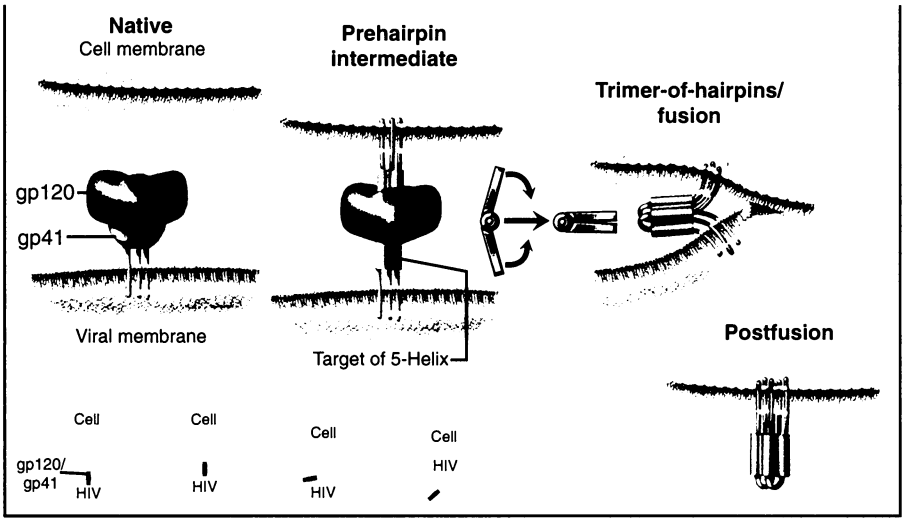
quickly replenish another estuary's stock that has been overfished," he says. Similarly, designers of protected reserves—often touted as nurseries that will supply fish to areas where fishing is allowed—may have to reshape plans. "Putting a reserve in one estuary may not do a lot of good" for another area's stocks, Thorrold says.

Although the study's policy impacts may not be felt for years, researchers say it is another sign of the otolith's growing value to scientists. European researchers, for instance, have recently launched a multimillion-dollar effort to use otolith signatures to track cod and other economically important fish. Steven Campana, a biologist at the Bedford Institute of Oceanography in Dartmouth, Nova Scotia, says otoliths "give you some very precise information not available from other kinds of studies." –DAVID MALAKOFF



Interference. A new compound, 5-Helix, stops HIV from fusing its membrane with a host cell's.

AIDS RESEARCH

HIV Inhibitor Blocks Virus From Cell

HIV, the virus that seemed invincible in the early days of the AIDS epidemic, has yielded ground to drugs that block its replication. But some strains of the wily virus have developed resistance to current drugs, and not all patients respond well to today's cocktail treatment. Searching for alternatives, researchers in the past several years have focused on another of the virus's vulnerable spots: the mechanism that snaps the virus into place against a host cell, allowing it to enter. Now, a team of researchers reports a new way to gum up that mechanism and prevent HIV's envelope from melding with a host cell membrane. They've designed a molecule that, in cell culture at least, prevents HIV from infecting cells.

"One wants to continue to identify new targets to attack HIV and add to the combination regime," says structural biologist Peter Kim of the Whitehead Institute for Biomedical Research at the Massachusetts Institute of Technology in Cambridge, whose team designed the molecule.

In the early 1990s Kim, recently tapped to head research and development at Merck Research Laboratories worldwide, and other research teams figured out how influenza infiltrates host cells. Many other viruses, including HIV, use a similar trick. The attack begins when HIV encounters a CD4 receptor on a T cell. This triggers a protein called gp41 that's anchored to the surface of the virus. The gp41 protein shoots out a harpoonlike projection that pierces the T cell's membrane. Then the two ends of the stretched-out gp41 protein snap together, pulling the virus's envelope and the cell membrane together. They fuse and allow the virus to penetrate the T cell.

Once this harpoonlike mechanism was understood, researchers began looking for wrenches to throw in the works. They've found two, and this week, in a paper published online today by *Science* (www.scienceexpress.org), Kim's group reports designing a third.

