Treatment of acute lung injury using one-component LNP to deliver TGFβ mRNA to the lower lung

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CRS 2025 ANNUAL MEETING & EXPOSITION
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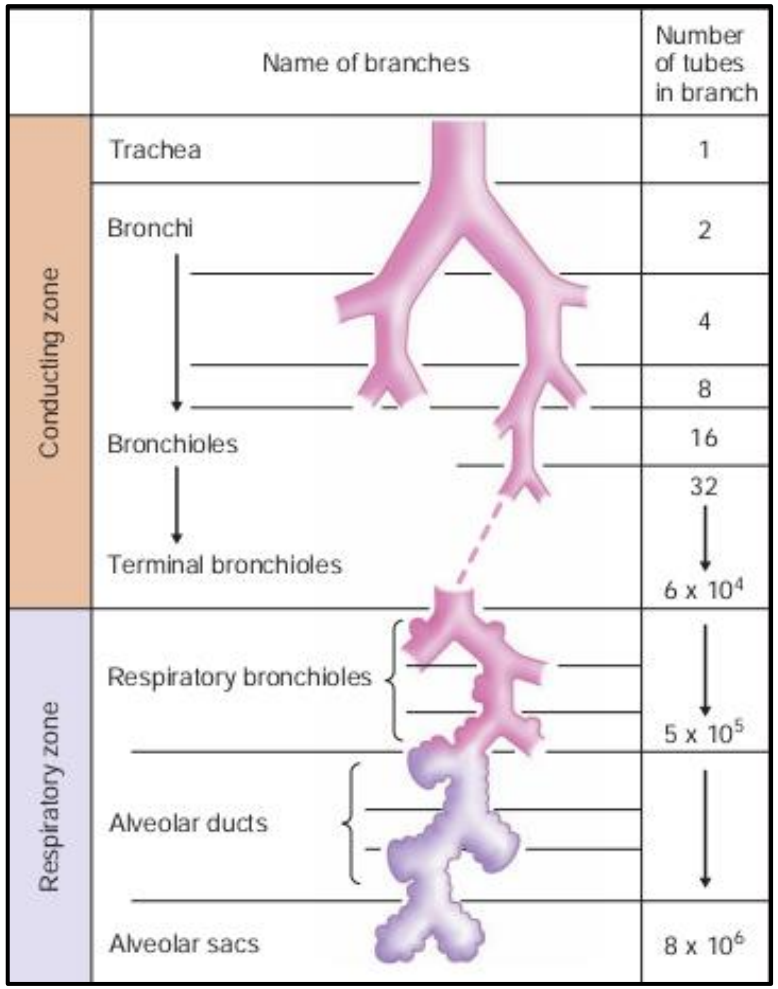
NEXT-GENERATION DELIVERY INNOVATIONS

Clinical need to target the respiratory airway



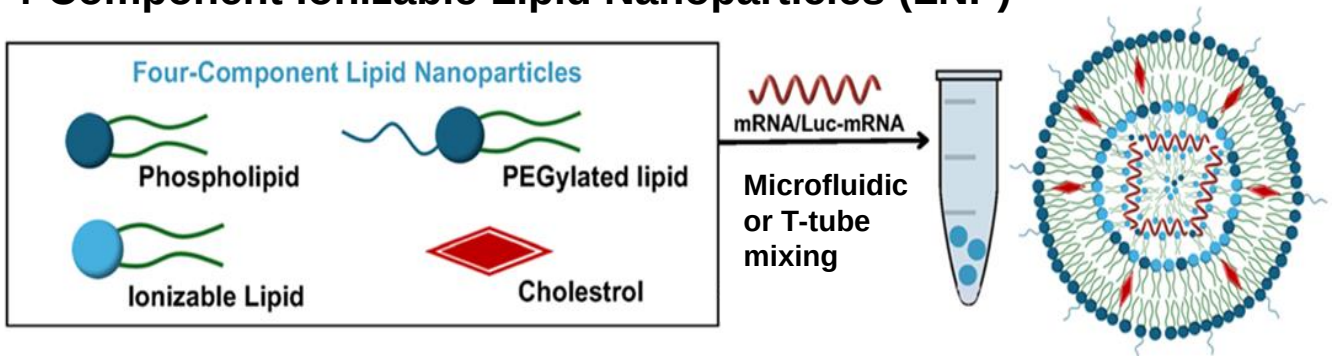
- Two major regions of the lung
- Pathologies in these two areas are diverse
- Therapies that target the respiratory epithelium exclusively are extremely limited

