Body clock researchers prevent liver cancer growth in mice

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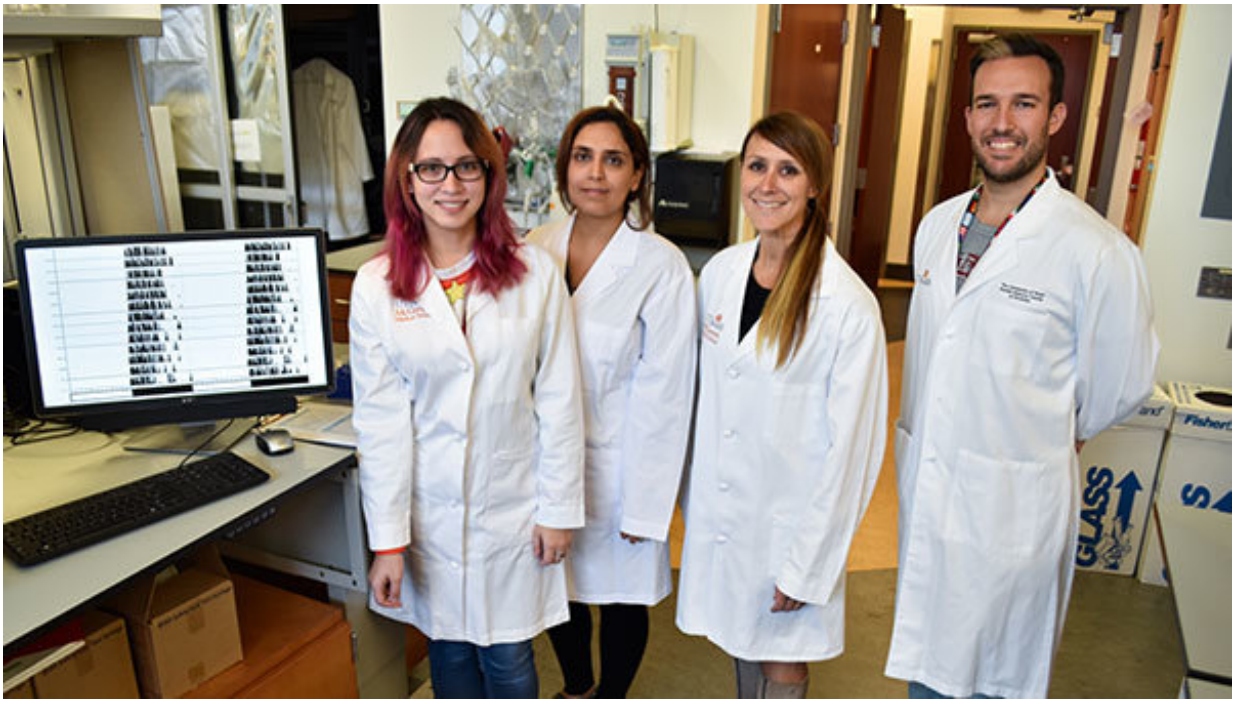

Working on the link between circadian rhythms and cancer at UTHealth, from the left, are Corrine Baumgartner; Baharan Fekry, Ph.D.; Kristin Eckel-Mahan, Ph.D.; and Aleix Ribas Latre, Ph.D. Credit: Rob Cahill, UTHealth

The body's internal clock could play a critical role in the fight against certain types of liver cancer, according to a preclinical study by scientists from The University of Texas Health Science Center at Houston (UTHealth). The results were published recently in the journal *Nature*

Communications.

The body's clock, called the circadian clock, is an intrinsic, 24-hour timekeeping system that operates in all cells of the body and regulates sleep, metabolism and other vital body functions.

"We were able to inhibit the growth of liver cancer in a mouse model by manipulating the circadian clock at the cellular level," said Kristin Eckel-Mahan, Ph.D., the study's senior author and an assistant professor with the Center for Metabolic and Degenerative Diseases at McGovern Medical School at UTHealth.

Eckel-Mahan said researchers confirmed their findings in human tissue samples.

In 2015, 32,908 new cases of liver cancer were reported, and 25,760 people died of liver cancer in the United States, reported the Centers for Disease Control and Prevention.

Eckel-Mahan's team identified a malfunctioning protein that was inhibiting the expression of a key circadian transcription factor and blocking the ability of a tumor suppressor to perform its normal 24-hour cellular functions. When investigators forced the tumor cells to re-express the deficient circadian protein, the tumor cells died.

Fifty percent of liver tumors express this malfunctioning protein, which induces circadian dysfunction in those cells, said Eckel-Mahan, whose laboratory is in the Brown Foundation Institute of Molecular Medicine for the Prevention of Human Diseases at UTHealth.

The study focused on hepatocellular carcinoma (HCC), the leading liver malignancy found in humans and the second-leading cause of all malignancy-related cancer deaths. Hepatocellular carcinoma is on the

rise and has been linked to obesity-associated fatty liver disease.

"These results suggest that targeting the circadian clock in HCC may be a promising treatment for the growth and progression of HCC tumors," the authors wrote.

She said the next steps are to determine how to prevent disruption of the clock in the first place and to study whether pharmacological approaches known to improve clock function can also prevent the growth of these liver tumors.

More information: Baharan Fekry et al, Incompatibility of the circadian protein BMAL1 and HNF4α in hepatocellular carcinoma, *Nature Communications* (2018). DOI: 10.1038/s41467-018-06648-6

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