Genetic Cloning and Testing

BACKGROUND

Genetic Cloning

For years, humans successfully have used myriad genetic techniques—from selective breeding to genetic manipulation—to create plants and animals with desirable characteristics. Corn has been genetically engineered to improve resistance to fungus and viral infections, rot, and drought, and calves have been genetically altered to accelerate the growth process, to cite two examples.

Genetic cloning is a comparatively new process that uses the DNA contained in cells to "clone," or duplicate, strands of DNA, cells, or organisms to achieve exact copies of the original. These genetic clones are analogous to identical human twins—two genetically identical individuals whose development can be traced to the division of a single embryo. For some time, scientists have known that multiple animals could be created in the same way that human twins are created: by dividing a single embryo into multiple embryos shortly after fertilization. This creates offspring that are genetically identical to each other and have received their genetic information from each sexual parent (half from the male, half from the female).

In the early 1980s researchers discovered another cloning method. In nuclear transplantation cloning, scientists remove the DNA from a donor somatic cell (typically an embryonic or fetal cell) and implant it into an egg cell from which the DNA has been removed. The egg then is implanted into a female animal and carried to term. The new embryo will develop into an animal genetically similar to the *donor* animal, regardless of whether the donor or a foster mother carries it to term. Researchers have used this technique to clone sheep and cows from embryonic cells.

Until 1997 researchers were successful only at cloning organisms using cells from an embryo or fetus; no animal had been successfully cloned from the cells of an adult animal. But in February 1997 researchers at the Roslin Institute in Edinburgh, Scotland, announced that they had done just that. Dolly, a Finn Dorset sheep, was produced from the cell nuclei of a mammary gland in a six-year-old ewe. To create Dolly, the Scottish researchers performed 277 nuclear transfers of the DNA contained in the adult sheep's mammary gland cells into egg cells. Of these "reprogrammed" eggs, only 29 developed into viable embryos, and only one developed into a live lamb.

A CNN/*Time Magazine* poll, released two days after publication of the article announcing the cloning, revealed that two-thirds of the respondents believe it is

GLOSSARY

Chromosome
Units in the nucleus of a cell, composed of DNA, that contain genes; normal human somatic cells contain 46 chromosomes (23 pair).

Clone
Duplicate.

DNA
Deoxyribonucleic acid; the material inside the nucleus of a cell that carries genetic information.

Embryo
The prefetal product of conception from implantation through the 12th week of development. An embryo conceived through sexual reproduction receives half its genetic information from each sexual parent—that is, half comes from the sperm and half from the egg. A cloned embryo receives all its genetic information from one parent—the DNA donor.

Gene
A hereditary unit that occupies a specific location on a chromosome and may help to determine a particular characteristic in an organism; genes exist in various forms and can undergo mutation.

Genetic marker
A known DNA sequence associated with a particular gene or trait; some are associated with certain diseases or conditions.

Genetic profile
A record of a person's genetic makeup.

Genome
The complete collection of an organism's chromosomes.

Somatic cell
One containing a full complement of chromosomes, one set from each sexual parent.

morally unacceptable to clone animals, and 89 percent believe it is morally unacceptable to clone humans. On March 2, 1997, another group of scientists—this time in Oregon—announced they had cloned monkeys from multiple embryos. Together, these developments are believed to mean that is possible to genetically clone humans.

Reaction to the announcement of Dolly's birth was swift. On March 4, 1997, President Clinton banned using any federal funds for human cloning research, called on privately funded researchers to implement a temporary, voluntary moratorium on the same, and directed the National Bioethics Advisory Commission to study the issue. The commission's report was released in June 1997.

After fading from the public mind for several months, the cloning debate emerged again in late 1997 when a physicist announced his plan to build a clinic in Chicago to clone humans for infertile couples. Shortly thereafter, the Michigan House passed three bills to

- amend the Public Health Code, to make anyone who clones a human being subject to a civil fine of up to $10 million and permanent loss of any Michigan health care license;
- amend the Michigan Penal Code, to make cloning a human being a felony punishable by up to 10 years in prison, a fine of $5,000, or both; and
- prohibit people from using state funds to conduct research on human cloning or clone a human being.

