

PEGylated lipid screening, composition optimization, and structure–activity relationship determination for lipid nanoparticle-mediated mRNA delivery

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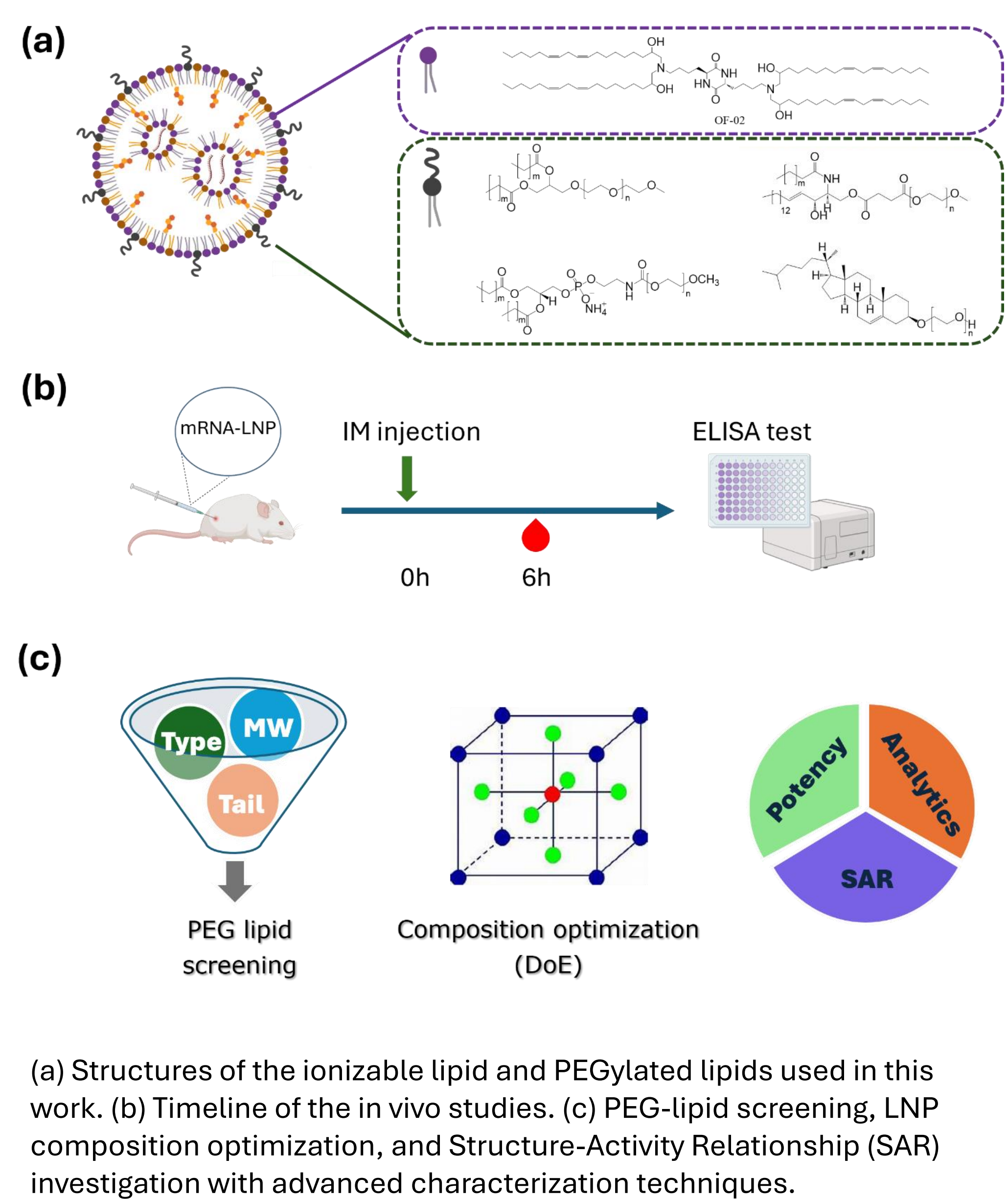
INTRODUCTION

Lipid nanoparticles (LNPs) have emerged as effective carriers for mRNA delivery in vaccine and therapeutic applications. This study systematically screened PEGylated lipids for intramuscular mRNA delivery, optimized formulation composition, and investigated structure-activity relationships to improve delivery efficacy and elucidate mechanisms driving differences in protein expression.

