Gene therapy to target ER stress in brain diseases

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© 2016 Elsevier B.V. Gene therapy based on the use of Adeno-associated viruses (AAVs) is emerging as a safe and stable strategy to target molecular pathways involved in a variety of brain diseases. Endoplasmic reticulum (ER) stress is proposed as a transversal feature of most animal models and clinical samples from patients affected with neurodegenerative diseases. Manipulation of the unfolded protein response (UPR), a major homeostatic reaction under ER stress conditions, had proved beneficial in diverse models of neurodegeneration. Although increasing number of drugs are available to target ER stress, the use of small molecules to treat chronic brain diseases is challenging because of poor blood brain barrier permeability and undesirable side effects due to the role of the UPR in the physiology of peripheral organs. Gene therapy is currently considered a possible future alternative to circumvent these problems by the delivery of therapeutic agents to selective regions and cell types