Nature Reviews Gastroenterology & Hepatology | Published online 10 Feb 2016; doi:10.1038/nrgastro.2016.21

HEPATOCELLULAR CARCINOMA

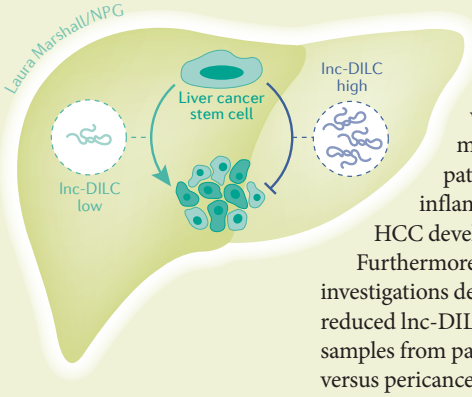
A role for lncRNA in liver cancer

New findings published in the *Journal of Hepatology* suggest a functional role for long non-coding RNAs (lncRNAs) in the development of hepatocellular carcinoma (HCC), which could ultimately aid prognosis and treatment of the disease.

As the sixth most prevalent human malignancy, there is an urgent need to clarify the mechanisms of HCC progression. Liver cancer stem cells (LCSC) are believed to be critical in the chemoresistance and recurrence of HCC. Recent studies have also reported the aberrant expression of lncRNAs in malignancies including HCC, but their role in LCSC propagation was previously unknown.

Now, using microarrays, the consistently reduced expression of one lncRNA in multiple HCC cell lines has been found, termed lnc-DILC (lncRNA downregulated in LCSC). The investigators assessed the role of lnc-DILC in hepatoma spheroids, in which knockdown of lnc-DILC was shown to enhance LCSC expansion whereas overexpression suppressed propagation. Lnc-DILC knockdown spheroids also exhibited enhanced xenografted tumour growth *in vivo*, demonstrating an inhibitory role for lnc-DILC in HCC.

The investigators also showed that transcription of the inflammatory cytokine *IL-6* was downregulated by lnc-DILC, and a putative binding locus was found within the *IL-6* promoter. "We found that lnc-DILC suppressed LCSC expansion by inhibiting IL-6–STAT3 autocrine signalling," reports author Hongyang Wang, and that it also, "mediates crosstalk between NFκB signalling and the IL-6–STAT3 cascade, which are the most important pathways involved in inflammation-associated HCC development".



Furthermore, clinical investigations demonstrated reduced lnc-DILC in tumour samples from patients with HCC versus pericancerous normal tissue, as well as possible correlations between lnc-DILC levels and LCSC biomarkers, suggesting potential prognositc value. "Considering the pivotal role of lnc-DILC in LCSC expansion, we will explore whether it could serve as a potential therapeutic target in HCC treatment in the near future," concludes Wang.

Iain Dickson

> "…there is an urgent need to clarify the mechanisms of HCC progression"

ORIGINAL ARTICLE Wang, X. *et al.* Long non-coding RNA DILC represses self-renewal of liver cancer stem cells via inhibiting autocrine IL-6/STAT3 axis. *J. Hepatol.* http://dx.doi.org/10.1016/j.jhep.2016.01.019