

TARGETING HEPATIC ARGININE METABOLISM FOR TREATMENT OF METABOLIC DISEASES

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Background

Over 30% of adults in the world are overweight or obese. Lifestyle management has proven to be impractical and ineffective in real-life settings and there are no current treatments available for metabolic disease.

Technology Summary

Pharmacological or genetic activation of the Arginine 1 or Arginine 2 genes as a method of treating metabolic disease via depletion of hepatic arginine.

Work by the DeBosch lab has shown *in vivo* that hepatic arginine depletion, via viral transfection of the Arginase 2 gene, resulted in enhanced whole-organism energy homeostasis. Overexpression of Arginine 2 in the liver cells of diabetic mice improved heat generation and reduced fat in the liver, while overexpression decreased body fat and increased lean mass in wild-type mice.

It is hypothesized that Arginase 2-polyethylen glycol conjugate (ADI-PEG) can induce hepatic arginine depletion, which then in turn induces thermogenesis and blocks hepatic steatosis. ADI-PEG and other means of arginine depletion would be suitable therapeutics for metabolic diseases such as obesity, non-alcoholic fatty liver disease, and type II diabetes.

Patent

Pending