DNA `edge' creates new sports worry

Scientists concerned about `gene doping'
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For years after he won two gold medals in the 1964 Winter Games, Eero Mantyranta was dogged by rumors of deceit: The Finnish cross- country skier had something in his blood, people whispered, something that had given him an edge.

He never failed a drug test - but the rumors turned out to be true.

Scientists eventually discovered that Mantyranta harbored a rare mutation in his DNA, a genetic quirk that caused his body to crank out more red blood cells than the average athlete. The extra cells bathed his laboring muscles in oxygen, providing the boost he needed to glide past competitors.

Now, on the eve of the Winter Games in Salt Lake City, sports officials and scientists fear the day may not be far off when athletes born without such lucky genes could simply add them later, cheating not with drugs but DNA.

It's called "gene doping," and the idea behind it is simple: to hijack gene therapy techniques for curing disease to become better, stronger, faster. Unlike drugs, such genetic tinkering would be all but impossible to detect, scientists say.

Nobody expects genetically enhanced super jocks to turn up in Salt Lake City - the technology isn't there yet. But the World Anti- Doping Agency, which leads the charge against drugs in sports, is concerned enough about future events that it's planning a summit on gene doping next month in New York. Officials are eager to gain an edge on dishonest athletes, but after more than three decades of playing catch-up, few are optimistic.

"Athletes are probably already ahead of us," says Theodore Friedmann, director of the human gene therapy program at the University of California at San Diego and a conference organizer. "They've always used whatever they needed to win. Death is a secondary consideration."

Ancient Greek athletes, historians know, popped hallucinogenic mushrooms. Roman gladiators took the equivalent of speed before entering the Circus Maximus. Victorian-era jocks routinely used a variety of performance-enhancing chemicals, including caffeine, alcohol, nitroglycerine, ether, heroin, cocaine - even strychnine, a stimulant more famous for its role in rat poison.

Although drug tests for racehorses were initiated as early as 1910, doping

among two-legged athletes was mostly ignored until the 1960s, when drugs were blamed for a rash of high-profile deaths in international cycling. The first Olympic drug tests were conducted in 1968 at the Mexico City games.

Officials ban a long list of stimulants, narcotics, steroids, hormones and beta blockers. Most are detectable with a urine or blood test - 3,500 of which are being given to Salt Lake City athletes before the opening ceremonies this week. The notion of genetically engineered athletes may sound like science fiction, but researchers working on therapies for atherosclerosis, cystic fibrosis and other diseases have pinpointed genes that have the potential to become popular in the locker room.

Take research subject No. F66-52, aka "Mighty Mouse."

Caged in the cluttered and somewhat smelly laboratory of Johns Hopkins molecular biologist Se-Jin Lee, F66-52 is not your ordinary rodent. As Lee attempts to remove the furry brown lump from its pen, Mighty Mouse clings stubbornly to the cage bars. "He's just flexing to show off," jokes Lee.

But it's true: This rodent is ripped. Every time F66-52 squirms, thick knots of muscle ripple visibly beneath its shoulders and rump. An unaltered mouse cowering in the corner of a nearby cage looks wimpy by comparison. To create Mighty Mouse, Lee and his team blocked the action of myostatin, a gene the Hopkins researchers have found plays a key -albeit mysterious - role in muscle development. Blocking the gene causes muscles to balloon. The strongest of these genetically altered mice have four times the muscle mass of a typical rodent and weigh about 30 percent more, Lee says.

The genetic tinkering hasn't resulted in any noticeable health problems - although, Lee says, his muscle-bound mice appear a tad more docile. Like other scientists working with so-called "Schwarzenegger" mice, Lee hopes his research leads to new drugs for people with muscular dystrophy, cancer and other conditions that cause muscles to wither. But he knows the sick aren't the only ones who may find myostatin irresistible. "Clearly, there's going to be the potential for abuse," Lee says.

Genes that beef up muscles would be ideal for sprinters, lifters and athletes who need quick bursts of power. Marathoners, cross- country skiers and others who prize endurance could get a boost from genes that affect the blood.

