

# Genetic Fixes and Future Generations

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Researchers at the University of Florida recently reported successful gene therapy in rats, permanently altering the genetic control of blood pressure. This is not the first successful gene therapy in an animal model, but it is the first time a specific and useful genetic change has been passed on to the animal's offspring and even to the animals in a third generation. This feat was achieved by performing the gene therapy not only on somatic cells but on germ-line cells as well.

This success signals the possibility of germ-line gene therapy in humans. But the incredible potential of permanently curing both present patients as well as their future children and grandchildren also brings significant new risks and questions. Who can consent for future individuals? What are the risks of creating unwanted changes in future generations? How should we decide which kinds of gene therapy are acceptable to be applied to the germ-line?

The goal of gene therapy is to cure disease or ailments by permanently repairing problems caused by flaws in our genes. For example, gene therapy could potentially be used to fix a genetic flaw that causes diabetes. There are 2 choices for the target of such therapies—either to cure just the individual by targeting the defective cells in his or her body (such as in the pancreas) or to also modify the genes in that individual's sperm or eggs so that the genetic defect is removed from that family's gene pool forever. So part of the promise of germ-line gene therapy is the prospect of treating not only affected individuals but all their future descendants before they exist. Parents would no longer pass genetic disease on to their children and their children's children.

Whatever change is achieved through germ-line gene

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therapy is permanent, for good or for bad—permanent not only for individual patients but a permanent change to the gene pool that will last as long as descendants continue to pass on their genes. That means that both the benefits and the risks of germ-line gene therapy are magnified, since a treatment's effects don't stop with the patient, as in other sorts of medicine, but continue on across generations. How sure must we be that the changes created by gene therapy won't be harmful—especially to future people—before using this new technology?

Even if we can agree that germ-line gene therapy is a sufficiently safe and acceptable way to permanently cure genetic disease, how can we guarantee respect for the interests of all those who are affected by it? The basis for ethical medical decision-making is that patients give their informed consent—especially when significant risk accompanies a treatment option. But how can consent be obtained from future people? Since that's impossible, under what conditions can people today make decisions for the people of tomorrow?

It turns out that we frequently confront this problem in other areas—decisions about federal budget deficits affect the economic outlook of future generations; and decisions about the use of natural resources today determine the state of the environment we leave for the future. We make judgments about these and other issues by weighing the current risks and benefits against those expected to occur in the future. Future effects are inevitably perceived as less valuable, both because they are off in the distance and because we can't truly foresee what the future will hold. New breakthroughs may render current thinking obsolete.

When the health of future humans is at stake, however, such calculations seem insufficient. Changes to our genetic legacy offered by germ-line gene therapy demand higher standards of certainty and safety, because once we start, going back is not an option, and continuing forward may alter the future. The challenge, then, is to think not only about ourselves, but also about how our decisions will affect those who come after us. The effect of medical decisions on future generations is not a typical consideration for most physicians, but the advent of effective gene therapy and its potential use on the germ-line means it may be part of physician-patient discussions sooner rather than later.