

TREATMENT OF CHRONIC LIVER INJURY USING A THERAPEUTIC mRNA

Two research groups from CIBER, Universidad Miguel Hernández, Univesitat Politècnica de Valencia, FCIPF and ISABIAL have developed a new treatment system of liver injury using therapeutics mRNAs.

The Need

Chronic liver injury, including liver cirrhosis, is characterized by persistent inflammation, dysregulated T cell responses, progressive fibrogenesis, and loss of hepatic function. Existing clinical management primarily addresses underlying etiologies, mitigates complications, or culminates in liver transplantation, and pharmacological options that restore immune tolerance, reduce hepatocellular death, or reverse fibrosis can be limited and may present safety concerns. There is therefore a need for new, safe, and effective therapies that selectively modulate pathological immune pathways in the liver, attenuate inflammation and fibrosis, and can be delivered with hepatic selectivity to maximize efficacy while minimizing systemic toxicity.

The Solution

The present invention describes an mRNA encoding cellular receptor that can be used in the treatment of chronic liver injury, such as liver cirrhosis. To optimize the therapeutic effect, the present invention includes the formulation of several lipid nanoparticles (LNPs) loaded with said mRNA and functionalized with an antibody specifically directed to endothelial cells, to ensure the restoration of the expression of therapeutic mRNA in the correct target cells of the host. The proposed therapeutic mRNA has been reported to play a role in limiting T cell immune responses in the liver. Interaction of this receptor with its ligand, which is expressed on activated T cells, has been described to inhibit T cell activation, proliferation, and effector functions, consistent with mechanisms of tolerance in the healthy liver. Expression of this gene on hepatic antigen-presenting cells is reduced in experimental models of cirrhosis, and this reduction correlates with induction of a Th17 adaptive immune response.

Innovative Aspects

The present invention has been tested in mouse models. The use of the mRNA/LNP/specific antibody system to treat liver cirrhosis carries the following innovative aspects:

- 1.- Efficacy:** In experimental cirrhosis, this therapy restores the hepatic expression of the therapeutic gene and positively impacts on: (1) the liver inflammatory response, (2) liver function measured by serum test profile, (3) liver fibrosis, and (4) brain inflammation.
- 2.- Targeted and controlled delivery:** The conjugation of therapeutic mRNA to specific antibodies increases the specificity and selective delivery of mRNA contained in the LNPs to the body endothelium, mostly in the liver sinusoid cells.
- 3.- mRNA protection:** Encapsulation of therapeutic mRNA in lipid nanoparticles prevents enzymatic degradation by proteins of the extracellular milieu.
- 4.- Biocompatibility:** The use of lipids, which are similar to the ones found in cell plasma membranes, ensures low immunogenicity and cytotoxicity as confirmed in *in vitro* and *in vivo* experiments.
- 5.- Production:** The controlled synthesis of the system is scalable, a desirable feature for commercialization purposes.
- 6.- Regulatory approval:** This technology follows the same rationale SARS-CoV-2-mRNA-LNP loaded vaccines.

Intellectual Property:

- Priority European patent application filed (February 2026)

Aims

Looking for a partner interested in a license and/or a collaboration agreement to develop and exploit this asset.

Contact details