Liver cancers are a major cause of cancer-related deaths. Large-scale genetic analyses have associated liver cancer with dysregulation of numerous molecular pathways, but disruptions in insulin signaling pathways appear to have a particularly important contribution to liver tumor formation. Obesity is a major risk factor for developing liver cancer, and the nuclear receptor PPAR? critically controls fat uptake and storage in the liver by regulating the transcription of metabolism-associated genes. However, whether PPAR? also plays a role in promoting the growth of liver tumors is not clear.

This week in the *JCI*, research led by Ganna Panasyuk at INSERM examined the link between PPAR? and liver tumor formation. The findings identify a metabolic pathway with pro-tumor effects that can be suppressed by selectively blocking PPAR?.

Researchers initially observed that increases in PPAR? expression and activity in human liver tumors were associated with loss-of-function of the transcription factor hepatocyte nuclear factor 1? (HNF1?). In a mouse model, they determined that loss of HNF1? led to abnormal increases in PPAR? expression that in turn led to increased tumorigenesis.

Pharmacological activation of PPAR? in a mouse model of liver cancer exacerbated tumor formation; in contrast, treatment with a PPAR? inhibitor had positive therapeutic effects.

Taken together, these findings demonstrate a role for PPAR? in the metabolic pathway disturbances that promote liver tumorigenesis and reveal that PPAR? is a potential target for anti-tumor therapies to treat liver cancers.

**More information:** Cecilia Patitucci et al, Hepatocyte nuclear factor 1? suppresses steatosis-associated liver cancer by inhibiting PPAR?