LUNAR®-CF: An mRNA Replacement Approach for Cystic Fibrosis Lung Disease

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Mutation agnostic treatment for CF lung disease

**Cargo:** hCFTR mRNA  
**Delivery vehicle:** LUNAR®  
**Delivery format:** Aerosol
Effects of Aerosolization and Stability in CF Mucus

Aerosolized LUNAR®, A Lung Delivery Platform

Encapsulation Efficiency is Maintained

Aerosolized LUNAR-mRNA maintains activity

LUNAR® Protects mRNA in CF Sputum

Different mesh nebulizers were tested for particle integrity using aerosolized LUNAR®-mRNA

Encapsulation efficiency is maintained in all tested nebulizers

Translational efficiency of aerosolized LUNAR®-EGFP mRNA is maintained after nebulization

Nine different LUNAR® formulations were tested for mRNA stability in sputum from two CF patients

All LUNAR® encapsulated mRNA was intact, and unencapsulated mRNA was degraded
Targeting LUNAR®-mRNA Delivery to Airways Epithelium

LUNAR®-mRNA Transduction is Maintained Across Species
Penetration of LUNAR®-mRNA through CF mucus

LUNAR®-Cre in a G551D CF ferret

Trachea

Bronchus

Low-res

High-res

[Images of Trachea and Bronchus with high and low resolution views]
Epithelial Cell Profiling with LUNAR®-mRNA (TdT)

Apical transduction in non-CF HBE cell population

Transduction efficiency ~31%

Ionocytes

Ciliated

Goblet cells

Basal cells

Transduction efficiency in epithelial cell types (% Log2)

Airway Epithelial cell types

- Ciliated cells
- Basal cells
- Goblet cells
- Ionocyte (BSND)
- Ionocyte (FOXI1)
Functional Restoration of Cl⁻ Current with LUNAR®-hCFTR in vitro

Ferret BE cells (G551D)  HBE cells (F508del⁺/⁺)

High levels of mature CFTR protein  Restored chloride activity

Western Blot

CFTR Cl⁻ Transport Activity

AUC/min [µA/cm²]
Functional Restoration of Cl⁻ Current with LUNAR®-hCFTR *in vivo*

NPD assessment in G542X Mouse Model after topical nasal instillation of LUNAR-hCFTR

![Graph showing functional restoration of Cl⁻ current with LUNAR®-hCFTR](image)

- **LUNAR® buffer control**
- **LUNAR®-hCFTR mRNA**

**** p = 0.0005*
Aerosolized LUNAR® LNPs are stable and protect mRNA from degradation in CF sputum

Target engagement of epithelial cells *in vitro* and *in vivo* across species and cell types

Codon-optimized hCFTR mRNA generates high levels of mature CFTR protein

Proof-of-activity for LUNAR®-hCFTR mRNA *in vitro* and *in vivo*

These data strongly support further development of LUNAR®-hCFTR for treatment of CF lung disease
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