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Isthmin Protein Therapeutics for the Treatment of Non-Alcoholic Fatty Liver Disease

Stanford inventors in the Katrin Svensson laboratory have identified the protein Isthmin-1 (ISM1) as a treatment for nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH). Both NAFLD and NASH are characterized by an increase in lipids stored in the liver and can lead to inflammation, scarring, and damage over time. While there is a growing prevalence of NAFLD that is fueled by increasing obesity rates, there are no FDA-approved pharmacological treatments. Researchers in the Svensson laboratory have shown that therapeutic treatment of ISM1 improves the clinical indicators of NAFLD, including liver weight, blood glucose, and lipid levels in the liver, in mice with established disease. ISM1 is a secreted bioactive peptide that regulates glucose uptake in skeletal and adipose tissue while suppressing lipid synthesis and inducing protein synthesis in the liver. Mechanistically, ISM1 is thought to inhibit cleavage and downstream activity of Sterol Regulatory Element-Binding Proteic-1c, a known regulator of lipid synthesis. The ISM1 signaling pathway is distinct from other pharmaceuticals in development and directly targets the disease on a molecular level, offering a distinct and novel approach to treating and reversing NAFLD.

Stage of Development
Proof of concept

Applications

- Nonalcoholic fatty liver disease
- Nonalcoholic steatohepatitis
- Co-treatment of nonalcoholic fatty liver disease and diabetes

Advantages

- Utilizes novel therapeutic target with distinct mechanism of action that could circumvent adverse effects of other available treatments
- Increases glucose uptake without side effects of fact accumulation in the liver and weight gain that often accompany insulin-based therapies
- Improves insulin sensitivity

Publications

- Jiang, Z., Zhao, M., Voilquin, L., et al. (2021). Isthmin-1 is an adipokine that promotes glucose uptake and improves glucose tolerance and hepatic steatosis . Cell Metabolism, 33(9), 1836-1852.

Patents

- Published Application: WO2023010049
- Published Application: 20240342244

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