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Mice gene research aims at modified food

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MGH scientist sees a potential method to improve nutrition

By Gareth Cook, Globe Staff, 2/5/2004

A scientist at Massachusetts General Hospital said yesterday that he has genetically altered mice to produce a healthy compound found in fish oil and hopes to use the technology on other animals to create a new generation of more nutritious meat, eggs, and milk.

The challenging procedure, described in today's issue of the journal *Nature*, takes DNA from a tiny worm and places it in the mice, giving them the ability to turn common nutrients into omega-3 fatty acids. Omega-3s, which are found in salmon and other fatty fish, are known to protect the heart.

The research, led by MGH's Dr. Jing X. Kang, would have to overcome many scientific and government hurdles before heart-healthy T-bones are a reality at the local supermarket. But the advance could be a sign of the fast pace of progress in genetic engineering as well as a harbinger of a coming debate over its proper role in the food we eat.

The potential stakes for the public, proponents and critics agree, are enormous: Modified food could prevent a wide range of diseases without the need to coax people onto restrictive diets, and it could cause unforeseen health and environmental problems.

"There is an awful lot of research that needs to be done before this could have any benefits for humans," said Jane Rissler, a senior staff scientist with the Union of Concerned Scientists in Washington, D.C.

The Food and Drug Administration has approved a variety of genetically engineered plants -- including tomatoes, potatoes, corn, and soy -- for human consumption.

It has not approved any genetically modified animals for consumption, though a handful of such projects are underway, including one at Aqua Bounty Technologies in Waltham, which has engineered salmon to grow faster.

Kang and other scientists believe that the modern diet is too low in omega-3s and is too rich in a related family of fatty acids known as omega-6s.

In prehistoric eras, humans probably ate a diet, including wild plants and animals that fed on them, which was more balanced between the two, said Dr. Artemis P. Simopoulos, a former nutrition researcher at the National Institutes of Health and leading proponent of the health benefits of omega-3s. The products of modern agriculture, and especially processed foods, are tilted heavily towards omega 6s.

Kang, an associate professor at Harvard Medical School, has long sought to understand how omega-3s function in the body.

In addition to preventing heart attacks, a growing body of research suggests they may have broader protective effects, such as fighting against arthritis, neurodegenerative diseases, and some cancers.

Kang knew that researchers had identified a gene that can transform omega-6s into omega-3s in a widely studied worm, *C. elegans*. He and colleagues at the hospital took this gene, called "fat-1," and then made subtle modifications to it so that it could function in the mouse. This gene was inserted into the nucleus of the mouse embryo cell.

The resulting mice had dramatically more omega-3s throughout their body, including the muscle, heart, and

milk, according to the paper in Nature.

The omega-3s were present in the right levels and the right forms to be potentially beneficial if eaten, said Joyce Nettleton, an omega-3 specialist and nutrition scientist who works as a consultant in Denver.

The mice were able to reproduce, and their offspring had the same trait, Kang said. The mice appeared healthy, but the team has not done extensive testing on them, Kang said.

To be viable as a food technology, scientists will have to transfer the gene into other animals, a challenging step that could have unforeseen consequences.

The gene could cause health problems for the animals, said James D. Murray, professor in the department of animal science at the University of California, Davis.

Even if that hurdle is cleared, Murray said, genetically modifying the fat content of animals can change the taste and texture in ways that consumers might find unacceptable.

For example, he said there is a genetic mutation in some sheep that makes their hindquarters very large, and the meat's taste is less appealing.

With genetic engineering, scientists have no choice but to do all the work, prove it is safe, and then get the government's permission to feed it to humans before they know how it tastes.

"The only way to do that it is to put it to a taste panel," said Murray, who has genetically engineered the milk-producing cells in goats so that their milk contains healthier fats. Murray's goal is to do the same in cows.

Kang hopes to try inserting the gene into a salmon, so that farmed salmon can produce their own omega-3 and be raised using vegetable products instead of fishmeal, avoiding some health concerns. He also hopes to try chickens soon if he can find collaborators. "I don't have a farm in my lab," Kang said.

Yet even if the omega-3 technology is never used in food animals, the modified mice could help solve human health problems, Kang and other scientists said.

The mice give researchers a convenient model for testing how omega-3s work to fight disease. Underway are several experiments to see whether the omega-3 mice are more resistant to cancer.

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