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July 18, 2001

Genetically Engineered 'Mighty Mice' May Shed Light on Muscle-Wasting Diseases

Four years ago, a group of Johns Hopkins researchers created a line of genetically engineered "mighty mice" by removing a growth-regulating gene. Now they have engineered another batch of overly muscular rodents. The first set of mice (*see image*) lacked the myostatin gene from their genetic codes. But in the new research, published in the July 17th issue of the *Proceedings of the National Academy of Sciences*, the pumped-up mice retained their myostatin. Instead the scientists altered the animals' physiques by tweaking three proteins capable of blocking myostatin's activity to varying degrees.

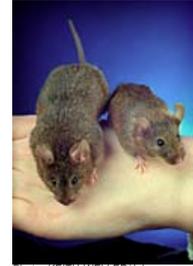


Photo: KEITH WELLER/Johns Hopkins Medical

Myostatin acts as a negative regulator of skeletal muscle mass. If it is unable to function, muscles can grow uninhibited. Mice engineered to produce excess amounts of the protein follistatin had the most powerful muscles: one such mouse exhibited average muscle weights 261 percent greater than control animals. Mice with excess mutant activin II receptors and those with myostatin propeptide also showed increased muscle mass compared with their ordinary mousy counterparts.

"By expressing high levels of these proteins in mice, we have been able to increase muscle mass to levels comparable to those seen in mice completely lacking myostatin," Se-Jin Lee, the study's lead author, says.

Because the function of myostatin appears to be conserved across species, the researchers are hopeful that the findings will be beneficial in shaping treatments for muscle-wasting diseases. Lee cautions, however, that more testing is necessary to determine whether administering the proteins directly, instead of altering the genome, can provide similar results. "The agricultural implications are probably more straight forward, since conceivably, one could try to find ways to block myostatin activity early during development," he says. "For human applications, this research is just the beginning."

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