Early Results of Gene Therapy Encouraging

Less than three months after she received the first federally approved infusion of genetically engineered cells to cure a disease, a young girl with a life-threatening immune deficiency shows signs of improvement, researchers reported last week. National Institutes of Health (NIH) gene therapist W. French Anderson told an FDA panel that preliminary findings leave him "cautiously optimistic" the novel therapy is working.

But Anderson also told reporters that related studies, in which cancer patients will receive genetically enhanced tumor-killing cells, remain stalled because of technical problems and because of a previously unpublicized "hold" placed on the procedure by some FDA reviewers who – despite the agency's approval last month – remain concerned about a potential risk of the experimental procedure.

Speaking before the FDA's Biological Response Modifiers Advisory Committee in Rockville, Md., Anderson and NIH co-worker R. Michael Blaese provided the first public progress report for a four-year-old girl with an inherited immune disorder called ADA deficiency (SN: 9/22/90, p.180). To date, she has received four infusions of gene-altered white blood cells. The researchers reported that for the first time in her life, the youngster's bloodstream now contains normal numbers of disease-fighting T cells, a kind of white blood cell normally destroyed in victims of ADA deficiency.

Anderson noted that her improved white cell count could not have resulted from the mere addition of the laboratory-reared cells; the number of white blood cells circulating in her body has doubled since she received a number of cells equal to about 10 percent of her original count. This suggests the engineered cells are somehow nurturing the girl's handicapped white blood cells, perhaps by secreting growth factors that her own cells cannot make.

Blaese says tests indicate the engineered cells, which live in the girl's circulation for at least three weeks after each infusion, may have a survival advantage over ADA-crippled cells – a finding researchers had hoped to see. He says other measures of the girl's immune status, while "not discouraging," remain too preliminary to release. The girl remains healthy and a second child with the same disease may begin receiving the same treatment in January, Blaese says.

Clinical trials of a similar genetic therapy for malignant melanoma could begin within the next three weeks, Anderson told the FDA committee. But he also noted that the team performing the therapy, which is led by Steven A. Rosenberg of NIH and includes Anderson and Blaese, had experienced problems getting patients' gene-altered cells to grow properly in culture. The cells have been engineered to produce supplemental quantities of a naturally occurring cancer-fighting compound called tumor necrosis factor (TNF).

Anderson also revealed that the FDA's highly publicized "approval" of the cancer procedure in November included a proviso requiring the resolution of certain unanswered questions before the first infusions begin. As of this week, the FDA's hold remains in effect, Anderson told SCIENCE NEWS. He said the agency wants to know how much TNF produced by the engineered cells remains bound to those cells' outer membranes. Most of the altered cells get trapped and destroyed by the liver before ever reaching the tumor site, Anderson notes. He says some FDA reviewers worried that if large amounts of TNF remain bound to the membranes of cells captured by the liver, then toxic TNF concentrations could build up in that organ.

Jay J. Greenblatt, chief of the National Cancer Institute's drug regulatory affairs section, says the Rosenberg team this week provided the FDA with new evidence that very little TNF remains membrane bound, suggesting the therapy poses little risk of liver damage. He suspects the first infusions into cancer patients may begin during the first week of January. *– R. Weiss*

Reading climate changes in an Ice Age map

Long before the age of automobiles, long before the invention of the wheel, natural events caused atmospheric carbon dioxide levels to climb dramatically at the end of the last Ice Age. Uncovering reasons for that increase may help researchers better predict the climatic impact of the present carbon dioxide buildup caused by human activities.

European botanists now report on one piece of the puzzle: how the continents affected atmospheric levels of this gas. After constructing a global map of vegetation at the peak of the glacial age, the researchers found that soils and land plants actually helped damp some of the carbon dioxide increase at the end of the last Ice Age.

Jonathan M. Adams of Cambridge University in England and his colleagues from France and Germany produced their map of the vegetation existing 18,000 years ago by sifting through published reports on ancient pollen and other plant remains in sediments from around the world. They then estimated how much carbon dioxide was locked within the plants, soil and peat in specific regions.

Continental vegetation and soils contained far less carbon dioxide during the Ice Age than they do today, the researchers report in the Dec. 20 NATURE. Carbon storage on the continents totalled 968.1 billion tons 18,000 years ago, compared with 2,319.4 billion tons now, an increase of 140 percent.

The atmospheric level of carbon dioxide increased at the end of the Ice Age, from 200 parts per million (ppm) during glacial times to 280 ppm in the 1800s. While many researchers believe that oceans supplied this extra carbon dioxide, they wondered what was happening on land. The work by Adams' group suggests that as the climate warmed after the Ice Age, land plants and soils worked against the oceans by absorbing some of the ocean-liberated gas – a finding that runs counter to earlier studies based on computer models.

The issue of carbon storage on the continents remains a major question for those studying the current rise in carbon dioxide, caused by fossil fuel burning and forest destruction. Only about half the carbon dioxide emitted each year remains in the atmosphere, indicating that "sinks" on land or in the ocean must absorb the rest. While experts have long considered the world's oceans as the major sink, Pieter Tans of the National Oceanic and Atmospheric Administration in Boulder, Colo., and his co-workers suggested last year that land vegetation takes up and stores a major portion of the carbon dioxide that does not stay in the atmosphere (SN: 8/26/89, p.132).

William H. Schlesinger, a biogeochemist from Duke University in Durham, N.C., debates that theory. The new work by Adams' group suggests land vegetation and soils absorb carbon dioxide slowly and can only store a small fraction of the gas emitted into the air each year by human activities, comments Schlesinger in the same issue of NATURE.

Adams, however, cautions against using the new study to judge current events because the changes at the end of the Ice Age occurred over thousands of years. Soils and vegetation could respond quite differently to the more rapid carbon dioxide increase occurring today and may in fact absorb a large fraction of the emitted gas, he told SCIENCE NEWS. *– R. Monastersky*