Liver cancer, among the top-10 cancer killers, is on the increase as obesity leads to fatty livers which predispose to liver cancer. Fat can damage the liver in much the say way as alcohol abuse or hepatitis, two major risk factors for liver cancer.

Removing HSF1 thwarts liver cancer by decreasing access to two critical elements: glucose and lipids or fats.

Tumors use glucose for energy as well as the rapid cell division essential to cancer growth, said Dr. Xiongjie Jin, GHSU Assistant Research Scientist and the study's first author. Cancer also needs more lipids to make membranes needed for new cells and so those cells can communicate, Jin said. Lipids also serve as an additional energy source.

Mice lacking HSF1 are hypersensitive to glucose, able to efficiently turn it into energy that can be used by the body so little can be diverted to cell division, said Dr. Nahid Mivechi, Director of the GHSU Center for Molecular Chaperone, Radiobiology and Cancer Virology and the study’s corresponding author. As added bonuses, the mice stay slim even on a high-fat diet and avoid diabetes.

The mice also produce fewer lipids because they more easily make active protein kinase, or AMPK, which helps regulate energy levels and inhibits lipid synthesis, Moskophidis said. Lipid-hungry tumors don’t like AMPK, he notes.

The studies, funded by the National Institutes of Health's National Cancer Institute, were done in genetically altered mice that were later exposed to a carcinogen known to produce cancer in 100 percent of male mice within five to seven months. Now the scientists are removing HSF1 from mice that already have cancer to see if this approach - which better reflects how treatment would be used in humans - works as well. They also are exploring the potential of HSF1 inhibitors in advanced breast
cancer and melanoma.

They note that HSF1 levels vary normally, typically increasing after eating. In a high-metabolism, disease state such as cancer, HSF1 becomes more important, Moskophidis said. The researchers believe short-term inhibition of HSF1, as might one day be used in cancer patients, would be safe since it's one of a family of transcription factors with similar functions. However, HSF1 seems to be the family member with the biggest role in cancer.

The football-shaped liver helps the body use food and drink as energy and nutrients and helps detoxify the body. According to the American Liver Foundation, liver cancer tends to be asymptomatic until later stages of the disease. Symptoms may include fatigue, pain on the right side of the upper abdomen or around the right shoulder blade, nausea, loss of appetite, unexplained weight loss or jaundice. It may be discovered during a routine checkup if a doctor feels hard lumps in the abdomen, or incidentally by imaging studies.

Provided by Georgia Health Sciences University

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