Drug delivery strategy eliminates myotonia symptoms in mice with myotonic dystrophy

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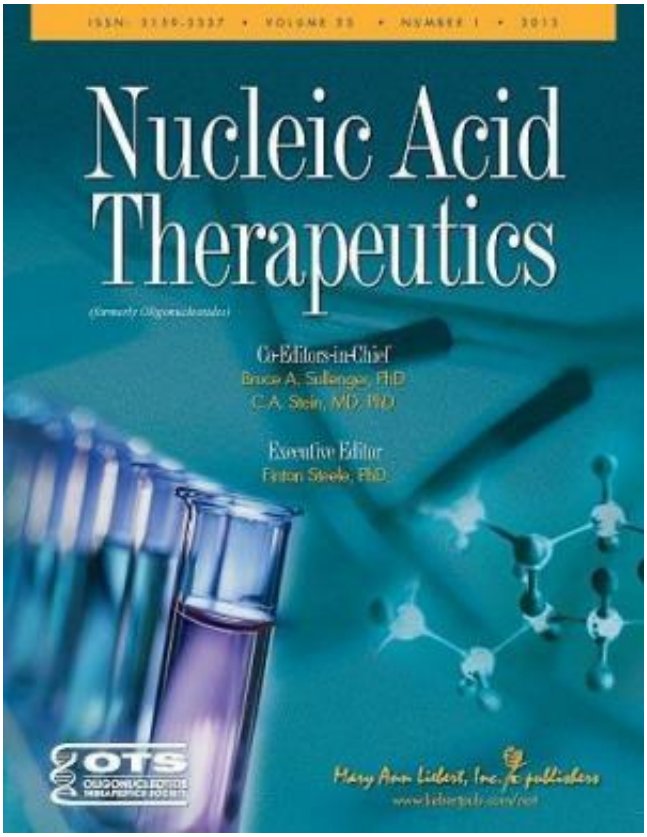

By targeting the specific mutation that causes the hereditary neuromuscular disease myotonic dystrophy, it is possible to neutralize the mutant RNA toxicity and minimize or even eliminate the disabling symptoms of the disease. New classes of drugs called antisense

oligonucleotides are being designed to achieve this. Innovative work to develop a modified antisense drug that can be administered intravenously and achieve the desired therapeutic effect is described in an article in *Nucleic Acid Therapeutics*.

Andrew Leger and coauthors from Genzyme, a Sanofi Company (Framingham, MA) added a peptide to an oligonucleotide strand designed to bind to and inactivate the mutated RNA region associated with myotonic dystrophy type 1 (DM1). The disease can affect function of the heart, central nervous system, and gastrointestinal tract, and a characteristic symptom is myotonia, in which muscles are slow to relax following contraction.

In the article "Systemic Delivery of Peptide-Linked Morpholino Oligonucleotide Neutralizes Mutant RNA Toxicity in a Mouse Model of Myotonic Dystrophy," the authors describe how the peptide is intended to enable systemic delivery of the drug, protecting it from being damaged or destroyed in the body before it can reach its target, the muscles. They report that intravenous introduction of the drug in a mouse model of DM1 led to good biodistribution of the drug, evidence that the problems previously caused by RNA toxicity were corrected, and complete elimination of myotonia in the treated mice.

"One of the greatest challenges to the therapeutic use of nucleic acids is effective and safe delivery," says Executive Editor Fintan Steele, PhD, SomaLogic, Inc., Boulder, CO. "The work of Leger and his colleagues demonstrates a potentially powerful way to meet that challenge for many diseases."

More information: The article is available free on the *Nucleic Acid Therapeutics* website.