



reply to requests for comment.) One donor, mathematician Nakhle Asmar of the University of Missouri, Columbia, says “national security” was the reason he gave McCain \$2300, the maximum allowed from an individual for the general election. Has he done anything more for the candidate? “I don’t have time,” he says, adding that he believes “both [candidates] will be good for education and science.”

Some who have volunteered for Obama say they would have preferred to remain nonpartisan but that the stakes are too high. Holz, who has written to local papers, recorded YouTube videos, and canvassed for Obama, worries that such activism could “compromise the scientific enterprise” by politicizing it. But the bigger problem, he says, is that “the scientific enterprise has already been compromised and politicized

by Republicans.” White House science adviser John Marburger says he opposes “scientists using science to support their partisan views.” The problem, he says, is that they could “lose credibility with the public.”

Durand doesn’t pretend to know if her efforts have helped Obama. But she’s got her fingers crossed. “I feel so much more optimistic now than I did in 1968,” she says.

—ELI KINTISCH

SELF-EXPERIMENTATION

Eat, Drink, and Be Wary: A Sugar’s Sour Side

In 2001, Ajit Varki’s dream came true when he drank an extract from pig spit. Varki’s strange culinary excursion was part of an experiment that he believed might help explain the unique susceptibility humans have to some infectious diseases, cancers, and heart ailments.

A prominent researcher in the dual disciplines of sugar biology and evolutionary biology, Varki first purchased a few kilos of glands taken from the jaws of pigs. Next, his lab at the University of California, San Diego (UCSD), minced and homogenized them to extract the mucins. From these mucins, proteins secreted by mucosal surfaces, they plucked off a sugar called Neu5Gc for short. And that’s what Varki’s sweet tooth craved.

Neu5Gc, which is also known as a sialic acid, is made by chimpanzees and many other mammals but not humans, and Varki’s group earlier had found the genetic mutation that prevents us from making it. Varki suspected that when we are exposed to Neu5Gc, it incorporates into our cells, where it somehow makes humans more susceptible to a variety of diseases. The first step was to figure out how it entered the body—thus, the pig spit experiment.

Varki reasoned that Neu5Gc could enter humans through food that contains it, such as red meat and milk products. To prove it, he proposed ingesting huge amounts of pig Neu5Gc and seeing where it went. But when Varki asked his institutional review board for permission to drink the Neu5Gc, some members balked. “I was at first told that self-experimentation was not allowed any more,” says Varki. He assured them that he would assess results using objective measures such as mass spectrometry to prove its presence—



Diet-conscious. Ajit Varki long suspected a link between disease and Neu5Gc in red meats and dairy products.

and he slyly asked if any members of the committee wanted to be the volunteers, he recalls. They gave him a green light.

To establish a baseline, Varki restricted what he put in or on his body for 2 days before the experiment: no red meats, milk products, or lanolin shampoos, all of which contain Neu5Gc. Then he checked into a clinical research center at UCSD and drank 150 milligrams of the Neu5Gc dissolved in 100 milliliters of water. “It was slightly sweet and sour, slightly acidic,” says Varki, pig-spit connoisseur. He wasn’t particularly worried that the Neu5Gc (full name, *N*-glycolylneuraminic acid) would make him sick. “It was like eating 14 pork steaks,” he says. “People do that on July 4th.” But to be safe, the clinical center

kept him under observation all day, taking blood samples every 2 hours. No side effects surfaced. Urine, saliva, and hair trimmings over the next week all showed increased levels of Neu5Gc. Closer analyses showed that his cells had actually taken it up and incorporated it on their surfaces, as they do with other sialic acids in the synthesis of new glycans. Two of Varki’s colleagues did the same self-experiment with similar results, which they published in the 14 October 2003 issue of the *Proceedings of the National Academy of Sciences*. “There’s no other example I know of where you eat something foreign that outfoxes the biochemical systems and becomes part of you, no different from molecules made in your body,” Varki says. ▶

Varki has since taken that observation a step further. This week, *Nature* is publishing a new study online, led by Varki and two teams of researchers in Australia, that strongly ties Neu5Gc to a human disease and ingestion of red meat. "It's a very concrete example of how our susceptibility to disease might be governed by our diet," says Carolyn Bertozzi, a carbohydrate chemist at UC Berkeley. "Ajit is an incredibly creative guy. Sometimes he's chasing strange meteors and comets, and sometimes he hits something. This is a really interesting story, and I'm very excited by it."

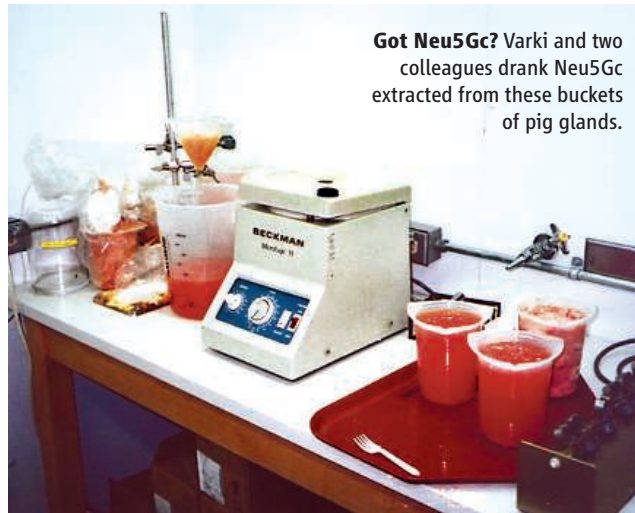
Varki has long wondered why chimpanzees and humans are genetically so similar but suffer from different diseases, and he sees Neu5Gc as one key to solving that mystery. But so far, speculations have outnumbered evidence. "He's been looking for that direct link with disease, and it's been elusive," says Bertozzi. That is, until the new *Nature* study, which she says is thoroughly convincing.

