

Seeking the source of a sugar-storage flaw

Most Type II diabetics have a disorder called insulin resistance, in which cells fail to respond fully to insulin's message to store sugar. Two small studies now strengthen the suggestion that these diabetics — as well as seemingly healthy people with insulin resistance — have a defect in the glucose transporter system that brings sugar into cells for processing, rather than a flaw in the insulin itself or in the cellular receptors for it. Though preliminary, the findings raise hopes that scientists might eventually develop treatments for insulin resistance, which some view as a very early sign of Type II diabetes.

Past attempts to unlock the mechanism behind insulin resistance focused primarily on the insulin receptor, a cell-surface protein that serves as this hormone's docking site. But in recent years, several studies have suggested that something goes wrong *after* insulin binds with its receptor, possibly involving a sugar-processing enzyme or the glucose transporters — proteins in the cell that move to the cell surface to snare sugar from the bloodstream and deliver it into the cell for processing. At this week's meeting of the American Diabetes Association, held in Atlanta, researchers reported new results that add to the evidence implicating glucose transporters.

Scientists at the Yale University School of Medicine used nuclear magnetic resonance, a noninvasive technique, to study how well muscle cells take up glucose and convert it to an intermediate sugar form called glucose-6-phosphate. Douglas L. Rothman, Gerald I. Shulman and their colleagues measured baseline cellular levels of glucose-6-phosphate in four men with Type II diabetes and in four healthy men without insulin resistance. Next, they injected the eight volunteers with glucose and insulin — a technique that approximates the postmeal "sugar surge" in the bloodstream. In the healthy men, muscle cells showed a 30 percent rise in intracellular glucose-6-phosphate levels 20 minutes after the injections, whereas the diabetics showed no increase. This may signal a malfunction in transporter proteins, the researchers speculate.

In a related report, W. Timothy Garvey and his colleagues at the Indiana University School of Medicine in Indianapolis suggest that people with insulin resistance have fewer transporter proteins to carry glucose into the cells. The team studied fat cells surgically removed from 11 lean control subjects, 11 obese people with Type II diabetes, and 11 obese people with insulin resistance but normal blood sugar levels. (Such people secrete more insulin to compensate for the cellular resistance to its message.)

Garvey's group found that the people with insulin resistance — whether dia-

betic or not — had fewer transporter proteins in their fat cells than did controls. In addition, he says, the results show decreased expression of the gene that directs fat cells to produce transporter proteins.

Scientists emphasize that the new findings remain preliminary and do not rule out other possible causes. "It's an evolving story," says Philip E. Cryer of the Washington University School of Medicine in St. Louis. Still, Garvey says, if researchers can pinpoint the defect responsible for insulin resistance, they may find a way to prevent progression to Type II diabetes, which usually strikes after age 40.

— K.A. Fackelmann

Quasar light points to younger galaxies

Astronomers have usually assumed that most galaxies formed early in the history of the universe, perhaps as much as 10 billion years ago. Two researchers now say they have strong evidence that gas clouds were still coalescing into galaxies as recently as just a few billion years ago. In fact, their observations of the effect of intervening gas clouds on the passage of light from distant quasars to Earth suggest that star formation within nascent galaxies may have reached a peak about 5 billion years ago rather than at an earlier time.

"It may be that there never really was an epoch of galaxy formation," says Donald G. York of the University of Chicago, who presented the new evidence at last week's American Astronomical Society meeting in Albuquerque, N.M. "It looks as if galaxies are created at different times in different places."

To detect pockets of early star formation associated with the collapse of vast gas clouds, York and Brian Yanny first examined the spectra of distant quasars, looking for the characteristic imprint left when light passes through a large cloud of molecular hydrogen. Such clouds make their presence felt by absorbing certain well-defined wavelengths of light.

York and Yanny found such clouds, but direct observation of a forming galaxy is tricky. Normally, the faint light emitted by clouds just starting to collapse into galaxies would be lost in the background light of the night sky. To overcome that problem, the Chicago team developed a technique for filtering out all but a narrow band of wavelengths of light typically emitted by hot, bright, young stars. By applying this technique to the clouds they identified by quasar light, they could map each cloud's star-formation regions.

"No one had really thought to apply

Fermat-number factors

Two computer scientists have reached an important milestone on the road toward factoring ever-larger composite numbers. Last week, Arjen K. Lenstra of Bellcore in Morristown, N.J., and Mark S. Manasse of the Digital Equipment Corp. Systems Research Center in Palo Alto, Calif., finished factoring the tenth Fermat number, proving that this 155-digit behemoth is the product of three prime numbers.

Fermat numbers have the form $2^m + 1$, where $m = 2^n$ and n is zero or a positive whole number. More than three centuries ago, French mathematician Pierre de Fermat conjectured that all numbers of this form are prime—that is, divisible evenly only by themselves and 1. His conjecture proved true for the first five Fermat numbers (ranging from $n = 0$ to $n = 4$). A century later, however, Leonhard Euler successfully factored the next Fermat number in the sequence. Since then, mathematicians have tried to factor larger Fermat numbers, reaching the eighth number ($n = 7$) in 1970 and the ninth ($n = 8$) in 1981.

To crack the tenth Fermat number ($n = 9$), Lenstra and Manasse used a recently invented method that significantly speeds the factoring of Fermat-type numbers. Various computers in a number of different locations provided essential information for the factorization, and the final step required a type of large computer known as the Connection Machine.

The computations show that the tenth Fermat number has a 49-digit and a 99-digit factor to go with the previously computed factor, 2,424,833. Both of the large factors start and end with the digit 7.

At the moment, reaching the next Fermat number appears out of the question. The number is so large that it easily overwhelms any known techniques for efficiently factoring large numbers. □

this trick," York says. "But if you block out most of the skylight, suddenly all these galaxies come popping out at you."

The resulting images show pockets of star formation, looking like bright sparks scattered against a dark background. "We may be seeing the first bursts of light from the extended gas clouds that eventually create fully developed galaxies," York says. Each patch of light apparently represents a small, collapsed piece of cloud that had reached a density large enough to initiate star formation.

By measuring how long it takes light from these collapsing clouds to reach Earth, astronomers can figure out what galaxies looked like billions of years ago and deduce when galaxies started to form.

— I. Peterson