KDDF
Korea Drug Development Fund

Asset #4
Boston Children's Hospital

ApoM-Fc Fusion Protein in Complex with S1P for the Treatment of Vascular Diseases

Therapeutic Area	Cardiovascular Disease	**Indications**	Hypertension, Ischemic Heart Disease, Atherosclerosis, Peripheral Vascular Disease
Modality	Protein	**Development Stage**	Pre-clinical

Overview

Background

- Endothelial cell function is critical for normal cardiovascular homeostasis. Endothelial dysfunction hence leads to the development of cardiovascular diseases such as hypertension and Ischemia. Recently, endogenous factors –such as plasma Apolipoprotein M-containing high density lipoproteins (ApoM-HDLs) –have been shown to promote the well-being of the endothelium. Thus, ApoM-based therapeutics have a great potential in reducing the burden of cardiovascular disease, which is the leading cause of death globally.
- ApoM-HDL is the physiological carrier of the bioactive lipid sphingosine-1-phosphate (S1P) and engages S1P receptors to promote endothelial survival.

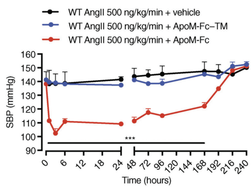
Technology Advantages

- ApoM-Fc has increased in vivo stability with half-life of 93.5 hours
- ApoM-Fc does not activate immune and hematopoietic S1P receptors, hence circulating numbers of lymphocytes, white blood cells, red blood cells and platelets not altered
- In vivo: ApoM-Fc bound S1P was stabilized and potently reduced blood pressure in a mouse model of hypertension
- In vivo: ApoM-Fc administration attenuated ischemia/reperfusion (MI/R) injury in the brain and heart in mouse models.

Key Data

Sustained blood pressure reduction in hypertensive mice after ApoM-Fc administration

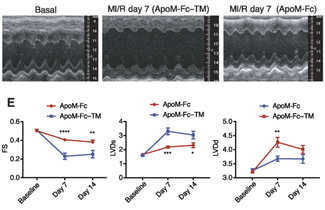
A



(A) In C57BL/6 mice, ApoM-Fc but not ApoM-Fc– TM administration potently reduced blood pressure by ~40 mmHg at 2 hours after treatment. The effect of ApoM-Fc was sustained and therapeutic efficacy was maintained for 192 hours after a single dose.

Effect of ApoM-Fc–bound S1P on cardiac function after myocardial infarction

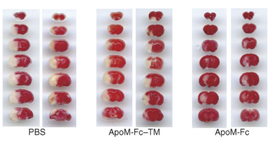
B



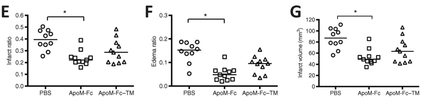
Echocardiographic analysis 1 to 2 weeks after I/R injury showed that ApoM-Fc administration significantly preserved myocardial function (B) Representative images of two-dimensional (2D) guided M-mode echocardiography of the LV at baseline and 7 days after MI/R injury (C) LV end-diastolic (LVDd) diameter, LV end-systolic (LVDs) diameter, and fractional shortening (FS) of (D) were measured at the indicated time points after MI/R injury.

Effect of ApoM-Fc–bound S1P on brain tissue damage and vascular barrier function after cerebral ischemia

D



(D) Representative images of TTC staining of seven, 1-mm-thick brain coronal slices 23 hours after reperfusion



(E, F) Administration of ApoM-Fc resulted in a decrease in both the infarct size and total edema region, which is the sum of cytotoxic and vasogenic edema (G) Infarct volumes (corrected for edema) were reduced to ~39% in ApoM-Fc–treated mice compared to PBS-treated mice.

IP Status & Publication(s)

Intellectual Property

Patent Number
US 10870689 B2 (2020.12.22)

Patent Family
PCT, US, EP, JP, CN, CA

Publication(s)

- Swendeman, Steven L et al. (2017) An engineered S1P chaperone attenuates hypertension and ischemic injury. Science signaling vol. 10,492 eaal2722.
- Christoffersen, Christina, and Lars Bo Nielsen. (2013) Apolipoprotein M: bridging HDL and endothelial function. Current opinion in lipidology vol. 24,4: 295-300.