Lipid nanoparticles for pulmonary delivery of mRNA

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INTEGRATING
Delivery Science
ACROSS DISCIPLINES

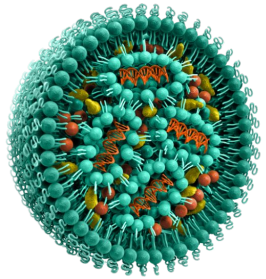
Background

- Systemic and localized gene therapy using lipid nanoparticle (LNP)-based delivery platforms have gained recent successes.
- Inhalation-based gene therapy and mucosal immunization remain challenging for treating various lung diseases.
- Intranasal (IN) administration of nucleic acids-encapsulated nanoparticles can directly access the pulmonary system.
- Mostly, mucociliary clearance and nasal membrane impermeability are the key barriers to effective IN delivery.

Study plans

NanoAssemblr™
Ignite™

Optimization



LNP

+

IN solution

Characterization

- Size
- PDI
- EE
- Gel run
- Stability
- Rheology
- Viscosity

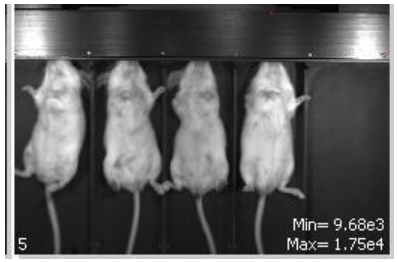
In vitro testing

Preclinical testing

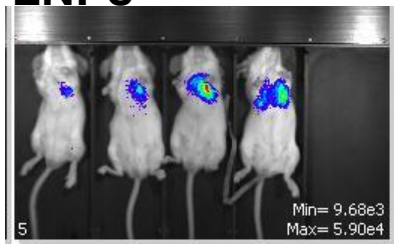
PDI=Polydispersity Index
EE = Encapsulation efficiency

Protein translational efficacy

A

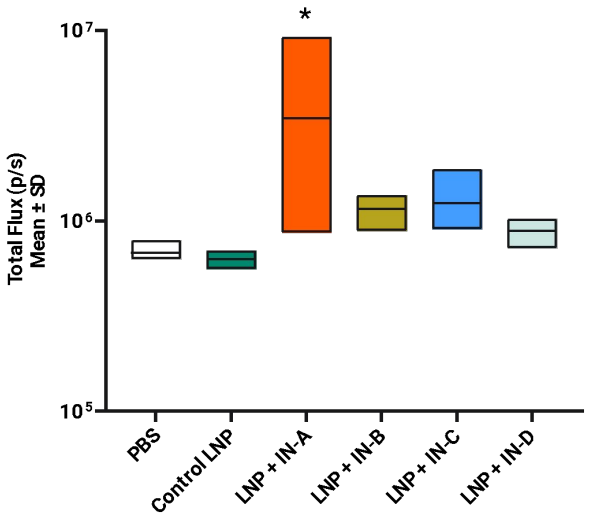


FLuc-mRNA LNPs



IN-specific FLuc-mRNA LNPs

B



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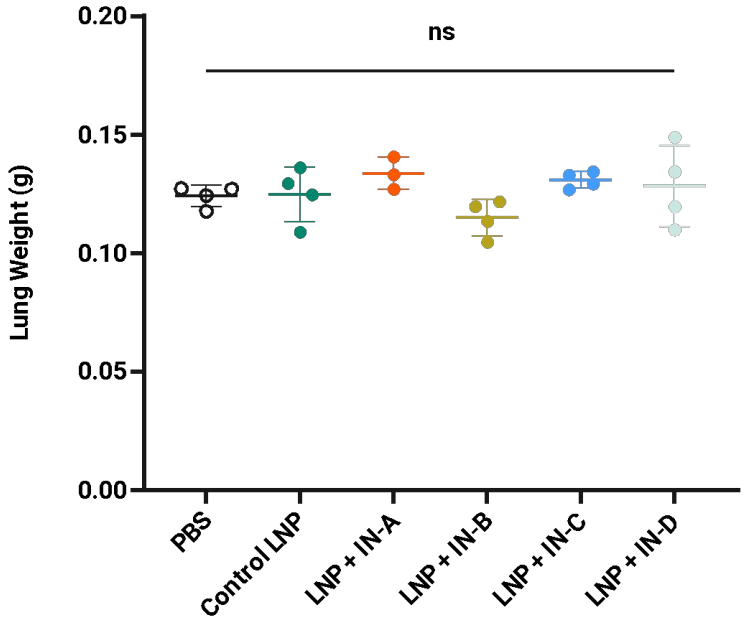
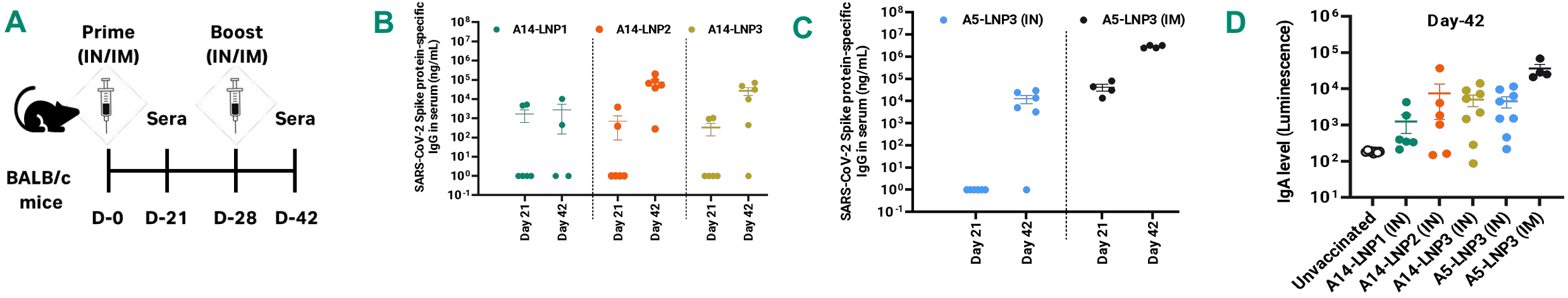


