Cuadernos de Bioética
ISSN: 1132-1989
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Asociación Española de Bioética y Ética Médica
España

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The post-humanist embryo: genetic manipulation, assisted reproductive technologies and the principle of procreative beneficence
Cuadernos de Bioética, vol. XXV, núm. 3, septiembre-diciembre, 2014, pp. 427-443
Asociación Española de Bioética y Ética Médica
Madrid, España

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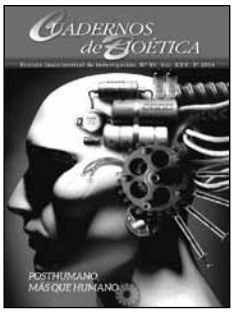

THE POST-HUMANIST EMBRYO: GENETIC MANIPULATION, ASSISTED REPRODUCTIVE TECHNOLOGIES AND THE PRINCIPLE OF PROCREATIVE BENEFICENCE

EL EMBRIÓN POST-HUMANO: MANIPULACIÓN GENÉTICA, REPRODUCCIÓN ASISTIDA Y EL PRINCIPIO DE BENEFICENCIA PROCREATIVA

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ABSTRACT:

Keywords:
Transhumanist, procreative beneficence, enhancement, genetic manipulation, assisted reproductive technologies (ART).

Drawing from Julian Savulescu's argument for the obligation to use technological interventions for the enhancement human life, the Principle of Procreative Beneficence (PPB) states that parents have a moral obligation to use available reproductive technologies, including techniques of genetic manipulation, to create children who have the best chance of enjoying the best possible life. The aim of this study is to analyse the extent to which the possibility of using genetic manipulation to promote specific personality traits and thereby enhance human life is actually supported by current scientific knowledge and to determine whether the techniques employed in embryo selection comply with the PPB. In light of this analysis, the importance of involving the scientific community in the enhancement debate will be made clear. Moreover, when current knowledge of genetic and epigenetic processes and evidence of the risks of assisted reproductive technologies are taken into account, we find sufficient reason—even when guided by the PPB—to abstain from the use of current techniques of genetic manipulation and embryonic selection.

RESUMEN:

Palabras clave:
Tranhumanismo, beneficiencia procreativa, enhancement, manipulación genética, técnicas de reproducción asistida.
Recibido: 15/03/2013
Aceptado: 25/06/2014

El principio de beneficencia procreativa (PPB), propuesto por Julian Savulescu, establece que los padres tienen la obligación moral de utilizar las técnicas de manipulación genética y reproducción humana asistida disponibles para crear niños que tengan la mejor oportunidad de disfrutar de la mejor vida posible . El objetivo de este trabajo es analizar, por un lado, hasta qué punto la manipulación genética para la obtención de rasgos concretos tienen en consideración el paradigma actual de la ciencia y, por otro lado, si las técnicas implicadas en la selección embrionaria propuestas cumplen con el objetivo perseguido por el PPB. Además, esta exposición pretende mostrar la importancia de implicar en la discusión sobre el *enhancement* a la comunidad científica. Teniendo en cuenta el conocimiento científico sobre los procesos genéticos y epigenéticos del desarrollo y los riesgos asociados a las técnicas de reproducción asistida, nos encontramos con razones suficientes para tomar la decisión de no someter a los niños a las técnicas actuales de manipulación y selección embrionaria.

1. Introduction

According to Nick Bostrom, a co-founder of the movement, transhumanism is a philosophy that "promotes an interdisciplinary approach to understanding and evaluating the opportunities for enhancing the human condition and the human organism opened up by the advancement of technology."[1] The principal aim of transhumanism is to "focus on radically improving the quality of life through biological manipulation."[2] To achieve this goal, genetic manipulation and assisted human reproduction techniques are given a central role.[3] The pre-implantation embryo is at the centre of the debate: if the embryo can be biologically manipulated to increase the possibility of living a better life, why not do it? In this context, biological manipulation is seen as a favourable, safe, reliable, and convenient form of intervention.

Some authors have taken the argument for enhancement further, going one step beyond those who support the voluntary application of reproduction technologies.[4] Such is the case of Julian Savulescu, the current occupant of the Uheiro Chair in Practical Ethics at the University of Oxford. Savulescu argues that there is a positive obligation to make use of technological interventions to enhance human life.[5] "Not only can we enhance, we should enhance,"[6] is the position defended by Savulescu. Genetic manipulation, from this perspective, is not just an opportunity; it's an imperative.

As viewed by Savulescu, the aim of genetic modification is to create happier people: "We want to be happy people, not just healthy people."[7] Back in 2003, in the book "Beyond Therapy," the American Council of Bioethics anticipated the potential danger of this application of biotechnology to the pursuit of happiness, which emerges when the distinction between *enhancement* and *therapy* is not taken seriously.[8] Although this distinction remains a subject of debate, it has been effectively blurred in the last decade by transhumanism, and this ambiguity has benefited the theoretical development of *enhancement.*[9]

In recent years, transhumanists have devoted considerable effort to defining the meaning of a "better life" and to specifying the physical and psychological traits required for its achievement. Although these efforts have not satisfied critics,[10] the transhumanist project has not lost any momentum. Indeed, if anything, its proponents are more convinced than ever, and take it for granted that these basic questions have been answered.

At this basic level, some of the deepest criticisms of transhumanism come from those who maintain that there is an established natural law whose moral demands are contrary to transhumanist aspirations. However, establishing a constructive dialogue on the basis of such considerations is difficult at best, as proponents of transhumanist enhancement tend to consider any position that invokes a pre-defined essence of life or a pre-established natural order as vain illusion. Indeed, such criticisms have been dismissed as the ideology of a "bio-conservative" group and are assumed to be uncritically opposed to the use of technology for human betterment.[11] In this oppositional context, the moral ob-

1 Bostrom, N. [On line publication] «Transhumanist Values». 2012 <http://www.nickbostrom.com/ethics/values.html> [consulted: 5/05/2013].

2 Savulescu, J. «Genetic interventions and the ethics of enhancement of human beings». In: *The Oxford Handbook of Bioethics*, Oxford University Press, Oxford, 2007, 518.

3 Bostrom, N. «Human Genetic Enhancements: A Transhumanist Perspective». *Journal of Value Inquiry* 4 (37), (2003), 493-506; Savulescu, J. «The moral obligation to create children with the best chance of the best life». *Bioethics* 5 (23), (2009), 274-290.

