

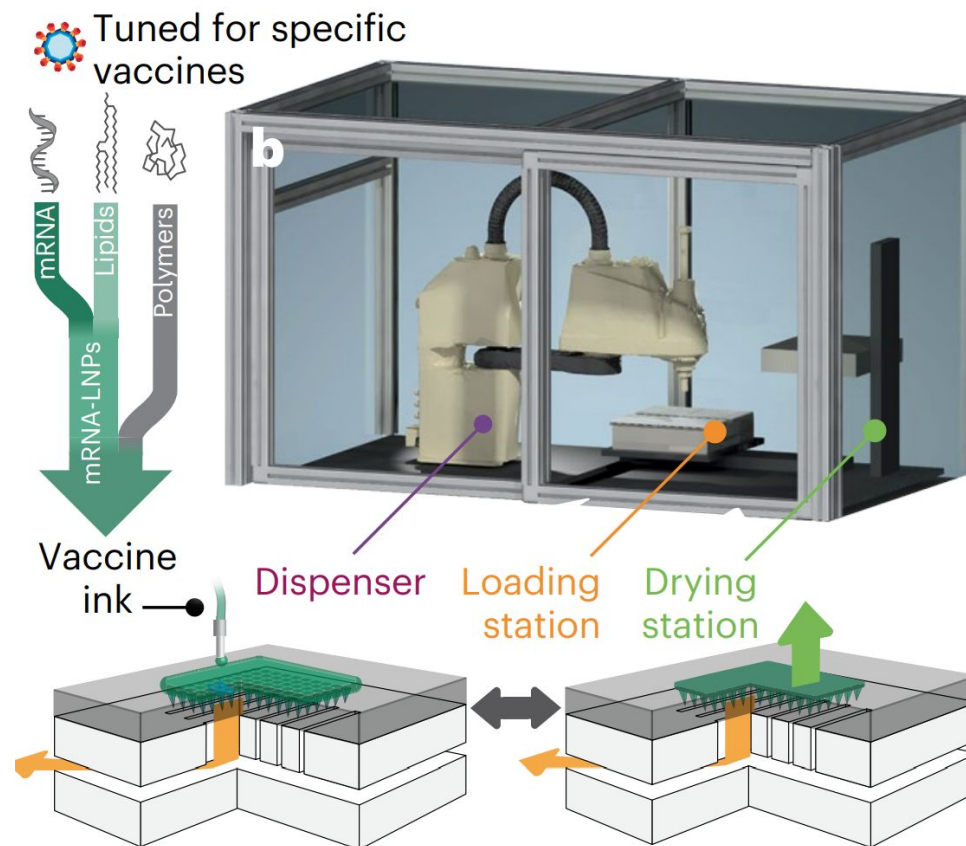
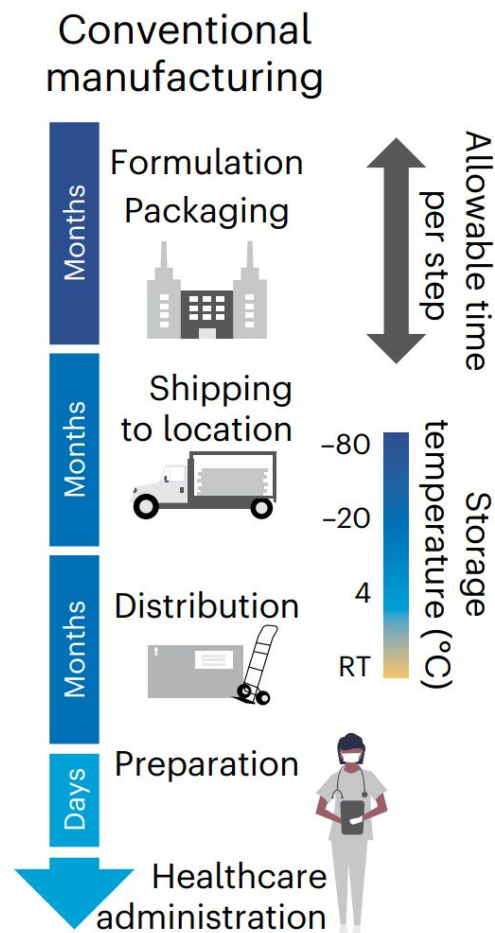
# Delivery Technologies for Diversified Products

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

Behnaz Eshaghi, Ph.D.



