Evolution and the Future of Humankind

(Die Evolution und die Zunkunft des Menschen)

Lee M. Silver, Ph.D. Department of Molecular Biology and Woodrow Wilson School of Public and International Affairs Princeton University Princeton, NJ 08544

Translated into German and published in the book volume Evolution: Geschichte und Zukunft der Lebensdauer

Translated and Edited by: Ernst Peter Fischer and Klaus Wiegandt Publisher: Fischer Taschenbuch Verlag, Berlin Year of Publication: 2003 Pages of chapter: 324-337

English language copyright held by Lee M. Silver, 2004

Future Evolution by Natural Selection?

"It is simply not true that natural selection has ceased to operate in the human species. To make this clear, let us ask ourselves how one could possibly do away with natural selection, if that were desirable. . . [One] fantastic way to abolish natural selection would be to have the number of children that a couple may produce determined by drawing lots, so that the fertility of the parents would in no way depend on their genes, to have all children survive to maturity, and then either all to marry, or some, chosen by lot, to remain unmarried. Surely nothing like this ever happened anywhere in recorded history."

-- Theodosius Dobzhansky, 1964¹

Most educated people accept the fact that we have evolved from more primitive species. The obvious result of our evolution (over the last several million years) has been our enhanced mind with the human-unique attributes of language and a science-based understanding of the universe around us. Since it's happened in the past, it is commonly assumed that it will continue to happen in the future. If our minds expanded in the past, won't they continue to expand in the future? B-rated science fiction movies and television shows from the 1950s and 1960s showed the consequences of this expansion in the form of future humans with over-sized foreheads housing over-sized brains.

But is this necessarily so? Before we can answer this question, we must understand how evolution takes place. The basic answer is actually quite simple but often misunderstood. All members of a species carry the same set of genes. You and I have about 70,000 of the same genes (the exact number will be known once the human genome provides a complete catalogue). The genetic difference between us lies in the small changes – rare mutations.

Now let us imagine that within the individual members of a species, a particular gene exists in two different forms. If, on average, those conceived with second form of the gene ultimately have more children than those conceived with the first form of the gene, then with each generation, a larger and larger proportion of the population will carry the second gene form. Eventually, there will come a time when the first form of the gene disappears, and only the second form survives in all members of the species. It is the change in the forms of genes that a population carries that defines evolution. This is not what most non-scientists think of when they conceive of evolution. They usually imagine large-scale changes in the way a population looks or behaves. This "macro-evolution" is simply a result of large numbers of miniscule changes in many genes. My short description of evolution cannot possibly do justice to the subtle details of the process, but I simply want to emphasize the critical point that evolution can only occur when a new form of a gene increases the average number of children produced by those who carry it. Scientists refer to this property as "reproductive fitness"

With this basic understanding of evolution, we can appreciate the point that Dobzhansky was trying to make, and then ask whether he was right or not. Dobzhansky's claim was that human genes continue to play an important role in determining whether a child survives to adulthood, whether she marries, and how many children she has. He made fun of the idea suggested by unnamed contemporaries that survival, marriage, and childbearing might have little to do with genes.

While Dobzhansky is recognized as one of the most important early 20th century geneticists (he made this pronouncement near the end of his career), his notions concerning future human evolution are naïve. What he thought to be fantasy is now reality in the modern industrialized societies of North America and Europe and more and more countries throughout the world. Except for a small percentage of children born with certain congenital diseases (and even this exceptional group becomes smaller with time), both survival to maturity and likelihood of marriage are independent of genes. The survival of nearly all children is due, of course, to modern emphasis on sanitation and medicine. The ascendancy of individual autonomy as *the* defining human right means that the question of marriage really does come down to "drawing lots." Finally, the miracles of new reproductive technologies have, and will continue to reduce the impact that genes have on family size. Perfectly fertile people have far fewer children than they are capable of, and greater and greater proportions of infertile people are using reproductive technologies to match them child for child.

But let us consider the possibility of the future emergence of a highly infectious lethal disease. Wouldn't natural selection choose people who were genetically resistant to the new disease over people who were susceptible?

Let us grant that natural selection of our immune system could occur in the future (although this is by no means a given). What impact would this have on the essence of human nature? The answer is absolutely none at all. Disease resistance genes are not the ones that define us as human beings. Our immune system is not only indistinguishable from that of the other apes, it is indistinguishable from the immune systems present in every other mammal, even down to lowly mice. And only a small percentage of our genes actually play a role in protecting us from infectious disease. The attributes that make us uniquely human are two in number. They are minds and our looks. So the question of future human evolution should really be reduced to the question of whether our minds or appearances will change according to Darwinian principles, and as I have argued above, I believe the answer is no..

