fidence-building experience of unparalleled proportion in my life."

Kevan M. Shokat, then a grad student teaching assistant for one of Bertozzi's bioorganic chemistry classes at UC Berkeley and now a professor at UC San Francisco, encouraged her to take a great leap into a totally different field and environment for her postdoctoral studies.

Then Rosen took a chance on Bertozzi, a synthetic chemist, when he invited her to postdoc in his immunology lab and taught her the basics of cell biology and genetics.

While working on her degrees, Bertozzi had very positive experiences overall. When asked what difficulties women face in the field of chemistry, she recalls a few encounters with instructors and fellow students that left her feeling alienated and isolated. Women were a minority, or absent, in most labs at that time.

The situation changed when she arrived at UC San Francisco, where there were many more women at all levels, including the senior faculty.

"I felt more enfranchised and included in the profession during those years," she says. "The experience made a lasting impression, and I try to propagate it with the students in my own lab."

She believes the field is now different from 10 years ago and her female students appear to be more confident and have higher expectations and a greater sense of entitlement than did women of her own generation.

But challenges still exist, she says, even for successful senior faculty. Women chemists in academia are challenged to find ways to deal with the sense of isolation that comes with being outnumbered by men in venues such as committees, faculty meetings, review panels, and conferences. The number of women participating at these levels needs to be increased, she says, adding that she has noticed better atmospheres in chemistry departments that include more women.

When asked what advice she would give young women, and men, beginning careers in chemistry, Bertozzi replies: "I would tell them to invest in finding out their own scientific interests and to follow them in whatever direction they lead and that they are headed for a tremendously exciting, multifaceted career with numerous opportunities. I would tell them that they made a good choice."

This profile was written by C&EN Contributing Editor **Kevin MacDermott**, *a former associate editor in C&EN's ACS News department.*

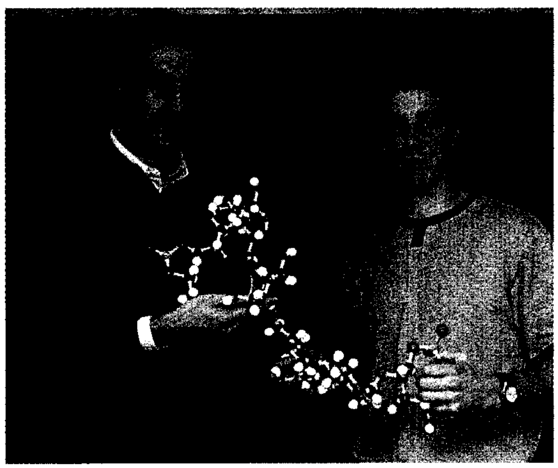
CARBOHYDRATES

VACCINES BY AUTOMATED SYNTHESIS

Oligosaccharide-based vaccines show promising activity against malaria, leishmaniasis

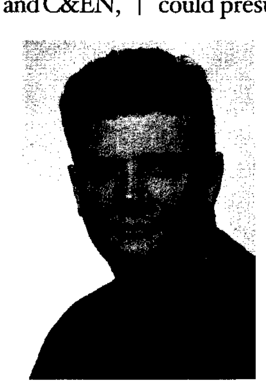
Carbohydrates are notoriously hard to synthesize, but recently several research groups have made major advances in simplifying and accelerating the process.

One of those is the team of assistant professor of chemistry Peter H. Seeberger at Massachusetts Institute of Technology, which developed a novel automated solid-phase oligosaccharide synthesizer that eases access to carbohydrate structures [*Science*, **291**, 1523 (2001) and C&EN, Aug. 28, 2000, page 8]. The automated oligosaccharide synthesis technology makes it possible to produce biologically interesting oligosaccharides in about 1% of the time previously required, Seeberger tells C&EN.



AUTOMATED Seeberger (left) and Hewitt hold a structure of the malaria toxin oligosaccharide analog they synthesized.

Now, he and his coworkers are beginning to apply this technology to specific medical applications. At last fall's Welch Conference on Chemical Research, in Houston, Seeberger described fully synthetic carbohydrates that in preliminary studies showed promising activity as malaria and leishmaniasis vaccines.



