Targeting the lower regions of the lung: a novel platform for pulmonary mRNA delivery

Rachel Sun
PharmD/ PhD student
Rutgers University

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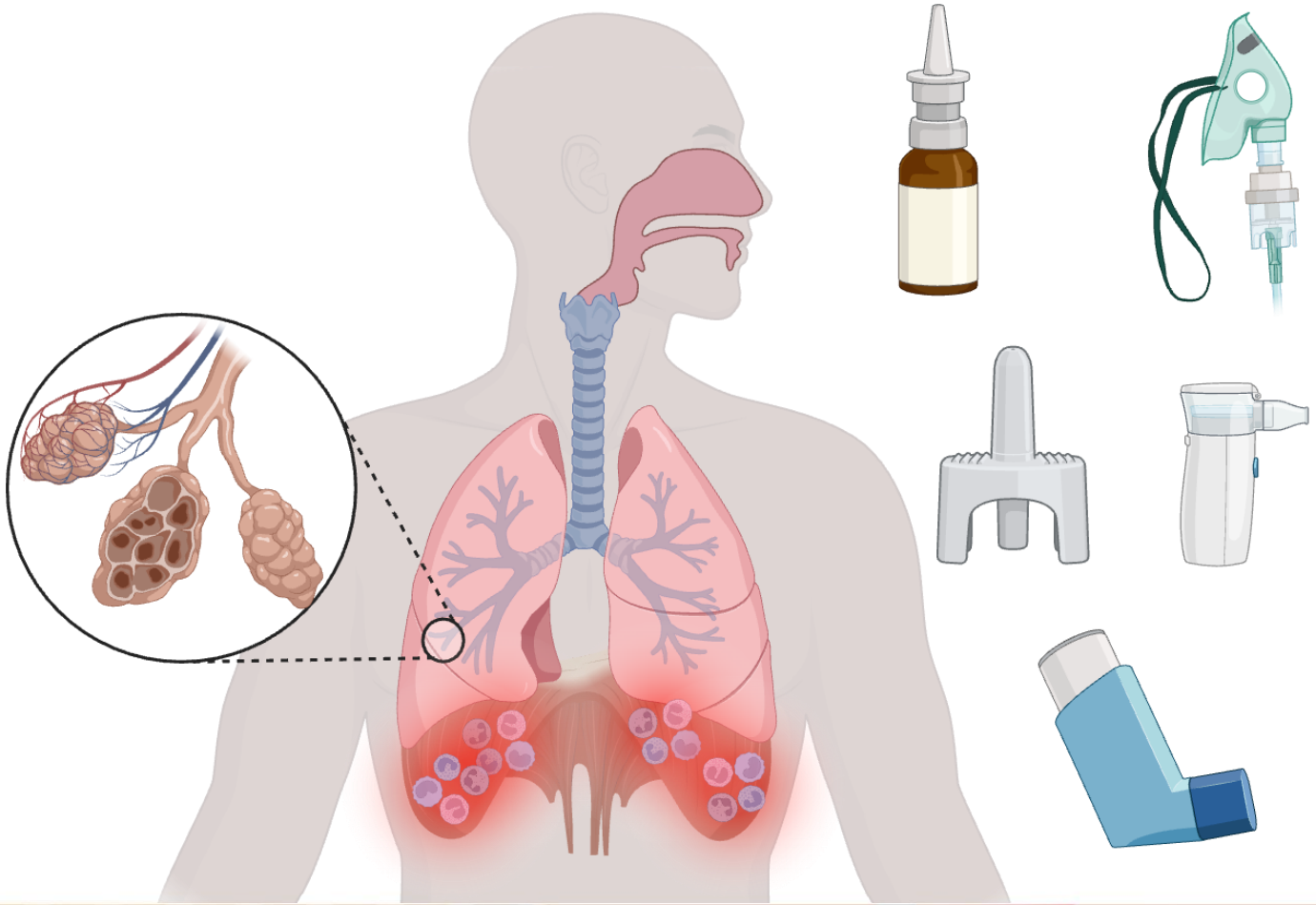
NEXT-GENERATION DELIVERY INNOVATIONS

Barriers to lung-targeted therapies

- Primarily target the upper airways of the lung
- Limited targeted delivery to the lower regions of the respiratory system



Ionizable amphiphilic Janus dendrimers (IAJDs)

Delivered mRNAs can be used to increase the expression of protein therapeutics

- Examples include cytokines, peptide hormones, and antioxidant enzymes

Key to therapeutic delivery is:

- Tissue specificity
- Time frame
- Functional processing

IAJDs: one-component Ionizable Amphiphilic Janus Dendrimers

- Single component lipid
- Self assembling

One-Component Ionizable amphiphilic Janus dendrimers (IAJDs)

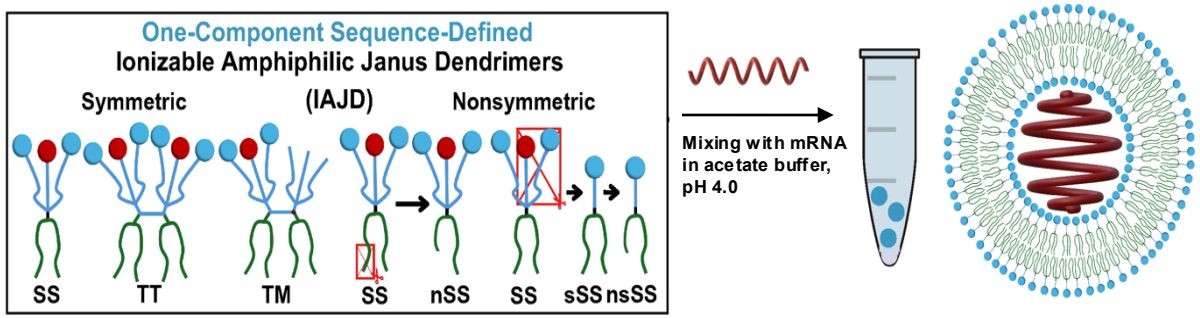


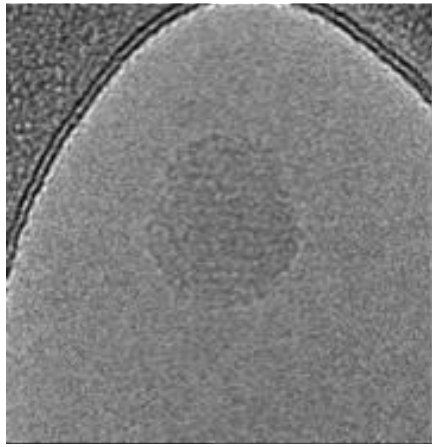
Image adapted from: **https://doi.org/10.3390/pharmaceutics15061572**

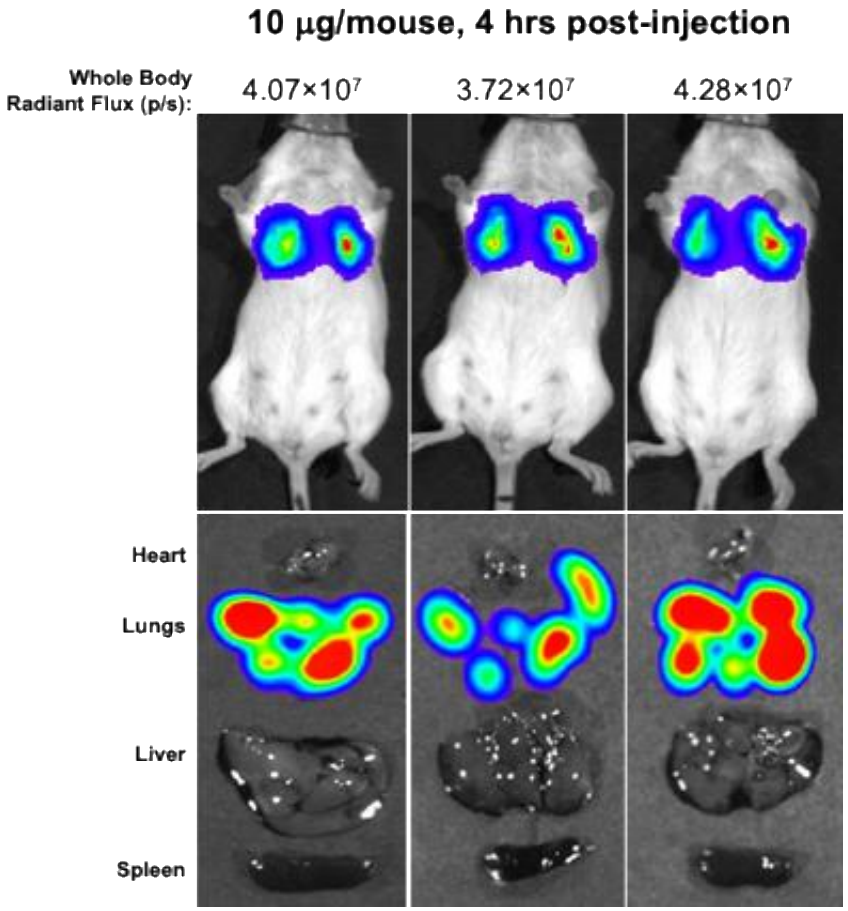
IAJD34 was selected for further characterization

