# Brave New World of Genetic Engineering

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With the debate on stem cell research still very hot and the debate on cloning heating up, little attention has been paid of late to genetic engineering technologies. Yet the ability to replace or alter individual genes within our DNA has perhaps a more profound potential—when compared to stem cells and cloning—to alter our view of human life; indeed, these technologies have the ability to alter what it means to be human. Each of these new medical technologies challenges our understanding of human life and humanity, and they are in many ways interrelated, one leading to another. Each in its own way raises a fundamental question about what it means to be human, and what respect we will give to human life.

Human embryonic stem cell research forces a utilitarian view of human life; some human beings are sacrificed for the potential benefit (and it is *only* a potential benefit) of others. The prospect of human cloning gives us the power to create new life (although it actually only re-creates existing or previously existing life) outside of a natural context, without the necessity for male or female; we would be able to create in our own image with this technique, copying ourselves or others at will. But to what purpose? Again, the purpose is a utilitarian one, using created life to fulfill our own desires either for a high-tech child, or even more selfishly, sacrificing new life for our own health. Genetic engineering, specifically germline gene engineering, takes this a step further by allowing us truly to create new life, to shape new designs for humanity, making new human beings to our own specifications.

# **Genetic Engineering Technology**

What is genetic engineering? It is the use of molecular techniques to alter the genome, the very DNA sequence itself, in some or all of the cells of an individual. The techniques have their roots in the recombinant DNA technologies developed in the 1970s. These techniques have allowed scientists to isolate, purify, and determine the base sequence of the DNA for genes which code for specific proteins in the cell,

to synthesize genes *de novo*, to cut and splice whole genes or pieces of genes together, recombining DNA into new configurations (hence the term recombinant DNA), to replicate these gene sequences innumerable times, and to transplant these gene sequences into any cell. The techniques have led to the Human Genome Project with the mapping of the entire human genome, identification of new genes and their function, and to actual and proposed uses of these genes in therapeutic applications for human diseases.

Genetic engineering can be subdivided into two main categories: somatic genetic engineering (also termed noninheritable genetic modification), and germline genetic engineering (also termed inheritable genetic modification). Somatic genetic engineering modifies or replaces genes within somatic cells, i.e., any cell of the body except the sperm or egg cells or their immediate precursors. These modifications alter the genome of the particular cell or tissue, with the primary goal being to correct some genetic defect which causes disease in the treated individual. Germline genetic engineering specifically alters the genes in the sperm or egg cells (or their immediate precursors) or in the zygote or early embryo. While the goal may be the same as somatic genetic engineering, i.e., to correct a defective gene which can lead to disease, the changes made affect prospective individuals, including not only the child so engineered, but also all of that child's descendants. Both techniques could be abusedeither could be used for enhancements of genetically determined abilities, rather than for therapeutic treatments of disease, but germline genetic engineering also gives the ability to select desired characteristics in a prospective child, providing a "designer baby" with preferred characteristics.

Technically, both somatic and germline genetic engineering rely on the same tools: (1) the gene of interest, and (2) a vector to contain and control the gene and deliver (transfect) it into the appropriate cell. The gene itself is one which has been identified, characterized, and replicated in multiple copies. With the actual base sequencing of the human genome near completion, the identification and analysis of many individual genes is moving into high gear. Previously, many genes involved in single-gene disorders had been identified, including muscular dystrophies, hyperlipidemias, and some cancers. It is likely that identification and characterization of many more genes with possible therapeutic applications will accelerate with the information coming from the Human Genome Program, and lead to more possible applications of gene therapy based on our increased knowledge of gene func-

<sup>&</sup>lt;sup>1</sup>E.H. Kaji and J.M.Leiden, "Gene and Stem Cell Therapies," *Journal of the American Medical Association* 285 (2001): 545–550.

