Abstract Submitted
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Cholesterol improves the transfection efficiency of lipoplexes by increasing the effective membrane charge density CYRUS R. SAFINYA, ALEXANDRA ZIDOVSKA, HEATHER M. EVANS, KAI K. EWERT, Materials, Physics, and Molecular, Cellular and Developmental Biology Departments, University of California, Santa Barbara — Motivated by its important role in lipid-mediated gene delivery, we have studied the effect of cholesterol on the transfection efficiency (TE) of lamellar, cationic lipid-DNA (CL-DNA) complexes. A successful *in vivo* liposome mixture seems to require cholesterol. Recent work in our group has identified the membrane charge density (σ) as a universal parameter for TE of lamellar, DOPC containing CL-DNA complexes (A.J. Lin et al, *Biophys. J.*, 2003, K. Ewert et al, *J. Med. Chem.*, 2002, A. Ahmad et al., *J. Gene Med.,* 2005), with TE following a universal bell-shaped curve as a function of σ. Theoretical calculations considering the headgroup area of cholesterol and thus necessarily counting for an increase in σ, when DOPC is replaced by cholesterol, show that TE strongly deviates from the TE universal curve. However, experimental determination of σ via X-ray diffraction shows full agreement with the TE universal curve demonstrating that the real σ is higher as predicted, therefore the effective headgroup area of cholesterol is lower as expected by theory, suggesting that cholesterol is inserted deep into lipid bilayer partially hidden by the neighboring lipids. Funding provided by NIH GM-59288 and NSF DMR-0503347.

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