between 0 and 99 degrees," he says, "and then all of a sudden at 100 degrees it evaporates." With co-movers, on the other hand, the disappearance of J/psi's with increasing collision energy should be gradual.

In the meantime, however, there are several other hints that a phase transition might be taking place in the CERN heavy-ion collisions. Theorists predict that as matter gets hotter and quarks move toward deconfinement, they should also appear to get lighter. In protons, for instance, quarks appear to have a mass of about 300 million electron volts. "This is not the bare quark mass," Satz says. "It arises from the quark binding itself with gluons all around it. In a hot enough quark-gluon plasma, the quark shakes off all the gluons and gets its naked mass back." At the Heidelberg meeting, physicists from a CERN experiment called CERES reported seeing an excess of low-mass particles in lead-gold collisions, confirming hints from both CERES and another CERN experiment known as HELIOS 3. The data, however, are far from strong enough to rule out more mundane explanations for the excess.

The ambiguity should end when Brookhaven fires up its new Relativistic Heavy-Ion Collider (RHIC) in 1999. If the CERN results really are the first evidence of a quark-gluon plasma, then RHIC, colliding nuclei at higher energies, should have little trouble establishing an iron-clad case. As Pisarski puts it, "I would assume a quark-gluon plasma has been produced for short periods of time and small volumes at CERN. You just can't pick it out definitively. Once we go to RHIC ... it should all be much clearer."

–Gary Taubes

BIOCHEMISTRY

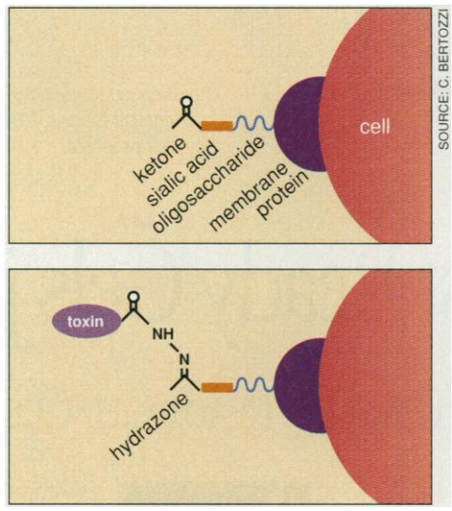
Making Cells Selectively Sticky

Living cells are coated with sticky sugars, and a group of researchers at the University of California, Berkeley, has now found a way to alter what those sugars will stick to. The sugar molecules—long chains of them called oligosaccharides—are attached to the ends of the protein receptors and other structures on the cell surface. Investigators have long pictured turning these sugars into the molecular equivalent of Velcro, by modifying them to bind specific molecular partners, such as drugs aimed at specific cells. Past sugar-altering techniques have either damaged the cells or been viable only in the test tube. But at a meeting of the American Chemical Society in Orlando, Florida, 2 weeks ago, the Berkeley group, led by organic chemist Carolyn Bertozzi, reported a scheme for harnessing cells' own machinery to alter their sugars.

"It looks like very nice work," says Steve Withers, a carbohydrate chemist at the University of British Columbia in Vancouver. If the Berkeley researchers can find a way to alter the sugars on the surface of cancer cells while leaving normal tissue untouched, for example, they might be able to turn anticancer toxins into smart weapons, says Withers. Bertozzi says that the altered sugars could also be used for fastening cells to artificial substrates to create engineered tissues.

The strategy isn't new. In the late 1970s, for instance, researchers led by Carl Gahmberg at the University of Helsinki in Finland began showing that they could oxidize cell-surface sugar groups to make compounds known as aldehydes, which could selectively interact with amines and other compounds. But the oxidants used to alter the sugars often damaged the cells they modified. Another approach has relied on specialized enzymes capable of transforming specific cell-surface sugars. "But that approach doesn't work for modifying cells in vivo," as there is no way to deliver the sugar-transforming enzymes to cells in the body, says Bertozzi.

In search of a scheme that might have a better chance at making the jump from the test tube to the clinic, Bertozzi and her colleagues Lara Mahal and Kevin Yarema looked for a means of co-opting cells' own biochemical machinery to alter their surface sugars. Enzymes in cellular organelles called the endoplasmic reticulum and the Golgi apparatus typically attach these sugars to newly synthesized protein receptors just before the proteins make their way to the cell membrane. The last chemical group on each chain of sugars is often a sugar called sialic acid, and it was this outermost sugar that the Berkeley researchers targeted for modification.



Hook and eye. A ketone group added to a cell-surface protein could provide a target for toxins or other drugs bearing a matching chemical group.

The team decided to alter these terminal sialic acids by attaching small chemical groups called ketones to them. Ketones are abundant within cells but virtually absent from cell surfaces, notes Bertozzi. So the researchers hoped that ketone-tipped sialic acids could act as a target for compounds designed to interact only with ketones.

Carrying out this plan turned out to be relatively simple. Cells normally modify a precursor sugar called N-acetylmannosamine to create the sialic acid, then attach it to the oligosaccharides decorating a protein receptor. To hijack the process, the researchers simply attached ketones to the mannosamine, creating a compound known as ManLev. They then fed the ManLev to cancerous lymphocytes in culture and waited to see if the cells would convert it to ketone-modified sialic acid and attach the acid to cell surfaces. The scheme worked. Bertozzi and her colleagues found that the ketones were expressed on cell-surface proteins, right at the end of the sugar complexes.

In addition, Bertozzi and her colleagues showed that the modified sugars can serve as hooks for other compounds—the other part of the molecular Velcro. Researchers have long known that a small chemical group known as a hydrazide selectively reacts with ketones. To see if they could exploit this affinity, the Berkeley group indirectly linked fluorescent dyes to the hydrazides, then added the combination to ketone-bearing cells. The dye-bound hydrazides promptly bound to the modified cells. The researchers are now trying to link toxins to hydrazides to see if these compounds will home in on ketone-bearing cancer cells. Because many kinds of cancer cells overexpress sialic acid—and would therefore bear more ketones—the researchers hope that hydrazide-linked drugs will selectively target cancer cells.

In addition to guiding cancer drugs to their targets, Bertozzi believes the ketone-hydrazide linkage could prove useful for anchoring cells to artificial matrixes. That would give researchers working to design complex tissues such as an artificial liver a new tool for arranging different cell types in specific regions of a scaffold. "It's a creative approach," says Joseph Gardella, a tissue engineering expert at the University of Buffalo in New York, who like most tissue engineers tries to come up with scaffold materials that normal cells will stick to. The new approach, by contrast, could anchor cells to a broader set of scaffolds. If the scheme works, sticky sugars could give researchers a whole new handle on cells.

–Robert F. Service