<sup>&</sup>lt;sup>2</sup>M. Koenig, et al., "Complete cloning of the Duchenne muscular dystrophy (DMD) cDNA and preliminary genomic organization of the DMD gene in normal and affected individuals," *Cell* 50 (1987): 509–517; C.G. Davis, et al., "The J.D. mutation in familial hypercholesterolemia: amino acid substitution in cytoplasmic domain impedes intemalization of LDL receptors," *Cell* 45 (1986): 15–24; S.H. Friend, et al., "A human DNA segment with properties of the gene that predisposes to retinoblastoma and osteosarcoma," *Nature* 323 (1986): 643–646; Y. Miki, et al., "A strong candidate for the breast and ovarian cancer susceptibility gene BRCA1," *Science* 266 (1994): 66–71.

tion.<sup>3</sup> This will include candidates for more complex, multi-gene disorders such as diabetes and Alzheimer disease, and could also include elucidation of genetic predispositions to other conditions such as alcoholism. As the studies proceed, we should note with caution any reports that claim to have identified genes which control complex behavioral phenomena; we are much more than just the sum of our genes. Nonetheless, the "menu" from which to pick in terms of correcting genetic disorders, as well as in selecting other genetic traits, will not be a limiting factor in genetic therapies.

The vector which contains and delivers the DNA of the gene to the cell is a critical component of the system. While the DNA of the gene could simply be thrown onto cells and allowed to be taken inside the cells, this is an inefficient and relatively uncontrollable method to achieve the desired expression of the gene. Instead, a vector, itself a constructed piece of DNA, is used to deliver the gene efficiently and precisely to the cell, ideally inserting itself (with the gene as part of its own DNA sequence) stably into the cell's genome and controlling the expression of the gene as needed in the host cell. Plasmid vectors derived originally from bacteria have been used in the past, but these pieces of DNA tend to be inefficient at delivering the gene to nongrowing cells and can elicit an immune response. Most current therapies use viral vectors.<sup>4</sup>

The elements of the viral genome which allow infection of a cell and insertion into the host genome are kept as part of the vector, and the other viral genes are replaced with the therapeutic gene and other DNA sequences to target and control the gene's expression. This allows efficient and stable transduction of the cell with the therapeutic gene, and depending on the construction of the control elements within the vector, allows specific expression of the gene in certain tissues or in response to certain signals.

Several different viruses have been used with some success, but the ideal vector that targets the gene to the appropriate cells or tissues, stably transfects the cells, and allows control of gene expression, all without causing an immune response or other adverse response, has yet to be achieved. A good example is seen in a recent volume of the journal *Gene Therapy*. A promising pair of reports were published on the use of adeno-associated virus as a vector for gene therapy, used in these studies to treat rare diseases in mice. Adeno-associated virus is not linked to human disease and is considered safe for gene therapy. However, the two reports were accompanied by a jointly authored cautionary paper from the two research groups publishing

<sup>&</sup>lt;sup>3</sup>F.S. Collins and V.A. McKusick, "Implications of the human genome project for medical science," *Journal of the American Medical Association* 285 (2001): 540–544.

<sup>&</sup>lt;sup>4</sup>Kaji and Leiden,"Gene and Stem Cell Therapies."

<sup>&</sup>lt;sup>5</sup>T.M Daly, et al., "Prevention of systemic clinical disease in MPS VII mice following AAV-mediated neonatal gene transfer," *Gene Therapy* 8 (2001): 1291–1298; S. Song, et al., "Stable therapeutic serum levels of human alpha-1 antitrypsin (AAT) after portal vein injection of recombinant adeno-associated virus (rAAV) vectors," *Gene Therapy* 8 (2001): 1299–1306.

the positive results, because one group had found evidence of tumor formation in some of the mice.<sup>6</sup> While the data suggest that the viral vector used in the gene therapy did not cause the tumors, this possibility cannot be excluded without further study. Design of an appropriate vector for target tissues is a matter of continuing development, including early work on a human artificial chromosome<sup>7</sup> which could function as a sort of "super vector," containing multiple genes to be added to a cell, as well as any desired sequences for control of the individual genes, and the ability to be replicated along with other chromosomes and passed on to daughter cells as a discrete chromosome.

