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**Transfection efficiency and structural studies on non-viral gene carriers containing cholesterol and other sterols**

HEATHER EVANS, ALEXANDRA ZIDOVSKA, KAI EWERT, C. R. SAFINYA, Materials, Physics, and Molecular, Cellular and Developmental Biology Departments, University of California, Santa Barbara — Lipid based nonviral gene delivery currently focuses on cationic liposomes, which typically consist of a mixture of cationic and neutral (helper) lipids. Motivated by the plasma membrane composition of mammalian cells, which contain large amounts of cholesterol, this molecule is often used as a helper lipid. The presented work investigates the effect of cholesterol and structurally related molecules on the transfection efficiency (TE) of cationic lipid-DNA (CL-DNA) complexes in mammalian cells. Previous studies have identified the membrane charge density as a universal parameter, predicting TE for CL-DNA complexes in the lamellar  $L\alpha^C$  phase [1,2]. Addition of cholesterol to low transfecting CL-DNA complexes results in dramatic improvements in TE that significantly deviate from the TE model for lamellar complexes. A model system using negatively charged giant vesicles has been developed to mimic the cell membrane and understand the behavior pattern of CL-DNA complexes containing cholesterol. Funding provided by NIH GM-59288. [1] Lin AJ, Slack NL, Ahmad A, George CX, Samuel CE, Safinya CR, *Biophys. J.*, 2003, V84:3307 [2] Ahmad A, Evans HM, Ewert K, and Safinya CR, *J. Gene Med.*, accepted

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