Eliminating tumor suppressor C/EBP alpha explains cancer in aging liver

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Understanding how the tumor suppressor protein C/EBP alpha is eliminated in aging livers gives important clues to the mechanism by which cancer occurs in that organ and could point the way to new therapies and prevention, said Baylor College of Medicine researchers in a report that appears online today in the *Journal of Clinical Investigation*.

A variant of C/EBP alpha called the S193-ph isoform is such a powerful tumor suppressor protein that it must be eliminated before liver cancer can occur, said Dr. Nikolai A. Timchenko, professor in the Huffington Center on Aging and the department of immunology and pathology at BCM.

"Understanding the molecular mechanism behind the development of liver cancer will help develop new ways to prevent the disease," he said.

The process is multi-step. Another protein - gankyrin, short for gann ankyrin repeat protein (Gann means cancer in Japanese) - must be elevated first.

"It is a small molecule that is part of the protein degradation system in the cell," he said. "Previously, it has been shown that this protein eliminates the p53 and RB (retinoblastoma) proteins, both tumor suppressor proteins in other cancers. This is a tumor suppressor killer."

To demonstrate how the mechanism works, he and his colleagues compared tissues from young mice expressing a specific variant of

C/EBP alpha and tissues from wild type old mice. If part of the liver is removed in these mice, this tumor suppressor prevents generation of new liver tissue - indicating that it stalls rapid growth. Uncontrolled growth is a hallmark of cancer.

In these special mice, they found that gankyrin plays an important role in making C/EBP alpha a target for degradation within the cell.

"Cancer is increased in many tissues of older people," he said. "The information we have is specific for the liver, but it might also be important for other kinds of cancer. We do not know yet."

Provided by Baylor College of Medicine