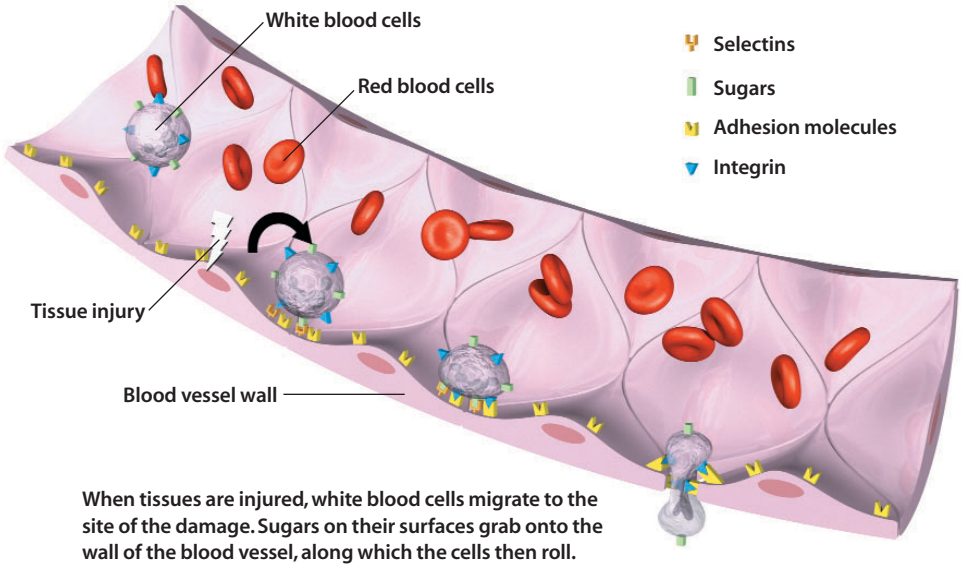

When tissues are injured, white blood cells migrate to the site of the damage. Sugars on their surfaces grab onto the wall of the blood vessel, along which the cells then roll. The white blood cells ultimately squeeze between the cells making up the blood vessel and address the injury.

JOHN MACNEILL

GLYCOMICS

Sugars could be biology's next sweet spot.

The 1990s may well be remembered in biology as the decade of the gene, culminating in the completion of the Human Genome Project's working draft. And the next big thing in medicine may be the study of the proteins coded for by all those genes *(see "The Proteomics Payoff," p. 54)*. But even as doctors and drug companies struggle to interpret and exploit the recent explosion of data on genes and proteins, yet another field of biology is waiting to break out: glycomics. This emerging discipline seeks to do for sugars and carbohydrates what genomics and proteomics have done for genes and proteins—move them into the mainstream of biomedical research and drug discovery.

For years, carbohydrates were one of the least glamorous subjects in biochemistry research. At best, scientists thought, these molecules created structure (in the cell walls of plants, for example) or were used to store energy (think potato); at worst, they hindered the study of important biological molecules like DNA and proteins. However, a very different portrait of sugars is gradually emerging. Biologists are finding that minor differences in sugar structures can have a huge impact on biological functions; in fact, sugars are involved in everything from embryonic development to regulation of the immune system. "Sugars are everywhere, in all organisms," says David Zopf, a vice president at Horsham, PA-based Neose Technologies, one of a number of research groups and companies working to exploit glycomics.

The commercial buzz is being created by the realization that a better understanding of sugar biology could ultimately lead to new drugs, new targets for conventional drugs and even improvements in the activity of existing drugs. Modifying protein-based drugs with the appropriate sugars, for example, could create far more efficient treatments and reduce the required doses. That's because current methods of making protein-based drugs do not always modify the proteins with the same sugars found on natural versions; this causes the liver to quickly flush the protein therapeutics out of the body. Cancer is another area where sugars turn out to play a big role, helping to transmit the signals that trigger unchecked cell growth; companies are looking to exploit this knowledge to tackle or slow the progress of the disease.

One reason that sugar biology, or glycobiology, has lagged behind the study of genes and proteins is that, until very recently, researchers lacked effective tools for studying carbohydrate molecules. Part of the problem is the complexity of sugars. While DNA and proteins have essentially linear sequences, sugars branch; DNA has just four basic building blocks and proteins have 20, but sugars have more than 30. "We truly haven't cracked the code yet," says MIT glycobiologist Ram Sasisekharan. "We are just beginning to unravel the mysteries of sugars."

Indeed, Sasisekharan's lab developed the first practical method for sequencing sugars only two years ago. And MIT chemist Peter H. Seeberger demonstrated the first automated machine for sugar synthesis in February. Just as the invention of the automated DNA sequencer and synthesizer in the mid-1980s opened up the field of genomics, the availability of such tools is heating up glycomics.

Knowledge of sugars' functions could affect medicine far beyond improving drug doses and fighting cancer. Researchers are looking into how sugars influence the development of Parkinson's, Alzheimer's and infectious diseases like AIDS and herpes, to name a few. Sugars also seem poised to influence stem cell biology, organ transplantation and tissue engineering. If these promising areas of research prove successful, "sugar pills" will take on a whole new meaning. —*Erika Jonietz*

CARBO LOADING

GROUP	FOCUS
Consortium for Functional Glycomics (La Jolla, CA)	Understanding protein-carbohydrate interactions
Glycodata (Ashdod, Israel)	Computer- and biochip-based analysis
Neose Technologies (Horsham, PA)	Sugar-based drugs; protein modification
SafeScience (Boston, MA)	Sugar-based drugs to treat cancer