

Scalable Synthesis of Phospholipids for Stable, Tunable Drug Delivery Vesicles and Surface Coating

Stanford chemists have developed a scalable synthetic process to create a new class of viscous, stable phospholipid bilayer vesicles with tunable properties. Specifically, this is the first synthetic method to create pure ladderanes (lipids produced in nature by anammox bacteria) and can be adapted to generate either naturally-occurring molecules, their intermediates, or novel lipids with unique, tunable properties. The resulting ladderanes self-assemble into vesicles, which is particularly useful for capturing cargo such as drugs or imaging agents. Because of their viscosity, low compressibility, and slow diffusion, ladderane-based drug delivery vehicles are likely to be relatively impermeable and more stable than traditional liposomes. They could be used to target molecules to a therapeutic site, to perform basic research of biological systems, or to create nanofabricated coatings.

Stage of Research

The inventors have used the synthetic process to create prototypical self-assembled, fluid, viscous, bilayer ladderane vesicles and characterized the vesicle properties. They found that ladderane vesicles have low compressibility and exceptionally slow diffusion compared with common straight-chain lipids.

Professor Noah Burns gives an overview of the technology.

Applications

- **Drug delivery** - create lipid vesicles to deliver molecules for therapeutics and imaging

- **Biological research** - create vesicles for selective delivery of molecules to cells for basic scientific studies
- **Nanofabrication and coating** such as surface passivation

Advantages

- **Stable** - ladderane vesicles demonstrate reduced compressibility
- **Dense and highly viscous** - likely to minimize leakage of vesicle contents and increase circulation half-life
- **Tunable** - enables synthesis of novel molecules to optimize properties for intended use (for example, vesicles could be designed to melt at a specified temperature to customize time and location of drug delivery)
- **Self-assembly** to encapsulate drugs or other cargo
- **Scalable synthesis** to enable large scale production

Publications

- Frank R. Moss III, Steven R. Shuken, Jaron A. M. Mercer, Carolyn M. Cohen, Thomas M. Weiss, Steven G. Boxer, and Noah Z. Burns, [Ladderane phospholipids form a densely packed membrane with normal hydrazine and anomalously low proton/hydroxide permeability](#), *PNAS* 2018
- Jaron A. M. Mercer, Carolyn M. Cohen, Steven R. Shuken, Anna M. Wagner, Myles W. Smith, Frank R. Moss, III, Matthew D. Smith, Riku Vahala, Alejandro Gonzalez-Martinez, Steven G. Boxer, and Noah Z. Burns. "[Chemical Synthesis and Self-Assembly of a Ladderane Phospholipid](#)." *J. Am. Chem. Soc.*, 2016, 138 (49), pp 15845–15848. DOI: 10.1021/jacs.6b10706

Patents

- Published Application: [WO2018045094](#)
- Published Application: [20190177347](#)
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