

Delivery Technologies for Diversified Products

Impact of Lipid Composition on Maintaining Bioactivity of mRNA-LNPs in Thermostable mRNA-Vaccines

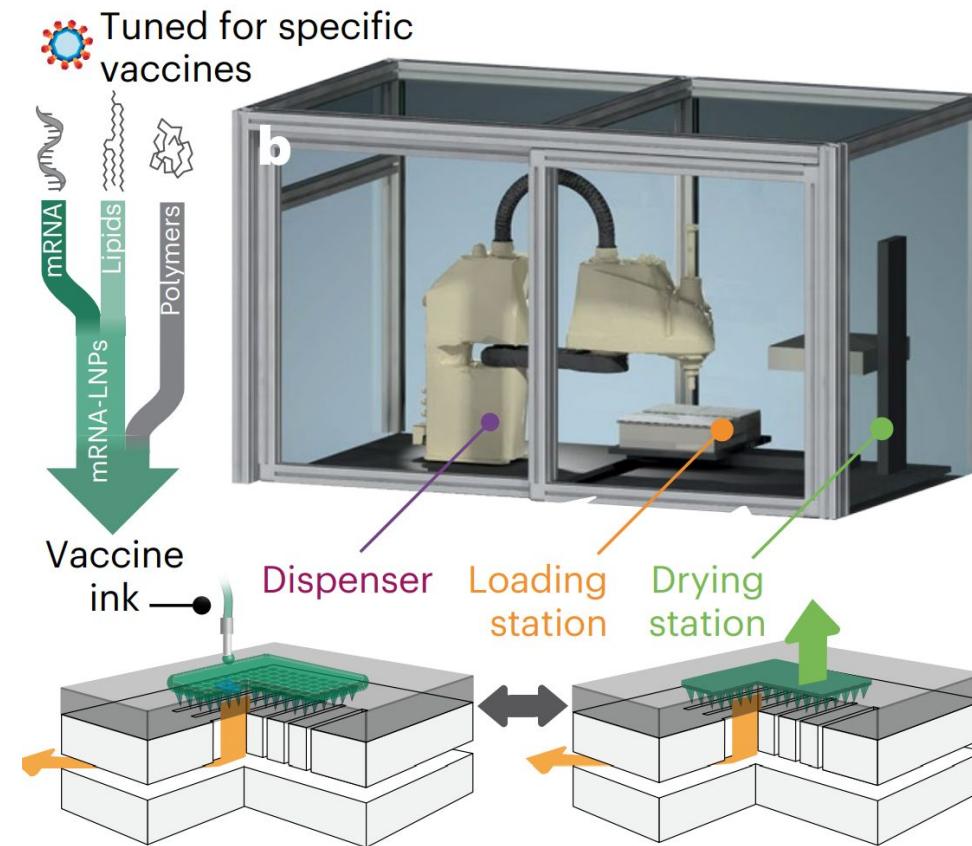
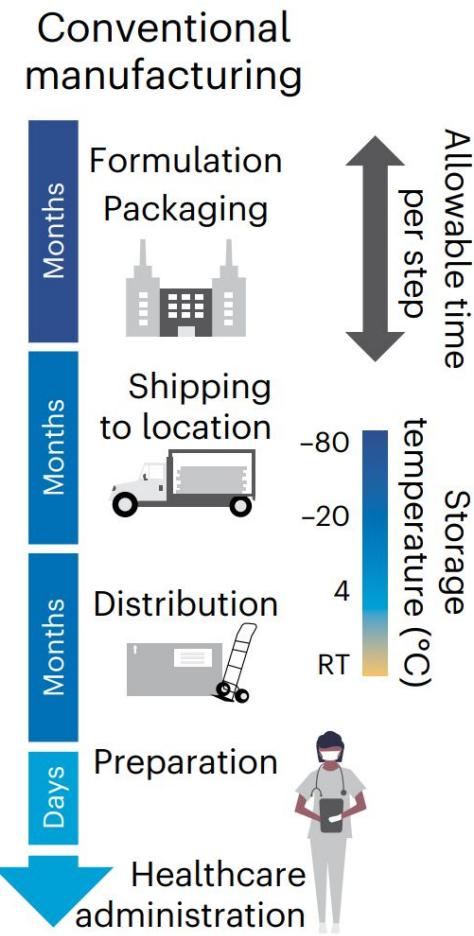
Behnaz Eshaghi, Ph.D.



