

Liver cancer: Molecular signaling pathway of tumor development decoded

April 23 2024



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As a malignant disease of the liver cells, hepatocellular carcinoma (HCC) is one of the main causes of cancer-related deaths. While the treatment options for this aggressive type of cancer remain limited, the incidence is increasing.

A research team led by Latifa Bakiri and Erwin Wagner from MedUni



Vienna's Clinical Institute for Laboratory Medicine has now described a molecular signaling pathway that plays a key role in the development of liver cancer, thereby identifying a potential new starting point for the development of therapeutic treatments. The results of the study have just been published in the journal *Proceedings of the National Academy of Sciences*.

In their research, the international team led by MedUni Vienna, built on earlier study results that had suggested the involvement of certain transcription factors (c-Fos and c-Jun) in the development of hepatocellular carcinomas. Transcription factors are proteins involved in numerous cellular processes, including the control of genes associated with the development of HCC. To advance these findings, the scientists developed a new mouse model.

The experiments carried out with these proteins showed that the combination with previously unexplored (Fra) proteins in this context triggers the cascade of tumor formation. Specifically, this involves the interaction between c-Jun and Fra-2, which the studies showed to be essential in the development of liver cancer.

"It is remarkable that we were able to reverse <u>tumor growth</u> by switching off the <u>protein</u> combination of c-Jun and Fra-2," reports the head of the study Wagner.

The study also showed that tumor growth can be stopped by blocking a specific gene (c-Myc). "Accordingly, our research results suggest that the molecular signaling pathway we have identified represents a promising starting point for further research into HCC and the development of new therapeutic measures," concludes first author Bakiri.

Hepatocellular carcinoma is an aggressive tumor with rapid progression



and limited therapeutic options. Even though the incidence has increased significantly in Western countries in recent decades, this type of cancer is still comparatively rare. However, due to its <u>poor prognosis</u>, HCC is one of the most common causes of cancer-related deaths. HCC occurs in particular in the context of advanced <u>liver</u> disease (cirrhosis, chronic hepatitis B) and is often only diagnosed at a late stage.

More information: Bakiri, Latifa et al, Liver cancer development driven by the AP-1/c-Jun~Fra-2 dimer through c-Myc, *Proceedings of the National Academy of Sciences* (2024). DOI: 10.1073/pnas.2404188121. doi.org/10.1073/pnas.2404188121

Provided by Medical University of Vienna

Citation: Liver cancer: Molecular signaling pathway of tumor development decoded (2024, April 23) retrieved 26 June 2024 from https://medicalxpress.com/news/2024-04-liver-cancer-molecular-pathway-tumor.html

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