# Electron Microscopy Analysis of Lipid Nanoparticles: Effect of Lipid Components on Morphology


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## Background

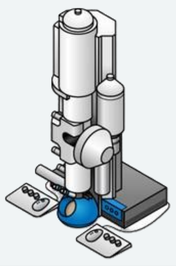
**Lipid nanoparticles** (LNP) as the leading gene delivery platform

Design remains largely **empirical** – based on transfection efficiency

Morphology is a critical factor influencing transfection efficiency[1]

But the effect of lipid components on LNP structure remains unclear.

## This study – TEM analysis



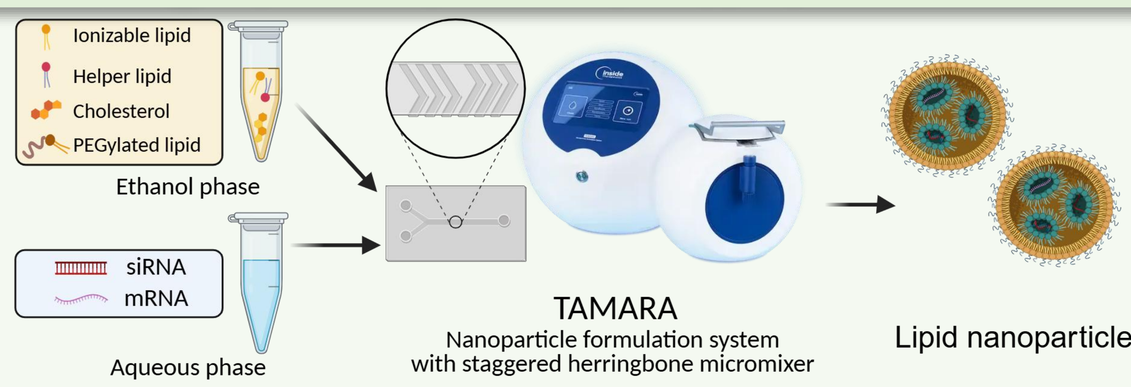
**LNP Formulation parameters**

1. PEGylated lipid
2. Ionizable lipid
3. RNA cargo

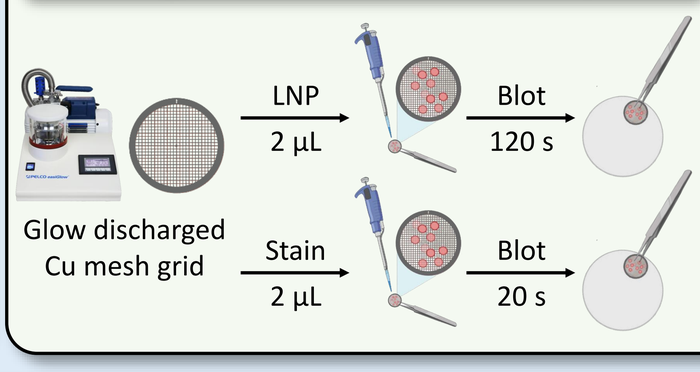
**Aim**: Provide basis for rational LNP design based on morphology

## Method

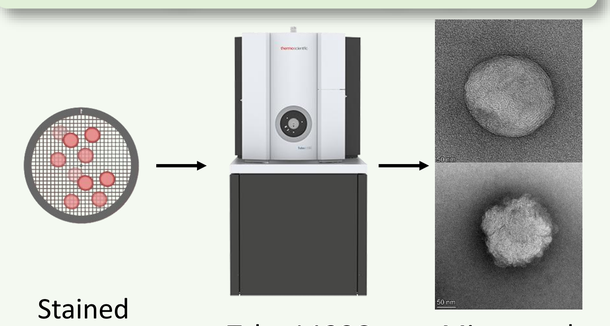
### ① Lipid nanoparticles (LNP) preparation



