

Liver progenitor cells are involved in the development of hepatic tumors

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The malignant transformation of hepatocytes is the origin of most hepatocellular carcinomas, an aggressive type of liver cancer with high mortality rates. But these cells do not act alone. Research conducted by scientists at the Spanish National Cancer Research Centre (CNIO) reveals how hepatocytes "recruit" and "instruct" liver progenitor cells to contribute to the hepatic lesions.

"The cellular origin of [liver cancer](#), as well as the origin of tumour heterogeneity, are not clear yet and may be context-dependent," say the authors in the journal *Cell Reports*. Hepatocytes -the main liver cells- have been considered the main source of hepatocellular carcinomas but the results of this research provide various novel perspectives.

"What we are showing here is that hepatic [progenitor cells](#) expand during tumorigenesis and, at one point, they become transformed because of oncogenic hepatocyte cross-talk; this makes them participate in liver tumour development in general, and in hepatocellular carcinomas in particular," explains Nabil Djouder, head of the Growth Factors, Nutrients and Cancer Group at the CNIO and main author of the paper.

Thanks to an animal model -generated by Djouder and his team- that fairly reproduces the tumour formation process seen in human hepatocarcinogenesis, and to other genetic experiments, the authors have tried to follow the formation of the lesions and to define the histopathology of the various tumours that develop in this organ, whether benign (regenerative nodules, adenomas) or malignant (hepatocellular

[carcinoma](#) or HCC).

"This is what we've seen: oncogenic hepatocytes lead to hepatocellular carcinoma but, in a model that mimics human hepatocarcinogenesis, progenitor cells also participate in [liver](#) tumour heterogeneity. They mostly lead to benign tumours but sometimes they can lead to aggressive carcinomas", points out Djouder. In other words, progenitor cells become oncogenic even though they were not initially transformed.

Malignant hepatocytes crosstalk and instruct neighbouring progenitor cells to become activated, maintaining them in an undifferentiated state while at the same time proliferating, becoming oncogenic themselves, and contributing to the lesions. This activation occurs, as shown by this study, when the hepatocytes secrete two substances (α -ketoglutarate and galectin-3) that act and transform [progenitor](#) cells.

"Blocking galectin-3 can block the cross-talk between these [cells](#) thereby reducing tumourigenesis", a finding that could have therapeutic implications, explains Djouder.

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