Another aspect of genetic engineering techniques that must be mentioned is the fact that the genetic transformation of the patient's cells can be accomplished either in the laboratory (ex vivo gene therapy) or within the patient's body (in vivo gene therapy). In ex vivo gene therapy, the cells that will receive the new gene are removed from the patient's body and transfected in cell culture to accomplish the genetic transformation. Then the genetically altered cells are placed back into the patient. For in vivo gene therapy, the therapeutic gene in its vector is delivered directly through a catheter or other instrument into the target organ or tissue to be treated, and the genetic transformation takes place within the patient's body. Each method has its own advantages. Ex vivo gene therapy allows easy manipulation of the cells in the laboratory, and the efficiency and success of the genetic transformation can be easily monitored. The genetically modified cells can be selected and expanded in number before reimplantation into the patient. However, some cells are difficult to grow in culture, necessitating in vivo treatment to deliver the therapy.

### **Somatic Genetic Engineering**

Somatic gene therapy has been attempted clinically since the early 1990s.<sup>8</sup> Early work involved attempts at treating single-gene defects by replacing a defective gene with a normal copy of that gene, such as in patients with cystic fibrosis and familial hypercholesterolemia.<sup>9</sup> More recent studies have shown some progress in

<sup>&</sup>lt;sup>6</sup>A. Donsante, et al., "Observed incidence of tumourigenesis in long-term rodent studies of rAAV vectors," *Gene Therapy* 8 (2001): 1343–1346.

<sup>&</sup>lt;sup>7</sup>K.A., Henning et al., "Human artificial chromosomes generated by modification of a yeast artificial chromosome containing both human alpha satellite and single-copy DNA sequences," *Proceedings of the National Academy of Sciences USA* 96 (1999): 592–597; B. Grimes and H. Cooke, "Engineering mammalian chromosomes," *Human Molecular Genetics* 1 (1998): 1635–1640.

<sup>&</sup>lt;sup>8</sup>K.W. Culver, et al., "Lymphocyte gene therapy," *Human Gene Therapy* 2 (1991): 107–109; R.M. Blaese, et al., "Treatment of severe combined immunodeficiency disease (SCID) due to adenosine deaminase deficiency with CD34+ selected autologous peripheral blood cells transduced with a human ADA gene. Amendment to clinical research project. Project 90-C-195, January 10, 1992," *Human Gene Therapy* 4 (1993): 521–527; R.M. Blaese, et al., "T lymphocyte-directed gene therapy for ADA-SCID: initial trial results after 4 years," *Science* 270 (1995): 475–480.

<sup>&</sup>lt;sup>9</sup>M.R. Knowles, et al., "A controlled study of adenoviral-vector-mediated gene transfer in the nasal epithelium of patients with cystic fibrosis," *New England Journal of Medi*-

developing potential techniques for cancer treatments, in growth of new blood vessels to treat arterial blockage in limbs and after a heart attack, and in what is considered the first real success in human somatic gene therapy, infants were apparently cured of an inherited immunodeficiency. <sup>10</sup> Currently, the National Institutes of Health Office of Biotechnology Activities database (<a href="http://www4.od.nih.gov/oba/">http://www4.od.nih.gov/oba/</a>) lists 472 clinical trial records, including a recent attempt at treatment of Alzheimer's disease using implantation of genetically modified skin cells into the brain of a patient. <sup>11</sup>

So far this all sounds wonderful. The possibility of being able to treat genetic diseases opens a whole new realm for medicine in the relief of suffering. What antibiotics and vaccinations have done to relieve mankind's suffering from infectious diseases could now be possible using genetic therapies for inheritable diseases. But the comparison is not completely parallel, nor is the future for a world without genetic diseases as clear as for one without infectious diseases. While these technologies are obviously still in their infancy, showing only the glimmer of their potential, their impact on man's future and the ability to shape that future must be considered.

