Using novel biological aging clock, team finds obesity accelerates aging of the liver

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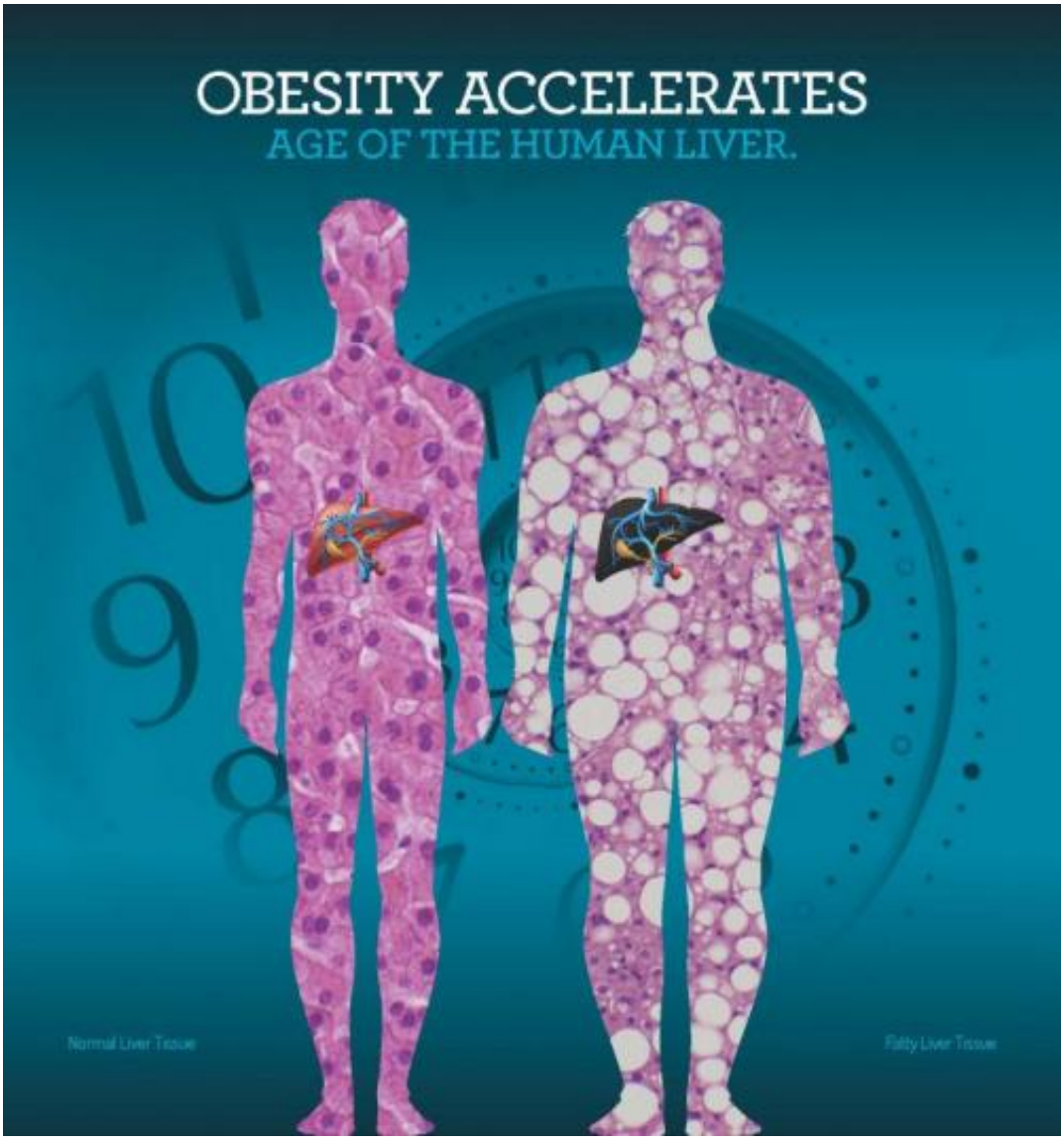

Obesity increases the age of liver. The patterns of the figures provides a microscopic view of liver cells from lean (left figure) and obese subjects (right

figure), respectively. Credit: UCLA

Using a recently developed biomarker of aging known as an epigenetic clock, UCLA researchers working closely with a German team of investigators have found for the first time that obesity greatly accelerates aging of the liver. This finding could explain the early onset of many age-related diseases, including liver cancer, in obese subjects

Although it had long been suspected that obesity ages a person faster, it hadn't been possible to prove the theory, said study first author Steve Horvath, a professor of human genetics at the David Geffen School of Medicine at UCLA and a professor of biostatistics at the UCLA Fielding School of Public Health. Using the epigenetic clock Horvath developed last year, he and Jochen Hampe from the University Hospital Dresden showed that carrying excessive weight can negatively impact select human tissues.

"This is the first study that evaluated the effect of body weight on the biological ages of a variety of human tissues," Horvath said. "Given the obesity epidemic in the Western world, the results of this study are highly relevant for public health."

The findings appear Oct. 13, 2014, in the early online edition of the peer-reviewed journal *Proceedings of the National Academy of Sciences*.

Horvath's aging clock uses a previously unknown time-keeping mechanism in the body to accurately gauge the age of diverse human organs, tissues and cell types. He and his collaborators focused on a naturally occurring process called methylation, a chemical modification of the DNA molecule.

Horvath used this epigenetic clock to measure the biological age of several tissues. The aging clock proved accurate in matching biological to chronological age in lean subjects. But liver tissues from obese subjects tended to have a higher biological age than expected.

In this study, Horvath looked at almost 1200human tissue samples, including 140 liver samples, to study the relationship between epigenetic age acceleration and body weight. While obesity doesn't affect the epigenetic age of fat, muscle or blood tissue, he and his collaborators found that, on average, the epigenetic age of the liver increased by 3.3 years for every 10 Body Mass Index (BMI) units.

For example, a woman who is 5 feet 5 and weighs 140 pounds has a BMI of 23.3. A woman the same height but weighing 200 pounds would have a body mass index of 33.3. Her liver would be about three years older than the woman who weighed 140 pounds, the study found.

"This does not sound like a lot, but it is actually a very strong effect," Horvath said. "For some people, the age acceleration due to obesity will be much more severe, even up to 10 years older."

Horvath also found that rapid weight loss induced by bariatric surgery did not reverse the accelerated aging, at least in the short term.

Going forward, Horvath and his team want to determine if the premature epigenetic aging of liver tissue in obese people can be prevented to possibly reduce their risk of diabetes and liver cancer. They plan to work on models that allow them to dissect the exact molecular mechanisms behind this aging process - which is not known at this point - in order to find the right targets for therapy and prevention.

"The increased epigenetic age of liver tissue in obese individuals should provide insights into common liver-related comorbidities of obesity,

such as insulin resistance and liver cancer," the study states. "These findings support the hypothesis that obesity is associated with accelerated aging effects and stresses once more the importance of maintaining a healthy weight."

More information: "Obesity accelerates epigenetic aging of human liver," by Steve Horvath et al. *PNAS*, 2014.

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