

levels correlated with the complete or partial protection of seven monkeys. In 13 unvaccinated control animals that easily became infected by the challenge virus, chemokine levels were much lower. This suggests that the vaccine, by some unknown mechanism, stimulated the immune system to produce higher levels of these chemokines, which in turn blocked receptors needed by SIV and prevented infection. "I do not believe any single candidate is the correlate of protection," says Lehner. "But I think [these chemokines] are at least as good a candidate as any of the others."

Lehner currently is conducting experiments to follow up on this work but, for competitive reasons, declines to describe them publicly. "I'm amazed at the speed at which this is moving, and there's a total silence about what people are doing," he says. Jonathan Heeney, an AIDS researcher at the Biomedical Primate Research Centre in Ryswick, the Netherlands, is tight-lipped, too, but says he recently completed a study that looked at chemokines and the protection offered by an AIDS vaccine in monkeys. "We've got a hint that there's something interesting going on there," says Heeney.

Marc Girard of the Pasteur Institute in Paris says he also has intriguing preliminary data from studies of chimpanzees given HIV vaccines. Girard challenged four vaccinated animals and one control chimp with HIV, which readily infects these primates but doesn't usually cause disease. Three vaccinated animals were protected, and all had higher levels of RANTES, MIP-1 α , and MIP-1 β than the one that became infected. (Unfortunately, the control animal did not become infected, confusing the results, but it, too, had elevated levels of these chemokines.) "We had very good correlation between high level of secretion of chemokines and protection," says Girard. But he doubts that chemokines are the sole explanation and says he needs to repeat the experiment.

Gallo is convinced that chemokines play a large role in protection, which he is attempting to prove by directly injecting them into monkeys and then challenging them. "I think chemokines and CTLs are going to be the answer for vaccines," says Gallo. If indeed his challenge experiments succeed, the next hurdle—and it too is a high one—will be to design a safe vaccine that can teach the immune system to boost production of these chemokines should it ever meet HIV.

New models

The third quest invigorated by the chemokine discoveries is the search for an animal that can develop AIDS. Experiments with monkeys and chimps have provided critical data for AIDS drug and vaccine developers, and for researchers studying disease progres-

sion. But these primates are expensive and, except for a few cases in chimps, they do not actually get sick from HIV. So, several groups now are trying to use the new chemokine-receptor advances to genetically engineer a small animal that would provide a more practical model. The aim is to create animals that sprout CD4s and the various HIV-related chemokine receptors on their cells. This effort, too, is far from a shoo-in.

Most researchers working in this area have focused on genetically engineering HIV-infectable mice. Although several groups are believed to have succeeded in getting these receptors expressed, that's just the first step. "For those who think it's just sticking these genes in and making a mouse that's infectable, I think they'll be disappointed," says Dan Littman of New York University's Skirball Institute, whose lab is a leader in this field.

One major problem is that even if HIV can be induced to enter a mouse cell, it has great difficulty copying itself because some viral genes don't work well in murine cells. "Clearly, there are blocks [to viral replication] that are very important, and I think they'll prevent the mouse from being an excellent model for AIDS pathogenesis," says Didier Trono of the Salk Institute for Biological Studies in La Jolla, California. Others are more hopeful. "With a bit of work, we may be able to overcome postentry replica-

tion restrictions," says the University of Pennsylvania's Doms, who is working with Frank Jirik of the University of British Columbia to make HIV-receptive mice. "It's well worth trying."

Mark Goldsmith of the Gladstone Institute of Virology and Immunology in San Francisco and colleagues hope to exploit the chemokine discoveries to create a different animal model for AIDS: a transgenic rabbit. Several years ago, NIAID's Thomas Kindt developed a transgenic New Zealand white rabbit that expressed human CD4 receptors. Although the animals did not develop disease, HIV could replicate more efficiently in their cells than in the mouse. Now, Goldsmith and others at the Gladstone have teamed up with Kindt to add chemokine receptors to these animals. "The challenge associated with rabbits is transgenesis methodology is substantially less efficient [than in mice] for reasons that aren't clear," says Goldsmith. Rabbits also have longer gestations, smaller litters, and nearly 20 times the housing costs of mice. Still, says Goldsmith, "we're optimistic."

On every front, the revelation that HIV and chemokines have an intimate relationship holds an equal measure of promise and problems. But the gap between these basic studies and their application is narrowing fast.

—Jon Cohen

MATHEMATICS

In Mao's China, Politically Correct Math

SAN DIEGO—Karl Marx may be best remembered for inspiring the 20th-century revolutions in Russia and China. But during another upheaval, the Cultural Revolution in China during the 1960s and 1970s, his little-known musings on calculus may have saved mathematics.

