Small Molecules That Facilitate Exon Skipping

Tech ID: 29874 / UC Case 2014-258-0

SUMMARY

UCLA researchers in the Departments of Microbiology, Immunology, and Molecular Genetics, and Human Genetics have discovered a novel small molecule therapy that facilitates treatment of Duchene Muscular Dystrophy.

BACKGROUND

Duchenne Muscular Dystrophy (DMD) is a genetic disorder caused by a mutation in the dystrophin gene. In DMD patients, muscles quickly degenerate, leading to muscle weakness and early death. The mutation typically found in DMD is a multiexon deletion which causes dystrophin protein levels to be unusually low.There is currently no cure, and steroids are currently the only therapeutic to help manage the symptoms.Gene and stem cell therapies are being tested in the lab but have yet to make it to the clinic. Antisense oligo therapy is currently being tested as a treatment option for DMD patients.These antisense oligos promote exon-skipping of the mutated region on a patient's dystrophin transcript, and thus, hoping to restore nominal dystrophin protein levels.This method has proven successful in mouse models of DMD and is currently being evaluated in clinical trials, however currently they appear to only restore minimal amounts of functional protein.Methods to improve exon-skipping in combination with antisense therapy would be highly beneficial to patients.

INNOVATION

UCLA researchers led by Profs. Stanley Nelson and Carrie Miceli have discovered a novel small molecule that supports antisense oligo therapy in inducing exon skipping, restoring dystrophin levels in cell culture and mouse models of DMD. Furthermore, this molecule is FDA approved and has been shown to have minimal side effects in DMD patients.Additionally, it was demonstrated that this adjunctive agent for antisense oligo therapy works through calcium signaling, a potentially safe mechanism of action.

APPLICATIONS

- An agent to facilitate antisense oligo therapy for DMD

ADVANTAGES

- Potentiates existing antisense oligo therapies
- Discovered from a library of FDA approved molecules, meaning its safe and approved for human use

STATE OF DEVELOPMENT

This novel agent has been validated in cell culture and mouse models for DMD.

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	9,982,260	05/29/2018	2014-258

RELATED MATERIALS

- G. C. Kendall, E. I. Mokhonova, M. Moran, N. E. Sejbuk, D. W. Wang, O. Silva, R. T. Wang, L. Martinez, Q. L. Lu, R. Damoiseaux, M. J. Spencer, S. F. Nelson, M. C. Miceli, Dantrolene enhances antisense-mediated exon skipping in human and mouse models of Duchenne muscular dystrophy. Sci. Transl. Med. 4, 164ra160 (2012).

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INVENTORS

- Nelson, Stanley F.

OTHER INFORMATION

KEYWORDS

antisense oligo, antisense therapy, antisense oligo therapy, Duchenne Muscular Dystrophy, DMD, exon skipping, adjunctive therapy, combination therapy, antisense exon skipping therapy

CATEGORIZED AS

- **Biotechnology**
  - Health
  - Other
- **Medical**
  - Disease: Musculoskeletal Disorders
  - Therapeutics

RELATED CASES

2014-258-0

▶ Barthelemy F, Wang D, Nelson SF, Miceli MC. Validation and Detection of Exon Skipping Boosters in DMD Patient Cell Models and mdx Mouse. Methods Mol Biol. 2018;1828:309-326. doi: 10.1007/978-1-4939-8651-4_19. PubMed PMID: 30171550.

▶ Wang DW, Mokhonova EI, Kendall GC, Becerra D, Naeini YB, Cantor RM, Spencer MJ, Nelson SF, Miceli MC. Repurposing Dantrolene for Long-Term Combination Therapy to Potentiate Antisense-Mediated DMD Exon Skipping in the mdx Mouse. Mol Ther Nucleic Acids. 2018 Jun 1;11:180-191. doi: 10.1016/j.omtn.2018.02.002. Epub 2018 Feb 13. PubMed PMID: 29858053; PubMed Central PMCID: PMC5992346.

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

▶ Small Molecules to Facilitate Therapeutic Exon Skipping

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