Exon skipping prevents formation of toxic protein fragments in Huntington's disease

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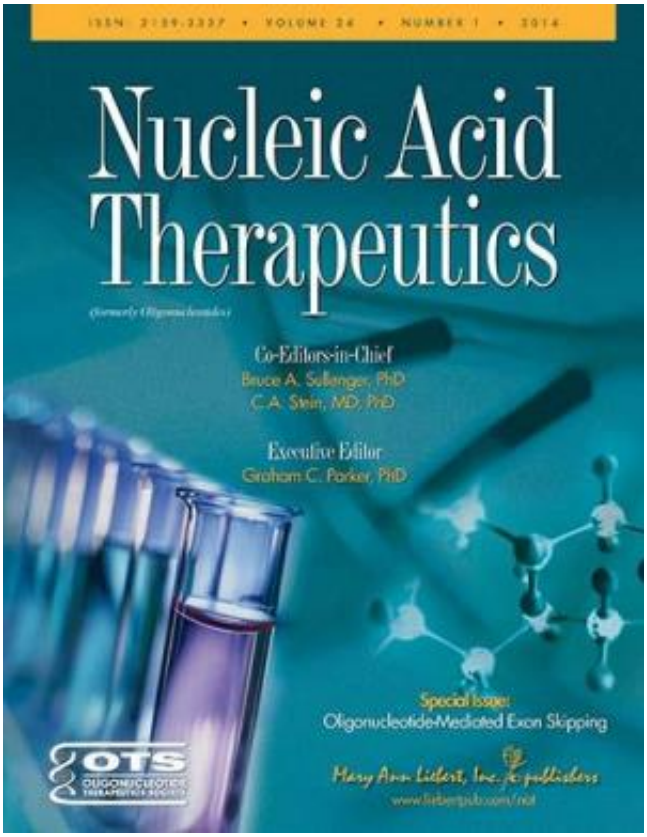

An innovative therapeutic strategy for reducing the levels of toxic protein fragments associated with Huntington's disease uses a new approach called exon skipping to remove the disease-causing component of the essential protein, huntingtin. Proof of concept using antisense

oligonucleotides to "skip over" the specific exon in a mouse model of Huntington's disease is reported in an article in *Nucleic Acid Therapeutics*.

Melvin Evers et al., Leiden University Medical Center, The Netherlands, describe the successful use of antisense oligonucleotides to target the mutated exon that causes Huntington's disease in the article "Preventing Formation of Toxic N-Terminal Huntingtin Fragments Through Antisense Oligonucleotide-Mediated Protein Modification."

"No field of therapeutic development is moving faster, with more imminent clinical translation than the nucleic acid based treatment of central nervous system conditions," says Executive Editor Graham C. Parker, PhD, The Carman and Ann Adams Department of Pediatrics, Wayne State University School of Medicine, Children's Hospital of Michigan, Detroit, MI. "The novel therapeutic strategy outlined in Evers et al. gives us a proof of concept of how a previously intractable condition can be treated by modifying rather than removing the toxic protein."

The special issue also includes the Review article "A Chemical View of Oligonucleotides for Exon Skipping and Related Drug Applications." by Peter Järver, Liz O'Donovan, and Michael Gait, Medical Research Council, Cambridge, U.K. The authors explore the complex chemistry and design of antisense oligonucleotides used for exon skipping and progress in developing new chemistries to improve their stability and binding.

Annemieke Aartsma-Rus, PhD, Leiden University Medical Center, Guest Editor of the issue, emphasizes the need for scientists, clinicians, patients, regulators, and drug manufacturers to work closely together to develop exon skipping therapeutics, which are currently in clinical trials for neuromuscular disorders such as Duchenne muscular dystrophy and

spinal muscular atrophy. These complex drugs and the challenging diseases they are targeting require a collaborative effort, she states in her Editorial "Antisense-Mediated Exon Skipping: Networking to Meet Opportunities and to Overcome Challenges."

Nucleic Acid Therapeutics is under the editorial leadership of Co-Editors-in-Chief Bruce A. Sullenger, PhD, Duke Translational Research Institute, Duke University Medical Center, Durham, NC, and C.A. Stein, MD, PhD, City of Hope National Medical Center, Duarte, CA; and Executive Editor Graham C. Parker, PhD.

More information: The article, part of a special focus issue on exon skipping, is available on the *Nucleic Acid Therapeutics* website.

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