## Alice Phillips BioChem 158 Spring 2015

Grappling With the Ethics of Non-Disease Genetic Selection

The growth of biotechnology, and specifically reproductive biotechnology, has been closely followed by a rise in the number of ethical questions about the use of such technology. Some questions are fairly straightforward to answer, so much so that the general population will accept an answer without much debate. Others lie in a gray area, where different people can come up with rational opposing arguments. An example of the former is in vitro fertilization (IVF). Even groups who object to all sorts of biotechnology in the field of reproduction, such as conservative religious groups, are traditionally supportive of the procedure (although support is never universal) on the basis that IVF helps people have families.<sup>1</sup> Other issues are far more divisive, such as the use and degree of use of pre-implantation genetic diagnosis. Past the grey area lie uses of genetic technology that are fairly universally denounced, such as government-mandated genetic selection for certain traits (population scale genetic engineering, or eugenics).<sup>2</sup> There are myriad ways to approach answering questions in the grey area—questions about selection for non-disease traits, for example—but this paper will approach them from the standpoint of minimizing harm. Barring a rational argument as to why a use of genetic technology poses harm to either an individual or society as a whole, and provided that that harm is not outweighed by a provided benefit, then the use would be ethical. When it comes to selection for non-disease traits, this paper will argue that such selection is allowable under most circumstances, but that genetic engineering of those traits should not be allowable: the consequences of doing so could be a bifurcated classist society, and it could eliminate valuable genetic diversity. Both of these reasons stem from the aforementioned harm principle, as a classist society harms all those who are not able to afford a "designer" baby without providing commensurate benefits to those who can, and eliminating genetic diversity has the potential to harm future generations who could have benefited from that diversity.

<sup>&</sup>lt;sup>1</sup> Moser, Whet, "Naperville Right to Life Activists Protest IVF Clinic," *Chicago Magazine*, 28 March 2012. <u>http://www.chicagomag.com/Chicago-Magazine/The-312/March-2012/Naperville-Right-to-Life-Activists-Protest-IVF-Clinic/</u>

<sup>&</sup>lt;sup>2</sup> Caplan, Arthur L., Glen McGee, and David Magnus, "What is immoral about eugenics?" *BMJ*, 13 November 1999, Volume 319. <u>http://biochem158.stanford.edu/Ethics/Eugenics.pdf</u>

Pre-implantation genetic diagnosis is a procedure that can be performed after fertilized eggs are produced through IVF.<sup>3</sup> Cells are removed from the blastula-stage embryo and then genetically tested for any known gene sequence. The desired embryo is then implanted into the womb. Uses of pre-implantation genetic diagnosis are varied, including screening embryos for autosomal dominant and recessive disorders, sex-linked disorders, sex selection, and chromosomal abnormalities such as aneuploidy (to prevent miscarriages), selecting an embryo who is a human leukocyte antigen profile match for an existing diseased sibling (a "savior sibling" embryo), and screening for non-disease traits.<sup>4</sup> At present the known gene sequences that correlate to specific adult non-disease traits are limited but, for the purposes of this paper, consider that almost all traits can be selected for genetically. This hypothetical will allow us to examine the logical extremes of pre-implantation genetic diagnosis technology-hypothetical extremes that may be reality in the not too distant future. In addition, assume that IVF treatment is ethically acceptable. (A common objection involves the objection to discarded embryos, particularly from those who would not allow use of those embryos in stem cell research for other reasons. However, exploring the veracity of that ethical argument would waylay this discussion about PGD selection for non-disease traits before it could get started.)

