



Proteomic and Single-cell Landscape Reveals Novel Pathogenic Mechanisms of HBV-infected Intrahepatic Cholangiocarcinoma

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BACKGROUND

Despite the epidemiological association between intrahepatic cholangiocarcinoma (ICC) and hepatitis B virus (HBV) infection, little is known about the relevant oncogenic effects. Therefore, we sought to identify the genomic, proteomic and single cell transcriptomic architecture of HBV-infected ICC tumors.

METHODS

A cohort of 32 HBV-infected ICC and 89 non-HBV-ICC were characterized using whole-exome sequencing, proteomic analysis, and single cell RNA sequencing.

ACKNOWLEDGEMENTS & CONTACT

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RESULTS

The Epithelial-to-Mesenchymal Transition (EMT) related gene FAT1 had a significantly higher mutation rate in HBV-ICC patients than nonHBV-ICC patients.

Further proteomic analysis revealed decreased cell-cell junction levels in HBV-ICC patients. In addition, the cell-cell junction level had an inverse relationship with EMT program in ICC patients.

Single cell analysis indicated that TGF β -signaling related EMT program changes increased in tumor cells of HBV-ICC patients.

Analysis of the immune landscape found that more CD8 T cells and Th2 cells were present in HBV-ICC patients.

ICAM1⁺ tumor-associated macrophages were correlated with a poor prognosis and contributed to the EMT in HBV-ICC patients.

Immune checkpoints analysis indicated the immunosuppressive landscape of CD8 T cells in HBV-ICC patients. A prominent co-inhibitory signal via the TIGIT–NECTIN2 axis was identified in complementary T cells and tumor cells.

The results were shown in Fig 1.

FIGURES

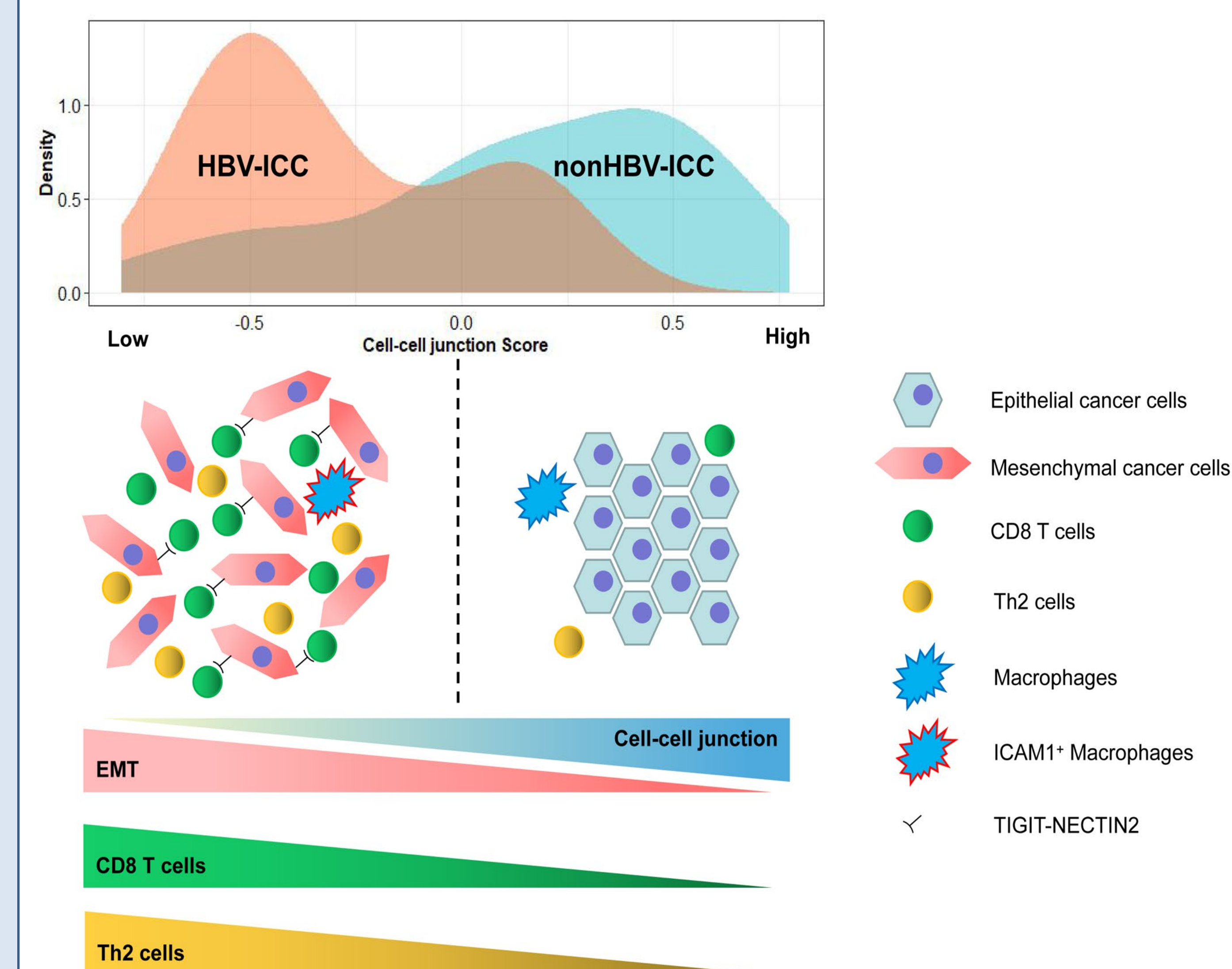


Fig 1. Graphical representation of the differences between HBV-ICC and nonHBV-ICC.

CONCLUSION

Our findings provide new insights into the behavior of HBV-infected ICC driven by various pathogenic mechanisms involving decreased cell junction levels and increased progression of the EMT program.

Our analysis of the immunosuppressive landscape provides mechanistic information useful for the design of efficacious immune-oncology treatments in ICC.