Asian Transplantation Week 2023

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Session Title : Biology of organoids

Harnessing the Potential of Organoids for Modeling Liver Diseases and Therapy

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We will present our research on the use of organoids for advancing translational studies in pediatric liver cancer and metabolic liver diseases. Our work is performed within the Princess Máxima Center in Utrecht, Netherlands, which is currently the largest pediatric oncology center in Europe. This unique environment allows us to investigate these rare liver diseases in children effectively. Hepatoblastoma, the most common pediatric liver cancer, is almost always associated with a WNT-activating CTNNB1 mutation. However, it exhibits remarkable molecular diversity. To explore this diversity and discover potential targeted therapies, we conducted an extensive analysis of hepatoblastomas and tumor-derived organoids. Our approach involved single-cell RNA-seq, spatial transcriptomics, single-cell ATAC-seq, and high-throughput drug profiling. Through this comprehensive study, we unveiled two distinct tumor epithelial signatures: hepatic 'fetal-like' and WNT-high 'embryonal-like' signatures, each characterized by distinct WNT signaling patterns. Furthermore, we conducted high-throughput drug screening using patient-derived tumor organoids, identifying notable sensitivity to various inhibitor classes, with HDAC inhibitors showing particularly promising results. Our findings shed light on the molecular landscapes of hepatoblastoma and offer insights into potential targeted therapeutic approaches. In addition to our work on hepatoblastoma, we are also exploring metabolic liver diseases, which can lead to the early onset of hepatocellular carcinoma (HCC) in adolescents. Our research has demonstrated the capacity of murine hepatocyte organoids to engraft and repopulate nearly the entire liver in mouse models. We will discuss how cell replacement therapy, utilizing in vitro expanded cell sources, holds significant promise for the treatment of metabolic diseases.