

Study identifies a role for the metabolism regulator PPAR-gamma in liver cancer

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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 γ critically controls fat uptake and storage in the liver by regulating the transcription of metabolism-associated genes. However, whether PPAR γ 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 γ and liver tumor formation. The findings identify a metabolic pathway with pro-tumor effects that can be suppressed by selectively blocking PPAR γ .

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

Pharmacological activation of PPAR γ in a [mouse model](#) of [liver cancer](#) exacerbated tumor formation; in contrast, treatment with a PPAR γ inhibitor had positive therapeutic effects.

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

More information: Cecilia Patitucci et al, Hepatocyte nuclear factor 1 α suppresses steatosis-associated liver cancer by inhibiting PPAR γ transcription, *Journal of Clinical Investigation* (2017). [DOI: 10.1172/JCI90327](#)

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