# Gene therapy success depends on ability to advance viral delivery vectors to commercialization

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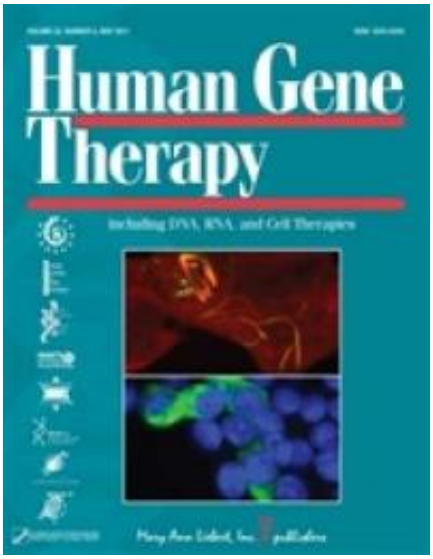


*Human Gene Therapy*, the official journal of nine international gene therapy societies, is an authoritative peer-reviewed journal published monthly in print and online that presents reports on the transfer and expression of genes in mammals, including humans. Credit: ©2011, Mary Ann Liebert Inc., publishers

Many gene therapy strategies designed to deliver a normal copy of a gene to cells carrying a disease-causing genetic mutation rely on a modified virus to transfer the gene product into affected tissues. One technology platform that is well suited for in vivo delivery of genes is based on adeno-associated viruses (AAV). As these novel therapies

move closer to commercialization, so do the methods for large-scale production and efficient delivery of AAV vectors, which are documented in a series of articles published online ahead of print in *Human Gene Therapy*, a peer-reviewed journal published by Mary Ann Liebert, Inc.

A collection of papers explores the progress and challenges in refining the production and use of AAV-based vectors. Allay et al. describe a large-scale, commercially relevant method for producing and purifying an AAV vector for use in a clinical study in "Good Manufacturing Practice Production of Self-Complementary Serotype 8 Adeno-Associated Viral Vector for a Hemophilia B Clinical Trial." In "Mycophenolate Mofetil Impairs Transduction of Single-Stranded Adeno-Associated Viral Vectors," Montenegro-Miranda et al. show that an immunosuppressive drug used in conjunction with gene therapy to treat an inherited liver disorder impaired the activity of certain types of AAV gene delivery vectors but not others. Yuan and coworkers present an improved and simplified method for generating producer cell lines that yield large amounts of AAV and exhibit stable growth, in "A Versatile Adeno-Associated Virus Vector Producer Cell Line Method for Scalable Vector Production of Different Serotypes."

Lu et al. developed a strategy for minimizing the unwanted production of AAV capsid protein by contaminating replication-competent virus that can provoke an immune response, as reported in "Systemic Elimination of de novo Capsid Protein Synthesis from Replication-Competent AAV Contamination in the Liver." In "A Simple Method to Increase the Transduction Efficiency of Single-Stranded Adeno-Associated Virus Vectors In Vitro and In Vivo," Ma and colleagues have further optimized their method for delivering a mixed population of AAV2 vectors to enable high-efficiency transfer of large genes.

Finally, a provocative commentary by J. Fraser Wright, "New Adeno-

Associated Virus Strategies to Support Momentum in the Clinic," explores how the design, manufacture, and characterization of gene therapy products have evolved based on the experience gained and lessons learned from first-generation clinical studies.

"Clinical proof of concept of AAV gene therapy has been realized in several diseases. The focus is now on issues related to commercialization including methods for large scale and high quality production of vectors," says James M. Wilson, MD, PhD, Editor-in-Chief, and Director of the Gene Therapy Program, Department of Pathology and Laboratory Medicine, University of Pennsylvania School of Medicine, Philadelphia.

**More information:** The articles are available free online at www.liebertpub.com/hum

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