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ETHICAL PROBLEMS WITH THE PREIMPLANTATION GENETIC DIAGNOSIS OF HUMAN EMBRYOS

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Abstract: The purpose of preimplantation genetic diagnosis by embryonary biopsy is to identify genetic alterations prior to the implantation of embryos produced by *in vitro* fertilization. The most important aim is the selection of genetically healthy embryos due to their genetic indemnity, but it can also be used to select the sex or, eventually, other detectable traits accrding to the wishes of the parents. This procedure has been the subject of scientific debates, in relation to the harm that it can cause to healthy embryos that are going to be implanted, and in relation to the interpretation of the genetic tests made. Ethical debates have also focused on the production of and respect for the life and the integrity of developing human beings. In this work, it is argued that most of the uses of PGD are morally reprehensible, because they are done with disregard to the dignity that should be granted to embryos as human persons.

Key words: preimplantation genetic diagnosis, human embryos, ethical status of embryos, persons, dignity

Problemas éticos con el diagnóstico genético preimplantacional de embriones humanos

Resumen: El diagnóstico genético preimplantacional (DGP) mediante biopsia embrionaria tiene como objeto la detección de alteraciones genéticas previamente a la implantación de embriones producidos por fertilización *in vitro* (FIV). Su finalidad más significativa es la selección de embriones por su indemnidad genética. También se puede emplear para seleccionar el sexo o eventualmente otras características detectadas según el deseo de los padres. Este procedimiento ha sido objeto de debates en el ámbito científico, por el eventual daño que puede ocasionar la técnica en embriones sanos que serán implantados y por las interpretaciones de los exámenes genéticos realizados. También ha sido objeto de debates en el ámbito ético-antropológico, en cuanto a la producción y al respeto a la vida e integridad de los seres humanos en desarrollo. En este trabajo se argumenta que los usos que se hacen del DGP son, en su gran mayoría, moralmente reprochables, por hacerse con desprecio de la dignidad que debe darse al embrión como persona humana.

Palabras clave: diagnóstico genético preimplantacional, embriones humanos, estatus ético de los embriones, personas, dignidad

Problemas éticos com diagnóstico pré-implantacional de embriões humanos

Resumo: O Diagnóstico genético pré-implantacional (PGD) por meio de biópsia embrionária visa a identificação de alterações genéticas prévias à implantação de embriões produzidos por fertilização in vitro (FIV). Seu propósito mais significativo é a seleção de embriões por sua característica genética. Ele também pode ser usado para selecionar o sexo ou, eventualmente, outras características identificadas de acordo com os desejos dos pais. Este procedimento tem sido tema de debate em âmbito científico, por eventual dano que pode ocaciosionar a técnica em embriões saudáveis que serão implantados e pela interpretações dos exames genéricos realizados. Ele também tem sido objeto de debate na área ético-antropológica, no que concerne a produção e o respeito à vida e integridade do ser humano em desenvolvimento. Este artigo argumenta que os usos que são feitos do PGD são, em sua grande maioria, moralmente condenáveis, por ser instrumentalizado com desrespeito pela dignidade que deve ser dada ao embrião como uma pessoa humana.

Palavras-chave: diagnóstico genético pré-implantacional, embriões humanos, status ético dos embriões, pessoas, dignidade

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The development of preimplantation genetic diagnosis ("PGD" hereon in) has raised numerous ethical issues, which is reflected in policy and legal debates around the legitimacy of this technique and its limits*(1-6)*. PGD can be used to detect genetic diseases in embryos and if its use were extended, it could allow for determining if an embryo has certain features desired by the parents, even though these may be related to diseases that require treatment. PGD may have limited use in detecting and treating pathologies, but has in fact been used as a source of information for eliminating defective embryos. One of the applications of PGD that has received more attention from the media and that has been presented as a justification for its use is the generation of "savior babies", that is, the possibility of choosing a child that could be a useful source for transplants for a sibling. On the other hand, children that do not have favorable characteristics will end up frozen and then dead*(7)*. It is obvious that the development of these technical possibilities requires reflection on their implications. What is in question is what children represent for their parents. Are they a product or a gift? And if they have a genetic flaw, do they lack dignity and deserve to be condemned to die? Do parents have the right to decide what characteristics their children will have? There are important reasons to maintain that children cannot be disposable objects like consumer products*(8-10)*[3].

