Developing endosome membrane mimics to study lipid nanocarrier interactions

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Lipid nanoparticles (LNPs) are established vehicles for intracellular RNA delivery [1,2,3]. They are uptaken through endocytosis and transported to the endosomal compartment, which is separated from the cell cytosol by a lipid membrane bilayer. For RNA cargo to be therapeutically active, it must be released from the endosome into the cytosol through a process called "endosomal escape" [4]. However, this remains a major barrier in RNA delivery, with a significant proportion of RNA remaining trapped in the endosome [5].

To better understand the process of endosomal escape, we probe interactions of LNPs with supported lipid bilayers (SLBs). Using QCM-D and TIRF, we examined how vesicles interact with SLBs that mimic the endosomal membrane. Additionally, during a neutron reflectometry (NR) experiment, we investigated vesicle interactions with SLBs and floating supported bilayers (FSBs), which serve as more biologically realistic membrane models. Notably, the nature of the membrane bilayer deposition (FSB vs SLB) of membranes with the same lipid composition was also found to influence their interaction with nanocarriers.

Together, we show that endosome-mimicking lipid bilayers of increased lipid complexity can be formed using SLB and FSB methods. These membranes can provide insights into lipid organization and applied to study LNP/vesicle fusion and lipid exchange processes. Such improved endosomal membrane mimics are highly relevant tools for uncovering mechanisms behind endosomal escape.

References:

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