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

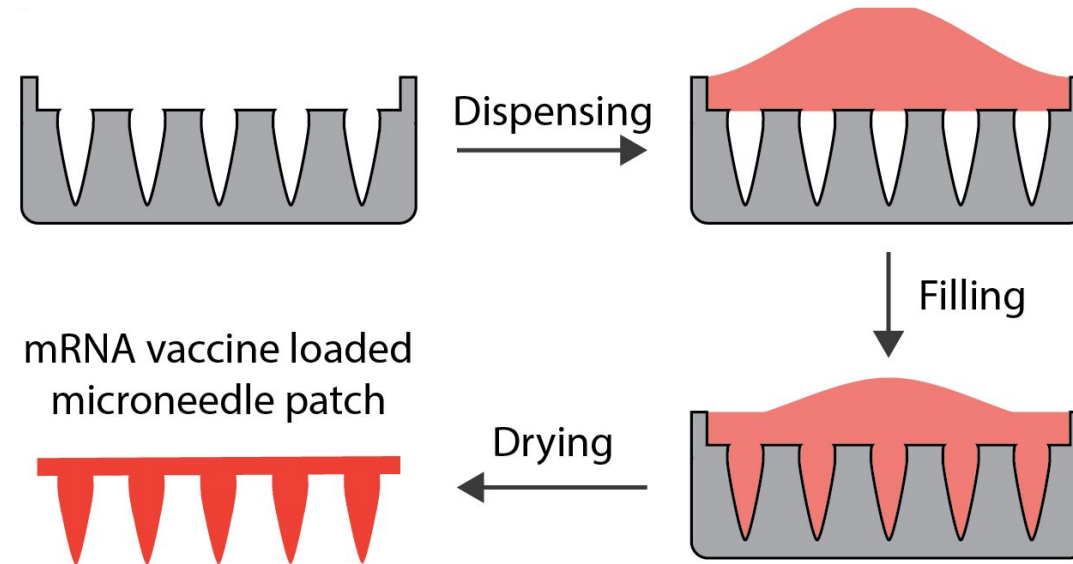
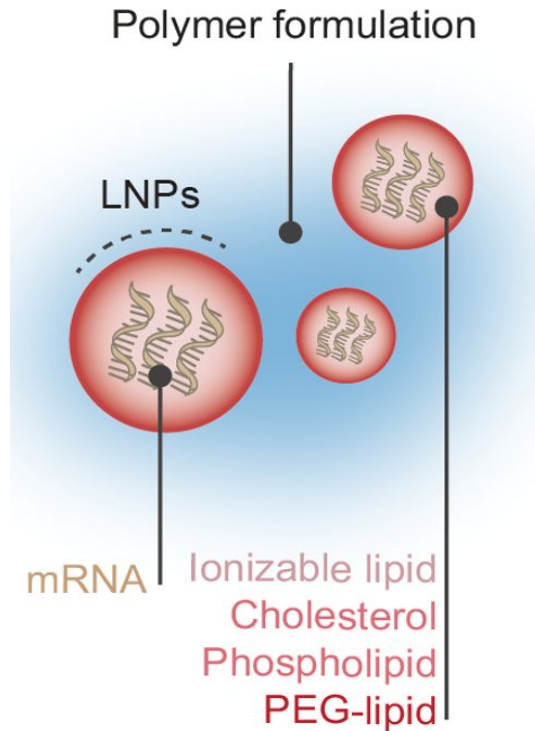


Straeten et al., Nat Biotechnol, 2023



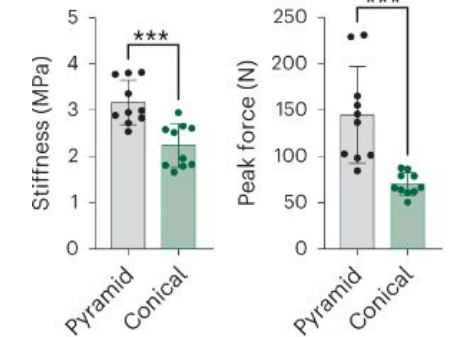
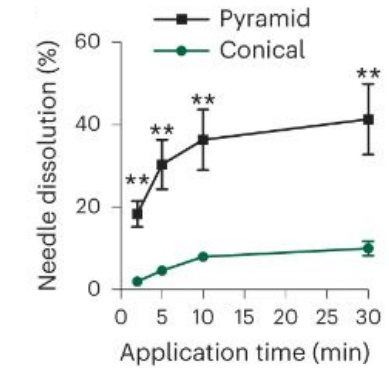
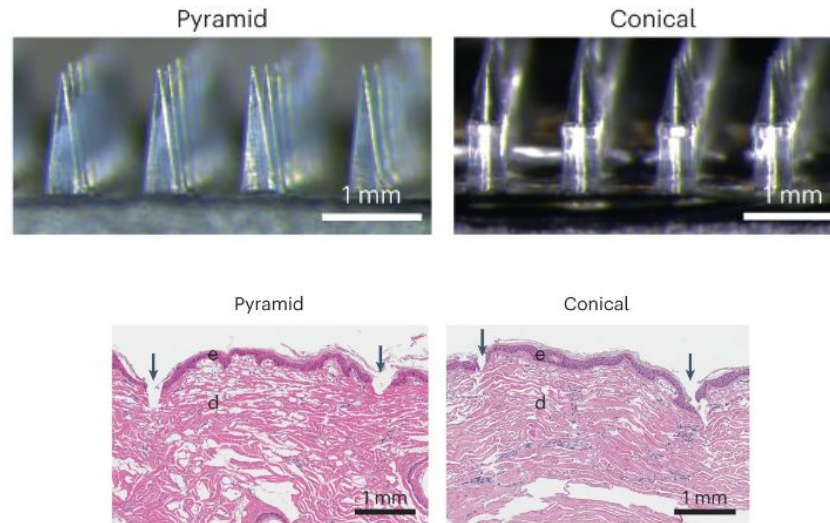
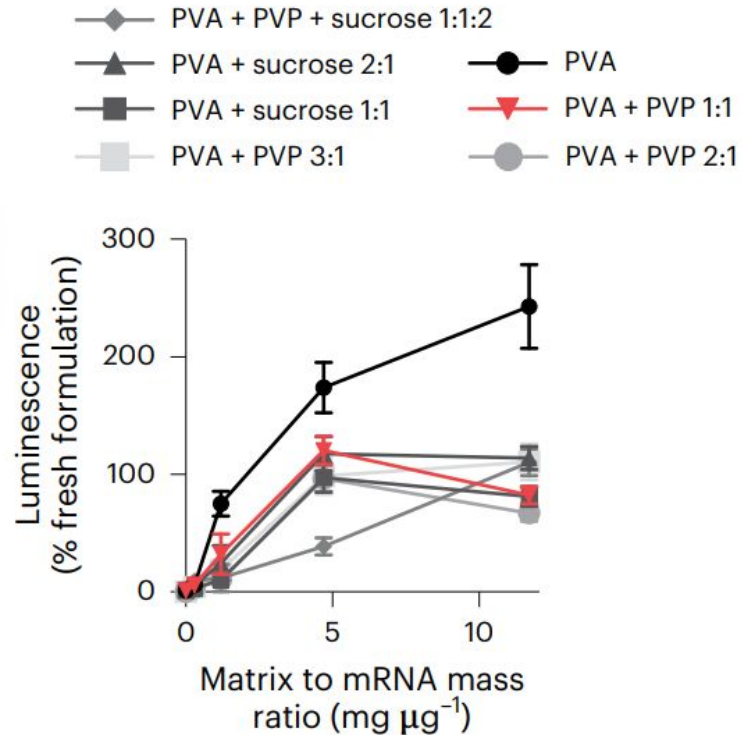
# Fabrication of mRNA-LNP-loaded MNPs

