ANOTHER "MILESTONE"

GENE THERAPY SURGES FORWARD

WASHINGTON, D.C.—These days gene therapy is the main review task before the National Institutes of Health Recombinant DNA Advisory Committee (NIHRAC, Bethesda, MD). Last month it recommended approving two closely related human gene-therapy tests at NIH and a third "milestone" proposal from the University of Michigan (Ann Arbor). But it rejected a proposal from the University of Rochester (Rochester, NY).

A contradiction was illustrated by committee handling of a proposal presented by Scott Freeman of the University of Rochester School of Medicine, which was not approved, and its handling of other proposals that were okayed. Freeman's protocol, which calls for treating patients with refractory ovarian cancer, proposes inserting a thymidine-kinase gene into a fraction of tumor cells from patients to make the cells more susceptible to the drug gancyclovir.

The exchange between Freeman and committee members quickly grew uneasy, with reviewers questioning the proposal on several technical points but also objecting to his calling the procedure an anti-cancer "vaccine" and a "treatment" instead of an "experiment." The committee, moreover, criticized Freeman for not completing several tests of cell lines that its subcommittee had called for. Freeman countered that he was being "asked to meet standards that other investigators have not met."

Later, the committee did not object to similar language—"to immunize patients against their own tumors"—in a proposal (actually two nearly identical proposals) from Steven Rosenberg of the National Cancer Institute (Bethesda, MD) and his collaborators at NIH. Indeed, the Rosenberg proposal sailed through the committee. The proposal entails the extraction of tumor cells from patients with advanced cancer. In one component, the cells will have a gene for interleukin-2 (IL-2) inserted before being injected back into the patients. In the other component, the gene for tumor necrosis factor (TNF) will be used. The committee approved the study of up to six patients with IL-2 and six others with TNF.

The committee also recommended approving a gene-therapy test on patients with familial hypercholesterolemia, a condition in which a missing cell receptor for lipid metabolism leads to accelerated deposition of cholesterol in the circulatory system, resulting in heart disease and, often, death at an early age. James Wilson at the University of Michigan Medical Center plans to insert the gene for the missing receptor into liver cells placed in culture after being removed surgically from patients. The risks to patients arise mainly from the surgery, says Wilson, adding that "we're treating a lethal disease."

Although several committee members urged Wilson to restrict the first test of the procedure to adults, a substantial majority agreed that imposing a formal restriction seemed ill-advised "biologically." Wilson says the test is "much more feasible and likely to be successful if done in children." After an intense debate, the test was approved for three patients without restrictions regarding age. NIHRAC chairman Gerard McGarrity, president of the Coriell Institute for Medical Research (Camden, NJ), calls the decision another "milestone," pointing out that it represents the first time the committee has approved a direct attempt to correct an inherited disease by genetically engineering somatic cells. —**Jeffrey L. Fox**