Muscle-Bound Boy Offers Hope for Humans

Scientists Work to Isolate Secrets of a Genetic Mutation That Could Alleviate Weakness Accompanying Disease and Aging

[FINAL Edition]

The Washington Post - Washington, D.C.
Author: Rob Stein
Date: Jun 28, 2004
Start Page: A.07
Section: A SECTION
Document Types: News
Text Word Count: 1086

As soon as he was born, doctors noticed something odd about the boy: He had unusually large muscles, which bulged from his little arms and legs.

Today, the 41/2-year-old is extraordinarily strong: Most children his age can lift about one pound with each arm -- he can hold a 6.6- pound dumbbell aloft with each outstretched hand. Otherwise, the boy appears normal, at least so far.

But scientists say the child is much more than a curiosity -- he could help them develop new treatments for a host of muscle disorders, most notably muscular dystrophy, and perhaps find ways to prevent the inexorable frailty that accompanies aging. He is the first human confirmed to have a defect in a gene that scientists have suspected could lead to new approaches for building muscles in people.

"This will certainly intensify efforts to move forward aggressively on this research," said Se-Jin Lee, a professor of molecular biology and genetics at the Johns Hopkins Medical Institutions in Baltimore, who helped study the boy.

At least one drug company, Wyeth Pharmaceuticals, has begun preliminary testing of a drug designed to mimic the effects of the defective gene as a possible treatment for the most common form

of muscular dystrophy, a devastating muscle disease that primarily afflicts boys.

At the same time, the discovery is raising concerns that athletes and body-builders will try to exploit the discovery to enhance their abilities, and some companies are already marketing products that claim to use the approach.

"Athletes find a way of using just about anything," said Elizabeth M. McNally of the University of Chicago, who wrote an article accompanying the findings in last week's New England Journal of Medicine. "This, unfortunately, is no exception."

The new research on the muscle-bound German boy follows work reported in 1997, when Lee and his colleagues used genetic engineering to create a breed of mouse with muscles at least twice as big as those of normal mice.

The rodents, dubbed "mighty mice," created a sensation. They also triggered a flurry of research by scientists hoping to use the work to help cure human ailments, including muscular dystrophy, cachexia - - a muscle-wasting condition that affects cancer and AIDS patients - - and perhaps the normal muscle weakening that comes with aging, called sarcopenia.

"That's a major health problem throughout the world. As people get older, and weaker, they are more susceptible to falling down and breaking bones, and those things have major health consequences," Lee said.

In agriculture, researchers hope it could lead to genetically engineered animals that would provide more meat. "If we could interfere with this gene in livestock, the idea was that we could improve meat production," Lee said.

In fact, scientists quickly determined that some breeds long prized for their massive muscles, such as Belgian Blue cattle, had naturally occurring mutations in the same gene the scientists altered to produce the mighty mouse.

The gene's instructions direct muscle cells to produce a protein known as myostatin, which regulates the growth of new muscle. When the gene is deactivated, muscles grow unusually large.

But while the findings in animals raised hopes that the gene played the same role in humans, there was no direct evidence of that.

"All this work was going on the assumption that . . . it would have applications in humans. We were all going on the assumption that it worked the same way in humans," Lee said. "But there was no proof."

That changed with the birth of the unusually muscular boy in Berlin. Markus Schuelke, a neurologist at the Charite University Medical Center in Berlin, was called to the hospital shortly after the boy's birth. When tests determined there was nothing else wrong with the boy, Schuelke contacted Lee and his colleagues and another team at Wyeth.

A detailed genetic analysis and blood tests determined that the boy's myostatin genes were damaged, and that he had none of the protein circulating in his blood.

"This is now the first case of a human with a myostatin mutation that's been identified," Lee said. "We think this is quite important, because it says for the first time that myostatin does in fact play an important role in regulating muscle growth in humans. The implications are that people will be more optimistic about the possibility of targeting myostatin for human therapeutic applications."

As it turns out, the boy's mother, a former sprinter, has one damaged version of the gene. He has two. No other family members were tested, but several are reported to be unusually strong. One male relative, for example, was a construction worker renowned for his ability to unload heavy curbstones by hand.

It could turn out that subtle variations in the myostatin gene explain why some people are more muscular, stronger or more athletic than others, McNally said.

"We all know that we're a little different that way. This is a good candidate gene for modulating some of that," McNally said. "There may be more subtle mutations that only slightly affect muscle growth."

Several dietary supplements are already on the market that claim to affect myostatin and help build muscles. None, however, has been shown to work, Lee said, adding that he was concerned that if drugs become available that affect myostatin, they could be subject to abuse.

"Unfortunately, I think anything that we do along these lines to improve muscle mass in patients will almost certainly have the potential for abuse by healthy individuals," Lee said. "We're going to have to work hard to make sure these drugs don't get into the wrong hands. But the potential for helping patients in dire need is important. I think it would be unfortunate to focus on that and slow the research down."

It is unclear whether the boy, whose identity is being withheld, will suffer problems later in life. One fear is that the lack of myostatin could cause his body to use up its natural supply of replacement muscle cells prematurely.

"We fear it might happen that this regenerational capacity of the muscle might be exhausted too early," Schuelke said. "It's like an account you live on, and if you live on it too lavishly you don't have enough for old age."

But inasmuch as no one has ever encountered a child such as this boy or studied animals with defective myostatin genes into old age, his health -- and eventual strength -- remains unknown.

"We don't really know," Schuelke said. "We'll just keep observing him and making tests."