4 Agar, N. *Liberal eugenics: in defense of human enhancement*, Blackwell Publishing, Oxford, 2004, p. 205.

5 Savulescu, J. (2007), *op cit.* 518.

6 Ibid, 517.

7 Ibid, 520.

8 President's Council on Bioethics, *Beyond therapy: biotechnology and the pursuit of happiness*, Dana Press, New York, 2003, 1-27.

9 "Transhumanists (advocates of human enhancement) are unaffected by the problems associated with maintaining that there are important differences between enhancement and therapy". Bostrom, N., Roache, R. «Ethical Issues in Human Enhancement». In: *New Waves in Applied Ethics*, Pelgrave Macmillam, New York, 2008, 122.

10 Postigo, E. «Transumanesimo e postumano: principi teorici e implicazioni bioetiche». *Medicina e Morale* 2, (2009), 267-282; Ballesteros, J., Fernández, E. (ed.). *Biotecnología y Posthumanismo*, Editorial Aranzadi, Navarra, 2007; Kass, L. *Life, Liberty, and the Defense of Dignity: The Challenge for Bioethics*, Encounter Books, San Francisco, 2002. Habermas, J. *Die Zukunft der menschlichen Natur: Auf dem Wege zu einer liberalen Eugenik?*, Suhrkamp, Frankfurtam Main, 2001.

11 Bostrom, N. «In Defence of Posthuman Dignity». *Bioethics* 3 (19), (2005), 202-214; Bostrom et al., *op cit.*122; Feito, L. «Hacia una mayor comprensión del papel de la naturaleza en los debates bioéticos». *Veritas* 23, (2010), 111-129; Roache, R., Clarke S. «Bioconservatism, bioliberalism, and the wisdom of reflecting on repugnance». *Monash Bioethics Review* 28 (1) 4, (2009), 1-21.

ligation for biological manipulation has been expressed in the form of a simple, guiding principle: The Principle of Procreative Beneficence (PPB).

The PPB was presented by Savulescu for the first time in 2001[12] and was later modified in 2009.[13] It states that parents have the moral obligation to use reproductive technology to select the child with the best chance of having the best possible life. Again, this proposal has aroused fierce criticism,[14] including arguments that equate transhumanism with eugenics.[15] Just to accept this label would seem to constitute a major concession to the critics of PPB, and yet Savulescu argues instead that he advocates a new kind of eugenics that is essentially different from the early eugenics movement: what was particularly objectionable about that movement, he says, was the coercive imposition of a state-approved vision for a healthy population.[16] We also find defenders such as Andrew Hotke, who argue that it is not morally wrong to be a eugenicist,[17] and others who, encouraged by the PPB, go one step further and propose the Principle of *General* Procreative Beneficence.[18]

Another strong criticism of the transhumanist approach is directed at the ethical implications of embryo selection assumed by PPB. If selecting some embryos implies the death of others, we are facing a serious threat to the right to life of individuals. But again, similar to natural law arguments, this criticism is easily dismissed by the transhumanists: anyone who does not recognize the dignity and personal status of the pre-implantation embryo will not see a problem with the selection and destruction of embryos. In this respect, the law is clearly on the side of transhumanism: the fact that laws allow assisted human reproduction clinics implies consent for the destruction of embryos.

Whatever the force of these criticisms, it could be argued that the credibility of transhumanist arguments and aspirations are based more on seemingly benign feelings of optimism and naïve faith in the power of science and technology than evidence and solid reasoning. There is no doubt that what started as a marginal phenomenon has become a significant movement that is increasingly sure of its goals and the way to pursue them. For transhumanists, at least, the path toward a better future has been cleared of obstructions.

In this paper we are not going to reproduce any of the aforementioned criticisms. Instead, we will develop a critical approach[19] that involves the biomedical community in the transhumanist enhancement debate, demonstrating the importance of taking the most current scientific knowledge and experimental data into account. We intend to analyse the scientific-technical premises of PPB in the light of evidence from developmental biology and biomedicine. The objective of this reflexion is limited in scope. First, we consider the extent to which scientific-technical assumptions underlying the transhumanist project in its current form—namely, assumptions about the possibility of attaining specific personality traits through genetic manipulation—are compatible with the latest theories and findings of biomedical science. Second, we will investigate whether the techniques and technologies currently used in genetic manipulation and embryo selection are in fact capable of offering our children the best chance of the best life, in keeping with the guidelines of the PPB.

12 Savulescu, J. «Procreative Beneficence: Why we should select the best children». *Bioethics* 15, (2001), 413-426.

13 Savulescu (2009), *op cit.* 274-290.

14 Hotke, A. «The Principle of Procreative Beneficence: Old arguments and a new challenge». *Bioethics*, (2012), doi: 10.1111/j.1467-8519.2012.01999.x; Herissone-Kelly, P. «Wrongs, preferences, and the selection of children: a critique of Rebecca Bennett's argument against the Principle of Procreative Beneficence». *Bioethics* 26 (8), (2012), 447-454; Bennett, R. «The fallacy of the Principle of Procreative Beneficence». *Bioethics* 23 (5), (2009), 265-273; Stoller, S. «Why we are not morally required to select the best children: a response to Savulescu». *Bioethics* 22 (7), (2008), 364-369.

15 Sparrow, R. «A not-so-new eugenics: Harris and Savulescu on human enhancement». *Hastings Center Report* 41 (1), (2011), 32-42.

16 Savulescu, J. [On line publication] «The maverick: It's our duty to have designer babies». (2012). http://www.readersdigest.co.uk/magazine/readers-digest-main/the-maverick-its-our-duty-to-have-designer-babies [consulted: 23/04/2013].

17 Hotke, A. [On line publication] «The principle of Procreative Beneficence is eugenic, but so what?». (2012). http://hdl.handle.net/1974/7580 [consulted: 20/04/2013].

18 "The Principle of General Procreative Beneficence states that couples ought to select children in view of maximizing the overall expected value in the world, not just the welfare of their future child". Elster, J. «Procreative beneficence: cui bono?». *Bioethics* 25 (9), (2011), 482-488.

19 Another approach for reflexion that I will not elaborate on in this paper, but which could, in my opinión, be fruitful, would be to attempt to analyse the risks *enhancement* views pose to the interests of politicians.

2. The Scientific Paradigm and the Mystery of "Missing Heritability"

When considering the possibility of *enhancement* the transhumanist position assumes that there are specific, objective physical and mental traits that can be selected in the embryo or obtained by genetic manipulation in order to ensure that a child can achieve a better life or perhaps even the best of all possible lives. This proposal presupposes the existence of single-gene phenotypic traits and gene therapies that can treat pathologies associated with a change in one gene or a group of genes.

