KDDF
Korea Drug Development Fund

Asset #3
Weill Cornell Medicine

A MicroRNA Mimic for the Treatment of Familial Hypercholesterolemia and Atherosclerosis

Therapeutic Area	Cardiovascular Disease, Metabolic Disease	**Indications**	Hypercholesterolemia and Atherosclerosis
Modality	Nucleotide	**Development Stage**	Hit to Lead/Lead Optimization

Overview

Background

- Impaired cholesterol and fat metabolism linked to cardiometabolic diseases
- Various regulatory factors influence lipid metabolism, presenting therapeutic potential
- SREBP-2 drives LDL receptor transcription for LDL removal
- Post-translationally, SREBP-2 and LXR limit LDLR-mediated cholesterol uptake
- Mechanisms preventing LDLR degradation during transcription are unknown
- Unmet Need: Improved understanding of LDLR regulation to inform development of novel treatments

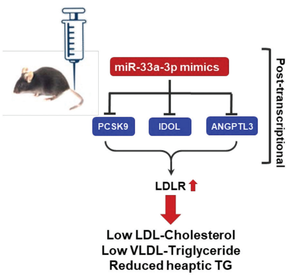
Technology Advantages

- miRNAs can regulate multiple genes in the same biological process with as individual ~22 nucleotide transcripts
- miRNAs can be administered in a tissue-targeted manner to enhance specificity and efficacy while minimizing side effects
- miRNA-33a-3p successfully reduced LDL cholesterol and hepatic steatosis in a mouse model of obesity

Key Data

MicroRNA mimics for the treatment of cardiometabolic diseases

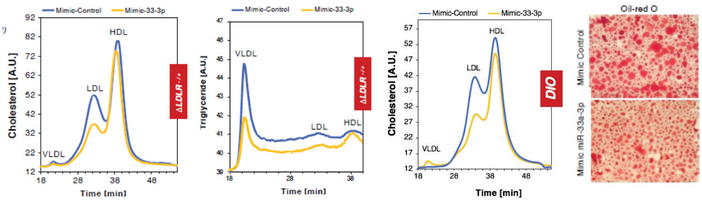
A



miR-33a-3p mimics are potent inhibitors targeting PCSK9, IDOL and ANGPTL3 expression

- Treatment and prevention of cardiometabolic diseases and NAFLD/NASH
- Reduction of hypercholesterolemia and hypertriglyceridemia in patients with atherosclerosis and insufficient response to statins and dietary changes alone

B



miRNA-33a-3p lowers plasma LDL-cholesterol and VLDL triglyceride levels and attenuates hepatic steatosis in diet-induced obese mice and heterozygous LDLR KO mice

IP Status & Publication(s)

Intellectual Property

Patent Number
PCT-US2022-029884 (2022.05.18)

Patent Family
PCT

Publication(s)

- Ramachandran at al. (2022). MicroRNA 33A controls SREBP-2 and LXR dependent regulation of the LDL receptor pathway. Atherosclerosis (Abstract)