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Genetically altering female mice prevents diet-induced obesity, study shows

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Researchers at The Ohio State University Wexner Medical Center seeking a way to combat the growing epidemic of obesity have found that deleting microRNA-155 in female mice prevents diet-induced obesity.

The findings are published online in the journal *Scientific Reports*.

"Obese individuals are susceptible to heart disease and metabolic syndrome, which is why it's important to find new ways to protect them from the effects of a high fat diet," said lead author Phillip G. Popovich, professor of neuroscience and director of The Center for Brain and Spinal Cord Repair at Ohio State's Neurological Institute.

In their study, researchers deleted a specific microRNA (miR) which is a small, non-coding RNA that influences and regulates gene transcription in cells and affects how they function. Researchers hypothesized that a specific miR—miR-155—would be a good target because it may regulate several signaling pathways that are involved in the development and maintenance of obesity.

Researchers studied female wild-type mice and miR-155 knockout mice that were fed a control diet or a high-fat diet for 12 weeks. Surprisingly, despite eating a high-fat diet for 3 months, miR-155 knockout mice did not become obese. Compared to wild-type mice, weight gain in miR-155 knockout mice was reduced 56 percent with a 74 percent reduction in accumulation of fat. Experiments using male mice produced similar

results.

The study also found that miR-155 deletion could enhance metabolic rate, an effect that could explain the reduced obesity in these mice. Compared to female wild-type mice, miR-155 knockout mice lost 78 percent more body weight after overnight fast, and miR-155 knockout mice increased energy expenditure (heat production) by 14 percent over wild-type mice.

"MicroRNAs target hundreds of mRNAs simultaneously, so they represent a promising class of molecules for improving outcomes of disease," said first author and former Ohio State researcher Andrew D. Gaudet, who is now at the University of Colorado Boulder. "Our study shows that manipulating miR-155 improves how cells respond to high fat intake. This suggests that altering microRNA expression is an attractive potential therapy for obesity."

Provided by The Ohio State University Wexner Medical Center