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Next-Generation Sports Doping

New drugs in clinical trials for muscle-wasting diseases could become the next big thing for athletes.

By Emily Singer

Two new classes of experimental drugs shown to have powerful muscle-building capabilities--selective androgen receptor modulators (SARMs) and myostatin inhibitors--have been added to the [World Anti-Doping Agency \(http://www.wada-ama.org/en/\)](http://www.wada-ama.org/en/)'s (WADA) list of prohibited substances for 2008. Neither class of drugs is yet on the market. But the agency, an international, independent organization based in Lausanne, Switzerland, that coordinates anti-doping regulations across sports, is gearing up for future abuse by limiting use among athletes and by developing new detection methods. "We now have convincing data on those drugs and what they can do," says [Olivier Rabin \(http://www.wada-ama.org/en/dynamic.ch2?pageCategory_id=306\)](http://www.wada-ama.org/en/dynamic.ch2?pageCategory_id=306), science director at WADA. "We have a duty to act as early as we can when drugs have the potential to be doping agents."

Unlike with testosterone and other anabolic steroids, the action of SARMs and myostatin inhibitors is restricted to muscle, likely limiting side effects. That's a very good thing for patients, but it also makes the drugs more attractive to those looking to bulk up. "I think there's a whole new horizon for anabolic therapies, and the potential for abuse will be exceedingly high," says [William Evans \(http://centeronaging.uams.edu/faculty/detail.asp?offset=10&ID=62\)](http://centeronaging.uams.edu/faculty/detail.asp?offset=10&ID=62), director of the Nutrition, Metabolism, and Exercise Laboratory at the University of Arkansas for Medical Sciences.

Compounds of both classes are currently in clinical trials for muscle wasting related to diseases such as cancer and muscular dystrophy. There have been no official reports of athletes using these drugs, but because there previously have been cases of athletes gaining access to compounds in clinical development, WADA officials say that they want to act early.

SARMs work similarly to testosterone but in a more targeted way. "They are effective by binding to the steroid receptor in only specific tissue, like muscle," says Evans, who is also a scientific advisor to [GTx \(http://www.gtxinc.com/\)](http://www.gtxinc.com/), a company developing the drugs. "They are not steroid drugs, but they produce the anabolic effect of the steroids." GTx, based in Memphis, TN, has shown in a clinical trial that one compound being developed for muscle wasting and bone loss can significantly boost lean muscle mass in older people.

Myostatin inhibitors work through a fundamentally different mechanism. They block myostatin, a naturally occurring protein in the body that stops growth of skeletal muscle. Cattle, sheep, dogs, and, in one confirmed case, a human with mutations in this gene are extremely muscular. (See "[Mimicking the Massively Muscular \(http://www.technologyreview.com/Biotech/19589/\)](http://www.technologyreview.com/Biotech/19589/)".)

Scientists have developed antibodies to myostatin and other molecules that can boost lean muscle mass in animals by as much as 60 percent. It's not yet clear how well myostatin inhibitors will work in humans. Clinical studies of two myostatin inhibitors are now under way for muscular dystrophy and other muscle-wasting diseases.

WADA is developing detection methods for both SARMs and myostatin inhibitors, although the agency declined to say how far along those tests are. "In fairness to athletes who stay clean, we don't say when detection tools are available," says

Rabin. "We say when we detect the first athletes using the drugs."

Other groups are more public about their progress. [Acceleron](http://www.acceleronpharma.com/content/company/index.jsp) (<http://www.acceleronpharma.com/content/company/index.jsp>), a company based in Cambridge, MA, that is developing a myostatin inhibitor, says that it has already developed a test for research purposes that is capable of detecting the drug in blood. And scientists at the Center for Preventive Doping Research, [German Sport University Cologne](http://www.dshs-koeln.de/index_neu.htm) (http://www.dshs-koeln.de/index_neu.htm), are working on a test for SARMs.

Fortunately, scientists say that detecting abuse of these two new classes of drugs is likely to be easier than detecting two doping agents that have plagued the sports world in recent years. Erythropoietin, which stimulates growth of red blood cells and is used to treat anemia patients, is processed quickly by the body, making it difficult to detect. Human growth hormone, which boosts cell growth, is a naturally occurring hormone. Tests must be able to discriminate between the natural hormone and the pharmaceutically derived version. "People who are trying to cheat like to use a steroid naturally present in the body, because it makes it much more difficult for labs to detect," says Don Catlin, founder of [Anti-Doping Research](http://antidopingresearch.org/index.html) (<http://antidopingresearch.org/index.html>), a nonprofit research institute based in Los Angeles.

Myostatin inhibitors present a particularly interesting case for WADA. In 2004, scientists published a paper describing an abnormally muscular German toddler who carried mutations in both copies of his myostatin gene. The boy's mother, who had been a professional athlete, was found to have one defective copy of the gene, raising questions about how to deal with athletes who have naturally occurring genetic mutations that give them benefits similar to those offered by performance-enhancing drugs. "We have ethicists thinking about those issues and guiding us in the future," says Rabin. "We need to maintain fair play for all competitors." The issue is likely to grow as advances in genomics allow scientists to uncover additional variants linked to muscle, or other factors related to athletic ability.

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