Major clinical gap for treatment of lower airways disease and injury

Image adapted from: https://doi.org/10.1016/B978-0-323-44887-1.00006-7

4-component LNP vs one-component IAJD

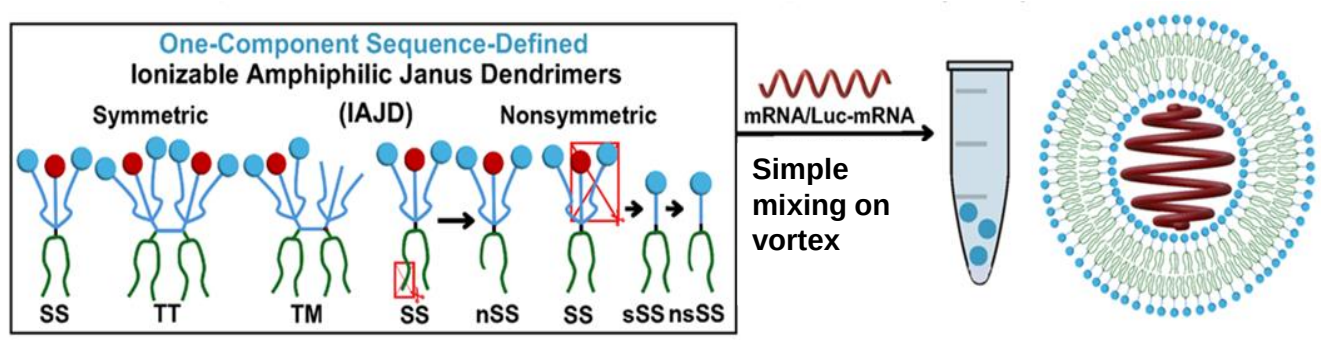
4-Component Ionizable Lipid Nanoparticles (LNP)



4-components

- Microfluidics
- PEG dilemma; adverse reaction
- Storage at -80 ℃

1-Component Ionizable Amphiphilic Janus Dendrimers (IAJD)



