

Gene therapy reduces obesity and reverses type 2 diabetes in mice

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Researchers used a CRISPR interference that decreases the expression of *Fabp4* and reduces lipid storage in adipocytes. Credit: Jee Young Chung

The obesity epidemic affects nearly half a billion people worldwide, many of them children. Obesity-related diseases including heart disease, stroke, type 2 diabetes, and cancer are a leading cause of preventable death. Obesity is caused by both genetic and environmental factors, confounding the development of effective anti-obesity drugs, which exhibit severe off-target effects. In a study published today in *Genome Research*, researchers developed a gene therapy that specifically reduces fat tissue and reverses obesity-related metabolic disease in obese mice.

To overcome the side effects of current anti-obesity drugs, researchers Jee Young Chung and colleagues developed a specific gene silencing therapy against a fatty acid metabolism gene, *Fabp4*. Researchers used a CRISPR interference

system wherein catalytically dead Cas9 protein and single guide RNA was targeted to white adipocytes with a tissue-specific fusion peptide. The complex is internalized with little toxicity to the cells and upon internalization, the molecule complex decreases the expression of *Fabp4* and reduces lipid storage in adipocytes. Demonstrating that this delivery method performed well in cells, Chung and colleagues tested their therapy on [obese mice](#). Mice were fed a diet high in fat leading to [obesity](#) and insulin resistance. *Fabp4* repression resulted in a 20% reduction of body weight and improved insulin resistance and inflammation after just six weeks of treatment. Additional systemic improvements were observed, including a reduction in fatty lipid deposition in the liver and reduced circulating triglycerides.

The current standard FDA-approved treatment showed just 5% of body weight loss after one year of treatment in humans. However, while this therapy displays promising results in mice, further studies are required before it can be used in clinical treatment against human disease. Importantly, this work highlights the advances in precision gene editing technology, which can be translated to other types of therapies.

More information: *Genome Research* (2019). [DOI: 10.1101/gr.246900.118](https://doi.org/10.1101/gr.246900.118)

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