These ethical questions are presented in a global context of significant differences in the treatment of embryos under distinct jurisdictions. Far from being a guide in relation to shared moral intuitions, legislation has been a source of confusion. In effect, although biology has shown beyond any doubt that the development of a new human being begins with fertilization, legislation in several countries questions whether the life of an embryo prior to implantation is that of a human being and whether an embryo deserves respect under these conditions*(11)*. Some countries have gone further and have even affirmed that respect for a human being is conditioned by his/her state of development or capacity to completely express his/her potential. For example, in the European Economic Community it is considered that the human nature of the embryo is acquired after fourteen days of development, given that it is at this point that the embryonic nervous system becomes evident. This also coincides with the process of gastrulation, when conjoined twins can be generated. Consequently, in these European countries the human embryo is a subject that merits respect from day 14 post-fertilization onward, and before which the embryo is an "object" or "thing" (referred to as a "pre-embryo") and consequently susceptible to manipulation. Law 20.120 (2006) in Chile regulates scientific investigation involving human beings and the human genome and prohibits cloning. It establishes the respect deserving human beings from conception and explicitly prohibits the manipulation of embryos. Debates continue in other countries about regulating PGD*(12,13)*.

In what follows we will first explain what the PGD technique consists of and discuss the risks that it implies or could imply for the development of the embryo. Secondly, we will argue that the embryo should be treated morally as a person and thirdly we discuss the implication of this on ethical reflections about PGD.

§ 1. **What is preimplantation diagnosis?**

The fertilization of an oocyte (egg) by a spermatozoid occurs naturally in the Fallopian tubes and results in the formation of a zygote that represents the first stage in the development of a new human being. The egg nucleus (pronucleus) contains the 23 maternal chromosomes and the spermatozoid contains the 23 paternal chromosomes. Both sets of chromosomes have genetic changes (in DNA structure) and epigenetic changes (in gene expression) that are complementary and required to biologically generate human beings. The maternal mitochondria contribute her DNA to complete the genome of the zygote. By successive divisions and differentiation the zygote forms all the cell types present in human beings. There is no doubt that the zygote has a new genetic structure. With this the first stage in the development of a new human organism begins. It is an ongoing and predictable development that ends with the complete development of the organism*(14,15)*. The

[3] This kind of ethical questioning has become particularly urgent with the development of CRISPR/Cas9 gene editing. This work does not deal with the problems associated with gene editing, which will be the focus of a future work.

zygote contains a new genome, the fundamental structure of which is maintained throughout its development and identifies the unicellular embryo as biologically human and specifies its individuality*(11)*. The zygote is a totipotential cell capable of generating the entire organism.

After the membrane of the spermatozoid fuses with the egg, a series of biological events begin that lead to the development of the embryo*(16,17)*. The genome begins to express itself within a few hours of fertilization*(18)*. The first division of the zygote occurs around 30 hours after fertilization, resulting in the first two cells, which are termed blastomeres, each of which has 46 chromosomes. The two blastomeres then divide in two and the embryonic genome begins to be expressed more massively, that is, an epigenome is configured*(19)*. At three days post-fertilization the embryo is full of cells (blastomeres) and a morula is formed. By the fourth or fifth day the embryo grows and produces a cavity, generating a blastocyst. Cellular territories appear in the blastocyst with specific functions. Stem cells appear that are responsible for producing the distinct cellular tissue of the body*(20)*. By day 7 post-fertilization the embryo reaches and lodges in the uterus, where hormone production begins, the detection of which in laboratory tests provides the clinical identification of pregnancy. This supports the definition of pregnancy of the World Health Organization. It is important to note that the mother hosts the embryo in her body unknowingly seven days prior to implantation. There is currently no reliable test to confirm that fertilization has occurred. The implanted blastocyst subsequently continues developing and gastrulation begin by day 14 to 16 post-fertilization, which gives rise to the fetal organs. Thus the central nervous system begins to develop on day 14 and up to day 14 or 16 it is possible that the embryo divides and generates conjoined twins*(21)*.

