Development and application of glycosylated particulate carriers for delivery of nucleic acid medicine

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Successful gene therapy depends on the development of efficient delivery systems. Although pDNA and oligonucleotides are novel candidates for nonviral gene therapy, their clinical applications are generally limited owing to their rapid degradation by nucleases in serum and rapid clearance. A great deal of effort had been devoted to developing gene delivery systems, including cationic liposomes. The main problem with cationic liposomes seems to be the lack of organ or cell selectivity because the lung has the highest level of gene expression after intravenous injection. Applying cell-specific targeting technology to liposomes would improve in vivo gene delivery and reduce any unexpected side effects. Among the various receptors, asialoglycoprotein receptors and mannose receptors are the most promising for gene targeting since they exhibit high affinity and are rapidly internalized. Both liver parenchymal and non-parenchymal cells exclusively express large numbers of high-affinity asialoglycoprotein and mannose receptors, respectively. Receptor-mediated gene delivery systems are able to introduce foreign DNA into specific cell types in vivo. Using this technology, cell-selective delivery systems of pDNA by galactosylated, mannosylated, and fucosylated liposomes were developed by the optimization of physicochemical properties of glycosylated liposomes/pDNA complexes. Based on the findings of glycosylated liposomes/pDNA complexes, targeted delivery system of oligonucleotides, such as siRNA, NFκB decoy, and CpG DNA were also developed.