

Myostatin Protein and Skeletal Muscle in Mice

In 1997, scientists McPherron, Lawler, and Lee identified a protein in the muscles of animals. The protein is called myostatin. They thought this protein was related to the heavily muscled phenotype in some animals. So, they decided to test their thinking using mice. They found the specific region of the chromosome - called a gene - that they thought was correlated with the myostatin protein. They changed the shape of this specific gene on the chromosome in a few mice cells using a technology called gene targeting. Gene targeting allowed the scientists to swap a “donor” piece of genetic information that had the structure they wanted with the “target” piece of genetic information to give it a different shape.

This shape change to the gene created a different allele of the gene - a different version of it. After a while, the cells with the different allele had proteins that were similar to the original myostatin, but a little bit differently shaped. The scientists predicted that this differently shaped protein would not do the same job as the typical one.

To test their thinking, they raised mice who had this different allele of the gene for myostatin. Some of the mice in the study only had one changed allele (along with one typical one), some had two copies of the changed allele, and some had two copies of the typical allele (which is how they were naturally without any copies of the allele that had been changed). The combination of copies of an allele is called an organism’s genotype. The mice in the study whose genotype at the myostatin gene was two copies of the changed allele also only had the differently shaped version of the myostatin protein. They also weighed 2-3 times more than the mice with the typical genotype. When the scientists counted the fibers in samples of the mice’s leg muscles, the mice with the double-copy changed-allele genotype had 86% more muscle fibers than the typical mice had. So, the scientists concluded that changing the gene resulted in the cell producing the differently shaped myostatin protein, which then resulted in mice with the heavily muscled phenotype.

Summarized from:

McPherron, A., Lawler, A. & Lee, S. Regulation of skeletal muscle mass in mice by a new TGF- β superfamily member. *Nature* 387, 83–90 (1997) doi:10.1038/387083a0