Preimplantation genetic diagnosis (PGD)*(22-26)* was first described by Handyside et al. in a 1990 issue of *Nature(27)*. The technique involves extracting blastomeres by biopsy from embryos that are at the two-cell stage to the blastocyst stage to obtain DNA for genetic molecular analysis with microchips that simultaneously analyze the DNA in thousands of genes*(28)*. And now the same embryo can be re-biopsied*(29)*. The potential harm that biopsy can cause embryos in early stages of development has been assessed and it has been shown that biopsies of blastomeres at day 3 (in the morula stage) significantly reduces subsequent implantation and results in fewer live births*(30)*.

The DNA from a single cell is sufficient to research thousands of genetic mutations responsible for many genetic disorders*(31)*, for example, alterations in just one gene, as in cystic fibrosis, in many genes, as in breast cancer, or in chromosomes, as in Down syndrome. It is important to consider that finding genetic mutations in embryonic DNA does not necessarily mean that the disorder will emerge, given that genes do not have a predetermined role but rather a probabilistic one that requires interaction with many other genes and with the environment in which the embryo develops*(8)*. In fact, there has been a debate recently about the significance of findings of genetic variants of clinical uncertainty*(32)*. The absence of any alteration in the genes examined by the technique does not ensure that the embryo will be healthy given that there may be alterations in other genes that were not tested. In terms of the degree of risk involved in embryonic biopsy, it cannot be ensured that extracting cells does not have harmful consequences for the subsequent development of the embryo*(33,34)*. With the discovery that the cells of preimplanted embryos have a certain orientation in their role in the organism*(35)*, concerns have been raised as to whether the removal of a cell can result in alterations in the embryo's development or if the remaining blastomeres can reprogram themselves to compensate for the loss. In this regard, samples have been taken from other parts of the embryo where biopsy would be potentially less harmful. Thus, biopsy of the trophectoderm (structure that gives rise to embryonic appendages like the placenta) in the blastocyst state appears to be a safer technique*(33)*. Biopsies of polar bodies have also been used to explore genetic alterations in embryos*(36)*.

A technical problem that remains unresolved is the detection of numeric chromosome alterations (aneuploidy) in only one or two cells of an 8-cell embryo, while the rest are normal (termed

mosaicism) and in particular the final result of a pregnancy*(37,38)*. PGD also presents limitations in relation to specific genetic diseases such as mitochondrial disorders*(39)*. When a genetic alteration is found in an embryo, it is not implanted and most often is eliminated. In some cases the embryo is frozen at –180° C and subsequently eliminated. In relation to the safety of the technique, effects on the growth and behavior of animals born after PGD have been shown*(40)*. Nevertheless, such effects on humans have not been observed in preliminary studies*(22,41-43)*.

One variant of the PGD procedure is preimplantation genetic screening (PGS), which emerged in 2011 with the introduction of the next-generation sequencing method, which was used to identify more than 400 genes associated with recessive genetic disorders. This technology is currently being used to detect changes in the number of chromosomes (aneuploidy) in embryos obtained from genetically normal parents by *in vitro* fertilization*(44)*.

§ 2. **Is the embryo morally a person?**

Ethical consideration of PGD not only requires careful attention to the specifics of the techniques that are used and their effect on the development of the embryo, but it is also critical clarity as to whether or not the embryo is a person. There are important differences that turn on this question in evaluating the risks involved in PGD.

A relevant fact for this question is that the human organism begins life with fertilization. There is no serious doubt that embryo is the same biological organism that later becomes a fetus, then a child and then an adult person. The question posed by several philosophers, however, is whether or not we should identify a human person with a human organism. The central motivations to differentiate between a human being and a biological organism have arisen at least since John Locke*(45, II, cap. 27)*. In the earlier philosophical tradition, well represented by Boecio, a person is an individual substance of rational nature (*rationalis naturae individua substantia*; ML 64, 1343). A "substance" is an entity that exists by itself and does not depend on other entities. It continues over time and is the same at different moments. Taking into consideration that this substance has a rational nature, it is argued that it has an intrinsic form of being that, if not impeded, tends to foster the rational activity of mature human. A human being is typically capable of higher cognitive activity and of deliberate and conscious decision-making. This reflective capacity endows human beings with a special moral responsibility for their actions and makes them responsible for their moral character. In their rational and free character, persons are endowed with a certain dignity by which they should be treated as ends in themselves (Santo Tomás de Aquino, *Summa theologiae*, I, q. 29, a. 3, c.). However, in the philosophical tradition, the morally special character of persons is not related to the actual exercise of freedom and rationality. One does not exercise these capacities when in a deep sleep, nor do small children or, of course, embryos. This does not prevent them from being persons as we are dealing with the same substance that because of its intrinsic nature has an internal dynamism destined to give rise to freedom and rationality provided this dynamism is not in some way impeded[4].

