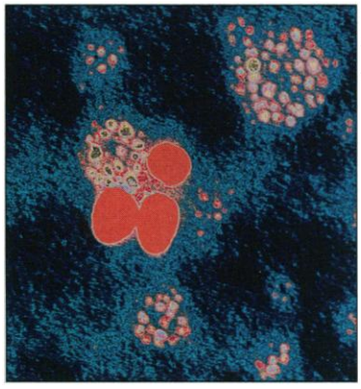
Chemists Get a Taste of Life At Gathering in San Diego

Chemists often deal with things as inanimate as metals and minerals, but more and more, they find themselves trying to imitate or exploit the chemical talents of life. That trend was amply evident when more than 10,000 members of the American Chemical Society (ACS) met from 13 to 17 March. Among the 5700 papers were presentations on the secret of spider's silk, how to prop up proteins to make a convincing vaccine, and enlisting microorganisms to break down PCBs and make fuel.

A Scarecrow Vaccine

Nir Kossovsky says that in his quest for a new kind of vaccine, he was inspired by the principle of the scarecrow: "The more it looks like Farmer John, the better it works." At the ACS meeting, Kossovsky, a University of California, Los Angeles (UCLA) pathologist, described building artificial virus particles that, like scarecrows, have the shape as well as the attire of the real thing—in this case, HIV (the AIDS virus), and Epstein-Barr virus. But instead of having potentially harmful genetic material beneath their coat of viral proteins, Kossovsky's "decoy viruses" conceal a tiny grain of ceramic coated with sugars.



KOSSOVSKY

Fooled again. In a colorized electron micrograph, antibodies *(orange)* bind to a "decoy virus" made up of diamond particles *(white)* sheathed in Epstein-Barr virus proteins.

These decoys, Kossovsky told the meeting, have already shown that they can fool the immune system into mounting a response, at least in animal tests. And some of his listeners thought he's on the right track. But at least for AIDS, noted Genentech's Michael Powell, other vaccine candidates that have done equally well in initial tests are further along in development; in addition, he said, immune response in animals doesn't always predict success in humans.

Kossovsky was looking for a way to stimulate the immune system without exposing the patient to the danger of viral genes. To avoid this possibility, some vaccine researchers administer only part of the pathogen, such as pieces of proteins. Others have tried to mimic a virus's shape with gene-free decoys made of clumps of protein bound together with detergent and other materials. But Kossovsky says his decoys may prove more convincing because the ceramic cores give them the correct overall shape, and the sugars stabilize each protein. The approach makes sense, says Powell. "I think the closer you get to the proteins' shape on the virus, the better it should work."

Kossovsky says he got the idea several years ago when a Japanese materials scientist at UCLA returned from a trip home with a sample of virus-sized grains of diamond. But he realized that the process of sticking viral proteins to this core would dehydrate them and cause them to denature, or lose their shape, and with it some of their ability to stimulate the immune system.

After securing research money from a group of venture capitalists, he says, he began searching for a way around the problem. He recalled that spores and fungi can dry out and come back to life, with their proteins intact, because of the sugar molecules packed in with the proteins. Because sugar molecules sport hydroxyl groups (OH) that resemble part of a water molecule, they can fool dehydrated proteins into acting as if they were still in water. So Kossovsky coated his grains (which he was now making out of a ceramic material he thought might be more benign than diamond) with a sugar called cellobiose before attaching the viral proteins.

Kossovsky has confirmed that the resulting assemblages resemble real viruses. Measurements of their surface charges indicate that the viral proteins hold the same shape as the ones on live viruses. More to the point, when the decoys for Epstein-Barr virus and HIV were injected into rats, rabbits, and guinea pigs, they elicited specific antibody production and cellular immunity. But vaccine expert Larry Arthur of the National Cancer Institute cautions that earlier decoys also looked promising at this stage. When he and other vaccine researchers tested an HIV decoy called an ISCOM, "we saw blazing immune responses"—in rats, rabbits, and goats. Unfortunately, he adds, "when we worked with monkeys and chimpanzees, we got almost nothing."

PCBs Into Pussycats

Even before one of its pipelines exploded a week ago in New Jersey, Texas Eastern Gas Pipeline company had a major mess on its hands. The company owns more than 50 gas compression stations where the soil is contaminated with PCBs (polychlorinated biphenyls), once-popular industrial lubricants that are now considered environmental villains because they may cause cancer and harm wildlife. Because the compounds are extraordinarily difficult to get rid of, the cleanup can involve stripping off contaminated soil and shipping it to an incinerator. Faced with that costly prospect, Texas Eastern turned to PCB researchers, among them Princeton chemist Jeffrey Schwartz.