LNPs + PVA/PVP (Ink)



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

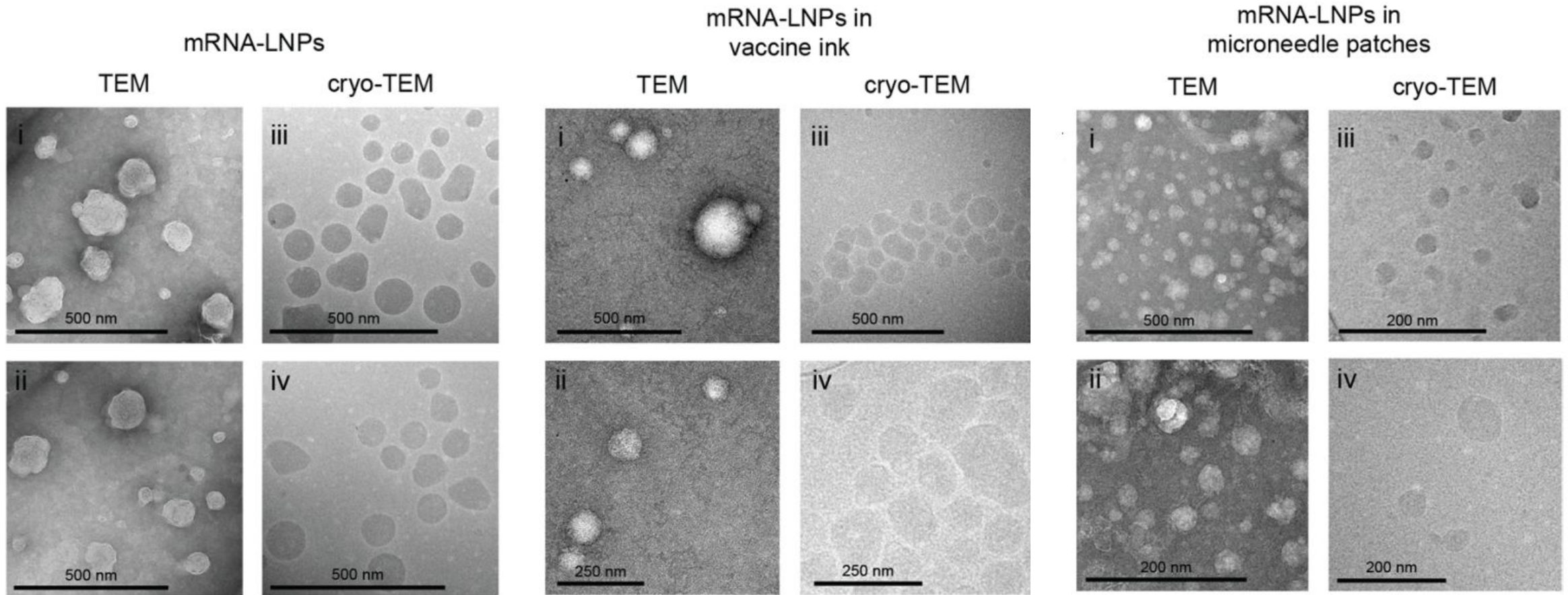
# Ink composition and needle geometry were optimized for mRNA-LNP bioactivity and MAP application



