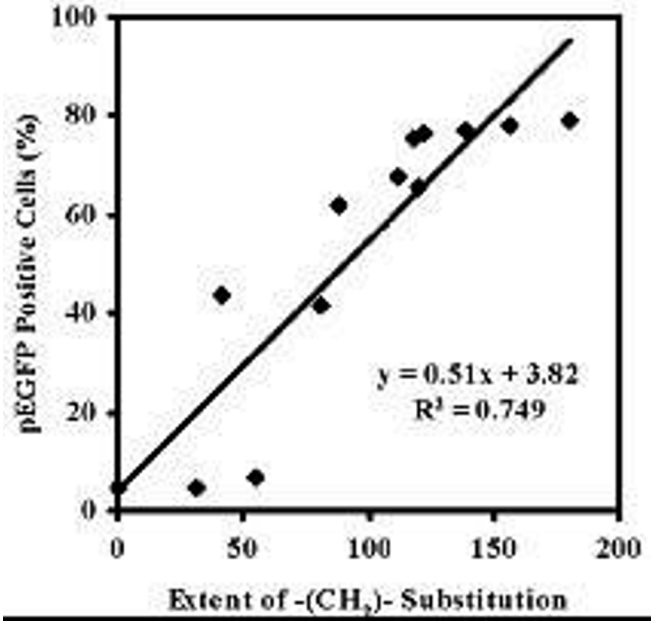
showed that successful protein expression was obtained with PLLs substituted with myristic and stearic acid, the latter displaying a relatively lower toxicity. **Conclusion:** We conclude that substituting lipids on PLL results in effective gene carriers and the extent of substitution, rather than the individual lipid, appeared to be critical for effective plasmid delivery.



881. Nanoparticle-Mediated Delivery of Antisense Oligoribonucleotides Allows Restoration of Dystrophin Expression in the mdx Mouse

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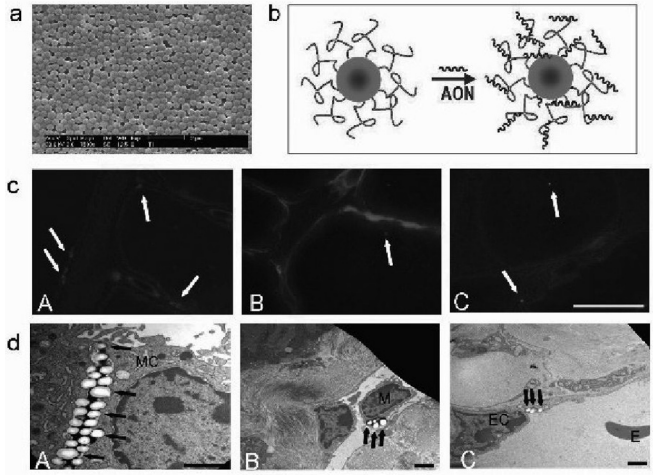
For subsets of Duchenne muscular dystrophy mutations, antisense oligoribonucleotide mediated exon skipping has proven to be efficacious in restoring the expression of dystrophin protein. In the *mdx* murine model systemic delivery of antisense oligoribonucleotide, recognising the splice donor of dystrophin exon 23, has shown proof of concept. We have been able to restore dystrophin expression in body-wide striated muscles of mdx animal model using different formulations of cationic nanoparticles. These were loaded with low doses of 2'OMePS antisense oligoribonucleotide, ranging from 0.9 to 4.5 mg/kg/week, and delivered by weekly intraperitoneal injection. Transcription, western and immunohistochemical analysis showed increased levels of dystrophin transcript, protein and correct localisation at the sarcolemma. We characterised the physical properties, the interaction between nanoparticles and AON, and their diffusion pathways both by fluorescence and electron microscopy analysis. We therefore showed that cationic nanoparticles have the capacity to both deliver antisense oligoribonucleotides in body-wide muscles and reduce the dose required for dystrophin rescue. This non-viral approach may improve the therapeutic usage of antisense oligoribonucleotides in Duchenne muscular dystrophy as well as the delivery of RNA molecules with many implications in both basic research and medicine.



1a: T1 nanoparticle scanning electron microscope. 1b: Interaction between AON and T1 nanoparticles. 1c: Biodistribution in the mdx mouse of fluorescent T1 A: diaphragm; B: gastrocnemius; C: heart. 1d: Biodistribution of T1 by electron microscope analysis.

882. Synthesis and Evaluation of Amphiphilic Poly(tetrahydrofuran-b-Ethylene Oxide) Copolymers for DNA Delivery into Skeletal Muscle

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Purpose Amphiphilic triblock copolymers such as the pluronic poly(ethylene oxide-b-propylene oxide-b-ethylene oxide) L64 (pEO13-pPO30-pEO13) have been shown to mediate more efficient gene transfer in muscle as compared to naked DNA. We were interested in studying the effect of a chemical change of the central block of pluronic polymers on the transfection activity. Methods We synthesized new amphiphilic copolymers in which the hydrophobic pPO block was replaced by poly(tetrahydrofuran) (pTHF) chains. The resulting triblock pEO–pTHF–pEO polymers have been characterized by NMR and SEC and assayed for in vitro and in vivo gene transfer. Results The animal experiments showed that the new copolymers are able to significantly increase the transfection efficiency of plasmid DNA after intramuscular injection. Conclusions These results indicate that the capacity to enhance plasmid DNA transfection in skeletal muscle is not restricted to pEO–pPO–pEO arrangements.