The question about reshaping humanity's future primarily revolves around germline genetic engineering, but should also be considered in relation to somatic genetic engineering and its possible uses for enhancement. In this sense, the treatment would not be given to a diseased individual to correct some defect, but rather to a healthy individual to augment the person's normal functions, or possibly even to add additional genetic capabilities. The same techniques apply; it is only the intent of the individual (as well as the willingness of the scientist or physician to perform the procedure) that is different. Rather than being a far-fetched idea, the desire of some individuals to alter themselves genetically should be expected. We are all too familiar with the idea of plastic surgery to change external appearances, or with stories of

*cine* 333 (1995): 823–831; M. Grossman, et al., "Successful ex vivo gene therapy directed to liver in a patient with familial hypercholesterolemia," *Nature Genetics* 6 (1994): 335–341.

<sup>&</sup>lt;sup>10</sup>J.A. Roth, et al., "Gene replacement strategies for treating non-small cell lung cancer," *Seminar in Radiation Oncology* 10 (2000): 333–342; I. Baumgartner, et al., "Constitutive expression of phVEG<sub>165</sub> after intramuscular gene transfer promotes collateral vessel development in patients with critical limb ischemia," *Circulation* 97 (1998): 1114–1123; D.W. Losordo, et al., "Gene therapy for myocardial angiogenesis. Initial clinical results with direct myocardial injection of phVEGF<sub>165</sub> as sole therapy for myocardial ischemia," *Circulation* 98 (1998): 2800–2804; T.K. Rosengart, et al., "Angiogenesis gene therapy. Phase I assessment of direct intramyocardial administration of an adenovirus vector expressing VEGF121 cDNA to individuals with clinically significant severe coronary artery disease," *Circulation* 100 (1999): 468–474; P.R. Vale, et al., "Left ventricular electromechanical mapping to assess efficacy of phVEGF<sub>165</sub> gene transfer for therapeutic angiogenesis in chronic myocardial ischemia," *Circulation* 102 (2000): 965–974; M. Cavazzana-Calvo, et al., "Gene therapy of human severe combined immunodeficiency (SCID)-XI disease," *Science* 288 (2000): 669–672.

<sup>&</sup>lt;sup>11</sup>Susan Okie, "Alzheimer's operation is a gene therapy first," *Washington Post*, April 11, 2001.

athletes using drugs or hormones to enhance their physical performance. Evidence even exists that expression of genes can be altered via diet.<sup>12</sup> It is a short step to the idea of making such alterations a more permanent change, by altering the genome. To be sure, this will not come soon given the current uncertainties and difficulties in success with somatic genetic engineering. However, it will be hard to stop some from wanting to increase the energy-generating capacity of their muscles, or the oxygencarrying capacity of their blood, in an attempt to gain an advantage.

Another certainly wilder but not inconceivable notion in somatic genetic engineering will be the addition of other genetic capabilities. But what form might such additional genetic capacities take? Though hard to imagine, some capabilities could be borrowed from other species, or more likely as designed genes that add some desired ability. I once had a student who speculated on the possibility of a photosynthetic cow. The student surmised that such a cow would need little space, little in the way of feed, and certainly no pasture. (I think she was going to keep it on her apartment balcony so that she could get some fresh milk each morning.) Though the idea of a photosynthetic human is unlikely, the ability to have our own cells manufacture all of our vitamins or amino acids rather than rely on our diet or supplements is an appealing one.

Another possibility might be the facility to make antibiotics or disease-resistance proteins. When couched in terms of the potential health benefits, proposals for additional genetic capabilities beyond those normally associated with humans become more compelling. Using somatic genetic engineering to accomplish these ends will be an arduous task, as it must be done on a person-by-person basis, and would only involve some few altered cells in each individual. This brings us to the concept of germline genetic engineering, and the possibility of altering the genome of every cell in a human being.