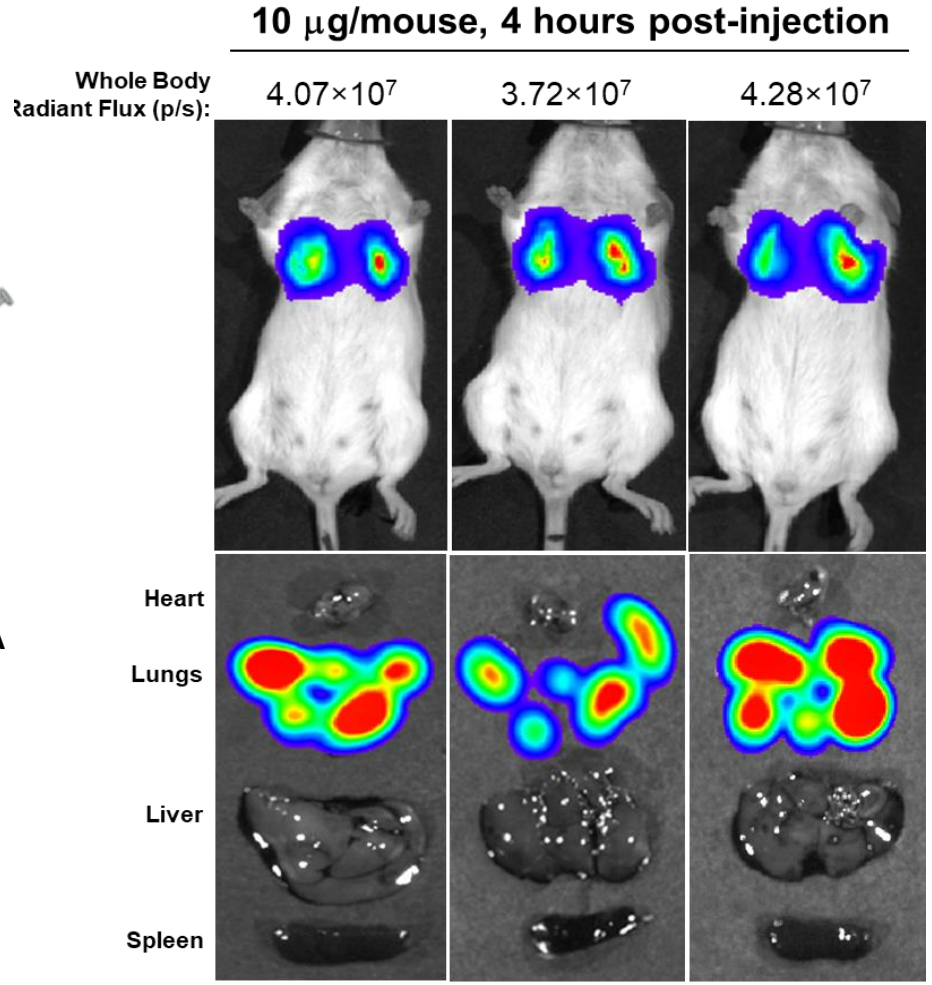
1-component

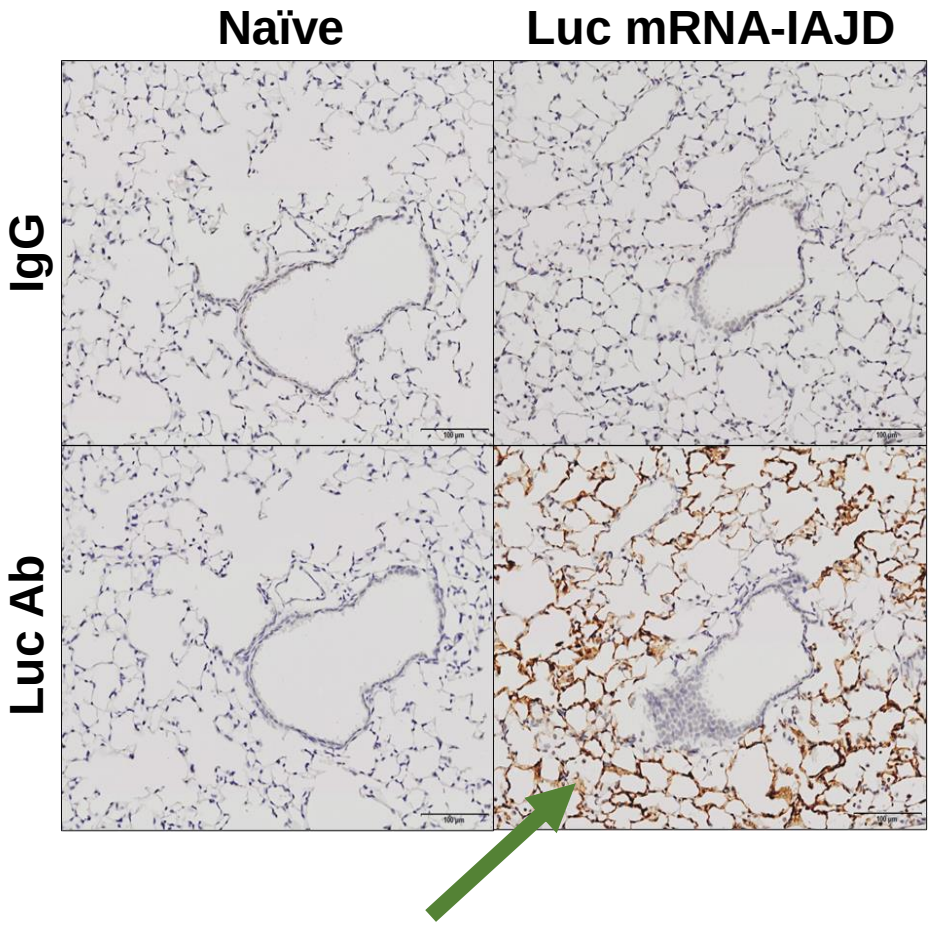
- Simple mixing on vortex
- No need for cholesterol or PEG
- Stable
- Cost-effective and fast production

Image adapted from: **https://doi.org/10.3390/pharmaceutics15061572**

Specificity of IAJD for mRNA delivery to the lung

10 µg, R.O.
IAJD34+Luc mRNA





See Abstract 2027354 for more information on how IAJD34 was characterized

Use of IAJDs to deliver protein therapeutics

- **Key to therapeutic delivery is:**
  - -Tissue specificity
  - -Time frame
  - -Functional processing
- **TGF-β in a model of acute lung injury**
  - -Potent anti-inflammatory
- **Can also be done with other mRNAs:**
  - -Other cytokines
  - -Vaccine components

