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SINGLE CELL RNA SEQUENCING OF THE NATIVE HUMAN LIVER AND ITS SPATIAL RESOLUTION REVEAL NEW SUBPOPULATIONS OF NON-PARENCHYMAL CELLS.

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Abstract Text:

Background: The liver's multitude of vital functions are tightly linked to its complex assembly of highly specialized parenchymal and non-parenchymal cells in collaborative sinusoidal units. Following the recent advancement in single-cell analyses, today whole organ heterogeneous cell populations can be studied without the need to separate the cells, opening avenues to provide comprehensive maps of an organ's different cell populations and their distribution in distinct functional subpopulations. In the present study we aimed at providing the first high-resolution transcriptomic map of the infant and adult human liver by single-cell RNA sequencing.

Methods: Approximately 80,000 liver cells obtained after collagenase digestion of two human livers (Hepatic Tissue Bank and Biobank; Cliniques Universitaires Saint-Luc) were loaded in a 10X Genomics instrument to generate 8 independent libraries. The libraries were sequenced using the Illumina technology in order to reach an average of 65,000 reads/cells. The data generated for both donors were analyzed separately and cell clusters were identified, annotated and zoned according to previously established functional, transcriptional and histological studies performed in mice and human.

Results: A total of ~28,000 single-cell transcriptomes were generated, of which ~78%, 3% and 18% corresponds to hepatocytes, cholangiocytes and non-parenchymal cells, respectively. Taking specific gene expression patterns related to zoned liver functions (i.e. glutamine metabolism, urea cycle, bile acid synthesis, xenobiotic metabolism and albumine production) as a reference, the single-cell transcriptomes obtained for hepatocytes have efficiently been organized along the porto-central axis, revealing the pericentral-, periportal- and midzonal-specific hepatocyte transcriptomes. Within the clusters of cholangiocytes and non-parenchymal cells, our preliminary results identify multiple subpopulations, including 2 distinct populations of hepatic stellate cells, of which the transcriptomic disparities hint to intriguing functional subspecializations.

Conclusion: Our study provides a transcriptomic atlas of the human native liver at an unparalleled resolution and contributes to a better understanding of the heterogeneity of the cellular compartments that underlies the physiology of the human liver.

Title:

SINGLE CELL RNA SEQUENCING OF THE NATIVE HUMAN LIVER AND ITS SPATIAL RESOLUTION REVEAL NEW SUBPOPULATIONS OF NON-PARENCHYMAL CELLS.

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Presentation Type:

Oral or Poster

Sponsorship:

The Walloon Region of Belgium and Promethera Biosciences

Category:

Liver Fibrogenesis and Non-Parenchymal Cell Biology

Description:

Basic Fibrosis Research and Stellate Cell Biology

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