Understanding the role of structure and lipid composition in lipid nanocarriers using bulk and single particle analysis

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Lipid nanocarriers are versatile structures with tunable physicochemical properties that are ideally suited for therapeutic applications. A key barrier to rational design is the inability to relate composition and structure to intracellular processing and function. During cellular processing, phospholipases, specific lipid-modifying enzymes, can alter the composition and structure of phospholipids contained within lipid nanocarriers. The phospholipase D (PLD) family are found in the endosomal pathway and are dysregulated in breast cancer. PLD cleaves phosphocholine headgroups releasing choline and generating anionic lipids within the lipid bilayer.

We have combined Single Particle Automated Raman Trapping Analysis (SPARTA®) with small angle scattering (SAXS / SANS) and fluorescence techniques for multiscale characterization of lipid nanocarriers. This enables us to determine the phase and internal structure of the nanoparticles and couple this to dynamic measurements of lipid composition to study their interaction with PLD.

Our analysis demonstrates that PLD, a key intracellular trafficking mediator, can access the entire lipid membrane in structured lipid nanoparticles (LNP) to generate stable, anionic LNPs. PLD activity on vesicles with matched amounts of enzyme substrate was an order of magnitude lower, indicating that the lipid membrane structure can be used to control enzyme interactions.

References

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