

Technology Opportunity, Ref. No. UA-22/027

Treatment of Congenital Myopathy

The technology relates to pharmaceutical compositions for the treatment of RYR1-related congenital myopathy.

- Keywords** congenital myopathy, RYR1 mutation, DNMT inhibitor, 5-aza'-2-deoxycytidine, class IIa HDAC inhibitor
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- Reference** <https://doi.org/10.7554/eLife.73718>
- Background** Congenital myopathies are rare neuromuscular disorders that are caused in approximately 30% of the patients by mutations in the RYR1 gene. Patients present a variety of symptoms and phenotypes depending on whether the mutations are dominantly or recessively inherited. Patients with recessive RYR1 mutations, for example, often display involvement of extraocular muscles leading to ophthalmoplegia and or ptosis as well as involvement of respiratory muscles, often requiring assisted ventilation. Severe forms of the disease are observed at infancy with major complications in every-day life. In addition to the depletion of RyR1 protein, muscles of patients with recessive RYR1 mutations exhibit striking epigenetic changes, including an increased content of HDAC-4 and HDAC-5 and hypermethylation of more than 3600 CpG genomic sites.
- Invention** The present invention relates to pharmaceutical compositions comprising an HDAC inhibitor, and/or a DNMT inhibitor, in particular 5-aza'-2-deoxycytidine, for the treatment of RYR1-related congenital myopathies. The pre-clinical proof-of-concept was achieved in an innovative and proprietary mouse model with knocked in RyR1 mutations, isogenic to those identified in a severely affected child with recessively inherited multi-minicore disease (MmD), a form of congenital myopathy. This model recapitulated not only the physiological and biochemical changes, but also the major muscle epigenetic signatures observed in muscle biopsies from multi-minicore disease patients. An investigator-initiated clinical trial is planned.
- Fields of Use** Treatment of RYR-1-related congenital myopathy
- Patent Status** patent application filed
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