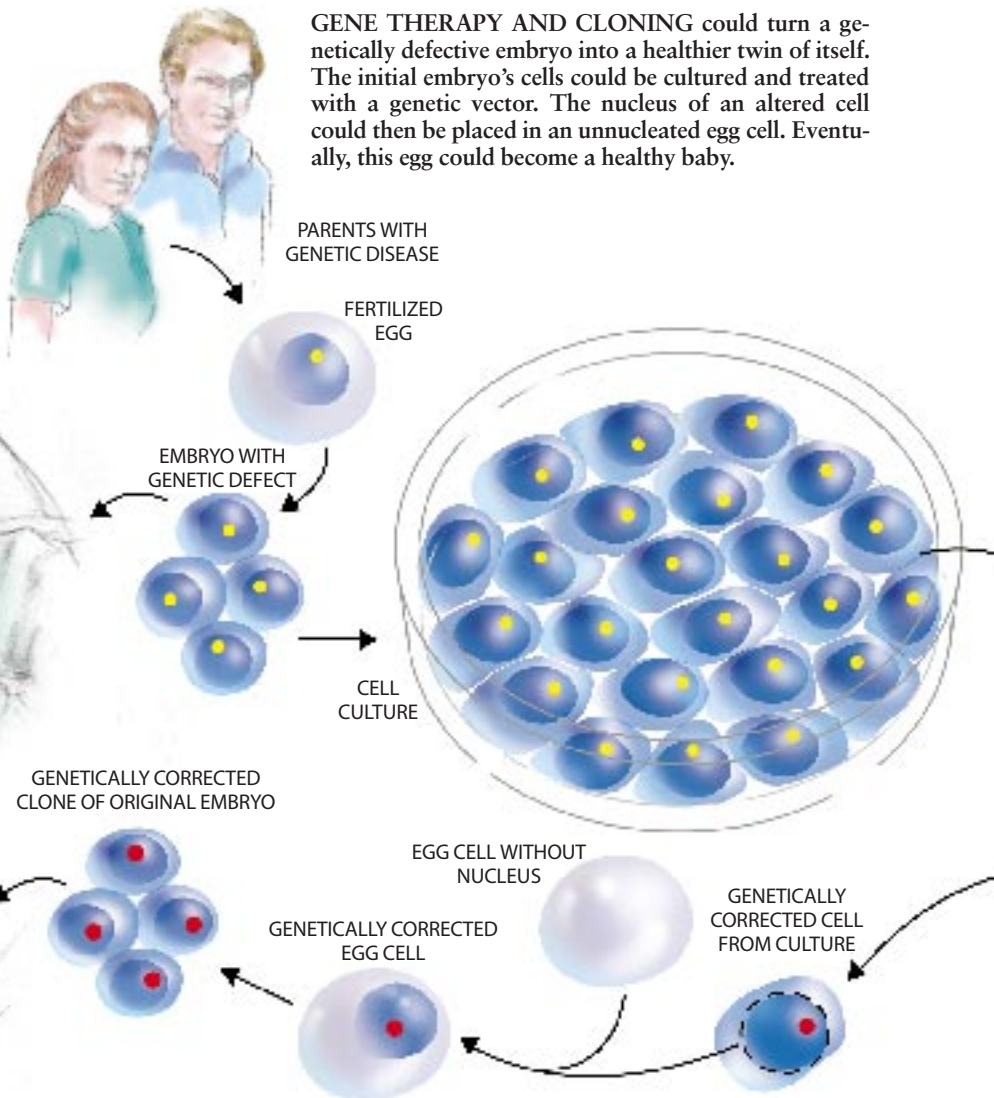
What Cloning Means

The recently debuted technology for cloning is usually discussed as a means of creating genetic copies of whole adult individuals. This is far from its only use, however. Cloning could be combined with other biotechnologies, either to achieve more novel goals or to improve on previous methods. Although the technique is still in its infancy, and needs to be studied and developed much further, educated musings about cloning's ability to inform gene therapy are already being brought to the table. An area that might particularly benefit is germ-line gene therapy—genetic modifications that could correct a problem for future generations. "I think cloning is going to be used as a tool that will make gene therapy work," comments Lee Silver, a molecular biologist at Princeton University and an expert on reproductive technologies. "For the first time, germ-line gene therapy becomes realistic."

Germ-line therapy, which is not yet being studied in humans, could ideally prevent deadly or debilitating disorders such as sickle cell anemia or cystic fibrosis. Such diseases are typically transmitted silently from generation to generation by people carrying one copy of a defective gene; the disease becomes manifest when two carriers have a child who inherits two copies.

