A Tumorigenic Index to Determine Liver Cancer Initiation and Prognosis

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BACKGROUND

The incidence and mortality of liver cancer, mainly hepatocellular carcinoma (HCC) and intrahepatic cholangiocarcinoma (ICC), are increasing rapidly worldwide. Diverse risk factors for primary liver cancer have been identified, including infection of hepatitis B virus (HBV) and hepatitis C virus (HCV), alcohol abuse and non-alcoholic steatohepatitis (NASH) as well as intake of aflatoxin B1. Consistent with the complex and multifactorial etiologies, multiomics analyses of human HCC and ICC samples have identified vast genomic heterogeneity, molecular and cellular defects, metabolic reprogramming, and subtypes of tumors as well as altered tumor microenvironment in the liver. However, it remains to be determined if any common molecular signatures in the transcriptomes exist for liver cancer, despite their considerable genomic heterogeneity. Furthermore, little is known about the kinetics and fashions, either gradual accumulation or dramatic transition, in generation of cell-intrinsic and -extrinsic signals that are intertwined to drive malignant transformation of hepatocytes and tumor initiation.

TECHNOLOGY DESCRIPTION

Researchers at UC San Diego have come up with stepwise mechanisms to probe hepatocarcinogenesis, by examining the interrogated temporal gene expression profiles in several mouse models with hepatic steatosis, fibrosis, inflammation and consequently tumorigenesis. Instead of anticipated gradual changes, a sudden molecular switch at a critical pre-cancer stage was identified by developing a new analytical approach that focuses on transcription factor (TF) clusters. Coarse-grained network modeling further demonstrated that the abrupt transcriptomic transition occurred once changes were accumulated to reach a threshold. Based on the experimental and bioinformatic data analyses, as well as mathematical modeling, a tumorigenic index (TI) was devised to quantify tumorigenic signal strengths, which can effectively predict tumor stages and prognosis of liver cancer patients and for triage of liver cancer patients with diverse backgrounds.

APPLICATIONS

The present invention provides methods for determining liver cancer initiation and prognosis as well as develops methods of using changes in transcription factor clusters for determining liver cancer tumorigenesis.

ADVANTAGES

The researchers developed a novel transcriptome-based tumorigenic index (TI) as a quantitative tool to measure tumorigenic signal strength and tumor progression in the liver.

STATE OF DEVELOPMENT

This quantitative approach developed for liver cancer may be generally applicable to other types of cancer upon optimization or adjustment.

INTELLECTUAL PROPERTY INFO

The invention is patent-pending and is available for licensing and collaborations.

PATENT STATUS

Patent Pending