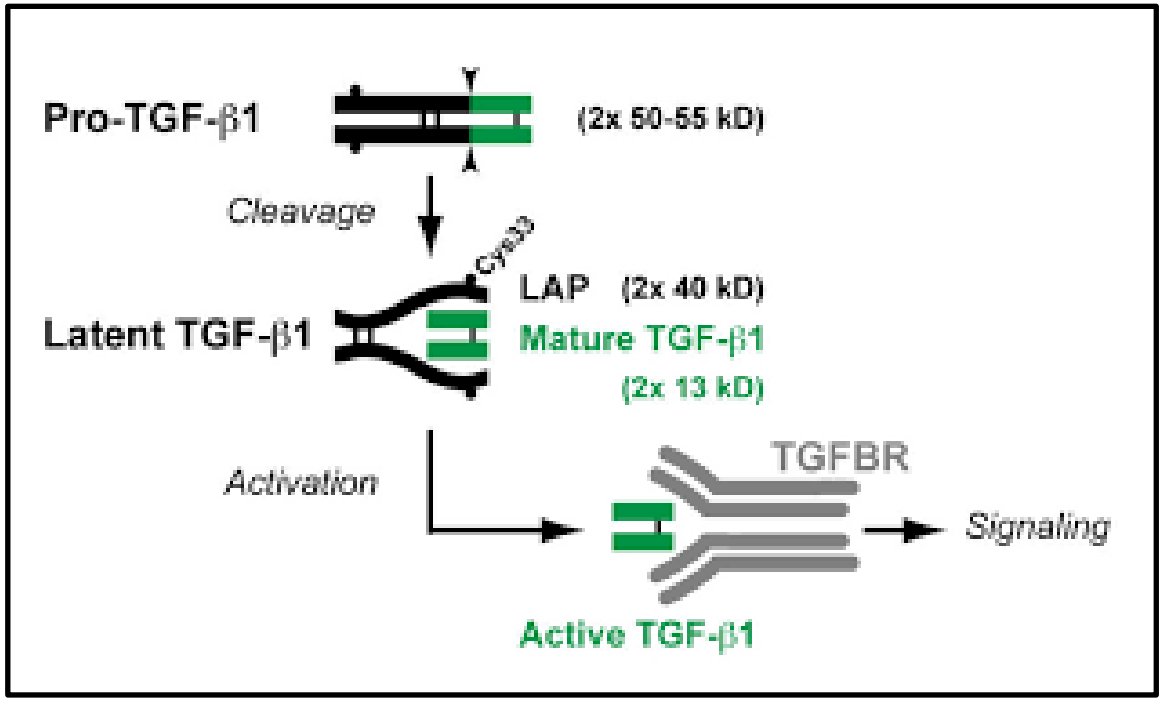
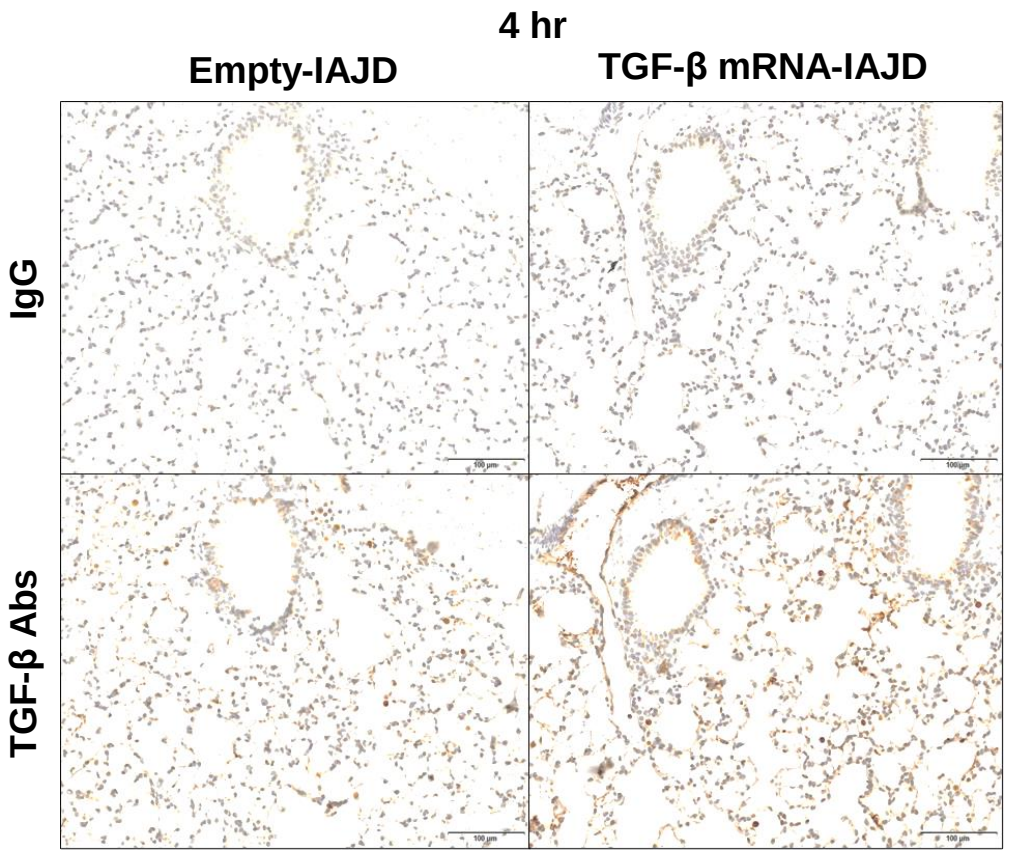
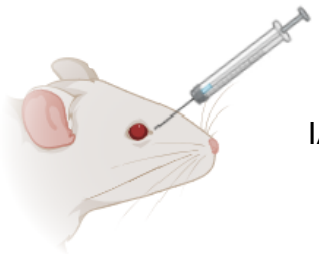


