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ONE STRONG TYKE

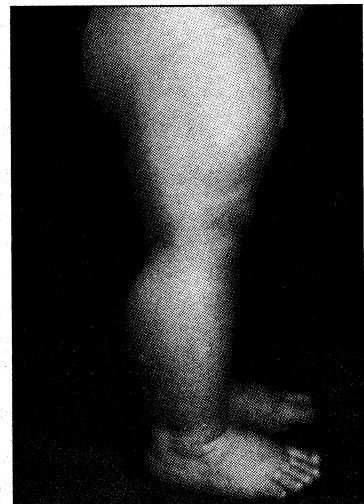
## Gene mutation in muscular boy may hold disease clues

By Andreas von Bubnoff  
Tribune staff reporter

He has the look of an überkid, a 4-year-old version of Arnold Schwarzenegger.

But to scientists, the German boy is something more: the first confirmed case of a human with a genetic mutation that removes a fundamental barrier to muscle growth, causing a markedly pumped-up body and unusual strength. Already, he has twice the muscle mass of children his age and can lift weights that some adults would find challenging.

More important, experts say the boy's condition, described Thursday in the New England Journal of Medicine, sheds light on basic questions about how muscles form. That could lead to



New England Journal of Medicine

**At 7 months, this boy's muscles were big due to a mutated gene. At 4, he's fit and strong.**

treatments for muscle-wasting diseases such as muscular dystrophy or for muscle deterioration related to age and illness, such as cancer and AIDS.

The myostatin gene affected in the boy's condition has long been suspected to inhibit muscle growth, based on experiments in mice and cattle, but

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# MUSCLE: Boy comes from unusually strong family

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this is the first case to illustrate the gene's role in humans.

The boy's abnormality was discovered by Dr. Markus Schuelke at the Charité Hospital in Berlin on the day of the boy's birth in 1999.

"It was just chance," said Schuelke, the lead author of the study. "There was a child on our neonatal ward that was trembling with his arms and legs. We first thought he might have epilepsy."

The trembling went away after a couple of weeks, Schuelke said, but he noticed the boy was very muscular.

Schuelke and his colleagues suspected that the boy might have a mutation in the myostatin gene because they were aware of earlier research involving mice. In 1997, Dr. Se-Jin Lee of Johns Hopkins University's School of Medicine had shown that eliminating the myostatin gene in mice leads to muscle overgrowth.

Schuelke collaborated with Lee's group and Wyeth Pharmaceutical Co. in Cambridge, Mass., to prove that the boy's genetic mutation resulted in loss of the myostatin protein.

The finding is important because researchers often are unsure whether genes shown to have an effect in animals produce the same results in people, experts said.

"This really says pretty clearly for the first time that myostatin plays an important role in regulating muscle growth in humans, as we already knew to be the case in both mice and cattle," Lee said.

Elizabeth McNally, a University of Chicago muscular dystrophy researcher not involved in the study, said the finding

"does make people feel a lot better about pushing this pathway for therapeutic intervention" in humans—such as in the treatment of muscular dystrophy, a class of genetic diseases leading to muscle wasting.

Drugs that inhibit myostatin have the potential to help people with muscle-wasting conditions by spurring muscle growth to counteract the degeneration. Studies have demonstrated that when an antibody that inhibits myostatin is injected into mice with a genetic defect similar to one form of muscular dystrophy, the mice show improvement.

"The mice didn't lose as much muscle," Schuelke said.

There are many forms of muscular dystrophy. Patients with

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—Dr. Se-Jin Lee

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the most common and severe form, called Duchenne muscular dystrophy, carry a mutation in a muscle protein called dystrophin.

"By the time they are 10 or 12 they are in a wheelchair, and then eventually their breathing muscles go," McNally said. "Later they get heart-muscle weakness as well."

Wyeth Pharmaceuticals started a Phase I clinical trial a few weeks ago in which healthy human volunteers are injected with an antibody—dubbed myo-029—that inhibits myostatin, said Gerald Burr, vice president of scientific communications at Wyeth.

Scientists involved in the re-

search caution that treating muscular dystrophy with myostatin inhibitors would not necessarily cure patients of the disease, because the new muscle generated would still be sick.

"We don't expect this to cure the disease, but we expect that this could have an effect on longevity," said James Tobin, a researcher at Wyeth involved in the study.

Other than being especially muscular, the German boy looks none the worse for his atypical genes, and his doctors say he has suffered no obvious ill effects.

He is "a normal, vibrant boy," Schuelke said. "He goes to school next year."

It's unclear, however, whether his genetic abnormality might eventually harm his health. Too much muscle growth theoretically could hamper the heart's pumping, but the myostatin gene has less of a role in the heart than in other muscles. Schuelke said the boy has had no heart problems.

Other members of the boy's family are also unusually strong, though not to the same degree. His mother was a sprinter competing at the national level, and the boy's grandfather was a construction worker who could unload curbstones from his truck by hand.

The boy's condition is the result of carrying two mutated copies of the myostatin gene. His mother has only one such mutation.

The 4-year-old can hold a 6.6-pound dumbbell in each hand with his arms extended, the researchers write in their report.

"That's a lot," Schuelke said. "Have you tried?"

The new findings are likely to spur renewed debate about possible abuses, such as creating genetically engineered athletes. But Schuelke believes that is easier said than done.

"It's a long way off," he said.

Screening for mutations in the gene to identify potential athletes, however, could be feasible.

"That will happen, I think," Schuelke said.