New AIDS Vaccine Stimulates Hope

An ideal AIDS vaccine must pack a one-two punch. It would generate immune cells that destroy infected cells and elicit HIV-binding antibodies that block infection.

Scientists have grown increasingly frustrated at the inability of potential vaccines to do the latter, that is, to induce neutralizing antibodies. "Last year was probably one of the low years for antibodies," says David C. Montefiori of the Duke University Medical Center in Durham, N.C.

A research group led by Jack H. Nunberg of the University of Montana in Missoula has now developed a possible vaccine for AIDS that, at least in mice, coaxes the immune system to secrete potent antibodies that block HIV's infectivity surprisingly well.

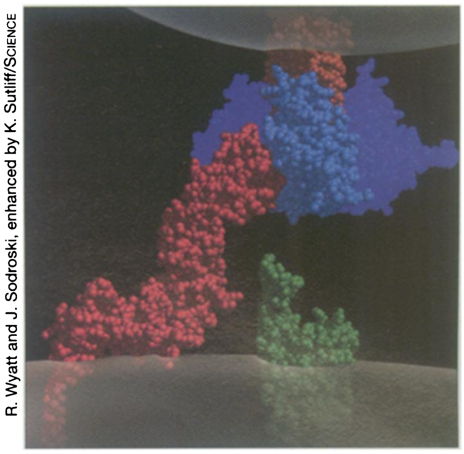
The vaccine has drawbacks that likely preclude its use in people. Nonetheless, it offers evidence that a human AIDS vaccine should be able to induce potent neutralizing antibodies, and it suggests what that vaccine might look like.

"In terms of proof of concept, if the results are correct, [the study] represents a major breakthrough for HIV-vaccine development," says Montefiori.

Vaccine developers have sought to provoke antibodies with pure gp120, a viral protein that HIV uses to attach to and infect cells. Human trials of gp120 vaccines are ongoing (SN: 7/11/98, p. 31).

Yet most AIDS researchers are openly skeptical of current gp120 vaccines. The antibodies generated in response to gp120 alone don't work against the wide variety of HIV strains found in people, apparently because they don't target the regions of the protein crucial to infection. Those regions show themselves only when gp120 snags CD4, a protein on the surface of the immune cells that HIV infects. Then, gp120 undergoes changes in shape that allow it and another viral protein, gp41, to sneak the virus into cells (SN: 11/7/98, p. 292).

Nunberg and his colleagues believe they've found a way to let the immune system see the vulnerable spots of these viral proteins. They added viral genes to skin cells, forcing them to make gp120 and gp41. They also engineered some tumor cells to make CD4 and one of the other human proteins that the AIDS virus latches onto. By mixing the two groups of cells and then dousing them with formaldehyde, the investigators hoped to catch the cells in the process of fusing, when critical parts of the viral proteins would be exposed.



R. Wyatt and J. Sodroski, enhanced by K. Sutliff/SCIENCE

This model shows how molecules on the surface of HIV (top), such as gp120 (blue), bind to immune-cell proteins (red and green) to infect the cell.

When the researchers injected the formaldehyde-fixed cell fusions into mice, the animals' immune systems made antibodies that, in test-tube experiments, prevented the AIDS virus from infecting cells. The antibodies thwarted 23 out of 24 HIV strains taken from patients worldwide, Nunberg's team reports in the Jan. 15 SCIENCE.

"This is one of the first really new ideas to come along in thinking about how to make a vaccine [that creates] an antibody response to the virus. It's exciting," says David Baltimore of the California Institute of Technology in Pasadena, who heads the national effort to develop an AIDS vaccine.

Several teams already plan to test this vaccine strategy in nonhuman primates. "We hope to begin those studies in several months," says Nunberg.

"Often, you can generate antibodies in mice, but you won't be able to generate them in larger animals, especially primates," notes Montefiori.

Researchers also caution that this particular AIDS vaccine is impractical for use in people, in part because it uses tumor cells. Nevertheless, the investigators are confident that they will learn how to duplicate its success with a safer, more practical vaccine preparation. —*J. Travis*

Fossil ancestor pursued varied tastes

Ancient members of the human evolutionary family, who lived before the emergence of our direct ancestors around 2.5 million years ago, favored forested areas where they ate mainly leaves and fruit, several studies of fossil teeth have indicated. These findings, which apply to the creatures known as australopithecines, feed into the view that meat eating first caught on later, among members of the bigger-brained *Homo* species, who needed more energy and protein.

A new analysis of dietary clues in 3-million-year-old teeth from *Australopithecus africanus*, however, suggests that it consumed a wider variety of food than has often been assumed, including a fair amount of meat.

A. africanus might have eaten about as much meat as the early *Homo* species that inhabited the same part of southern Africa, contend Matt Sponheimer of Rutgers University in New Brunswick, N.J., and Julia A. Lee-Thorp of the University of Cape Town, South Africa. Only *Homo*, however, appears to have used stone tools to cut body parts off carcasses and to break open and dig marrow out of bones, they hold.

"The primary dietary difference between *A. africanus* and *Homo* may not have been the quality of their food but their manner of procuring it," Sponheimer and Lee-Thorp say in the Jan. 15 SCIENCE.

The researchers examined two forms of the element carbon preserved in tooth enamel from four *A. africanus* individuals whose partial remains were unearthed at South Africa's Makapansgat Limeworks. For comparison, they also analyzed tooth enamel from other 3-million-year-old animals found at that site.

A. africanus consumed not only leaves and fruits but also large amounts of foods rich in carbon-13, which include grasses, sedges, and animals that ate those plants, the scientists report. A previous study directed by Lee-Thorp reported a similar pattern in the teeth of *Paranthropus robustus*, a member of a related line of upright walkers living from around 2.5 million to 1 million years ago. The wear on *A. africanus* teeth also suggested that the species ate meat.

"This is good science that questions the assumption that meat-eating was only possible among tool-using *Homo* species," comments Kaye E. Reed of the Institute of Human Origins at Arizona State University in Tempe. "But at this point, we still have no conclusive evidence that any australopithecines regularly ate meat."

A. africanus may have acquired its dental traits by eating tubers and roots from marsh grasses, supplemented by occasional meat treats, Reed says. Further studies need to examine whether modern chimpanzees that sometimes eat meat exhibit dental-carbon patterns similar to those of *A. africanus*, she adds. —*B. Bower*