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Glycotargeting to hepatocytes using novel cationic liposomal formulations

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The efficiency of liver gene therapy largely depends on the ability to specifically target hepatocytes for corrective gene transfer. Receptor-mediated gene transfer has shown potential for the treatment of liver diseases. The asialoglycoprotein receptor is a cell-surface receptor that is highly expressed on hepatocytes (liver cells). Genes targeted to this receptor can be delivered in a highly selective manner to the liver via glycotargeting. Glycotargeting relies on carrier molecules possessing carbohydrates that are recognized and internalized by these receptors. Glycosylation of liposomes have shown immense potential in the targeting of specific liver cells and can be achieved by incorporation of synthetic glycolipids into the liposomal bilayer. This study is aimed at producing synthetic targeted cationic liposome gene carrier systems for study in a human hepatoma cell line (HepG2). Targeted transfection was facilitated by the formulation of liposomes comprising of glycosylated cholesterol (MSβGal), novel cationic cholesteryl derivative *N,N*-dimethylaminopropylamidosuccinylcholesterylformylhydrazide (MS09), dioleoylphosphatidylethanolamine (DOPE) and polyethylene glycol (PEG_{2000}). The sugar moiety present in the liposomal bilayer is intended to bear specificity towards the membrane lectins, and the cationic component to bind electrostatically to the negatively charged DNA. Gel retardation, nuclease digestion and ethidium intercalation assays confirmed that DNA was fully liposome-associated, stable and protected from serum nucleases. Transfection activity of the cationic lipoplexes was determined using the luciferase reporter gene assay and cytotoxicity *in vitro* was evaluated using the MTT test. These findings support the notion that these lipoplexes could prove to be useful targeted gene carriers to liver hepatocytes and may be extended to an *in vivo* system.