siRNA therapy to treat Obesity/ NASH and Obesity/ NASH-driven cancer

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Obesity-associated nonalcoholic steatohepatitis (NASH) and liver cancer are increasing. Treatments are not currently available that reverse both the steatosis and fibrosis hallmarks of NASH. The leading causes of this disease are lipogenesis and fibrosis. GW researchers found that a high-fat diet (HFD) induced an increased expression of SPTBN1 and CASPASE3. Thus, identifying new potential targets for therapeutic intervention in NASH and liver cancer. Further study demonstrated that β-spectrin (SPTBN1) promotes lipogenesis and liver cancer development with a HFD. Targeting SPTBN1 holds great promise for treating or preventing cancers linked to obesity/NASH.

GW inventors then tested siRNA therapy to regulate Sptbn1 expression. The siSptbn1-treated mice accumulated less visceral body fat, had lower blood triglycerides (TG) concentrations, and similar blood glucose concentrations relative to controls. The treated mice also had normal liver architecture, low lipid accumulation, and low expression of pro-fibrotic and inflammatory genes in the relative to control mice.

Applications:

- Treat Obesity, and its complications e.g. NASH (fibrosis as well as steatosis)
- Obesity driven cancers

Advantages:

- Targets the causes of NASH/liver cancer (steatosis and fibrosis)
- Targets a specific gene
- Target tissue (liver) is reached easily

SiSptbn1-treated Mice Accumulated Less Visceral Body Fat, Had Lower Blood Triglycerides (TG) Concentrations Than SiCtrl-treated Mice.
Inventors

Lopa Mishra, M.D.

Dr. Mishra's work is in developing new therapeutics targeting liver cancer. She discovered that the TGF-β pathway is the effector pathway for the human stem cell syndrome with an 800 fold risk of cancer (Beck-Wiedmann Syndrome).

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