The role of tumor induced immune tolerance by tumor associated macrophages in hepatocellular carcinoma

Madeline Sauer, M2, Primary Presenter
Xiaoqiang Qi, PhD
Kevin Staveley-O'Carroll, MD, PhD, MBA
Guangfu Li, DVM, PhD

Department of Surgery

INTRODUCTION:
Hepatocellular carcinoma (HCC) is a lethal disease with limited treatment options. Immunotherapy is revolutionizing cancer care, but FDA approved immune checkpoint inhibitors still only function in a minority of patients. Elucidating the underlying mechanism is required to improve targeted immunotherapy. This study explores the role of tumor-associated macrophages (TAMs) on tumor growth and tumor-induced immune tolerance.
[58 words]

METHODS:
Using intrasplenic inoculation of oncogenic hepatocytes into wild type (WT) mice, we made a clinically relevant mouse model of HCC. Enzyme digestion followed by gradient centrifugation were used to isolate non-parenchyma leukocytes. Flow cytometry was used to detect frequency and phenotype of immune cell subsets. Flow sorting was used to purify macrophages for further analysis. Real time PCR, western blot and immunohistochemistry we detected CD47 and SIRP expression in WT and tumor-bearing mice.
[73 words]

RESULTS:
Monocyte derived and embryonic derived macrophages were highly purified with flow sorting to extent of more than 95%, and were separated based on moderate or high expression of CD11b. Tumor growth significantly increased the frequency of monocyte-derived macrophages and decreased the embryonic derived macrophages. Analysis of the macrophage subpopulation revealed a significant increase in the SIRPα/CD47 axis at the mRNA and protein level in embryonic derived macrophages with no significant change in the monocyte derived macrophages.
[76 words]

CONCLUSION:
Selective upregulation of the SIRPα/CD47 axis in embryonic macrophages suggests suppression of phagocytosis within this population may enhance tumor progression. Tumor growth drives change in macrophage populations and expressions, giving insight into the mechanism underlying HCC induced immune tolerance.
[39 words]

Total word count [244] without headers, title or authors