INTEGRATING
Delivery Science
ACROSS DISCIPLINES



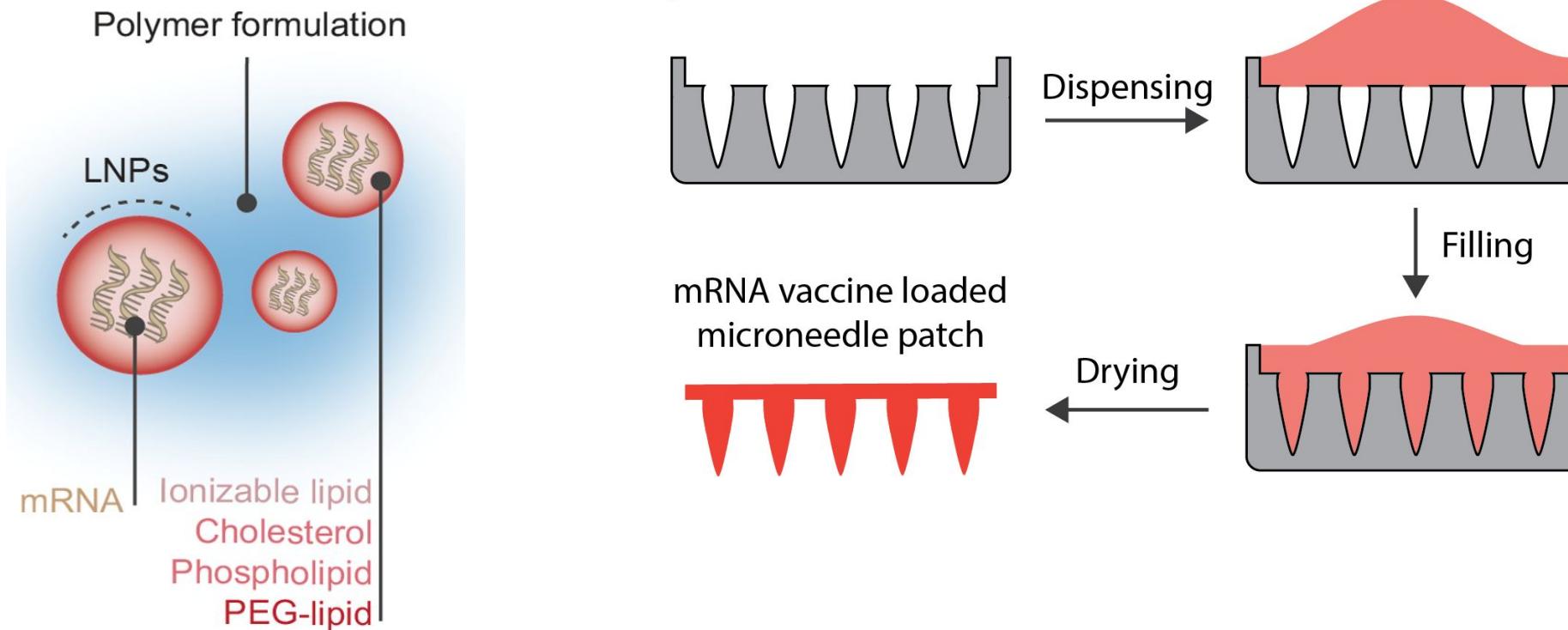
mRNA vaccines in a microneedle array patch (MNP) could enhance vaccine accessibility



Straeten et al., *Nat Biotechnol*, 2023

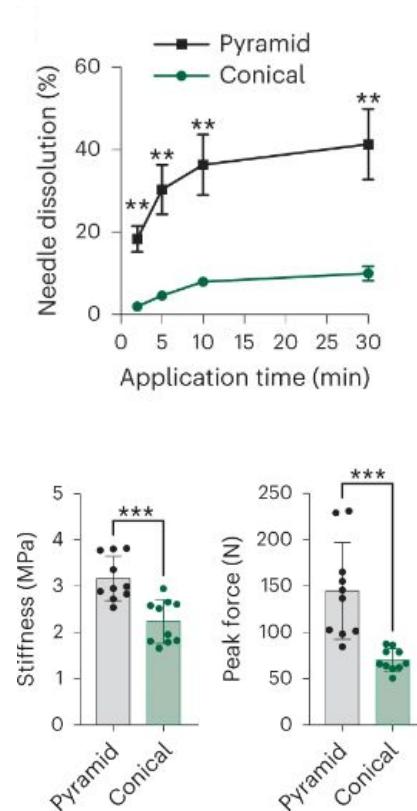
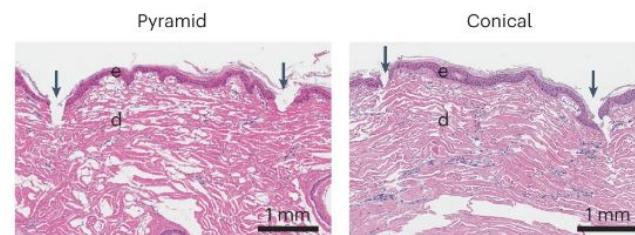
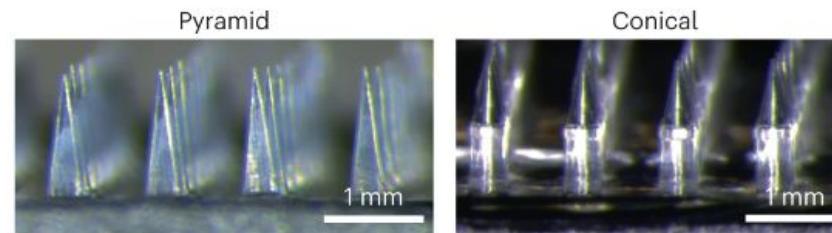
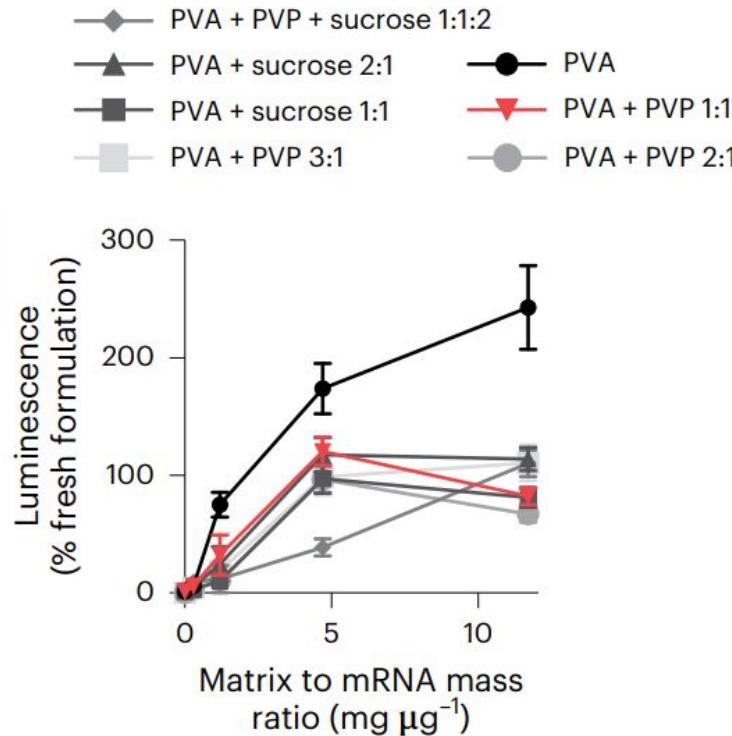
Fabrication of mRNA-LNP-loaded MNPs