Before we analyse these assumptions, we must clarify an important issue. If technology permits, and the associated risks are weighed and reasonably assumed, there does not appear to be any problem with genetically modifying the carrier of a mutation with pathological consequences to ensure that he (or she) has the best possible life. Such interventions could be seen as analogous to the "improvements" obtained through dietary methods, as when a mother takes folic acid during the first months of pregnancy to reduce the risk of neural tube defects. However, transhumanist *enhancement* proposes to engage in genetic manipulation and embryo selection for a different reason: "We want to be happy people, not just healthy people." Thus, in this analysis we are specifically concerned with the phenotypic traits that are relevant to the "happy" or "better than well" dimension of transhumanist enchancement (for example, empathy, imagination, congeniality, justice, honesty and moral character).[20] Accordingly, we will leave aside traits associated with reductions in the risk of various pathologies such as schizophrenia, cancer or malformations. Nor will we refer to techniques associated with the selection of gametes or embryos, or nuclear or pronuclear transference to enucleated ovules or zygotes, if these are used to avoid pathologies or decrease their risk. Rather our specific concern is what experimental science and developmental biology have revealed in recent decades about the possibility of controlling non-pathological personality traits by means of genetic manipulation.

20 Savulescu (2009), *op cit.* 516-535.

At least until the end of the twentieth century, the reigning dogma of molecular biology assigned to all genes a one-to-one correlation between DNA sequences of genes and their products (ARN and proteins), which had been established for certain genes.[21] At the beginning of the twenty-first century, having completed the human genome project, the scientific community had hopes of identifying the genes and genetic variants responsible for variation in phenotypic traits. However, after more than a decade of research, the results of these efforts have been disappointing. Scientists now have no problem admitting that

> "Genetic studies have attempted to elucidate causal mechanisms for the development of complex disease, but genome-wide associations have been largely unsuccessful in establishing these links."[22]

The so-called concept of "missing heritability" is indicative of the current state of affairs. The missing heritability problem refers to the gap between heritability estimates for complex human traits based on quantitative genetics, and the small magnitude and unreliability of contemporary molecular genetics, especially genome wide association studies.[23] If we look at mental traits, the total variance we can explain is only a few percent even after aggregating all the genetic variants for which an effect is corroborated by scientific evidence.[24]

Scientists have offered various explanations for what has been described as the mystery of "missing heritability." Two of these explanations adhere to the paradigm of the trait as a product of gene expression, massive polygenicity and rare genetic variants. For the first, thousands of genes contribute to the production of a

21 To be exact, we should say in certain transcriptionally active sequences of the genome.

22 Nagy, C., Turecki, G. «Sensitive periods in epigenetics: bringing us closer to complex behavioral phenotypes». *Epigenomics* 4 (4), (2012), 445-457.

23 Turkheimer, E. «Still missing». *Research in human development* 8 (3-4), (2011), 227-241.

24 DeYoung, C. G., Clark, R. «The gene in its natural habitat: the importance of gene-trait interactions». *Development and psychopathology* 24 (4), (2012), 1307-1318.

trait, such that it is nearly impossible to identify them, let alone manipulate them. For the second, the gene variants are not sufficiently common in the general population to be detected. Other explanations view phenotypic traits as the result of gene interactions, either gene-gene or gene-environment interactions.

Among these latter alternatives, new explanation has been recently proposed, the so-called gene-trait interaction[25] (GxT), which is of particular interest because it pays special attention to psychological traits. The concept underlying the GxT interaction "is that the effects of the genotype at a single genetic locus are likely to vary, depending on the differences in psychological traits"[26]. In other words, it has been shown that the neural effects of some genetic variants depend on the personality of the carrier.[27] This suggests that the modification of embryonic genes in the hope of achieving specific psychological traits in adults, as is proposed in *enhancement*, is not feasible, since "in order to understand thoroughly the effect of variation in a single gene, we need to understand the gene in the context of the brain as a whole"[28]. Moreover, the effects of specific variants in candidate genes that have been proposed to influence a given trait are often not replicable.[29] This has been systematically demonstrated for the Intelligence Quotient,[30] one of the examples favoured by transhumanists when presenting the concept of *enhancement*. In this respect, the science is clear:

> "There is no evidence of anything even resembling a 'gene for' intelligence, and no promising signs that all the infinitesimal genetic associations are about to produce a meaningful genetic account of the development of intelligence."[31]

So far, the most fruitful way of explaining "missing heritability" has been epigenesis, with epigenetics becoming a new scientific paradigm in its own right. Science has shown that the mechanics of gene expression, in other words the regulation of what genes are expressed, how many times a gene is expressed, and when and where it is expressed, has a considerable influence on phenotypic traits. This regulation of gene expression is primarily achieved by epigenetic regulation mechanisms. Furthermore, this regulation affects not only gene transcription but also gene products, and in recent years it has been demonstrated that post-transcriptional regulation is largely responsible for the observed phenotypic differences amongst individuals and species.

A clear example of the influence of epigenesis is found in bees.[32] The queen bee and her workers are clones, yet despite their identical DNA profile, queen bees and their worker bees display prominent differences of anatomy, reproductive ability and behaviour. The cause lies in the fact that, unlike other bees, queen bees are fed exclusively on royal jelly as larvae.[33] The component in royal jelly responsible for producing this effect is royalactin, a protein that is in turn regulated by a growth factor which produces changes in a hormone that determines phenotypic traits in the adult.[34]

The upshot of epigenetics for transhumanism is that, from a scientific perspective, it is now highly questionable to maintain that the modification of traits such as intelligence, memory, patience, empathy or sense of humour, can be achieved by modifying our genetic material. The role of epigenetic regulation in the production of phenotypic differences is especially clear among cloned individuals—yet the implications for all individuals must be taken into account by transhumanists.

For example, consider the views of H. S. Faust, a transhumanist theorist who proposed the hypothetical

25 Ibid.

26 Ibid.

27 Mier, D., Kirsch, P., Meyer-Lindenberg, A. «Neural substrates of pleiotropic action of genetic variation in COMT: A meta-analysis». *Molecular Psychiatry* 15, (2010), 918-927.

28 DeYoung (2012), *op cit.* 1307-1318.

29 Ibid.

30 Chabris, C. F., Hebert, B. M., Benjamin, D. J., Beauchamp, J., Cesarini, D., Van der Loos, M., Johannesson, M., et al. «Most reported genetic associations with general intelligence are probably false positives». *Psychological science* 23 (11), (2012), 1314-1323.

