Gene Therapy
Restoring Health

or Playing God?

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[W]ho has been able, in the course of near six thousand years, to evade the execution of [the] sentence, passed on Adam and all his posterity? Be men ever so great masters of the art of healing, can they prevent or heal the gradual decays of nature? Can all their boasted skill heal old age, or hinder dust from returning to dust? (John Wesley, 1771)

IN MOST scientific research, technologists manipulate something separate from themselves: the nature of the stars, the nuclei of atoms, the strata of rocks, and the rules of numeric computation. They attempt to discover everything from the hidden rhythms of ocean tides to the composition of the air. But recent activities in human genetics have transformed the technologists *into* the technology they study.

The Basics of Human Genomics

- *Deoxyribonucleic acid (DNA) molecules,* the chemical compound containing the instructions to develop and direct the activities of living organisms, are made of two twisting, paired strands, often referred to as a double helix. Each DNA strand is made of four nucleotide bases: adenine (A), thymine (T), guanine (G), and cytosine (C). Bases on opposite strands pair specifically. That is, an A always pairs with a T, and a C always pairs with a G. The order of the A's, T's, C's, and G's determines the meaning of the information encoded in that part of the DNA molecule.
- An organism's complete set of DNA is called its *genome.* Virtually every cell in the body contains a complete copy of the approximately 3 billion DNA base pairs, or letters, that make up the human genome. With its four-letter language, DNA contains the information needed to build the entire human body.
- A *gene,* located on 23 pairs of chromosomes packed into the nucleus of a human cell, refers to the unit of DNA that carries the instructions for making a specific protein or set of proteins. Each of the estimated 20,000 to 25,000 genes in the human genome codes for an average of three proteins. Proteins make up body structures (organs, tissues), control chemical reactions, and carry signals between cells. If a cell's DNA is mutated, an abnormal protein may be produced, which can disrupt the body's usual processes and lead to a disease.
- *DNA sequencing* means determining the exact order of the bases in a strand of DNA. Sequencing can be used to search for genetic variations and/or mutations that may play a role in the development or progression of a disease, such as the substitution, deletion, or addition of a single base pair or the deletion of thousands of bases.
- *The Human Genome Project (HGP),* conducted at the U.S. National Institutes of Health by the National Human Genome Research Institute and completed in April 2003, produced a very high quality version of the human genome sequence, freely available in public databases. The sequence is a composite derived from nearly 100 anonymous volunteer donors.
- In October 2005, the *International HapMap Project* published a comprehensive map of human genetic variation that is speeding the search for genes involved in common diseases such as heart disease, diabetes, blindness, and cancer.
- The 3-year *Cancer Genome Atlas Pilot Project,* launched in December 2005, will develop and test strategies for a comprehensive exploration of the universe of genetic factors involved in cancer.—**KSS**

Adapted from The National Human Genome Research Institute. *A brief guide to genomics,* updated December 2006. Accessed June 12, 2007 at http://www.genome.gov/18016863.

Completion of the Human Genome Project has provided a transcript of the human genetic code, although its full interpretation still lies in the future (to learn more, see The Basics of Human Genomics above). Genome scientist Elbert Branscomb (1996) has said, "We are just chipping a hole into the sarcophagus of knowledge and peering into the darkness." As the data "hole" widens, researchers will be able to understand the genome's meaning and will have the power to manipulate it. People will have more control over their biologic lives than ever before.

The ethical implications are unsettling. Bioethicist Leon Kass (1985) has said:

> [B]ecause we belong to the nature we study and seek to control, our power over nature eventually means power also over ourselves. We are not only agents but also and increasingly *patients* of our scientific project for the mastery of nature. Our self-conception, if not also our very being, lies upon the table science—biology, medicine, psychology—has prepared. (p. xi)

There is a sense of uneasiness about the process and its potential, based on recent advances in genetic engineering. Even the definition of "human" is questioned:

> What happens to human dignity when test tube babies are conceived in order to be tissue donors for other family members—a practice already underway at the turn of the millennium? What happens to our definition of human nature when researchers create human–animal hybrids—also underway in 2000? In one case, the nuclei of human cells were extracted and inserted into a pig's egg cells; the hybrids were allowed to grow to 32-cell embryos before being destroyed. Researchers [look] forward to using such subhuman creatures for research—even for use as living meat lockers for growing transplantable organs and tissues. (Pearcey, 2001)

Many Christians have instinctive fears and a feeling of revulsion at such possibilities. Yet, as Kass (2002) has stated, "In crucial cases . . . repugnance is the emotional expression of deep wisdom, beyond reason's power fully to articulate it" (p. 557).

