The cell type specific function of JNK-1 in the development of hepatocellular carcinoma

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HCC represents the most common form of liver cancer type and the third largest cause of cancer death worldwide. Besides other risk factors, such as alcoholic liver disease or nonalcoholic steatohepatitis, obesity has been identified as an additional major risk factor for HCC development by creating an inflammatory, tumor promoting environment. The development and progression of obesity associated HCC is a complex process which depends on a multiplicity of events. One molecule that appears to be involved in almost all events is JNK. The exact mechanism how JNK contributes to the development and progression of HCC is not completely known but it appears to be strongly cell type specific.

Previous work on this project has demonstrated a higher tumor burden in mice which were deficient for JNK-1 in the myeloid lineage (JNK-1M-KO) and exposed to high fat diet feeding. The goal of our study was to investigate the origin of this increased tumor burden. The obtained results exhibited no alterations of apoptotic activities, neither on the expression level nor on the protein level. The expression of TNFα and IL-6 remained unchanged in JNK-1M-KO animals upon HFD feeding. Marker genes for M1 macrophages on the other hand, showed a lower expression in mice lacking JNK-1 on HFD feeding, indicating a diminished presence of pro-inflammatory macrophages. This was accompanied by a reduced expression of IL-1β since this cytokine is mainly released by M1 macrophages. In contrast to these findings, the expression of IL-22, a cytokine with tissue protective properties, was up-regulated in JNK-1M-KO mice up HFD feeding compared to the control animals. This was consistent with a slightly elevated cell proliferation in these mice. Nevertheless, more experiments are mandatory in order to confirm these results and to elucidate further effects of JNK-1 in macrophages to obesity associated HCC development.