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Exploiting immunity of hepatocellular carcinoma (HCC) to improve the treatment of patients

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ABSTRACT

Hepatocellular carcinoma (HCC) is the most common liver tumor and among the deadliest cancers worldwide. Environmental risk factors for developing HCC include chronic hepatitis B or C virus infection, alcohol abuse and the metabolic syndrome. Despite a significant therapeutic advance in the treatment of advanced HCC with the arrival of immune checkpoint inhibitors (ICI), ~75% of patients do not respond to these immunotherapies for unclear reasons. Such a heterogeneous response highlights the need to further explore etiology- and organ-specific immunity towards improved patient stratification and the development of new combination therapies. To better characterize the HCC immune microenvironment, we have employed 3′ end massively parallel single cell RNAseq (scRNAseq) with a 10x Genomics Chromium pipeline of live immune cells, FACS-sorted from dissociated tumors to particularly study the myeloid and innate lymphoid immune landscapes of HCC with respect to etiology and mutations in the β-catenin pathway that distinguish an immune-excluded class of HCC patients resistant to ICI. Our preliminary results uncovered marked differences in the HCC immune landscape compared to that of adjacent non-tumoral tissue and identified specific immune subsets according to etiology. This analysis will be expanded in a validation cohort, and in HCC patients receiving ICI. The geographical distribution of the identified immune cell subsets and their expression of specific biomarkers will be analyzed using multispectral immunofluorescence analysis (Vectra-Polaris) and spatial transcriptomics (10x Genomics Visium technology). Collectively, our project is expected to uncover immune biomarkers to better select patients who are likely to respond to current immunotherapies and identify novel therapeutic entry points for improved HCC patient care.

BIOGRAPHY

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