In Matthew 5:13–14, Christians are called to be "the salt of the earth" and "the light of the world." Ideally, believers speak from divine principles, understanding the biblical reasons for their instinctive uneasiness toward the extremes of genetic technology. Is there a limit to the uses of genetic science? Or is it too late for limits? What does Scripture teach on these matters?

Chapter 1 of Genesis reveals man's great worth as the highest point of creation, made in God's image and

likeness (Genesis 1:26). God gave man dominion over the rest of creation (1:28). Adam was given the task of naming the animals. The garden was beautiful, and limitations were few.

Deception intruded upon this idyllic scene in Genesis 3. Many interpret "knowing good and evil" (3:22) as having moral autonomy. Theologian V. Hamilton (1990) has commented:

> What is forbidden to man is the power to decide for himself what is in his best interests and what is not. This is a decision God has not relegated to the earthling. This interpretation also has the benefit of according well with 3:22, "The man has become like one of us, knowing good and evil." Man has indeed become a god whenever he makes his own self the center, the springboard, and the only frame of reference for moral guidelines. When man attempts to act autonomously he is indeed attempting to be godlike. (p.166)

The New Testament frequently mentions death as a penalty of the fall. Paul declares that "through one man sin entered into the world, and death through sin, and so death spread to all men" (Romans 5:12, NASB). The death penalty on man is irrevocable and cannot be undone. This is clear from God's banishment of Adam from the garden and from access to the tree of life (Genesis 3:22b). Although bodily death is part of the curse, it also may be a kindness, for a merciful Creator does not want fallen man to live in his broken state forever (von Rad, 1972). One thing is clear: God does not intend for natural (unglorified) bodily existence to extend indefinitely, a principle that has many implications for bioethics.

HEALING AND THE FALL

As a result of the fall of humankind, "the whole creation groans and suffers the pains of childbirth together until now" (Romans 8:22). The sickness of creation led not only to the ultimate toll of death, but also to daily suffering and disease. The essence of health as wholeness, completeness, and well-being has been lost.

God's plan for creation's recovery from the fall intends more than physical health, although the plan still includes it. Physical health cannot be accomplished by men, for it is a gift from God. As physician John Wilkinson (1998) has pointed out: "In God alone can we know the wholeness of our being and the rightness of our relationships which make up what the Old Testament means by health" (p. 12). God's goal is the restoration of bodily and spiritual integrity in the face of suffering and disease brought on by the fall. In his compassion and love for fallen men, God sent his Son to make men whole once again (John 3:14–18).

On this understanding of biblical health, the role of the human healer is to imitate God in reversing the effects of the fall. The healing ministries of Jesus and his disciples often went well beyond physical healing to include the spiritual dimension. In fact, the spiritual aspect of healing was often foremost. Jesus demonstrates this, for example, with the healing of the paralytic in Luke 5 when he says, "Friend, your sins are forgiven you" (Luke 5:18–20).

Spiritual healing was foremost in the minds of both Jesus and those who had faith to be healed: forgiveness from the ravages of sin. Jesus performed the subsequent physical healing from paralysis almost as an afterthought, "in order that [the Pharisees] may know that the Son of Man has authority on earth to forgive sins" (Luke 5:24). In this case, complete wellness or wholeness began with forgiveness from sin and ended with the man taking up his pallet to walk home.

How might these scriptural insights apply to bioethics and the use of modern medicine? Technologies such as penicillin, surgery, physical therapy, and magnetic resonance image (MRI) scanning seem entirely within the purview of the healing ministry of the healthcare professions. Compassionate physicians and nurses use every natural means at their disposal to cure disease. With regard to genetic intervention, how might the insights from Scripture be applied?

In the ethical discussions that began in the late 1960s, commentators on human gene therapy sometimes seemed to assume that this technique was qualitatively different from other types of therapeutic interventions. However, as the ethical discussion of gene therapy has progressed, somatic cell gene therapy has increasingly been

at a Glance

- **Human genome mapping** *has opened up many biologic possibilities while raising numerous ethical concerns.*
- **The use of gene therapy** *for* healing *appears to fit under a biblical framework of restoring health.*
- **The use of gene therapy** *for* enhancement *appears to enter into the realm of "playing God."*

GENE THERAPY FAQS

WHAT IS GENE THERAPY?

Gene therapy is an experimental technique that hopes to use genes to treat disease, inherited disorders, or infection by inserting a gene into a patient's cells. Approaches may include

- Replacing a mutated gene that causes disease with a healthy copy of the gene
- Repairing, inactivating, or "knocking out" a mutated gene that is functioning improperly
- Introducing a new gene into the body to help fight a disease.