Before gp41 snaps the two membranes together, it's elongated in an intermediate formation. The two arms of the protein, called the C-terminal (anchored to the virus) and the N-terminal (hooked into the T cell) regions, are exposed. Drugs that bind to either end prevent the extended protein's two arms from clicking together into the final structure. Compounds that grab hold of the N-terminal region are currently in clinical trials, where they've been shown to reduce the viral load in people infected with HIV. Now Kim's team has designed a compound that binds to the C-terminal region.

The new molecule, dubbed 5-Helix, is the product of a "very clever, rational drug design," says HIV researcher John Moore of Cornell's Weill Medical College in New York City. The compound closely mimics the final structure that gp41 assumes when it fuses the viral and cellular membranes. That conformation contains six interconnected coils that fold together to look like a cluster of three hairpins. 5-Helix has five of the six coils, and it desperately wants another coil to fill in the gap. It does so by binding to the C-terminal end of the stretched-out gp41 much more effectively than the N-terminal end of the protein, thus preventing gp41 from folding together.

"The issue now," says Moore, "is not, 'Does [such a compound] work in vitro?,' but 'Can you translate it to in vivo?' " If 5-Helix or a related compound does work in humans, it probably won't dominate the market, he says. The protein would be digested if taken orally and so would have to be injected, limiting its appeal. But such a compound could help people who don't respond to other drugs.

Although he admits it's a long shot, Kim thinks 5-Helix might also serve as the basis for a new AIDS vaccine—ultimately, the only hope for curtailing the worldwide epidemic. The linear sequence of amino acids that make up gp41 varies a lot among different HIV strains, so antibodies against the unfolded protein wouldn't protect very efficiently. But the surfaces of the coiled protein that are exposed just before gp41 snaps into place are highly conserved—that part of the protein looks similar in all HIV clades. And that, says Kim, suggests that antibodies to 5-Helix, which displays some of the same coiled fragments of protein as gp41, might also attack the virus.

Robert Lamb, a virologist at Northwestern University in Evanston, Illinois, says that using 5-Helix as the basis for an AIDS vaccine is an "exciting possibility" and worth trying. Conceptually, he says, the same sort of strategy would also apply to other viruses, including Ebola, that use a similar harpoon-protein mechanism to fuse their membranes with a host's.

–LAURA HELMUTH

PALEONTOLOGY

Mammoth Hunters Put Hopes on Ice

CAMBRIDGE, U.K.—In an anticlimactic ending to last year's TV special, a block of permanently frozen ground hewn from the Siberian tundra appears to contain only scattered remains of a woolly mammoth. But researchers say that the team's brute-force method of hauling remains to a lab for study while they are still frozen holds promise for more-intact

ILLUSTRATION: CAMERON SLAYDEN

Headier days. The hunt proved more rewarding than the trophy for scientific coordinator Dick Mol.

specimens unearthed on future expeditions.

Sponsored by the Discovery Channel, a team led by Bernard Buigues, a Paris-based North Pole tour operator, chiseled the 23-ton block from the Taimyr Peninsula in October 1999 and airlifted it by helicopter more than 300 kilometers to the northern Siberian town of Khatanga. The previous year, Buigues had excavated the skull of the 20,380-year-old male mammoth, nicknamed "Jarkov" after the family of indigenous Dolgans who had found its tusks sticking out of the snow. Ground-penetrating radar readings hinted that substantial portions of the carcass remained underground. But after inspecting the block, a Russian project scientist argued that it was unlikely to harbor mammoth remains (*Science*, 29 October 1999, p. 876).

After moving the block into a tunnel in Khatanga used to store reindeer meat and fish, Buigues and company began thawing it with hair dryers last October. Near the top of the block they found three thoracic vertebrae, two of which lay in anatomical position, and a pair of ribs lying haphazardly, like crossbones. But the bones were devoid of flesh. Indeed, the only flesh uncovered during the season's final thawing session, witnessed by *Science*, was a 10-centimeter-long strip of tissue that looked like beef jerky. "I was expecting a lot and got a little," Buigues said at the time.

