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## Mighty mice could yield human treatments

**Super-sized animals may pave way for new drugs and bigger livestock.**

**Michael Hopkin**

It might sound like a cartoon scene from *Tom and Jerry*, but a biologist has come up with a real-life genetic recipe to create mice with four times more muscle than normal.

The mutant mice, created by Se-Jin Lee of Johns Hopkins University School of Medicine in Baltimore, Maryland, have two key genetic differences compared with normal mice. They cannot produce a protein called myostatin, and they produce too much of another protein, follistatin. Both changes boost muscle mass in mice.

The muscly mice differ significantly from normal mice — their muscle fibres are more than twice the size, and they have 73% more of them, Lee reports in the journal *PLoS One*<sup>1</sup>.

The fact that muscle mass was boosted in two ways — both the number and size of muscle fibres — is good news for medical researchers who are looking for ways to restore muscle in people with diseases such as muscular dystrophy, AIDS or cancer, Lee adds.

### Double whammy

Myostatin restricts muscle development, which is why mice without this protein tend to bulk up. And follistatin binds to myostatin, possibly preventing its action, which is why Lee was investigating its effects. But he did not expect the mice to become so huge when given both treatments at once.

The fact that follistatin boosts muscle development in the absence of myostatin suggests that there is more than one mechanism. Mice also have higher levels of myostatin than people, notes Lee, suggesting that the protein is less important in humans. "In humans it's virtually undetectable — that's always left a nagging feeling," Lee says. "Clearly, there are other players."

If biologists can identify more proteins to which follistatin binds, it could spawn new and more-promising drugs for boosting muscle development in humans. So far, efforts to develop a drug that targets myostatin have not met with much success, although the drug company Wyeth is trialling an antibody-based treatment that could relieve muscular dystrophy by cancelling out myostatin's effects.

### Muscle madness

Drugs to preserve human muscle mass could also help elderly people to avoid losing their muscle, Lee suggests. "It's not that people want to create 80-year-old Schwarzeneggers — it's just that elderly people get weak, and they can fall over and break their hip."

The discovery might also add to livestock breeders' idea of what creates muscular animals, which could help in breeding cattle or sheep that carry lots of meat. Several 'double-muscle' breeds, such as Belgian Blue cattle and Texel sheep, carry mutations in the myostatin gene.

The spectre of drug-enhanced sporting performance also looms over Lee's field of research. Clearly, any development that offers the prospect of more muscle growth will be tempting to athletes. Although no drug has yet been passed for human use to boost these muscle-development pathways, Lee says that there is no guarantee that people are not already experimenting with such compounds.

"I certainly wouldn't recommend it or attest to it even working," he says. "But there's this whole subculture [of risky drug-taking in sport] out there that's crazy. This will be an issue and will be a challenge [to regulatory authorities] for sure."

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Mutant mice (right) are massively more muscular than normal ones (left).

*Se-Jin lee*

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## References

1. Lee, S.-J., *Plos One* **8**, e789 (2007).

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