Boy's brawn raises hope for treatments

Blocking of a protein could encourage growth in human muscles
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A remarkably brawny German toddler has given researchers new insight into human muscle growth - knowledge that could lead to breakthrough therapies for muscular dystrophy and other diseases, perhaps even for diabetes and obesity.

These potential treatments, involving a protein that controls muscle growth, could also have a dark side, giving athletes yet another chemical means to boost their performance.

In a study published today in the New England Journal of Medicine, scientists reported on a 4-year-old boy with a genetic mutation that allows his skeletal muscles to grow unusually large. His body produces no myostatin, a naturally occurring protein that blocks muscle growth.

Researchers knew that myostatin regulates muscle in animals, but this was the first time the protein has been shown to affect humans. The study raises hopes that myostatin-blocking treatments could encourage muscle growth.

"It's a huge step," said Johns Hopkins University geneticist Se- Jin Lee, one of the study's authors. "Based on animal studies, we thought it worked in humans. But there was lingering uncertainty."

Ever since Lee and another Hopkins researcher discovered myostatin seven years ago, scientists have studied the chemical as a potential treatment for diseases that destroy muscle.

Most have focused on muscular dystrophy, a genetic illness that progressively damages skeletal muscle. There is no effective treatment, and most patients die in their 20s from a combination of heart and breathing problems.

A 2002 study found that mice with a version of the disease improved after being given myostatin blockers. But no one was sure whether myostatin had an effect on humans. By confirming it, the new study will spur more research, Lee said.

"It's a big step," said Dr. Elizabeth McNally, a muscular dystrophy specialist at the University of Chicago.

Wyeth Pharmaceuticals has created a protein that disables myostatin, and is beginning a human safety trial of the substance, known as MYO-029. The company, which has a patent on all human therapeutic uses of myostatin, is also planning a study with muscular dystrophy patients.

"There's a big medical opportunity in this," said Wyeth biochemist James Tobin, who is overseeing the research. Tobin was also involved in the study of the German boy.

The child's condition was discovered the day he was born, when a doctor became concerned that the infant's unusually well-defined muscles might be a sign of illness.

Pediatric neurologist Markus Scheulke examined the boy and found him normal, but by chance he had read one of Lee's myostatin papers and wondered whether the infant had an abnormal myostatin gene. Tests confirmed his suspicion, and Schuelke contacted Lee and Wyeth about his discovery.

At first, doctors worried that the absence of myostatin would cause physical problems, perhaps impairing the boy's heart. But so far, he seems normal, except for his physique and strength.

The condition is inherited, at least in part: His mother, 24, was a professional sprinter, and several other family members are muscular.

Doctors believe myostatin blockers could treat other muscle- related diseases, including an age-related muscle loss known as sarcopenia and an aggressive variant called cachexia, which afflicts cancer and HIV patients, among others.

Researchers have also found lowering myostatin levels in mice significantly decreases obesity and improves symptoms of Type 2 diabetes.

Unknowingly, humans have been modifying myostatin genes for more than a century by breeding several varieties of beef cattle known for their bulging muscles and lack of fat. In tests, these "double- muscled" breeds, which include Belgian Blue and Piedmontese, displayed an altered myostatin gene and produce almost none of the substance.

If they work on humans, myostatin blockers will almost certainly find another use - as an athletic performance booster. Researchers say such compounds would likely provide a significant advantage.

"It's going to have a lot less side effects than steroids, and probably bigger effects on muscles," said University of Pennsylvania physiologist H. Lee Sweeney, who studies a related hormone called IGF-1, which spurs muscle growth.

"I wouldn't be surprised if somebody out there isn't [already] trying to block myostatin in some of these athletes," said University of Maryland geneticist Stephen Roth, who is studying how the protein works.

Despite the illicit potential, scientists emphasize that myostatin blockers would help many desperate patients. Says Lee: "There are people in dire need."

[Illustration]
Photo(s); Caption: 1. In breeding, humans have developed the bulging Belgian Blue cattle, which produce almost no myostatin. 2. A genetic mutation allows this 7-month-old baby's muscles to become unusually well-defined.; Credit: 1. PHOTO COURTESY OF THE JOHNS HOPKINS UNIVERSITY 2. NEW ENGLAND JOURNAL OF MEDICINE

Credit: SUN STAFF

Abstract (Document Summary)

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