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Possibilities and Responsibility

Society stands at the precipice of a new world. The recent completion of the Human Genome Project opens up a wealth of knowledge with the possibility of understanding the simple, yet essential, components of our being; DNA and the genes encoded within. The scientific and medical communities are presently working to decipher this monumental discovery and integrate the information into their pre-existing data. Once the function of each gene and protein in the human genome has been determined, scientists, researchers and doctors will possess the capability to make advances in bioinformatics, analyze and produce effective drugs more efficiently and economically, create novel cures for genetic diseases, and, or, possibly remove genetic diseases from the gene pool forever. Although this goal remains far from complete, current data about genes, proteins, and their functions have produced gene therapy techniques that are on the brink of curing genetic diseases or eliminating them all together.

At present there are two main types of gene therapy; somatic cell gene therapy and germ-line gene therapy. Somatic gene therapy involves all body cells other than those involved in reproduction, those of sperm or eggs. This new technology is being developed to cure those affected by genetic diseases, previously thought incurable. One gene therapy technique involves altering a virus to infect the body and insert normal DNA of the afflicted gene into the individual's cells. The degree of success varies

between diseases, but seems to work best against diseases where the individual's genes can be altered so that a few normal working cells can produce enough of the missing protein or enzyme to overcome the disease, as in the case of cystic fibrosis. When successful somatic gene therapy cures the individual, however, the genetic transformation does not manifest itself in the person's gametes, and therefore, is not passed on to future generations.

This paper, however, focuses on germ-line gene therapy, or, engineering. Unlike somatic cell gene therapy, germ-line gene therapy is the manipulation of the gametes, sperm or eggs, or an early embryo. This type of gene therapy does not affect the individual from which the gametes are derived, but instead, the resulting progeny and every generation thereafter. Germ-line engineering (GLE) does not correct manifest genetic diseases, but instead, prevents them and forever changes the genetic make-up of the resulting individual.

Currently there exist two methods of germ-line engineering. The first is similar to methods used in somatic cell gene therapy, where viruses are altered to infect cells and insert DNA. This procedure, however, leaves open the possibility that inserted DNA could integrate itself into chromosomes at crucial points along the chain of life, leading to harmful, or even lethal, mutations. Thus, because scientists cannot control where the DNA introduces itself, the process remains too dangerous to practice on human gametes or pre-embryos. This sort of genetic alteration has been tested on animals, though, and presently produces a range of animals such as cows with increased milk production, mice used for genetic tests, and sheep that can secrete specified hormones into their milk.

The second, and extremely innovative approach utilizes human artificial chromosomes (HACs). Created by microbiologist Huntington Willard and his colleagues at the Case Western Reserve Medical School, HACs are man-made chromosomes. The technology involved in HACs has the potential to allow scientists a controllable and predictable way of engineering complex custom-made genetic material, and then reliably introducing them into human embryo cells.

Both techniques open up far-ranging possibilities and show amazing technological advances in the manipulation of human genes. Yet, as with all developing technologies, germ-line engineering brings with it awesome opportunities that have not been perfected. Researchers cannot successfully perform GLE on human gametes or pre-embryos, and even if they could, they cannot predict the long-term affects of such alterations on future generations. Another lingering problem looms as to whom, or how, people will manipulate this technology.

Like somatic cell gene therapy, there are two types of germ-line gene therapy; negative and positive. Negative gene therapy aims to correct genetic diseases or conditions. Current negative gene therapy methods include preimplantation techniques such as in vitro fertilization or embryo selection, and prenatal screening methods such as amniocentesis. Once perfected, GLE could be added to the list of negative gene therapy options. Germ-line engineering may involve eliminating a defective gene from the prospective parent's gamete, and, or, taking a normal allele of the gene from either a pre-screened cell of the prospective parent's, or from another human being's, and inserting it into a sperm, egg, or pre-embryo.

Benefits of negative gene therapy include: permanently eliminating inherited diseases within a family, money-saving preventative action by eradicating the disease gene, before there is a disease to cure, and allowing inherited disease carriers to procreate without worrying about passing on defective genes to their offspring. Protests to negative gene therapy, however, arise with the moral, ethical and religious issues of tampering with the "natural" order of reproduction, selecting and discarding flawed pre-embryos, and the idea that genetic manipulation is man trying to play God.

There are also scientific objections in that certain diseases, such as sickle cell anemia, actually are evolutionary advantages for people living in particular climates of the world, and that by selecting our genes, humans run the risk of diminishing diversity within the gene pool which could adversely affect the whole species.

Germ-line engineering also raises specific medical concerns. Not only is GLE too dangerous to practice now, but even if the technology were found to be safe and effective, many feel that this is an unnecessary procedure. From a medical standpoint they believe the current negative gene therapy methods are sufficient for all genetic diseases except the rare case of a parent with two copies of a dominant disease gene, and even then, they suggest adoption or abstention from reproduction to GLE. They do not feel that recessive hereditary disease genes pose a great enough threat to warrant GLE, since presumably the other allele will be normal, and therefore expressed. In the case of two recessive disease alleles, or one dominant disease gene, they still believe that preimplantation or prenatal screening presents a better option to GLE, and is just as effective in guaranteeing the birth of a normal and healthy child.

One of the main reasons people are so opposed to gene therapies generally, and germ-line engineering specifically, are because of their potential. There is a fine line between what one person considers a disease, and what another considers a disadvantage. Myopia for example, is it a disease or a disadvantage, and does it warrant GLE? Thus, the therapeutic procedures developed to cure necessary medical diseases could theoretically be applied to other, cosmetic, improvements.