31 Turkheimer (2011), *op cit.* 227-241.

32 Weiner, S. A., Toth, A. L. «Epigenetics in social insects: a new direction for understanding the evolution of castes». *Genetics research international*, 2012, (2012), ID 609810, doi:10.1155/2012/609810

33 Kucharski, R., Maleszka, J., Foret, S., Maleszka, R. «Nutritional control of reproductive status in honeybees via DNA methylation». *Science* 319, (2008), 1827-1830.

34 Kamakura, M. «Royalactin induces queen differentiation in honeybees». *Nature* 473 (7348), (2011), 478–483.

existence of the MoralKinder haplotype (MK+), which would predispose individuals to a higher level of morality than average.[35] Although Faust claims that he is only conducting a "thought experiment," his hypothesis reveals his dependence on a scientific framework that is now obsolete. Similar oversights can be found in the book, "Unfit for the Future: The Need for Moral Enhancement."[36] Here, Savulescu and Persson advocate "moral bioenhancement," a project which, as pointed out by Briggle and Wenlong, is "in the spirit of James Watson, the co-discoverer of the structure of DNA, when he quipped 'If we could make better human beings by knowing how to add genes, why shouldn't we?'"[37]

The truth is that, by the beginning of the twenty-first century, there were already serious doubts amongst experts about the technological assumptions underlying arguments for genetic manipulation aimed at producing specific traits such as higher intelligence, better memory, perfect pitch, calmer temperament, sunnier disposition or greater ambitiousness. For instance, in a book published in 2003, the prospects of genetic manipulation were summarized as follows:

> "Growing recognition of the complexity of gene interactions, the importance of epigenetic and other environmental influences on gene expression, and the impact of stochastic events is producing a strong challenge to strict genetic determinism. Straightforward genetic engineering of better children may prove impossible, not only in practice but even in principle"[38].

A decade has passed since then, and the evidence for enhancement has not improved. Moreover, close look at the results of detailed research studies and the direction scientific activity has taken since then corroborates the view that the attainment of specific traits by means of genetic manipulation is not just a question of time.

3. Embryo Selection Techniques Implicated by PPB

As mentioned above, in 2009 Savulescu revised his first (2001) statement of the PPB, adding:

> "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 life can be expected, in light of the relevant available information, to go best or at least not worse than any of the others."[39]

In that article Savulescu identifies various methods that can enable parents to choose a child with optimal characteristics. For example, "pre-conception" methods enable parents to choose the sex of an embryo by separating the spermatozoa that carry the X and Y chromosome. The post-conception selection methods indicated by Savulescu include prenatal testing (chorionic villus sampling, amniocentesis, serum screening or ultrasound), In Vitro Fertilization (IVF) and pre-implantational genetic diagnosis. Currently, the technical resources that enable embryos to be obtained for genetic manipulation and selection are found within the context of assisted reproductive technologies (ARTs). Accordingly, to evaluate Savulescu's case for obligatory intervention, we must turn to the state of ARTs.

The principal phases of ARTs are: pituitary suppression; controlled ovarian stimulation; monitoring of ovule maturation; retrieval of oocytes; classification and culture of oocytes; collection and preparation of semen; insemination and in vitro fertilization of oocytes; control of embryo development; embryonic biopsy; pre-implantation genetic diagnosis (PGD); and uterine transfer. In

35 Faust, H. S.. «Should we select for genetic moral enhancement? A thought experiment using the MoralKinder (MK+) haplotype». *Theoretical medicine and bioethics* 29 (6), (2008), 397-416.

36 Ingmar, P., Savulescu, J. *Unfit for the Future: The Need for Moral Enhancement*, Oxford University Press, Oxford, 2012.

37 Briggle, A., Wenlong, L. [On line document] «Unfit for the Future: The Need for Moral Enhancement». Book review forthcoming in *Environmental Value* (2013). <http://www.erica.demon.co.uk/EV/reviews/52_Persson.pdf> [Consulted: 18/05/2013].

38 President's Council on Bioethics, *op cit.* 38.

39 Savulescu (2009), op cit. 276.

short, gametes are collected, selected and prepared; fertilization is induced; embryo development is monitored; and the embryos are analysed with a view to transfer some of them to the uterus. There is a close connection, therefore, between ARTs and PPB. Indeed, one could even say that the premise of PPB was born decades ago in assisted reproduction clinics. The procedures of ART have adopted as a foregone conclusion the principle that doctors should choose the embryo or embryos most likely to have a better life for transfer to the uterus. This is why PGD is performed.

In this study, our goal is to determine whether the techniques implicit in embryo selection meet the objective "select the child whose life can be expected to go best or at least not worse than any of the others."[40] Now that we are familiar with the techniques of ART, let us examine the scientific studies that have analysed their impact on children.

First of all, we need to take into consideration the fact that the likelihood of obtaining embryos which are suitable for implantation (i.e. healthy embryos) is low. Depending on the source, the exact figures vary. The Society for Assisted Reproductive Technology (SART) is the most important organization of professionals dedicated to the practice of ART. On its webpage it includes the statistics for reproductive techniques collected in 2011 from 85% of the ART clinics in the United States.[41] Although the information is very detailed in most respects,[42] among the data that is considered to be relevant to the success rate of ART, the ratio of zygotes obtained to live births is not published by SART or any other centre that I know of. We can get a rough idea of this figure from the fact that, according to SART, the success rate for implanted embryos that reach term is 36% in the best of cases (fresh embryos from non-donor oocytes taken from women under 35 years of age). In the specialist literature, a recent review highlights the fact that we can find no reliable data in the studies published from 1985 to 2012.[43] So we have to make do with the figures of the European Fertility Institute, whose global estimate for the technique is 18 to 20% for each attempt.[44] Whatever the case, the data available to us shows the importance of obtaining enough embryos to ensure the selection of healthy embryos that can reach term—in other words to boost the rate "success."

That said, let us concentrate our attention on the impact of the techniques used in the development of the embryo. Much research has focused on the need to satisfy the metabolic requirements of the pre-implantation embryo once the oocyte has been fertilized. As these needs are different at each developmental stage—that is to say, virtually every 24 hours—the culture medium must be changed regularly. Currently, what are known as "sequential culture media" are used, a type of culture medium that attempts to imitate the growth factors supplied by the mother during the embryo's journey to the uterus along the fallopian tube. Indeed, scientific research shows us that the culture media used at this developmental stage can affect the expression of imprinted genes and influence the phenotype of the conceptus, although the mechanisms of epimutations are still unknown.[45] We also know that the content of the culture medium is related to the success of implantation, although we don't know how. Curiously, a recent systematic review of all the scientific studies on IVF published in the last 25 years concludes that the information gathered from the literature is insufficient to establish which of the culture conditions is the most appropriate.[46]

Embryos that reach day three of development can be subjected to a PGD. To conduct a PGD, a biopsy must

40 Ibid.

41 All SART Member Clinics [On line publication] «Clinic Summary Report 2013".<https://www.sartcorsonline.com/rptCSR_PublicMultYear.aspx?ClinicPKID=0> [Consulted: 24/05/2013].