HOW MIGHT THIS BE ACCOMPLISHED?

A carrier molecule called a *vector* must be used to deliver the therapeutic "normal" gene to the genome in targeted cells. The most common vector is a virus that has been genetically altered to carry normal human deoxyribonucleic acid (DNA). In research, after target cells have been "infected" with the viral vector, the vector unloads its therapeutic genetic material into the cell. The subsequent generation of a functional protein product from the therapeutic gene restores the target cell to a normal state. Viral vectors being investigated are

- Retroviruses (e.g., HIV virus)
- Adenoviruses ("common cold" virus)
- Adeno-associated viruses (single-stranded DNA)
- Herpes simplex virus (cold sores).

Nonviral gene delivery options being researched are

- Naked DNA application involving direct introduction of therapeutic DNA into target cells
- Liposome, an artificial lipid sphere with an aqueous core carrying therapeutic DNA
- Chemical linking of therapeutic DNA to a molecule that will bind to special cell receptors and be engulfed by the cell membrane
- Introduction of a 47th artificial human chromosome into target cells
- Nano-sized bioceramic particles. (Tan, Cheang, Ho, Lam, & Hui, 2007)

WHAT OBSTACLES MUST BE OVERCOME?

- *Short-lived nature of gene therapy:* The nature of the genetic material and normal cell division means patients will have to undergo multiple rounds of gene therapy.
- *Immune response:* Gene therapy could stimulate the immune system in unknown ways. In addition, the immune system's enhanced response to invaders it has encountered before may make it difficult for gene therapy to be repeated.
- *Problems with viral vectors:* Viral toxicity, immune and inflammatory responses, gene control and targeting issues, virus reversion back to a disease-causing form may occur.
- *Multigene disorders:* Most disorders (heart disease, high blood pressure, arthritis, diabetes) are caused by variations in many genes. Gene therapy best treats single-gene diseases.

WHAT ARE THE CLINICAL REALITIES?

Little progress has been made since the first gene therapy clinical trial began in 1990, and several major setbacks have occurred:

- In 1999, 18-year-old Jesse Gelsinger died of multiple organ failures 4 days after starting a gene therapy trial for the treatment of ornithine transcarboxylase deficiency, a genetic liver disease that causes poisonous levels of ammonia to accumulate in the body. It is believed that his death was triggered by a severe immune response to the adenovirus carrier.
- In January 2003, the U.S. Food and Drug Administration (FDA) placed a temporary halt on gene therapy trials using retroviral vectors in blood stem cells after a leukemia-like condition developed in a second child treated in a French gene therapy trial. Both this child and another who had experienced a similar condition in August 2002 had been successfully treated by gene therapy for X-linked severe combined immunodeficiency disease (X-SCID), also known as "bubble baby syndrome."

WHAT DOES THE FUTURE HOLD?

Researchers are testing gene therapy in laboratory models to treat HIV infection, genetic illnesses, and multiple diseases, and to promote wound healing. All these therapies are targeted at somatic body cells. Gene therapy could be targeted to egg and sperm cells (germ cells), which means the inserted gene would be passed on to future generations. Although germ-line therapy could spare future generations in a family from having a genetic disorder, it might affect fetal development in unexpected ways or have long-term side effects. Currently, the U.S. Government does not allow federal funds to be used for research on germ-line gene therapy for people.—**KSS.**

Adapted from the National Institutes of Health. (2007, June 8). Handbook: Help me understand genetics. *Genetics home reference*. Retrieved June 13, 2007 at http://ghr.nlm.nih.gov/handbook.

Tan, K., Cheang, P., Ho, L. A. W., Lam, P. Y. P. & Hui, K. M. (2007). Nano-sized bioceramic particles could function as efficient gene delivery vehicles with target specificity for the spleen. *Gene Therapy*, 14(10), 828–835. Retrieved June 13, 2007 at http://www.nature.com/gt/journal/v14/n10/abs/3302937a.html.

viewed as a natural and logical extension of current techniques for treating disease (Walters & Palmer, 1997).

Somatic cell gene therapy involves altering the genes of a diseased individual, sometimes those of only one specific organ and sometimes those of the entire individual. The word *somatic* comes from the Greek "soma," meaning body, and refers to the type of genetic therapy that affects the adult cells of an individual's body alone without affecting subsequent generations. This may be accomplished through the use of a vector such as a virus to insert a normal gene into the DNA of cells to compensate for a nonfunctioning defective gene (Human Genome Project, 2005) (see Gene Therapy FAQs above).

