J Control Release. 2020 Oct 19;S0168-3659(20)30607-6. doi: 10.1016/j.jconrel.2020.10.029. Online ahead of print.

Development of A2G80 peptide-gene complex for targeted delivery to muscle cells

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PMID: 33091529 DOI: 10.1016/j.jconrel.2020.10.029

Abstract

Therapeutic strategies based on antisense oligonucleotides and therapeutic genes are being extensively investigated for the treatment of hereditary muscle diseases and hold great promise. However, the cellular uptake of these polyanions to the muscle cells is inefficient. Therefore, it is necessary to develop more effective methods of gene delivery into the muscle tissue. The A2G80 peptide (VQLRNGFPYFSY) from the laminin α2 chain has high affinity for α-dystroglycan (α-DG) which is expressed on the membrane of muscle cells. In this study, we designed a peptide-modified A2G80 with oligoarginine and oligohistidine (A2G80-R9-H8), and prepared peptide/plasmid DNA (pDNA) complex, to develop an efficient gene delivery system for the muscle tissue. The peptide/pDNA complex showed α-DG-dependent cellular uptake of the A2G80 sequence and significantly improved gene transfection efficiency mediated by the oligohistidine sequence in C2C12 myoblast cells. Further, the peptide/pDNA complex promoted efficient and sustained gene expression in the Duchenne muscular dystrophy mouse models. The A2G80-R9-H8 peptide has the potential for use as a specific carrier for targeting muscle in gene therapy in muscular dystrophy.

Keywords: Dystroglycan binding peptide; Gene delivery; Muscle targeting; Peptide/gene complex; Treatment for hereditary disease.