However, this philosophical tradition has changed profoundly since Locke's time. For Locke, the conditions of identity of a person arise from the continuity of psychological states, among which memory plays a crucial role*(45, II, cap. 27)*. For the psychological view introduced by Locke, what makes a person P_1 at time t_1 the same as P_2 at t_2 is the fact that there is continuity between the psychological states of P_2-at-t_2 and P_1-at-t_1. Psychological continuity has preeminence with respect to the continuity of the same biological organism. What is essential to a person are her/his mental states, of which the individual is conscious in a first person perspective. What supports such mental states is something secondary. The question then is whether only one with mental

[4] One can appreciate that the idea has long been maintained that the embryo and later the fetus go through a process of "retarded animation" in which it gradually acquires a human character (cf. Saint Thomas Aquinas, *Expositio super Iob*, III, 395-400). This does not cast in doubt the central concept that a person is a substance that persists over time, being the same at different moments and possessing a rational nature that tends toward rationality and freedom. It is simply that knowledge of the biological process in the past was much more limited. The knowledge available today through embryology leaves no doubt that from fertilization onward we are dealing with a human organism.

states of this type is a person. Only those are individuals that have a sense of continuing over time as a person. It can be appreciated then that there are motives of the philosophical tradition present in these ideas, but profoundly transformed. For the philosophical tradition, a person is one that possesses a nature that tends to produce mental states of a rational character. In contrast, according to Locke's conception, a person is a set of mental states of a rational character. The states should be localized in one human organism or another, if you will, but this localizing is ultimately accidental.

During much of the last century the debate about personal identity was a continuation and refinement of the psychological Lockean conception*(46,47)*. It isn't strange that this psychological conception of personal identity and of the person has been drawn upon in debates on ethical questions. Two philosophers that have taken up this point of view very notably are Michael Tooley and Peter Singer. For them, only those who are conscious of themselves in different moments, have interests and are capable of planning for their lives in the long-term are persons*(48,49)*. For Singer, the fetus does not fall under this characterization of a person, while many animals do. However, very young children and persons with highly limited cognitive capacities also do not meet this characterization. The same reasons for excluding embryos from the condition of a person also serve to exclude many other human beings that are already born.

Many find this position excessive, although it seems more coherent if one has accepted the psychological conception of identity in any of its forms. A variety of alternative theories have been explored that are less shocking in terms of their moral consequences, in which the character of the unborn person is acquired between fertilization and birth*(50:56-90)*. For example, it has been argued that the fetus only becomes a person when it has conscious desires or interests*(51:115-129)*. It has been argued that the fetus becomes a person when it has the capacity to feel pain or pleasure. It has also been argued that the fetus becomes a human being when it has a functioning brain. All these theories are derived from the psychological conception, and they partly relaxe the requirements of the Lockean tradition followed by Tooley and Singer. Other theories have proposed the instant when the fetus becomes viable as the critical moment, that is, when it is able to survive without its mother help. It is clear that we do not use a criterion of this type to judge the personal character of a seriously ill person, because of which it be ruled out from hereon. It has also been proposed as a criterion the moment in which the fetus shows movement or when it begins having a "human appearance". These criteria make the character of a person depend on certain "recognition" that one can grant to a fetus as an "equal". These criteria can rapidly be ruled out given that the character of a person cannot consist in an extrinsic property or set of properties[5]. For a long time it was considered that blacks or other groups did not appear human. Another criteria proposed to fix the moment at which the embryo begins to be a person is implantation. This is not a psychological criterion like the former. The argument behind this proposal is that before implantation we are not dealing with an authentic organism but rather a collection of totipotential cells. In effect, the formation of twins can occur before implanting. The assumptions on which this theory rests have been shown empirically to be false*(35)*. It is evident that from the moment of fertilization the embryo is an organism. Even at the point of the first mitosis there is a certain evident degree of specialization of the two cells that make up the embryo.