One necessary preamble to a discussion of PGD is a discussion of what if any obligation parents have to their children regarding the children's genetic make-up, and specifically whether parents are obligated to procreate to produce only the most advantaged child. Julian Savulescu and Guy Kahane argue in their essay "The Moral Obligation To Create Children With the Best Chance Of the Best Life" that parents are required to produce the best children they can.<sup>5</sup>

If couples (or single reproducers) have decided to have a child, and selection is possible, then they have a significant moral reason to select the child, of the possible children they could have, whose

<sup>&</sup>lt;sup>3</sup> "Pre-implantation genetic diagnosis (PGD)," *Human Fertilisation & Embryology Authority*, last updated 1 April 2014. <u>http://www.hfea.gov.uk/preimplantation-genetic-diagnosis.html</u>

<sup>&</sup>lt;sup>4</sup> Appold, Karen, "Preimplantation Genetic Diagnosis: How Should Labs Grapple With Ethics?" Clinical Laboratory News, American Association for Clinical Chemistry, 1 January 2014. https://www.aacc.org/publications/cln/articles/2014/january/preimplantation

<sup>&</sup>lt;sup>5</sup> Savulescu, Julian, and Guy Kahane, "The Moral Obligation o Create Children With the Best Chance Of the Best Life," *Bioethics*, June 2009, 23(5): 274-290. http://onlinelibrary.wiley.com/doi/10.1111/j.1467-8519.2008.00687.x/full

life can be expected in light of the relevant available information, to go best or at least not wore than any of the others.<sup>6</sup>

Savulescu and Kahane call this the Principle of Procreate Beneficence. At first blush, it seems unobjectionable, but there are several problematic aspects of this proposed moral obligation. Firstly, it insists on the necessity of an arms race in child rearing, such as in the height of boys. Yes, short boys may want to be taller, but somebody always has to be the shortest. Secondly, it seems impossible to saddle the parents with a moral obligation to procreate a child who will have the best possible life, since the parent and the child's conception of best possible life may, years later, turn out to be quite disparate.<sup>7</sup> Moreover, Savulescu and Kahane ignore possible methodological problems in carrying out this moral obligation:

Even those who deny that parents are allowed to select the most advantaged child will often admit that parents should hope for a child who is naturally endowed with talents and capacities that will make it likelier that she will lead a good life.<sup>8</sup>

Savulescu and Kahane mention this as if to point out the preposterism inherent in an objection to genetic engineering for excellence if parents naturally desire excellence anyways. But there is no such preposterism. Hoping for excellence still leaves the child's genetics to chance, and it seems perfectly reasonable that a parent may themselves be satisfied with his genome and not want to bother with designing his baby. And what if environmental factors change between the time when the parent designs the baby and the time when the baby is an adult? What if, today, a parent selected for a baby who is a computer science genius, but by the time that baby is 40, computer science has been overtaken by some other talent as the most desirable. Is it not possible that actively designing a baby due to the parent's contemporary perception of excellence actually hinders the chances that the child will be especially well equipped in the future? It is clear that there is no moral obligation for the parent to actively produce the child with the best

<sup>&</sup>lt;sup>6</sup> Savulescu, Julian.

<sup>&</sup>lt;sup>7</sup> Savulescu and Kahane even discuss the possible complexity of a trait like manic depression, which a parent would likely be inclined to select against but which the 'sufferer' may value and identify with. Unfortunately, the authors do not fully explore the implications of such an example on their proposed moral imperative, which puts decision-making in the hands of parents who have a particular set of perceptions. <sup>8</sup> Savulescu, Julian.

possible future life, if only because there are so many unanswered questions as to how a parent is practicably supposed to do that.

Now that any moral imperative to produce the most excellent possible child has been dismissed, this paper can examine the ethics of doing so at all. There is a spectrum of possible ways to select for a child's genetics, ranging from the selection of mate to the possibility of cloning. After careful examination of each, it will become clear that in accordance with the principle of minimizing total harm stated above, genetic selection for offspring's non-disease traits is allowable only so long as the parents do not genetically engineer the child to possess a trait that the parents could not have naturally passed on to her. The spectrum runs as follows: selection of when to procreate, selection of mate (or sperm), selection regarding disease-associated traits, selection regarding non-disease associated traits in existing embryos, and genetically engineering non-disease.

