amazing things PODCAST

REPAIRING THE GENES THAT CAUSE DUCHENNE MUSCULAR DYSTROPHY

Thousands of diseases are rooted in our genes, occurring when something goes wrong during cell multiplication and causes a mutation in the gene's DNA sequence. This is why researchers the world over heralded the 2012 revelation of the CRISPR-Cas9 system, a groundbreaking tool for editing faulty genes. CRISPR-Cas9 allows scientists with relative ease and precision to snip out a segment of mutated or damaged DNA, correcting genes that are disease-causing and opening the door to potential treatments for diseases where there currently are none.

Duchenne muscular dystrophy (DMD) is one of those diseases. Dr. Amy Wagers of the Harvard Stem Cell Institute has been looking at ways to use stem cells to treat DMD. Duchenne results from mutations in the gene on the X chromosome that encodes for a protein called dystrophin, which is necessary for proper muscle function and regeneration. Duchenne is a particularly debilitating and rapidly progressive form of muscular dystrophy affecting about 1 in every 3,500 male births worldwide. Most patients are confined to a wheelchair by their teens, and few survive to age 30.

Stem cells are unique in that they don't yet have a specific function in the body. Rather, they are what make it possible for us to recover after injury and repair and replace cells that are lost. Several years ago Wager's lab began looking at using stem cells to provide the missing dystrophin protein to muscle affected by Duchenne muscular dystrophy, essentially by transplanting cells from healthy muscle into diseased muscle. While promising, this approach requires finding a way to get enough muscle stem cells to treat all of the affected muscles and then getting those cells to all of the muscles in the body. Another way to achieve the same end is to edit the mutated dystrophin-encoding gene so that when stem cells replicate, the edited version of the gene is reproduced. Enter CRISPR-Cas9.

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REPAIRING GENES
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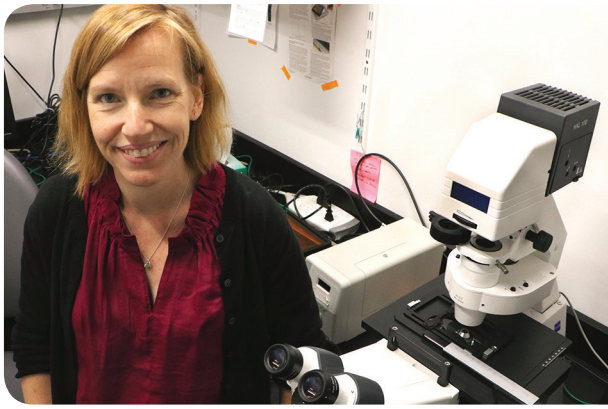

Building on previous work in the muscular dystrophy community demonstrating that the dystrophin protein can function with pieces of its middle missing, Wager's team used the new gene editing tool on mice bred with Duchenne muscular dystrophy. They wanted to see if simply cutting out the mutation that caused the loss of the dystrophin protein could restore expression of the DMD gene and production of the muscle-building protein; their experiment worked. They found that, despite missing a small chunk in the middle, the gene was still partially functional, and now had an improved capacity for protection against muscle damage.

While much work remains — studies in mice are not proof of effectiveness in humans — the findings by Wagers and her team are a momentous first step toward her goal of providing hope to patients and families affected by this devastating disease. "All you have to do is meet someone with the disease to understand that this is something worth dedicating your energy and your efforts to fighting," she said.

Wagers has received significant support from the National Institutes of Health throughout her career, including funding for the most recent mouse study. She credits an NIH "New Innovator" award early in her career as having had a "catalytic effect" on the direction of her work.

PHOTOS COURTESY OF AMY WAGERS