

**Online**

News from Harvard Medical, Dental, and Public Health Schools

September 1, 2006

[Back Issues](#)

[Contact Us](#)

[Keyword Search](#)

[Calendar](#)

### [Immunology](#)

Regulatory T Cells Tactful in Controlling Killer Cousins

### [Genetics](#)

Gene Linked to Beak Length in Darwin Finch

### [Molecular Medicine](#)

Light Shone on Disease-fighting Effect of Omega-3s

### [Resources](#)

Drosophila RNAi Screening Center Flies into the Future

[Research Briefs](#)

[Molecular Switch](#)

[Regulates Fat, Cholesterol](#)

[Metabolism](#)

[Corneal Transparency](#)

[Made Clearer](#)

[Bulletin](#)

## MOLECULAR MEDICINE

### Light Shone on Disease-fighting Effect of Omega-3s

*Benefit Seen in Raising Ratio of Omega-3 to Omega-6 Fatty Acids*

Omega-3 fatty acids regularly make headlines for their potential to prevent diseases such as arthritis, cardiovascular disease, depression, asthma, inflammatory bowel disease, and cancer. But as intriguing as the news is, the medical community has not been racing to take advantage of these fats' therapeutic potential, perhaps because studies have been equivocal and have not answered questions about how the fats work in the body. Recently, research on the effects of omega-3s has begun to bring them into the realm of molecular medicine.

Two years ago, Jing Kang, HMS associate professor of medicine at Massachusetts General Hospital, revealed a transgenic mouse that converts omega-6 fatty acids into omega-3s. These mice generated a great deal of interest as a tool for studying the effect of changing the ratio of essential fats in the diet—something that has been hypothesized to be important for health. Since then, Kang's group as well as several other laboratories have begun to use the mice to study a variety of diseases. Kang's lab recently published two papers in *Proceedings of the National Academy of Sciences* showing that higher levels of omega-3 fatty acids protect mice from colitis and slow melanoma growth.

For both studies, he collaborated with Charles Serhan's lab at Brigham and Women's Hospital, which has been uncovering specific molecules produced by omega-3 fatty acids that actively dampen inflammation. These studies "nicely demonstrate in molecular terms why you need to eat your tuna fish," Serhan said.

#### **Fatty Acid Pathways**

The mice that Kang's lab developed borrow the gene *fat-1* from worms. The gene encodes an enzyme that can slip an extra double bond into an omega-6 fatty acid, turning it into an omega-3. This seemingly minor change in chemistry brings a major change in function.

Both omega-6 and omega-3 fatty acids are considered essential for normal development and function and must be found in food. Both of the fats get converted into a host of substances that have far-reaching impacts on the body. "The two classes of fatty acids compete for the same enzymes," said Kang, including cyclooxygenase, the



Photo courtesy of Jing Kang

**Jing Kang developed mice that can do what no other mammals can: create their own endogenous omega-3 fats. The mice let researchers study the benefits of omega-3s in the body without changing diets.**

[HMS Researchers Gain Millions from Gates Foundation to Develop HIV Vaccine](#)

[Two at HMS Receive Freedom to Discover Awards](#)

[Martin Wins International Prize for Innovation in Health Care](#)

[New Appointments to Full Professor](#)

[Honors and Advances](#)

[News Briefs](#)

[In Memoriam](#)

[Forum](#)

[Cancer Vaccine Gears Up for Global Delivery](#)

[Front Page](#)

target of COX-2 inhibitors. Most scientific attention has focused on the omega-6 pathway, which produces several classes of molecules that mediate inflammation, such as pro-inflammatory prostaglandins and thromboxane. This pathway, as the intended target of COX-2 inhibitors, has been a major subject for drug development.

Meanwhile, despite epidemiological and clinical evidence for the actions of omega-3 fatty acids, they have not received the same attention. Many people have assumed that omega-3s are beneficial simply because they counteract the effects of omega-6 fatty acids. But the lab of Serhan, the Simon Gelman professor of anesthesia at HMS and BWH, has recently uncovered potent products biosynthesized from omega-3 fatty acids, called resolvins and protectins, that counteract inflammation. The discovery of these molecules is important, Kang said, because it shows the function of omega-3s is “not just to compete with omega-6. The metabolites of omega-3s are also bioactive.”

Nutrition research has suggested that the ratio of omega-6 to omega-3—as much as 20 to one in Western diets—should be less uneven. Kang said that the *fat-1* mice give researchers a chance to study the potential benefits of increasing the proportion of omega-3 fatty acids in the body without the potential confounding effects of changing diets. Kang has received requests from about 30 other labs wanting to study the *fat-1* mice. Among them is Lois Smith, HMS associate professor of ophthalmology at Children’s Hospital Boston, who is testing the hypothesis that omega-3 fatty acids could ameliorate abnormal blood vessel growth in retinopathy. “In the general public and the scientific community, fats are just thought to be something that you eat,” Smith said, “but they can be as important as proteins in how they signal.”

