Netrin-1 and UNC5B as Novel Targets in Metabolic Liver Diseases: NAFLD & NASH

Innovative and effective therapies for treating Non-Alcoholic Fatty Liver Disease (NAFLD) and Non-Alcoholic SteatoHepatitis (NASH)

Technology

This invention from the Moore Lab at NYU Langone Health pertains to the identification of a ligand-receptor pair as a novel therapeutic target for the treatment of metabolic liver diseases. Netrin-1 is a secreted, laminin-related protein which binds to its cognate receptor Unc5b. In macrophages, expression of Netrin-1 leads to chronic inflammation by promoting macrophage retention. Interestingly, the Moore Lab demonstrates in proof-of-concept studies, that the loss of Netrin-1 in a diet-induced obesity (DIO) mouse model reduces hepatic steatosis (fat build-up) and liver macrophage content. Additionally, a human antibody (co-owned with LifeArc) has been engineered to selectively target Netrin-1 and reverse macrophage accumulation in tissues in preliminary studies. Taken together, these results strongly suggest that Netrin-1 and/or Unc5b represent new and promising therapeutic avenues for NAFLD and NASH drug development.

Background

NAFLD and NASH are metabolic disorders caused by excessive lipid accumulation in the liver. NASH is a more severe form of NAFLD and is characterized by chronic inflammation and hepatocyte death. At later stages, NASH can cause liver fibrosis and an increased risk of hepatocellular carcinoma. In the U.S., NAFLD affects up to 25% of the population, while NASH is a growing epidemic (affecting between 2 and 5% of Americans) and quickly becoming a leading cause of cirrhosis and liver failure. Consequently, there is an obvious need for new and efficacious NAFLD and NASH treatments. However, there are presently no FDA-approved therapeutics for these indications.

Applications

- Metabolic liver diseases
  - NAFLD
  - NASH
- Atherosclerosis

Advantages

Technology ID

MOO02-06

Category

Life Sciences/Biologics
Life Sciences/Therapeutics/Metabolic Diseases
Life Sciences/Therapeutics/Liver Disease
Life Sciences/Therapeutics/Cardiovas
Disease
Doug Brawley

Authors

Kathryn Moore, PhD

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- Non-intracellular targets: Netrin-1 is a secreted extracellular protein and Unc5b is a cell-surface receptor. Both are amenable to therapeutic intervention
- Validated target function: Netrin-1 plays a well-characterized role in cell migration, but has also been shown to mediate de-novo lipid metabolism pathways
- Lead molecule identification: A human antibody has already been engineered which selectively targets Netrin-1 and promotes macrophage migration

IP Status

Two provisional patent applications pending

References

1. Sharma M, Schlegel M, Brown EJ, et al. , Netrin-1 Alters Adipose Tissue Macrophage Fate and Function in Obesity