

Germline Outline: Treating Muscular Dystrophy by editing germline DNA
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Problem: There is no cure for muscular dystrophy

- There is somatic gene therapy and PGD, but both are costly and not fully effective
- PGD is not applicable for couples that both have DMD

Solution: Germline modification to correct mutation in exon 23

- This is effective in mice
- Also provides insight into myofiber function after correction and beneficial for somatic cell therapy

Regulatory Issues: Not applicable in humans yet

- Long term effects are unknown
- Must be tested in larger animals

Proposed Regulations: Test on larger animals and perform long term studies

- Human testing should not be considered until percentage of correction is nearly perfect
- Apply these techniques to other genetic diseases such as cystic fibrosis and sickle cell anemia

References

1. Long, C., McAnally, J. R., Shelton, J. M., Mireault, A. A., Bassel-Duby, R., & Olson, E. N. (2014). Prevention of muscular dystrophy in mice by CRISPR/Cas9-mediated editing of germline DNA. *Science (New York, N.Y.)*, 345(6201), 1184–1188. doi:10.1126/science.1254445
2. Long, C., L. Amoasii, A. A. Mireault, J. R. McAnally, H. Li, E. Sanchez-Ortiz, S. Bhattacharyya, J. M. Shelton, R. Bassel-Duby, and E. N. Olson. 2016. Postnatal genome editing partially restores dystrophin expression in a mouse model of muscular dystrophy. *Science* 351(6271):400-403.
3. Nelson, C. E., C. H. Hakim, D. G. Ousterout, P. I. Thakore, E. A. Moreb, R. M. C. Rivera, S. Madhavan, X. Pan, F. A. Ran, and W. X. Yan. 2016. In vivo genome editing improves muscle function in a mouse model of Duchenne muscular dystrophy. *Science* 351(6271):403-407.
4. Fernández, R. M., Lozano-Arana, M. D., Sánchez, B., Peciña, A., García-Lozano, J. C., Borrego, S., & Antiñolo, G. (2017). Preimplantation Genetic Diagnosis for Myotonic Dystrophy Type 1 and Analysis of the Effect of the Disease on the Reproductive Outcome of the Affected Female Patients. *BioMed research international*, 2017, 9165363. doi:10.1155/2017/9165363