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The influence of size, lipid composition and bilayer fluidity of cationic liposomes on the transfection efficiency of nanolipoplexes

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Abstract
Among non-viral vectors, cationic liposomes are the most promising carriers in gene delivery. But the most critical issue about their application is their low transfection efficiency compared to viral vectors. In this study, we tried to make a comparison between transfection efficiency of different liposomal formulations and to investigate the effect of membrane fluidity and other physical properties of liposomes and lipoplexes such as size and charge ratio on the transfection efficiency in in vitro environment. Different gene delivery systems were developed by using liposomes composed of ١،٢-dioleoyl-٣-trimethylammonium-propane (DOTAP) or ٣-β-[N-(N′N′-dimethylaminoethane)-carbamoyl] cholesterol (DC-CHOL) in combination with other lipids including ١،٢-dipalmitoyl-sn-glycero-٣-phosphocholine (DPPC), ١،٢-dioleoyl-sn-glycero-٣-phosphoethanolamine (DOPE), egg L-α-phosphatidylcholine (EPC) and ١،٢-dipalmitoyl-sn-glycero-٣-phosphoethanolamine (DPPE). These multilamellar vesicle (MLV) liposomes were extruded through ١٠٠ nm polycarbonate filters to produce small unilamellar vesicles (SUVs). Transfection activity of these lipoplexes in Neuro٢A cells was tested using pRL-CMV encoding Renilla luciferase. We could not establish any direct correlation between high fluid membranes and high transfection efficiency because DOTAP:DPPE had a better result than DOTAP:DOPE while DC-CHOL:DOPE was more successful in gene transfer than DC-CHOL:DPPE. It was revealed that the use of these two helper lipids with different Tm (DPPE: ٦٤ °C and DOPE: -١١ °C) along with DOTAP increased transfection efficiency but formulation of these phospholipids with DC-CHOL was led to a significant reduction in transfection activity. Generally, DOTAP:DPPE, DC-CHOL:DOPE and DOTAP:DOPE:DPPE formulations showed the highest transfection activity. The results of this study showed that, in designing of liposome based non-viral vectors, different parameters such as size, lipid composition and the use of helper lipid should be considered.

Author keywords
Helper lipid; Liposome; Size; Transfection efficiency

Indexed Keywords
Bi-layer; Carbamoyl; Cationic liposomes; Charge ratio; Critical issues; Dipalmitoyl-sn-glycero-٣-phosphocholine; Fluid membrane; Gene Delivery; Gene delivery systems; Helper lipid; In-vitro; Lipid composition; Lipoplexes; Liposomal formulation; Membrane fluidity; Multilamellar vesicles; Nonviral vectors; Phosphatidylcholine; Phosphoethanolamine; Polycarbonate filters; Renilla luciferase; Size; Small unilamellar veside; Transfection activity; Transfection efficiency; Viral vectors

Engineering controlled terms: Fluidity; Gene transfer; Liposomes; Phospholipids; Propane; Sugar (sucrose)

Engineering main heading: Nucleic acids

EMTREE drug terms: ١،٢ dioleoyl ٣ trimethylammoniopropane; ١،٢ dioleoyl sn glycero ٣ phosphoethanolamine; ١،٢ dipalmitoyl sn glycero ٣ phosphoethanolamine; ٣ beta [n (n'n' dimethylaminoethane) carbomoyl] cholesterol; dipalmitoylphosphatidylcholine; egg alpha phosphatidylcholine; lipoplex; liposome; phospholipid; polycarbonate; Renilla luciferin ٢ monooxygenase; unclassified drug