Transfection efficiency and structural studies on nonviral 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 LαC 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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