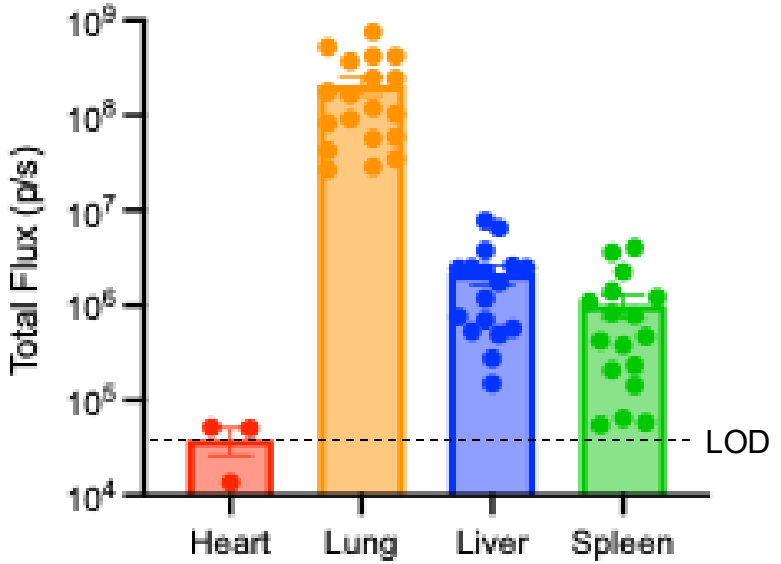
Characteristics of one-component IAJD34

Luc mRNA-IAJD34	
Size, nm	97.0 ± 2.4
PDI	0.250 ± 0.01
Encapsulation, %	98.9 ± 0.2
Zeta potential, mV	48.8 ± 4.3

