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Kelsey Lloyd
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Ethical Dimensions of Pre-Implantation Genetic Diagnosis

Modern applications of germ-line gene therapy are able to provide lifesaving treatments to otherwise fatal diseases. This was first demonstrated in the year 2000 with the case of the Nash family, who owes the life of their young daughter, Molly, to pre-implantation genetic diagnosis (PGD). At just six years old, Molly was dying from Fanconi anemia, a rare genetic disease, and hematopoietic stem cell transplantation was her only chance of survival. In order to limit the risks associated with allogenic stem cell transplantation and graft versus host disease, Molly's parents opted to have another child and genetically ensure that it would be a well-matched donor for Molly. Through processes of *in vitro* fertilization (IVF) and PGD, an embryo with matching tissue type was selected, implanted, conceived, and ultimately born as Adam Nash – a perfectly matched stem cell donor for his older sister, and the first genetically designed human being. Within months of his birth, transplantation efforts showed signs of success and Molly Nash eventually achieved full remission.[1] This first foray into embryonic genetic modification and gave promising insight to the future possibilities of germ line therapy.

The rapid advancements of germ line gene therapy are as problematic as they are promising. With the successful creation of "donor baby" Adam Nash, it became clear that applications of PGD had come a long way from their humble beginnings in simple embryonic sex determination screening, now occupying a new and uncertain realm of deliberate human design that challenges fundamental cultural concepts of ethicality, legality, and the role of medicine as a whole. If the technology exists to select for embryos with desirable traits and weed out those with undesirable traits, then

1 Dobson, Roger. "'Designer Baby' Cures Sister." 2000.

reproduction could conceivably take on a consumerist quality much like shopping. Indeed, if gene therapy lives up to its promises, doctors may soon be able to create "designer babies" with any specified assortment of attributes ranging from eye color to intelligence, stature to disposition.[2] Moral judgment is struggling to keep pace with the ever-advancing frontline of genetic technology, and many questions have yet to be answered. Are these actions acceptable in the absence of medical need, or do prospective parents have a right to access all available technology regardless of motive? Is it ethical to create a human being with the primary intention of harvesting its tissue for another person's benefit? These questions of human creation teeter on the theological but must be answered, for society's stance on such matters will surely have enormous implications for future medical practice.

This paper will first examine pre-implantation genetic diagnosis more closely to differentiate it from other, less controversial forms of gene therapy, and to elucidate why there is such an intense demand for this therapy in the medical realm. We will then consider the realistic capabilities and limitations of this technology in order to quell sensationalized public fears. From this, we will be able to focus our questions of ethics and legality on a realistic set of conditions in which we find ourselves now and anticipate how the technology will likely evolve in the near future.

For the purposes of this paper, gene therapy can be categorized into in three main forms: somatic gene therapy, pre-implantation genetic diagnosis (PGD), and pre-implantation genetic modification (PGM). Each is distinguished by its own set of aims, limitations, and capabilities, and therefore each incurs its own unique set of ethical dilemmas.

Somatic gene therapy is characterized by the genetic alteration of non-reproductive cells for medical purposes. It can be used to repair muscle and brain cells after injury.[3]

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2 Lemonick, Michael D. "Designer Babies." 1999

3 Reiss, Michael J. ""What Sort of People Do We Want." 1999.

Somatic gene therapy is the relatively unproblematic in terms of ethical acceptability; however, it is limited by the fact that it cannot prevent genetic disease.

PGD (also referred to as embryonic screening) can prevent genetic disease.[4] PGD is a form of germ line therapy that, at its most basic level, is an extension of other assisted reproduction therapies. The technique is characterized by screening the genetic material of an individual's reproductive cells with the intent to confer a health benefit to the descendants and/or another individual.[5] PGD enables early identification of genetic disease in embryos, and it is mainly used in conjunction with IVF with at-risk parents who wish to avoid implantation of an embryo with an identified monogenic disease. When the fertilized embryos have grown to be eight to ten cells in vitro, one cell is removed from each embryo and analyzed for the genetic disorder of interest. Once a desirable, "healthy" embryo is found, it is implanted in the womb.[6] PGD developed in the early 1990s with the simple purpose of differentiating sex before implantation in an effort to avoid sex-linked disorders such as fragile X syndrome and haemophilia A, but PGD is now able to screen for many malignant and non-malignant monogenic diseases, including leukemia, sickle cell disease, Hodgkin's disease, thallassemia, and Fanconi anemia.[7] In light of these capabilities, some doctors are already stating that, "it should be criminal to bring handicapped babies into the world," exhibiting the doctor's opinion that medicine is obligated to treat and prevent disease to the best of their abilities.[8]

PGD is not only able to prevent certain genetic diseases; it can also be used to indirectly treat existing cases. PGD fills a glaring void in hematopoietic stem cell therapy. While stem cell transplantation has become the treatment of choice for many the

4 Ibid.

5 Ibid.

6 "PGD". Institute for Reproductive Health. 2012.

