Projektexamenskod: KBTX16-23-07

Avdelningen för kemi och biokemi
Institutionen för kemi och kemiteknik, Chalmers tekniska högskola

Projektförslag för kandidatarbete inom inst. Kemi och kemiteknik och Biologi och bioteknik

Developing biocompatible stabilisers for lipid nanoparticles

Bakgrund

Lipid nanoparticles (LNPs) are an established non-viral drug delivery platform used for the Pfizer-BioNTech and Moderna vaccines against COVID-19. Despite the clinical success of LNPs, there are rising concerns about undesirable side-effects caused by immunogenic PEGylated lipids. To replace PEGylated lipids, we must replicate the complex role performed by these stabilisers. To allow recruitment of apolipoprotein E (ApoE) to the particle surface (Figure 1), PEGylated lipids are designed to shed *in vivo*.

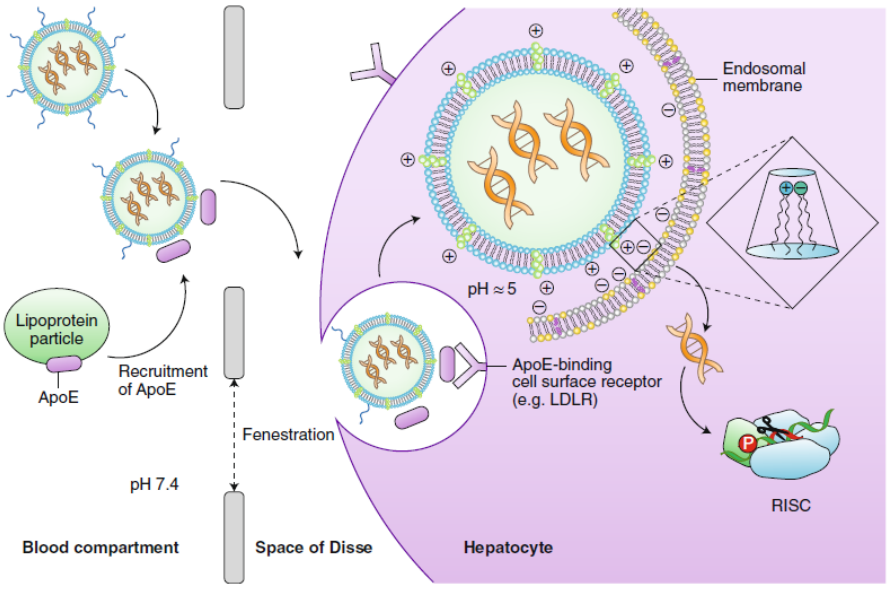

Figure 1. Illustration of PEG shedding from LNPs, and subsequent endosomal trafficking. Reproduced from Akinc, A. *et al. Nat. Nanotechnol.* **2019**, *14*, 1084–1087.

Problembeskrivning

A supramolecular stabiliser—for which shedding can be carefully controlled by tuning the strength of intermolecular interactions—may be a highly effective alternative to PEGylated lipids. In this project, you will decorate the outer surface of LNPs with a supramolecular host. Unlike PEG, this host exhibits no known immunogenicity. This strategy is accompanied by an additional advantage over the current state-of-the-art: the supramolecular nature of the interactions between the host and the LNP surface will impart a high degree of control over the rate of stabiliser shedding, allowing us to tune the interactions between the LNP platform and the cellular environment with unprecedented resolution.

Genomförande /Viktiga moment/teknikinnehåll

1. Synthesize the stabilizer (2 steps x 3 stabilizers) (organic synthesis, NMR)
2. Fabricate and characterize novel LNPs (microfluidics, DLS)
3. Investigate cargo delivery *in vitro*

Speciella förkunskapskrav: Ideally, I'm looking for a group of students in which some (not all) have experience in organic synthesis, and some (not all) have experience in cell culture. It is okay if you have neither skillset – it is more important that you love to learn, and are comfortable asking questions!

Möjlig målgrupp: K, Kf, Bt

Gruppstorlek: 4-6 studenter

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