p53 critical to recovering from acetaminophen overdose

26 April 2017

Results from a new study show that after an acetaminophen overdose the p53 protein plays a key role in preventing the progression of liver damage and signaling the liver to repair itself. The findings could lead to new treatments for people who overdose on this popular pain reliever and fever reducer. Overdoses can lead to sudden liver failure and bring more than 50,000 people to emergency rooms in the U.S. every year.

Prachi Borude, a graduate student at the University of Kansas Medical Center and recipient of this year's American Society for Investigative Pathology (ASIP) Experimental Pathologist-in-Graduate Training Award, will present the new findings at the ASIP annual meeting during the Experimental Biology 2017 meeting, to be held April 22-26 in Chicago.

"Current treatment options for acetaminophen overdose are very few, and liver transplant is not feasible in all cases, so there is immediate need for new therapy," said Udayan Apte, associate professor at the University of Kansas Medical Center and leader of the research team. "Understanding the mechanisms that connect liver injury progression and liver regeneration could lead to new, more effective therapies for acetaminophen overdose."

Previous studies conducted by Apte's group and other scientists showed that liver regeneration after acetaminophen overdose is critical for survival. In the new study, the researchers examined the role of p53 protein—a tumor-suppressor protein that also helps regulate cell division and multiplication—in liver injury and repair after acetaminophen overdose.

The researchers administered acetaminophen to normal mice and mice deficient in p53. Compared with the normal mice, the p53-deficient mice showed significantly higher liver injury 24 hours after receiving acetaminophen. However, the p53-deficient mice also showed rapid liver regeneration. These findings show that activation of p53 is important for preventing progression of acetaminophen-induced injury while inhibition of p53 helps stimulate liver regeneration—and thus recovery—after acetaminophen overdose.

"Current therapy and other research examining acetaminophen overdose target the initial injury process, however most of the times patients come to emergency room at late stages," said Apte. "By focusing on later stages of injury and recovery, we have revealed the critical link to preventing injury progression and helping liver regeneration."

The researchers plan to confirm their findings with additional studies and want to move toward developing new therapies for acetaminophen overdose by identifying drugs that inhibit or activate p53.

More information: P53 Regulates Progression of Injury and Liver Regeneration After Acetaminophen Overdose, app.core-apps.com/eb2017/abstr … e96fd9b3196099be300d

Provided by Experimental Biology 2017