Schofield

According to the Malaria Foundation International, each year 300 million to 500 million people become ill with malaria. The disease causes chills, fever, sweating, and anemia, and it sometimes affects the brain and kidneys. Several million people annually die of the disease, including 200 to 300 children per hour worldwide. Chloroquine and a number of other antimalarial drugs are available to treat it, but many variants of *Plasmodium falciparum,* the malaria organism, have developed resistance to the drugs.

Alternative drugs are thus needed. But research on such drugs has not been well supported, largely because malaria patients tend to be poor and are unable to afford expensive advanced medicines.

An effective vaccine could help solve the malaria problem, and vaccine candidates have exhibited some efficacy in animal tests. But a safe and effective malaria vaccine for people has yet to be developed, in part because funding for research and clinical trials has been inadequate.

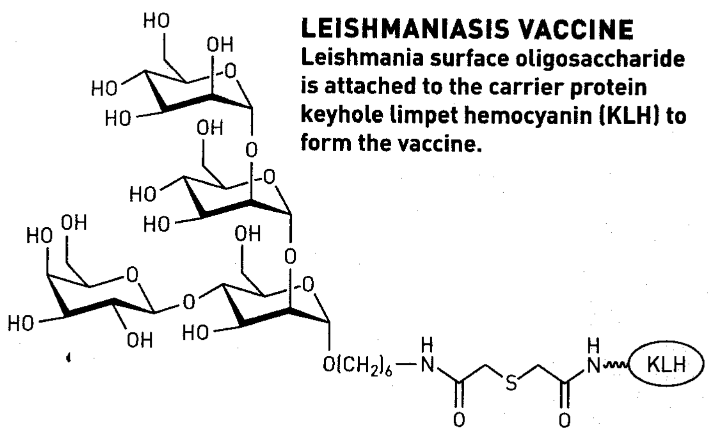
The malaria toxin produced by *P. falciparum* contains a carbohydrate moiety that could presumably be mimicked to create a vaccine. Louis Schofield and coworkers in the Infection & Immunity Division of the Walter & Eliza Hall Institute of Medical Research, Melbourne, Australia, identified the complex native oligosaccharide. In an initial vaccine study, "they found that they could give healthy mice the native oligosaccharide vaccine, and in about two-thirds or three-quarters of the cases the mice did not die when challenged with malaria," Seeberger said.

He and graduate student Michael C. Hewitt used their solid-phase automated synthesis technology, in combination with solution-phase methods, to synthesize a complex oligosaccharide with a structure similar to that of the natural product. "Schofield put it into mice and found exactly the same immune response as was found with the native material," Seeberger said. "We found very good protection—over 65%—and we believe the level of protection can be brought up to almost 100% by changing the formulation of the vaccine."

In experiments in a mouse model for malaria, he said, "the Australian group conjugated the synthetic carbohydrate to an immunostimulant, injected the constructs in three booster shots, and almost three-quarters of the mice survived perfectly fine—compared with 100% fatalities in unimmunized controls. We are now starting to make larger quantities of the carbohydrate for primate studies, and at the same time we're synthesizing related structures to understand exactly how the vaccine works."

Leishmaniasis is another tropical parasitic disease, with about 2 million new cases each year, according to the Centers for Disease Control & Prevention. Symptoms include serious skin sores, fever, weight loss, and organ enlargement.

The leishmania parasite has a very complex oligosaccharide on its surface that includes a key tetrasaccharide cap. Seeberger's group members used their automated synthesis technology to produce the tetrasaccharide in a matter of days and then covalently linked the carbohydrate to a protein carrier [*Org. Lett.*, **3**, 3699 (2001) and *J. Org. Chem.*, **66**, 4233 (2001)]. The Schofield group has begun to test the conjugate for vaccine activity and has obtained encouraging initial results.



LEISHMANIASIS VACCINE
Leishmania surface oligosaccharide is attached to the carrier protein keyhole limpet hemocyanin (KLH) to form the vaccine.

Seeberger notes that the collaboration between his group and Schofield's validates "a basic potential for synthetic carbohydrate vaccines in research aimed at addressing some of the important public health problems of developing nations." And it helps demonstrate potential real-world applications for Seeberger's automated solid-phase oligosaccharide synthesizer technology as well.—STU BORMAN