University of Pennsylvania, Philadelphia, and colleagues. Such an extended childhood would give predators and disease ample time to pick off animals before they reproduced, says Gregory Paul, an independent dinosaur artist and paleontologist in Baltimore, Maryland. But if Curry's rapid growth rate is right, young sauropods probably weren't picked on for long.

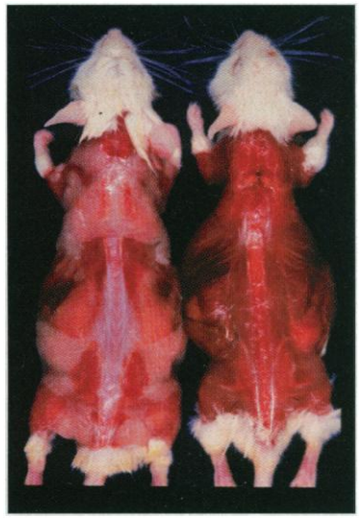
–ERIK STOKSTAD

BIOMEDICINE

From Fat-Free Mice, The Skinny on Diabetes

When it comes to body fat, extremes can have extreme consequences. Obesity can lead to health problems such as diabetes. And now comes a dramatic illustration of the ills of having no fat at all. Two independent groups have shown that mice genetically engineered to lack fat cells also get diabetes, with symptoms even more severe than those of their obese counterparts. The animals suffer all the signatures of adult-onset diabetes in humans: high blood sugar, high insulin levels, and a ferocious thirst and appetite.

Reported in last week's issue of *Genes and Development* by Nobel laureates Michael Brown and Joseph Goldstein and their colleagues at the University of Texas Southwestern Medical Center in Dallas and by Marc Reitman and Charles Vinson's group at the National Institutes of Health in Bethesda, Maryland, the findings may yield clues to the enigma of adult-onset diabetes, also called type 2 diabetes or diabetes mellitus. Body fat plays a role in the illness, which afflicts at least 18 million Americans, but endocrinologists don't know exactly how. The mice also provide the first model ever for a rare human condition known as lipodystrophy, in which patients are born with an extreme scarcity of fat and the symptoms of adult-onset diabetes. "The insights that these models yield may provide more beneficial treatments for both diseases," says Reed Graves, a chemist at the University of Chicago who helped to pioneer the work in the current papers.



Baring all. A transgenic mouse (right) lacks the white fat seen under the skin of a control animal.

CREDIT: MARC REITMAN

Graves worked with Susan Ross in Bruce Spiegelman's laboratory at Harvard Medical School, where the trio was trying to figure out how fat influences diabetes and related disorders. In 1993, they successfully depleted fat in mice by engineering in a toxin gene and turning it on in fat cells. The mice developed some diabetic symptoms, but the researchers could not pin down the link between a lack of fat and diabetes because these mice did not lose fat cells until they reached middle age.

The more recent experiments do a better job of eliminating fat from the animals. Both groups of researchers genetically blocked the growth of fat cells by altering transcription factors, proteins that turn genes on or off and are crucial to cell growth and maturation. Reitman and Vinson's team inactivated the genes for two families of transcription factors that normally help fat cells grow and develop, while Brown and Goldstein altered the gene for another transcription factor so that cells would get an overdose of it. Both mutations were designed to affect only fat cells.

The changes had the same effect: The mice were born with little or no white fat. The transgenic mice also failed to develop mature brown fat, which normally serves a warming function in hibernating animals. "We had to use heating pads because the fat needed for [heat production] was gone," recalls Vinson, who notes that tending to the rodents "was certainly not trivial."

Many of the animals died before reaching adulthood, but those that survived developed diabetes: Their cells no longer responded properly to insulin, which stimulates cells to metabolize glucose. As a result, insulin levels in the bloodstream skyrocketed—up to 442 times normal levels for some of Reitman and Vinson's mice—and glucose levels at least tripled. Like human diabetics, the animals also had high levels of triglycerides and other fat building blocks in their circulation, and their livers became engorged with triglycerides. "These animals are really sick," Reitman says. "But they clearly don't get diabetes in the same way as normal type 2 diabetics," where excess body fat plays a role.

Brown and Goldstein speculated that the altered transcription factor in their mice might be the key to the diabetes, and they spent a great deal of effort trying to tease apart the molecular pathways triggered by the mutation. But they could find no clear answers. Reitman and Vinson have a different hypothesis, which could explain why both obesity and a complete lack of fat can lead to diabetic symptoms. They propose that excess fatty acids and triglycerides in the circulation and liver might somehow trigger the disease. The compounds might end up in the circulation either because they spill from stuffed fat cells, in the case of obesity, or because there are no fat cells to store them, as in lipodystrophy and the fatless mice.

If the conjecture can be proven, it could open the way to new therapies for both adult-onset diabetes and lipodystrophy. Indeed, Graves's group at the University of Chicago found that a drug called troglitazone—which helps trigger fat cell maturation—could lower blood glucose levels and reduce other diabetic symptoms in his group's transgenic mouse. That drug is now available as a treatment for human diabetes, and Graves hopes the researchers will explore the effects of similar drugs in the new transgenics.

For his part, Vinson says there is a message for diabetics and nondiabetics alike: "We learned that too much fat is bad and so is not enough fat. The punch line here is that a little fat is good. As Aristotle said, 'Everything in moderation.'"

–TRISHA GURA

Trisha Gura is a science writer in Cleveland, Ohio.

SPACE SCIENCE

NASA Craft to Take the Controls in Flight

TOKYO—Both science fiction fans and scientists are eagerly anticipating tomorrow's scheduled launch of NASA's Deep Space 1 mission. But it's not the destination—a close encounter with an obscure asteroid—that excites them. What's special about the mission, which begins a series of flights testing new technologies, is the onboard software that will, for the first time, assume complete control of the spacecraft. Computer scientists say it's a step toward a real-life HAL 9000, the fictional cyber-character in Arthur C. Clarke's *2001: A Space Odyssey*. Its success, they add, would be a boon to future deep-space probes and to the field of artificial intelligence (AI).

"This experimental system is a kind of 'HAL 1000,'" quips Nils Nilsson, a computer scientist at Stanford University. "NASA's willingness to test this technology in Deep Space 1 represents a step forward for AI. If it works, it will most likely be used in future NASA missions and will attract the attention of other potential users."

Deep Space 1 is the first mission of NASA's New Millennium Program, which