Today prenatal genetic testing can reveal whether a fetus or embryo is affected with many of these conditions. The parents then have the option of aborting and rolling the genetic dice again with another pregnancy. In some cases, however, the dice are guaranteed to come up snake eyes. "If both parents are sickle cell diseased," Silver says, "then all of their embryos will also carry the disease. You can't select, because there are no good embryos." But gene therapy, aided and abetted by cloning, could theoretically correct the condition for their children, and all subsequent progeny as well.

The recipe would begin with a fertilized egg growing, in the laboratory, into



GENE THERAPY AND CLONING could turn a genetically defective embryo into a healthier twin of itself. The initial embryo's cells could be cultured and treated with a genetic vector. The nucleus of an altered cell could then be placed in an unnucleated egg cell. Eventually, this egg could become a healthy baby.

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for Gene Therapy

a mass of early embryonic tissue. A functioning gene—say, for the blood's oxygen-carrying protein, beta globin, which is mutated in sickle cell anemia—would then be inserted into the embryonic cells by tailored viruses or other vectors. (A marker sequence inserted along with the gene might help identify which cells took up the gene correctly.) The DNA of one of those cells could then be implanted into a new egg cell from the mother, beginning the pregnancy afresh. In effect, this last step replaces the original embryo with a healthier clone of itself.

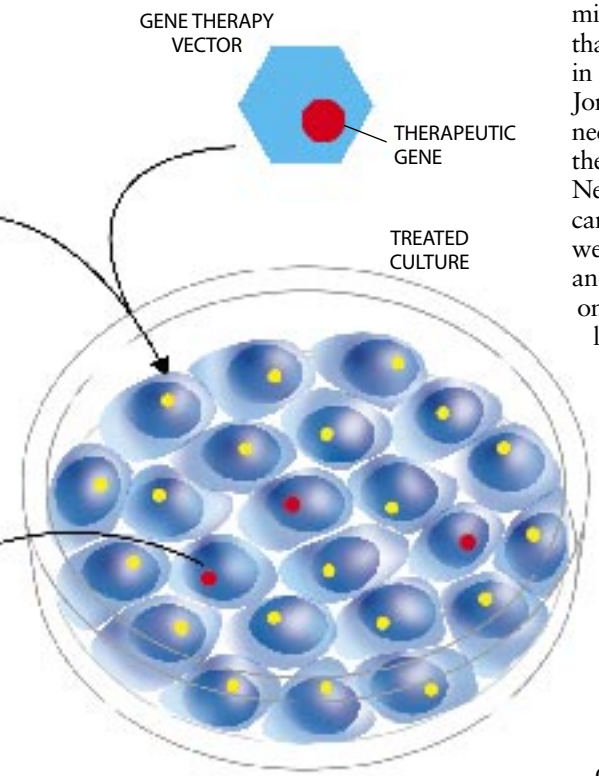
Germ-line therapy does not require a cloning step, but cloning might make it far easier. Very early stage embryonic cells, if separated, retain the ability to regenerate into whole embryos (indeed, that is how identical twins, triplets and quadruplets arise). Gene therapists could therefore alter the DNA of the embryonic cells and return one to the mother for gestation. The problem is that embryonic cells lose their "pluripotent" capacity after a few cell divisions, so the gene therapists would be forced to work on relatively few cells. The inefficiency of current gene manipulation techniques would consequently undermine many therapeutic attempts. With cloning, however, the age and number of cells eligible for manipulation is unlimited.

In theory, cloning would allow therapy on cells from a more advanced pregnancy (although this would raise more troubling ethical issues for many parents). In a variation on this theme, the gene therapy might also be conducted on cells from one of the parents. A child cloned from those altered cells would be free of the genetic defect but in other ways a genetic duplicate of its donor parent.

Cloning may remove some of the practical barriers to germ-line gene therapy, but it does not alter the ethical ones. Many researchers, not to mention the general public, are deeply concerned that germ-line techniques could be misapplied toward eugenic goals with authoritarian or even genocidal overtones. So even if cloning does enable the technology, there may not be a sudden rush to perform germ-line gene therapy.

Cloning may also benefit somatic gene therapy as a tool for basic research. By making it easy to obtain large numbers of genetically identical cells for study, cloning should help elucidate how embryonic cells commit to become a particular cell type. "That process of commitment involves shutting off genes that would otherwise have played a role in becoming a liver or a brain," reflects Jon Gordon, professor of obstetrics, gynecology and reproductive science at the Mount Sinai School of Medicine in New York City. "I think the fact that we can now reverse that gives us hope that we can understand that process better and understand diseases that are based on or manifest as errors in this process, like cancer." Cloning might therefore help therapists determine which genes they should be aiming to correct in various illnesses. If so, cloning's greatest utility may not be for making more people but for making more people healthy.

—Steve Mirsky and John Rennie



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