LNPs + PVA/PVP (Ink)



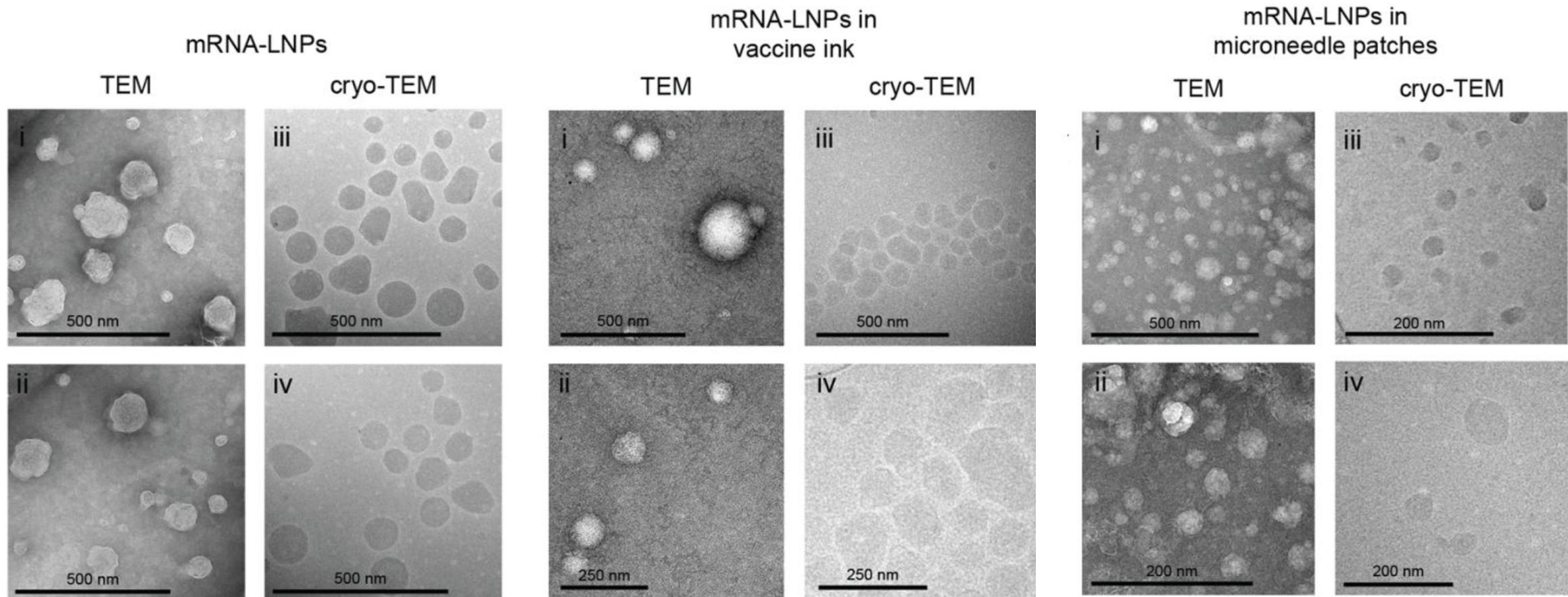
Straeten et al., *Nat Biotechnol*, 2023

Ink composition and needle geometry were optimized for mRNA-LNP bioactivity and MAP application



