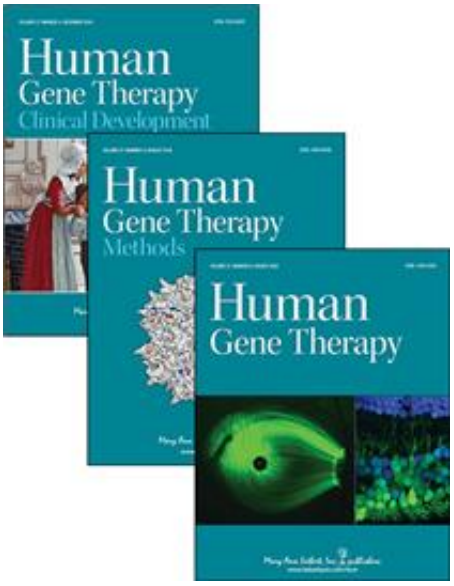
New system for therapeutic gene delivery increases transgene expression up to 100-fold

January 27 2017



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Advanced engineering of a mini-intronic plasmid (MIP) system designed to carry a therapeutic gene can significantly enhance the expression of the transgene delivered using an adeno-associated viral (AAV) vector. The ability to increase transgene expression by up to 40 to 100-fold, which would reduce the cost of manufacturing and perhaps also lessen the immune response of AAV/MIP-based gene therapy, is reported in *Human Gene Therapy*.

Authors Jiamiao Lu, Feijie Zhang, and Mark Kay, Stanford University,

Palo Alto, CA, and James Williams and Jeremy Luke, Nature Technology Corp., Lincoln, NE, describe the modified MIP expression system in the article entitled "A 5' Non-coding Exon Containing Engineered Intron Enhances Transgene Expression from Recombinant AAV Vectors in vivo." The researchers discuss the potential implications of enhanced transgene expression on the doses needed to achieve a therapeutic response and the flexibility the small intronic sequences offer, allowing them to be used in both DNA plasmids and viral delivery vectors.

"Careful observation of the expression characteristics of different vector designs sometimes leads to unexpected findings," says Editor-in-Chief Terence R. Flotte, MD, Celia and Isaac Haidak Professor of Medical Education and Dean, Provost, and Executive Deputy Chancellor, University of Massachusetts Medical School, Worcester, MA. "In this case, the authors found that a very substantial increase in the amount of transgene expression (up to 100-fold) could be achieved from rAAV vectors by including essential bacterial plasmid elements in an upstream intron. This could present substantial advantages for future in vivo gene therapy."

More information: Jiamiao Lu et al. A 5′ Noncoding Exon Containing Engineered Intron Enhances Transgene Expression from Recombinant AAV Vectors, *Human Gene Therapy* (2017). DOI: 10.1089/hum.2016.140

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