Study of Obese Mice Finds Exercise Helps Prevent Liver Cancer

This benefit was independent of weight control among the animals.

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Mice engineered to become obese and develop type 2 diabetes did not develop liver cancer when provided access to an exercise wheel in a recent study, whereas most of their counterparts with no wheel did develop the malignancy.

The mice in the experiments closely resembled humans with non-alcoholic fatty liver disease (NAFLD), a major driver of hepatocellular carcinoma, the most common form of liver cancer, among humans. In its more severe form, fatty liver disease can progress to non-alcoholic steatohepatitis (NASH).

“As yet there are very few effective therapies for liver cancer, so approaches to prevent liver cancer are greatly needed,” the study’s lead investigator Geoffrey C. Farrell, MD, of Australian National University, said in a press release. “Some population data suggest that persons who exercise regularly are less likely to develop liver cancer, but studies addressing whether this has a real biological basis and, if so, identifying the molecular mechanism that produces such a protective effect are few, and the findings have been inconclusive.”

As described in the Journal of Hepatology, researchers conducted experiments using the mouse model, in which mice are genetically driven to eat heavily. The investigators injected the animals early in their lives with a low dose of a cancer-causing agent.

The study authors provided half the mice with an exercise wheel, while providing the other half of the animals with no such exercise outlet. The mice with the wheel ran up to 25 miles per day.

Such exercise delayed the accumulation of fat in the mice with an exercise wheel. For the first three months, their weight gain was not particularly steep. Nevertheless, by the sixth-month mark, the exercising mice still had become obese. At this point, most of the non-exercising mice had liver cancer, while none of the exercising mice did.

Weight gain operated independently of the risk of liver cancer.

The scientists also studied the molecular signaling pathways that govern liver cancer development

to determine how exercise apparently prevented the condition. They found that exercise effectively switched off a stress-activated protein known as kinase JNK1. They studied mice that lack this protein and confirmed that JNK1 is involved with liver cancer development.

The investigators also found that activating the tumor suppressor gene p53 prevented the growth of altered cells that were on a path to becoming malignant.

“Exercise has already been shown to improve some outcomes for patients with cirrhosis. If the present studies in an animal model that closely resembles humans with fatty liver disease can be replicated in patients, it is likely that exercise could delay onset of liver cancer and mitigate its severity, if not completely prevent it—thereby greatly improving patient outcomes,” Farrell said. “Also, knowing the molecular pathways involved points to ways that drugs or pharmaconutrients could be employed to harness the powerful protective effect of exercise to lower risk of liver cancer in overweight people with diabetes.”

To read a press release about the study, click here.

To read the study abstract, click here.

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