P.42 Engineering DNA-linked janus liposome clusters towards applications in drug delivery

T Wild

University of Leeds, UK

We aim to develop controlled liposome clusters as potential multi-drug carriers for application in nanomedicine therapies. To this end, we are utilising a platform where different liposomes can be connected through DNA linkers, to deliver multiple species keeping the individual cargos separate. Liposome clusters can be formed using complementary saturated lipid DNA conjugates integrated into the liposome's surface. To ensure strong and directional liposome bridging, a patch of localised DNA will allow assembly of size-limited clusters due to the directionality of the adhesive interaction. Previous studies have localised DNA on the surface of a liposome though phase coexistence, where the mixing of saturated (DPPC) and unsaturated (DOPC) lipids with cholesterol lead to the formation of liquid ordered patches of saturated lipid, surrounded by a liquid disordered phase of unsaturated lipids [1]. However these studies display poor saturated lipid DNA partitioning to the liquid ordered patches, allowing unwanted weak DNA hybridisation between the liquid disordered phases [2]. Therefore to enhance saturated DNA partitioning to the liquid ordered phase cardiolipin (CL) was added. CL is a highly unsaturated lipid which adopts a negative curvature, 10 mole percent has been shown to increase saturated lipid DNA partitioning by an order of magnitude [2]; driven through CL increasing the free energy required for a saturated lipid to insert into the liquid disordered phase. However the addition of CL requires a new four component phase diagram to be plotted, where tie lines across the liquid-liquid coexistence region determine the relative domain sizes and hence the size of the adhesion plaques. Due to the nanoscale liposome size required for cellular uptake, we use liposome diameters of 100 nm, prohibiting the use of optical techniques to view the phase separation. Therefore to map out the four component phase diagram we use a Förster Resonance Energy Transfer (FRET) fluorescence spectroscopy technique, which reports the redistribution of dyes during phase separation due the change in mean inter-probe distances. We are investigating the cluster size formed between two populations of Janus liposomes as we vary the relative domain size of the DNA-functionalised phase. This platform will be further developed towards targeted drug delivery of combination therapeutics, for example to combat multi-drug resistance or to deliver prodrugs with an activating compound.

[1] Beales, P.A. and T.K. Vanderlick, *Partitioning of membrane-anchored DNA between coexisting lipid phases.* The journal of physical chemistry. B, 2009. 113(42): p. 13678-13686

[2] Beales, P.A., J. Nam, and T.K. Vanderlick, *Specific adhesion between DNA-functionalized "Janus" vesicles: size-limited clusters.* Soft Matter, 2011. 7(5): p. 1747-1755