The denouement comes as no surprise to many. But the revelation that the block does not contain a whole mammoth has drawn ridicule from some quarters. An editorial in the 6 January edition of *The Times* of London even suggested that the whole episode was a hoax. "Prehistoric hoaxes offer very good sport, as our dalliances with Piltdown man have long proven," *The Times* said.

However, Discovery Channel officials and project scientists reject that characterization. "Nobody ever said Jarkov was going to be Sue," says Ross MacPhee, curator of mammals at the American Museum of Natural History in New York City, referring to the nearly complete *Tyrannosaurus rex* skeleton.

Buigues's team takes some consolation from having succeeded in airlifting the remains, still frozen in place, to an environment where they could be thawed under controlled conditions. "Whether or not this mammoth is the epitome of frozen mammoths is immaterial," says Larry Agenbroad, a geologist at Northern Arizona University in Flagstaff. "We can now go out and get more." –RICHARD STONE

PALEOANTHROPOLOGY

Oldest Human DNA Reveals Aussie Oddity

Australian scientists say they have successfully extracted an extinct genetic sequence from an anatomically modern man who died on the shores of an Australian lake about 60,000 years ago. The sequence is so primitive that it raises questions about the leading model of human origins, the "Out of Africa" theory, which holds that our ancestors first arose in Africa, then spread throughout the world perhaps 100,000 years ago.

DNA studies from living populations have repeatedly pointed to such a recent African origin. But the new data, published in the 16 January 2001 *Proceedings of the National Academy of Sciences*, present a "serious challenge" to a "simplistic" Out of Africa scenario, says co-author Alan Thorne, an anthropologist at Australian National University in Canberra. Thorne argues that the results better fit a model known as multiregionalism, favored by a determined minority of anthropologists, in which people coming from Africa interbred with earlier humans already living in various parts of the Old World.

The researchers say they extracted mitochondrial DNA (mtDNA) from the remains of 10 ancient humans—a striking feat, as other scientists had extracted ancient human DNA from only a handful of subjects (including the 5300-year-old Alpine "Ice Man" and three 30,000-plus-year-old Neandertals). The 10 fossils—four from Lake Mungo in New South Wales, Australia, and six from Kow Swamp in nearby Victoria—range from 2000 to 15,000 years old, except for a Lake Mungo man known as LM3, who has been dated by three separate methods at more than 60,000 years old (*Science*, 21 May 1999, p. 1243). LM3 is "the oldest individual dated accurately and possibly the oldest human from which DNA has been recovered," Thorne says.

Far out. Mungo man bore a now-vanished sequence of mitochondrial DNA.

The key finding, Thorne says, is a sequence in LM3's mtDNA that differs both from that of the other fossils and from that of modern people. Now extinct in modern human mtDNA, it exists only as a remnant, or "insert," on chromosome 11 in the modern nuclear genome. Scientists have long suspected this sequence to be a copy of old mtDNA that found its way into the cell nucleus, as other sequences are known to have done.

Thorne says the data undermine studies that support the Out of Africa scenario with genetic evidence from living populations. By analyzing variations in modern DNA sequences and tracing their "roots" backward in time, scientists have concluded that everybody now alive stems from African ancestors who replaced earlier types of humans without interbreeding with them. Now, the most divergent, deep-rooted mtDNA sequence of any anatomically modern human has turned up thousands of miles from Africa. "We don't say that humans evolved in Australia," Thorne says—but the logic behind earlier genetic studies could lead to just such an absurd conclusion, he says. Instead, Thorne thinks the new data support the multiregional hypothesis, which holds that *Homo sapiens* may have inherited DNA from precursors such as *Homo erectus*, who spread into Eurasia more than 2 million years before the presumed Out of Africa migrants did. Thorne and Milford Wolpoff of the University of Michigan, Ann Arbor (see p. 231), are central proponents of multiregionalism.

"For many years people have been saying Out of Africa is correct because the genetic evidence is consistent," says John Relethford of State University of New York College at Oneonta. But the Australian study "suggests that if we saw more ancient sequences we might get a very different picture than we get from looking only at the DNA of living

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