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Efficient Delivery of Therapeutic Small Nucleic Acids to Prostate Cancer Cells Using Ketal Nucleoside Lipid Nanoparticles

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Abstract: A novel nucleoside lipid derived from dioleyl ketal was synthesized from uridine in three steps starting from dioleyl ketone. Electronic microscopy studies show that Ketals Nucleoside Lipids (KNL) self-assemble to form liposome-like structures in aqueous solutions. KNL is able to bind siRNA as demonstrated by electrophoresis experiment and standard ethidium bromide fluorescence displacement assay. Transfection assays of stable hepatic cell lines HupIRF, carrying a luciferase reporter gene demonstrate that KNL is able to transfect siRNA and exhibits protein knockdown more efficiently than its diester analogue (DOTAU) and lipofectamine. Herein, we also report that KNLs are suitable transfecting reagents for the development of novel therapeutic approaches involving either siRNA or antisense oligonucleotide against human prostate cancer PC-3 cells resistant to chemotherapy.