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



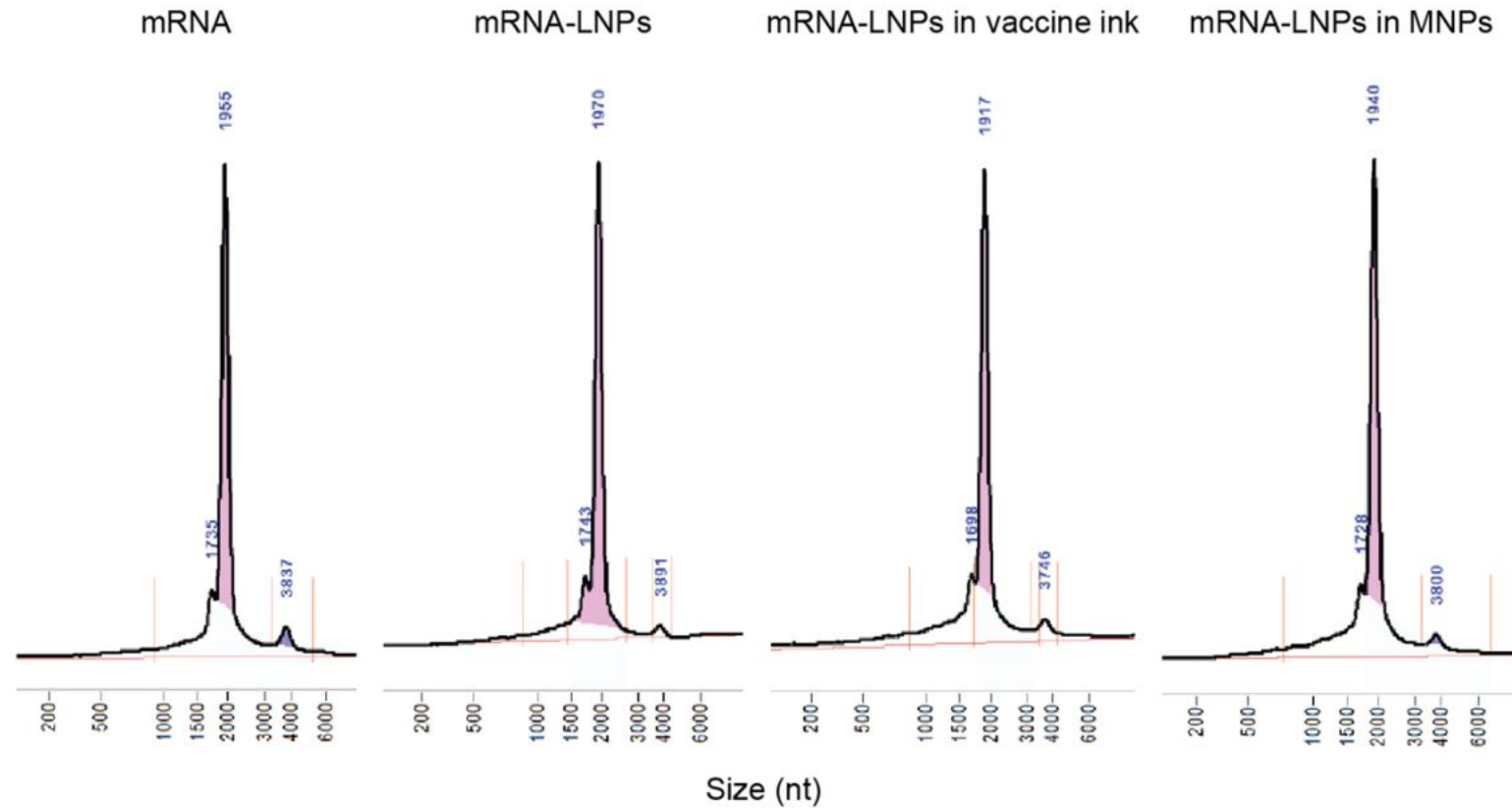
# TEM and Cryo-TEM results demonstrated intact mRNA-LNP structure in MNPs



