Subcommittee okays human gene transfer

After presenting new and previously withheld data to a National Institutes of Health (NIH) subcommittee, federal researchers last week received the panel's long-awaited approval to inject, for the first time, genetically engineered cells into humans.

The researchers still must gain final approval from NIH Director James B. Wyngaarden and the Food and Drug Administration. But the unanimous approval of the key NIH subcommittee dealing with human gene therapy appears to signal the end of a months-long controversy that has had researchers, NIH officials and scientific journal editors at odds over the circumstances under which new scientific data may be reported and published.

The experiments — proposed by W. French Anderson of the National Heart, Lung, and Blood Institute and Steven A. Rosenberg and R. Michael Blaese, both of the National Cancer Institute — are not designed to benefit patients directly but may aid in the development of better cancer therapies. They passed muster with the NIH's Recombinant DNA Advisory Committee (RAC) in October, despite a failure to win approval from the RAC's Human Gene Therapy subcommittee (SN: 10/8/88, p.228). Wyngaarden nixed the experiments later that month. He and others were reportedly miffed upon learning that the researchers had withheld from the RAC certain data so as not to jeopardize their publication in a major scientific journal. The NEW ENGLAND JOURNAL OF MEDICINE (NEJM) and SCIENCE, for instance, generally do not publish work scientists already have reported in detail elsewhere.

In a written response to Wyngaarden's statement that the "RAC will not be held hostage to the NEW ENGLAND JOURNAL OF MEDICINE," NEJM Editor-in-Chief Arnold S. Relman reassured the director that "our policy is not to interfere with authors responding to requests for information from duly constituted government bodies." NIH officials now want similar clarifications from other journal editors, according to Gerard J. McGarrity, a consultant to the Human Gene Therapy subcommittee that approved the Anderson proposal last week.

At that meeting, Rosenberg presented unpublished results of a novel cancer therapy in which the researchers remove tumor-attacking cells (called TIL cells) from patients with advanced melanoma. They cultivate those cells in the laboratory, then reinject about 1 trillion of them into the patient from whom the original cells were taken (SN: 6/25/88, p.404). "Given the information we now have, there's no question that some patients are benefited by this treatment," Rosenberg told the panel. "Of about 20 patients treated with TILs, we see a good response rate of 60 percent. So we're on to something that can cause a substantial number of tumor regressions, but it certainly requires a lot of improvement." The results are scheduled for publication in the Dec. 22 NEJM.

By adding a genetic marker to the TIL cells before reinfusing them, the researchers hope to determine the cells' fate in the body and to see whether some types of TIL cells attack tumors more efficiently than others do. "We're giving 10^{11} cells, but it's possible that a very tiny percentage are the effective cells. And if we can grow *them* 10^{11} we might improve the potency by hundreds of fold," Rosenberg said.

At the same meeting, Anderson presented new experimental evidence suggesting the chances of the procedure infecting a patient with a dangerous virus are less than one in a million. Anderson says he expects the FDA to complete its review within the next two months, and he hopes to perform the first human studies by March. The subcommittee limited its approval to 10 consenting patients with life expectancies of 90 days or less.

— R. Weiss

Heavy rock cast at claims of new force

Pushing measurements to finer and finer levels in recent years, geophysicists have disturbed the dust on Sir Isaac Newton's three-century-old law of gravity by finding evidence of an additional gravity-like force not included in Newton's famed equation. However, claims for such a new force are under siege.

Scientists reported last week at the American Geophysical Union meeting in San Francisco that unusual geological formations could explain the results of all three recent experiments detecting signs of non-Newtonian gravity. "There is a Newtonian explanation for the observed results," says Robert L. Parker, a geophysicist at the Scripps Institution of Oceanography in La Jolla, Calif.

While work by Parker and his colleagues calls into question the evidence for an additional force — thought to be about one-fiftieth the strength of gravity — it does not completely discredit the experiments. Above all, geoscientists say, the new analysis underscores the need for better experiments, some of which are in progress.

At stake is the accuracy of Newton's inverse square law of gravity, which holds that the gravitational attraction between two bodies is proportional to one over the square of the distance separating the bodies. If a new gravity-like force does exist, physicists will have to decide whether it is a previously unrecognized component of gravity or a completely novel fifth force.

Parker is one of 22 scientists from Scripps and from the Los Alamos (N.M.) National Laboratory involved in the most recent of the gravity experiments. In this project, researchers lowered gravity meters down a hole bored 2,000 meters into the Greenland ice cap. Led by Los Alamos' Mark E. Ander, the investigators tested the inverse square law by comparing actual measurements with values predicted using Newton's law.

After working through the preliminary data, Ander reported in August that they had found significant differences between the predicted and measured gravity. His team interpreted the results as an apparent violation of the inverse square law, although they cautioned that more analysis was needed (SN: 8/6/88, p.85).

Since then, the team has used a technique called ideal body analysis to show that their results need not mean Newton was wrong. This analysis relies on a well-known principle in physics, which holds that different objects can produce the same external gravity field. Therefore, one can imagine several unique arrangements of rock that would yield the same set of gravity measurements above ground.

Ideal body analysis proved that the gravity readings taken by the Greenland group could be explained by geological formations under the ice. Specifically, Ander's team has assumed that the bedrock density has a value of 2.70 grams per cubic centimeter. Yet if 25 to 35 percent of the bedrock has a density of 3 gm/cm^3 and it is arranged appropriately, their results would square with Newton's law.

No one knows what rock lies beneath the ice near the borehole. In the uncovered coastal bedrock, there are intrusions of dense material, but these fill only a small percentage of the rock, Ander says. "We got such a very large effect that we know some of it has got to be due to geology. The question is whether it is all due to geology, and it is hard to believe the entire thing is geology."

Parker also told scientists that the same kind of density variations could explain the results of two other projects that purportedly found signs of another force. In these experiments, researchers measured gravity in a mine shaft and on a television tower (SN: 12/19&26/87, p.388). Those involved with the tower experiment disagree with Parker's conclusions, saying it would require totally improbable geology to explain their results.

According to Parker, an ocean experiment now underway has the best chance of clearly measuring a non-Newtonian gravity force because researchers can survey gravity in several horizontal planes as well as in the vertical.

— R. Monastersky