Single cell RNA-seq revealed landscape of infiltrating T cells in HBV+ liver cancer

Subject Code: H16

With the support by the National Natural Science Foundation of China, a collaborative study by the research groups led by Prof. Zhang Zemin (**张泽民**) from the Biodynamic Optical Imaging Center (BIOPIC), Peking University, Prof. Peng Jirun (**彭吉润**) from Beijing Shijitan Hospital, Capital Medical University, and Prof. Ouyang Wenjun (**欧阳文君**) from the Department of Inflammation and Oncology, Amgen Inc. illustrated the landscape of infiltrating T cells in liver cancer via single cell RNA-seq sequencing, which was published in *Cell* (2017, 169: 1342—1356).

Primary liver cancer is one of the most common malignancies in China and results in 360,000 incident cases and 350,000 deaths a year currently. Chronic hepatitis B virus (HBV) infection is the major cause. Yet, limited treatment options are available. Cancer immunotherapies have provided great promises for oncological treatment in multiple cancer types including melanoma, lung and colon cancers over the past decades, but clinical effectiveness in liver cancer is seldom reported. Their group applied the state-of-the-art single cell transcriptome sequencing technology to treatment-naïve HBV+ hepatocellular carcinoma (HCC), and mapped the landscape of infiltrating T cells precisely, providing important insights into the immune status of HCC.

They isolated 5063 T cells from three tissue types (peripheral blood, tumor, and adjacent normal tissues) for six HBV+ HCC patients, and performed deep single-cell RNA sequencing (~1.2 million reads with paired 150bps for each cell on average). The dataset not only allowed characterization of the transcriptional profiles of individual cells but also enabled assembling full-length T cell receptor (TCR) sequences. They identified 11 T cell subsets with characteristic molecular and functional properties, among which exhausted CD8+T cells and regulatory CD4+T cells preferentially enriched in the tumor tissues. The enrichment is related to local clonal expansion of these T cells, as indicated by their TCR sequences. They further identified signature genes for each subset which may serve as potential drug target candidates. One of the genes, layilin, is upregulated on both exhausted CD8+T cells and regulatory CD4 + T cells. Further studies demonstrated that it can repress the CD8+T cell functions *in vitro*. The deep transcriptome data also revealed rarely observed CD8+FOXP3+ regulatory-like cells in one patient, demonstrating the potential to discover novel cell types.

This compendium of transcriptome data and the new findings provide valuable insights into the immune status of HBV+ HCC patients, and the signature genes of each T cell subset may also be good drug targets, facilitating the development of immunotherapies for liver cancers. However, more studies are needed to completely understand the interplay of tumor and immune cells and to fully evaluate the therapeutic values of the potential drug target candidates.

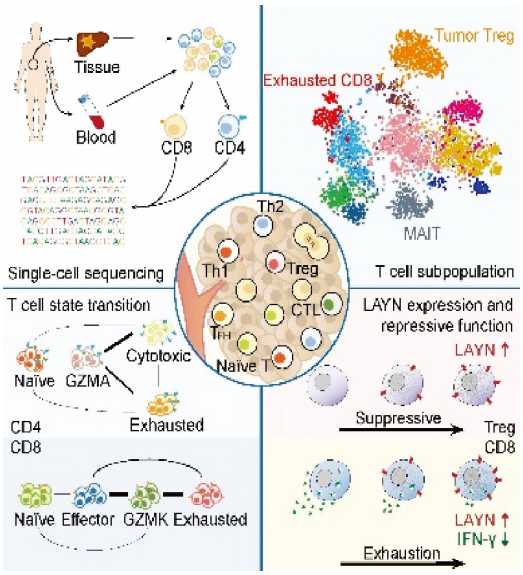

Figure T cell landscape of HBV+ liver cancers.