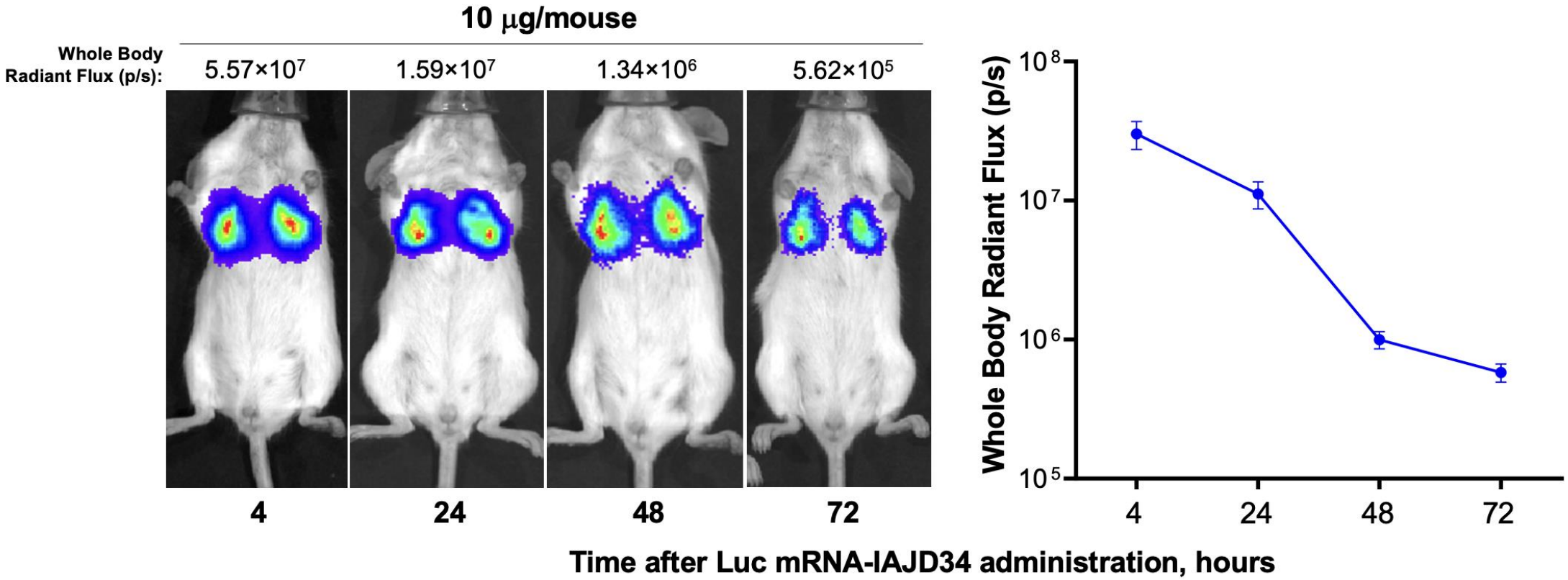
Cryo-TEM of IAJD 34







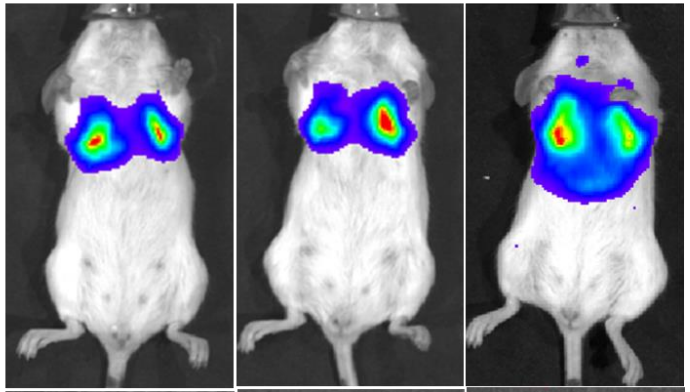
Specific and targeted lung delivery over time

