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Designing Biotinylated Lipids for Selective Partitioning to Liquid Ordered Phase

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Designing lipids to partition into specific membrane domains (e.g., lipid rafts) could provide routes towards labeling and characterizing assemblies involved with pathogen entry, signaling, and trafficking in cells. Commercially available lipids provide an array of functionality to label membranes but their partitioning behavior to ordered (Lo), the membrane phase associated with lipid rafts, or disordered (Ld) phases do not follow defined rules based on their molecular structure. We present work that lends insight into designing functionalized lipids for selective partitioning to the Lo phase. For this study, we focused on biotinylated lipids, which are useful for attaching ligands (e.g., antibodies) to the membrane surface. It is known that biotinylation of DPPE directly on the headgroup or with a caproyl spacer generate lipids that partition strongly towards the Ld phase, whereas using PEG2000 as the spacer enables partitioning to the Lo phase. However, because of PEG2000's considerable steric bulk and potentially unfavorable effects on membrane structure/stability we prepared and examined a series of shorter PEG spacers to determine if an optimal spacer length exists for Lo partitioning. Using FITC labeled streptavidin we found that as the length of the ethylene glycol chain increased from trimer to decamer selectivity of the lipids for the Lo phase improved reaching partitioning coefficients that exceeded DPPE-PEG2000-biotin by several fold.

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