Gene Regulatory Network Inference from Single-Cell Transcriptomic Data in Hepatocellular Carcinoma

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Master thesis in Bioinformatics and Computational Biology

Hepatocellular carcinoma (HCC) is one of the most lethal cancers worldwide and the most frequent form of primary liver malignancy. This malignancy typically arises on a background of chronic inflammation resulting from viral hepatitis or fatty liver disease. Various etiologies are associated with HCC and some studies have suggested that the treatment response differs depending on different underlying HCC etiologies. However, the biologically distinct mechanisms between different HCC etiologies remain still relatively unclear. Analysis of gene regulatory networks (GRNs) is critical to uncover the regulatory mechanism driving different HCC etiologies. Based on single-cell RNA-sequencing (scRNA-seq) data of HCC patients and non-tumoral/normal livers, I constructed GRNs from HCCs of different etiologies and non-tumoral/normal livers, for each cell cluster. Through comparing GRNs among different HCC etiologies and among HCCs and non-tumoral/normal livers, I revealed the most critical genes and transcription factors, and further explored the influence of specific central genes and specific regulatory interactions on biological functions and pathways. Besides previously reported dysregulated genes, this study provides novel candidate genes which might play a putative role in the development of HCC. Functional exploration further highlights specific biological processes and pathways which might be highly related to HCCs. Taken together, the construction of GRNs based on scRNA-seq data enables to detect regulatory changes between HCCs of different etiologies and non-tumoral/normal livers that are invisible to scRNA-seq analyses based on clustering or differential expression analysis, expanding insights that can be obtained with scRNA-seq technology.

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