The choice of when to procreate—as in, what time of the year to procreate seems like a relatively banal one, but there are perceived advantages that parents can try and angle to get for their kids. Conceiving such that the child's birthday will fall at the beginning of the athletic-year cut-off for organized sports, particularly for boys, can mean that the child will have a size and strength advantage on teammates. In theory, the child will find athletic confidence and success, and be more likely to succeed athletically overall. Similarly, it is not unimaginable to think a parent might try to conceive to make sure their child has a birthday during the school year in order to reap the social benefitsif they exist—of birthday recognition in school and high attendance at birthday parties, since kids are in town. These tactics are difficult to question, if they are indeed practiced, both because the attempts may not necessarily succeed if conception proves difficult and because it is hard to find any harm. (If a boy is boy earlier in the year, does that harm others? Perhaps athletically, although if too many people attempt this then the benefit is diminished, and perhaps late-blooming boys will find other advantages that result from lack of athletic talent.) These considerations of timing, however, are independent of actual genetic content. The selection of mate is not.

Either via selection of sperm through selection of mate or through selection out of a sperm bank, people discriminate about what genes to mix their own with to reproduce. There is no distinction, biologically, between the two processes. It is in regulation of sperm donation that we first find evidence of an established and accepted public interest in preserving the genetic diversity of the gene pool. Several countries, including the United Kingdom, the United States, Australia, and China, impose restrictions on the number of different families a donor's sperm can be used in.<sup>9</sup> For example, in the UK a donor's sperm can be used in no more than 10 different families or 10 live birth events (twins are one birth event), whichever comes first. Due to confidentiality restrictions that can accompany sperm donation, these sorts of restrictions are in place to minimize the possibility of future unintentional incest. If preventing people who are too genetically similar from reproducing together were not in the public interest (i.e. providing a public benefit greater than the harm done by restricting sperm use from a particular donor), these restrictions would not be so widely adopted. The cultural analog for mate selection, of course, is the fact that it is illegal in many states.<sup>10</sup>

One could counter that argument by stating that it is not illegal for two people who are both carriers for genetic disease to have sex. However, the harm of conceiving a child in that situation is perhaps more obvious to the general public, and so people take steps to avoid conception. These steps, which include pre-implantation genetic diagnosis via IVF procedure to screen for embryos who have the disease gene, are ethically allowable (and widely accepted/practiced). Remembering that this paper is assuming the ethical acceptability of IVF in general, this procedure in particular prevents future harm from being experienced by the hypothetical child. Moreover, there is no harm (and even benefit) from the societal perspective: parents can select for the embryos that do not carry a defective gene, thus helping future generations avoid the disease altogether. Hypothetically, the only genetic difference could be whether an embryo has the diseasecausing allele or not; there is no value in preserving the genetic diversity of alleles that are disease causing (e.g. genes that cause Huntington's) since those genes only produce harm for the sufferer and their family and friends.

However, there is plenty of debate about the ethical implications of couples who choose to select for the allele that causes a particular abnormality (not 'disease,' since

<sup>&</sup>lt;sup>9</sup> Gong, Dan, et. al., "An overview on ethical issues about sperm donation," Asian Journal of Andrology, 21 September 2009, 11(6): 645-652. <u>http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3735320/</u>

<sup>&</sup>lt;sup>10</sup> "Statuatory Compilation Regarding Incest Statutes," *National District Attorney Association*, March 2013. <u>http://www.ndaa.org/pdf/Incest%20Statutes%202013.pdf</u>

these couples obviously view the gene as in some way beneficial). Are those parents e.g. deaf people, dwarfs—depriving their offspring of a 'normal' life? That is a difficult argument to make. Take dwarfism, for example. For a parent to actively want a child who also has dwarfism, it is assumed that the parents find some benefit in being a dwarf. If both parents are dwarfs, the benefit to the child is clear: sharing a very meaningful characteristic with his parents. A deaf couple hoping to have a deaf child said, "A hearing baby would be a blessing. A deaf baby would be a special blessing."<sup>11</sup> This emphasizes the notion that, at least from the opinion of the deaf or dwarf community, there is no harm in being either of those things. If there is no harm experienced, and at the least a possibility of benefit, there is no ethical objection to selecting for such traits. One doctor who refuses to provide such selection says that parenting should be providing a better world for children, and that "deafness and dwarfism are not the norm"-making the obvious mistake of assuming normalcy to be the greatest available benefit.<sup>12</sup> Notably, the FDA has approved the use of human growth hormone for children with no birth defect so they can get taller for social reasons.<sup>13</sup> A set of dwarf parents might well contend that selecting for a dwarf child is ethically indistinct from that use of HGH.

