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Collaborative study takes aim at non-alcoholic fatty liver disease

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Texas A&M University System researchers in collaboration with the Department of Veterans Affairs and Baylor Scott & White Research Institute have completed a study identifying one of the mechanisms leading to the development of non-alcoholic fatty liver disease, or NAFLD, providing new possibilities for prevention and treatment of the disease.

The study, which included input from researchers affiliated with Wuhan University, Huazhong University of Science and Technology, Chongqing Medical University, Peking University, Augusta University and the Central Texas Veterans Health Care System was published in the journal *Hepatology*.

"Our research involved the adenosine 2A receptor, which plays a protective role against tissue damage," said Dr. Chaodong Wu, a Texas A&M AgriLife Research scientist in the nutrition and food science department of Texas A&M University in College Station. "It can reduce overactive immune cell activity, protecting tissues from being damaged by inflammation. However, until now its role in protecting from tissue damage relative to non-alcoholic fatty liver disease was largely unknown."

Wu said through this study, the researchers examined the effects disrupting this receptor would have on aspects of obesity-associated NAFLD so they could understand the underlying mechanisms.

"While these receptors normally serve as a protective mechanism, they

may be destructive if they become disrupted," he said. "For our study we used receptor-disrupted animal models for comparison to a control."

Both animal model groups were fed a high-fat diet to induce NAFLD, then were examined for inflammatory and metabolic responses.

"The results showed those models with the disrupted receptor had an increased severity of fatty liver disease and inflammation compared to the control model fed the same high-fat diet," said Dr. Gianfranco Alpini, distinguished professor in the medical physiology department at Texas A&M College of Medicine. Alpini is also a senior research scientist at Central Texas Veterans Health Care System and director of the Baylor Scott & White Digestive Disease Research Center.

Alpini said the study's investigation of the macrophages—large white blood cells that ingest foreign particles and infectious microorganisms—and liver cells of the receptor-disrupted animal models showed increased pro-inflammatory responses and enhanced fat deposition.

"Receptor deficiency also significantly increased the amount of a regulatory element-binding protein in the liver cells of fasted animal models," said Dr. Heather Francis, associate professor of medical physiology at Texas A&M College of Medicine and the study's co-author. "The increase in this protein was commensurate with an associated increase in the potential for fatty deposits in the liver."

Wu said the accumulative study results demonstrated receptor disruption in both macrophages and liver cells accounts for increased severity of NAFLD, likely through increasing inflammation and elevating fat deposits by stimulating the activity of a factor controlling protein expression of fat deposition.

"Overall, the study validates the importance of adenosine 2A receptor as a therapeutic and/or preventive target for NAFLD," Wu said. "This is significant in that it demonstrates the feasibility of targeting that receptor to treat non-alcoholic fatty liver disease by means of its activation."

He said based on the results generated, once bioactive food components capable of activating the receptor can be identified, these components and foods enriched with these components can be used to help prevent non-alcoholic fatty liver disease.

Wu said the study would not have been possible without the collaboration of the Central Texas Veterans Health Care System and Baylor Scott & White Research Institute's team at the Baylor Scott & White Digestive Disease Research Center.

"Many members of the study team, including Alpini and Francis, as well as Drs. Fanyin Meng and Shannon Glaser, associate professor of medical physiology at Texas A&M College of Medicine, are also affiliated with one or more of these institutions," he said.

Provided by Texas A&M University