7 Robertson et al. "Conception to Obtain Hematopoietic Stem Cells." 2002.

8 Ibid.

aforementioned life-threatening diseases, the treatment of many cases is limited for want of an immunologically compatible donor. According to the National Marrow Donor Program, approximately 7 million people in the United States are searching for a match, creating a "roughly one in 400 chance, depending on the patient's ethnic group, that an unrelated individual will be an acceptable match."[9] Even if a donor is found, indeed even if that donor is a sibling, allogenic stem cell transplantation carries extreme risks of graft versus host disease and opportunistic infection.[10] PGD offers an efficient solution for patients caught in this quandary. When tissue typing is employed in addition to IVF and PGD, an embryo can be selected so that it has human leukocyte antigen (HLA) compatibility with tissue type of the intended HSC recipient.[11] Parents with sick children are often very willing to initiate a PGD-assisted pregnancy in order to conceive a donor-baby who will be able to provide highly compatible HSCs to their older sibling.

Unfortunately, ethical problems arise with this form of embryonic screening because it does not confer a medical benefit to the baby but rather but to the individual who will someday receive the donation of lifesaving HSCs. The primary concern is that screening and creating a child for utilitarian purposes violates the Kantian imperative that humans exists as themselves rather than "means to an end".[12] In the words of Brigette Nerlich, a professor of Philosophy of Science of Nottingham, UK, "The very basis of human dignity, which in turn provides the foundation for human rights, is that we have to be treated as ends in ourselves".[13] By creating a child for a material purpose, one can argue that the parents are turning the child into an object. This argument, while commonly employed by the PGD opposition, can be easily rebutted. As Robertson

9 Robertson et al. "Conception to Obtain Hematopoietic Stem Cells." 2002.

10 Ibid.

11 Ibid.

12 Nerlich et al. "The First 'Designer Baby'". 2010.

13 Ibid

argues, “[The parents] are having a second child for a beneficial purpose. Nothing in the circumstances suggests that they will not be as loving and caring of the second child as they have been of the first. How a child is treated after it is born, not the motivation in conceiving it, determines whether reproduction is ethical.”[14] Parents have a right to conceive a child for any reason they deem fit, and though this circumstance “makes the purposeful nature of reproduction more transparent than usual”, it is a valid motive all the same.[15]

Additionally, pro-life supporters find issue with PGD because embryos left over from IVF are destroyed rather than implanted, which arguably is the destruction of life. This argument is often applied to assisted reproduction in general, and varies depending on religious and personal opinions dictating the moment that life begins. However, most people agree that PGD is at least preferable to prenatal genetic diagnosis, in which genetic screening is performed later in gestation and is likely to motivate the abortion of a fetus. Most academics and medical institutions agree that PGD screening for the avoidance of genetic disease is ethical.[16]

The most commonly invoked argument used against PGD screening is the “slippery slope theory”.[17] Even though much of what PGD currently does is negative selection (screening and exclusion), there is intense public fear that the tissue-typing part sets opens the door for future applications of PGD-based positive selection and widespread use for non-medical purposes such as human enhancement and cloning.[18] As Robertson et al. observe, “this slippery slope argument assumes both that the future genetic alteration

14 Robertson, John. "Embryo screening for tissue matching." 2002.

15 Ibid.

16 Wolf et al. "Using Preimplantation Genetic Diagnosis to Create a Stem Cell Donor: Issues, Guidelines & Limits." 2003.

17 Nelrich et al. "The First 'Designer Baby'". 2010.

18 Robertson et al. "Conception to Obtain Hematopoietic Stem Cells." 2002.

and manipulation will be unmitigatedly horrible, and that accepting the procedure now in question -- HLA typing of embryos prior to transfer -- will lead inexorably to abusive and uncontrollable genetic engineering of humans if only by changing attitudes that would make the next step towards genetic engineering easier to make."[19]

The next step towards genetic engineering is PGM. In contrast to PGD, PGM refers to the practice of *modification* an individual's genome before implantation in order to enhance valued traits in the subsequent offspring for *non-medical purposes*.[20] This practice, while not yet fully realized, holds promise to give parents the option of selecting their child's sex, features and perhaps even personality by manipulating embryonic genes. This scenario, by far the most controversial application of gene therapy, would result in the so-called "designer baby".[21] Germ line therapy is ethically troubling because embryonic selection and modification can be made to suit arbitrary choices rather than medically necessary interventions. Differential access to "designer" genes, fears of sex discrimination, and eugenics are areas of concern within germ line modification technology.