If that sort of genetic selection is allowable, though, what possible objections could be raised to selecting for non-disease genes? (Eye color, sex, etc.) The distinction lies in whether parents are merely allowed to choose from the existing embryos, or if the technology becomes available for parents to genetically engineer children as if assembling a Build-A-Bear. The latter is distinctly not allowable, both because it has the potential to create a classist society and because it could sharply decrease genetic diversity if certain alleles became 'fads' in a particular generation.

Non-disease selection is allowable so long as the embryo already had a chance to be conceived by the parents independent of technological interference. For example, selecting for sex is allowable. The clear example of a reason that this should not be allowed is that certain cultures put emphasis on male inheritance/having a first-born who is a male. China's one-child policy has made the problem of sex selection for males

<sup>&</sup>lt;sup>11</sup> Sanghavi, Darshak M., "Wanting Babies Like Themselves, Some Parents Choose Genetic Defects," *The New York Times*, 5 December 2006. http://www.nytimes.com/2006/12/05/health/05essa.html? r=0

<sup>&</sup>lt;sup>12</sup> Sanghavi, Darshak M.

<sup>&</sup>lt;sup>13</sup> Sanghavi, Darshak M.

rather horrific because it often results in rafts of orphaned girls.<sup>14</sup> However, in countries where there is no child-bearing limit, the empirical evidence shows that most people who take advantage of sex selection do so either to select for a girl or to select a child of the opposite gender of their existing child.<sup>15</sup> Neither of these choices poses harm: society is in no danger of advantaging females over males in a sexist fashion; gender balance is a benefit, if anything, because sociologic evidence suggests that gender-balanced societies are less prone to violence.<sup>16</sup> A more controversial example of non-disease trait selection is parents who want to choose an embryo who is an HLA type match for an existing child with a disease in order to harvest umbilical cord stem cells. However, this too should be allowed. Theoretically, it is logical to assume that if the parents are willing to go to the trouble of conceiving another child through IVF for the express purpose of helping the health of the existing child, then the parents are fairly invested/loving/responsible. Moreover, there is little rational reason to believe that the parents will love the second child less than the first, and may feel some gratitude towards the child. Because the only things that needs to be taken from the second child are umbilical cord stem cells (which can just barely be considered "taking from" to begin with), the second child experiences no harm. Therefore, with no reason to believe the second child suffers and with every reason to believe that the first child and family as a whole benefits, this is an ethical procedure.

If the parents are, hypothetically, able to engineer which alleles their children will inherit regardless of the alleles on the parental chromosomes, then the ethical questions become muddied by the imperative to do what benefits the gene pool at large; such engineering could result in a one-generation switch to a mono-allelic gene pool at a particular locus, depriving the pool of genetic diversity. This sort of artificial selection is unethical. A prime objection, and one that this paper subscribes to due to its roots in the harm principle, is that such engineering can create a classist society.<sup>17</sup> Even if the

<sup>&</sup>lt;sup>14</sup> Jian, Ma, "China's Brutal One-Child Policy," *The New York Times*, 21 May 2013. <u>http://www.nytimes.com/2013/05/22/opinion/chinas-brutal-one-child-policy.html</u>

<sup>&</sup>lt;sup>15</sup> Robertson, John A., "Extending preimplantation genetic diagnosis: the ethical debate," *Human Reproduction*, 2003, 18(3): 465-471. <u>http://humrep.oxfordjournals.org/content/18/3/465.full</u>

<sup>&</sup>lt;sup>16</sup> Szaflarski, Magdalena, "The Impact of Inequality: How to Make Sick Societies Healthier," *Preventing Chronic Disease*, 15 December 2005, 3(1): A26. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1500967/

<sup>&</sup>lt;sup>17</sup> Caplan, Arthur L.