Genetic Testing

Each gene on a chromosome can help influence a physiological, biochemical, or physical hereditary trait. Very simply put, a faulty or damaged gene can produce faulty proteins, and these may lead to disease. A genetic "marker" for some of these diseases has been pinpointed on one or another of the 46 human chromosomes. For example, researchers have linked the BRCA1 and BRCA2 genes to certain types of breast cancer and know that human chromosome #21 carries the gene for Down's syndrome. Genes may be faulty from the beginning of life, or they may become damaged at some point in an individual's life; they also may remain dormant until some event triggers a change that leads to disorder or disease.

Genetic testing is a process that examines human chromosomes for these marker genes. Currently, more than 450 tests for genetic disorders are available. Since 1965 the State of Michigan has required that newborns be tested for phenylketonuria (PKU), which leads to profound mental retardation if not detected early, carefully monitored, and treated with a special diet. Legislation enacted in 1986 expanded the testing requirement to several other diseases, including hypothyroidism and sickle-cell anemia, while a 1992 law requires testing for congenital adrenal hyperplasia, an easily treated adrenal gland condition.

Identifying exactly which gene combinations cause or are related to a specific disease or physical trait is a complicated, time-consuming process. Together, the human genome contains more than three billion "instructions" that produce 60,000 to 80,000 individual genes. In 1990 the U.S. Department of Energy and the National Institutes of Health jointly started the Human Genome Project, an international, 15-year project to identify the precise location of each human gene on the 46 individual chromosomes. As of October 1997 the project had mapped almost 5,800 genes to their location on specific chromosomes, with another 1,400 genes identified but not precisely located.

One variation on genetic testing is genetic *profiling*, a process by which an individual's genetic makeup is ascertained and recorded. One use of genetic profiling is to identify criminal assailants. Samples of a suspect's blood, semen, saliva, hair, skin, or even fingernail clippings are tested to reveal a DNA profile, which can be compared to that of materials taken from the crime scene or the victim; if they match, the results are offered as proof of guilt. Assuming that the tests have been carried out correctly and the samples handled properly, the reliability of the results rests on the uniqueness of human identity; with the exception of identical twins, the chance of any two humans having identical genetic "fingerprints" is roughly one in 270 million. Genetic profil-

ing also is used by the U.S. military to identify soldiers; new recruits are required to give blood and saliva samples to be stored for future use. Such profiles initially were used to correctly identify soldiers killed in the Persian Gulf war.

To date in the 1997–98 legislative session, Michigan legislators have introduced 17 bills regulating genetic testing. Common to many of the bills is a statement guaranteeing Michigan residents the right to genetic privacy. In addition, several bills either prohibit or strictly limit the situations in which health, life and disability insurers; health maintenance organizations; and Blue Cross and Blue Shield of Michigan may require and/or use genetic test results. In September 1997 Governor Engler established the Michigan Commission on Genetic Privacy and Progress in the Michigan Department of Community Health and charged it with recommending model statutes and policies that will protect genetic privacy, prevent discrimination, and guide acceptable use. The commission is conducting public forums statewide in April, May, and June and is expected to publish a report by November 1998.

DISCUSSION

Genetic Cloning

In response to Dolly's birth and President Clinton's charge, the National Bioethics Advisory Commission's (NBAC) report outlined several policies to clarify the U.S. position on cloning. Of greatest importance is the commission's finding that "at this time it is morally unacceptable for anyone in the public or private sector, whether in a research or clinical setting, to attempt to create a child using [cloning]." The NBAC further recommends that the moratorium on using federal funds for human cloning be continued and that all private firms and researchers agree to the same. The NBAC also recommends that any legislation enacted to codify the moratorium include a "sunset" (expiration) date, to ensure future review of the prohibition when more information and research about cloning have been accumulated. Another significant finding of the NBAC is that there is no consensus in any sector of society—political, religious, moral, or scientific—on the appropriate use of genetic cloning for animals or humans.

