Toxicity of dorsal root ganglia is widely associated with CNS AAV gene therapy

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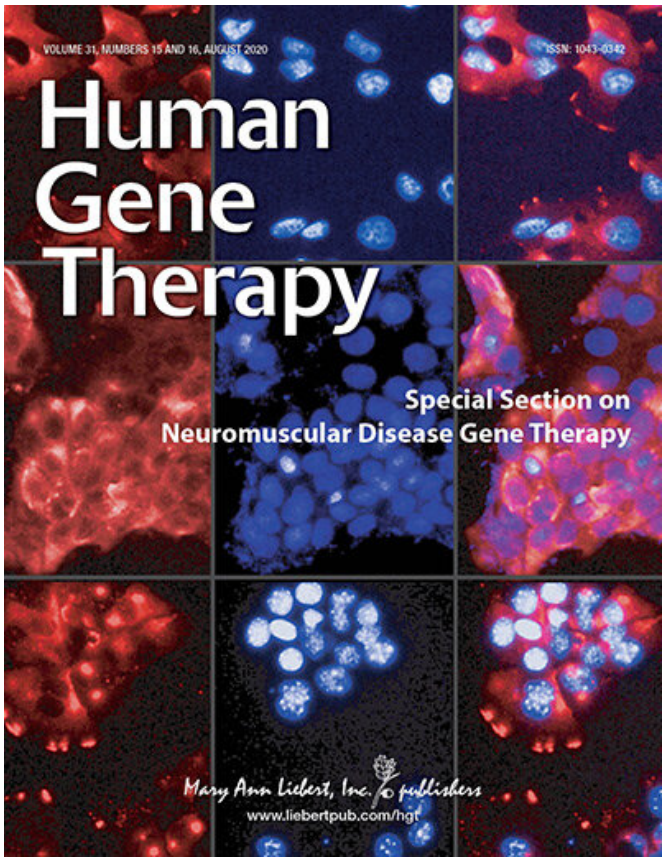

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A meta-analysis of non-human primate (NHP) studies showed that adeno-associated virus (AAV) gene therapy often caused dorsal root ganglion (DRG) pathology. There were no clinical effects. The study is reported in the peer-reviewed journal *Human Gene Therapy*.

The dorsal root ganglion is a cluster of neurons in the dorsal root of a spinal nerve. DRG pathology was present in 83% of NHP given AAV through the cerebrospinal fluid and 32% of NHP that received an intravenous injection.

The data suggest that "DRG pathology is almost universal after AAV vectors are delivered into the cerebral spinal fluid of nonhuman primates. However, none of the animals receiving a vector expressing a therapeutic transgene displayed any clinical signs," stated James M. Wilson, MD, Ph.D., a professor of Medicine and director of the Gene Therapy Program and the Orphan Disease Center, and coauthors from the Perelman School of Medicine at the University of Pennsylvania.

"The DRG pathology associated with AAV has triggered an increase in the intensity of preclinical evaluation of AAV vectors prior to initiation of clinical trials of new vectors," according to Editor-in-Chief of Human Gene Therapy Terence R. Flotte, MD, Celia and Isaac Haidak Professor of Medical Education and Dean, Provost, and Executive Deputy Chancellor, University of Massachusetts Medical School. "The insights offered by Dr. Wilson's paper provide an excellent summary perspective on this phenomenon, which could potentially eliminate the need for a number of redundant preclinical safety studies and thus shorten the path to the clinic for new vectors."

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More information: Juliette Hordeaux et al, Adeno-Associated Virus-Induced Dorsal Root Ganglion Pathology, *Human Gene Therapy* (2020). DOI: 10.1089/hum.2020.167

Provided by Mary Ann Liebert, Inc

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