But what about other changes in our environment? For the most part, we control our environments rather than our environments controlling us. Let us look at the last 60 million years for what the future might hold. Warming of the earth? Cooling of the earth? Increased carbon dioxide, increased pollutants? In the short run, it is hard to imagine environmental changes that would be so drastic that we couldn't simply figure out how to deal with them through technology as we always do.

But let us imagine that some drastic change does occur in the future that makes it very difficult for human beings to live without assistance. Let us say further that a small number of people have genes that help them to survive. What will everyone else do? Those who claim that we will have to evolve in response to changing environments of the future are often confusing natural selection with Lamarckianism. "We" can only evolve if new genes present in a small number of people (almost certainly not you or me) allow those select few to have more children than everyone else! But the drive to have children is intense, and most people will not forgo the chance to reproduce without a fight.

The brilliant evolutionary geneticist Dobzhansky got it wrong, like so many other scientists, because he fundamentally misunderstood the power of the individual in the modern world. Our species does not play by the rules of evolution. Individuals and couples are not going to say, "hey, you've got better genes than me so you go ahead and have children and I won't." It goes without saying that individuals will not simply lie down and give up life because they are missing protective genes. Furthermore, individuals will not accept not having children, and they will do everything within their power to overcome any genetic hindrance to fertility.

Future Evolution with Reprogenetics?

On July 25 1978, Louise Joy Brown was born as the first baby who had been conceived outside the human body. Her birth made headlines as it showed that in vitro fertilisation techniques could provide a cure for infertility, helping couples who could otherwise not conceive children. But Louise Joy Brown's birthday represents a singular moment in the history of humankind for another reason: science had brought the human embryo out of the darkness of the womb into the light of the laboratory.

Today, in vitro fertilisation has become a commonplace service. The best IVF clinics offer their customers success rates of up to 70%-twice as high as that naturally achieved by fertile couples actively trying to have a baby. At the same time that assisted reproduction techniques have been improving, there has been an explosion of knowledge in genetic research and technology. The "Human Genome Project," will eventually identify each and every human gene and characterise how it interacts with other genes and with the environment. The results from this immense undertaking will allow researchers to determine how individuals differ at each of these genes and how these variations influence unique personal characteristics. These differences will include resistance or susceptibility to infectious and inherited diseases, as well as the efficacy of drugs or therapies. With ever increasing knowledge, biologists will ultimately be able to make connections between genetic profiles and physical or mental attributes that we commonly refer to as innate talents.

New genetic technologies have implications for all fields in medicine, but when they are combined with reproductive technologies, the prospects are staggering. Indeed, the combination is so different from that of either technology alone that it deserves a new appellation: *reprogenetics*.² Reprogenetics refers to the use of genetic information and technology to ensure or prevent the inheritance of particular genes in a child.

Humans have always practised reprogenetics. At the simplest level, people look at a potential marriage partner and ask themselves, "Do I want to have children with this person?" Whether conscious or not, a marital choice made on the basis of this question will have a real effect on the genes that a child receives.

One step higher in technical sophistication is the selection of a sperm donor in cases of male infertility. Artificial insemination has been used for over 100 years to overcome infertility, and now some 50,000 children are born each year through the use of this procedure. The choice of the sperm donor has never been random. In the past, physicians selected donors based on health status, family history and other traits considered desirable such as intelligence, athleticism or character. Today, parents who need donor sperm can choose from catalogues on the World Wide Web. Similarly, egg donation is used in cases where a woman is unable to produce her own. The demand for egg donors with "superior qualities" is so large, and the number of women willing to donate eggs is so small, that "supply and demand" economics have taken over this process in the USA. A recent advertisement in the Princeton University student newspaper offered \$50,000 for eggs from a woman meeting certain criteria. Of course, many desired characteristics have little chance of being inherited, but the simple fact that people try to control their children's genes is a sign of reprogenetic intent.

Finally, any time a woman decides to abort a foetus based on the results of amniocentesis, she makes a negative choice against certain genes in her unborn child. And any time an abortion is chosen solely because a child would have been mentally retarded, reprogenetics is being practised for the sole purpose of increasing the intelligence of the child that is ultimately born through a later pregnancy.

Many bioethicists oppose all attempts by parents to actively control the genetic makeup of their children. They equate reprogenetics to clearly abhorrent eugenic practices used in the past. But in fact, reprogenetics and eugenics are fundamentally different from one another, both in terms of control and purpose.