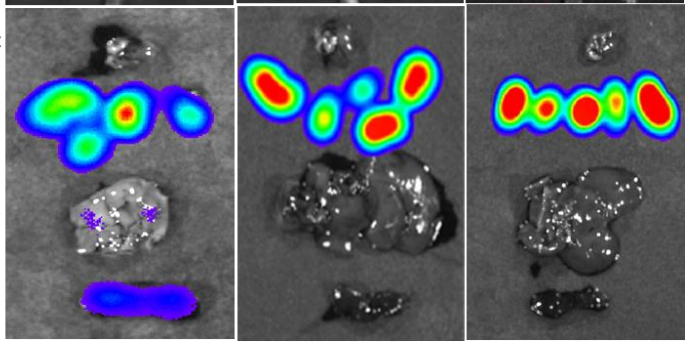


Dose-dependent mRNA delivery

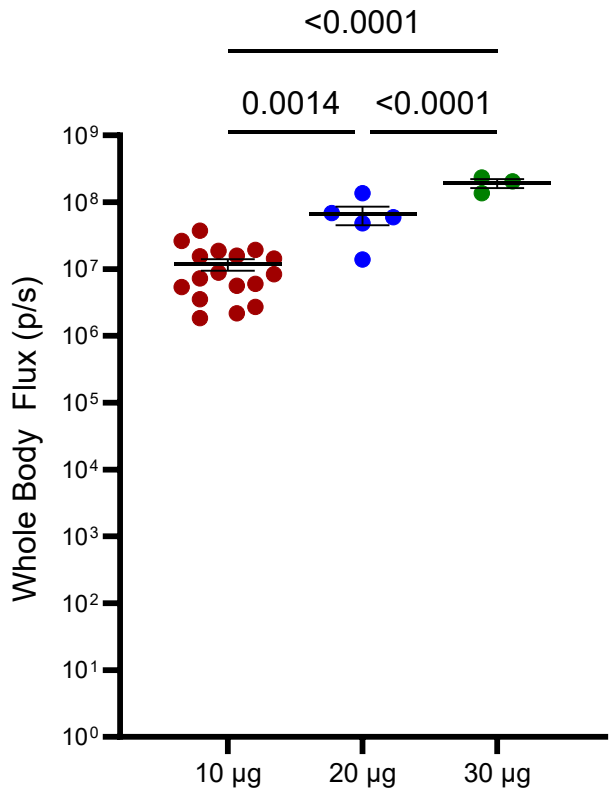
24-hours post-injection

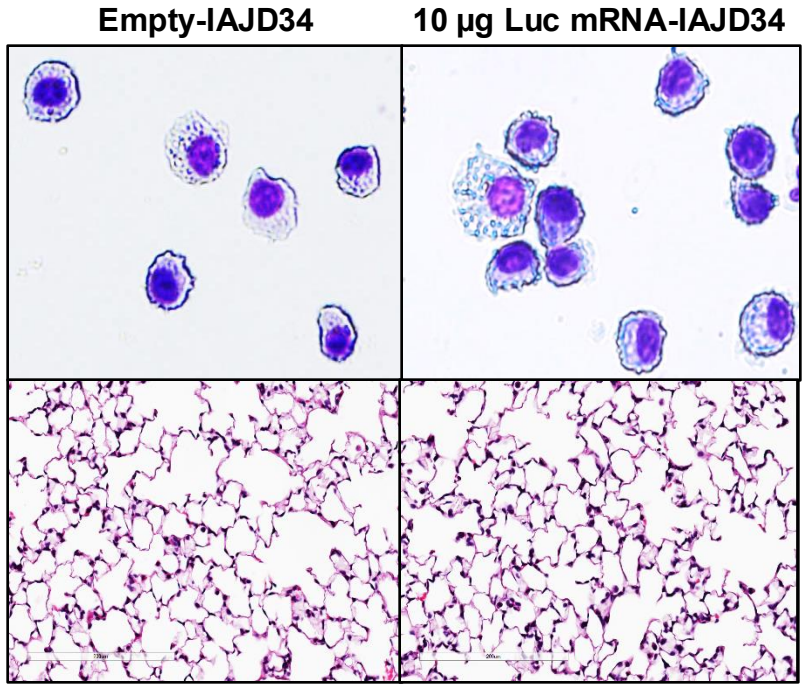
mRNA/mouse:	10 µg	20 µg	30 µg
Size/PDI:	95/0.240	111/0.255	123/0.269
Whole Body Flux [p/s]:	2.65e+07	1.37e+08	2.35e+08





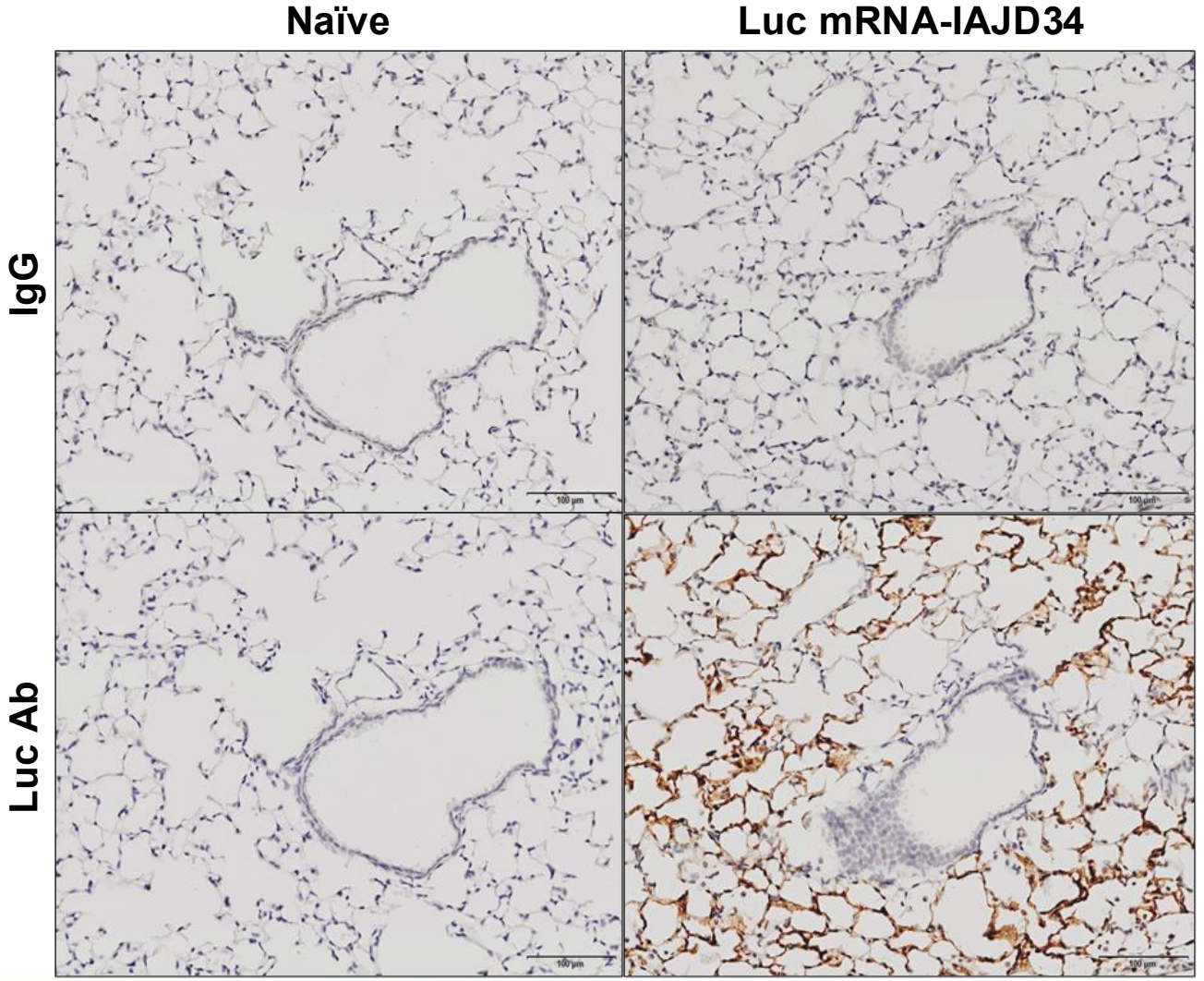
Heart Flux [p/s]:	5.69e+03	5.19e+03	4.32e+04
Lung Flux [p/s]:	1.26e+07	7.24e+07	9.31e+08
Liver Flux [p/s]:	8.18e+05	4.54e+04	4.56e+06
Spleen Flux [p/s]:	1.56e+06	5.21e+03	9.06e+05