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



# Capillary gel electrophoresis analysis confirmed the integrity of mRNA in MNPs

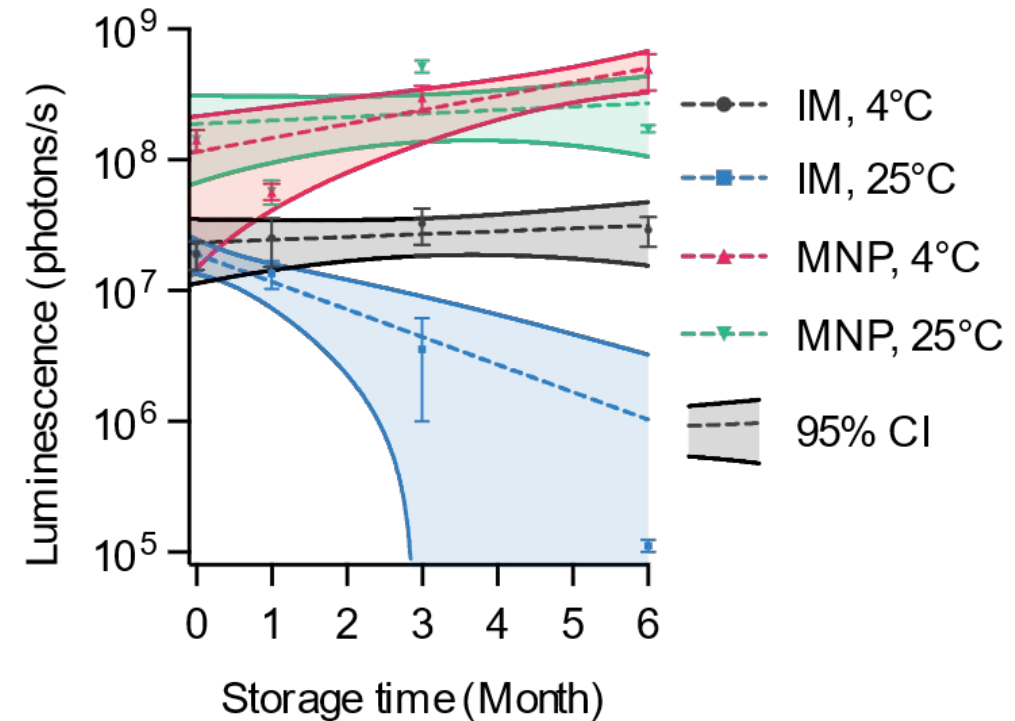
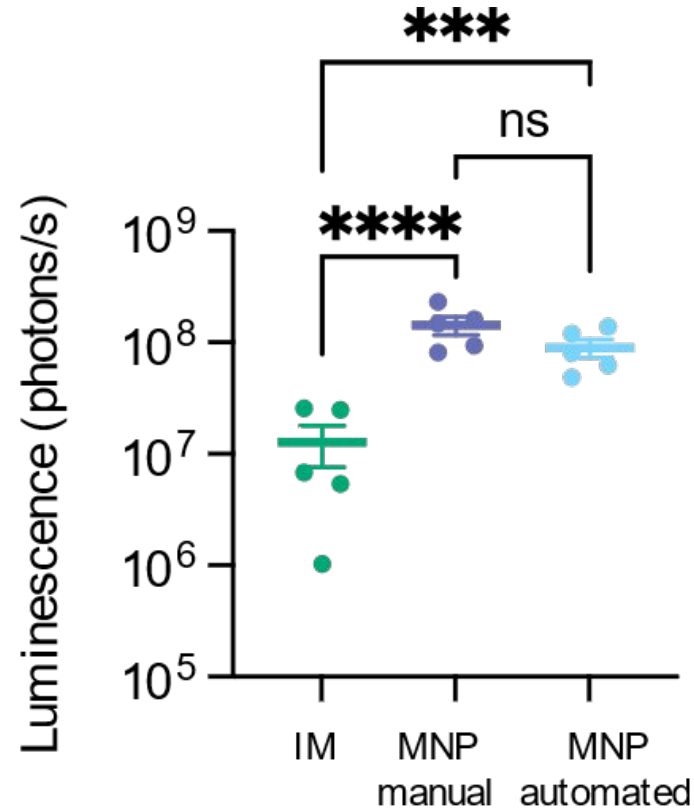


