Green light for gene therapy in healthy volunteers

A downsized, reconstituted version of the US National Institutes of Health (NIH, Bethesda, MD) Recombinant DNA Advisory Committee (NIHRAC) agreed in March that gene therapy researchers may begin studying recombinant vectors in normal, healthy volunteers. Committee members also are calling for the first special conferences under NIHRAC's new regime, recommending that the use of normal volunteers in research and also proposals to

test gene transfer as a means for human "enhancement" be scrutinized from an ethical as well as a scientific standpoint.

NIH officials now have some 174 gene transfer and gene therapy clinical research protocols in their databank, with 50 of those proposals considered adequately routine to be subject only to review by the US Food and Drug Administration (FDA; Rockville, MD) rather than by both FDA and NIHRAC.

Much of the recent streamlining efforts have aimed at simplifying this review and shifting most if not all of it to FDA (*Nature Biotechnology* 15:11, January 1997).

However, in all those cases, researchers planned to test their recombinant vectors in patients, often with life-threatening diseases such as cancer or AIDS. Now Ron Crystal and his collaborators at New York Medical Hospital-Cornell Medical Center (New York) are seeking to evaluate recombinant vectors in healthy volunteers. "We want to use volunteers because that's what's done in drug development under FDA phase I when subjects are closely monitored," Crystal says. Crystal's group plans to follow immune responses in skin, blood, and lungs elicited by an adenovirus-based recombinant vector administered in the skin. The vector will contain the *Escherichia coli* cytosine deaminase gene in a construction that is very simi-

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lar to the one Crystal's group is already using in patients with metastatic liver cancer.

"We want to develop a scientific database in humans," Crystal adds. He says that he takes his cue for such studies from the Motulsky-Orkin expert science panel that at the end of 1995 urged NIH officials and gene therapy researchers to return to basics as a way of overcoming some of the false hopes that have characterized the field (*Bio/Technology* 14:14, January 1996).

Some NIHRAC members were uneasy about allowing gene transfer procedures in volunteers who will not benefit medically. However, the committee endorsed Crystal's proposal. The uneasiness helped lead the committee to call for a special conference in which the general validity of such testing will be examined broadly. Moreover, the committee recommended review of the broad ethical questions raised if gene transfer and gene therapy procedures for enhancing either physical or intellectual traits were proposed for testing. No such proposals have yet been submitted to either NIH or FDA, officials say.

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