The conceptions that have rejected that the embryo has the character of a person by one means or another involve the psychological theory of personal identity. However, this theory has proven to be disastrous as an explanation of the conditions of the identity of a person*(52)*. The latest developments in this tradition have been so disastrous that they have rejected the notion of persons as entities that are identical at different moments over time. The fundamental difficulty is that psychological continuity is a vague relationship that is given in degrees that can be greater or lesser and not one-to-one. In contrast, identity is a precise one-to-one relationship, reflective, symmetric and transitive. One scenario that has

[5] A property *F* is extrinsic if and only if it is not intrinsic. A property *F* is intrinsic if and only if the fact of *x* is F or not, where *x* is any object, is founded on parts of *x* if it is founded on anything.

long been considered is the following: suppose that the brain of a person, P_1, is removed. There are cases of persons surviving the destruction of one hemisphere of the brain. And suppose that a method of brain transplanting has been developed, so that the right hemisphere of P_1's brain can be transplanted to another person, let's say P_2, whose brain had been removed earlier. And the left hemisphere of P_1's brain is transplanted to yet another person; let's say P_3, whose brain was also removed earlier. It the transplants are successful, P_2 will be psychologically continuous with P_1, and P_3 will be psychologically continuous with P_1. If one argues in general terms that personal identity is based on psychological continuity, then $P_1 = P_2$ and $P_1 = P_3$. But identity is symmetric and transitive, so that it follows that $P_2 = P_3$, which is clearly false.

Psychological continuity is not sufficient for personal identity, but neither can it be necessary for personal identity. Support a person P_4 suffers severe brain damage that causes him to lose practically all his memories. P_4's beliefs, intentions, preferences and character traits change radically such that he is psychologically discontinuous with pre-injury P_4. Wouldn't it be reasonable that we say that post-injury P_4 is different from pre-injury P_4? Suppose that after a year, P_4 recovers his memories, beliefs, preferences, intentions and character traits. Wouldn't it be reasonable to argue that P_4 had reappeared after a hiatus of a year? There are no "intermittent" persons. Consequently, psychological continuity does not appear to be necessary for personal identity.

The alternatives to the classic views of the person are not adequate. Our conception of the dignity of the person is related to the idea that people are substances that are identical at different moments over time and have an intrinsic nature that tends toward the development of rational thought and freedom. In this vision we must concede the character of a person to every human individual, and the embryo is clearly a human individual. The most recent and robust position on personal identity links this to the identity of the same organism over time*(53-56)*. This is exactly what should be supposed: a human embryo is the same organism that will subsequently be a mature human if its development is not impeded. If the mature human being is a person, then the embryo is as well.

§ 3. **Ethical evaluation**

According to what has been argued above, an embryo should receive the same treatment as a human person, although we are dealing with a little person that has not yet shown his/her rational capacities and autonomy. Nor do children o many ill persons have these capacities. A dignity should be granted to the embryo as an equal to any other person. There are two types of consequences that this dignity with respect to PGD:

(a) Risk evaluation

Firstly, given that the embryo is a person, the risks involved in the application of PGD are risks to persons. Normally in our individual and collective social decisions it is reasonable to assume certain risks if they are compensated for by corresponding benefits. Driving a car implies a certain probability of having an accident. When one takes out a term deposit there is a probability that the bank will not be able to meet its obligation. If these probabilities are low, it is rational to act in the face of such risks. When it is a matter of activities or processes that imply serious harm to persons, it is reasonable to be much more demanding with respect to the risks that are assumed. If a treatment is going to be introduced for example, it is required that there must be a clear understanding of the risks of using the treatment and its therapeutic effectiveness. A doctor that gives his patients medicine without knowing the risks that medicine poses would be criminal for doing so. Ignorance of the effects of a medication does not relieve criminal liability. In the case of the use of PGD, a lower standard cannot be applied. Ignorance of the adverse effects of a technology certainly does not make its use legitimate.

As noted above, there are well-founded reasons to doubt the safety of PGD. There is evidence with animal models that its use can be harmful. Until it has been clarified that PGD does not produce similar harmful effects in humans its use should be prohibited. Trophectoderm biopsy appears to offer less risk, but once again ignorance of adverse techniques does not make this technique legitimate. The complexity of epigenetic processes

obliges extreme caution with any interference in the development of the embryo.