Straeten *et al.*, *Nat Biotechnol*, 2023



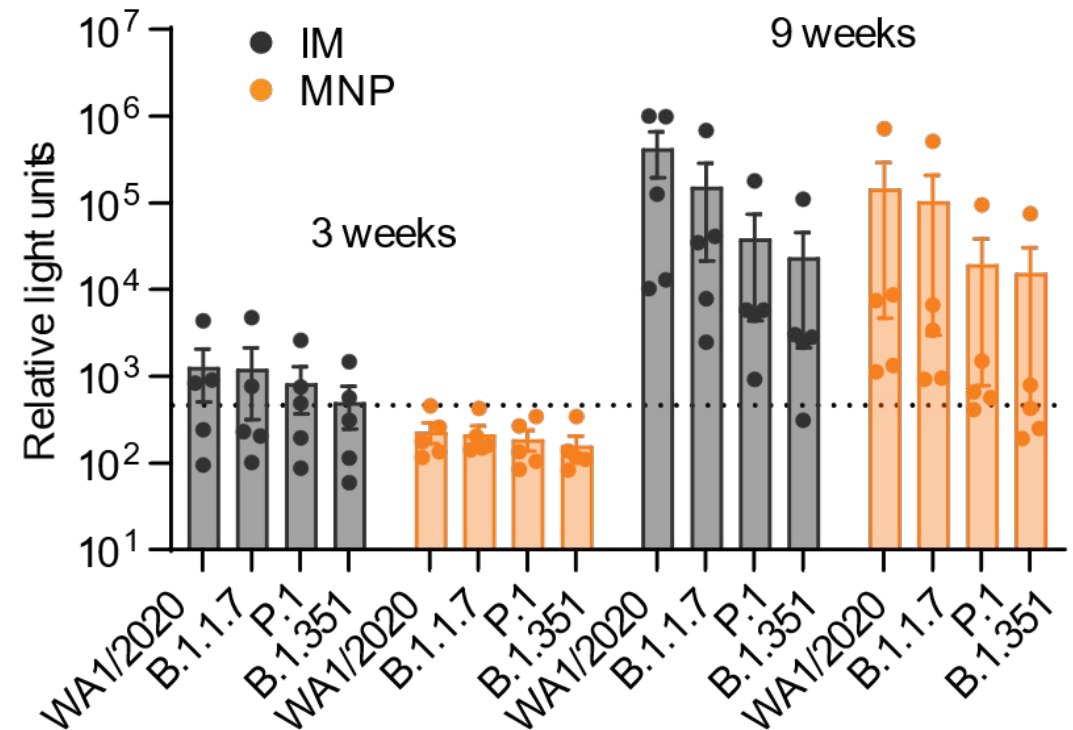
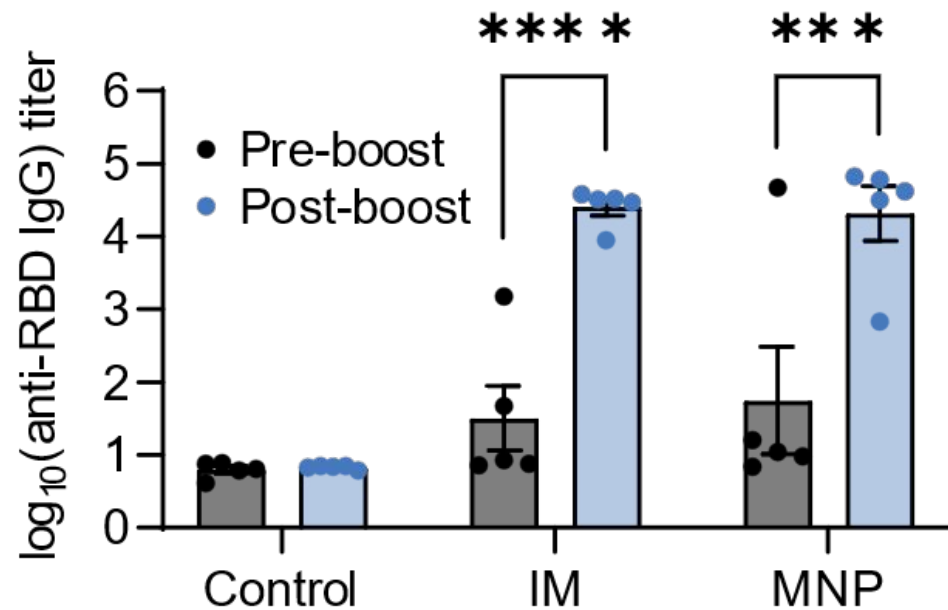


# Protein expression confirmed stability of MNPs for 6 months (stored at 4°C and RT)



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

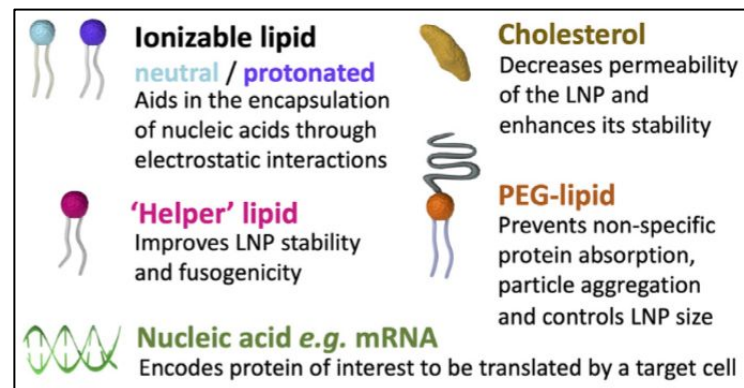
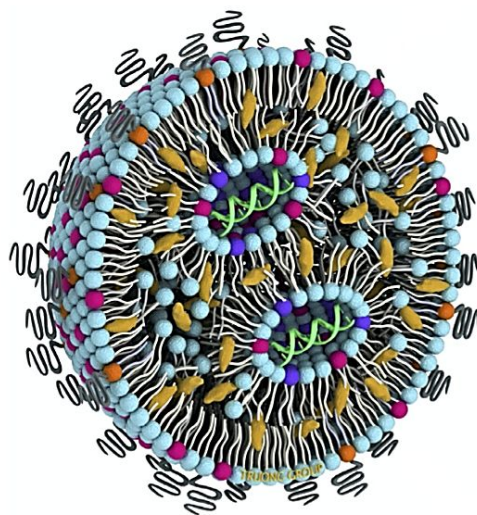
# anti-RBD IgG production demonstrated successful vaccination against SARS-CoV-2 using mRNA-LNP MNPs



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

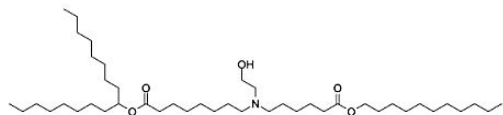
Pilkington *et al.*, *Acta Biomaterialia*, 2021



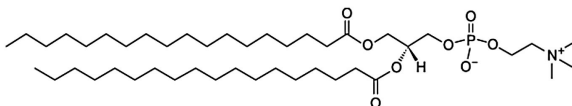
# Chemical structure of lipids used in mRNA-LNPs