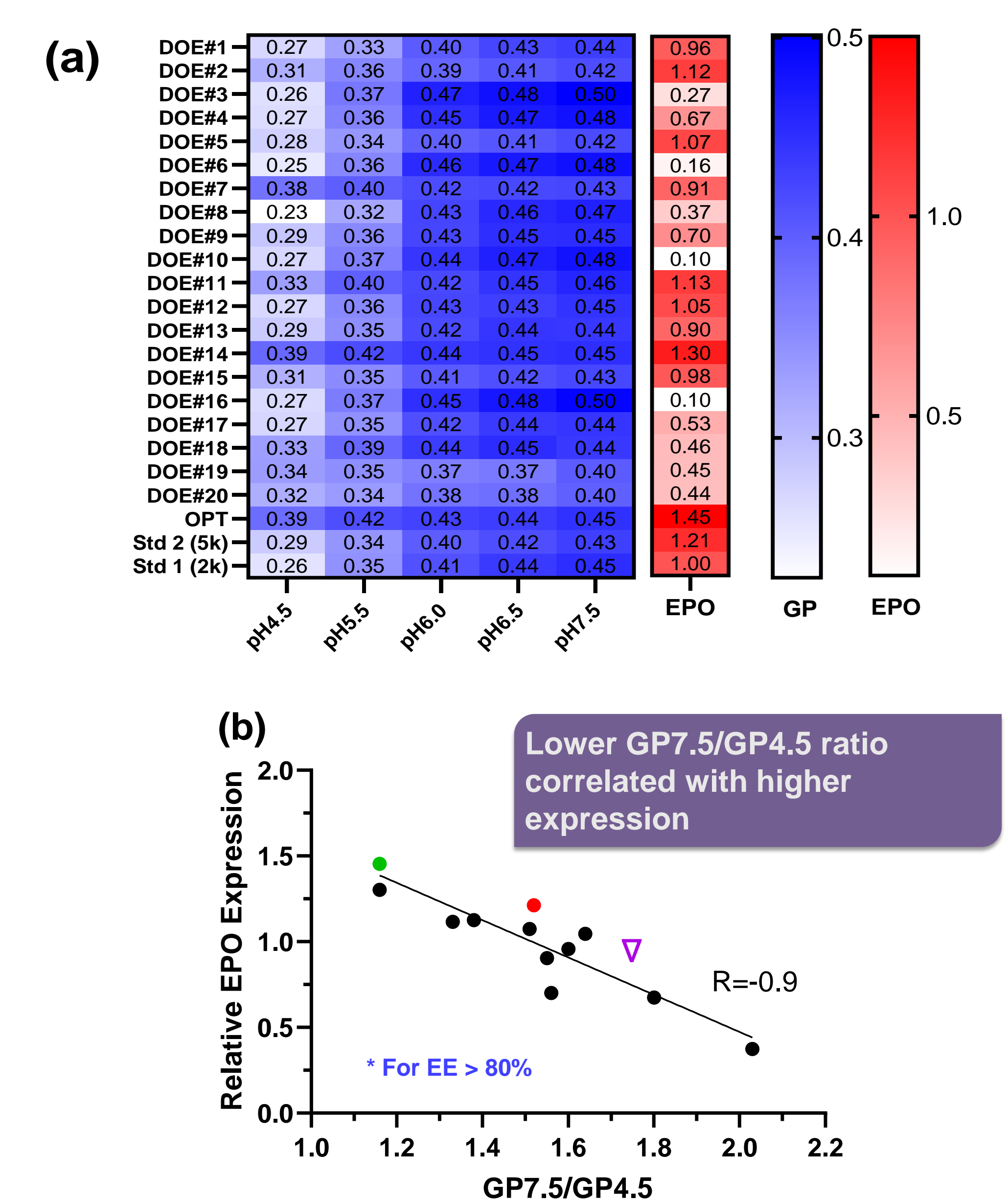
OBJECTIVE

–To identify key factors influencing transfection efficiency and provide guidelines for designing more effective next-generation LNPs for mRNA-based vaccines and therapeutics.