Positive gene therapy generally falls under this "enhancement" category. Since germ-line engineering has not yet been perfected, the closest reproductive interventions scientists have for positive gene therapies are preimplantation screening to select a specific embryo for implantation, or the utilization of sperm or egg donors to introduce desired traits into offspring. Although GLE therapies are still hypothetical, once geneticists determine the genes for nondisease characteristics such as skin, hair or eye color, height, or possibly even intelligence and personality, prospective parents may be capable of designing their children.

Pros for this sort of genetic manipulation follow from the advantages of being able to specifically choose the characteristics of one's own child. Your offspring could theoretically have not only the best possible genetic combination from you and your partner, but also possibly the finest genes available; and who does not want to give their children the very best? This self-selective process could also take the random chance[1] out of evolution and allow humans to decide their own future. With the world's

[1] Bioethicist John Harris says; "The best I can do here is repeat a perhaps familiar thought, namely that although this is often taken to be a difficult question (designer children) and indeed the idea of parents being able to choose such things very often causes outrage, I have found difficulty in seeing this question as problematic. It seems to me to come to this: either such traits as hair colour, eye colour, gender, and the like are important or they are not. If they are **not** important why not let people choose? And if they **are** important, can it be right to leave such important matters to chance?"

population over six billion and continuously growing, and our resources being finite, many of them non-renewable, some believe that humans need to start actively selecting who inherits the earth. Especially for those who fear dysgenics, the theory that the least educated, least well-off, least "fit" are "overreproducing," and as a result our species is on the decline[2], this technology provides for them a way to proactively choose the traits of future generations to come and reinstate the "survival of the fittest."

Cons against positive gene therapy are varied. Since positive gene therapy alterations are made, not so much for medically founded reasons, but for other aesthetic motives, they tend to conjure up ideas of eugenics and Nazi Germany. Sir Francis Galton, cousin to Charles Darwin, first coined the term "eugenics" in 1904 as: "the science which deals with all influences that improve the inborn qualities of a race; also with those that develop them to the utmost advantage." He went on to further suggest that his cousin's theory of natural selection should be applied to men[3].

A possible indication of the eugenic tendencies of positive gene therapy is that fetal sex, one of the few testable, nondisease, phenotypic characteristics, has already resulted in sex-selective abortions all over the world, most notably in China. Presumably

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[2] "Every day we are crippling and maiming the children of the future by injecting into them the genes that cause poverty, suffering, starvation, famine, disease, physical and mental retardation causing in effect the degeneration and anti-evolution of the human species. Paradoxically, we have been conditioned to believe that we are doing all this in the name of the highest morality. Indeed, we are told that it is the epitome of compassion, charity, social responsibility and even religious duty to spend time and money maintaining the unfortunate children who are retarded and incapable of taking care of themselves. What of our moral responsibility to protect the right of future generations to be born physically healthy and mentally capable? It is only because of our highly evolved intellectual capacity that we were able to develop the technology to keep these genetically poisoned individuals alive. Ironically, we are using the intellectual capacity that made us great in order to destroy that capacity itself." (Prometheus website, Eugenics and Dysgenics)

[3] Galton stated that although "no agreement could be reached as to absolute morality, the essentials of Eugenics may be easily defined. All creatures would agree that it was better to be healthy than sick, vigorous than weak, well fitted than ill-fitted for their part in life. In short that it is better to be good rather than bad specimens of their kind, whatever that kind might be. So with men."(Galton, 1904).

because prospective parents believe that one sex, generally male, provides advantages over the "lesser" sex. Others imply that if undesirable traits such as violence, or mental handicaps, were scientifically proven to be linked to specific genes, governments could take it upon themselves to enforce GLE as a societal preventative. Or, as many countries did during the recent 20th century, revert to forced sterilization, abortion or even genocide of those who were "genetically inferior."

An economical argument is that this technology applies only to the rich, and that it will further the cleavage between society's privileged elites who can afford these methods and those who are born without prenatal enrichments. This also raises questions over insurance and health care issues and who should be responsible if parents decide not to partake in positive GLE, or cannot manage to pay for such expensive therapy.

Others disagree with positive gene therapy on the basis that they feel it simply represents our consumerist society. Parents will continually want to somehow "up-grade" their children, like their computers, and the technology will forever be pushed to meet this demand. Bringing up as well the psychological implications of positive gene therapy and how parents will react to their "designed" child, how society will react to both the parents decision and the child, how the child will see themselves, their parents, and their interactions within their community, along with many other complex societal relations.

Those who fight for the rights of an unborn child are also usually anti-positive germ-line engineering. Some are against it because they feel the child loses part of its individuality and others believe that parents are not proxies for their children. Those concerned about the child's uniqueness worry that by choosing your child's

characteristics they lose their inherent identity and distinctiveness. Others say that parents cannot truly give consent for such a drastic genetic alteration of their children. They believe genetic decisions should be left up to the child, and if they want to genetically alter themselves they can look in to somatic engineering or other alternative methods.

As of now, the technology for germ-line engineering, either positive or negative, is still a prospect of the future. Yet as history has shown us, what the mind can imagine, someone will realize. Thus, as our technical and informational background increases, these possibilities will soon become realities. The Human Genome Project and the work being done on gene therapy techniques, whether they be somatic cell or germ-line cell, positive or negative, all represent valuable technical progress for the scientific community. The prospect for those living with genetically linked disorders is hopeful, as well as for their possible offspring and for generations to come. This new technology, however, brings with it awesome power, and with that comes the great responsibility of putting our knowledge to use wisely and handling this information seriously and cautiously. There are countless moral, ethical, religious, philosophical, psychological, societal, scientific and medical issues etc. regarding gene therapy, and specifically germ-line engineering, that this paper could only touch upon. All are extremely valid concerns and we, as a society, need to decisively address the issues surrounding this technology before the future all too soon become the present.

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