

LIVER CANCER

A model of fibrolamellar carcinoma

The first patient-derived transplantable xenograft model of fibrolamellar carcinoma (FLC; also called fibrolamellar hepatocellular carcinoma), has been developed.

FLC is a cancer that affects children and young adults. “A major concern is that FLCs have been increasingly diagnosed over the past ~45 years, have no known aetiology and there are no known successful forms of treatment,” write corresponding authors Lola Reid and Praveen Sethupathy.

Ascites from a patient with FLC was cultured under conditions selective for endodermal stem or progenitor cells. These cells were transplanted into mice and formed tumours. Histological analysis of the xenograft tumour showed similarities with the patient’s tumour. RNA-seq analysis of the model tumour revealed the existence of the *DNAJB1-PRKACA* fusion gene, present in ~80% of FLCs. Based on these results, the authors believe this is a genuine model of human FLC.

Further characterization of the xenograft tumours (after depletion of mouse cells), revealed a high percentage (60% or more) of tumour cells expressed stem cell markers such as, CD44 and LRG5. Immunohistochemical assessment of primary human FLC tissue also showed expression of stem cell markers. Global transcriptomic data suggests that FLCs arise from biliary tree stem cells.

High expression of multidrug resistance genes might be why FLCs are resistant to chemotherapy. Loss of *HDAC9* was seen, but the effect on pathogenesis is unknown.

“It is our hope that this study might lead to novel diagnostic procedures and therapies that will help patients,” conclude Reid and Sethupathy.

Gillian Patman

Original article Oikawa, T. *et al.* Model of fibrolamellar hepatocellular carcinoma reveals striking enrichment in cancer stem cells. *Nat. Commun.* doi:10.1038/ncomms9070