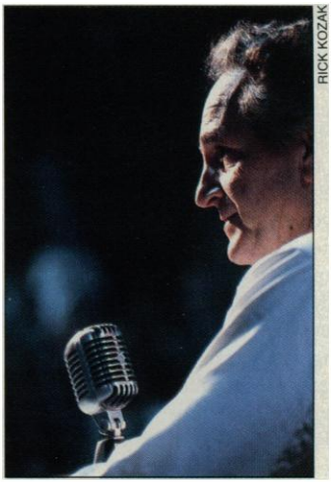
GENE THERAPY

Harkin Seeks Compassionate Use of Unproven Treatments

AIDS activists recently persuaded the Food and Drug Administration (FDA) to modify its rules to give terminally ill patients broader access to experimental and unproven therapies. Now the National Institutes of Health (NIH) is under similar pressure to change the rules on gene therapy. And the pressure is coming from somebody NIH can't ignore: Senator Tom Harkin (D–IA) who chairs the appropriations subcommittee that oversees NIH's budget.

Harkin wrote to NIH Director Bernadine Healy on 8 October to seek treatment for a politically well-connected patient who is dying of brain cancer. Some gene therapy researchers were angered—partly because the experimental therapy in question had already been turned down by NIH's Recombinant DNA Advisory Committee (RAC) because there was too little data to justify trying it. They see the political pressure as an attempt to avoid peer review. "This is monstrous," RAC member Robert Haselkorn at the University of Chicago wrote to the committee. "The manipulation of a U.S. senator coupled with the threat of further congressional action is...unconscionable."

Harkin's letter made it clear he is interested in more than this one case, however. He urged Healy to find a way to "give timely consideration to individual compassionate plea requests for approval of gene therapy procedures for terminally ill individuals," and requested "a temporary solution to this problem until an appropriate permanent legislative solution...can be achieved next year." Last week, Harkin's staffers sought to soften the senator's position, saying he was "not suggesting that there should be no review process. It would have to be approved by NIH. His letter was saying that they should be looking at possible ways...to act more quickly." RAC, which last week met to consider several gene therapy proposals (see box) established a working group to look into the issue.



RICK KOZAK

Special case. Senator Harkin sought help for a cancer patient.

Harkin's interest was spurred by the plight of Clemma Hewitt, a 51-year-old San Diego woman with grade 4 glioblastoma, a uniformly fatal brain tumor. Hewitt was originally from Iowa; her sister-in-law worked in Harkin's political campaigns; and her attorney husband, James O. Hewitt of Pacific Basin Enterprises in San Diego, served in four administrations, starting with President Kennedy.

Hewitt's cancer was discovered in January 1992. Since then, she has undergone brain surgery twice, including the removal of her entire right temporal lobe, three rounds of chemotherapy, radiation therapy, and an experimental treatment with radioactive monoclonal antibodies at Duke University. In the past 2 weeks, James Hewitt said, the size of his wife's tumor has increased by more than 30%.

As a last-ditch remedy, Ivor Royston, president and scientific director of the San Diego Regional Cancer Center, has proposed treating her with an experimental vaccine made by inserting the gene for interleukin-2 (IL-2) into glioblastoma cells. The IL-2-producing cancer cells would then be injected into her body. Theoretically, the production of IL-2 by the tumor cells will attract white blood cells, and generate a strong immune response to the tumor cells. Her immune system, primed by the genetically changed cancer cells, would then attack regular tumor cells anywhere in the body. Although similar approaches are under development at the National Cancer Institute and Johns Hopkins University, among other places, there is no evidence that such a treatment would work.

Indeed, Royston, a scientist-entrepreneur, and cofounder of Hybritech Inc. of San Diego, asked RAC to approve a similar study in the fall of 1991, but the committee resoundingly rejected the proposal because it lacked safety and efficacy data. Royston says he plans to submit a new protocol in 1993. In the meantime, Healy has told Harkin that she cannot approve the therapy on Hewitt, but suggested that she might qualify for enrollment in a brain cancer trial to be conducted by NIH researchers. In an interview with *Science*, Healy said, "In the estimate of the institution, the work [Royston proposed] has not gone far enough yet to be able to be cleared on a compassionate use basis."

Although RAC was not asked specifically to rule on the Hewitt case, it has appointed a subcommittee headed by LeRoy Walters, a bioethicist at Georgetown University, to hammer out a policy for such cases. It will be discussed at RAC's 1-2 March 1993 meeting. But that is cold comfort for Hewitt's husband. "That is not going to do her one bit of good at all," James Hewitt said after learning of RAC's decision. "If nothing is done, she might have 4 to 5 weeks."

–Larry Thompson

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Cystic Fibrosis Trials Approved

Just 3 years after an international team of researchers isolated the gene associated with cystic fibrosis, CF is about to become the first major inherited illness to be treated with human gene therapy. The National Institutes of Health's Recombinant DNA Advisory Committee approved three CF clinical trials at its 3-4 December meeting. In two of the studies, researchers will attempt to put the normal gene into cells that line the lungs of CF patients; a third, more conservative, study will put the CF gene into nasal epithelial cells, testing the treatment before going into the lung.

CF, the most common lethal hereditary disease in the United States, afflicts some 25,000 Americans, and 50,000 cases have been reported worldwide. The gene defect disrupts mucus production in the lungs, causing chronic infections and death, and the digestive tract is also affected. Median survival is 29 years in the United States.

The trials will mark the first use of a new gene transfer vector made from defective adenovirus, a virus associated with upper respiratory infections and pneumonia (*Science*, 19 April 1991, pp. 374 and 431). All previous gene transfer trials in humans, 37 in all, have used mouse retroviruses. The research teams are led by Ronald G. Crystal of the National Heart, Lung, and Blood Institute; James M. Wilson of the University of Michigan Medical Center in Ann Arbor; and Michael J. Welsh of the University of Iowa College of Medicine and the Howard Hughes Medical Institute, who is doing the more conservative study. The trials must still get final approval from NIH Director Bernadine Healy and the Food and Drug Administration. The Michigan study is scheduled to start in early 1993, with the others following.

–L.T.