Gene Editing
A Strategy for the Future

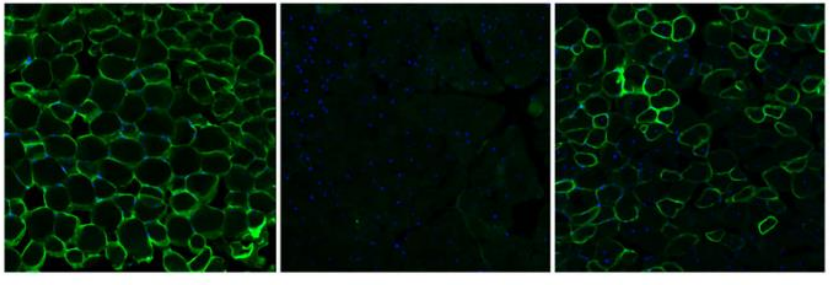
Parent Project Muscular Dystrophy
JOIN THE FIGHT. END DUCHENNE.

Kevin Flanigan, MD
June 30, 2018

SCIENCE

Gene Editing Offers Hope for Treating Duchenne Muscular Dystrophy, Studies Find

By NICHOLAS WADE DEC. 31, 2015



Three cross-sections of muscle tissue from mice. From left, normal, healthy tissue; tissue with Duchenne muscular dystrophy; and tissue after gene-editing treatment. Christopher Nelson

After decades of disappointingly slow progress, researchers have taken a substantial step toward a possible treatment for Duchenne muscular dystrophy with the help of a powerful new gene-editing technique.

Cite as: C. E. Nelson *et al.*, *Science* 10.1126/science.aad5143 (2015).

In vivo genome editing improves muscle function in a mouse model of Duchenne muscular dystrophy

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Cite as: C. Long *et al.*, *Science* 10.1126/science.aad5725 (2015).

Postnatal genome editing partially restores dystrophin expression in a mouse model of muscular dystrophy

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Cite as: M. Tabebordbar *et al.*, *Science* 10.1126/science.aad5177 (2015).

In vivo gene editing in dystrophic mouse muscle and muscle stem cells

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The CRISPR/Cas system

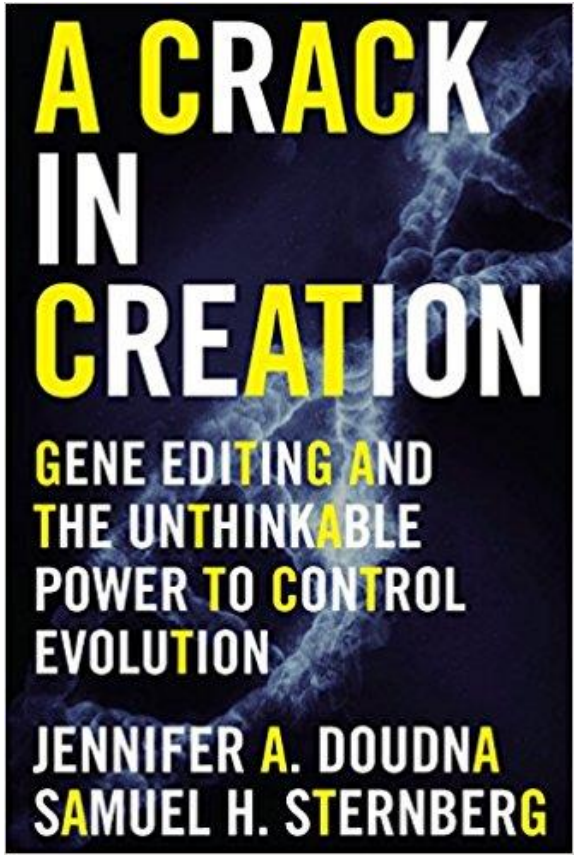
- **CRISPR: C**lustered **R**egularly **I**nterspaced **S**hort **P**alindromic **R**epeats
  - Originally identified in bacterial genomes
- CAS (CRISPR-associated system) genes
- Cas9: **nuclease** (protein that cuts DNA)
- Nuclease is targeted to a specific sequence by a guide RNA (gRNA)
- Cellular mechanisms exist to repair cuts in DNA
- Therapeutically those cuts are targeted so that repair results in a functional gene

Challenges for DMD therapy

- Targeting muscle – 40% of muscle mass – efficiently and specifically
- Delivery of the Cas9 and the guide RNA
  - Viral (AAV) using one or two vectors
  - Nanoparticles (gold)
- Relatively low efficiency of gene correction
- Avoiding off-target DNA cutting

- “CRISPR” isn’t a single treatment, but is a **platform** for therapeutic approaches – <u>one that holds enormous promise</u>.
- Somatic gene editing still faces pre-clinical efficacy, safety, and regulatory challenges before it will reach the clinic
- One can’t forgo standard of care therapies “waiting for CRISPR”.

Highly engaging and informative look at the science and ethics of CRISPR, intended for the interested lay reader



#PPMDConference

Thank you!