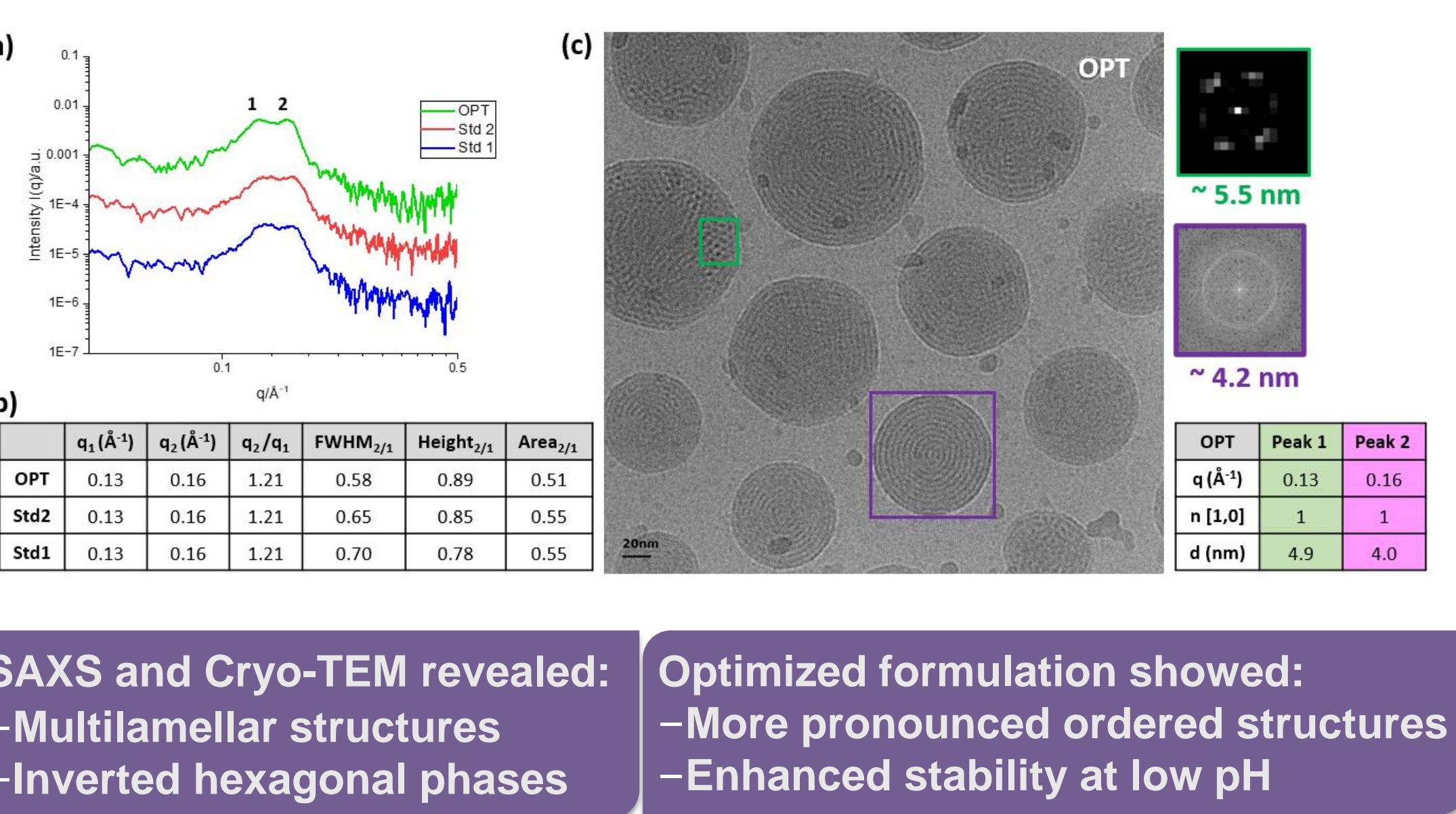
METHODS



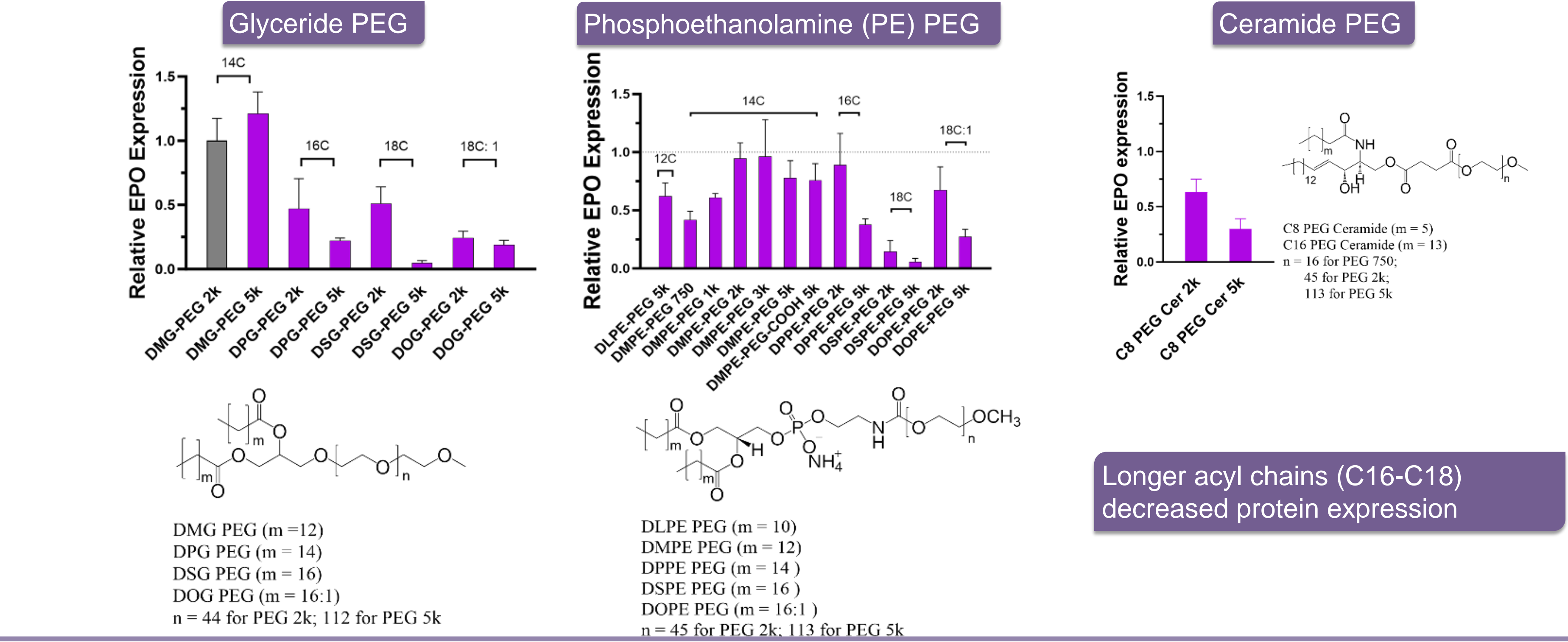
RESULTS: Figure 3, Lipid Packing



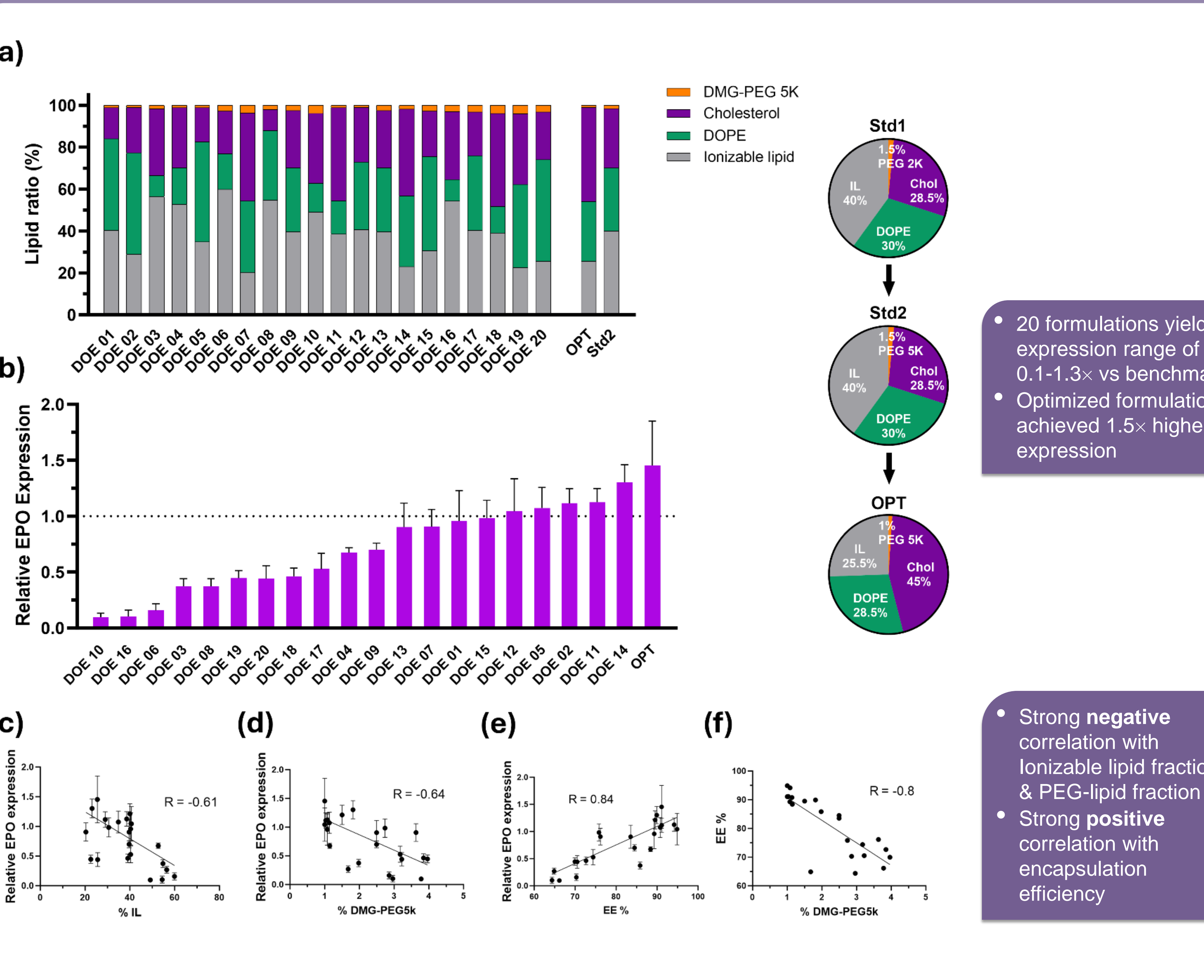
RESULTS: Figure 4, Internal Structure



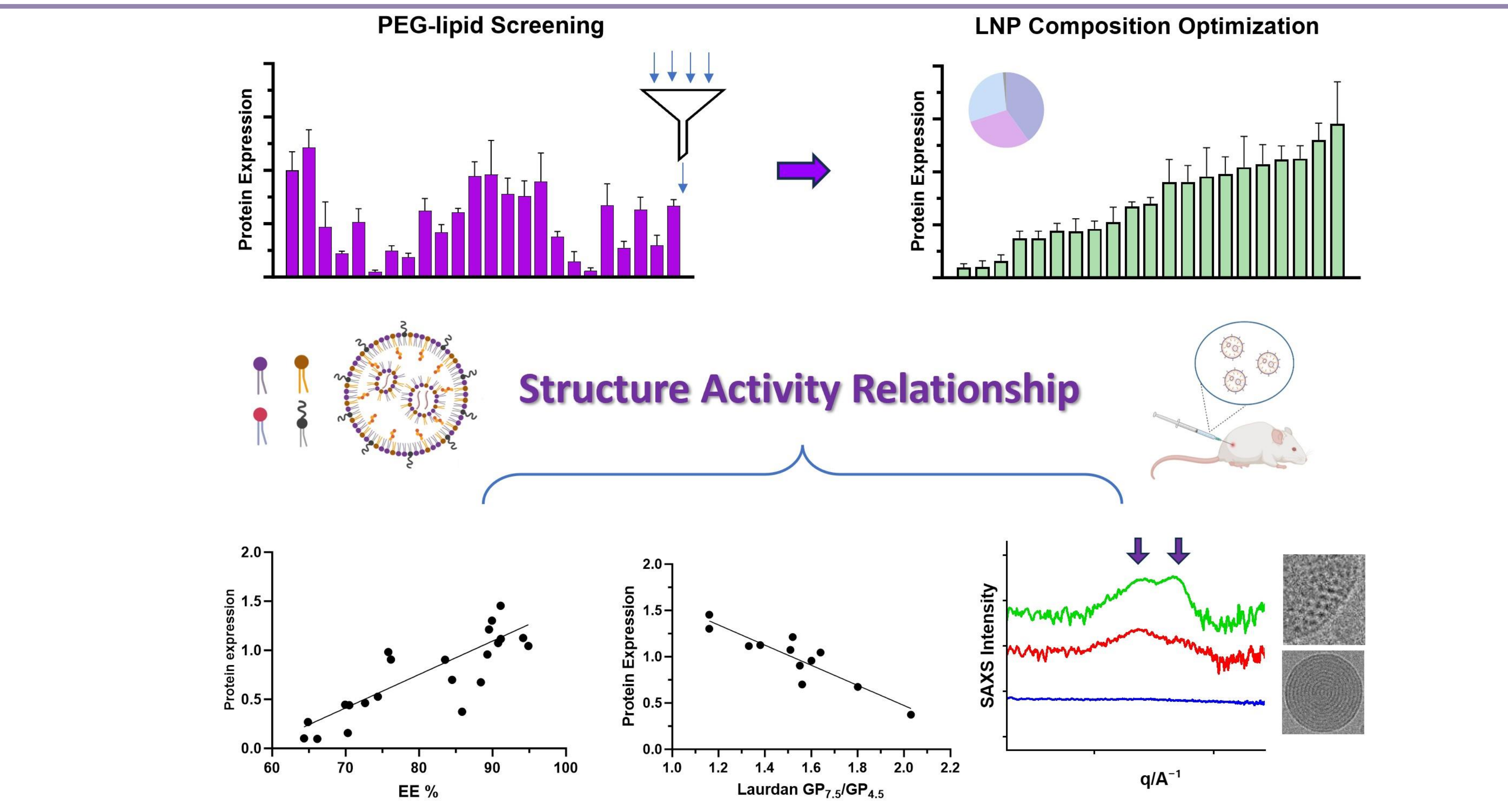
