Single-Step Manufacture of Multi-Functional Lipid-Based Nanoparticles

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A variety of uniform nanoparticles (**NP**s) such as discoidal micelles [**Fig 1 (A)**] and unilamellar vesicles can be manufactured through self-assembly in a lipid mixture composed of long- and short- chain lipids. This is a low-cost and chemically-green process, allowing for large scale production, thus suitable for industrial setting. Through our research supported by this NSF-grant (Nanomanufacturing program), several important achievements have been made. First, the formation of the discoidal micelles is robust and the platform can entrap and solubilize a variety of hydrophobic molecules (e.g., drugs, cholesterol). The NPs can be further stabilized by polyethylene glycol conjugated lipids [1]. Upon the elevation of temperature above the melting transition temperature of the long-chain lipid, small uniform unilamellar vesicles (radii ranging from 20 to 30 nm) can be obtained. It has also been shown that the cellular uptake of discoidal NPs is higher than that of the vesicles made of the same lipid composition. This is presumably attributed to more internalization pathways taken by the discoidal NPs than vesicles, which only utilize clathrin- and caveolae-mediated endocytosis. Last, both spontaneously forming discoidal NPs and vesicles can be "strung" by a polymer linker forming visible clusters as shown in **Fig 1 (B)** and **(C)**, respectively. Our preliminary study has shown that such clustering behavior can be applied for high-sensitivity biosensing (using *E coli O157:H7* pathogen as a model system), capable of detecting pathogen in a solution at a bacteria concentration as low as 10^2 CFU/mL, potentially leading to an instrument-free and low-cost pathogen detection platform.

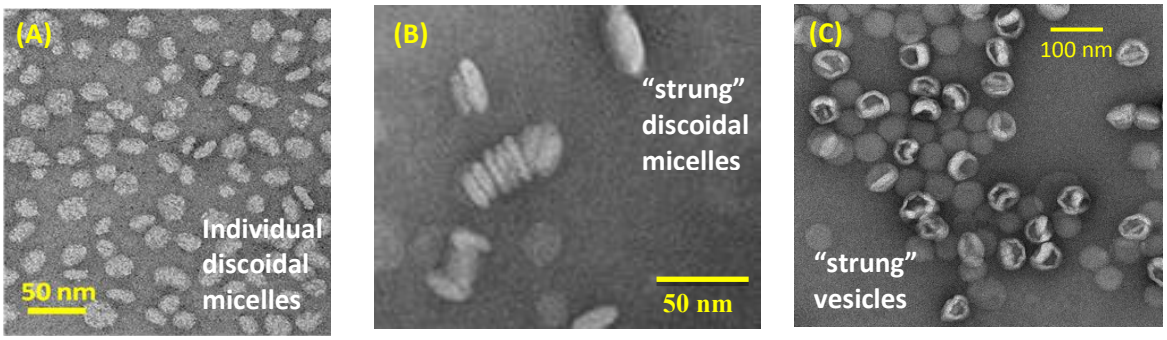

Figure 1 The negatively-stained transmission electron microscopic images of (A) individual discoidal micelles, (B) "strung" discoidal mcielles and (C) "stung" vesicles.

References

[1] Y. Liu, Y. Yang, M.-P. Nieh "The Effects of Temperature, Salinity, Concentrations and PEGylated Lipid on the Spontaneous Nanostructures of Bicellar Mixtures" Biochim. Biophys. Acta. – Biomembr 1838 1871–1880 (2014).