Study shows loss of key estrogen regulator may lead to metabolic syndrome and atherosclerosis

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UCLA researchers demonstrated that loss of a key protein that regulates estrogen and immune activity in the body could lead to aspects of metabolic syndrome, a combination of conditions that can cause Type 2 diabetes, atherosclerosis and cancer. Called estrogen receptor alpha, this protein is critical in regulating immune system activity such as helping cells suppress inflammation and gobble-up debris.

This early preclinical study in female mice demonstrated that removing estrogen regulator alpha alone was enough to reduce the immune system's protective process and promote increased fat accumulation and accelerate atherosclerosis development. Without this protein, the mice developed additional aspects of metabolic syndrome such as glucose intolerance, insulin resistance and inflammation.

This estrogen receptor is also expressed in many other non-reproductive tissues such as fat, muscle and liver and can also act independent of the hormone estrogen. However, little is known about the receptor's actions in these tissues that are involved in blood-sugar regulation, which plays an integral role in metabolic syndrome.

Researchers hope that these early findings may provide insight into the development of metabolic syndrome, which affects millions of people worldwide. A better understanding of the activity of this receptor may lead to improved future therapies.

"Impairment of this receptor's function could also play a role in the heightened incidence of metabolic syndrome being seen in younger women," said senior author Andrea Hevener, Ph.D., associate professor of endocrinology, diabetes and hypertension, David Geffen School of Medicine at UCLA. "We may find that action of this estrogen receptor is just as important as that of circulating estrogen, which is key in multiple therapies such as HRT."

Hevener notes that her team will next study the status of this estrogen receptor in pre and postmenopausal women.

More information: The study will appear in the early edition of the *Proceedings of the National Academy of Sciences (PNAS)* during the week of Sept. 5.

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