# Moderna

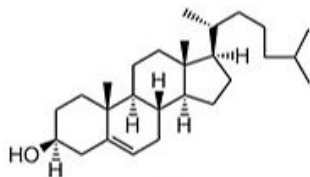
SM-102



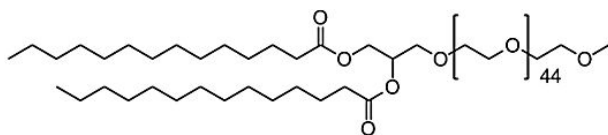
DSPC



## Cholesterol

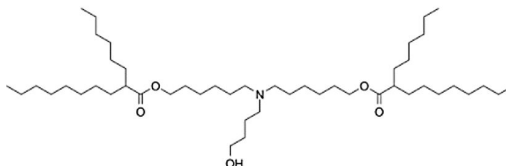


# PEG2000-DMG

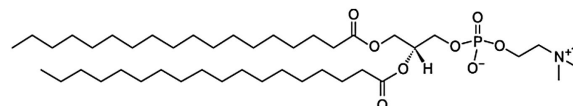


**Pfizer**

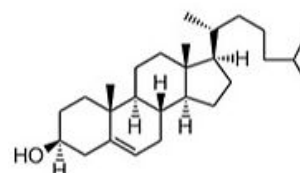
ALC-0315



DSPC



## Cholesterol

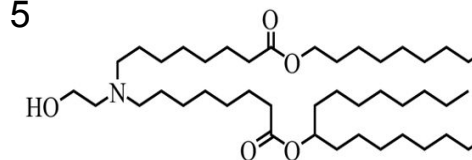


ALC-0159

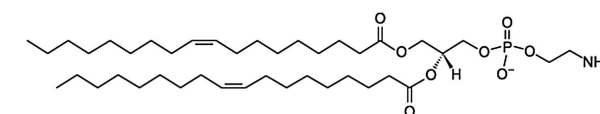


## Jaklenec Group

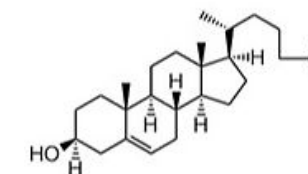
Lipid 5



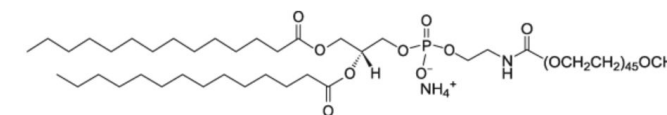
DOPE



## Cholesterol

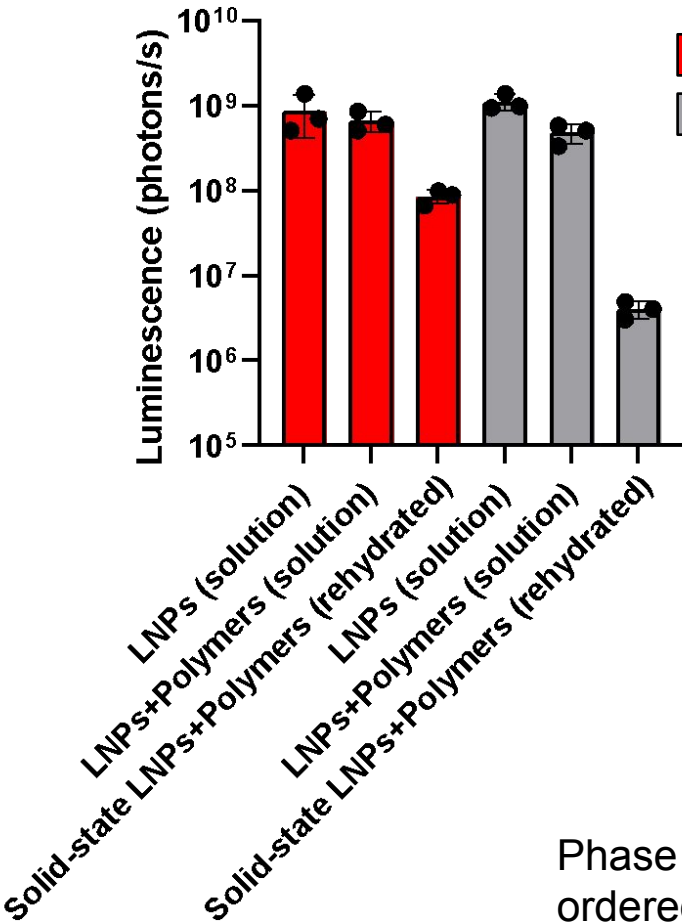


14:0 PEG2000 PE

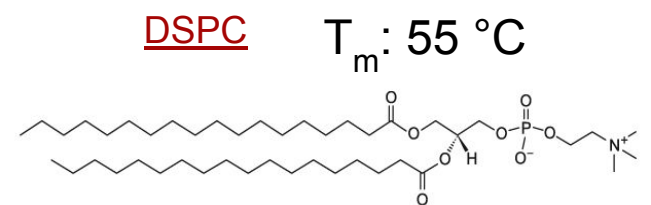
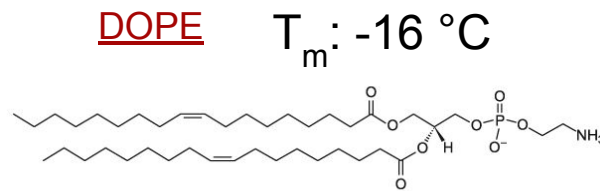