## **Germline Genetic Engineering**

The ability to pass on heritable traits to our offspring is at once both appealing and frightening. We would like to pass on intelligence, good looks, physical prowess, and other traits which we value. But we recoil at the thought of passing on the opposites to those traits, and especially at the thought of passing on a death sentence—a fatal genetic disease. It is especially this latter possibility that drives proposals for germline genetic engineering. If somatic genetic therapies are to genetic disease what antibiotics are to infectious disease, then germline genetic therapies are the equivalent of vaccinations—prevention rather than recovery. However, this form of prevention affects *prospective* individuals, and not just the one individual, but all of the generations of progeny from that individual.

Germline genetic engineering has been practiced in animals for almost twenty years, primarily with mice. It is used routinely in the production of transgenic animals (animals with added genes from another species) that have specific genetic alter-

<sup>&</sup>lt;sup>12</sup>S.X. Cao, et al., "Genomic profiling of short and long-term caloric restriction effects in the liver of aging mice," *Proceedings of the National Academy of Sciences USA* 98 (2001): 10630–10635.

ations.<sup>13</sup> These alterations allow scientists to study the effects of normal and aberrant genes in terms of development and function, both in individual cells and tissues as well as in whole individuals, and have been a useful tool in discovering the roles and interactions of numerous genes. Transgenic animals themselves are useful tools, allowing the modeling of various human diseases, or even the production of useful human proteins. Once the transgenic animal is made, it can be perpetuated in a breeding program, insuring that there is always a stock of this particular "design" for future use.

What about human germline genetic engineering? The technology is certainly progressing, though not yet to the point where anyone has directly and knowingly attempted such manipulation. Human artificial chromosomes have been proposed as ideal vectors for use in germline genetic engineering, since they could be easily added to the egg, sperm, or zygote.

Initial research shows that these artificial chromosomes are stable in human cells in culture, and can be used successfully for germline gene transmission in animals. However, current federal policy declines to consider research proposals for germline genetic engineering in humans, or even somatic genetic therapies on unborn individuals that might have the possibility of altering the germline, primarily in the interests of safety. Internationally, the UNESCO Universal Declaration on the Human Genome has been adopted unanimously and by acclamation at the twenty-ninth session of UNESCO's General Conference on November 11, 1997, and the following year, the United Nations General Assembly endorsed the Declaration. The Declaration calls for respect for human dignity and the uniqueness of the individual's genetic endowment, and prohibits use of genetic manipulation to "improve" humans. In fact, outside of the United States, germline genetic engineering is overwhelmingly prohibited or considered ethically unacceptable.

Yet proponents of germline engineering are moving ahead. A one-day symposium was held in 1998 at UCLA to discuss the possibilities of engineering the human germline. Though admitting that such technology could change humanity's path

<sup>&</sup>lt;sup>13</sup>L-N. Wei, "Transgenic animals as new approaches in pharmacological studies," *Annual Review of Pharmacology and Toxicology* 37 (1997): 119–141.

<sup>&</sup>lt;sup>14</sup>T. Voet, et al., "Efficient male and female germline transmission of a human chromosomal vector in mice," *Genome Research* 11 (2001), 124–136.

<sup>&</sup>lt;sup>15</sup>"NIH Guidelines for Research Involving Recombinant DNA Molecules, Appendix 'M'." Available at: <a href="http://www4.od.nih.gov/oba/rac/guidelines/guidelines.html">http://www4.od.nih.gov/oba/rac/guidelines.html</a>; "RAC in utero statement," March 11, 1999. Available at: <a href="http://www4.od.nih.gov/oba/rac/racinutero.htm">http://www4.od.nih.gov/oba/rac/racinutero.htm</a>.

<sup>&</sup>lt;sup>16</sup>"The Universal Declaration on the Human Genome and Human Rights." Available at: <a href="http://www.unesco.org/ibc/en/genome/index.htm">http://www.unesco.org/ibc/en/genome/index.htm</a>.

