Abstract Submitted
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New Dendritic Lipids for Improved Gene Delivery by Cationic Liposome-DNA Complexes KAI EWERT, HEATHER M. EVANS, AYESHA AHMAD, NATHAN F. BOUXSEIN, ALEXANDRA ZIDOVSKA, CYRUS R. SAFINYA, University of California, Santa Barbara — Cationic Liposome-DNA (CL-DNA) complexes are widely used in non-viral gene delivery, including clinical trials, but their efficiency still requires optimization. Membrane charge density is a universal parameter for transfection with lamellar CL-DNA complexes (Lin AJ et al., *Biophys. J.* 2003; **84**: 3307; Ahmad A et al., *J. Gene Med.*, accepted). Newly synthesized lipids with dendritic headgroups, based on an ornithine scaffold, have headgroup charges of +4e to +16e. These lipids form lamellar complexes if the headgroup charge is small or the fraction of dendritic lipid in the membrane (in mixtures with DOPC) is low. Higher contents of highly charged lipids exhibit a novel phase of CL-DNA complexes, whose structure was determined by synchrotron x-ray diffraction. Cylindrical micelles of lipid are arranged on a hexagonal lattice, with DNA rods placed around them in the interstices. Complexes with this structure are highly transfecting, preventing the previously observed drop in transfection efficiency at very high membrane charge densities. Funded by NIH GM-59288.

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