engineered allele itself confers no benefit (e.g. eye color), the ability to afford such an allele becomes a status symbol. If it does confer benefit (e.g. cognitive acuity), then the classism is merely rooted in actual ability-the harm to the have-nots still exists, and this is still not a society it would be ethical to create. Ultimately, this could result in the human species bifurcating into two subspecies: those who can afford to Build-A-Human, complete with superior cognitive and athletic abilities, and those who cannot.<sup>18</sup> The critical distinction between this pre-utero parenting and other types of parenting (tennis lessons, SAT prep courses) that society accepts, even if they exacerbate socioeconomic differences<sup>19</sup>, is that designing a baby results in hard-coded changes. While socioeconomic depravity certainly takes a horrendous toll, that person is still not hardcoded differently than anybody else. It is clear that the have-nots would certainly suffer harm. Yes, the haves would benefit in pure ability, but it is also likely that society would be harmed by the perpetually self-fulfilling lack of incentive for the have-nots to work hard. They do not have as high cognitive or athletic ability, so they cannot make as much money, and therefore cannot afford the market price of designing a baby of their own. Thus, any scenario in which only some members of society can participate in the genetic design on this scale is unethical.

The second objection is to the potential for such genetic engineering to eliminate genetic diversity entirely, making it unethical even if everybody can participate. Aside from the argument that genetic (and thus person) diversity would benefit society and homogeneity would harm it, the biological problems also indicate that genetically designing a human is ethically objectionable. Say that there is a trait that, for the current economic climate, is the most desirable. In theory, parents will want their children to succeed, so everybody builds in that trait. Then, two generations from now, it turns out some natural disaster causes a very different trait to be highly useful to society in lieu of the fad trait. How is society to recover from the natural disaster? What if the natural

Sandel, Michael, "Genetic Engineering," *KQED* (Forum with Michael Krasny), 7 May 2007. <u>http://www.kqed.org/a/forum/R705070900</u>

Greely, Henry T., "Legal, Ethical, and Social Issues In Human Genome Research," *Annual Review of Anthropology*, 1998, 27: 473-502.

http://biochem158.stanford.edu/Genome%20Papers/human\_genome\_research.pdf <sup>18</sup> Sandel, Michael, "The Case Against Perfection," *The Atlantic*, April 2004.

http://www.theatlantic.com/magazine/archive/2004/04/the-case-against-perfection/302927/ <sup>19</sup> Sandel, Michael. (*The Atlantic*)

disaster was a pandemic, and there was some other allele for that locus that, by chance, encoded resistance to the pathogen? Yes, society could engineer a host of new members with these impressive genetic engineering capabilities, but that would take years. In the meantime, society would suffer a great amount of harm for not being able to cope with the natural disaster. Cloning is merely the logical extreme of this example, where every possible trait has been homogenized across society. Of course, this also assumes that every baby is now being genetically engineered to avoid mutation resulting from inbreeding—if not, the harm would be even greater in this hypothetical.

In summary, genetic selection of humans is allowed where there is no harm, or where the harm is outweighed by the benefits of doing so. From the historical evolutionary perspective, it is perhaps necessarily ethical to select offspring's genes by selection the mating partner either romantically or via sperm bank since that is the definition of a sexually reproducing species. Selecting against disease traits clearly reduces harm and benefits future society by minimizing the prevalence of disease-causing genes in gene pool, and thus is ethical. In cases where there is the gene codes for a neutral trait such as eye color, or even a trait that confers kinship among members of a family such as dwarfism, there can be no ethical objection as long as the trait is available in naturally occurring embryos from a couple. There is no harm to society here because the requirement that the trait be a natural possibility in the family should diminish the possibility that this will create classism, since genes are quite diverse. Historical problems with eugenics of superficial traits (e.g. Nazi Germany) were associated with coercive reproduction (or a coercive lack thereof), in which there is clear harm and which is strictly unethical. Selection for non-disease traits by engineering those non-disease traits, however, is unethical both because it could well lead to a needlessly (and harmfully) classist society and because it could diminish valuable genetic diversity.

While some of these discussions have involved hypothetical biotechnological capabilities, it is important to continue to think ahead in the field of bioethics as the technology continues to grow. These ethical issues deserve a healthy debate, part of which I have attempted to offer here, but it will continue to be important that many voices from may corners of society engage with these issues.