The protein p62 helps liver cancer-initiating cells survive

The most common form of adult liver cancer is hepatocellular carcinoma (HCC), which is the third-leading cause of cancer deaths worldwide. HCC arises from persistent liver inflammation related to hepatitis B or C infection, alcohol consumption, or obesity.

A collaborative study led by Jorge Moscat, Ph.D., deputy director of the NCI-designated Cancer Center at Sanford Burnham Prebys Medical Discovery Institute, and Michael Karin, Ph.D., distinguished professor of Pharmacology and Pathology at UC San Diego School of Medicine, sheds light on the how liver cancer begins. The found that a protein called p62 is involved in the process, and that levels of the protein can be used to predict a liver cancer patient's prognosis.

The team looked at non-cancerous liver samples collected from people who had previously undergone treatment to eliminate their liver cancer. They found that people with higher levels of p62 were significantly more likely to see their cancer return and less likely to survive cancer-free compared to people with low or no p62.

They went on to define how high levels of p62 enable damaged liver cells, which can become cancerous, to survive. They found that the increase in this protein keeps cells from 'committing suicide' when they accumulate lots of damaging reactive molecules that cause mutations. This condition, called oxidative stress, is a natural consequence of injury and inflammation.

p62 does this by activating several proteins, including NRF2, which turns on genes for enzymes that detoxify reactive molecules, and c-Myc, which turns on genes that promote proliferation and block cell death.

While years of further testing are necessary before doctors might be able to use p62 information to make treatment decisions, new liver cancer detection and prevention methods are sorely needed. Liver cancer doesn't usually cause symptoms until later stages, so it's often diagnosed late, contributing to its low survival rate. Fewer than 20 percent of patients survive beyond the first five years after diagnosis.

The findings also suggest that drugs that block p62's survival-permitting action may help prevent chronic liver disease from progressing to liver cancer. How such drugs would be designed is not yet clear, as p62 has multiple functions.

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Publication

p62, Upregulated during Preneoplasia, Induces Hepatocellular Carcinogenesis by Maintaining Survival of Stressed HCC-Initiating Cells.

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