42 Amongst other parameters, the success rates correlate ovarian cycles (OC) with pregnancies (PR), OC with live births (LB), transferred embryos (TE) with PR and TE with con LB.

43 Mantikou, E., Youssef, M. A. F. M., Van Wely, M., Van der Veen, F., Al-Inany, H. G., Repping S., Mastenbroek, S. «Embryo culture media and IVF/ICSI success rates: a systematic review». *Human Reproduction Update* 19 (3), (2013), 210-220.

44 Instituto Europeo de Fertilidad [On line publication] «Nuestras soluciones: resultados».<http://www.iefertilidad.com/nuestras-soluciones/inseminacion-artificial> [Consulted: 24/05/2013].

45 Dupont, C., Sifer, C. «A review of outcome data concerning children born following assisted reproductive technologies». *ISRN obstetrics and gynecology* 2012, 405382, doi: 10.5402/2012/405382

46 Mantikou et al., *op. cit*. 210-220.

be performed on the 6-10 cell embryo. First, the zona pellucida that covers the embryo is perforated using a laser beam and then one or two cells are detached from the embryo by aspiration. These cells provide the genetic information necessary to select the embryo, an essential step for compliance with the tenets of PPB.

Having arrived at this point, we have now to assess the damage and consequent risk to development that results from forcibly removing 12 to 20% of the embryonic mass (i.e. one or two cells from an embryo of six to ten cells) to which we want to offer the best of possible lives. We need to remember that the destiny of the majority of the tissues that will be derived from the embryo depends on the state of each cell. It is certain that the embryo is capable of adapting to this insult, i.e. recovering from the loss of cells, and we are aware of the subsequent success of IVF. Nevertheless, and bearing in mind the low success rate of implantation, it makes sense to ask ourselves to what extent selection techniques pose a risk to the development and the future quality of life of the embryo. Although the specific effects that these techniques could have on the embryo are still unknown at the molecular level, the scientific community has begun to express its doubts in scientific publications. A recent study observed:

> "Preimplantation genetic diagnosis (PGD) or screening (PGS) used to detect and eliminate embryos with single-gene disorders or aneuploidy is quite invasive and demands more embryo handling and may be at risk of altered embryo and fetal developments."[47]

It would seem from the above that if the intention is to offer a child the best of all possible lives, the procedures employed in the selection process should be closely examined to determine the possible risks that they pose to the health of the child. A closer look at the epigenetic dimension of the issue may help us to understand what these risks might be.

47 Dupont et al., *op cit.*

4. The Epigenetic Repercussions of the Techniques Used in Embryo Selection

We will now focus on the embryonic stage at which one or two cells are extracted in order to perform a PGD. To understand the possible risks posed by these techniques requires some basic knowledge of the biology of the embryo, which I will try to explain clearly and succinctly.

The DNA of each cell (or blastomere) that makes up the 8-cell embryo has the same sequence of nucleotides. It is from this sequence of nucleotides, which repeated in every cell of the organism, that the concept of the "genome" has been developed—each individual has a genome and each species shares virtually the same genome. Now it is important to distinguish between the *sequence* of nucleotides that constitutes the DNA, and the biochemical and structural *configuration* of the chromatin fiber of DNA,[48] which I have defined elsewhere as the "epigenome." [49]

The crucial point is that while the DNA sequence is the same in all the cells of an organism, the configuration of the DNA is different. Epigenesis refers specifically to alterations of DNA configuration by means of changes to chemical signals (commonly called "epigenetic marks") inherited from the cell's lineage or previous developmental stage. These changes of configuration normally do not involve a change in the nucleotide sequence of DNA—in other words, the "epigenome" changes while the genome remains the same. The precise configuration of genetic material in each of the eight cells in the embryo determines gene expression, which is why the expression in each blastomere may be different.[50] Changes in epigenetic marks may be inher-

48 For further details regarding the roles of DNA, nucleotides, nucleosomes and chromatin fibers, and an overview of biochemical changes involving both nucleotides and histones, see (Güell, F., *El estatuto biológico y ontológico del embrión humano: el paradigma epigenético del siglo XXI desde la teoría de la esencia de Xavier Zubiri,* Peter Lang, Berna, 2013, pp. 312-333)

49 For a systematic explanation of the concept of "epigenome" and other related concepts (Güell, F., *El estatuto biológico y ontológico del embrión humano: el paradigma epigenético del siglo XXI desde la teoría de la esencia de Xavier Zubiri*, Peter Lang, Berna, 2013, pp. 348-357).

50 Wong, C. C., Loewke, K. E., Bossert, N. L., Behr, B., De Jonge, C. J., Baer, T. M., Reijo Pera, R. A. «Non-invasive imaging of human embryos before embryonic genome activation predicts

ited, can be temporary or permanent, and, as just indicated, affect gene expression by changing the configuration of DNA.[51] Differential expression also depends on the composition of the cytoplasm, in other words on the available cell machinery, and on the cellular and nuclear conformation that is required to initiate and regulate the process of gene expression.

In summary, each blastomere in the 8-cell embryo has a different biochemical and spatial DNA configuration and it is this configuration, which in turn depends on the epigenetic marks, that determines which genes are expressed and which are silenced, as well as the intensity of expression. This differential expression also depends on the cytoplasmic composition in the region of the cell in which the gene regulation machinery is located.

What concerns us now is the way in which these epigenetic marks and the cell machinery are inherited. At the end of the cell cycle, a cell "disappears"[52] in order to give rise to two new cells. Before dividing, the original cell replicates (duplicates) its DNA so that the cells that are produced through this process each possesses the complete nucleotide sequence of DNA. The DNA double helix of each daughter cell produced is made up of one strand inherited from the cell from which it originated and the other strand of the double helix is that which is newly synthesized–which is why the replication of DNA is described as "semi-conservative." As a result, only the inherited strand carries the epigenetic marks of the original DNA molecule. In addition, the daughter cell requires a set of complex regulatory machinery that can re-establish or modify the configuration of the original double helix. Like the DNA, the cytoplasmic machinery of the daughter cell is partially derived from the cytoplasm following cytokinesis (cell division) and partially constructed as newly synthesized machinery. In summary, gene expression depends on the configuration of the DNA, and this configuration is in part inherited from the original DNA molecule and partly generated de novo by the existing cell machinery. With this in mind, we can see that the differential expression and cytoplasmic load of the cells of the 8-cell embryo are determined by the prior status of the cells in the 4-cell embryo.

