

Scientists identify specific markers that trigger aggressiveness of liver cancer

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Hepatocellular carcinoma (HCC) or primary liver cancer forms in the epithelial tissue of the liver and is most commonly caused by the hepatitis B virus (HBV) or hepatitis C virus (HCV). In the U.S., the National Cancer Institute (NCI) estimates that 15,000 men and 6,000 women are diagnosed with HCC each year. Worldwide, HCC accounts for 632,000 cases with the highest regions being Western Pacific and Africa according to a 2004 World Health Organization (WHO) report.

Researchers from Taipei Veterans General Hospital investigated the molecular mechanisms of HCC, one of the most common tumors found in Taiwan and largely caused by the high prevalence (15%-20%) of HBV in the country. The study, funded in part by a grant from the National Science Council, is the first to provide a comprehensive profile of multiple Epithelial-Mesenchymal Transition (EMT) markers and to demonstrate that Snail and Twist, but not Slug, are the major inducers of EMT in HCC. Results of the study are published in the November issue of *Hepatology*, a journal of the American Association for the Study of Liver Diseases.

EMT is critical in the development of invasiveness and metastatic potential of human cancers, and described as process where epithelial cells no longer adhere to one another, taking on fibroblastic properties. The EMT process is initiated by suppression of E-cadherin function through the major EMT regulators (Snail, Slug, and Twist). E-cadherin (calcium dependent adhesion molecules) is a type of protein found in the epithelial cells that ensure [tissue cells](#) bind together. When E-cadherin

function is lost, cancer is able to progress and metastasize.

Professor Jaw-Ching Wu and colleagues obtained samples of primary HCC with adjacent non-tumorous liver tissues from 123 patients who had hepatic resection surgery between 1990 and 2002 at Taipei Veterans General Hospital. Reduced E-cadherin function was observed in 60.2% of patients. "We found a significant decrease in cancer-free intervals and overall survival for those patients who had a reduction in E-cadherin function," explained Dr. Wu. A downregulated expression of E-cadherin was also associated with large tumor size and multi-nodular tumors.

Results show that co-expression Snail and Twist (transcription factors or proteins that control when genes are switched on or off) indicates the worst prognosis for HCC patients. "Our research is the first to prove that the two proteins (Snail and Twist) work independently, but together promote EMT," noted Dr. Wu.

According to the study, overexpression of Twist is correlated with HCV-related HCC, partially explaining the highly invasive behavior and poor prognosis for patients with this form of liver cancer. Dr Wu added, "Our results provide essential information for determining HCC prognosis in patients and identifies possible new treatments for future HCC management."

More information:

Article: "A Comprehensive Analysis of the Independent Effect of Twist and Snail in Promoting Metastasis of Hepatocellular Carcinoma," Muh-Hwa Yang, Chi-Li Chen, Gar-Yang Chau, Shih-Hwa Chiou, Chien-Wei Su, Teh-Ying Chou, Wei-Li Peng, and Jaw-Ching Wu. *Hepatology*; Published Online: August 10, 2009 ([DOI: 10.1002/hep.23221](https://doi.org/10.1002/hep.23221)); Print Issue Date: November 2009. [www3.interscience.wiley.com/jo ... /122542499/abstract](http://www3.interscience.wiley.com/jo.../122542499/abstract)

Editorial: "The Epithelial Mesenchymal Transition: fact or fiction in cancer?" Gianluigi [DOI: 10.1002/hep.23329](https://doi.org/10.1002/hep.23329)gy; Published Online: October 29, 2009 (DOI: 10.1002/hep.23329); Print Issue Date: November 2009.

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