Next-Generation Midi-Dystrophin Gene Therapy Strategy Reported in Nature

Breakthrough gene replacement strategy for patients with Duchenne muscular dystrophy reported in Nature using gene-splicing technology to create midi-dystrophin

SEATTLE, WASHINGTON, USA, July 17, 2024 /EINPresswire.com/ -- Kinea Bio, Inc., a patient-dedicated gene therapy company focused on developing innovations to fight Duchenne muscular dystrophy (Duchenne) is excited to announce the publication of a breakthrough gene replacement strategy for patients with Duchenne, in the journal, Nature.

The report describes experiments in a mouse model of Duchenne that address a key limitation to existing gene replacement strategies for Duchenne, mainly the limited packaging capacity of adeno-associated viral vectors (AAVs). Current AAV gene therapy approaches use a shortened micro-dystrophin transgene. While micro-dystrophin proteins can provide benefits to patients, they are missing significant protein domains compared to the full-length dystrophin protein.

Additionally, present AAV gene therapy strategies require very high doses of viral vector to effectively shuttle the micro-dystrophin transgenes into muscle. These high vector doses can greatly increase the safety risks associated with receiving the therapy.

Lead author, Hichem Tasfaout, PhD, Scientific Advisor for Kinea Bio and acting assistant professor of Neurology at the University of Washington, reports results of dual and triple vector approaches to enable the delivery of larger constructs (called a midi-dystrophin for the dual vectors, and full-length dystrophin for the triple vectors) to individual muscle cells, tested in a mouse model of Duchenne. The dual vector midi-dystrophin is a larger dystrophin protein, containing significantly more functional domains of the dystrophin protein than current micro-dystrophins. The results reported in Nature indicate that midi-dystrophin provides superior benefits to muscle than micro-dystrophin. Delivery of full-length dystrophin leads to further benefits, even in very old, highly dystrophic mice. Further, the experiments described utilize next-generation AAVs that increase the efficiency of viral delivery to muscle cells, enabling lower AAV doses and thereby decreasing the risk of serious adverse events to patients. The authors also used a miniaturized and highly active muscle-specific expression cassette to produce high levels of midi-dystrophin exclusively in muscle cells.

Jeffrey Chamberlain, PhD, Kinea Bio co-founder and senior author, and professor of Neurology at the University of Washington, explains:

“Our goal is to use a midi-dystrophin or a full-length dystrophin transgene, which contain more functional protein domains than current micro-dystrophins, along with a muscle regulated & targeted AAV to increase transduction efficiency to muscle tissue and dramatically improve muscle function and quality of life for patients living with this genetic disorder. Our gene therapy approach potentially overcomes many of the limitations of currently approved and investigational micro-dystrophin replacement therapies and builds on the learnings and research from my lab that has helped to shape where gene therapy for Duchenne is today.”

Casey Childers, DO, PhD, Chief Executive Officer of Kinea Bio, adds:
“This publication in Nature provides compelling evidence that Kinea’s dual vector midi-dystrophin approach can provide improved benefits compared to micro-dystrophin replacement therapies currently on the market. Our goal is to advance the development of a midi-dystrophin product in the hopes of improving the health and function of dystrophic muscle in patients living with Duchenne.”

ABOUT KINEA BIO, INC.
Kinea Bio, Inc., located in Seattle, Washington, is a patient-dedicated gene therapy company focused on developing innovations to fight devastating neuromuscular diseases like Duchenne. Kinea strives to find new solutions for current limitations in gene therapy through advancing capsid engineering, muscle-specific expression cassette design, non-viral delivery, and gene-splicing technology. Kinea’s engineered myotropic AAV capsids together with a suite of muscle-specific promoters enable more effective dosing that can fine-tune the delivery of genetic cargo. Kinea’s protein splicing technology enables the delivery of genes previously considered undeliverable due to the size limitations of AAV vectors. This splicing innovation is especially important for treating Duchenne, for which previous treatments relied on truncated versions of the dystrophin gene.

Media Contact:

Seung Wook Oh, PhD
Kinea Bio, Inc.
swoh@kineabio.com