*** IN-(X) = IN composition types**

A) Representative whole body IVIS images of the female BALB/c mice of two groups where one is the control group (top-left) treated with FLuc-mRNA/LNPs and the other (top-right) is one of the test groups receiving IN-specific Fluc-mRNA/LNPs. Mice received one dose of 0.1 mg/Kg FLuc-mRNA with a volume of 12.5 µL into each nostril by pipette drop. B) Analysis of the comparative efficacy of the treatment groups after IVIS imaging. C) Relative lung weights for the mice groups (n = 4).

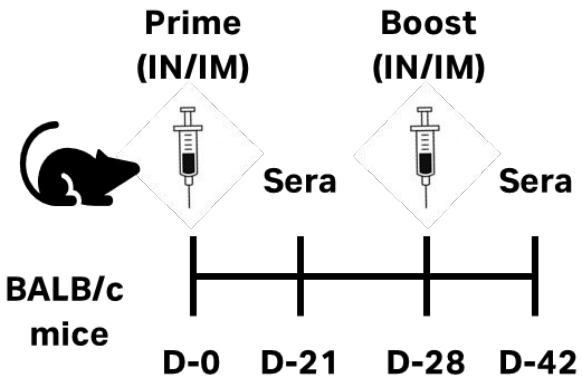
Immunization efficacy



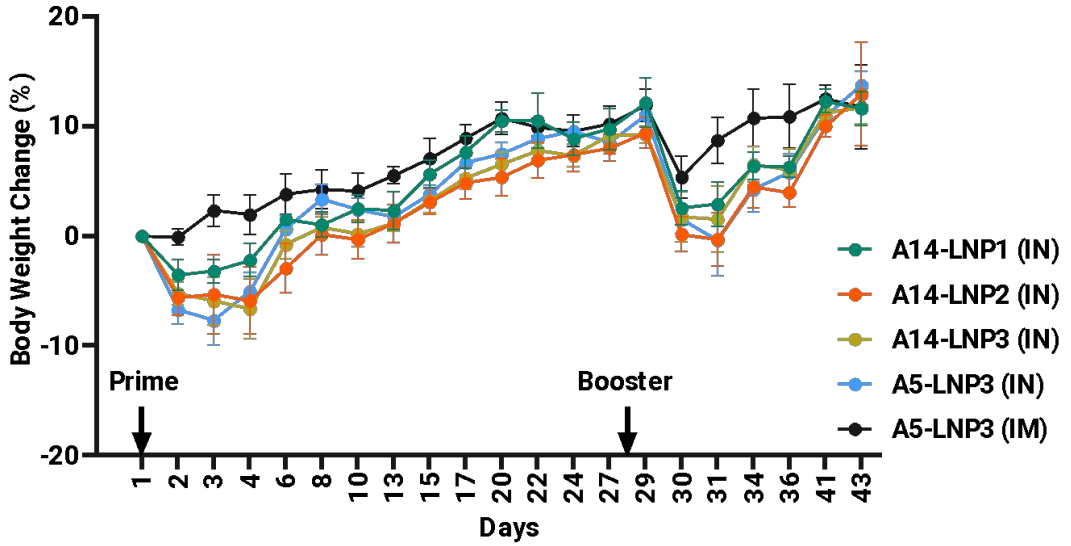
A) Vaccination study outline in female BALB/c mice. B-D) Relative humoral immune responses (IgG and IgA) in the plasma of vaccinated female BALB/c mice at day 21 and day 42. Mice received the IN vaccinations after mixing saRNA-encapsulated IN-specific LNPs. LNP# represents the different Cytiva proprietary ionizable lipids.

Immunization efficacy

A



E



A) Vaccination study outline in female BALB/c mice. E) Relative body weight changes (%) of all the vaccinated mice groups. LNP# represents the different Cytiva proprietary ionizable lipids.

Summary

- Our IN-delivery platform can deliver nucleic acids-loaded nanoparticles into the lungs by retaining the drug product's **critical quality attributes (CQAs)**.
- Our preclinical screenings exhibited desired *in vivo* protein translational efficacy in lungs.
- Mucosal vaccination showed a desirable immune response.
- Further studies include other types of antigenic mucosal immunization and effective delivery of genes for other pulmonary genetic disorders such as cystic fibrosis, and α1-antitrypsin deficiency.

Thank you!

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