Straeten et al., *Nat Biotechnol*, 2023

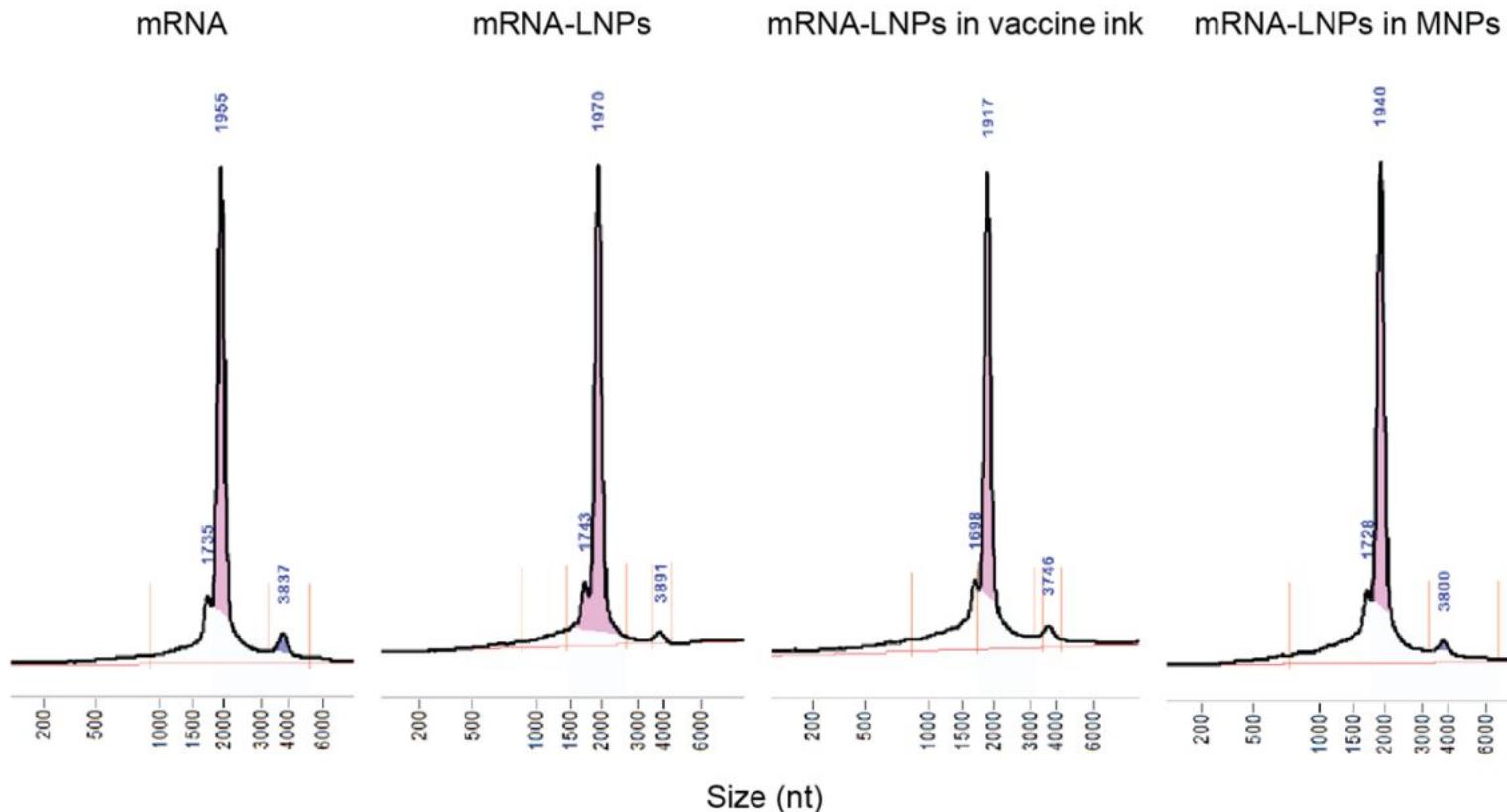
TEM and Cryo-TEM results demonstrated intact mRNA-LNP structure in MNPs



Straeten *et al.*, *Nat Biotechnol*, 2023



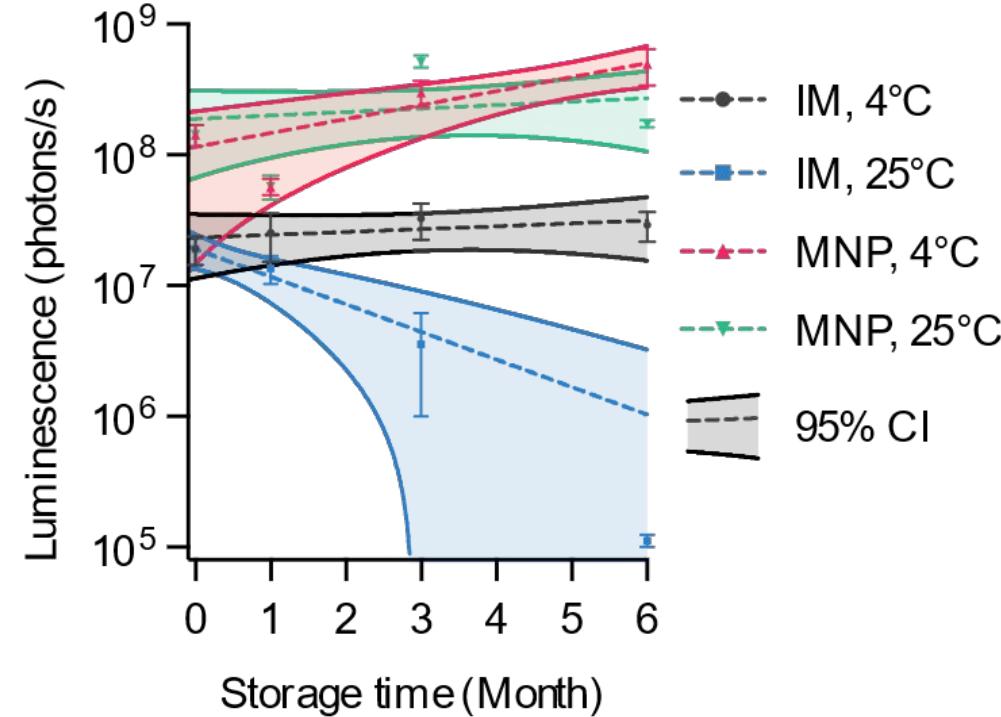
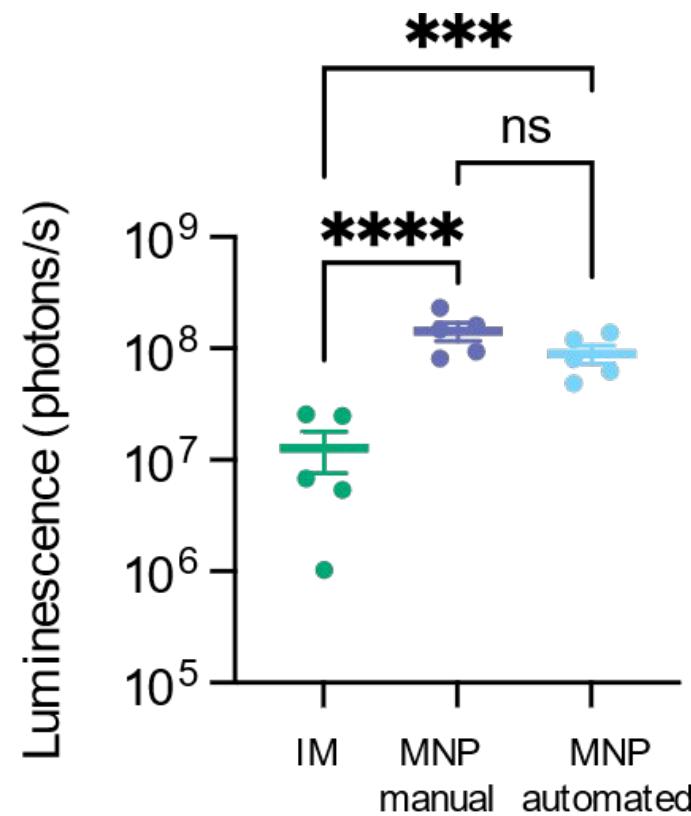
Capillary gel electrophoresis analysis confirmed the integrity of mRNA in MNPs