<sup>&</sup>lt;sup>17</sup>M.S. Frankel and A.R. Chapman, "Facing inheritable genetic modifications. Supplementary material. International perspectives on germ line research and applications," *Science* 292 (2001): 1303. Available at: <a href="http://www.sciencemag.org/cgi/content/full/292/5520/1303/DC1">http://www.sciencemag.org/cgi/content/full/292/5520/1303/DC1</a>.

<sup>&</sup>lt;sup>18</sup>"Engineering the human germline symposium." Available at: <a href="http://www.ess.ucla.edu/huge/report.html">http://www.ess.ucla.edu/huge/report.html</a>.

and needed serious discussion, the participants were virtually unanimous in supporting the technology. Some proposals included the possibility of designing germline modifications in such a way that they could be activated or inactivated depending on the wishes of the next generation. The public policy recommendations included revising current policy of the NIH Recombinant DNA Advisory Committee to accept germline engineering proposals, resisting efforts by UNESCO or other international bodies to block human germline engineering, and resisting any legislation that would regulate germline genetic engineering. The general tone of the meeting is best summed up in a statement made by Nobel laureate James Watson: "I mean, if we could make better human beings by knowing how to add genes, why shouldn't we do it?"

In September 2000, a panel set up by the American Association for the Advancement of Science (AAAS) issued a report in which they recommended that the focus of genetic engineering should be on making changes in cells that would not be passed on to succeeding generations.<sup>19</sup> They note that the effect on future generations makes germline genetic engineering a category of research deserving special consideration in development of public policy. The report urges scientists to focus on making genetic changes that will not be passed to the next generation.

Tight regulation and oversight are needed, according to the AAAS panel, because unintended genetic changes could be passed to a child along with intended benefits. <sup>20</sup> However, if governmental oversight is all that is believed needed to curb the rush into germline genetic engineering, past incidents involving somatic genetic engineering provide a cautionary tale. The death of 18-year-old Jesse Gelsinger during a gene-therapy experiment in 1999, and the subsequent exposure of a lack of adequate oversight by government agencies and research laboratories for gene therapy clinical trials, does not engender great confidence in the ability of oversight bodies to contain potentially dangerous experimentation. <sup>21</sup>

Indeed, neither oversight nor scientific peer pressure have prevailed thus far. In fact, a form of human germline genetic alteration has already taken place, with the intermingling of mitochondrial DNA during in vitro fertilization.<sup>22</sup> In these treatments, cytoplasm from donor human oocytes was transferred to other, older oocytes to "rejuvenate" them prior to fertilization.

This first crossing into germline genetic modification has been excused because it involved an inadvertent side effect of a procedure that had a medical benefit, and

<sup>&</sup>lt;sup>19</sup>M.S. Frankel and A.R. Chapman, "Human inheritable genetic modifications: assessing scientific, ethical, religious, and policy issues" (American Association for the Advancement of Science, Washington, D.C., 2000). Available at: <a href="http://www.aaas.org/spp/dspp/sfrl/germline/main.htm">http://www.aaas.org/spp/dspp/sfrl/germline/main.htm</a>.

 $<sup>^{20}\</sup>mbox{Paul Smaglik},$  "Germline gene therapy needs tight control, says US panel," Nature 407 (2000): 278.

<sup>&</sup>lt;sup>21</sup>"Gene therapy's trials," *Nature* 405 (2000): 599.

<sup>&</sup>lt;sup>22</sup>J.A. Barritt, et al., "Mitochondria in human offspring derived from ooplasmic transplantation: Brief communication," *Human Reproduction* 16 (2001): 513–516.

minimized due to its relatively innocuous alteration.<sup>23</sup> And federal oversight was a moot point, since the genetic transfers used naturally-occurring DNA and did not involve federal funds.

In an article responding to the news of this first germline genetic modification, the authors of the original AAAS report note that

... inheritable genetic modification (IGM) techniques developed for therapeutic purposes are also likely to be suitable for genetic alterations intended to improve what are already "normal" genes. IGM for such enhancement purposes could widen the gap between "haves" and "have-nots." A market economy, where techniques for IGM are available on the basis of ability to pay, would add inherited advantage to the benefits of nurture and education already enjoyed by the affluent.<sup>24</sup>

The authors note that the first likely sites for germline genetic engineering will be infertility clinics (as has already occurred). This is an almost completely unregulated environment, and not necessarily a safe or responsible environment for genetic treatments.