***In vivo* luminescence data suggests that lipid composition can affect bioactivity of mRNA-LNPs**

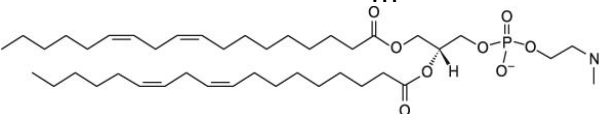
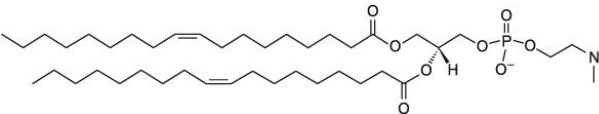
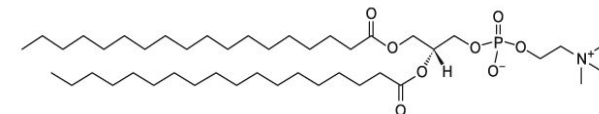
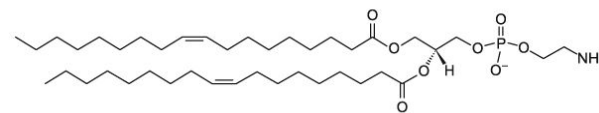
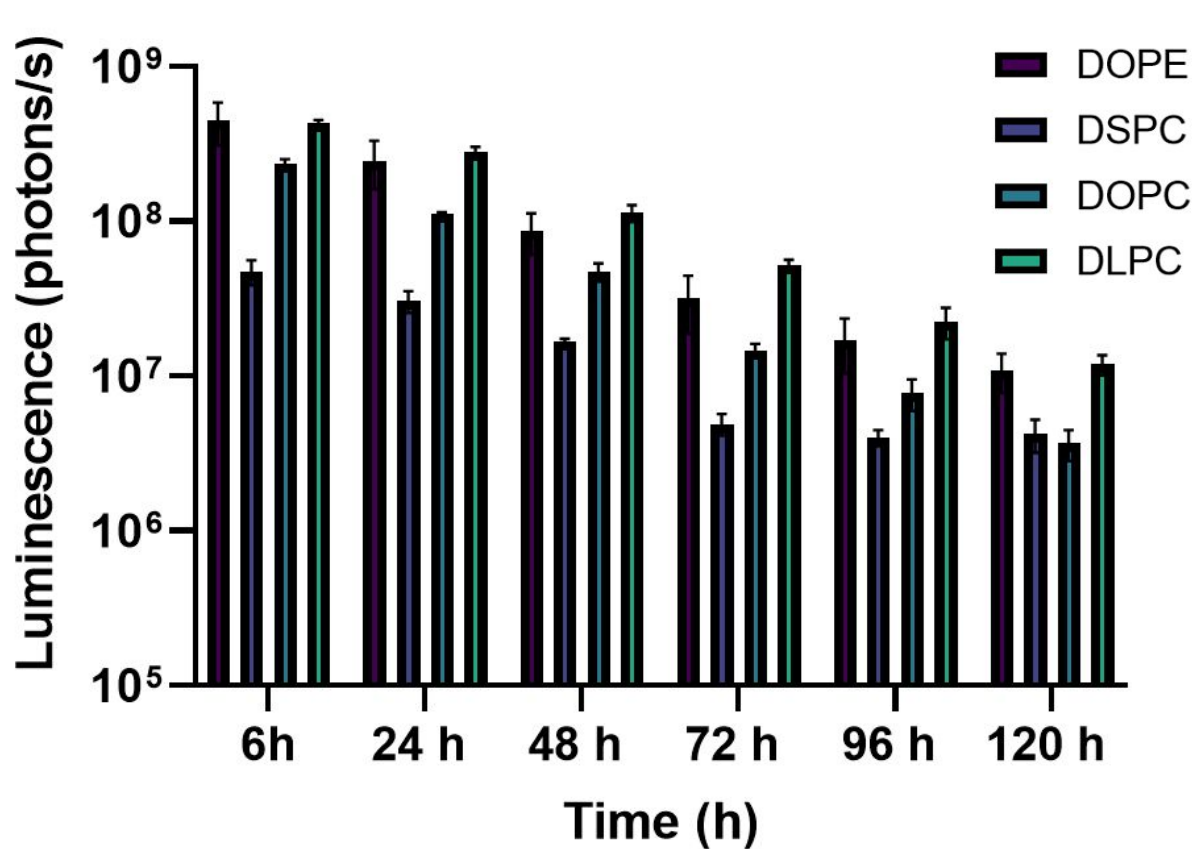


## Phase transition temperature of DOPE vs DSPC



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





# 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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- Tim Forster
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- Robert Langer
- Ana Jaklenec



**The Jaklenec Group**

Engineering delivery systems for global health



**Langer Lab**

MIT Department of Chemical Engineering

**Barouch Lab**

**Virology and Vaccine Research**

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