

Creation of a Novel Humanized Dystrophic Mouse Model of Duchenne Muscular Dystrophy and Application of a CRISPR/Cas9 Gene Editing Therapy.

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Public Summary:

Duchenne muscular dystrophy is caused by mutations in DMD which disrupt the reading frame. Therapeutic strategies that restore DMD's reading frame, such as exon skipping and CRISPR/Cas9, need to be tested in the context of the human DMD sequence in vivo. We have developed a novel dystrophic mouse model by using CRISPR/Cas9 to delete exon 45 in the human DMD gene in hDMD mice, which places DMD out-of-frame. We have utilized this model to demonstrate that our clinically-relevant CRISPR/Cas9 platform, which targets deletion of human DMD exons 45-55, can be directly applied in vivo to restore dystrophin.

Scientific Abstract:

Duchenne muscular dystrophy is caused by mutations in DMD which disrupt the reading frame. Therapeutic strategies that restore DMD's reading frame, such as exon skipping and CRISPR/Cas9, need to be tested in the context of the human DMD sequence in vivo. We have developed a novel dystrophic mouse model by using CRISPR/Cas9 to delete exon 45 in the human DMD gene in hDMD mice, which places DMD out-of-frame. We have utilized this model to demonstrate that our clinically-relevant CRISPR/Cas9 platform, which targets deletion of human DMD exons 45-55, can be directly applied in vivo to restore dystrophin.

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