Straeten et al., *Nat Biotechnol*, 2023

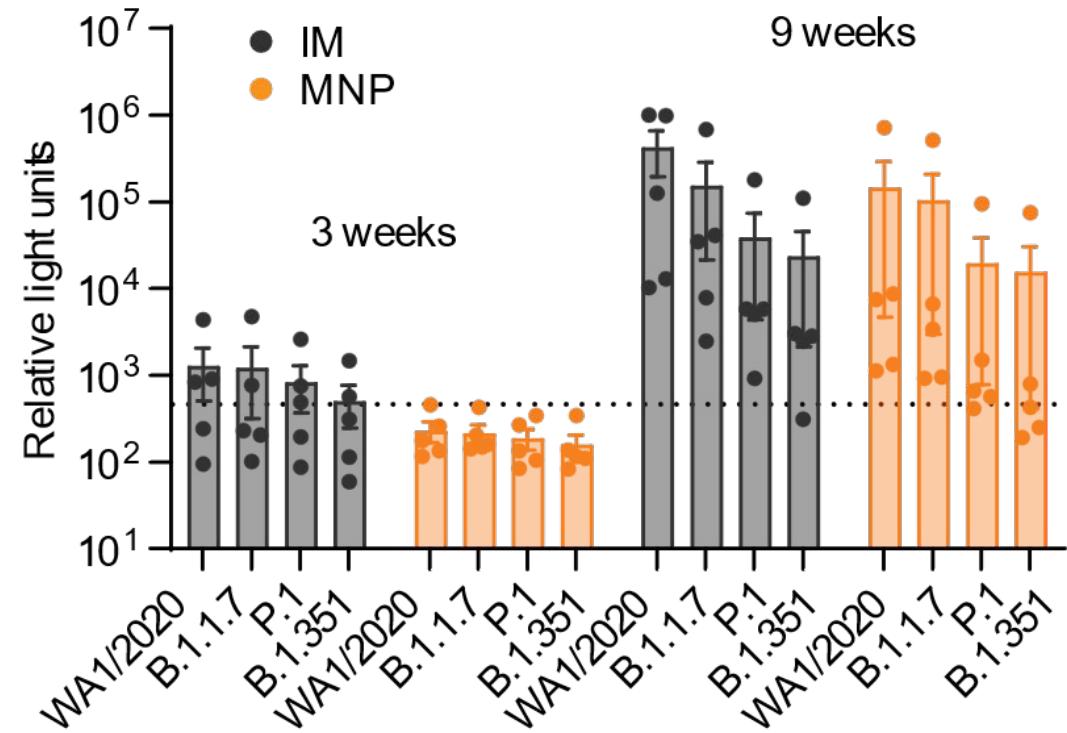
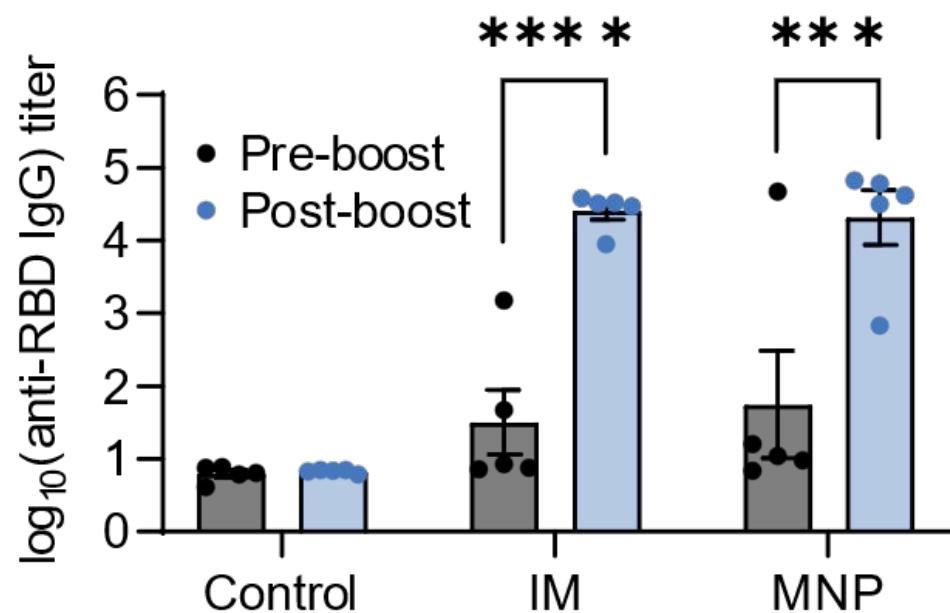


