CRISPR INTERFERENCE FOR OBESITY TREATMENT: A NOVEL GENE THERAPY APPROACH

THIS ABSTRACT WAS INDEPENDENTLY WRITTEN BY SILVIA BOLZANI AS A PORTFOLIO SAMPLE. IT SUMMARIZES THE FINDINGS OF THE ORIGINAL PAPER

Targeted Delivery of CRISPR Interference System Against Fabp4 to White Adipocytes Ameliorates Obesity, Inflammation, Hepatic Steatosis, and Insulin Resistance

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ABSTRACT

Obesity is a global public health emergency resulting from the combination of genetics and environmental factors. Obesity rates have increased significantly worldwide. Since 1990, the number of obese adults has doubled, while adolescents have quadrupled (WHO, World Health Organization). The excessive accumulation of white adipose tissue (WAT) triggers inflammation by promoting the release of pro-inflammatory cytokines. This highlights the need for WAT-targeted therapy to reduce inflammation and decrease fat mass. To date, the most prominent gene editing tool is CRISPR, clustered regularly interspaced short palindromic repeats.The authors proposed to adapt a CRISPRi (CRISPR interference) system to treat obesity and obesity-induced type 2 diabetes.

A CRISPRi system incorporating a dead Cas9 protein was created with the aim of targeting the Fabp4 gene, which encodes a protein predominantly expressed in adipose tissue. This protein plays a critical role in regulating fatty acid storage and has been identified as a potential factor in obesity. The study employed a non-viral delivery system that utilized a fusion peptide (ATS-9R) to target the cellular adipose tissue marker prohibitin. The dCas9/sgFabp4 + ATS-9R system selectively targeted adipose tissue in obese mice, downregulating Fabp4 mRNA expression. Silencing this important factor led to considerable reductions in body weight and blood glucose levels, as well as improvements in obesity-related inflammation and hepatic steatosis.

In the treatment of obesity, this non-viral targeting method has proven to be highly effective in the delivery of gene therapy. The findings indicate that prohibitin and Fabp4 are significant and prospective targets, suggesting the CRISPRi system as a valuable tool for future translational research, from a mouse model to human patients.