One candidate is VEGF, or vascular endothelial growth factor, a substance that triggers blood vessels to sprout. Although researchers hope it might help people with clogged arteries and other circulation troubles, scientists fear the gene could be hijacked by athletes to pipe more blood to their muscles. Marathoners, notes molecular biologist Peter Schjerling of the Copenhagen Muscle Research Center in Denmark, typically have four times more blood vessels feeding their muscles than sprinters. So when it comes to boosting endurance, "the more blood vessels you have, the better," he says.

Athletes also are probably eyeing the gene for erythropoietin, or EPO, a hormone that regulates red blood cell production. Synthetic versions of the hormone, used by doctors to treat anemia, have become one of the most widely abused drugs in sports today. The allure of EPO is simple: By boosting the number of oxygen-carrying red-blood cells, muscles stay fresher longer. (EPO is what skier Eero Mantyranta's body overproduced as a result of his genetic quirk.)

Gene therapy experiments with erythropoietin in animals have shown promise. In one University of Chicago experiment, scientists boosted red blood cell

concentration in mice to 81 percent from 49 percent with a single injection of the EPO gene. Even a year later, the mice's red blood cell levels remained high.

But after more than a decade of research and hundreds of experiments, gene therapy for humans has succeeded in treating only a couple of disorders. (Athletes take notice: One of them involves the VEGF gene.) And there have been other setbacks: A University of Pennsylvania volunteer died during an experiment in 1999. The biggest hurdle has been delivering the therapeutic gene to the cells. To do it, researchers often turn to one of nature's most efficient DNA delivery services for help: the virus.

A virus makes a person sick by inserting its genetic material into the DNA of its host. In gene therapy, scientists disarm the virus, replacing its genetic material with the therapeutic gene they want to deliver. But even if they get the virus to deliver the gene to the right target in the body, researchers face problems. "Once you turn the gene loose, how are you going to turn it off?" asks Donald Catlin, director of Olympic Analytical Lab at the University of California, Los Angeles.

Most genes in the body aren't designed to be continuously switched "on," but therapeutic genes delivered by a virus are always on. And that, says Catlin, could prove deadly.

With erythropoietin, for example, an always-on EPO gene could flood the blood with so many red blood cells that it turns as viscous as syrup, increasing the risks of clots and strokes. In one EPO gene- therapy experiment on baboons, scientists were forced to constantly dilute the animals' blood to keep them alive. (For similar reasons, the synthetic drug has been blamed for the deaths of more than 20 cyclists since 1987.)

If athletes did pull off gene doping, it might be all but impossible to detect, says Catlin, whose office oversees testing for the U.S. Olympic Committee and others. Because engineered genes would look identical to natural ones, officials would need to find other evidence, such as the virus that delivered the gene. To do that, says Catlin, officials would have to know the precise spot where the virus was injected, a process that would probably require a muscle biopsy.

Sports officials, who have encountered resistance to getting urine and blood samples, doubt that athletes would surrender a piece of muscle. Even if they did, that sample might not provide ironclad evidence because one of the most popular gene therapy delivery vehicles is the virus that causes the common cold.

Some scientists have begun to discuss - only half in jest - whether the only way to stop cheating might be to lift the ban on doping altogether. Without a black market for rogue drugs, the argument goes, at least fewer athletes might die.

"There will always be those who cheat, whether it's on their income taxes or anything else," says Dr. Gary Wadler, author of Drugs and the Athlete. "It gets back to the issue of money, fame, fortune."

But opening the door to gene doping and other performance- enhancing drugs would probably mean whole new record books and a very different Olympics. "We've actually been joking that we should have an Olympics competition of scientists," says Schjerling. The theme? "Who can make the best athlete by any means."

[Illustration]
PHOTO(S) / CHART(S); Caption: 1. Muscle-bound: The strength of a mouse at a Johns Hopkins lab has been genetically enhanced. 2. The future of athletic cheating; Credit: 1. JOHN MAKELY : SUN STAFF 2. LAMONT W. HARVEY : SUN STAFF

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Abstract (Document Summary)

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