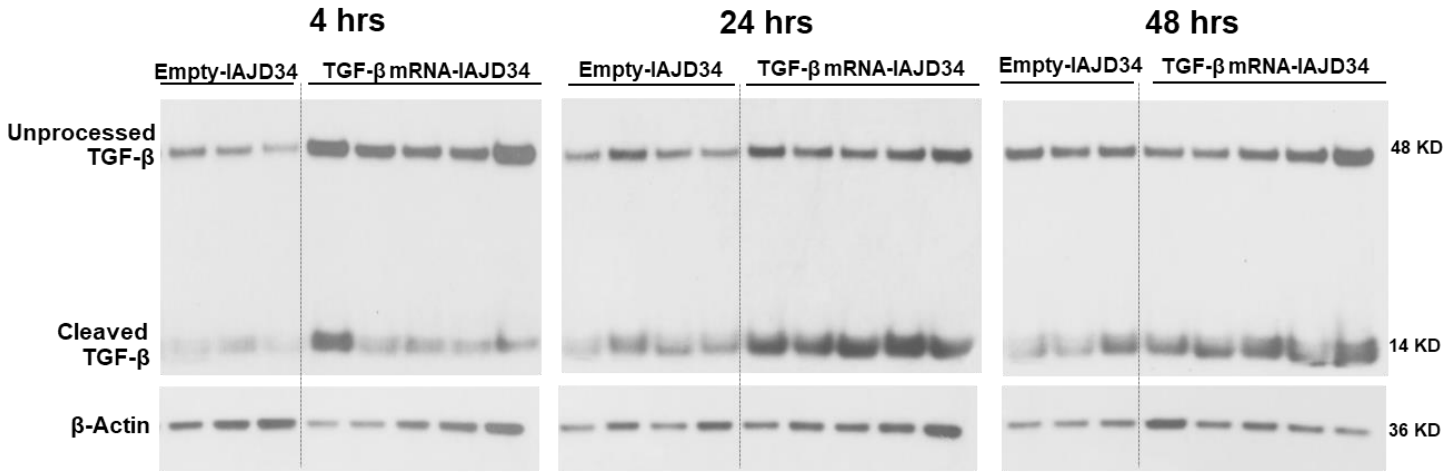
Image adapted from https://doi.org/10.1371/journal.pone.0076186

TGF-β expression following delivery to lung





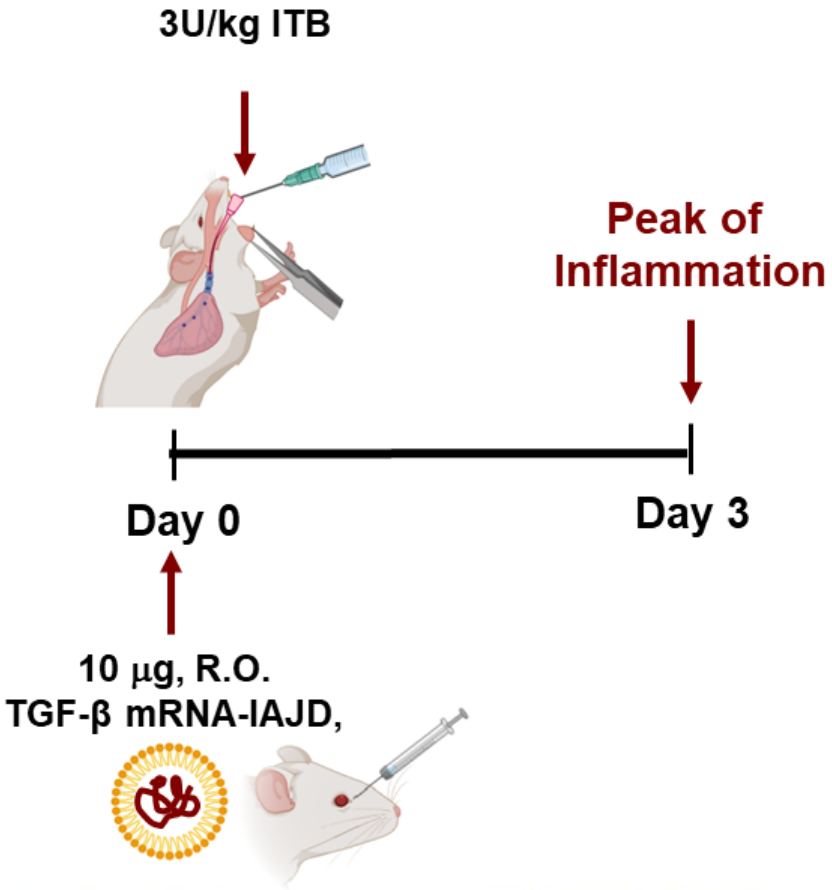
10 µg, R.O.
IAJD34+TGFb mRNA
Lung tissue