The purpose of eugenics was to improve a society's so-called "gene pool" by controlling the breeding practices of its citizens. In the early twentieth century, the USA put this idea into practice by the forced sterilisation of people deemed genetically inferior because of supposedly reduced intelligence, minor physical disabilities or criminal character. Further "protection of the American gene pool" was endeavoured by congressional enactment of harsh policies to restrict the immigration of people from Eastern and Southern Europe–regions whose populations (from which all four grandparents of the author of this paper came) were considered to harbour undesirable genes. Eugenic practices were not restricted to the USA, but were also used in Sweden and more recently in China when mentally retarded people were sterilised. Nazi Germany's version of eugenics was the most horrendous approach, eliminating all those who were deemed to carry any undesirable genes. In the aftermath of World War II with the repulsion against the atrocities committed by the Nazis, eugenics was finally and rightly repudiated as discriminatory, murderous and infringing upon the natural right of humans to reproduce freely.

While eugenics is controlled by the government, reprogenetics can be controlled at the level of individual prospective parents. And while eugenics is concerned with the vague notion of a societal gene pool, reprogenetics is concerned with the very real question of what genes an individual child will receive. While the promulgation of eugenic practices led to a restriction of reproductive freedom and worse, reprogenetics will do exactly the opposite. It could give parents children with a higher likelihood of being healthy, without bringing direct harm to anyone else.

Fundamentally, reprogenetics can be understood through its sole motivation: the desire of parents to give all possible advantages to their children. Indeed, this evolutionarily derived instinct is expressed by parents of many species who use all available resources to maximise their children's survival chances. Reprogenetics allows parents to reach for this goal before their child is even born. Affluent parents provide environmental advantages to their children after birth; reprogenetics will allow them to add genetic advantages. It is important to point out that

both genetic and environmental advantages simply enhance probabilities-nothing is

guaranteed. But the lack of guarantee does not stop parents from spending \$150,000 to send their children to Princeton University.

If democratic societies allow money to buy environmental advantages for children, how can they prohibit parents from buying genetic advantages, as both are aimed at the same goal of helping a child? If reprogenetics is used to increase chances of health, happiness and success, what could be wrong with it? I will not answer this question now. Instead, I will first consider future reprogenetic technologies and the potential impact on naturally existing biological inequities.

Two reprogenetics technologies based on the use of IVF are currently available: embryo selection and genetic engineering of the germ line. For embryo selection, DNA analysis is performed on a single cell taken from an 8-cell human embryo. Thus, once certain genes are characterised, for example, parents could select embryos that will develop into taller children, or children with increased potential for longevity or long-term happiness–which has a strong genetic correlate. Embryo selection does not involve modification of the genome. It just allows parents to select one embryo over another; it is equivalent to placing the dices on the table rather than throwing them for a random reproductive outcome.

However, embryo selection is severely limited as a reprogenetic technology for two reasons. First, if parents do not carry a particular gene, none of their embryos will either. Second, parents can choose any gene to select, but they cannot choose many. Because our genes are re-shuffled like cards before we hand off 50% to our child, the probability that any one embryo will get any set of genes decreases exponentially as the gene number increases. Simple probability calculations suggest that it will never be feasible to select for more than five genes. Since traits like height, health and personality are influenced by large numbers of genes, it is unlikely that embryo selection will ever go beyond avoidance of simple genetic diseases.

All of these limitations disappear with genetic engineering of the germline. Any gene imaginable and any number of genes could be modified in, or added to, an embryo. Over the last 20 years, the technology of germ line engineering has been used with increasing efficiency to alter embryos in a variety of species–including mice, pigs, and sheep–in an increasingly sophisticated manner (Hogan et al., 1994). Until recently, however, the possibility that this technology might be applied to human embryos was not given serious consideration because of three major problems. First, the technology was extremely inefficient, with success rates typically less than 50%. Second, the application of the technology was associated with a high risk of newly induced mutations. Finally, there was–and still is–a general sense that genetic

engineering can never be performed on people because of the possibility that a particular modification might have unanticipated negative side effects. The existence of any one of these problems alone would be sufficient to label genetic engineering of the human germ line as unethical and irresponsible.

But as we move into the new millennium, the technological landscape is improving dramatically. It now seems possible that all three problems can be overcome. Powerful new modification and screening technologies could soon allow scientists to alter the genomes of embryos and identify only those in which the desired genetic change has been implemented without any damage to the pre-existing genome. This technical advance could eliminate the first and second problems associated with genetic engineering. But the third problem seems to remain. Even if the embryo's genome is engineered exactly as intended, how can we rule out unintended, unanticipated and deleterious side effects?

Before we can answer this question, we must understand that while there is a near-infinite number of possible germline genetic modifications, they can all be placed into two categories. Type I genetic changes are those that provide the embryo with a genotype substantially equivalent to one that people get naturally. Type II genetic changes provide enhancements that no human beings get naturally.