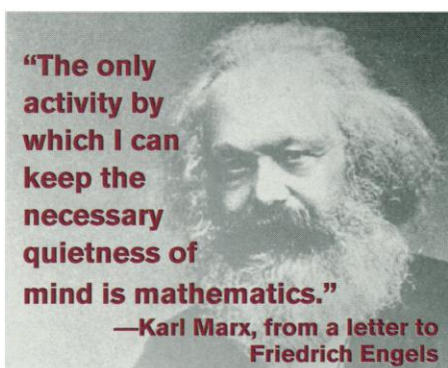
According to Joseph Dauben, a historian of mathematics at the City University of New York, mathematicians in China seized on Marx's comments about "dialectical" processes in mathematics, along with related passages in the writings of Chairman Mao, to justify research activity that might otherwise have been denounced as a decadent, imperialist abstraction. They did so, Dauben said here at the joint meetings of the American Mathematical Society and the Mathematical Association of America, with the help of a highly abstract theory imported from the capital of Western imperialism, the United States.

The starting point for Dauben's account, which Chinese mathematicians corroborate, is Marx's own fascination with the interplay of thesis and antithesis—the dominant process in

history, as he saw it—in certain mathematical procedures. Taking a limit, for example, entails thinking of a variable as both zero (thesis) and nonzero (antithesis—or possibly the other way around). "Marx regarded the analysis of the derivative, for example, as the analysis of a dialectical process, as the negation

of a negation," notes Dauben. Mao, too, commented favorably on the ideological implications of mathematics, linking the "internal contradictoriness" of positive and negative numbers with the paramount importance of motion and incessant, revolutionary change.

So when revolutionary change threatened intellectual endeavors during the Cultural Revolution, Dauben says, mathematicians in China took refuge in research that arguably



carried Marx and Mao's stamp of approval. Their safe haven, he says, lay in an approach to calculus known as nonstandard analysis, which epitomizes the mathematical qualities that appealed to Marx and Mao. The method, developed in the early 1960s by Abraham Robinson at the University of California, Los Angeles, uses sophisticated principles of mathematical logic to create a model of the real number system that includes infinitely large and infinitely small numbers along with such familiar values as 1, 2, $\sqrt{5}$, and π .

The model's infinitely small numbers provide a rigorous basis for the original concept of vanishingly small increments that Newton called "fluxions" and Leibniz labeled "infinitesimals"—they put flesh on what Bishop Berkeley, an early critic of calculus, derided as "the ghost of a departed quantity." As such, Robinson's theory gives a precise meaning to some of the intuitions that mathematicians and physicists bring to the study of functions, and it has led to solutions to a handful of problems that had eluded standard approaches. But it hasn't caught on widely, at least in the United States.

For Chinese mathematicians, though, Robinson's extension of the standard real numbers could be viewed as the dialectical synthesis of zero and nonzero—a use of the theory that Dauben learned about from Chinese mathematicians while he was writing a biography of Robinson. Nonstandard analysis provided "a means of reinterpreting the infinitesimal calculus within a materialist framework, to justify and promote their own mathematical study," Dauben says. "This saved many of them from being shipped out to the countryside."

Marx's mention of infinitesimals "made nonstandard analysis seem more acceptable than other fields to the authorities at the time," agrees Renling Jin, a nonstandard analyst at the University of Wisconsin, who grew up in China during the Cultural Revolution. Although he was too young then to witness what was going on in the Chinese universities, he says it is "very likely" that many mathematicians held on to their jobs by being politically correct à la Mao.

Interest in Robinson's theory led to an all-China symposium on nonstandard analysis in 1976. And although the revolutionary fervor of those days is long past, enthusiasm for nonstandard analysis remains high, as indicated by meetings in 1984, 1987, 1989, and 1996. Most of the research presented there has appeared only in Chinese, Dauben notes. But he thinks it's only a matter of time before its influence will be felt in the West. As Mao put it (albeit in a different context), "We must encourage our comrades to think, to study the method of analysis, and to cultivate the habit of analysis." Even bad times, it seems, can give birth to good—if nonstandard—mathematics.