No toxicity or signs of inflammation have been observed

Targeted lung parenchyma delivery confirmed by IHC



Summary

- IAJD34 formulated with mRNA specifically targets the lower regions of the lung
- IAJD34 is a potential platform for the treatment of pulmonary injury and disease

Acknowledgements

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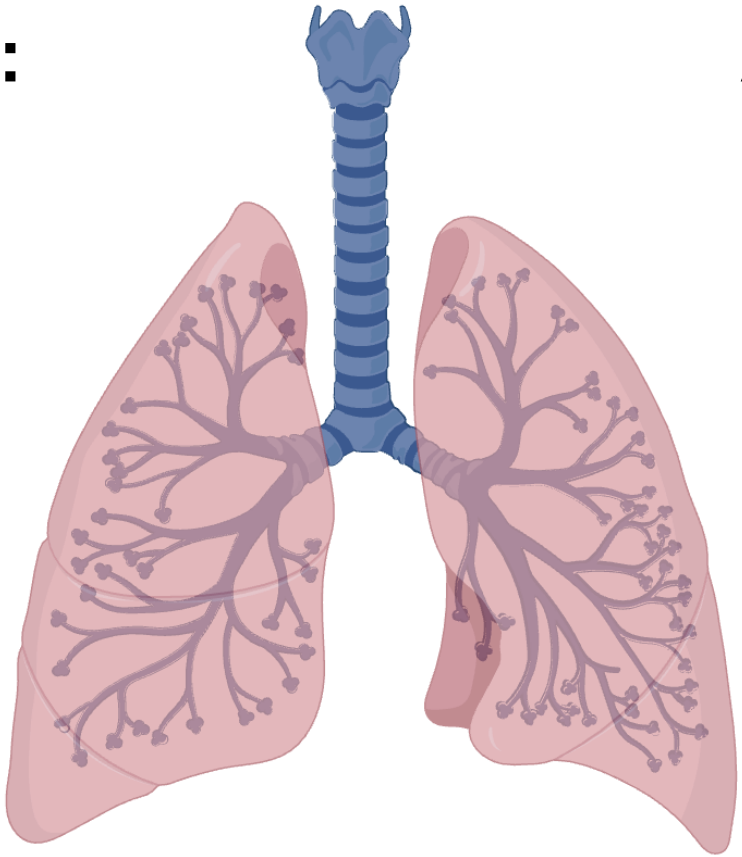
The Weissman Lab
Bringing mRNA therapeutics to the world

leap R3



Andrew Gow Lab:

Andrew Gow
Changjiang Guo
Elena Abramova

RUTGERS THE STATE UNIVERSITY OF NEW JERSEY ERNEST MARIO SCHOOL OF PHARMACY 1892

NIEHS CEED Center for Environmental Exposures and Disease

rs1893@pharmacy.rutgers.edu