B3

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Unraveling the Impact of IL-23 Signaling on Hepatocellular Carcinoma Progression: Insights from Transgenic Murine Models and Cellular Profiling

Background: Interleukin-23 (IL-23) is a pro-inflammatory cytokine that is primarily secreted by dendritic cells and macrophages, leading to the differentiation and maintenance of Th17 cells. Although the role of IL-23 in hepatocellular carcinoma (HCC) has been controversial, more recent studies have shown its role in promoting HCC and the tumor microenvironment.
Methods: Transgenic mice with the deletion of the IL-23 receptor on CD4 expressing cells (IL-23CD4cre) were generated utilizing the Cre-LoxP recombination system. These mice were injected with 8,000 MC38 cells (murine colon adenocarcinoma cells) via the portal vein. After 4 weeks, liver tumors were assessed and tissues were prepared for flow cytometry analysis.
Results: Using liver weight as an indirect gauge of tumor volume, IL-23CD4cre mice had a significantly greater liver weight than IL-23 competent mice. Although no statistically significant disparity in tumor count or burden was observed, a trend consistent with liver weights was discernible. The absence of statistical significance could be attributed, at least in part, to the small group size utilized in this investigation. Furthermore, employing flow cytometry analysis, we detected a significantly heightened prevalence of neutrophils, monocytes, and T regulatory cells within non-tumor liver tissue from IL-23CD4cre mice, alongside a notably reduced frequency of macrophages compared to the IL-23 competent mice.
Discussion: The observed variations in flow cytometry analysis predominantly emanating from non-tumor tissue in contrast to tumor tissue suggest a potential involvement of IL-23 in augmenting the tumor microenvironment conducive to metastatic proliferation. Notably, this effect appears to be primarily mediated through modulation of myeloid cell frequencies within the non-tumor liver tissue.