Now we are in a better position to articulate key questions about the risks of genetic manipulation. We can confirm that the embryo from which one or two cells have been removed recovers because evidently cell proliferation continues. Yet, on the other hand, it is reasonable to conclude that these embryos will not have exactly the same epigenetic configuration and, as a matter of course, they will not have the same cytoplasmic load. So we might ask ourselves the following question: If the cells with the expected epigenetic configuration are not available, does this affect the next and subsequent stages of development? Let us see what science has to say about this.

Epigenetic alterations are increasingly recognized as causes of human disease, and these alterations are likely to arise during the pre-implantation stage of mammalian embryos, when the epigenomes of cells are most vulnerable.[53] Although this process is only partially understood because of the experimental inaccessibility of early-stage embryos, research in fetal, postnatal and adults increasingly suggests the central role of DNA methylation in human brain development and function.[54] For instance, studies of new-borns have shown that early-life disruption of epigenetic marks may contribute to the origins of mental illness.[55] Changes in DNA during early childhood could partially explain the dis-

development to the blastocyst stage». *Nature biotechnology,* 28 (10), (2010), 1115-1121. For a review of gene expression in pre-implantation embryos and a critical analysis of the idea of "genome activation" see: (Güell, *op cit*. 481-484)

51 These epigenetic mechanisms include DNA methylation, chromatin conformational changes through histone modifications, ncRNAs and, most recently, 5-hydroxymethylcytosine. (Nagy et al., *op cit.* 445-57). For a summary of the genetic and epigenetic aspects implicated in organic development see: (Güell, *op cit*. 303-333).

52 By saying that the cell "disappears" I mean to emphasize that the originating cell -or so called "parent cell"- no longer exists *as such*, that is, as a functional and anatomical unity. Notions of "generation," "inheritance," and "daughter cell" are analogies from the organism level of reproduction, but such analogies have an essential limitation, as the cell cycle necessarily entails the disappearance of the "parent cell" as a distinct entity.

53 Lorthongpanich, C., Cheow, L.F.,; Balu,S., Quake, S.R., Knowles, B.B. et al. Single-Cell DNA-Methylation Analysis Reveals Epigenetic Chimerism in Preimplantation Embryos *Science* 341 (2013), 1110-1112.

54 Lister, R. et al. «Global epigenomic reconfiguration during mammalian brain development». *Science* 341 (2013), 6146.

55 Lee, E. R., Alisch, R. S. «Early-life disruption of epigenetic marks may contribute to the origins of mental illness». *Epigenomics* 4 (4), (2012), 355–357.

cordance of psychiatric disease in monozygotic twins, and behavioural epigenetics is poised to alter our fundamental understanding of psychiatric disease.[56] There is also evidence that implicates epigenetic factors, such as DNA methylation and histone modifications, in the link between social experiences occurring during the postnatal period and in adulthood, including altered neuroendocrine and behavioural outcomes.[57]

The repercussions of epigenetic changes in the development of the early human embryo is therefore a latent problem of ART that requires further attention. To quote from a recent review:

> "It is critically important to evaluate in detail the impact of ART on the genetic, epigenetic and phenotypic outcome in relation to genome-wide epigenetic regulation in early development."[58]

The scientific data suggests that environmental factors exert a crucial influence on epigenetic regulation in early mammalian development, including, although not limited to, genomic imprinting.[59] As we will discuss below, there is evidence that environmental influences during mammalian development lead to persistent changes in the epigenome that can alter the individual's susceptibility to disease.[60] Accordingly, if we know that environmental influences produce alterations in the development course and health of the future infant, it is reasonable to conclude that the elimination of 20% of the genetic material of the embryo during one of its stages will have significant consequences. Although the mechanisms underlying epimutations remain unknown, we have ways of determining whether the techniques used for embryo selection represent a risk to the health and happiness of the infant: for instance, we can analyse the health of children born as a result of ART.

5. Implications of ART on the Well-Being of IVF Children

Now let us consider the quality of life of the 36% of embryos which reached term following ART. The first IVF-conceived child was born in 1978 and, 35 years later, five million children have been born as a result of ART throughout the world. The scientific research now includes enough cases for us to analyse the health of these children, although we are dealing with a population that has not yet reached the age of forty. We can start by making the following observation: according to SART, as indicated above, the success rate for implanted embryos that reach term is 36% in the best of all cases. The implication of this data is that the embryos that supply the necessary first stage of selective enhancement, the embryos subjected to the biological manipulations of ART, have a mortality rate of 64%.

Here we focus on the health of the 36% that survive implantation. There are currently over a hundred published studies relevant to this issue, including eight reviews that compare birth defects in ART and non-ART infants. Using different methodologies and criteria, these reviews select a group of studies for meta-analysis and provide an overview of their individual results. Let us briefly summarize their conclusions. The first review from 2004 included 19 studies and concluded that there is an approximately 29% increase in the risk of major malformation in ART infants.[61] The second review was published a year later, included 25 studies, and increased this risk to 35 to 40%.[62] The third review, published in the same year, concluded that twins produced by in vitro fertilization have an increased risk of

56 Dempster, E.L., Pidsley, R., Schalkwyk, L.C. et al. «Disease-associated epigenetic changes in monozygotic twins discordant for schizophrenia and bipolar disorder». *Human Molecular Genetics* 20 (24), (2011), 4786-4796.

57 Champagne, F. A. «Interplay between social experiences and the genome: epigenetic consequences for behaviour». *Advances in genetics* 77, (2012), 33-57.

58 Kohda, T., Ishino, F. «Embryo manipulation via assisted reproductive technology and epigenetic asymmetry in mammalian early development». *Philosophical transactions of the Royal Society of London. Series B, Biological sciences*, 368 (1609), (2013), 20120353. doi:10.1098/rstb.2012.0353

59 Ibid.

60 Gluckman, P. D., Hanson, M. A., Buklijas, T., Low, F. M., Beedle, A. S. «Epigenetic mechanisms that underpin metabolic and cardiovascular diseases». *Nature reviews Endocrinology* 5 (7), (2009), 401-408.

