Glycofection: gene transfer with the help of cationic glycopolymers.

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Glycosylated cationic polymers, called Glycofectins™, such as glycosylated polylysines (M_r ~25 000) interact with plasmid to give a glycoplex, a compacted form of a polymer/DNA complex. We recently developed a simple method to convert reducing saccharides (mono-, di- or oligosaccharides) into glycosynthons (glycoamino-acids or glycopeptides) in a very high yield within a day. Such glycosynthons are easily either converted into clusters or used directly to synthesize glycoconjugates including neoglycoproteins and cationic glycopolymers.

A glycoplex, prepared with a given glycofectin, is preferentially taken up by the cells which express, at their surface, a lectin which recognizes the carbohydrate moieties born by that glycofectin and usually leads to an enhanced gene expression, up to thousands times that obtained with glycoplexes prepared with glycofectins bearing irrelevant carbohydrate moieties or with polyplexes prepared with the sugar-free polymer.

However, in some cases, there is an inverted relationship between the uptake extent of the glycoplex and the gene expression level. It is, for instance, what happens with cystic fibrosis airway epithelial cells. These cells actively take up neoglycoproteins as well as glycoplexes containing α-mannopyranosyl residues but they very poorly take up glycoplexes containing lactosyl (Galβ-4Glcβ-) moieties; while lactosylated glycoplexes lead to a quite high gene expression, mannosylated ones lead to an extremely poor gene expression. These paradoxical results will be discussed on the basis of a differential intracellular trafficking of glycoplexes.

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