At the meeting Schwartz announced his solution: a way to turn these tough pollutants into pushovers. His strategy is to use a catalyst to pry off the chlorine atoms that account for PCBs' stability, allowing ordinary soil bacteria to break them down into harmless byproducts. Schwartz says his method is cheap and has already worked in the laboratory. If a planned field test is successful—and if he can convince the Environmental Protection Agency (EPA) of the virtues of the method—he may have found a way to alleviate PCB nightmares for companies like Texas Eastern.

Schwartz isn't the first chemist to look for a way to break down PCBs. "Many things have been proposed that work under controlled conditions," says EPA chemist John Smith. But that often means extreme temperatures and pressures. Furthermore, in some cases the cure is as bad as the disease: Some schemes leave behind other toxins, such as dioxin.

Schwartz says these methods are taking the wrong approach. The chlorine in PCBs renders them invulnerable to the oxidation reactions that break down most materials exposed to the elements—and yet some of these cleanup strategies try to force oxidation on the PCBs. Luckily, says Schwartz, the compounds most resistant to oxidation are also the most susceptible to the opposite kind of chemical reaction: reduction. And, he says, "if we could reductively lop off the chlorines, we could be left with PCB species that could be easily oxidized by native flora." End of problem—in theory.

Other chemists have tried to reduce PCBs into a degradable form, but most techniques, he says, are either difficult to scale up or rely on metal catalysts that are difficult to remove from the soil later. The method he came up with relies on a titanium-based reducing

agent that, he says, gets rid of the chlorine and leaves nothing but acceptably safe products behind—salt, borate, and titanium dioxide (which is used in food coloring). In laboratory tests, the method removes chlorine from PCBs in solution in less than 24 hours; tested in soil, it's only a little slower.

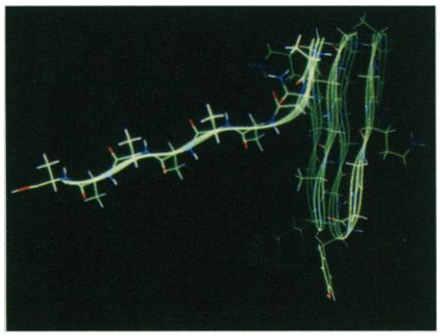
Few others know about the technique, since Schwartz announced it for the first time at the ACS meeting. But Princeton chemist Thomas Spiro, who chaired the session in which Schwartz spoke, was impressed. Though he is not an expert on PCBs, Spiro thought the method sounded chemically plausible, adding that "it's inexpensive—and the products left over are nonhazardous materials already found in the earth."

Schwartz says Princeton has licensed the technology to a startup company called Xetex, which will try it out at one of Texas Eastern's contaminated sites in Pennsylvania. Before the technique can be used on a wider scale, however, it will have to gain EPA approval. "To convince us," says EPA's Smith, "they will have to demonstrate it under the conditions it's proposed to be used for." Schwartz isn't worried. "As far as we can see this is really unprecedented—and it works."

A Spider's Stratagems

Rock climbers, bungee jumpers, and spiders all spend at least part of the time with their lives hanging by a thread. In spite of recent advances in synthetic polymers, the spider still has the best material to bet its life on. But humans may not have to envy the strength and toughness of spider's silk forever: At the ACS meeting, biochemist Randy Lewis of the University of Wyoming reported steps toward understanding and imitating the silk's miraculous combination of qualities.

Lewis told attendees he has identified



LEWIS

Molecular slinky. A computer model shows where spider's silk gets its spring.

the molecular architecture that underlies those properties and taken a key step toward harnessing the material for human purposes: outfitting bacteria with the genes for the silk proteins. The gene transfer, he says, turns the bacteria into factories that pump out the raw materials of the silk in commercially useful quantity. "You can't get that from the spiders."