Some members of Congress are troubled that the NBAC does not condemn human cloning outright; instead, the NBAC condemns human cloning at this time, leaving the door open for continued debate. Other opponents of genetic cloning in general point to the large failure rate of Dolly's creation: More than 277 cellular transplants were needed to produce 29 embryos, which then were implanted into surrogate sheep. Of the 29 embryos, only one live birth—Dolly—resulted, an embryo-to-live-birth success rate of just over three percent; the others were miscarried, stillborn, or born with genetic defects and died shortly after birth.

But recent research shows that the success rate is increasing. In December 1997 researchers at the Roslin Institute announced the birth of Polly and Molly, cloned sheep that had been genetically altered to produce milk containing the human blood clotting factor IX for treating hemophilia. From the 425 cellular transplants, 62 embryos were implanted in surrogates, and 6 live births resulted, an embryo-to-live-birth rate of 9 percent. Further research and experimentation likely will continue to increase cloning's success rate, although observers point out that 100 percent success never is to be expected: miscarriages, stillbirths, and birth defects will occur, just as is the case with sexual reproduction.

There are many points of view about cloning. Some observers fear that genetic cloning gives humans too much control over the creation of life; we are one step closer to "playing God" with plants, animals, and ourselves. Others take the position that genetic cloning merely is another step in the genetic experimentation involving plants and animals that dates back more than 100 years to Gregor Mendel's work that led to the principles of heredity. Some fear the potential for misuse of cloning: If humans can be cloned, what will stop a millionaire or dictator from cloning him/herself, to continue the dynasty? Others make the point that while genetics are important

in human development, they do not account for the *totality* of a person's development: The natural environment and interaction with others, among other factors, also influences behavior, so a millionaire may find that his/her cloned child is no less rebellious—or no more interested in the family business—than is a natural child.

By definition, cloning means that the offspring only has one "parent," and therefore only one source of DNA and genes. Widespread cloning of any living thing may dangerously decrease the gene pool and make future generations more susceptible to diseases unknown at this time. Supporters counter, however, that it makes a difference *what* is cloned or genetically manipulated: Tampering with a single gene to ensure, for example, that no more children are born with cystic fibrosis represents only a minor alteration in the gene pool; that is much different from replicating an entire human's DNA hundreds or thousands of times to create multiple clones.

There are divergent views on cloning's religious, moral, and ethical implications. While some religious leaders and ethics scholars believe that cloning anything is dangerous, others believe that cloning animals is an appropriate step in the quest for scientific knowledge. In the National Bioethics Advisory Commission's report, one hypothetical instance speculated on cloning a child who has a serious disease—such as leukemia—and needs identical bone marrow for treatment. Some religious leaders condemn such an action, and others do not—expressing their belief that such action is appropriate from both a moral and religious standpoint as long as the parents raise the second child as they would in any other circumstance.

If research continues to be successful, genetic cloning of animals holds out the potential for near-term returns in both research and commerce. Scientists already rely on selective breeding to create large numbers of genetically identical animals to use in research; for example, mice currently are bred with specific human antibodies and other genetic markers for cancer research. Also for research purposes, genetically manipulated animals may be cloned so that their tissue is more compatible with the human immune system.

On the commercial front, genetic cloning may replace existing selective-breeding techniques by offering a more efficient way to produce a large number of embryos from "best of breed" livestock. Currently three companies are engaged in genetic activity—for pure research and/or commercial purposes—with animals: PPL Therapeutics, the operating arm of the Roslin Institute in the United Kingdom; ABS Global, a U.S. firm, and its subsidiary, Infigen; and Advanced Cell Technologies, another U.S. firm. In conjunction with University of Massachusetts researchers, Advance Cell Technologies announced in early 1998 that it had created two calves through a combination of genetic engineering and cloning. Five additional calves, which have been engineered to produce milk with the human serum albumin, currently are being carried to term. Albumin, a protein used to maintain fluid balances in patients, represents a current worldwide market of roughly $1.5 billion.

