Single-Step Manufacture of Affinity Nanodiscs for Drug Delivery

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Designing targeting nanoparticles (**NP**s) for effective carriers of cancer diagnostics and therapeutics has been an ongoing effort in current biomedical and pharmaceutical fields. Although targeting NPs can show high efficacy in many cases, one of the more important issues for their applications is robustly manufacturing the designed NPs in large quantities with chemically green, simple and low-cost methods. In this project, we have utilized the principle of self-assembly to construct lipid-based nanodiscs in aqueous lipid mixtures. The fundamental understanding of molecular architectures and mismatching solubility of the lipids is key to controllably form uniform nanodiscs with a diameter of 20 ~ 30 nm (polydispersity < 15%) and a thickness of 5 nm (**Fig 1**), through homogenizing long- and short- chain lipids in water. These nanodiscs are capable of incorporating hydrophobic molecules or molecules with hydrophobic segments, thus providing an ideal template for entrapping hydrophobic pharmaceutics as well as cancer-targeting ligands. To lengthen the *in vivo* circulating time, the surface of the nanodiscs is modified with polyethylene glycol, **PEG** (also via self-assembly) to reduce possible *in vivo* immune response and enhance the stability of the nanodiscs. Such nanodiscs have shown a higher cancer cell uptake than that of 100-nm liposomes made of similar species (**Fig 2**) – an indication that cancer cell uptake can be morphologically dependent. The nanodiscs, in absence of PEG, coalesce with each other upon dilution and elevation of temperature following a diffusion-limited process mainly controlled by the Coulombic repulsion. However, PEG-modified nanodiscs show great stability in terms of morphology. The manufacturing protocol based on the fundamental understanding of the self-assembly is simple, scalable, environmentally green and possibly applicable to other relevant systems (surfactants, lipids, peptides, *etc.*), providing for potential industrial applications.

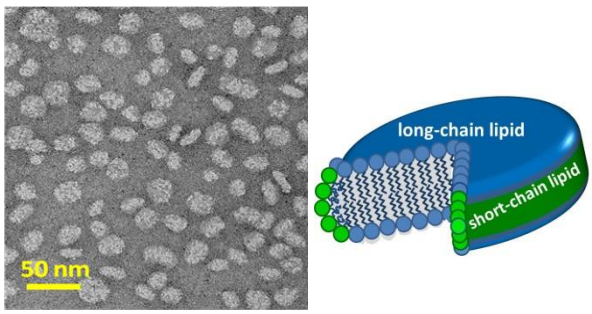

Figure 1 Transmission electron micrograph and a sketch of the lipid-based nanodiscs composed of long- and short- chain lipids.

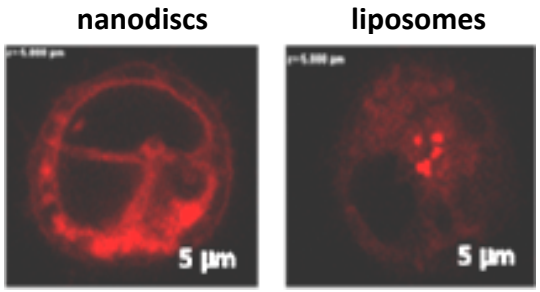

Figure 2 The fluorescence confocal micrographs of CCRF-CEM cancer cells after being incubated with Nile-Red containing nanodiscs and liposomes at 37 °C for 2 hours. The optical configurations are identical in both cases.

References

[1] For further information about this project link to http://www.ims.uconn.edu/~safn/SAFN_Research.html or email: mu-ping.nieh@ims.uconn.edu.