Protein expression confirmed stability of MNPs for 6 months (stored at 4°C and RT)



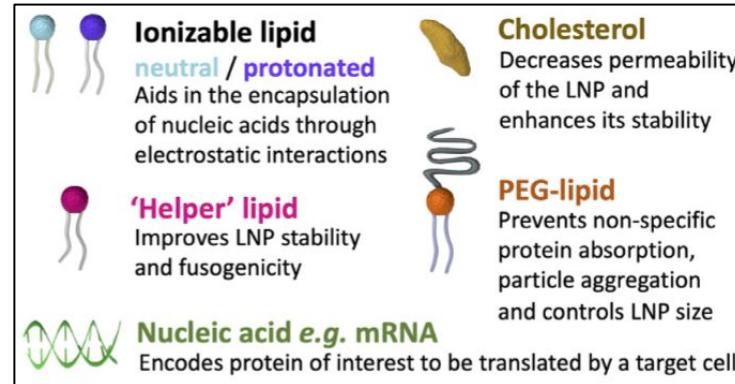
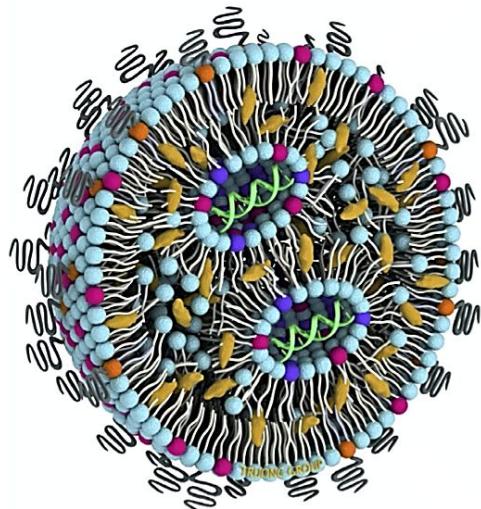
Straeten et al., *Nat Biotechnol*, 2023

anti-RBD IgG production demonstrated successful vaccination against SARS-CoV-2 using mRNA-LNP MNPs



Straeten et al., *Nat Biotechnol*, 2023

Composition of mRNA-LNPs



	Ionizable lipid	Phospholipid	Cholesterol	PEGylated lipids	Ratio
Moderna	SM-102	DSPC	Cholesterol	PEG2000-DMG	50:10:38.5:1.5
Pfizer	ALC-0315	DSPC	Cholesterol	ALC-0159	46.3:9.4:42.7:1.6
Jaklenec Group	Lipid 5	DOPE	Cholesterol	14:0 PEG2000 PE	50:10:38.5:1.5

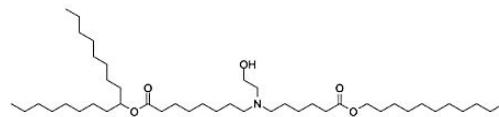
Pilkington *et al.*, *Acta Biomaterialia*, 2021



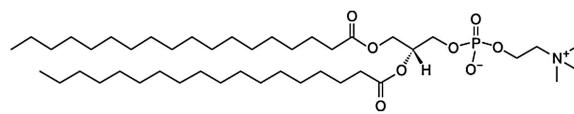
Chemical structure of lipids used in mRNA-LNPs

