



**IBT Researchers Learn a Novel Metabolic Regulator
Also Suppresses Tumors**December 18, 2008

Researchers at the Texas A&M Health Science Center Institute of Biosciences and Technology in Houston have found that a specific isotype of the fibroblast growth factor family that is beneficial for prevention of some aspects of metabolic syndrome is also a tumor suppressor.

The work, led by **Wallace McKeehan, Ph.D.**, director of the HSC-IBT Center for Cancer and Stem Cell Biology, appears in the journal *Molecular Carcinogenesis*.

Part of the fibroblast growth factor (FGF) family, *FGFR4* is an isoform in the liver that mediates metabolic homeostasis (cholesterol, lipid and glucose metabolism) similar to insulin.

The FGF family of extracellular matrix-controlled tyrosine kinases already has been shown to mediate cell-to-cell communication, thereby controlling a precise balance among different cell types during embryonic development or in the temporary regeneration of adult organs in response to stress, insult and injury. In most cases, unrestrained chronic FGF signaling has contributed to extreme growth of certain cells associated with birth defects and cancer.

In this study, Dr. McKeehan and his colleagues found the *FGFR4* in the liver serves to prevent liver cancer (hepatoma) rather than promote it. This is a logical but unexpected finding given the general contribution of other members of the FGFR family in diverse other tissues. In fact, when a closely related member of the FGFR family (*FGFR1*) appears abnormally in liver cells, it drives the cells' malignancy.

The researchers experimented on mice that had *FGFR4* missing in the liver. Their previous studies showed that such deficient mice were fatter and exhibited high blood levels of cholesterol, lipids and glucose, characteristics associated with obesity, cardiovascular diseases and diabetes.

After the *FGFR4*-deficient mice were exposed to a strong carcinogen called *diethylnitrosamine* (DEN), they exhibited a much higher rate of hepatomas that were larger and more deadly. And when *FGFR4* was introduced back into deficient hepatoma cells, the cells died – a contrast to the *FGFR1* that further promoted hepatoma growth and malignancy.

As a result, the normally resident *FGFR4* in liver cells (hepatocytes) serves to prevent hepatomas by causing the death of hepatoma cells, concurrent with its routine role of maintaining metabolic homeostasis, Dr. McKeehan said.

“Enhancement of *FGFR4* activity through pharmaceuticals could improve blood

levels of lipid and glucose and enhance weight loss while at the same time preventing liver cancer,” Dr. McKeehan said. “Few drugs have such a desirable side effect as the prevention or delay of cancer.”

Other contributors to the *Molecular Carcinogenesis* study were **Xinqiang Huang, Ph.D.**, now a researcher at the University of California, Los Angeles; and **Chengliu Jin, Ph.D.**; **Yongde Luo, Ph.D.**; and **Fen Wang, Ph.D.**, of the HSC-IBT Center for Cancer and Stem Cell Biology.

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