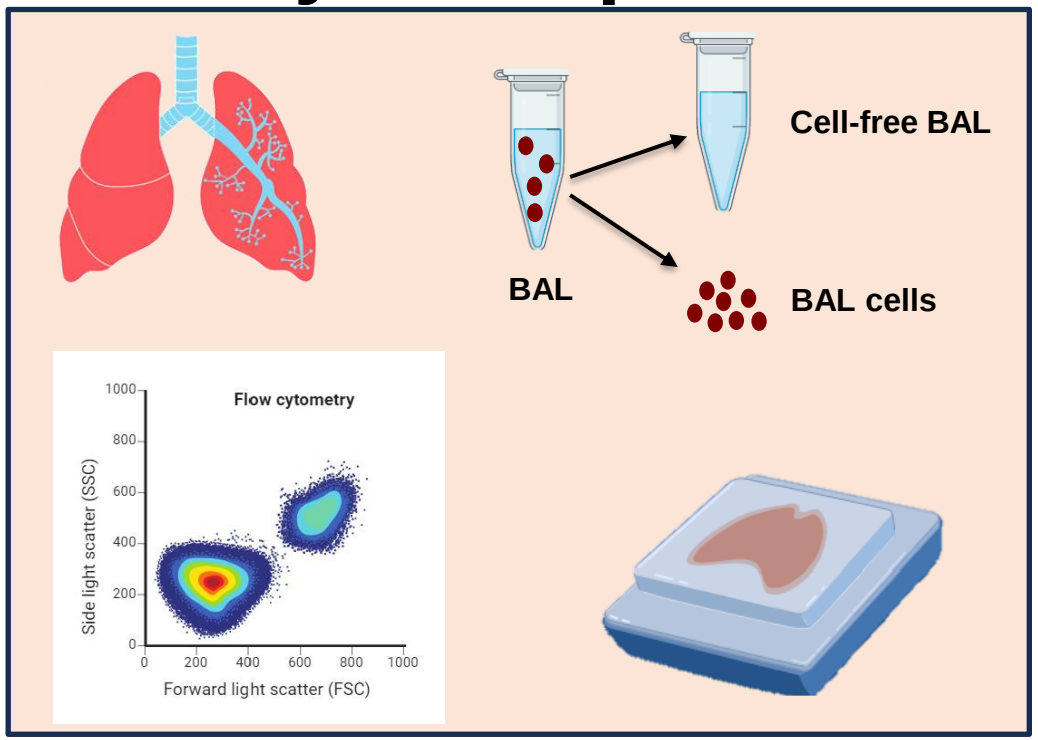
Showed no toxicity in lung, liver, spleen, or kidney

Using TGF-β mRNA-IAJD to treat ALI

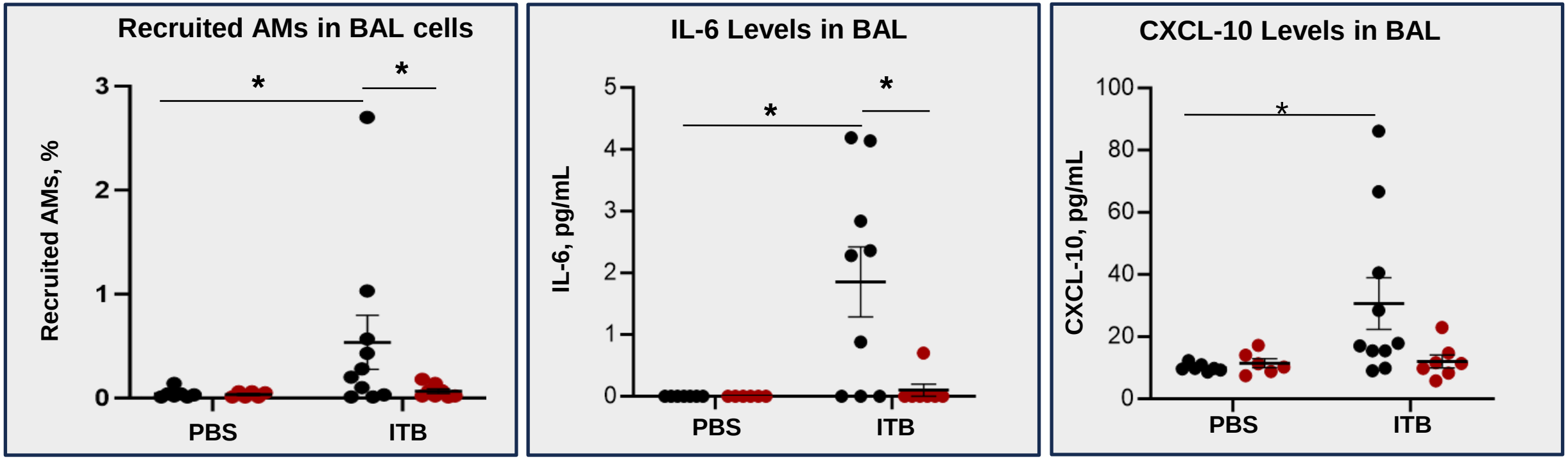
Use Bleomycin (ITB) as a model of Acute Lung Injury (ALI)