Moderna

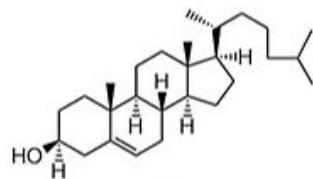
SM-102



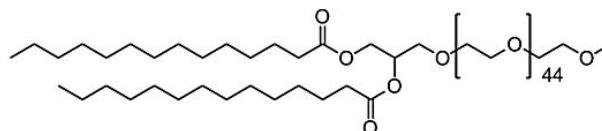
DSPC



Cholesterol

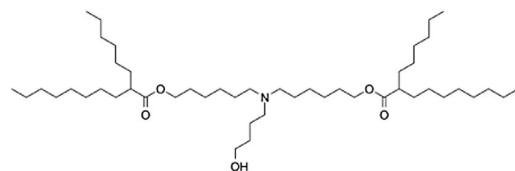


PEG2000-DMG

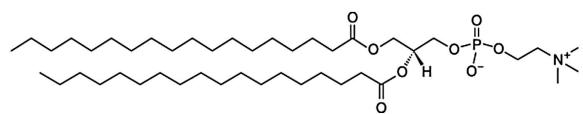


Pfizer

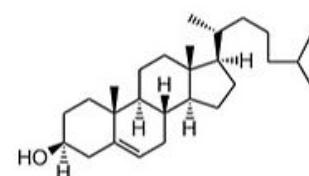
ALC-0315



DSPC



Cholesterol

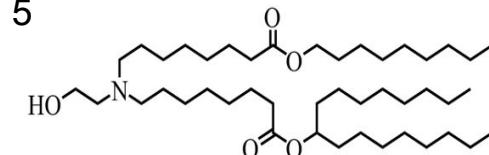


ALC-0159

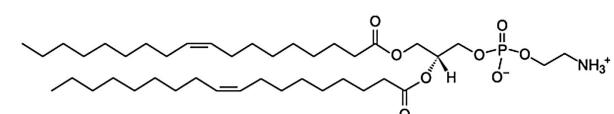


Jaklenec Group

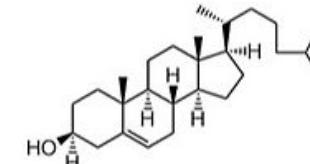
Lipid 5



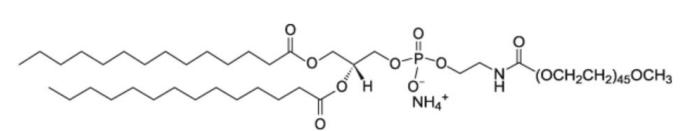
DOPE



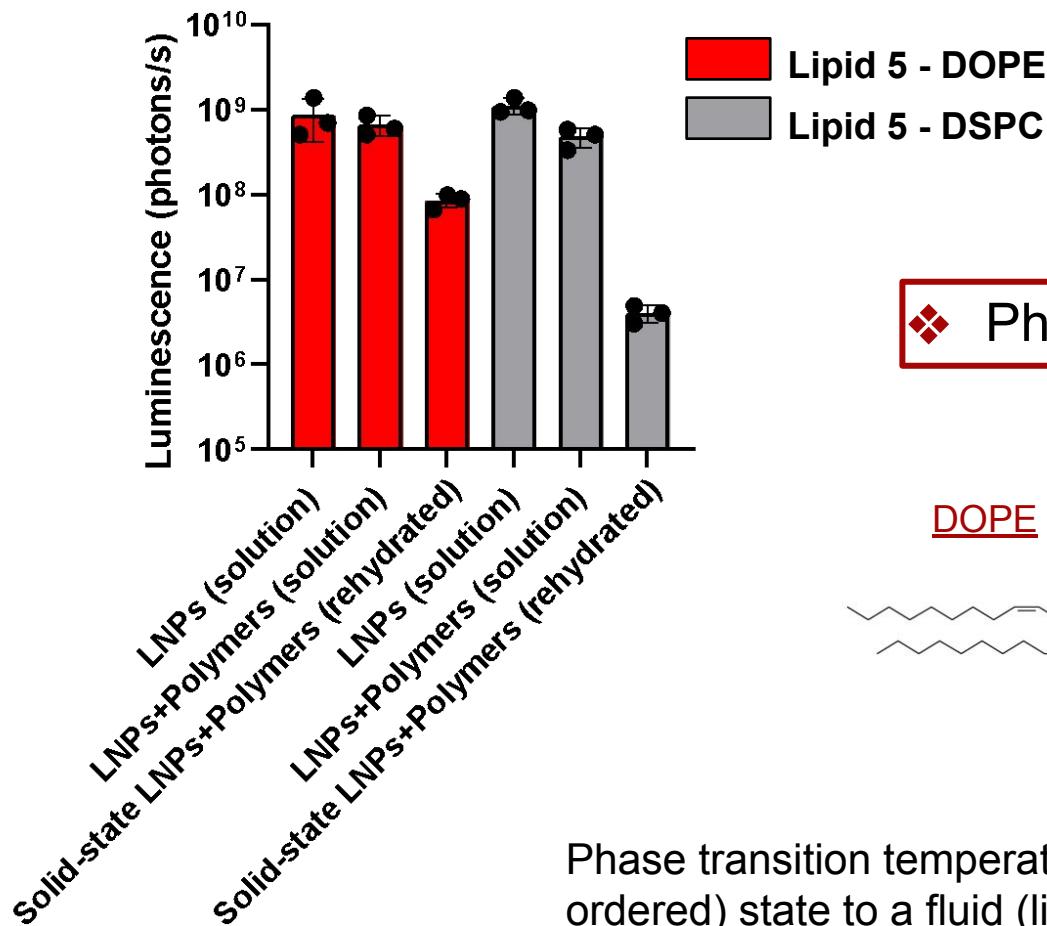
Cholesterol



14:0 PEG2000 PE

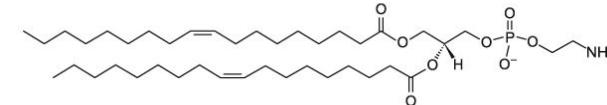


In vivo luminescence data suggests that lipid composition can affect bioactivity of mRNA-LNPs

