SCIENCE NEWS of the week

Human Gene Therapy Wins Crucial Victory

For the first time, a federal advisory committee has approved research proposals to treat volunteers with genetically altered cells. In the two studies, researchers would administer altered white cells to adults suffering a deadly form of skin cancer and to children with a serious immune disorder. The committee's decisions, announced this week, represent a landmark step toward the goal of using gene therapy to combat a variety of human diseases.

Both proposals passed review by the Recombinant DNA Advisory Committee (RAC), a panel of scientists, ethics experts and laypersons charged with advising the National Institutes of Health (NIH) on genetic engineering. The two proposals must now obtain final approval from the Food and Drug Administration and the director of NIH. The scientists involved say they hope to begin treating volunteers with the gene-altered cells within a month.

RAC unanimously approved the request of Steven A. Rosenberg of the National Cancer Institute to inject gene-altered white cells into 50 men and women with advanced melanoma. These cells, called tumor-infiltrating lymphocytes (TIL), home in on and destroy tumors. Rosenberg's previous research revealed that unmodified TIL cells — removed from the patient's tumor, grown rapidly in the laboratory, and then injected back into the bloodstream — shrank tumors in some, but not all, melanoma patients (SN: 12/17/88, p.389).

To improve TIL's tumor-destroying punch, Rosenberg and his colleagues now want to splice in a gene coding for tumor necrosis factor, a potent chemical proven to shrink tumors in mice. "It is almost miraculous in what it can do in mouse models," Rosenberg told reviewers. He believes the altered TIL cells will cluster around human melanoma tumors, where the gene can direct production of large amounts of tumor necrosis factor.

Review scientists asked Rosenberg whether people given such treatment could develop toxic blood levels of tumor necrosis factor, especially if the altered TIL cells persist in the body to churn out the powerful chemical. But Rosenberg's description of recent work with TIL cells marked with a nontherapeutic gene (SN: 9/23/89, p.197) seemed to allay reviewers' concerns. He presented data from a report scheduled for the Aug. 30 NEW ENGLAND JOURNAL OF MEDICINE, showing virtually no hint of TIL cells marked with a special tracer gene in tissues removed from two people who died of advanced melanoma. That finding, he said, suggests that the therapeutic TIL cells will deliver their tumor necrosis factor and then die. Nonetheless, Rosenberg says he will initially keep the doses at very low levels.

The other research proposal involves the long-awaited gene-therapy trial for up to 10 children with an inherited immune disorder called adenosine deaminase deficiency (SN: 6/16/90, p.380). These children lack a crucial enzyme that normally helps the body disarm toxic chemicals building up in T-lymphocytes. The defect destroys the body's immune system.

Each child in the study would receive T-lymphocyte cells removed from his or her bloodstream and altered to carry a gene coding for the missing enzyme, according to the proposal submitted by NIH researchers R. Michael Blaese and W. French Anderson.

In this case, however, the vote was not without dissent. Richard C. Mulligan of the Whitehead Institute for Biomedical Research in Cambridge, Mass., voted against the proposal, noting that children with this once-fatal disease now can obtain treatment with a new drug.

At the same time, a RAC subcommittee deferred action on a proposal by Malcolm K. Brenner of St. Jude Children's Research Hospital in Memphis, Tenn. Brenner's team hopes to administer gene-marked bone marrow cells to discover why some children treated for leukemia later suffer recurrence. — *K.A. Fackelmann*

Common origin cited for American Indians

The vast majority of American Indians most likely descended from a single migrating population from Asia, biochemist Douglas C. Wallace told a scientific gathering last week in Bar Harbor, Maine.

With that assertion, Wallace enters the long-running debate over who first settled in the New World. Much recent attention has focused on the linguistic research of Stanford University's Joseph Greenberg, who argues that Native American languages fall into three groups that descended from one ancestral tongue (SN: 6/9/90, p.360).

"Our findings support Greenberg's hypothesis," Wallace told SCIENCE NEWS. "If we go back far enough in time, most American Indians should genetically link up with one Asian population."

Wallace and his co-workers at Emory University in Atlanta studied mitochondrial DNA from South America's Ticuna Indians, Central America's Maya and North America's Pima. A total of 99 individuals, each with a different maternal ancestry, donated blood for genetic analysis.

Mitochondrial genes lie outside the nuclei of cells and are inherited only from the mother. Using DNA-cutting enzymes to snip mitochondrial samples at specific locations, the researchers pinpointed chemical sequences at those locations.

All three tribes have high frequencies of mitochondrial DNA containing at least three of four rare chemical sequences, two of which otherwise occur only in Asian populations, Wallace reports. Early Asian immigrants to the New World must have carried the four "master" sequences with them, he maintains. Moreover, most modern American Indians apparently descended from at least four women in an early migrating group, he adds.

Mitochondrial analysis has not yet yielded an entry date for the prehistoric settlers, although Wallace estimates that Asians first trekked into the Americas 15,000 to 30,000 years ago. Exceptions to the shared mitochondrial heritage include Eskimos, Aleuts, Navajos, Apaches and a few others who arrived later on, he says.

Wallace reported these results, detailed in the March AMERICAN JOURNAL OF HUMAN GENETICS, at last week's Short Course in Medical and Experimental Mammalian Genetics.

His group's findings contrast with those of another genetic study reported in March (SN: 6/9/90, p.361). Indians from predominantly Pacific Northwest tribes encompass up to 30 mitochondrial DNA lineages extending back 40,000 to 50,000 years, asserted a team led by Svante Pääbo of the University of California, Berkeley. A series of separate migrations must have fueled the observed genetic diversity, Pääbo proposed.

Pääbo and his colleagues studied chemical substitutions in a small section of mitochondrial DNA known to undergo rapid structural changes; Wallace's team searched for genetic markers along the entire thread of mitochondrial DNA.

Wallace says he has not seen Pääbo's data and does not know why the two studies arrive at opposite conclusions. However, he says the tribes he studied were largely free of the outside genetic influences that would obscure ancient mitochondrial mothers. Analysis of blood types and proteins affirms that the Ticuna and Pima tribes in his study had virtually no genes from non-native groups, while the Maya tribe possessed a small amount of European ancestry.

— *B. Bower*