New Gene Therapy Fights Frailty

By age 40, every man and woman begins losing muscle. Over the next 3 to 5 decades, this process—known as sarcopenia, or "vanishing flesh"—inexorably transforms even the most hale individuals into frail elders. While exercise can slow the weakening that accompanies this loss, there has been no way to halt the muscle wasting.

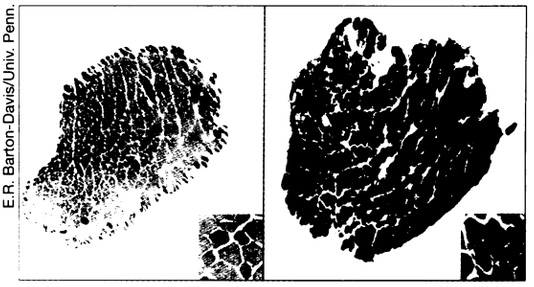
New research now suggests that this unrelenting process may be stoppable.

Working with mice, which experience a similar loss of up to 30 percent of their skeletal muscle during aging, scientists applied a novel gene therapy. They inserted DNA for a hormonelike substance into a virus gutted of the capacity to cause disease. The researchers then injected the virus into the right, back leg of young, middle-age, and elderly animals. They then observed the rodents, which were kept sedentary, for 3 to 9 months.

Comparing the treated leg with its left counterpart, they found roughly 15 percent more mass and strength in the right leg of young adult animals. In geriatric mice, the effect was even more pronounced: They showed 19 percent more muscle mass and 27 percent more power in the treated leg .

"Though I expected improvement in the old animals, I never dreamed we would basically preserve them at young-adult levels," says study leader H. Lee Sweeney of the University of Pennsylvania School of Medicine in Philadelphia. His team presented its findings Dec. 14 at a meeting in San Francisco of the American Society for Cell Biology. A report of the work also appears in the Dec. 22 PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES.

Previous studies suggested that sarcopenia might trace to a drop in the body's production or ability to use insulinlike growth factor 1 (IGF-1), explains Anna M. McCormick of the National Institute on Aging in Bethesda, Md. Normally secreted by injured muscle, this hormonelike substance recruits nearby satellite cells—local repair crews—to mend routine, small muscle rips (SN: 8/10/96, p. 90).



E.R. Barton-Davis/Univ. Penn.

Four months after gene therapy: Cross-section of untreated leg (left) and treated leg (right) from a 6-month-old mouse.

The new findings don't prove that an IGF-1 deficiency causes sarcopenia, says Nadia Rosenthal at the Cardiovascular Research Center of Massachusetts General Hospital in Charlestown, a member of Sweeney's team. However, she notes, this gene therapy "can arrest [muscle] degeneration and atrophy due to aging." And while it works in both young and old animals, she says, to get the most benefit, "the younger the better."

"This is exciting," says Charlotte A. Peterson of the University of Arkansas in Little Rock. "It's the first case of a molecule affecting muscle atrophy due to aging," she says. The technique used to provide it "is the closest anyone has come to something you might consider using as a therapy [for people]," she adds.

McCormick agrees that it's "a great proof of principle. But as with any gene therapy, we have a long way to go."

Still, "these dramatic findings signal a fountain-of-youth opportunity," says neurologist Leon I. Charash of Cornell University Medical College in New York City. He is a medical advisor to the Muscular Dystrophy Association, which funded Sweeney's team. The finding holds out the prospect, he says, "of helping older people lead healthier and better lives, with less need for medical care."

Rosenthal is also excited by the technique's potential use in helping aging cardiac muscle repair damage from a heart attack. Sweeney notes it may even help limit some of the wasting caused by the milder forms of muscular dystrophy.

However, because the treatment's effects are local, treating a human to prevent frailty might require hundreds of injections to augment all the skeletal muscles vulnerable to aging. Cardiac therapy would need far fewer injections. In either case, Sweeney says, "you'd only have to do it once." —*J. Raloff*

Fishing trawlers scrape rock bottom

Fishing boats in search of shrimp, flounder, and other bottom-dwelling seafood delicacies drag heavily weighted nets along the seafloor. Creatures not snared are crushed, buried, or exposed to predators. Marine researchers now say such trawling worldwide destroys a seabed area twice the size of the contiguous United States each year.

"Nobody had a clue that it was nearly this extensive," says Elliott A. Norse of the Marine Conservation Biology Institute in Redmond, Wash. The complete damage report appears in a suite of articles in the December CONSERVATION BIOLOGY.

Norse had long suspected that damage from bottom trawling is in the ballpark with that from clear-cutting forests on land (SN: 10/26/96, p. 268), but his new calculations show that it's 150 times more widespread. Logging flattens an area about the size of Indiana yearly.

Since the 1970s, new technology has allowed fishing fleets to trawl deeper. Not adapted to storm waves and other trials of shallow-water life, creatures in deep waters take longer to grow and recolonize than their near-shore relatives. Norse predicts that the deepest areas of the trawled seafloor may take as long as clear-cut forests to recover—from decades to centuries.

Skeptics point out that such estimates stem from incomplete research. "While we know species diversity from the trawl area drops, other species tend to thrive afterward," says Scott Smullen of the National Marine Fisheries Service in Silver Spring, Md. Smullen says that before sounding an alarm, his agency is trying to find out more about trawling's long-term effects on fish habitat. Norse and others are pushing to set aside areas for immediate protection. —*S. Simpson*

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A seafloor community before (left) and after a trawling net crashed through.