This presentation summarizes the evolution of organoid technology at the cell-, tissue-, and system-level complexities, emphasizing their transformative potential for precision medicine and tissue replacement therapy in hepatology medicine.