The object of Lewis' efforts is "dragline" silk, which serves as the spiders' lifelines when they hang in midair and also provides the scaffolding for their webs. In the lab, Lewis says he's pulled and yanked the dragline of a spider called the golden orb weaver and found it matches the most advanced polymers, such as Kevlar, in strength and far exceeds them in toughness. To find out why, Lewis has been using nuclear magnetic resonance and x-ray diffraction to examine the structure of key silk proteins. He says the proteins share structural features with two children's toys—LEGO blocks and slinkys. Like LEGOs, the proteins hold each other in a tight peg-and-hole fit, which, says Lewis, makes them difficult to pull apart. Embedded in the building blocks are slinky-like springs that impart elasticity.

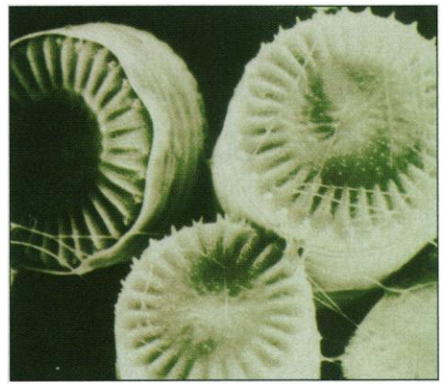
At the same time, Lewis has been making headway in large-scale production of these proteins. In 1992 he succeeded in cloning two silk protein genes from the golden orb weaver. Now he's finally succeeded in inserting those genes into bacteria. So far, though, the closest Lewis has come to spider's silk is a test tube full of protein. The next step, says biochemist Christopher Viney of the University of Washington, is figuring out how to transform those proteins into a fiber. "We want to duplicate the synthesis as it happens in the spider," says Viney.

If Lewis, Viney, and others can divine the remaining secrets of spiders' artistry, bioengineered silk might serve as surgical sutures, replacement ligaments, and even as a strong, resilient net for snagging planes landing on aircraft carriers. And climbers, jumpers, and others with a taste for the spider's dangling way of life might finally be able to suspend themselves from the real thing.

Fill 'Er Up–With Algae

The green movement is everywhere these days. Soon it may even be in one of the most improbable places of all: the local filling station. The reason is that oils made from plants—green oil, if you will—are cleaner than conventional fuels. Already tested in buses in Europe and experimental vehicles in the United States, "biodiesel" made from soybean and rape seed oils cuts down on the sulfur fumes, soot, and carcinogens produced by the burning of ordinary diesel. The trouble is that vegetable oil probably won't meet future demand, so Eric Jarvis and his colleagues at the National Renewable Energy Laboratory in Golden, Colorado, are trying to tap into a more abundant and even more environmentally correct source of oil: algae.

Now, you might not think algae produce oil. Like most plants, algae convert carbon dioxide and sunlight into sugars and proteins, but when starved of nitrogen, they turn to producing mostly oils. A simple reaction called esterification turns algae oil into a diesel-like fuel. And at the ACS meeting, Jarvis described how his colleague Paul Roessler had cloned an algae gene linked to oil production. By tinkering with this gene, he says, the group hopes to coax industrial quantities of oil from these microscopic organisms.



CAROL BOURNE

Oil riches? Lipids from micrometer-sized algae like these diatoms can be turned into biodiesel.

From an environmental point of view, biodiesels aren't perfect—they still generate nitrogen oxides, significant contributors to smog. But they offer enough improvement over the smelly stuff currently in use that Jarvis' group was eager to find sources to supplement existing vegetable oils. Algae looked like a good candidate: They can grow in salt water ponds on arid wasteland, and they might offer an environmental bonus by feeding off waste carbon dioxide from power plants, keeping it out of the atmosphere.

The gene cloned by the Colorado group encodes an enzyme known as acetyl-CoA-carboxylase, which catalyzes the first step in oil production. The next step, says John Sheehan, director of biodiesel production at the lab, is to increase expression of the gene to squeeze more oil out of their algae. If the researchers succeed, Sheehan and Jarvis expect many different applications for algae oil—as industrial lubricants and cosmetics, for example. But a bigger customer may be the city buses targeted by the tougher curbs on diesel emissions that take effect next year under the Clean Air Act, says Sheehan.

Still, it takes more than gene-splicing expertise to create a viable fuel, say others who have worked in the alternative fuels game. After the scientific research is done, "99% of the work is still ahead of them," says William Holmberg of the American Biofuels Association. "They still have to think about regulations, emissions testing, engine testing, and creating a market niche." Luckily, soybean biodiesel has already surmounted some of those hurdles, says Holmberg, which may help open the way for algae oil to flow into consumers' tanks.

–Faye Flam