—Barry Cipra

EXTINCTIONS

Cores Document Ancient Catastrophe

Last week, cores of ancient sea-floor sediment made a splash in the media, when a first look at deep-sea samples unloaded from the drill ship *JOIDES Resolution* revealed a layer of debris ejected from the great meteorite impact 65 million years ago. The cores, from off the U.S. southeast coast, were heralded by some as proof of the impact's potency. But researchers hardly needed proof beyond the 180-kilometer crater itself, identified nearly 5 years ago (*Science*, 14 August 1992, p. 878); for them, the real controversy is not whether the impact happened but whether it caused all or only a few of the extinctions that took place at the end of the Cretaceous period, 65 million years ago. And while public attention spotlighted the *Resolution* cores, another group of paleoceanographers has already retrieved—and analyzed—a similar core that they say convicts the impact of slaughtering most of the extinction's marine victims.

In a core drilled from a former seabed that now lies high and dry in southern New Jersey, Richard Olsson of Rutgers University and his colleagues in the New Jersey Coastal Plain Drilling Project found that many species of microfossils—remains of one-celled organisms such as foraminifera, nanoplankton, and dinoflagellates—flourished right up to the debris layer, then vanished. "It would be very hard to argue now that the impact did not occur precisely at" the time of the extinctions, says Olsson.

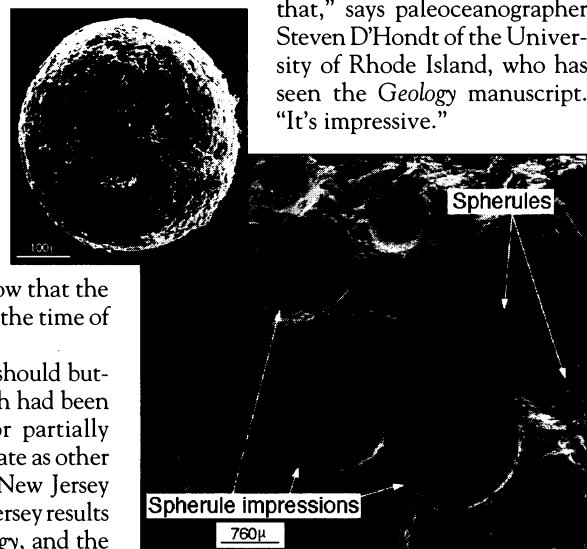
The chronology, Olsson says, should buttress earlier records, some of which had been disturbed, chemically altered, or partially eroded. Still, there's sure to be debate as other scientists get a look at both the New Jersey and the deep-sea cores. The New Jersey results were only just submitted to *Geology*, and the *Resolution* crew "just got off the boat," notes paleoceanographer Gerta Keller of Princeton University. "Any scientist will have to be skeptical" until the data become public.

Already, the cores establish the U.S. East Coast as a rewarding place to study the effects of the impact, which struck several thousand kilometers to the southwest on the Yucatán Coast. Closer to the crater, around the Gulf of Mexico and the Caribbean, the sea-floor record is a jumble of victims, survivors, and putative impact debris, perhaps because it was scrambled by giant tsunamis rushing out from the shallow-water impact (*Science*, 11 March 1994, p. 1372). "The effects [of the impact] were so large—boulders were moved around in some places—that there has been some uncertainty as to when the extinctions were in relation to

the geologic effects," notes Kenneth Miller of Rutgers, chief scientist of the New Jersey drilling team. The new cores, which are further from the impact and so undisturbed, should help remedy the dearth of convincing records.

Miller and his colleagues retrieved their core last November when they used a modest truck-mounted rig to drill in Bass River State Park just north of Atlantic City, New Jersey. Like the deep-sea cores, this core has each layer of sediment in the expected order, as indicated by each interval's distinctive microfossils. Between the last denizens of the Cretaceous and the few survivors of the subsequent Tertiary period are 6 centimeters of sand-size spherules of now-solidified melt: debris that splashed out of the crater while white-hot from the impact. The geologic instant of the catastrophe is so well preserved, says Olsson, that each spherule at the base of the impact layer can be seen to have left its own depression in the soft Cretaceous mud it settled on. "You can't get much finer physical resolution than

that," says paleoceanographer Steven D'Hondt of the University of Rhode Island, who has seen the *Geology* manuscript. "It's impressive."



Mark of extinction. Spherules of solidified impact melt (top) were nestled in mud from the end of the dinosaur age.

Olsson and his colleagues find that the denizens of the latest Cretaceous disappear precisely at the debris layer, while in the Tertiary new species appear thousands of years after the impact layer. The record "establishes a unique tie between ballistic ejecta from the Chicxulub crater and the extinction of marine organisms," says Miller, who concludes that the impact caused all the extinctions. That work will have to be confirmed by others, but between the New Jersey core and the three returned by *Resolution*, there should be plenty of slices of impact debris to go around.

—Richard A. Kerr