It is likely that many research and commercial decisions about cloning will be made long before the political, moral, and ethical debate surrounding genetic cloning—and especially the genetic cloning of humans—comes to a common judgment.

Genetic Testing

As with cloning, there are political, religious, and ethical implications involved in genetic testing; some of the unresolved issues are the same, and some are particularly pressing because genetic testing is in increasingly wide use.

Michigan legislation enacted in 1990 (Public Acts 191, 250, 251) directed the Michigan State Police to establish a computerized library of DNA profiles of people convicted since 1990 of criminal sexual assault in Michigan. People convicted of such crimes must provide samples of body fluids or tissue for inclusion in the library. If a sample is available, such information is included in the individual's profile that has been established under P.A. 295 of 1994. Despite the apparent certainty that one's DNA can be

used to accurately ascertain whether s/he was involved in a crime, there still are unresolved legal issues about the use and admissibility of evidence obtained from DNA samples.

Proponents of DNA testing maintain that its general reliability (1) makes identifying a culprit more certain in criminal sexual assault cases, (2) reduces the trauma victims suffer during a trial, and (3) makes mistaken identity unlikely. Opponents contend that (1) taking an individual's blood and other samples without consent is unreasonable search and seizure and an invasion of privacy, and (2) applying such techniques to only one class of offenders violates the traditional presumption of equal treatment under the law. And given at least the *potential* for human cloning, some also point out that in the future DNA tests may *not* be able to identify one specific individual; for example, if person B is a clone of person A, they will have identical DNA, regardless of an age difference or other factors.

Both genetic testing and profiling also raise concerns about privacy and the use of the resulting information. Who has the right to know the results of a genetic test performed voluntarily on a woman prior to starting a family or performed involuntarily on a man who must give a tissue sample as a condition of release from prison for a sexual crime? Is the woman's future employer entitled to know that she has a genetic disposition toward a disease that would be expensive to treat? What about an insurance company? Spouses? Intimate partners? Children? Parents? Should prison officials, when the DNA profile of the released man is completed, inform him if they discover that he has the genetic marker for an inherited disease?

Complicating the controversy surrounding genetic testing is the lack of understanding among many people about genetic markers. The presence of a genetic marker does not *necessarily* mean that someone will get a disease, since many other factors may affect a person's susceptibility. For example, genetic markers for colon cancer may be present, but research indicates a distinct possibility that diet (low fat, high fiber) may play a major role in frustrating the disease process. In other cases, there is a difference between *carrying* the disease and *having* the disease. Sickle-cell anemia, for example, is a recessive trait, meaning unless a person inherits the gene from both parents, s/he will not develop the disease; someone who inherits the marker from only one parent is referred to as a carrier; s/he may pass the disease along to a child, but s/he does *not* personally have the disease.

There are also issues surrounding whether individuals and health-care providers are able fully to understand the implications of genetic tests. For example, a study reported in 1997 in the *New England Journal of Medicine* finds that one-third of the doctors in a particular study do not fully understand the meaning of DNA results from one type of colon-cancer susceptibility test.

While employers are not prohibited from asking job candidates or employees to submit to genetic tests, federal and Michigan statutes forbidding discrimination against people with handicaps generally are understood to mean that employers cannot base hiring/firing decisions on genetic tests. Insurers in Michigan likewise are not prohibited from requiring coverage applicants to submit to genetic testing: Current regulations preclude insurers from excluding an individual from a group health plan because of his/her medical history, but they are permitted to turn down individual health insurance applicants who did not have coverage prior to applying. Only Blue Cross and Blue Shield of Michigan is required to insure all applicants.

Genetic cloning, testing, and profiling offer great possibilities for humans to control their environment; they also pose significant social, legal, and ethical questions. The findings of the governor's commission—as well as federal legislation—likely will help shape legislative action.

See also Early Childhood Development.

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