61 Rimm, A. A., Katayama, A. C., Diaz, M., Katayama, K. P. «A meta-analysis of controlled studies comparing major malformation rates in IVF and ICSI infants with naturally conceived children». *Journal of assisted reproduction and genetics* 21 (12), (2004), 437-43.

62 Hansen, M., Bower, C., Milne, E., De Klerk, N., Kurinczuk, J. J. «Assisted reproductive technologies and the risk of birth defects - a systematic review». *Human reproduction* 20 (2), (2005), 328-338.

pre-term birth and an increased rate of caesarean delivery.[63] The fourth review, which also dates from 2005, reported that IVF pregnancies were associated with a statistically significant increase in the rate of perinatal mortality, pre-term birth after less than 33 weeks' gestation and admission to neonatal intensive care units.[64] The fifth review, published in 2011, concluded that ART twins have an increased risk of adverse outcomes and a higher risk of perinatal death.[65] The sixth review, from 2012, concluded that singleton pregnancies after IVF are associated with a higher risk of obstetric and perinatal complications.[66] The seventh review, published the same year, indicated a significantly higher risk of birth defects for children conceived by IVF.[67] The most recent review dates from 2013 and includes the results of 45 studies out of a total of 95.671 infants. Its conclusions, like those of the previous reviews, leave little room for doubt:

> "ART infants had a higher risk of birth defects compared with naturally conceived infants. The risk further increased when data were restricted to major birth defects or singletons only."[68]

What type of risks do these studies refer to? A review recently published in *Molecular Human Reproduction* lists publications that have reported the complications that constitute a perinatal and paediatric risk associated with the use of ART.[69] The perinatal complications include pre-term delivery[70], low birth weight[71], pre-eclampsia[72], placenta previa[73], placental abruption[74] and caesarean section.[75] But what ought to surprise us most are the paediatric risks associated with ART. In the infants selected there is a higher risk of malformation[76], chromosomal anomalies[77], septal heart defects[78], oesophageal atresia[79], hypospadias[80], cancer (in particular, hepatoblastoma[81],

63 . McDonald, S., Murphy, K., Beyene, J., Ohlsson, A. «Perinatal outcomes of in vitro fertilization twins: a systematic review and meta-analyses». *American Journal of Obstetrics and Gynecology* 193 (1), (2005), 141-152.

64 McDonald, S. D., Murphy, K., Beyene, J., Ohlsson, A. «Perinatel outcomes of singleton pregnancies achieved by in vitro fertilization: a systematic review and meta-analysis». *Journal d'obstétrique et gynécologie du Canada* 27 (5), (2005), 449-459.

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66 Pandey, S., Shetty, A., Hamilton, M., Bhattacharya, S., Maheshwari, A. «Obstetric and perinatal outcomes in singleton pregnancies resulting from IVF/ICSI: a systematic review and meta-analysis». *Human reproduction update* 18 (5), (2012), 485-503.

67 Wen, J., Jiang, J., Ding, C., Dai, J., Liu, Y., Xia, Y., Liu, J., Hu, Z., «Birth defects in children conceived by in vitro fertilization and intracytoplasmic sperm injection: a meta-analysis». *Fertility and Sterility*. 97 (6), (2012), 1331-7.

68 Hansen, M., Kurinczuk, J. J., Milne, E., De Klerk, N., Bower, C. «Assisted reproductive technology and birth defects: a systematic review and meta-analysis». *Human reproduction update*, (2013), doi: 10.1093/humupd/dmt006

69 Feuer, S. K., Camarano, L., Rinaudo, P. F. «ART and health: clinical outcomes and insights on molecular mechanisms from rodent studies». *Molecular human reproduction* 19 (4), (2013), 189-204.

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71 Jackson et al., *op cit.* 551-563; Helmerhorst et al., *op cit.* 26; Schieve, L. A., Meikle, S. F., Ferre, C., Peterson, H. B., Jeng, G., Wilcox, L. S. «Low and very low birth weight in infants conceived with use of assisted reproductive technology». *New England Journal of Medicine* 346, (2002), 731-737; McDonald et al., *op cit.*105-113.

72 Jackson et al., *op cit.* 551-563.

73 Ibid; Romundstad, L. B., Romundstad, P. R., Sunde, A., Von During, V., Skjaerven, R., Vatten, L. J. «Increased risk of placenta previa in pregnancies following IVF/ICSI; a comparison of ART and non-ART pregnancies in the same mother». *Human Reproduction* 21, (2006), 2353-2358.

74 Shevell, T., Malone, F. D., Vidaver, J., Porter, T. F., Luthy, D. A., Comstock, C. H., Hankins, G. D., Eddleman, K., Dolan, S., Dugoff, L. et al. «Assisted reproductive technology and pregnancyoutcome». *Obstetrics & Gynecology* 106, (2005), 1039-1045.

75 Jackson et al., *op cit.* 551-563; Helmerhorst et al., *op cit.* 26.

76 Hansen et al. (2005) *op cit*. 328-338; Davies, M. J., Moore, V. M., Willson, K. J., Van Essen, P., Priest, K., Scott, H., Haan, E. A., Chan, A. «Reproductive technologies and the risk of birth defects». *New England Journal of Medicine* 366, (2012), 1803-1813.

77 Ibid; Bonduelle, M., Aytoz, A., Van Assche, E., Devroey, P., Liebaers, I., Van Steirteghem, A. «Incidence of chromosomal aberrations in children born after assisted reproduction through intracytoplasmic sperm injection». *Human Reproduction* 13 (1998), 781-782.

78 Reefhuis, J., Honein, M. A., Schieve, L. A., Correa, A., Hobbs, C. A., Rasmussen, S. A., The National Birth Defects Prevention Study «Assisted reproductive technology and major structural birth defects in the United States». *Human Reproduction* 24, (2009), 360-366.

79 Ibid.

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81 McLaughlin, C. C., Baptiste, M. S., Schymura, M. J., Nasca, P. C., Zdeb, M. S. «Maternal and infant birth characteristics and hepatoblastoma». *American Journal of Epidemiology* 163, (2006), 818-828.

retinoblastoma[82] and leukaemia[83]), metabolic disease[84], imprinting disorders[85] and cerebral palsy[86].