RESULTS: Figure 1, PEG-Lipid Screening (hEPO expression)



RESULTS: Figure 2, DOE Optimization



CONCLUSIONS

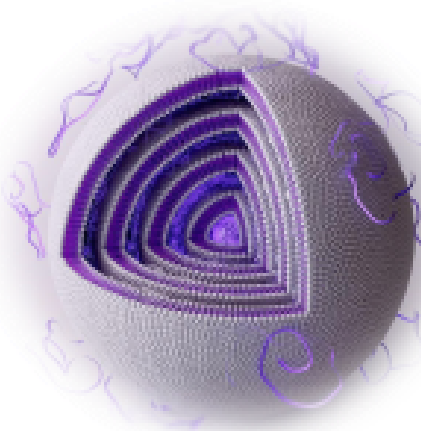


REFERENCES & FUNDING

REFERENCES
Liu, L., et al. (2025). "PEGylated lipid screening, composition optimization, and structure–activity relationship determination for lipid nanoparticle-mediated mRNA delivery." *Nanoscale* 17(18): 11329-11344.

FUNDING
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- Identified DMG-PEG5k as optimal PEGylated lipid for mRNA delivery
- Key factors for enhanced transfection:
 - ✓ High mRNA encapsulation (>90%)
 - ✓ Strong membrane integrity at low Ph
 - ✓ Ordered internal structures
- Balanced lipid ratios critical for LNP performance
- Findings provide framework for rational design of next-generation mRNA-LNPs



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