



Samenvatting proefschrift G. Zhou

‘Regulation of intra-tumoral T cell immunity in liver cancer’

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Liver cancer represents the second most common cause of cancer-related mortality worldwide. Hepatocellular carcinoma (HCC) is the most prevalent primary liver cancer, cholangiocarcinoma (CCA) second. Liver metastasis of colorectal cancer (LM-CRC) is the most frequent secondary liver cancer and a leading cause of death from CRC. The current therapeutic options for all three types of liver cancer are very limited. Hence, there is a pressing need for novel and effective treatments.

In this thesis we investigate some of the immune suppressive mechanisms in the tumor microenvironment of liver cancers with the goal of identifying new and potentially promising immunotherapeutic targets to overcome intra-tumoral immune inhibition and enhance anti-tumor reactivity of tumor-infiltrating T cells in patients with liver cancer. We study how to reduce the immunosuppressive capacity of pro-tumor regulatory T cells, and how to activate anti-tumor functions of effector T cells in HCC, CCA and LM-CRC by manipulating co-inhibitory and co-stimulatory pathways. For this purpose, we used leukocytes isolated from resected liver tumors, tumor-free liver tissues and peripheral blood collected from patients who underwent liver tumor resection, and performed flow cytometry analyses and in vitro immune cell culture assays. The ultimate aim of these studies is to provide new immunotherapeutic approaches to treat patients with primary liver cancer or CRC liver metastasis.

Part I focuses on two types of pro-tumor T cells, immunosuppressive conventional regulatory T cells and type I regulatory T cells. We have studied how to abrogate the immune suppression exerted by these cells in the tumor microenvironment.

Part II focuses on two types of anti-tumor T cells, CD8⁺ cytotoxic T cells and CD4⁺ T helper cells. We have studied how to invigorate effector functions of tumor-infiltrating T cells by targeting co-inhibitory and co-stimulatory immune checkpoint pathways.

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