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**Role of GPNMB in hepatic steatogenesis and cancer**

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**Background and aims**

Non-alcoholic fatty liver disease (NAFLD) is considered as the most common cause of chronic liver disease worldwide. With its progressive form, non-alcoholic steatohepatitis (NASH), is characterized by steatosis and inflammation with hepatocyte injury with or without fibrosis, and it is revealed as an evolving major cause of hepatocellular carcinoma (HCC). Noteworthy, a considerable fraction of patients may suffer from progression of the disease towards hepatocellular carcinoma (HCC). Gpnmb a transmembrane glycoprotein that is expressed in bones, calvaria, adipose, skin, pancreas, lung, liver. However, the role of Gpnmb in liver injury is still unknown. Therefore, we aim to identify the concentration of GPNMB in hepatic steatogenesis and cancer.

**Methods**

A NASH-based hepatocellular carcinoma model (STAM) was performed. 2-day-old male C57BL/6J mice were injected with streptozotocin (200 mg/mouse). Starting from 4 weeks of age, the mice were continuously fed a high-fat diet (HFD) for the duration of the study. We examined genes differentially expressed between 12W and 20W of STAM mice. To compare the STAM mice 12W with GSE48452 (Human NASH) and compare 20W with GSE14520 (Human HCC). Benjamini-Hochberg adjusted P values were calculated and an adjusted P value cutoff of 0.05, and a fold change threshold of 0.5, were used to compare significantly altered gene transcripts at each group. With IHC we saw GPNMB expressed in hepatocyte in normal mice but in hepatocarcinoma cells in HCC mice. From qPCR we checked the GPNMB expression in STAM tissue and HUH7/HCC. Modulating GPNMB to see its function in primary hepatocyte, AML-12 and HUH7.

**Results**

GPNMB expression is upregulated from steatogenesis and cancer. GPNMB staining shows cytoplasmic were positive with normal cells but accumulation in tumor cells in HCC. GPNMB inhibits lipid droplet formation and promotes apoptosis of HUH7 cell.

**Conclusion**

We can conclude that a STAM mouse is an optimal model to study NASH-based HCC for diagnostic and therapeutic targeting. GPNMB promotes fatty acid oxidation, and GPNMB is tumor suppressive and promotes apoptosis of HCC cells by inhibiting the PI3K/AKT pathway.