CRISPR EDITING FOR TREATING
Duchenne muscular dystrophy

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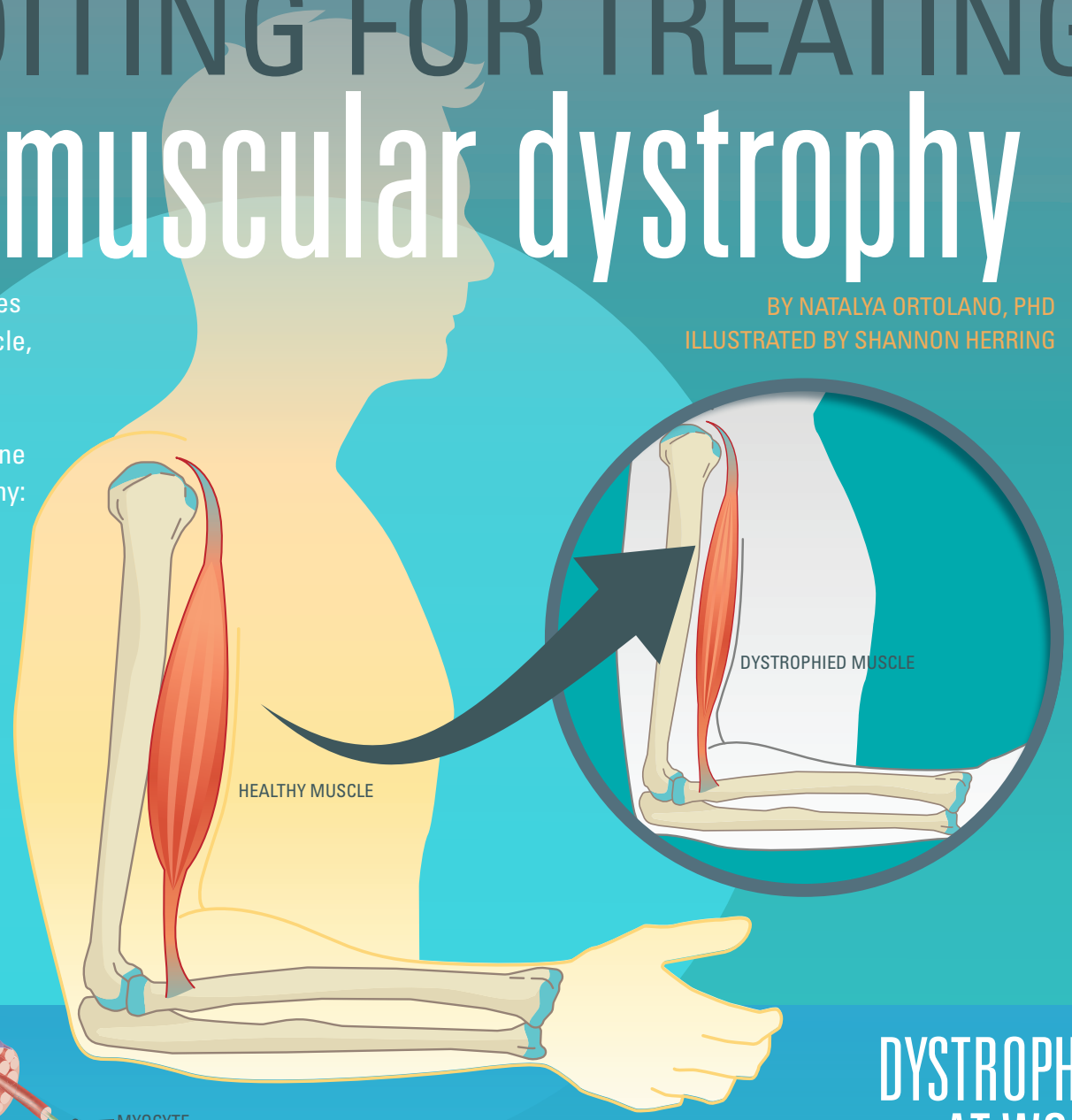
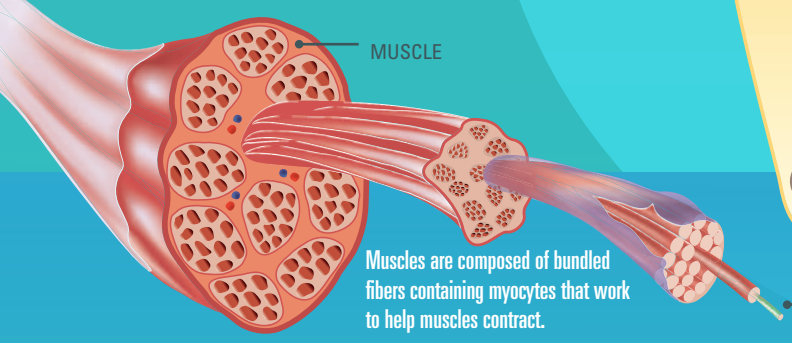
Muscular dystrophy is a group of genetic diseases that cause the progressive degeneration of muscle, resulting in symptoms such as difficulty walking, slow growth, learning disabilities, and heart problems. Mutations in the muscle-stabilizing gene dystrophin cause two types of muscular dystrophy: Duchenne muscular dystrophy (DMD) and Becker muscular dystrophy (BMD). Although DMD and BMD are caused by mutations in the same gene, BMD is less severe. BMD patients often reach their mid-40s, but DMD patients often succumb in their late teens or early 20s. Researchers use gene editing technology to make DMD mutations more like those found in BMD patients to lessen the disease severity.