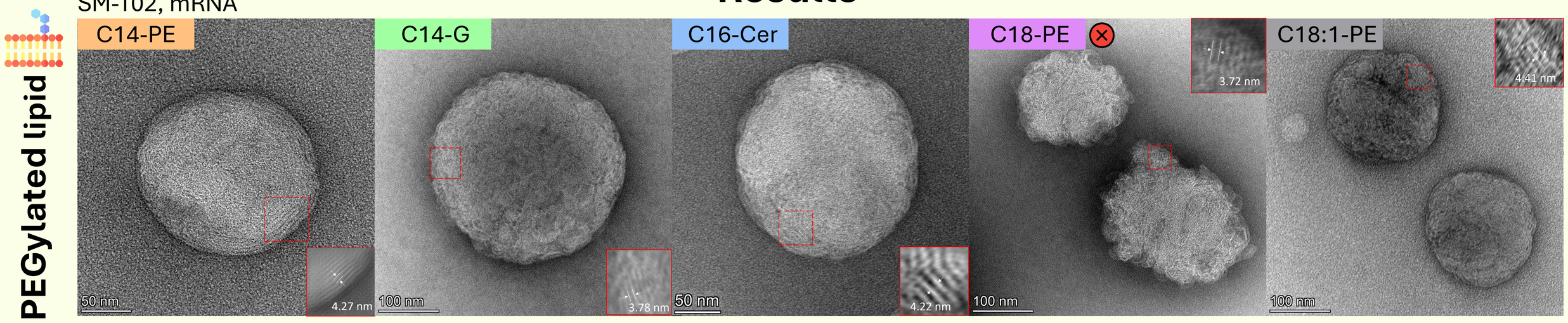

### ② Sampling & staining

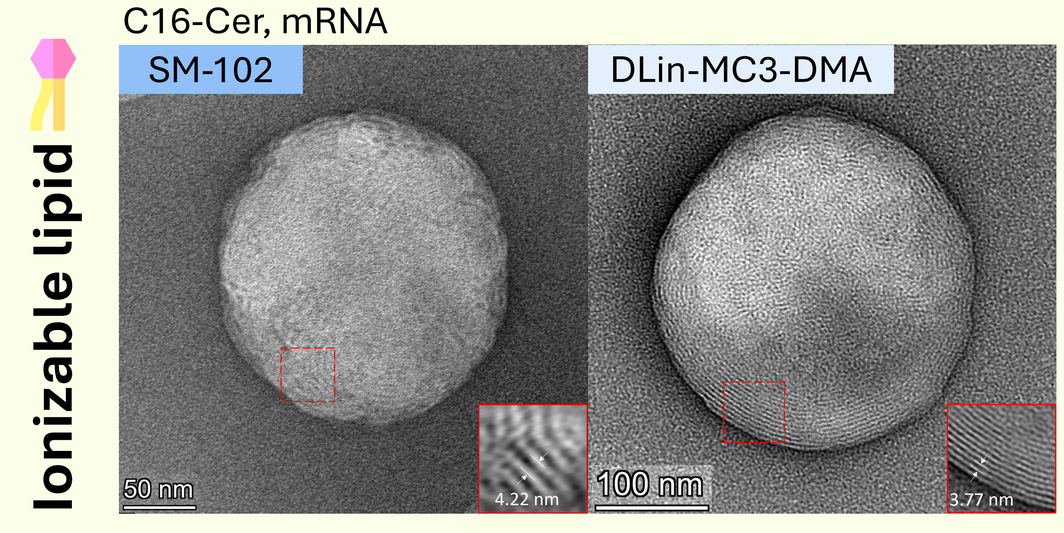


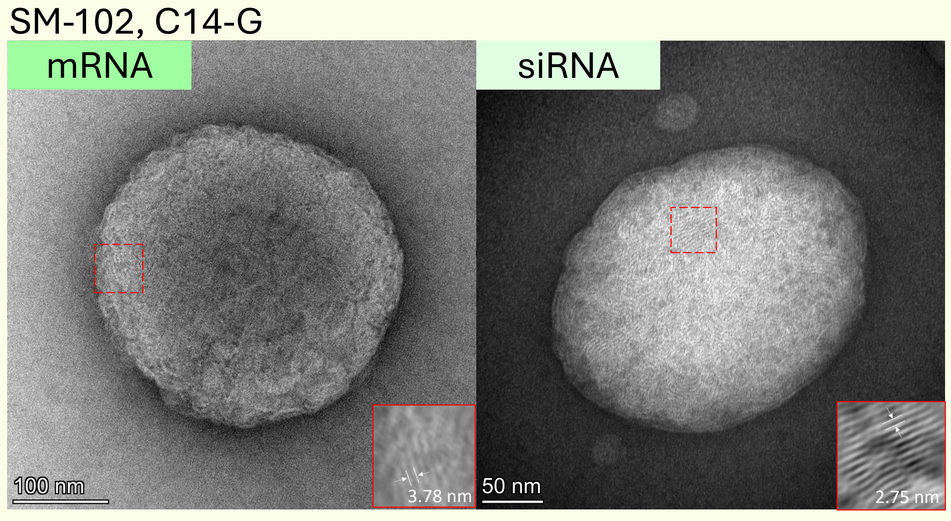

### ③ TEM Imaging



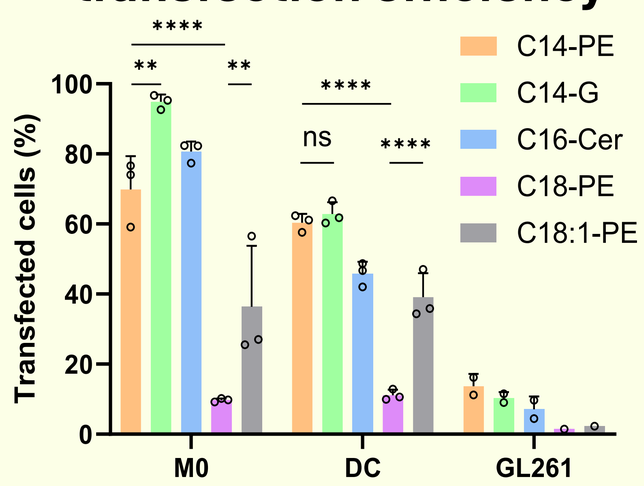

## Results




### Effect of PEGylated lipid on transfection efficiency




- Rounded LNP → High transfection
- Angular (C18-PE) → least effective

**PEGylated lipid**
Major influenced on lamellarity, membrane curvature and transfection efficiency

**Ionizable lipid**
Greatly affected lamellarity and the core structure

**RNA cargo**
Governed the packaging of the lipids and the internal structure

## Key takeaways

- Formulation parameters control LNP morphology.
- Rounded LNPs (multilamellar or amorphous) outperformed angular LNP, despite internal nanostructure differences.
- Further study needed to establish cause-and-effect relationship.

## References


1 Patel, S., Ashwanikumar, N., Robinson, E. et al. *Nat Commun*, **11**, 983 (2020)


## Acknowledgement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