

TRANSGENIC SPECIES

Engineered Fish: Friend or Foe of the Environment?

With the world's fish consumption rising, transgenic fish might alleviate pressure on wild stocks. But researchers worry that genetically engineered fish, if they escaped, could wreak ecological havoc

In fine weather, the floating pens full of salmon bob gently off the coast of Maine. They're designed to take the brunt of a storm, but a fierce nor'easter that hit Machias Bay in December 2000 was too much for them. The pens' steel rims gave way, and some 100,000 fish escaped. Fearing that the runaways would interfere with the few remaining wild salmon, conservationists demanded a moratorium on new fish farms in the state. Feral fish have also plagued North America's west coast, where an estimated half-million salmon escaped from 1987 to 1997; since then, farm-raised salmon have been found spawning in British Columbia.

Farmed salmon are big, hungry, and aggressive. When they were added to an experimental stream in a 2000 study, the number of native cousins dropped by a third. And imported alien species on the lam from farms have been known to overrun native species (*Science*, 23 November 2001, p. 1655). Researchers are paying renewed attention to such escapes as they debate the future of a new type of farmed fish: transgenic species. They have the potential to be even more of a menace than existing farmed fish. No genetically engineered fish are commercially farmed yet, but a modified Atlantic salmon is under review by the U.S. Food and Drug Administration (FDA), and others are nearing commercialization elsewhere. Says Eric Hallerman of Virginia Polytechnic Institute and State University in Blacksburg: "It's my sense that transgenic fish will go forward in some places in the world whether Greenpeace likes it or not."

Outfitted with an extra gene for growth hormone, the engineered salmon grow up to six times as fast as other domesticated salmon. That growth rate, and a 20% gain in efficiency at converting food to flesh, could offer fish farmers bigger profits. Broadly applied, such technology might provide better yields for developing countries, reduce pollution from fish farms, and ease pressure on wild fisheries. Yet a question lingers in the minds of many scientists: What would happen if the fish escaped?

The answer is unclear. A study* released

by the National Research Council (NRC) last month cited environmental impact—in particular, by highly mobile creatures such as fish—as the greatest risk associated with animal biotechnology (*Science*, 23 August, p. 1257). Bulk-up transgenic fish might out-compete wild fish for food. If outfitted with genes for cold tolerance, they could spread to

Image not available for online use.

Yearning for freedom. Fish raised in pens (right) have escaped to join their wild kin (above).

more extreme latitudes like an invasive species. And if they interbred with wild fish, any number of scenarios could result, including local extinction of natives.

To get a handle on those risks, scientists have been testing transgenic fish in the lab. Some have used hormone patches to simulate the effects of transgenes and then studied how well the fish survive in the wild. Others have taken a more theoretical approach by modeling what might happen to population genetics if transgenic fish escaped and interbred. Commercial developers insist that the risk is negligible, as transgenic fish currently in development will be sterilized. But most scientists say they simply don't yet

understand enough about the potential ecological impacts to approve of raising even sterile transgenic fish in the seas, as some producers propose. "It's a realm of unknown risks," says William Muir, a geneticist at Purdue University in West Lafayette, Indiana.

The contenders

One thing is certain: Demand for seafood is rising, and it might double by 2040, according to the Food and Agriculture Organization of the United Nations. Many wild fisheries are already depleted, so much of the supply will likely come from aquaculture, says James Carlberg of Kent SeaTech Corp. in San Diego, California. But intensive aquaculture has its troubles. For instance, when fish are crowded together, disease becomes more common and can spread to wild fish.

Transgenics offer potential solutions, and researchers around the world have been after them for more than 2 decades (*Science*, 2 August 1991, p. 512). Many kinds of fish have been engineered, some for disease resistance but most for faster growth. In Cuba, for example, molecular biologist Mario Pablo Estrada García of the Center for Genetic Engineering and Biotechnology in Havana and colleagues have added a viral promoter to tilapia, a freshwater fish from Africa, to increase expression of a native gene that codes for a growth hormone. In the lab, the fish grow twice as fast as domesticated tilapia. The group is a few years away from commercializing the fish, García says. Another group, led by

Norman Maclean of the University of Southampton, U.K., has tested a different type of growth-enhanced tilapia in field trials in Hungary. On average, the transgenic tilapia were three times heavier than nontransgenics at harvest. And Zhu Zuoyan of the Chinese Academy of Sciences' Institute of Hydrobiology in Wuhan has been working on fast-

growing transgenic Yellow River carp engineered to carry a growth hormone gene from grass carp. Field trials demonstrated that the first-generation offspring grow 42% faster than nontransgenic carp.

The most famous transgenic fish is a growth-enhanced Atlantic salmon made by Aqua Bounty Farms Inc. of Waltham, Massachusetts. By adding a growth hormone gene from Chinook salmon along with a promoter sequence, the company has creat-



* *Animal Biotechnology: Science-Based Concerns.*

ed a line of Atlantic salmon that can produce growth hormone all year long rather than just during spring and summer. The modified fish put on weight up to six times as fast as traditional hatchery salmon. Although the fish don't end up larger than normal farmed Atlantic salmon, they reach market size up to a year sooner. Before the company can sell eggs or young fish to farmers, FDA must give approval. Aqua Bounty has begun to submit safety data for human consumption, says the company's Joseph McGonigle. FDA hasn't published any guidelines for genetically modified fish and says it will use the recent NRC report on animal biotechnology to develop its regulations.

