NIH advisers endorse disputed vaccine trial

Top advisers to NIH Director Bernadine P. Healy voted last week to back a controversial congressional order to begin the first large-scale clinical trial of therapeutic vaccines designed to boost the immune systems of people infected with HIV, the AIDS-causing virus.

The advisory committee endorsed the recommendations of a scientific panel that last month favored a modified form of the mandated vaccine trial—based on preliminary medical evidence, the urgency of the AIDS epidemic, and the promise of $20 million in government funds. Such a trial could require 30,000 people if completed in two years; 14,000 if the trial lasted five years, according to NIH statistician Susan S. Ellenberg.

The results of many small, independent clinical studies suggest that *therapeutic* vaccines containing proteins called gp120 and gp160, cloned from HIV's outer shell, might slow or stop the progress of HIV in people already infected with the virus. In contrast, *preventive* AIDS vaccines are designed to bolster the immune defenses of uninfected people before exposure to HIV.

In October, Congress drew strong criticism from federal researchers and health officials when it set aside $20 million of the 1993 Department of Defense (DOD) appropriation specifically for a clinical trial of a gp160-based vaccine developed by MicroGeneSys, Inc., of Meriden, Conn.

Anthony S. Fauci, director of the National Institute of Allergy and Infectious Diseases, told SCIENCE NEWS that members of the panel were particularly displeased that Congress had singled out the MicroGeneSys vaccine after extensive lobbying by the company and its lobbyist, former Senator Russell B. Long.

Healy has criticized the appropriation repeatedly, calling it an attempt to dodge the peer review process, whereby qualified experts and researchers would evaluate the vaccine's scientific merits. Healy condemned the spending measure again at the advisory committee meeting last week, describing it as a "dangerous and possibly deplorable precedent for biomedical research."

Congress, however, did not exclude federal researchers completely from the decision process. The spending measure included a proviso that the trial could be stopped by the combined disapproval of NIH, the Food and Drug Administration (FDA), and DOD. In that case, the money would go to other AIDS research programs conducted by the military.

The bill also called on NIH to weigh the scientific merits of gp160 and advise on how a large-scale trial of the drug might proceed. This gave Healy an opportunity to convene a blue-ribbon panel, which met on Nov. 5 and Nov. 23. Its members included Fauci, FDA Commissioner David Kessler, representatives of DOD, and AIDS research advocates.

The panel concluded that currently available data on gp160, showing the vaccine is nontoxic and seems to provoke some immune response in those treated, would not ordinarily justify a large, expensive clinical trial. But in this case, because of the severity of the AIDS epidemic and the promising but inconclusive evidence that gp160 strengthens the body's defenses against HIV, the panel decided that the DOD appropriation should be spent on such a trial.

Panel members stipulated, however, that the trial should involve more than just the MicroGeneSys product. Other possible candidates include the gp120-based vaccines developed by Genentech, Inc., of South San Francisco, Calif., and the Biocine, Co., of Emeryville, Calif., and a gp160-derived vaccine from Immuno AG of Vienna, Austria.

Both Kessler and Fauci refused to speculate in interviews with SCIENCE NEWS about the criteria researchers would use to choose vaccines for the trial.

Participants in the DOD-funded trial should not be limited to military personnel but should include a diverse sample of the population, including minority groups, intravenous-drug users, and others whose incidence of HIV infection is high, the panel noted.

Besides backing Healy's blue-ribbon panel, the advisory committee recommended that another expert panel meet to draw up a proposed experimental design for the vaccine trial. This protocol would include the criteria for choosing candidate vaccines. *—D. Pendick*

Gold on silver: Laying down a mixed result

Layering gold on silver—a process as ancient as metallurgy itself—can still conjure up surprises. By carefully observing the deposition of gold atoms on the surface of a silver crystal, researchers have now uncovered a new, unusual kind of growth that leads to the formation of a thin gold film.

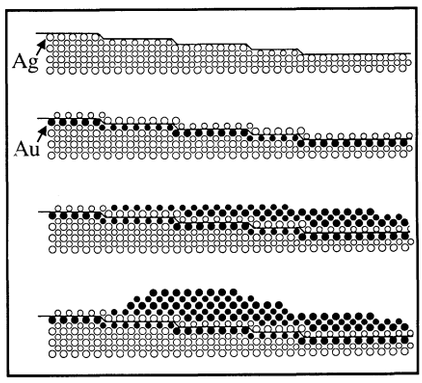
These experiments show that instead of forming a blanket atop a silver bed, gold atoms initially prefer snuggling down under the topmost sheet of silver atoms to form an "underlayer." Only after this submerged layer is nearly complete does growth of a gold film occur on top of the upper silver layer.

"We were all surprised by this counterintuitive and unexpected result," says Shirley Chiang of the IBM Almaden Research Center in San Jose, Calif. Chiang and her colleagues report their findings in the Nov. 30 PHYSICAL REVIEW LETTERS.

The IBM effort was inspired by the puzzling results of an experiment performed two years ago by researchers at Rutgers University in Piscataway, N.J. Their measurements of ions reflected from a gold-coated silver surface suggested that either the gold layer had to be two atoms thick, even when most of the silver surface was still bare, or the gold atoms had somehow mixed with the surface silver atoms.

By combining ion-scattering data with scanning tunneling microscope images of silver surfaces coated with varying amounts of gold, the IBM scientists concluded that gold atoms initially bury themselves beneath a layer of silver atoms. They saw no two-atom-thick gold steps.

These experimental results also confirm theoretical predictions made independently by physicist Che-Ting Chan and co-workers at Ames Laboratory of Iowa State University in Ames. The group's calculations, reported in the Sept. 14 PHYSICAL REVIEW LETTERS, had suggested that the formation of a gold underlayer would lower a silver surface's overall energy.



Deposition of gold on the stepped (110) surface of a silver crystal begins with the burrowing of gold atoms (solid circles) under the topmost layer of silver atoms (open circles). Only after this gold underlayer forms does gold begin to accumulate atop the silver surface. As deposition continues, finger-like plateaus of gold grow and coalesce into a solid film.

Because of the high mobility of surface silver atoms at room temperature, says IBM's David E. Fowler, "it seems plausible that the gold might end up underneath."

The IBM researchers also discovered that in later stages of deposition, gold atoms form long, flat, finger-shaped plateaus all pointing in the same direction on the silver surface. These two-dimensional formations, in turn, provide the foundations for three-dimensional gold "islands," which gradually enlarge and coalesce into a solid film.

"That's a behavior that's been talked about but not observed before," Fowler says. *—I. Peterson*