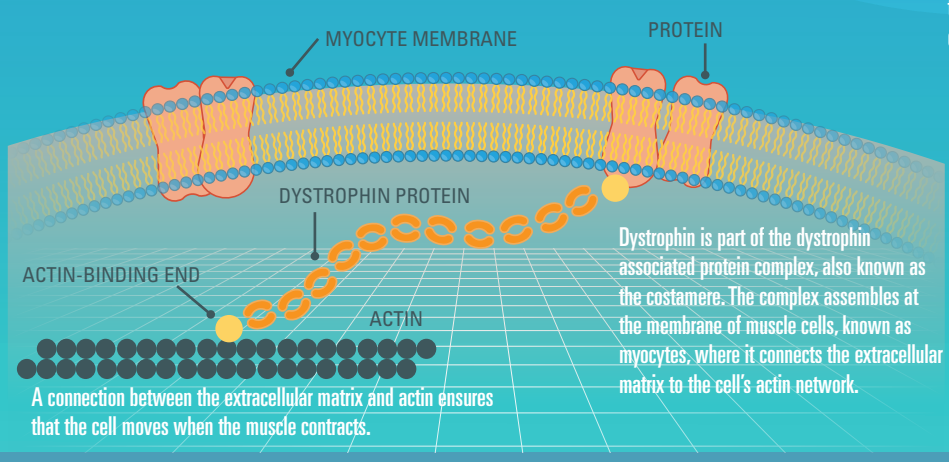




Muscles are composed of bundled fibers containing myocytes that work to help muscles contract.

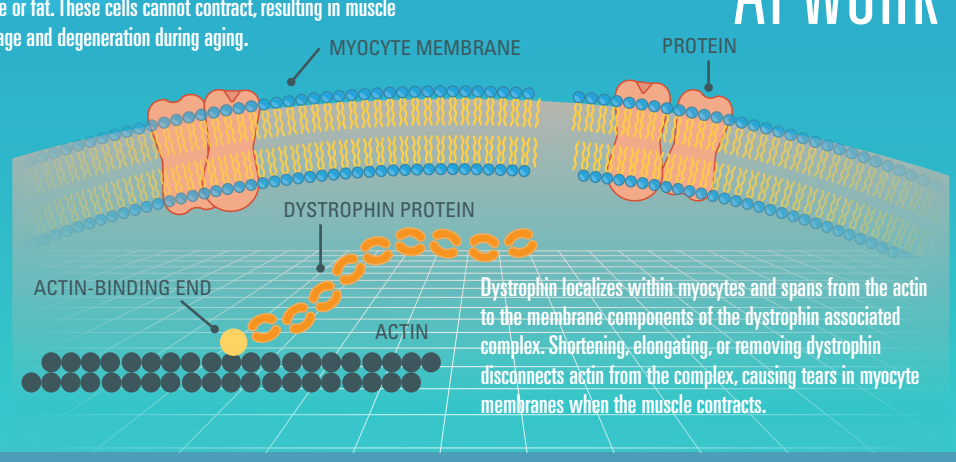
Damaged myocytes die and are often replaced by scar tissue or fat. These cells cannot contract, resulting in muscle damage and degeneration during aging.