Predicting trouble

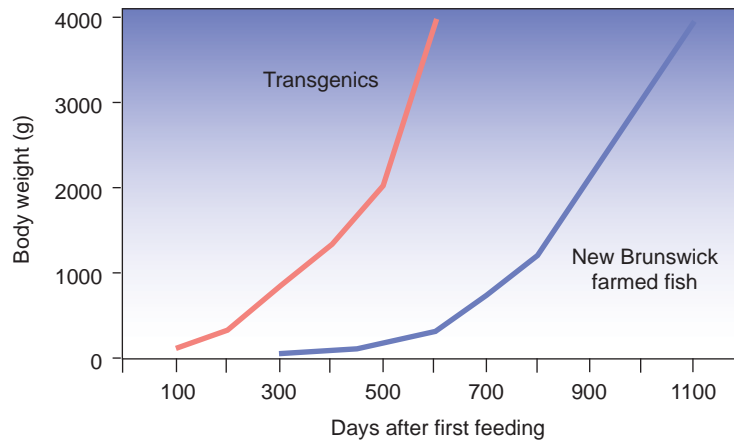
Aqua Bounty fish aren't likely to endanger human health: The transgenic growth hormone is identical to that already consumed in Chinook, and growth hormones are destroyed by cooking and digestion anyway, McGonigle says. But the environmental safety of transgenic fish raises more questions. In trying to answer them, many researchers have examined transgenic fish in the lab for traits that might influence their activity in the wild. Some of the results suggest that transgenic fish would outcompete natives. For instance, a study by molecular biologist Robert Devlin of the governmental organization Fisheries and Oceans Canada in West Vancouver, British Columbia, revealed that transgenic salmon eat almost three times as much food as nontransgenic peers of the same size.

Still, researchers say it's a stretch to conclude that the fish would sink wild fish, given the narrow range of conditions in the lab. "It's virtually impossible to scale up from these experiments to the real world," says Mart Gross, a conservation biologist at the University of Toronto.

To get a more realistic view, Jörgen Johnsson of Göteborg University, Sweden, and colleagues have studied brown trout in experimental streams. Because genetically engineered fish may not be released in the wild, they use fish with implants that slowly release growth hormone. Over 1 year, growth-enhanced trout grew 20% faster than wild trout and survived just as well, Johnsson's group reported last year in *Functional Ecology*. That result ruled out an earlier suggestion that growth-enhanced fish

might be more susceptible to predators or might starve from growing out of season, and it adds to fears that transgenics might outcompete wild fish, Johnsson says.

Other problems could arise if transgenics interbred with wild relatives. A model of population genetics developed by Muir and Richard Howard of Purdue calculates the likelihood that a transgenic fish would spread its genes. The program crunches just a few key measures of an animal's fitness: the age at which it reproduces, the likelihood that it will survive that long, its fertility or fecundity, its ability to attract mates,



Growth spurt. Engineered fish (largest individual, *right*) outpace nontransgenic brethren.

and how many times it might breed.

The mix can generate surprising results. In a 1999 paper in the *Proceedings of the National Academy of Sciences*, Muir and Howard reported that even if a transgene decreased one component of a fish's fitness, it could still harm a native population. For instance, a transgene that makes young fish less likely to survive but boosts their ability to mate if they do would still spread through a population. As transgenic fish mated with wild ones, both populations would shrink, generation by generation, until they disappeared.

But others caution against making decisions based on models at this time. "The models may be past our ability to plug in reliable data, so maybe we shouldn't be using them for management," Devlin says. Virginia Tech's Hallerman points out that there aren't enough data yet on Atlantic salmon or other species of interest to make it meaningful to run Muir's model. Complicating matters is the fact that the effect of a transgene can depend heavily on a fish's genetic background. This variability

was demonstrated by an experiment by Devlin's group, published in *Nature* last year. When rainbow trout were given a gene for growth hormone, wild fish put on much more weight than did domesticated ones. Among coho salmon, in contrast, the domesticated fish bulked up more than wild ones. Because different populations of a species can vary substantially in their response to certain gene products, Devlin says, a given genetic enhancement might not pose the same risk for all members of a wild stock. Muir notes that there isn't an alternative to the model at the moment: "It represents our best guess, and perhaps that is all we can do."

The safest approach to transgenic aquaculture, of course, would be to raise the fish in tanks on land. But the added cost—an increase of about 40%—would make it difficult for producers to compete with conventional marine salmon farmed off, say, Chile or Tasmania. So in its proposal to FDA, Aqua Bounty suggests a compromise: raising fertile broodstock in secure facilities on land and sending only sterilized fish to sea pens for rearing.

Opponents say the plan is still too risky. Aqua Bounty sterilizes eggs in pressure chambers, a process that adds an extra set of chromosomes, and says it achieves 100% effectiveness. But that's in lab conditions with only thousands of eggs, treated by experienced operators. Muir and others suspect that at the industrial scale, some eggs would be bound to become fertile females. Practically speaking, "there isn't anything such as 100% sterility," says Sue Scott of the Atlantic Salmon Federation in St. Andrews, New Brunswick, Canada. What's necessary, argues Anne Kapuscinski of the University of Minnesota, Twin Cities, is to have multiple barriers, such as sterility plus confinement on land.

"We've spent a decade developing and testing transgenic fish, and we're still not confident in our risk assessment," says Devlin, who has no plans to commercialize his lab's fish. Other researchers say the technology has a lot to offer: "I view it as a hopeful process for biodiversity, because it will ease harvesting pressure on wild populations," says Gross. The enhanced productivity of transgenic fish might make their advent—in at least some corners of the world—as likely as the rise of biotech plants.

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