For example, cystic fibrosis is a genetic disease that causes a defect in the cellular transport of chloride ions across cell membranes. This leads to thick mucous in the airways of the lungs, causing obstruction and infections. Gene therapy of this disease involves using a modified cold virus to "infect" the lungs of cystic fibrosis patients. The virus inserts a normal copy

How might scriptural insights apply to bioethics and the use of modern medicine?

of the affected gene into the DNA of the nucleus of airway cells, which hopefully then may function normally (Cystic Fibrosis Foundation, 2006). To date, therapeutic trials have had only limited success, but this form of treatment holds promise for the relief of symptoms and the prolongation of life.

Somatic cell gene therapies such as this affect only nonreproductive cells. There are no genetic alterations of germ-line cells (sperm and eggs), so no changes can be passed on to the patient's children. On the other hand, germ-line therapy would affect all subsequent generations of offspring (Walters & Palmer, 1997). This would represent a permanent change in the genetic heritage of human beings. For this reason, some ethicists have urged only cautious approval of germ-line genetic therapy as a way to rid mankind of certain loathsome genetic disorders.

As a way to alleviate human suffering and restore wholeness, genetic therapy for specific defects appears to fit under the broad umbrella of a biblical framework of restoring health. To date, however, this would not be genetic *enhancement*.

ENCHANCEMENT AND THE FALL

The practice of medicine has always had the goal of relieving suffering (Engelhardt, 1996). But when medicine moves beyond this mandate, it stretches into the realm of enhancement.

Enhancement has been concisely defined by ethicist Mark Frankel (2003):

> By "genetic enhancement" I mean improving human traits that without intervention would be within the range of what is commonly regarded as normal, or improving them beyond what is needed to maintain or restore good health. Examples could include increasing height, improving intelligence, altering behavior, or changing eye color, all of which have been shown to have some underlying genetic connection. (p. 33)

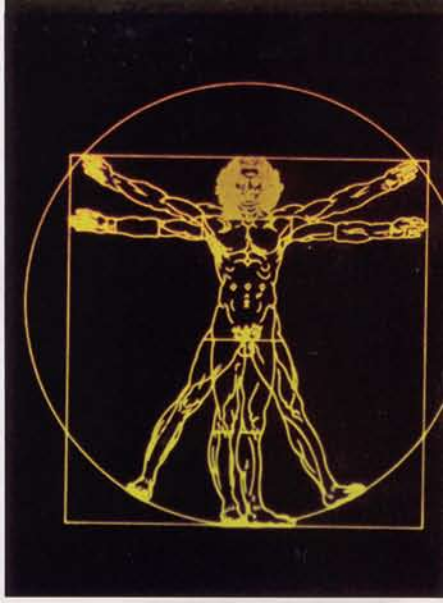
Genetic enhancement makes many thoughtful people suspicious because it raises a number of vexing questions. The diversity of our society is at issue because the possibility of enhancement runs the risk of market forces defining a "genetic ideal." What would happen to the concepts of hard work and competition if physical prowess could be genetically "programmed"? The principles embodied in sports and athletic competition might become meaningless. If the abilities to learn a foreign language or to master abstract mathematics can be genetically programmed, then what is the value of pursuing academic achievement? Indeed, the genetically "fit" and "unfit" may become segregated from each other, with good jobs going only to those with the "right" genes. Even further, what would become of the very nature of man?

Arthur Caplan (2003), the prominent director of the University of Pennsylvania Center for Bioethics, seems relatively unconcerned about these deep questions. He comments:

> If we started to enhance ourselves, we might be able to do more, but would we still be human when we were done? The main flaw with this argument is that it is made by folks who wear eyeglasses, use insulin, and have artificial hips or heart valves, benefit from transplants, ride on planes, dye their hair, talk on phones, sit under electric lights, and swallow vitamins. What are they really talking about? Have we become less human because we ride instead of walk to work? We might be less healthy, but does a reliance on technology for transportation make us unrecognizable as humans? Is there a natural limit beyond which our nature is clearly defiled by change? Surely not. It is the essence of humanness to try to improve the world and oneself. (p. 105)

Professor Caplan blurs the difference between healing and enhancement. His examples come from the normal practice of medicine to relieve suffering or use technology to make life easier. Yet genetic enhancement goes beyond current medical practice and runs the tangible and foreseeable risk of tampering with human nature itself. Suddenly, the question, no longer quite so rhetorical, asks: "Is there a natural limit beyond which our nature is clearly defiled by change?" It is the very "essence of humanness" that Professor Caplan calls upon that should *not* be subject to change.