### **Ethics of Genetic Engineering**

The arguments in favor of genetic alterations are almost always phrased in terms of the potential medical benefits and relief of human suffering that can result by treatment or eradication of inheritable genetic diseases. Most would have no problem with somatic genetic engineering that is aimed at treating an individual who has a genetic malady. This treatment relieves human suffering and meets the Hippocratic goal to "Help, or at least do no harm." However, somatic genetic engineering to achieve some enhancement is difficult to justify under this rubric. The ability to run faster or breathe easily at high altitudes confers an advantage, but could hardly be claimed as medically necessary to relieve human suffering. Should such genetic enhancements be considered acceptable? Perhaps such somatic genetic enhancements could be considered a form of individual rights and expression, in the same manner as a tattoo, a piercing, or a hairstyle. Yet augmenting normal physical abilities with performance-enhancing drugs is not allowed in world-class athletic competitions. The economic inequalities in terms of access to genetic enhancements would seem to side against the acceptability of this somatic genetic engineering. The use of somatic genetic engineering to achieve enhancements is of dubious value, both ethically and technically. However, it is much more likely that the push for genetic enhancements will come through germline genetic engineering, against which there are ample objections.

As with somatic genetic engineering, arguments in favor of germline genetic engineering always begin with the ubiquitous "medical benefit" justification of scientific research, promising freedom from health concerns related to genetics. The hope

<sup>&</sup>lt;sup>23</sup>E. Parens and E. Juengst, "Inadvertently crossing the germ line," *Science* 292 (2001): 397.

<sup>&</sup>lt;sup>24</sup>M.S. Frankel and A.R. Chapman, "Facing inheritable genetic modifications," *Science* 292 (2001): 1303.

to rid oneself of a "genetic sentence" of disease is a powerful one. But here we are not dealing with curing ourselves. Germline genetic engineering is done on *prospective* people, and directly affects not us but future generations. It is done because of our hopes for our children and other descendants, or more grandly for the "betterment of mankind." Yet this becomes a slippery slope of even greater incline than that of somatic genetic engineering. What exactly makes, as Watson phrased it, a "better human being"? Who decides what is better? In short, germline genetic engineering is simply a technologically advanced form of eugenics, with the ultimate goal of creating "perfect designer humans."

Germline genetic engineering is unpredictable and uncontrollable

The coordination of some thirty thousand to one hundred thousands genes is necessary for proper development of a human being. Development is a finely orchestrated ballet of cells forming tissues and organs at the right place and time; it takes only one gone awry at the wrong place and time to have a seriously flawed individual. It is sheer hubris to think that we can control such coordination, or anticipate what alterations in single or multiple genes will do to the coordination. Making such coordination work by "reprogramming genes" is also necessary during cloning, in this instance using only the usual and normal gene complement. A paper in the summer of 2001 showed that the failure to reprogram and coordinate gene expression properly was virtually inevitable, resulting in unstable gene expression and explaining why there are essentially no normal clones.<sup>25</sup> While some claim they will be able to detect subtle problems in the expression of genes in a cloning gone awry, most scientists doubt this will be possible.<sup>26</sup> A similar logic follows for germline genetic engineering. Even the removal of a "genetic disease" gene may have unforeseen consequences; the mutation which causes sickle cell anemia actually has a protective effect against malaria. There is no possible way to predict what will be the consequences of alterations to the germline and passage of that new "version" of the human genome to future generations.

