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TITLE

Enhanced gene expression in the brain following intravenous administration of lactoferrin-bearing polypropylenimine dendriplex

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ABSTRACT

The possibility of using gene therapy for the treatment of brain diseases such as brain cancer, Alzheimer's and Parkinson's diseases, is currently hampered by the lack of gene delivery systems able to cross the blood-brain barrier and deliver DNA to the brain following intravenous administration.

On the basis that lactoferrin can effectively reach the brain by using specific receptors for crossing the blood-brain barrier, we propose to investigate if a lactoferrin-bearing generation 3- diaminobutyric polypropylenimine (DAB) dendrimer would allow the transport of plasmid DNA to the brain after intravenous administration.

In this work, we demonstrated that the conjugation of lactoferrin to the dendrimer led to an enhanced DNA uptake by 2.1-fold in bEnd.3 murine brain capillary endothelial cells compared to the unmodified dendriplex *in vitro*. *In vivo*, the intravenous administration of lactoferrin-bearing DAB dendriplex resulted in a significantly increased gene expression in the brain, by more than 6.4-fold compared to that of DAB dendriplex, while decreasing gene expression in the lung and the kidneys. Gene expression in the brain was significantly higher than in any other major organs of the body.

Lactoferrin-bearing generation 3 polypropylenimine dendrimer is therefore a highly promising delivery system for systemic gene delivery to the brain.

KEYWORDS

Brain delivery; blood-brain barrier; gene expression; dendrimer; lactoferrin