(T1046) Multiomics study to elucidate the molecular pathogenesis of choledochal cysts

Clara Sze Man TANG - *The University of Hong Kong*

Qiongfen Lin – The University of Hong Kong; Zijing Yang – The University of Hong Kong; **Pak Sham** – The University of Hong Kong; **Paul Tam** – Macau University of Science and Technology

Abstract: Congenital bile-duct dilatation (CDD) is a rare complex anomaly most commonly found in Asians, which is characterized by abnormal dilatation of the extrahepatic and/or the intrahepatic bile ducts. Despite surgery, many patients still suffer from post-operative complications and an increased risk of hepatobiliary cancers. Our previous genetic study suggested a genetic predisposition in the pathogenesis of the disease. To further elucidate the genetic causes of CDD, we performed whole exome and genome sequencing on 78 trios of type I and IV CDD patients of Chinese and Vietnamese ancestries. De novo analysis identified thirty-seven damaging protein-altering variants, which were enriched in oncogenic MAPK signaling and focal adhesion pathways. Recessive and compound heterozygous damaging mutations were also enriched in associated oncogenic pathways. Spatiotemporal expression of these candidate gene was further evaluated using fetal single cell transcriptomic data and single nuclei RNA sequencing data of CDD extrahepatic bile duct. The findings suggest a link between genetic predisposition, cancer genes, and disease pathogenesis. Unravelling this relationship will help guide the stratification of patients based on the pathological mechanism and to correlate the genetic findings to disease prognosis, particularly the increased risk of malignancy.

Funding Source: The project is supported by General Research Fund 17113320