Geneticists now understand that people are not born equal when it comes to biological properties including physical and physiological characteristics, disease resistance or susceptibility. One percent of the population, for instance, carries a mutation that provides absolute resistance to HIV infection. Some people have superior cancer protection genes, and others are born with genes that greatly increase their life expectancy. With the results from the Human Genome Project it has now become feasible to study and characterise the physiological effects of each of these genes. Deleterious side effects can be identified or ruled out before genetic engineering is ever attempted with such "type I genes." In the case of people who carry the HIV resistance gene, for example, medical studies have demonstrated no significant negative impact on health or any physical characteristics. When the likelihood of negative sides effects is shown to be sufficiently low, parents will be able to use type I genetic enhancement to give their child a potentially beneficial gene that other children can get naturally. Type II genetic enhancements on the other hand will not be feasible in the near future because of the possibility of unanticipated side effects.

For the sake of analysis, let us assume that at some point in the future, technical problems associated with genetic engineering of the germ line are eliminated and it is possible to use the technology safely and efficiently. In practice, this means reaching a point when the risk of birth defects is lower than 4%-the risk encountered in cases of natural conception and gestation.

Until this goal is attained, the use of type I genetic engineering will be considered unethical and unacceptable. But if, and when, the risk of the technology is reduced below the natural level, we will have to consider the ethics of its use in terms other than safety. And these considerations will be greatly influenced by the political system within which such a discussion takes place.

All modern democratic societies must balance the opposing aims of individual autonomy and social justice. In the USA, individual autonomy is of paramount importance. If a society allows parents to buy their children advantages, it has no logical basis for banning type I genetic enhancements. Americans would respond to any attempt at a ban with the question, "Why can't I give my child beneficial genes that other children already get naturally?"

In most other Western countries, social justice plays a much larger role. Most European countries try to achieve it by providing equal healthcare and educational opportunities to all children, irrespective of the affluence of their parents. Here, type I genetic enhancements might seem immoral because they are unfair to those children who did not receive them. But there is a flaw with the fairness argument: children are not biologically equivalent to begin with. Everyone is born with advantages or disadvantages across a whole range of physical characteristics as well as innate abilities. Life is not fair.

In the future, the critical question therefore will be who decides how genetic advantages are distributed. Who decides which child will get the HIV resistance gene, which child will have the potential for a long life span and which one will have superior protection against cancer and heart disease? Should the decision be left to the randomness of nature, as it is now? Should it be determined by the parents' affluence? Or should it be controlled by the state? There may come a time in the future when an individual or society actually *is* making a decision in favour of randomness when it chooses *not* to make a decision. Alternatively, the desire of a European-style democracy to protect its citizens, may lead to an active responsibility of the state to perform type I genetic enhancements, just as childhood vaccination is performed in Europe.

Unfortunately, the provision and regulation of genetic enhancement technology will not be easy. Unlike healthcare, there are almost no limits to genetic enhancements. There can always be greater resistance to diseases, greater longevity, greater physical prowess, and greater mental capacity. Furthermore, the innate desire to advantage one's children is so powerful that affluent citizens may buy reprogenetics elsewhere even if their society bans or limits its use–just as Europeans now travel to the USA to purchase human eggs from selected donors.

The use of genetic enhancement could greatly increase the gap between "haves" and "havenots" in the world. A gap between classes within societies may emerge initially. But when the cost of reprogenetics drops like the costs of computers and telecommunications did, it could become affordable to the majority in Western and other industrialised countries. Ultimately, type II genetic enhancements will become feasible too, and then there really will be no limitations. When this happens, the economic and social advantages that wealthy countries maintain could be expanded into a genetic advantage. And the gap between wealthy and poor nations could widen further with each generation until all common heritage disappears. A severed humanity might be the ultimate legacy of unfettered global capitalism.

The only alternative seems remote today and it may never be viable: a single world state in which all children are provided with the same genetic enhancements and the same opportunities for health, happiness, and success. But politics are far more difficult to predict than science.

- Lee M. Silver

The author is at the Department of Molecular Biology and the Woodrow Wilson School for Public and International Affairs of Princeton University. He is also the author of *Remaking Eden: How Genetic Engineering and Cloning will Transform the American Family.*

Email: lsilver@princeton.edu

¹ Theodosius Dobzhansky (1964). Heredity and the Nature of Man (New American Library, New York), p. 157 (paperback edition).

² Silver, L. M. Remaking Eden: How Genetic Engineering and Cloning will Transform the American Family. Avon Books, New York, 1998.