Galactosylated DNA lipid nanocapsules for efficient hepatocyte targeting

Titre	Galactosylated DNA lipid nanocapsules for efficient hepatocyte targeting
Type de publication	Article de revue
Auteur	Morille, Marie [1], Passirani-Malleret, Catherine [2], Letrou-Bonneval, E. [3], Benoît, Jean-Pierre [4], Pitard, B. [5]
Editeur	Elsevier
Type	Article scientifique dans une revue à comité de lecture
Année	2009
Langue	Anglais
Date	11/09/2009
Numéro	2
Pagination	293-300
Volume	379
Titre de la revue	International Journal of Pharmaceutics
ISSN	1873-3476
Résumé en anglais	The main objective of gene therapy via a systemic pathway is the development of a stable and non-toxic gene vector that can encapsulate and deliver foreign genetic materials into specific cell types with the transfection efficiency of viral vectors. With this objective, DNA complexed with cationic lipids of DOTAP/DOPE was encapsulated into lipid nanocapsules (LNCs) forming nanocarriers (DNA LNCs) with a size suitable for systemic injection (109+/-6 nm). With the goal of increasing systemic delivery, LNCs were stabilised with long chains of poly(ethylene glycol) (PEG), either from a PEG lipid derivative (DSPE-mPEG(2000)) or from an amphiphilic block copolymer (F108). In order to overcome internalisation difficulties encountered with PEG shield, a specific ligand (galactose) was covalently added at the distal end of the PEG chains, in order to provide active targeting of the asialoglycoprotein-receptor present on hepatocytes. This study showed that DNA LNCs were as efficient as positively charged DOTAP/DOPE lipoplexes for transfection. In primary hepatocytes, when non-galactosylated, the two polymers significantly decreased the transfection, probably by creating a barrier around the DNA LNCs. Interestingly, galactosylated F108 coated DNA LNCs led to a 18-fold increase in luciferase expression compared to non-galactosylated ones.
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