DYSTROPHIN AT WORK



Dystrophin is part of the dystrophin associated protein complex, also known as the costamere. The complex assembles at the membrane of muscle cells, known as myocytes, where it connects the extracellular matrix to the cell's actin network.

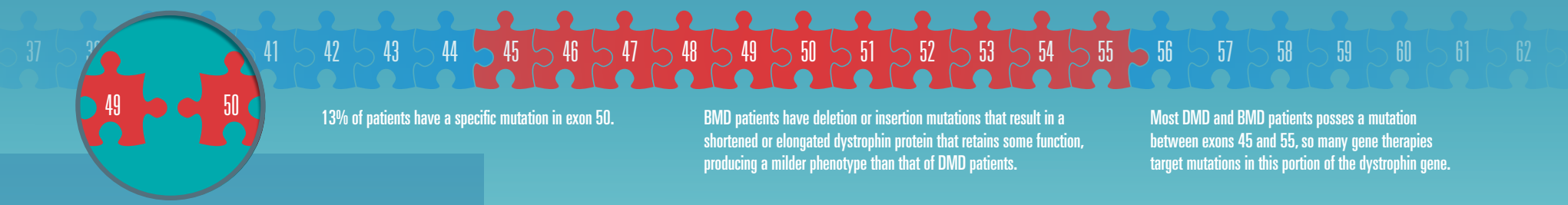
A connection between the extracellular matrix and actin ensures that the cell moves when the muscle contracts.



Dystrophin localizes within myocytes and spans from the actin to the membrane components of the dystrophin associated complex. Shortening, elongating, or removing dystrophin disconnects actin from the complex, causing tears in myocyte membranes when the muscle contracts.

DUCHENNE MUTATION

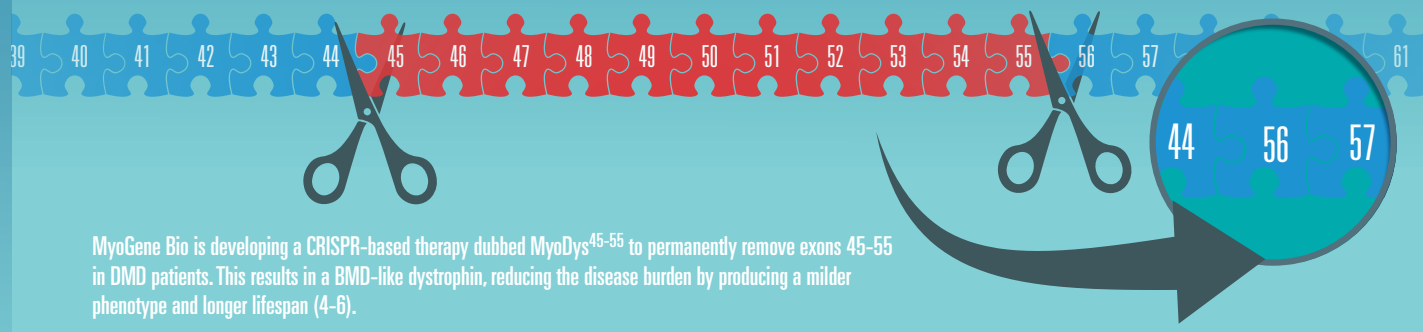
All DMD patients do not have the same mutation, but they all carry frameshift mutations that produce truncated dystrophin that does not function, or is quickly degraded (1).



13% of patients have a specific mutation in exon 50.

BMD patients have deletion or insertion mutations that result in a shortened or elongated dystrophin protein that retains some function, producing a milder phenotype than that of DMD patients.

Most DMD and BMD patients posses a mutation between exons 45 and 55, so many gene therapies target mutations in this portion of the dystrophin gene.



MyoGene Bio is developing a CRISPR-based therapy dubbed MyoDys$^{45\text{-}55}$ to permanently remove exons 45-55 in DMD patients. This results in a BMD-like dystrophin, reducing the disease burden by producing a milder phenotype and longer lifespan (4-6).

REFERENCES

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