Germline genetic engineering creates a genetic caste system

Similar to Huxley's *Brave New World*, or the movie GATTACA, germline genetic engineering will result in separation of the human species into different classes, the manufactured "genetics" versus the "normals," or even into different species if the modifications are extensive enough. The disadvantaged will be those who do not meet the desirable genetic standards, standards that will be set by society's elite, the economically and politically dominant groups. Those who are among the privileged few will increase their privileges, creating a "genetic aristocracy." Prejudices and discrimination will increase, rather than decrease. And most will be unable to afford enhancements, further exacerbating already-wide gaps between "haves" and "havenots," especially between technologically-advanced countries and Third World na-

<sup>&</sup>lt;sup>25</sup>D. Humphreys, et al., "Epigenetic instability in ES cells and cloned mice," *Science* 293 (2001): 95–97.

<sup>&</sup>lt;sup>26</sup>Aaron Zitner and Stephanie Simon, "Reprogramming of genes at core of cloning debate," *Los Angeles Times*, April 22, 2001.

tions.<sup>27</sup> Gina Maranto says it well: "Humans have long since possessed the tools for crafting a better world. Where love, compassion, altruism, and justice have failed, genetic manipulation will not succeed."<sup>28</sup>

Germline genetic engineering treats children as manufactured commodities

This type of genetic modification is not intended to save lives or alleviate suffering of existing people, but rather targets *prospective* people, dallying with the perfectibility of a new human being. An increasing number of scientists point to the inevitability, once established for medical purposes, of germline genetic engineering being used for purposes of enhancement.<sup>29</sup> This may be via a desire to rid a future child of a disease, but will more likely be to endow children with traits a parent wishes them to possess, such as intelligence, height, eye color, or hair color. There are already numerous stories of prospective parents who would like to select the sex of their future child, as well as other traits. As Leon Kass points out, the attitude will become that "not to do so will be socially regarded as a form of child neglect .... Never mind that, lacking a standard of 'good' or 'better,' no one can really know whether any such changes will truly be improvements."<sup>30</sup> Nevertheless, there will be a rush to manufacture "better children," for a "better humanity," creating a shopping mall mentality in the creation of human beings. Erwin Chargaff, renowned biochemist, calls this "a kind of capitalist cannibalism."<sup>31</sup>

Germline genetic engineering degrades human dignity and individuality

Manufacture of human beings to specification degrades not only the individual manufactured, making them mere commodity or artifact, but degrades all of humanity. It leads us back down a path where one human being becomes the property of another, except in this future scenario the new human is the *created* property of another, designed and crafted to meet the maker's desires. We end up with man making man in his own image, yet without any higher standard to which the craftsman is held. The product of this manufacturing process leads us to a dreary future, where some will no longer even be human, and as C.S. Lewis says in *The Abolition of Man*,<sup>32</sup> "the rule of the Conditioners over the conditioned human material, the world of post-humanity." It would be wiser to stop and ponder with the Psalmist, "What is man that thou art mindful of him?"<sup>33</sup>

<sup>&</sup>lt;sup>27</sup>"Gene cures 'will not help Third World'." Available at <a href="http://www.guardian.co.uk/">http://www.guardian.co.uk/</a> Archive/Article/0,4273,4134555,00.html.

<sup>&</sup>lt;sup>28</sup>Gina Maranto, *Quest for Perfection: The Drive to Breed Better Human Beings* (New York: Scribner, 1996), 278.

<sup>&</sup>lt;sup>29</sup>D. King, et al., "Risks inherent in fetal gene therapy," *Nature* 397 (1999): 383.

<sup>&</sup>lt;sup>30</sup>Leon R. Kass, "Preventing a Brave New World: Why We Should Ban Human Cloning Now," *The New Republic*, May 21, 2000.

<sup>&</sup>lt;sup>31</sup>Jordan Mejias, "Research Always Run the Risk of Getting Out of Control," *Frankfurter Allgemeine Zeitung*, June 4, 2001.

<sup>&</sup>lt;sup>32</sup>C.S. Lewis, *The Abolition of Man* (New York: HarperCollins, 1944), 75.

<sup>&</sup>lt;sup>33</sup>Psalm 8:4.