At present, PGD and PGM are limited to dealing with simple, monogenic traits, which of course limits the types of modifications that parents can make on their children. Media fuels the argument against PGM by sensationalizing the possibilities, likening the children of tomorrow as "Frankenbabies" and idealized super-humans.[22] But despite the fact that genetic research is continually expanding and the Human Genome Project has just recently identified the approximate 100,000 genes in the human genome, fertility clinics offering made-to-order babies with optional eye color, personality, musical capability, athleticism, height, weight, sexuality, and longevity are frequently thought to

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19 Ibid.

20 "PGD". Institute for Reproductive Health. 2012.

21 CBS. "'Designer Babies' Ethical?". 2009.

22 Nelrich et al. "The First 'Designer Baby'". 2010.

be distant possibilities. Such traits are almost always the result of unspeakably complex interactions between genes and environmental stimuli, and cavalier modification of interrelated genes are more likely to disrupt bodily function and produce pathogenic phenotype than create the intended, desirable phenotype.[23] Some have considered the attempt to unravel these complexities for commercial benefit an impossibility and a waste of time.

Perhaps we have been underestimating ourselves. New research has shown enormous progress into gene-identification for seemingly complex phenotypes that gives reason to believe that real, large scale DNA sequencing and multiplex gene expression are making real progress towards elucidating the interactions between genes. Some examples include: a mutation in the genetic code for the p66shc protein has been shown to "[result] in a 30% increase in life span in mice"; "variations in angiotensin gene have been linked with increased muscle performance, a theory that was replicated in US Army recruits"; "a genetic loci on chromosome 4 has been strongly correlated with extremely high intelligence in children". [24] Given these early successes, science seems to be on track to achieve the genetic understanding necessary to make designer babies a reality in our not-so-distant future.

Assuming that the technological capabilities and consumerist demand for PGM technology drive designer babies to fruition, there are many ethical concerns that deserve consideration. First, the rights and best interests of the child are again placed in jeopardy. There is a certain unease that accompanies the idea that an overbearing parent might be able to alter a child's genetic makeup to suit its own values and desires. One can imagine an eager father choosing muscle-enhancing PGM treatment to produce a future son who will likely become a professional football player. Not only would this action potentially selfishly infringe on the natural course of his son's lifetime, but could also be problematic

23 Reiss, Michael J. ""What Sort of People Do We Want." 1999.

24 Henn, Wolfram. "Consumerism in prenatal diagnosis." 2012.

for the child if he does not live up to his genetic expectation. Some point out that this situation would not be unique to genetically altered children; parents of normal children are constantly striving to develop their children to look, behave, and perform in a desirable way. Indeed this is what parenting is all about.[25] The only thing different about PGM is that the assisted development begins before birth and comes with a hefty price tag.

There are also fears that PGM can be abused in ways that are discriminatory and ultimately pose a threat to society. One such abuse would be through sex discrimination. Although studies within the United States have shown that Americans have little if no preference between male and female children, it cannot be ignored that PGD and PGM would facilitate sex discriminating policies that exist in other cultures like China and India.[26] The same way that PGM might favor intelligence and health, so too could it tend to favor males over females. If this effect is large enough, demographic balance could be altered and have profoundly negative societal ramifications. Underneath it all, there is always the looming shadow of eugenic practices, made infamous by the Nazi's, in which a set of culturally valued characteristics are fiercely promoted while other characteristics are discriminated against.[27] Opponents of genetic manipulation, such as Princeton's Lee Silver, fearfully foresee a future in which society becomes stratified first by those wealthy enough to seek PGM treatment and those who are only capable of reproducing the old fashioned way, and then by a society that is delineated between the "gene-rich" and the "gene-poor".[28] As troubling as such a future might be, would it not be more frightening to introduce legislation that could dictate our future reproductive decisions?

To conclude, this paper has examined several of the ethical issues involved with

25 Steinbock, Bonnie. "Choosing our Children's Genes". 2008.

26 Lemonick, Michael D. "Designer Babies." 1999.

27 Nelrich et al. "The First 'Designer Baby'". 2010.

28 Lemonick, Michael D. "Designer Babies." 1999.

embryonic genetic screening, manipulation, and selection, though all perspectives cannot be explicated, let alone resolved, here in the modest scope of this paper. It is my sincere hope that fear of the uncertain future will not overshadow the miraculous good that PGD treatment can do for families avoiding and combating devastating genetic disease. That being said, this paper also makes it clear that germ line therapy requires regulation and oversight to some degree in order to monitor abuses. Philosophers and politicians will undoubtedly quibble endlessly over where to "draw the line" of human ethics with regards to this technology, but I think that the moral experiences of normal people will determine the future of this treatment. The necessity of PGD to save a life will overcome our naïve grip on fragile notions of dignity, virtue, and tradition.

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