Estrogen receptors might hold key in obesity prevention

May 21 2019

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Despite countless fad diets, both obesity and metabolic diseases continue to plague communities across the U.S. Now, researchers from the University of Missouri believe that the clue to treatment might be related

to estrogen—for both men and women.

In two separate studies, Vicki Vieira Potter and Jaume Padilla, researchers in the Department of Nutrition and Exercise Physiology, have found that the estrogen receptor alpha, a protein found inside cells that is activated by estrogen, appears to be protective against obesity. Their research indicates that the protein reduces various metabolic diseases, including fatty liver disease.

"Reducing obesity and metabolic disease risks are urgent public health priorities," Vieira Potter said. "The key to finding treatments is understanding how estrogen receptor signaling impacts metabolism and how these proteins serve a protective function."

In a test of female mice, the researchers found that mice without functional estrogen receptor alpha were more obese and metabolically dysfunctional. The mice also were more susceptible to weight gain and metabolic dysfunction when fed a high-fat, high-sugar diet.

Furthermore, daily injections of a drug known to stimulate fat cells to burn calories effectively prevented metabolic dysfunction, both in the mice with and without the functional estrogen receptor. In both groups of mice, they found that the therapy was less effective when paired with the high-fat, high-sugar diet.

"These new findings suggest that drug-induced activation of specific metabolic pathways might have value in preventing those hormone changes that we know occur as people age," Vieira Potter said. However, we also found that the effectiveness of that therapy was reduced when combined with an unhealthy high-fat, high-sugar diet."

In a test of male mice, researchers found more evidence that the estrogen receptor alpha is required for optimal metabolic function, even

in males with less estrogen. In that study, they found that the presence of the estrogen receptor alpha was required for exercise to be effective in reducing fat storage in the liver.

"It seems as though the estrogen receptor alpha is mediating the boon of estrogen benefits when it comes to protecting metabolism," Padilla said. "These findings suggest that aging and obesity might increase susceptibility to disease by adversely affecting estrogen receptors. Our findings also suggest that exercise and targeted therapies appear to effectively mitigate that dysfunction."

"Beta 3 adrenergic receptor activation rescues metabolic dysfunction in female estrogen receptor alpha-null mice," was published in *Frontiers of Physiology*.

More information: Stephanie L. Clookey et al. Beta 3 Adrenergic Receptor Activation Rescues Metabolic Dysfunction in Female Estrogen Receptor Alpha-Null Mice, *Frontiers in Physiology* (2019). DOI: 10.3389/fphys.2019.00009

Provided by University of Missouri-Columbia