washingtonpost.com

Gene-Altered Mice Create Healthful Oils

Omega-3 Advance Could Be Applied to Foods

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Thursday, February 5, 2004; Page A03

Scientists in Boston have created a line of genetically engineered mice that make their own omega-3 fatty acids -- healthful oils, typically found in fish, that mice, humans and other mammals cannot normally make on their own.

The scientists have no interest in adding mice to the menus of health food restaurants, though the meat from these gene-altered mice is now about as heart-healthy as a piece of salmon. Nor do they advocate adding the omega-3 gene to humans -- an enhancement that would endow people with the capacity to convert the unhealthful fats in their diets into healthier oils but would open a Pandora's box of ethical concerns.

They do, however, foresee a future in which cattle will be engineered to have the gene in their muscles so a slab of beef could have a fat profile similar to that of a piece of salmon -- and without worries about mercury or other ocean contaminants that have recently plagued the seafood industry.

The Boston team also foresees putting the gene into chickens, to make leaner eggs, and into cow mammary tissues so the milk produced by those cows would be rich in omega-3s.

Omega-3 fatty acids have been shown to lower the risk of heart disease and other chronic conditions in humans.

But the immediate goal, the researchers said, is to put the gene into farmed salmon. Although fish are famed for being rich in omega-3s, even they cannot make those good compounds themselves. They get them by eating algae -- tiny floating plants packed with omega-3s.

Farmed fish are not free to graze on algae and are generally fed vegetable oils, which makes their meat hardly more healthful than that of other farm animals. To make up for that, fish farmers typically add ocean-derived fish meal to their farmed fishes' food -- an approach that is expensive and inefficient, requiring two to three pounds of fish meal to make one pound of farmed fish rich in omega-3s.

"If we put this gene into live salmon and then just give them vegetable oil, they can make the omega-3s themselves, and they'll be healthier and they'll be healthier to eat," said Jing X. Kang, the Harvard Medical School cell biologist who led the mouse study, which appears in today's issue of the journal Nature.

Kang and his colleagues started with a gene isolated from a tiny, soil-dwelling worm called *C. elegans*, an organism able to make its own omega-3 fatty acids from less healthful omega-6 fatty acids. Omega-6s are the prevalent fats in today's human diet.

They injected copies of that gene into mouse embryos and then placed the embryos into the wombs of surrogate mother mice to develop into mice with the unprecedented capacity to make omega-3s from the omega-6s in their diet. Their offspring inherit the same capacity.

Conventional mice fed conventional, fish-free diets have 20 or more times as much omega-6 fatty acids as omega-3 fatty acids in their muscles, blood and breast milk -- a ratio similar to that found in humans eating a standard American diet. That ratio has been linked to chronic inflammation, heart disease and related problems.

But with their newfound capacity to convert one fatty acid to the other, the engineered mice lowered their omega-6 levels and raised their omega-3 levels to the point where they had about equal amounts of each in their bodies -- a healthy 1-to-1 ratio that scientists believe is about what humans had thousands of years ago.

The mice seemed to suffer no ill effects, Kang said.

"This could be an enormous step forward for animal nutrition and for the nutritional value of animal products," said Norman Salem, a laboratory chief at the National Institute of Alcohol Abuse and Alcoholism, who studies fatty acid chemistry.

As fish, cows and other farm animals have been fed higher amounts of vegetable oils over the years, their meat has become increasingly unhealthful for humans, Salem noted. But there is another way that may help reverse that trend, he said: Change the fat profiles of the plants being fed to those animals.

Plant biotechnologists are already tackling that challenge, said David Stark, a vice president at Monsanto Co. in St. Louis, one of several companies pursuing the goal. Canola oil especially rich in mono-unsaturated fat -- the kind that makes olive oil healthful -- is already on the market, he noted. And scientists have begun to endow soybeans with an omega-3 gene like the one in Kang's mice.

Animals fed the engineered beans would produce milk and meat with more healthful fat profiles. But perhaps most important, Stark said, omega-3-rich soybeans could have a direct impact on heart disease rates, because more than 80 percent of the oil in the American diet comes from soybeans.