Neu5Gc connected Varki and his Australian collaborators through a circuitous route that dates back to the death of several children in 1993 who ate tainted hamburgers from Jack in the Box restaurants in the United States. The culprit was later identified as a deadly strain of the gut bacteria *Escherichia coli*, known as 0157:H7. A toxin secreted by this *E. coli*, Shiga, can lead to hemolytic-uremic syndrome (HUS), which causes kidney failure. Molecular microbiologists James and Adrienne Paton, a husband-and-wife team at the University of Adelaide in Australia, subsequently discovered several other Shiga-producing *E. coli* that caused HUS outbreaks there, and one secreted a second toxin as well, subtilase cytotoxin (SubAB).

Toxins must first bind to the surface of a cell to do their damage, which led the Patons to David Smith of Emory University School of Medicine in Atlanta, Georgia, who specializes in matchmaking ligands and receptors. Smith found that SubAB has a high affinity for Neu5Gc, and he told the Patons about Varki's work. Their subsequent collaborative studies make a compelling case that when humans eat meat or dairy products that have high levels of Neu5Gc, it becomes

incorporated into their cell surfaces, and SubAB can bind to it. "It's the first time we've seen an example of a component in food being the preferred receptor for a bacterial toxin," says James Paton.

The researchers next showed precisely how Neu5Gc binds to the toxin, which included crystallizing SubAB, an intensive effort done in Jamie Rossjohn's lab at Monash University near Melbourne.



Got Neu5Gc? Varki and two colleagues drank Neu5Gc extracted from these buckets of pig glands.

Human cells fed Neu5Gc also became much more susceptible to SubAB, the team found. And mouse experiments further clarified the connections between SubAB, Neu5Gc, and disease.

So consider the delicious irony. *E. coli* that produces the SubAB toxin contaminates red meat and milk products. Humans who ingest these foods incorporate Neu5Gc into their cells, making them hypersusceptible to SubAB—and much more likely to become seriously ill from the toxin.

Although these insights have no immediate practical application, Varki hopes they may open a door that eventually helps explain and even thwart major diseases. Some forms of Neu5Gc are seen as foreign by the human immune system, and we sometimes create antibodies to it. Varki suspects that these antibodies may contribute to autoimmune diseases, cancers, and heart problems seen in humans but not in chimps. Pathogens can also directly bind to Neu5Gc on cell surfaces, and one strain of the malaria parasite does just that, readily causing disease in chimps but not humans. Paton suggests that the greatest impact of the new findings may be in sparking epidemiological studies of, say, vegans, that prove these links. Any way you look at it, Neu5Gc proves the point like never before: You are what you eat.

—JON COHEN

Panel OKs Anthrax Shots for First Responders

A U.S. scientific panel thinks that police, firefighters, people who work with hazardous materials, and others running the risk of exposure to an anthrax infection may be offered the vaccine against the fatal disease. That suggestion, from an advisory panel to the U.S. Centers for Disease Control and Prevention (CDC), is a departure from current policies.

Anthrax vaccination is compulsory for military personnel serving in risk areas overseas. Although most experts believe the vaccine—six shots over a period of 18 months—is safe, some service members believe it has made them ill, and some have filed lawsuits. Relying on new safety data, CDC's Advisory Committee on Immunization Practices agreed on 22 October that first-responder agencies "may choose to offer" their staff the vaccines on a voluntary basis—but it stopped short of recommending they do so.

That caution reflects the panel's inability to assess the risk of future attacks, says the committee's chair, Dale Morse, who adds that the job site and duties affect a worker's risk of contracting anthrax as well. "We believe it's very low, but we can't say it's zero," Morse says. Meryl Nass, an internist at Mount Desert Island Hospital in Bar Harbor, Maine, who strongly opposes the military program, believes the recommendations will put more people at risk for adverse events. No first responders became infected during the 2001 anthrax letter attacks, which killed five people. —MARTIN ENSERINK

HAL the Cosmologist

Physicists know that the gravity from huge strands of dark matter distorts the images of distant galaxies and makes them tend to align, a bit like fish in a school. Now, computer scientists may help them to find new algorithms to measure that "weak lensing" distortion, which could be used to probe the mysterious dark energy that's accelerating the expansion of the universe. The competitors in the GRavitational lEnsing Accuracy Test 2008 (GREAT08) PASCAL Challenge will analyze a simulated data set of 30 million galaxies, preparation for the billions of galaxies that cosmologists expect to survey in coming decades. The challenge is the latest from the PASCAL Network, a consortium sponsored by the European Union. John Shawe-Taylor, a computer scientist at University College London, says the contest pushes machine learning in new directions by emphasizing large data sets and high precision. —ADRIAN CHO