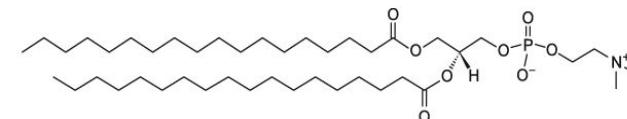


❖ Phase transition temperature of DOPE vs DSPC

DOPE $T_m: -16 \text{ }^\circ\text{C}$



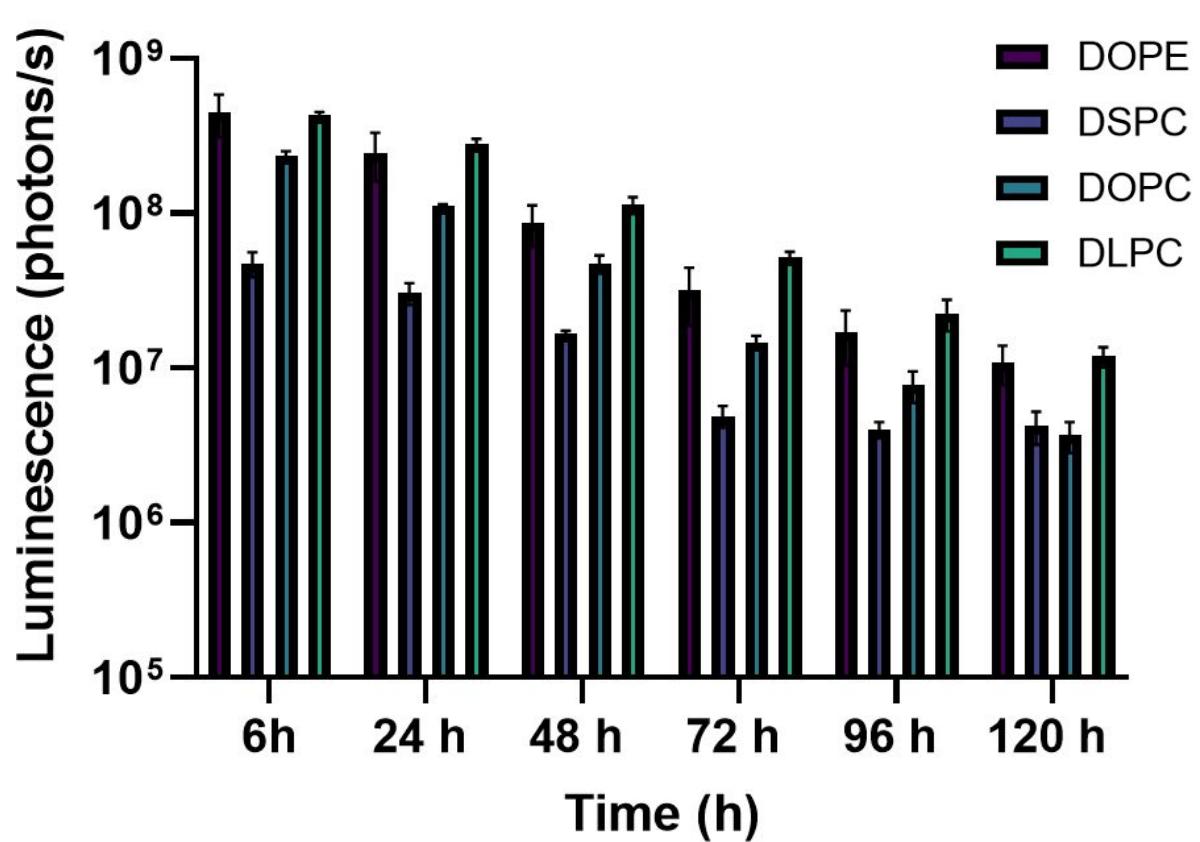
DSPC $T_m: 55 \text{ }^\circ\text{C}$



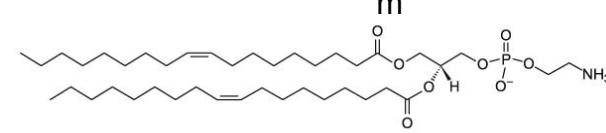
Phase transition temperature: Temperature at which the lipids converts from the gel (solid ordered) state to a fluid (liquid disordered) state.



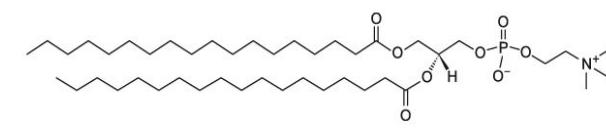
Luminescence signal in MNPs depends on the lipid composition



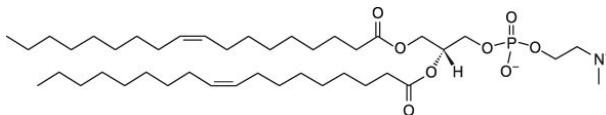
DOPE (18:1) $T_m: -16 \text{ }^\circ\text{C}$



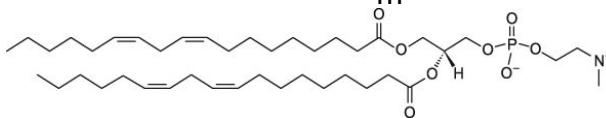
DSPC (18:0) $T_m: 55 \text{ }^\circ\text{C}$



DOPC (18:1) $T_m: -17 \text{ }^\circ\text{C}$



DLPC (18:2) $T_m: -57 \text{ }^\circ\text{C}$



Conclusion

- Fabrication of mRNA-LNPs in MNPs with retention of mRNA integrity and LNP structure
- Characterization of mRNA-LNPs using TEM, Cryo-TEM, and capillary gel electrophoresis
- Protein expression and antibody production after MNP immunization
- Dependency of protein expression on lipid composition



Acknowledgments

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