Cysteine Depletion as a Treatment for Obesity and Associated Metabolic Disorders

A rapid, safe, and tunable method of weight loss and metabolic regulation in the context of obesity and associated metabolic disorder treatment.

Technology

The research team recently discovered that dietary cysteine deprivation in conjunction with inhibition of cysteine synthesis leads to rapid and reversible weight loss in a murine model. Cysteine deprivation triggers a global reprogramming of metabolic processes culminating in (i) significant loss of adipose tissue lipid content, (ii) reduced lipogenesis, (iii) and excretion of intermediary metabolites. The observed weight loss was accompanied by the following effects: a global integrated stress response, an oxidative stress response, increased expression of GDF15 (Growth differentiation factor 15, a hormone associated with increased lipolysis and food aversion), and a drastic drop in coenzyme A (CoA) levels. Importantly, vital functions such as locomotion, circadian rhythm and tissue structure and integrity remained largely unaffected in these cysteine-deprived mice. To date, all studies have been performed through dietary cysteine depletion and genetic manipulation of the cysteine biosynthesis pathways by knockout of cystathionine-γ lyase (CSE), however pharmacological inhibition of CSE is expected to exhibit a similar phenotype. Additionally, this metabolite-dependent mechanism of weight loss was readily reversible upon reintroduction of dietary cysteine, thereby demonstrating the potential for this approach as a tunable weight management strategy.

Background

Obesity and associated metabolic disorders are a growing global health crisis, with the global prevalence of obesity expected to reach 24% of the population by 2035, affecting approximately 2 billion people. Current weight loss strategies often focus on overall caloric restriction or specific macronutrient reduction, which can be difficult to maintain and may have variable efficacy. Amino acid restriction has been explored as an alternative approach, however, the effects of specifically depleting cysteine, a semi-essential amino acid, on metabolic regulation and weight loss have not been fully investigated. This innovation presents a differentiated approach to weight loss and metabolic regulation by exploiting the unique role of cysteine in metabolic processes.

Development Stage

Researchers have performed preclinical murine *in vivo* experiments demonstrating the efficacy of this technology in inducing rapid weight loss without detrimental side-effects. NYU is seeking a partner to help develop this technology.

Applications

Category

Life Sciences/Diabetes
Life Sciences/Therapeutics/Metabolic Diseases
Life Sciences/Therapeutics/Cardiovas Disease
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Learn more

- **Obesity and associated metabolic disorders:** This technology could be developed into a novel weight loss and metabolic regulation strategy
- **Conditions of elevated cysteine levels:** This technology could be applied to treat cancer, neurological disorders, and autoimmune and cardiovascular diseases

Advantages

- **Rapid and significant weight loss:** Cysteine deprivation led to a 30% weight loss within a week in rodent models
- **Maintenance of muscle mass and function:** No adverse effect to muscle mass or function was observed following cysteine restriction
- **Controllable weight management:** The weight loss was readily reversible upon reintroduction of dietary cysteine
- **Disease-modifying:** Cysteine deprivation led to a global reprogramming of metabolic processes underlying obesity and associated disorders
- **Safe:** The induced weight loss did not adversely affect skeletal muscle or other vital organs

Intellectual Property

NYU has filed a U.S. provisional patent application covering the method of targeting cysteine levels for the treatment of obesity and other metabolic conditions.

References

1. Varghese A, Gusarov I, Gamallo-Lana B, et al. , https://doi.org/10.1101/2024.07.30.605703