KDDF
Korea Drug Development Fund

Asset #11
Boston University

mRNA Therapeutics for Acute and Chronic Liver Diseases

Therapeutic Area	Gastroenterology	**Indications**	Acute Liver Failure, Chronic Liver Failure
Modality	Nucleotide	**Development Stage**	Pre-clinical

Overview

Background

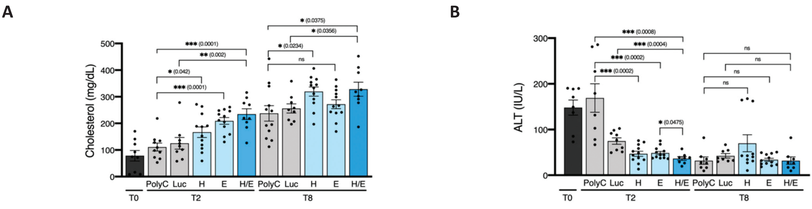
- Liver disease ranks as the 12th leading cause of death in the US, with liver transplantation being the sole remedy. The scarcity of donors poses a significant challenge. Although the liver can regenerate through hepatocyte proliferation, this falters in cases of severe damage.
- Thus, there's an urgent need for therapies to hasten recovery after acute damage and prevent chronic injury-related complications. A breakthrough technology utilizes modified mRNA within lipid nanoparticles to activate regenerative pathways, offering a safe and effective treatment for liver diseases.

Technology Advantages

- Modular applications depending on disease stage and severity
- Potent, non-integrative method for transient expression of mitogens into hepatocytes
- Rapid and effective resolution of hepatocyte necrosis and steatosis
- Efficient liver targeting using lipid nanoparticles

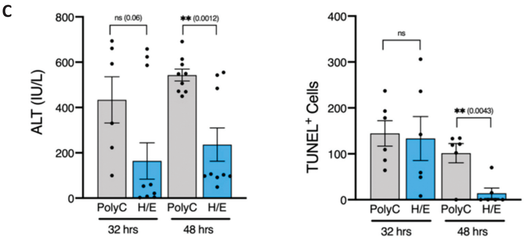
Key Data

HGF/EGF mRNA-LNP accelerate restoration of liver function during recovery from CDE-induced chronic liver injury



The scale bar represents 200 μm for all ×100 magnification images. Analyses of total serum cholesterol levels (A) and ALT levels (B) from 3 to 4 mice per group in duplicate or triplicate (n = 8–12) per time point treated with controls Poly(C) RNA-LNP or Luc mRNA-LNP, or single HGF(H), single EGF(E) or the combination H/E mRNA-LNP indicate sharp reversion of steatosis and restoration of basic levels of ALT after H/E mRNA-LNP injections. Data are presented as mean values ± SEM. Dark grey: T0, light grey: control RNA, light blue: single mRNA, dark blue: combined mRNA. P values were calculated by two-sided student's t test, ***<0.0001, **<0.001, *<0.05, n.s. = not significant. Source data are provided as a Source Data file

HGF/EGF mRNA-LNP accelerate liver recovery in the APAP-induced acute liver injury model



Data are presented as mean values ± SEM. Grey: control RNA, blue: combined mRNA. P values were calculated by two-sided student's t test, ***<0.0001, **<0.001, *<0.05, n.s. = not significant

IP Status & Publication(s)

Intellectual Property

Patent Number
-

Patent Family
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Publication(s)

- Rizvi at al. (2021). Murine liver repair via transient activation of regenerative pathways in hepatocytes using lipid nanoparticle-complexed nucleoside-modified mRNA. Nature Communications