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Leptin analogs to treat obesity

Stanford scientists in Chris Garcia's lab have developed leptin analogs that have potentially more favorable pharmacokinetic and pharmacological signaling properties for use as diabetes and obesity drugs.

Excess body weight is a primary underlying risk factor for a variety of human diseases including type 2 diabetes, cardiovascular disease, and several types of cancer. Although a variety of dietary and pharmacological interventions have emerged in the past several decades to combat obesity, therapeutics capable of safely promoting significant and sustained weight loss are still needed.

Leptin is a hormone that plays a critical role in regulating energy balance and body weight. When functioning properly, leptin suppresses hunger and increases energy expenditure, helping to maintain a stable body weight. Previous attempts to use leptin as a drug have been disappointing in part due to Leptin resistance and high serum leptin levels in obese patients also present an obstacles to the efficacy of wild-type-leptin-based drugs.

This invention describes engineered leptin variants that function as high affinity biased agonists, thereby decoupling activation of the anorexigenic LepR-STAT3 pathway from pathways associated with leptin resistance. Together with additional modifications that enhance the solubility and stability of these variants, these leptin analogs could overcome the challenges of the native Leptin protein and lead to novel pharmacological outcomes that help overcome leptin resistance.

Stage of Development
Research - in vitro

Applications

- Therapeutics for obesity, metabolic syndrome, type 2 diabetes, and dyslipidemia

Advantages

- Novel leptin variants with anti-obesity and anti-diabetic properties
- Improved pharmacokinetic and pharmacological signaling properties
- Large potential market due to growing obesity and diabetes epidemic

Patents

- Published Application: WO2024050285

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