Advances and caveats of novel therapies in neuromuscular disorders

Benedikt Schoser
Friedrich-Baur-Institute, Dep. of Neurology LMU Clinic Munich, Germany
benedikt.schoser@med.uni-muenchen.de

Different gene therapy strategies have become established, tested in preclinical and clinical trials, and evaluated as approved forms for long-term efficacy. The initiated paradigm shift from a purely descriptive and symptom-oriented diagnosis and therapy to gene therapy precision medicine poses various challenges for the patient, the doctor, and our healthcare system. The aim of every gene therapy is to modify or introduce the target gene with the initiation of degradation of dysfunctional proteins. Different techniques such as gene transfer, gene substitution or gene editing in-vivo and ex-vivo are now usable. For example, a modification of the pre-mRNA using antisense oligonucleotides or RNA interference (siRNA) can be used for exon skipping. Initiation of gene expression to produce the target protein can be based on DNA modification using gene replacement, cell-based therapies (iPS cells), regulation by compensatory proteins, or pharmacological therapy with small molecules. Each method has advantages and complex disadvantages that must be evaluated individually. Phenotypic peculiarities of a rare disease often only become apparent through specific translational therapy. It is already becoming evident that a very early point in timing gene therapy is probably the most effective. Newborn screening is gaining additional importance since early diagnosis can achieve the best possible success of therapies, possibly even preventively. Adequate long-term follow-up documentation in registries is essential for these specific therapies.