The dangers of tampering with human nature are not merely the concern of theistic philosophers. Francis Fukiyama (2002), in the book



Our Posthuman Future, warns of the dangers to humanity posed by recent technological advances. He speaks as an evolutionist, with a basic optimism about biotechnology. Yet he claims that genetic manipulation will seriously challenge the way man looks at himself. He is deeply concerned about a possible loss of human nature and human dignity, declaring that "denial of the concept of human dignity . . . leads us down a very perilous path" (p. 160).

The great 20th-century philosopher Mortimer Adler (1985) once wrote that the denial of human nature is one of the great "philosophical mistakes" of this age. Wilde (2002) writes of Adler:

> [He] affirmed that there may be more stability to human nature than early modern philosophers believed. It may not be fixed and immutable, but there is some reality to the concept of a *human* nature, for otherwise humans would not be distinguishable from other animals.

The pages of Scripture amplify these philosophical views on human nature and ascribe a high value to man and to his nature because he is made in the image of the Creator God. Genetic enhancement would go beyond mere amelioration of the effects of the fall. It would *recreate* original sin, tempting man to "be like God, knowing good and evil" (Genesis 3:5). As noted earlier, this knowledge is the sin of radical moral autonomy, a slap in the face to the Creator. This is the ultimate warning implied by traditional injunctions against "playing God." Such activity is clearly outside of the moral bounds of man, as expressed beautifully by the ancient King David of Israel in Psalm 8:5–6:

> You have made them [man]
> a little lower than God,
> and crowned them with
> glory and honor.
> You have given them
> dominion over the works of
> your hands;
> You have put all things
> under their feet.

God has given man great value—just as he is, just as God created him. In addition, God has vested his highest creature with the great role of stewardship over the rest of creation (compare this with the dominion mandate of Genesis 1:28). Such stewardship cannot and must not extend to dominion over *his own nature*, for then God's trust of man would become twisted, and a form of idolatry. The Apostle Paul sternly pronounces God's judgment on those who would confuse creature and Creator (Romans 1:21–25).

God pronounced his perfect creative work in Genesis 1:31 as "very good." With his technology, man now has the ability to say to his Maker: "It's not so good after all—I can improve on it." Such is the hubris of genetic enhancement. But Scripture clearly condemns this impulse.

Drawing a hard line between healing and enhancement will not be easy because the distinction is not always clear-cut. Frankel and Chapman (2002) have made this helpful comment on the uses of inheritable genetic modification (IGM) techniques, equivalent to the germ-line therapy discussed earlier:

> The dilemma is that IGM modification techniques developed for therapeutic purposes are likely to be suitable for enhancement applications as well. Thus, going forward with IGM to treat disease or disability will make it difficult to avoid use of such interventions for enhancement purposes even when this use is considered ethically unacceptable. (p. 499)

The difficulty of finding the exact margins notwithstanding, the healing–

Genetic enhancement goes beyond current medical practice and risks tampering with human nature.

enhancement distinction is vital because there are further prices that society would pay for its technological hubris. The "perfecting of humanity" is an important argument for the cloning of human embryos, either as "designer babies" (which most writers would condemn) or to provide the raw materials for stem cell therapy (a very acceptable alternative in the view of some). Either way, society runs the risk of creating superior and inferior subclasses of humanity, which may well lead to the philosophical excesses of eugenics. The National Bioethics Advisory Commission (NBAC, 1997) has warned:

> [A] eugenics program would propagate dogma about the sorts of people who are desirable and those who are dispensable. That is a path that humanity has trod before, to its everlasting shame. And it is a path to whose return the science of cloning should ever be allowed to give even the slightest support. (p.74)

GREAT DANGER

Herein lies the great danger of "perfecting" human beings through enhancement. If man is allowed to think he can "play God" and improve on his own nature, then human nature itself is at risk. Every individual life is no longer intrinsically of value for its own sake, but men compete with one another to develop the best and most perfect genetic traits. "[A]s history repeatedly has demonstrated, once we accept the pernicious premise that some people are 'superior' to others—the core principle of eugenic thinking—we open the door to great evils" (Smith, 2003).

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Web Resources

- Center for Bioethics: www.cedarville.edu/bioethics
- Genetics Home Reference: http://ghr.nlm.nih.gov/ghr/
- National Human Genome Research Institute: www.genome.gov/
- The Hastings Center: http://www.thehastingscenter.org/

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