NIHRAC okays gene therapy

WASHINGTON, D.C.—The National Institutes of Health Recombinant DNA Advisory Committee (NIHRAC, Bethesda, MD) approved seven gene-therapy clinical proposals—two for HIV-infected individuals and five for cancer patients—during its September meeting. NIHRAC has now approved 58 such gene-therapy protocols.

The committee also heard tantalizing, though preliminary, data from a safety trial now under way that suggests that gene-therapy protocols may be effective against adult brain tumors. The trial—sponsored by Genetic Therapy Inc. (GTI, Gaithersburg, MD)—involves the use of a retrovirus vector to introduce a gene for ganciclovir susceptibility into a patient's tumor cells, a procedure followed by intensive treatment with ganciclovir. So far five of eight patients appear to have responded to the treatment, with three patients showing tumor shrinkage.

Including the two gene-transfer protocols involving HIV patients just approved, NIHRAC has now approved a total of five such proposals. Earlier approvals include a proposal from Viagene (San Diego, CA), another from Gary Nabel of the University of Michigan Medical Center (Ann Arbor, MI), and one from a team at NIH.

One of the two HIV protocols just approved—described by Flossie Wong-Staal at the University of California, San Diego (La Jolla, CA)—proposes transferring a gene for a ribozyme that cleaves an HIV gene into virus-infected CD4 lymphocytes of AIDS patients, thereby interfering with replication of the HIV virus in these cells.

The other HIV proposal, which has already been approved for HIV-infected individuals with lymphomas, was outlined by Philip Greenberg of the University of Washington (Seattle, WA). This proposal is a cooperative venture with Immunex (Seattle, WA). It calls for removing CD8 lymphocytes from an HIV-infected individual, amplifying them *in vitro*, and then reinfusing them into the patient to combat HIV-infected CD4 lymphocytes, since CD8 lymphocytes generally keep CD4 lymphocytes in check. As a safety measure, the extracted CD8 lymphocytes will be engineered with a gene to make them sensitive to ganciclovir.

Of the five proposals approved for treating cancer, three call for the use of interleukin-2 (IL-2) genes. The first—submitted by Peter Cassileth at the University of Miami (Miami, FL)—aims at placing an IL-2 gene into the tumor cells of patients with lung cancer as a way of treating that malignancy. Increased IL-2 production by these tumor cells should signal the immune system to attack them.

The second IL-2 proposal—which was deferred at an earlier NIHRAC meeting and subsequently modified and resubmitted by Tapas Das Gupta of the University of Illinois College of Medicine (Chicago, IL)—outlines a broadly similar immune-system-based strategy for using IL-2 genes to treat patients with malignant melanoma. And the third IL-2 proposal—described by James Economou of the University of California, Los Angeles (Los Angeles, CA)—also involves an approach based on the transfer of an IL-2 gene into a patient's tumor cells as a way of treating metastatic melanoma.

Another cancer proposal that won approval from NIHRAC will be tested on patients with breast cancer. This proposal—which was resubmitted by Joyce O'Shaughnessy of the National Cancer Institute (Bethesda, MD)—calls for the insertion of a multidrug resistance (MDR) gene into a patient's stem cells as part of a bone-marrow-transplantation procedure. The MDR gene is expected to help patients better withstand the toxic effects of intensive chemotherapy to treat their malignancies.

The fifth cancer protocol that NIHRAC approved targets brain tumors in pediatric patients. Like GTI's protocol, the proposal—outlined by Larry Kun at St. Jude Children's Research Hospital (Memphis, TN)—entails using a retrovirus vector to introduce a gene for ganciclovir susceptibility into a patient's tumor cells followed by intensive treatment with that drug.

--Jeffrey L. Fox