Given the forcefulness of this data, the scientific community has been curiously unresponsive. For example, in a recent issue of *Circulation*, the official journal of the American Heart Association, a study reported clinical and experimental evidence that the processes involved in egg manipulation might be associated with epigenetic changes mediated by patterns of DNA methylation. In the conclusion, the authors state:

> "This study provides evidence that the use of ART in infertile couples is associated with fetal and postnatal cardiovascular remodeling, suggesting prenatal exposure to pressure overload."[87]

This statement would seem to indicate scientific grounds for caution, if not skepticism, concerning the reliability and safety of ART. However, the editors felt the need to qualify this statement, indicating a reluctance to draw any conclusions, positive or negative, from the relevant data:

> "The authors propose that epigenetic changes related to the technology at the time of conception could lead to permanent reprogramming of cardiac development. Although such a proposal is consistent with current experimental programs in the developmental origins of disease, there is, at present, no data to support such a hypothesis. The time course and stability for epigenetic changes are not established, and which particular pathways may lead to the specific cardiac changes is speculative"[88].

Insofar as the data *do* support an hypothesis, however, they seem to indicate caution and skepticism with regard to embryonic manipulation, rather than the unguarded optimism of the transhumanists. In any case, we can see how transhumanists could exploit the ambiguity of this scenario to claim scientific support for their "hypothesis" of a better future.

In this analysis, we have been concerned to determine the extent to which the processes involved in IVF, the very same processes that enable the embryonic selection required for transhumanist enhancement, might compromise the future health and happiness of children. Scientific research leaves no room for doubt: embryo selection poses a risk, not just to the happiness of the individual but to basic health and even to their physical integrity.

It is important to clarify that ART has been examined here as the actual context in which transhumanist genetic manipulation and embryonic selection could be put into practice. As stated above, the objectives of this article are therefore provisionally limited in scope and the analysis carried out here is limited to the biomedical techniques currently available to transhumanist proponents, as guided by the PPB. No doubt the future will bring new and better techniques and that the ethical implications of these techniques will be different. Yet this should not prevent us from undertaking a rigorous analysis the situation as it currently stands. To avoid the implications of current techniques, which is the most relevant context for judging the case for transhumanism, is to take refuge in an abstract and specious notion of prudence in order to evade concrete ethical responsibility.

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84 Ceelen, M. «Body composition in children and adolescents born after in vitro fertilization or spontaneous conception». *J. Clinical Endocrinology & Metabolism* 92, (2007), 3417-3423.

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87 Valenzuela-Alcaraz, B., Crispi, F., Bijnens, B. et al. «Assisted Reproductive Technologies are Associated with Cardiovascular Remodeling in Utero that Persists Postnatally», Circulation 128, (2013), 1442-1450.

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6. Conclusion

In my opinion, the use of biological manipulations to help a child have the best possible of lives is something we cannot renounce in toto. We cannot deny the obligation to use scientific knowledge and technology to ensure that our offspring are not only healthy but also happy. What is under consideration here is the more specific proposal of PPB, advanced by the transhumanist movement, which Savulescu defines as the selection and manipulation of gametes and embryos, interventions that are already a basic part of ART and IVF.

In the first part of this paper we have shown that the plan to modify a gene or group of genes in the embryo in order to obtain certain desirable personality traits rests on hypotheses that are no longer supported by developmental biology. The epigenetic dimension, not to mention the complex role of the genes in the context of brain and behaviour, exposes the fallacy of trying to correlate single gene modification (or that of a group of genes) in the early embryo with the improvement of traits such as memory, empathy or moral character. One could even go so far as to argue that the scientific hypotheses that underpin the transhumanist project are being abandoned by the scientific community in the 21st century.

In reference to personality traits, it has been a decade since the U.S. president's Council on Bioethics declared that "the reality that these traits are heavily influenced by environment will not be overcome by better technology."[89] Reviews of past and current research, and the direction in which future research is moving, merely serve to corroborate this view. The research carried out also suggests that exposing gametes or embryos to artificial conditions and PGD may provoke epimutations and alter the imprinting of genes, which may lead to deleterious consequences for development. The aim of the PPB proposed by Savulescu is "to select the child, of the possible children they could have, whose life can be expected, in light of the relevant available information, to go best or at least not worse than any of the others."[90] In the light of the relevant information available to us from current scientific and biomedical sources, we have shown that the process of embryonic selection entails a high risk of foetal and perinatal mortality. Moreover, the selected embryos that overcome these dangers have higher risks of cancer, malformation, chromosomal anomalies, septal heart defects, oesophageal atresia, hypospadias, metabolic disease, imprinting disorders and cerebral palsy. It is worth mentioning that several decades will have to pass before we can construct an accurate picture of the long-term health risks of ART, given that the study population has not yet reached 40 years of age.

Returning to transhumanist hypotheses, Savulescu maintains that "there is reason to obtain and use all genetic and other information about disease susceptibility and non-disease states to make a decision to select the most advantaged child."[91] As we have shown, if we consider the consequences of obtaining and using all the genetic and additional information about disease susceptibility in order to select the most advantaged child, we have sufficient grounds to oppose the use of child selection techniques.

89 President's Council on Bioethics, *op cit*. 38.

90 Savulescu (2009) *op cit*. 276.

91 Ibid.

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The post-humanist embryo: genetic manipulation, assisted reproductive technologies and the principle of procreative beneficence.Â Drawing from Julian Savulescuâ€™s argument for the obligation to use technological interventions for the enhancement human life, the Principle of Procreative Beneficence (PPB) states that parents have a moral obligation to use available reproductive technologies, including techniques of genetic manipulation, to create children who have the best chance of enjoying the best possible life. The aim of this study is to ana - lyse the extent to which the possibility of using genetic manipulation toâ€¦ CONTINUE READING. Save to Library. Principle of procreative beneficence Assisted reproductive technologies (ART) Epigenetics Embryo Gametes In Vitro Fertilization (IVF). This is a preview of subscription content, log in to check access. References.Â Journal of Assisted Reproduction and Genetics 29(9): 943â€“950.CrossRefGoogle Scholar. Kohda, T., and F. Ishino. 2013. Embryo manipulation via assisted reproductive technology and epigenetic asymmetry in mammalian early development. Philosophical Transaction Royal Society of London B 368: 20120353.CrossRefGoogle Scholar. Krisher, R.L. 2004. PROCREATIVE BENEFICENCE : THE MORAL OBLIGATION TO HAVE THE BEST CHILDREN I will argue for a principle which I call Procreative Beneficence: couples (or single reproducers) should select the child, of the possible children they could have, who is expected to have the best life, or at least as good a life as the others, based on the relevant, available information.Â Other Principles of Reproductive Decision-Making Applied to the Simple Case The principle of Procreative Beneficence supports selecting the embryo without the genetic predisposition to asthma. That seems intuitively correct. How do other principles of reproductive decision-making apply to this example?