### Molecular Disease Dampeners

The first of Kang’s studies, led by Christian Hudert and published on July 25, used the mice to study a drug-induced model of colitis. The transgenic mice were protected from clinical disease, and the researchers detected higher levels of anti-inflammatory molecules with fewer signs of inflammation.

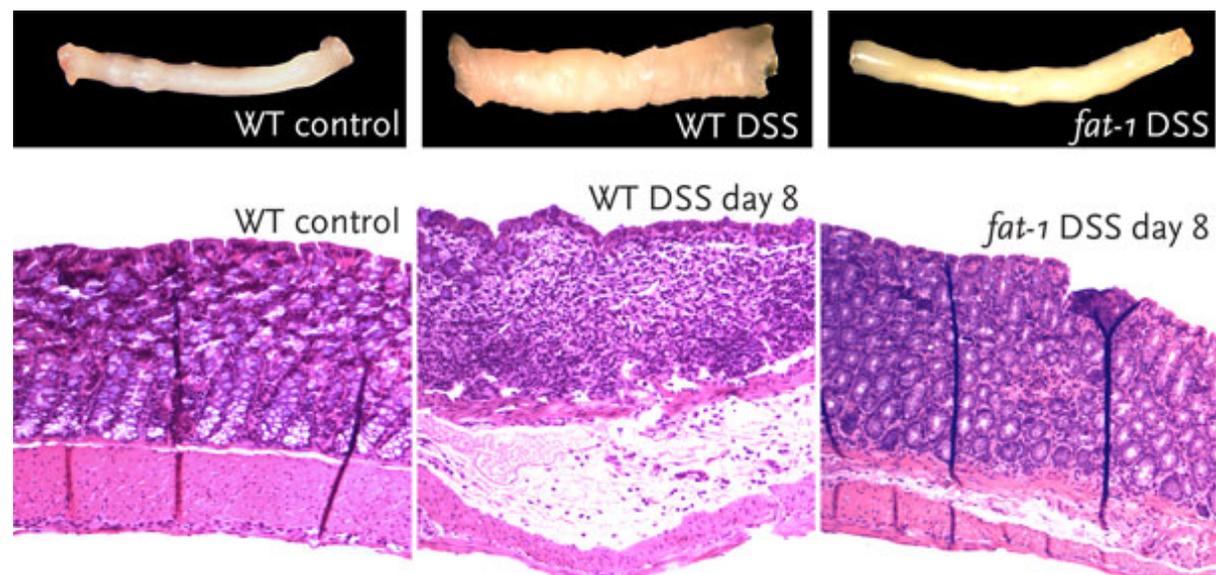


Image courtesy of Jing Kang

**Mighty mice.** Transgenic mice with tissues high in omega-3 fatty acids are protected from drug-

induced colitis. Above, sections of the colon show that wild-type mice given the drug develop severe inflammation (middle), while the tissue of transgenic mice (right) looks similar to untreated mice (left).

---

Another study, led by Shuhua Xia and published on Aug. 15, introduced mouse melanoma cells into both *fat-1* mice and wild-type mice. They found that tumors grew more slowly in the mice with the *fat-1* gene. Using mass spectroscopy to analyze the lipids in tissues of both sets of mice, the team found that metabolites of omega-3s were elevated in tumors and surrounding tissue of *fat-1* mice. The tumors of these mice also had higher levels of the tumor suppressor PTEN.

Serhan sees these studies as bridging two worlds that are traditionally very separate—nutrition and molecular medicine. “What is the pharmacological effect of the foods you eat?” Serhan asked. It seems obvious that foods may have important biological effects, but they are rarely understood the same way drugs are. In the case of omega-3 fatty acids, studies have been hampered by the inconsistency of supplements that are not regulated like drugs and vary in content and quality. With Kang’s mice, he said, “you take away all the problems with feeding studies.” Being able to describe the effects of the fats on a molecular basis is crucial to winning over skeptics who see omega-3s as little more than folk remedies.

Of course, nutrition and medicine will make use of these findings in different ways. Kang’s ultimate goal is to find a nutritional solution to the deficiency of omega-3 fatty acids in most modern diets. Ever since humans developed agriculture, our diet has been overloaded with omega-6–rich grains, oils, and meats, while sources of omega-3s—primarily fish and some nuts and vegetables—are lacking in most diets around the world. Kang has helped develop a transgenic pig carrying the *fat-1* gene, and he sees transgenic livestock as the best practical solution to adding more omega-3s to the diet. From the perspective of medicine and disease, Serhan says that identifying and characterizing molecules in the omega-3 pathway will help spur the pharmaceutical industry to explore drugs that mimic these compounds.

—Courtney Humphries

[top](#)