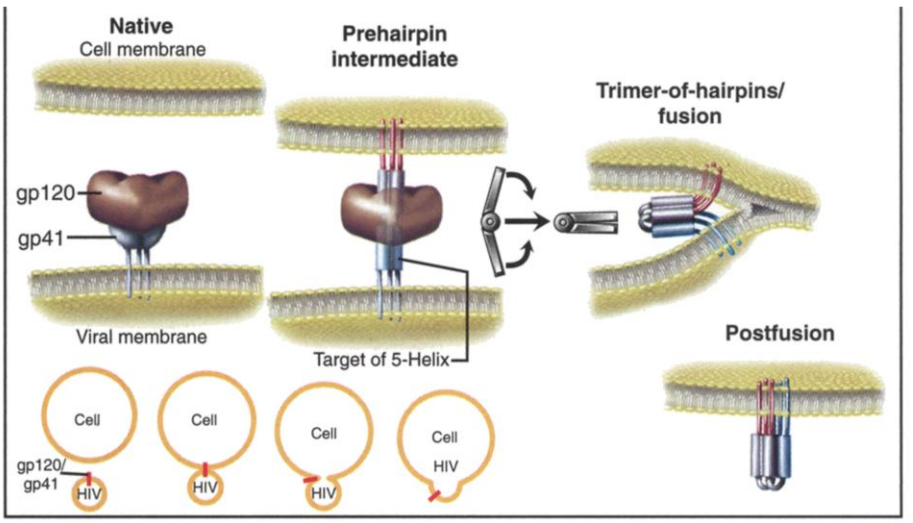
quickly replenish another estuary's stock that has been overfished," he says. Similarly, designers of protected reserves—often touted as nurseries that will supply fish to areas where fishing is allowed—may have to reshape plans. "Putting a reserve in one estuary may not do a lot of good" for another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