Liposomes with Silica Coated Shell for Protective Targeted Delivery of mRNA Vaccines

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Liposomes and other nanosized lipid-based vesicles, are currently widely used in various drug/nucleic acid delivery applications. Development of vaccines, including cancer and COVID-19 vaccines, based on the use of nucleic acids delivered by lipid nanoparticles currently attracts the most attention of researchers. However, a wide clinical application of mRNA-based vaccines is substantially tampered by a low resistance of mRNA against destroying action of relatively high temperature during their storage and harsh conditions during their traffic after injections in the enzyme rich blood and body fluids towards the site of the most efficient vaccine application. The current project explores a possibility of substantial increasing in stability and resistance of mRNA encapsulated in silica coated lipid-based nanoparticles during the storage and nanoparticle journey inside the body after injection towards the antigen presenting cells. We hypothesize that the coating of cationic liposomes with protective silica shells can be augment the stability of the internalized drug. Such research can be translated to work into mRNA carrying lipid nanoparticles. Experiments on this stage of investigation were aimed at developing a method of rapid fabrication and characterization of such nanoparticles. We are currently developing an innovative method of coating of cationic (positively charged) lipid vehicles with anionic (negatively charged) silica shells. The general idea behind the method can be illustrated in three main steps (Figure 1). Cationic liposomes were mixed with a concentrated silica precursor solution (1) forming a stable colloid solution. The negatively charged silica nanoparticles are attracted to the positively charged lipid bilayer (2) finally resulting under carefully selected conditions in the formation of stable silica coated lipid nanoparticles (3). The source components and final nanoparticles were characterized by their zeta-potential and size using a dynamic light scattering (DLS) instrument. Stability of the final nanoparticles will be evaluated by assessing the degradation profile versus various concentrations of Triton-X 100, a surfactant. Preliminary experiments showed that upon addition of liposomes to the silica sol excess silica precipitate was generated by the end of the reaction. Upon characterizing the size, shows that a heterogenous distribution with large particles (> 2 µm) which conflicts with data from researchers who have successfully produced silica coated liposomes. Further characterization was not conducted due to poor sample quality. A single Triton X stability assay of cationic liposomes shows definitive degradation at concentration 5% and 10% (v/v) Triton X-100. Future studies will mainly be focused on generating a silica solution without the excess generation of silica particulates. The effects of relative reagent concentration, reaction time, reaction temperature, and pH. More replicates of the Triton X assay will be done to verify the reproducibility of our results. This research was supported in part by NIH Grant R01CA238871 grant, the School of Graduate Studies, and the Rutgers Office for Research and Economic Development.