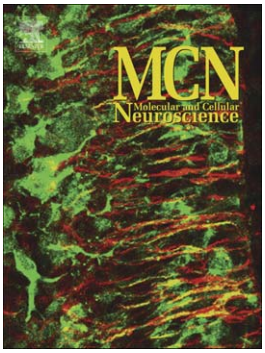

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Splicing therapy for neuromuscular disease

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Abstract

Duchenne muscular dystrophy (DMD) and spinal muscular atrophy (SMA) are two of the most common inherited neuromuscular diseases in humans. Both conditions are fatal and no clinically available treatments are able to significantly alter disease course in either case. However, by manipulation of pre-mRNA splicing using antisense oligonucleotides, defective transcripts from the *DMD* gene and from the *SMN2* gene in SMA can be modified to once again produce protein and restore function. A large number of *in vitro* and *in vivo* studies have validated the applicability of this approach and an increasing number of preliminary clinical trials have either been completed or are under way. Several different oligonucleotide chemistries can be used for this purpose and various strategies are being developed to facilitate increased delivery efficiency and prolonged therapeutic effect. As these novel therapeutic compounds start to enter the clinical arena, attention must also be drawn to the question of how best to facilitate the clinical development of such personalised genetic therapies and how best to implement their provision.

Keywords

DMD
SMA
antisense
splicing
exon skipping
exon inclusion

Abbreviations

2'OMePS – 2'-O-methyl phosphorothioate
2'MOE-PS – 2'-O-methoxyethyl phosphorothioate
AON – antisense oligonucleotide