Inflammation and Cancer: Friend or Foe?

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Abstract
Although antitumor immune response has been harnessed to combat cancer, tumor-promoting inflammation has long been noticed by the progression of chronic inflammation to cancer and has become one of the emerging hallmarks of cancer. Many questions arise as to which inflammatory cytokines or which subsets of immune cells directly or indirectly promote malignancy, which of these can be targeted or reprogrammed to instead combat cancer, and to what degree these properties are generic or tissue-specific. Many inflammatory cytokines play important roles during cancer development. Therapeutic strategies have also been developed to target pro-tumor inflammation.

Our laboratory focuses on the role of liver inflammation, especially inflammatory cytokines during the development and progression of hepatocellular carcinoma. IL-17A has been found in both murine and human tumor microenvironment, and shown to be critically involved in tumor development. However, the role of IL-17A in antitumor immunity remains controversial. Our recent finding demonstrated the immune-suppressive role of IL-17A in hepatocellular carcinoma and revealed a novel mechanism involving crosstalk between γδ T cells, MDSCs and tumor cells through IL-17A production in the tumor microenvironment. Therefore, IL-17A could be a potential target for future immunotherapy. IL-23 is another inflammatory cytokine, which can expand Th17 and other IL-17 producing cells. IL-23 can not only directly promote tumor cell growth but also regulate antitumor immune responses through the expansion of Tc17 cells in hepatocellular carcinoma.

Tumor vaccines to induce specific antitumor immune response did not achieve satisfying clinical efficacy because of the immune-suppressive tumor microenvironment caused by pro-tumor inflammation. Combining with other immunotherapy strategies, including inhibitory checkpoint blockade and targeted cytokine treatment, would greatly improve the outcome of tumor immunotherapy. Our laboratory is interested in oncolytic virus and targeted cytokine therapy. We have generated Newcastle Disease Virus expressing IL-7 with reverse genetic system. It was used to modify autologous tumor vaccine and achieved prophylaxis and therapeutic efficacy, which has been shown to be dependent on the CD8⁺ T cells. It warrants future studies for the development of an effective cancer vaccine based on our strategies.

Selected Publications
2. Yong Liang, Shoubao Ma, Yanming Zhang, Ying Wang, Qiao Cheng, Yan Wu, Yue Jin, Donghui Zheng, Depei Wu, Haiyan Liu (2014) IL-1β and TLR4 signaling are involved in the aggravated murine acute graft-versus-host disease caused by delayed bortezomib administration. Journal of Immunology 192(3):1277-85
4. Fen Liu, Fuyi Tong, Yan He, Haiyan Liu (2011) Detectable expression of IL-35 in CD4⁺ T cells from peripheral blood of chronic hepatitis B patients. Clinical Immunology 139:1-5