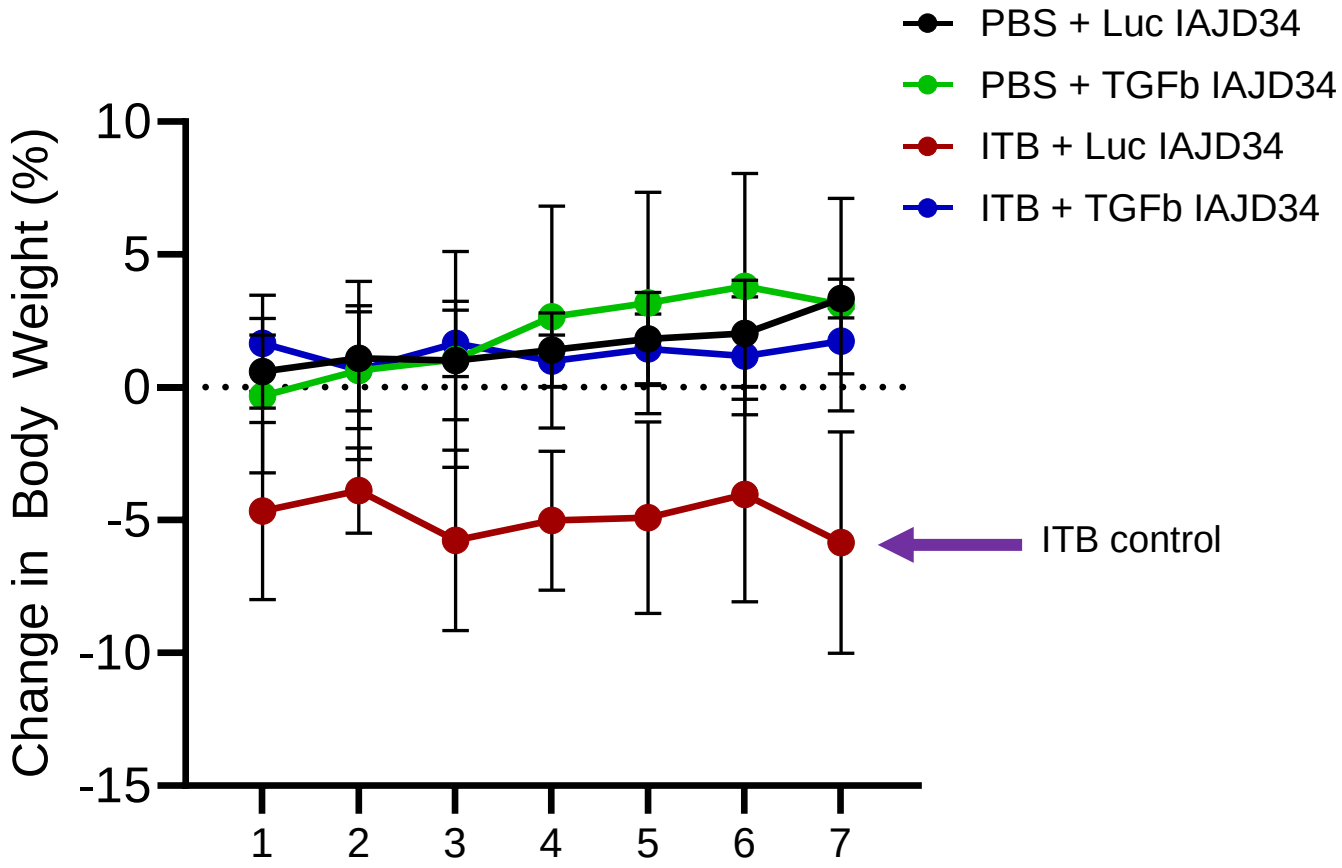
Day 3 Endpoints

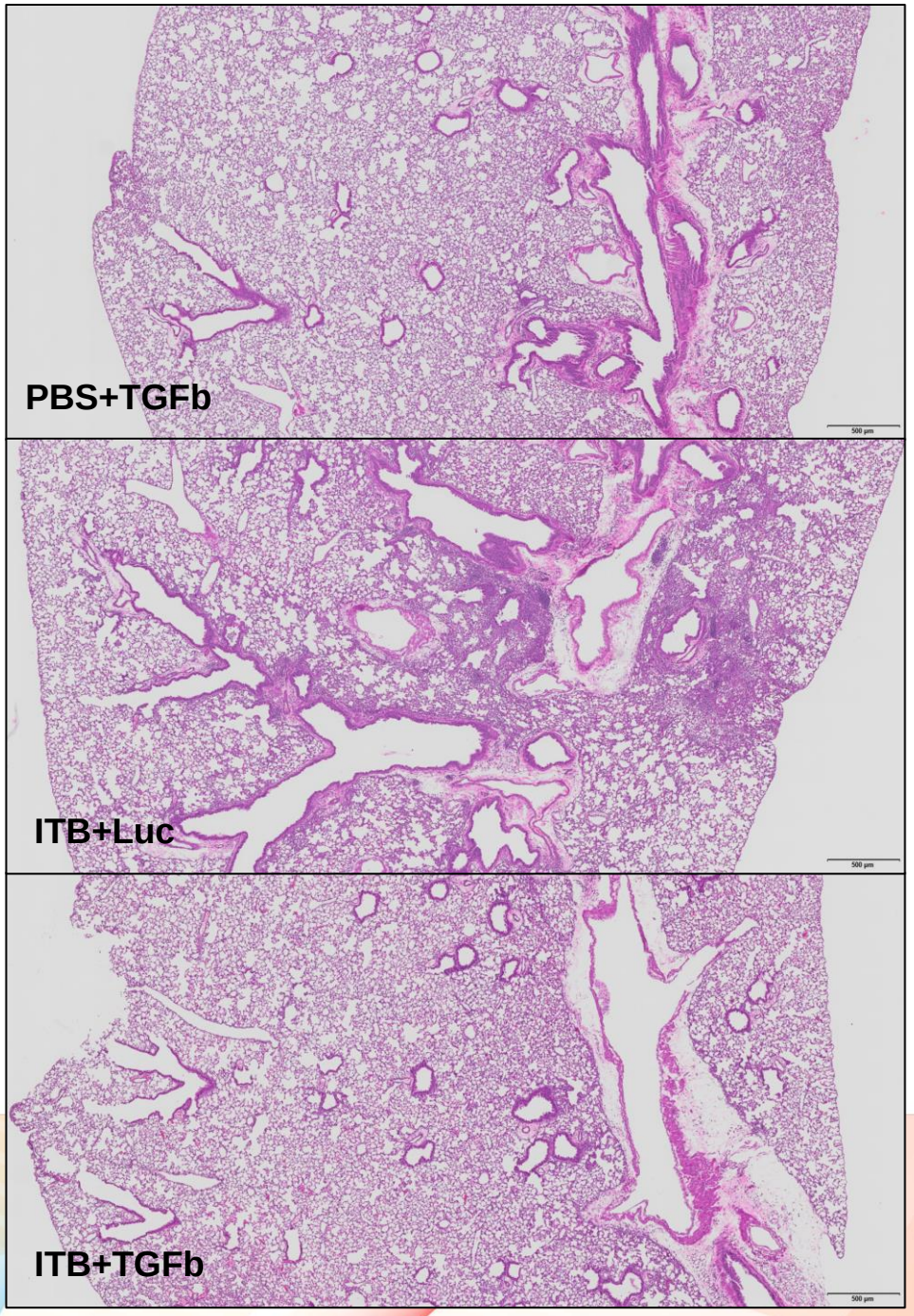


TGF-β mRNA-IAJD treatment reduces ITB injury



7 Days post-ITB injury (4U/kg)





n=4-6/group and graphs include 2 independent instillation days

Summary

This proof-of-concept study demonstrates the ability of one-component IAJD, formulated with TGF-β mRNA, to serve as a platform for efficient delivery to the lung

Currently pursuing other therapies for lung parenchyma

-Other mRNAs

-Genetic recovery models

Acknowledgements

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