(b) Illegitimate uses

PGD can simply determine whether or not an embryo has any pathology, which in itself is not morally questionable. In principle, it is better to know something than to be ignorant of it. If the use of PGD is for the purpose of applying treatment that can restore the health of the embryo, its use is not only legitimate but also morally laudable.

The most serious ethical problem emerges because the most common use of PGD is to determine if the embryo is "appropriate". The consequence of PDG revealing pathology is that the embryo is killed or frozen. Both intentionally causing the death of embryos and freezing them are seriously incorrect actions from a moral perspective. An action that in abstract is good or neutral because of the type of intent behind it can become wrongful if it has been done as a means toward a morally wrongful act. Thus if PGD is a means to killing embryos its use is morally reprehensible.

The use of PGD to select other features considered desirable in embryos is also morally reprehensible. It is likewise seriously wrong for parents or any other person to intentionally kill a person because that person is sick or because, for example, that person is not sufficiently intelligent or beautiful.

§ 4. **Conclusions**

This work has explained what PGD consists of. We have argued that the embryo is a person that deserves to be treated morally as an equal and not as a consumer product to satisfy the preferences of parents or anyone else. This imposes significant restrictions on the use of PGD. Firstly, its use can only be authorized with sufficient knowledge of the risks it poses for the embryo. This knowledge does not exist at present and there are well-founded reasons to think that there are serious objective risks. Secondly, any use of PGD that has the end result of intentionally killing embryos that do not comply with selected preferences is morally reprehensible. Its use for selecting embryos to be frozen is also morally reprehensible.

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References

1. Hens K, Dondorp W, Handyside AH, Harper J, Newson AJ, Pennings G, Rehmann-Sutter C, de Wert G. Dynamics and Ethics of Comprehensive Preimplantation Genetic Testing: A Review of the Challenges. *Hum Reprod Update* 2013; 19(4): 366-375.
2. Propping P, Schott H. Embryo Screening: Update German View of Genetic Testing. *Nature* 2014; 510(7506): 473.
3. Symons X. Response to Tomasz Zuradzki's 'Preimplantation Genetic Diagnosis and Rational Choice Under Risk or Uncertainty'. *Journal of Medical Ethics* Nov 2014; 40(11): 779.
4. Wapner RJ, Levy B. The Impact of New Genomic Technologies in Reproductive Medicine. *Discov Med.* 2014; 17(96): 313-318.
5. Zuradzki T. Preimplantation Genetic Diagnosis and Rational Choice Under Risk or Uncertainty. *Journal of Medical Ethics* 2014; 40(11): 774-778.
6. Zuradzki T. A Situation of Ethical Limbo and Preimplantation Genetic Diagnosis. *Journal of Medical Ethics* 2014; 40(11):780-781.
7. Whetstine LM. Ethical Challenges in Assisted Reproduction: The Place of Preimplantation Genetic Diagnosis in a Just Society. *J Child Neurol* 2013; [Epub ahead of print].

8. Santos MJ. Manipulación genética de seres humanos. *Ars Medica* 2006; 13: 91-102.
9. Fitzgerald K. PGD: Bio-Medical Insights and Ethical Considerations. In Sgreccia E, Laffitte J, (eds.). *The human embryo before implantation. Scientific aspects and bioethical considerations. Proceedings of the 12th Assembly of the Pontifical Academy for Life*, Vatican, 27 February -1 March, 2006. Libreria Editrice Vaticana, 2007: 158-166.
10. Rethoré MO. Prenatal and Preimplantation Diagnosis from the Parents' Viewpoint. In Sgreccia E, Laffitte J, (eds.). *The human embryo before implantation. Scientific aspects and bioethical considerations. Proceedings of the 12th Assembly of the Pontifical Academy for Life*, Vatican, 27 February -1 March, 2006. Libreria Editrice Vaticana, 2007: 167-176.
11. Burgess J. Could a Zygote Be a Human Being?. *Bioethics* 2008; 28.
12. De Wert G, Dondorp W, Shenfield F, et al. ESHRE Task Force on Ethics and Law 22: Preimplantation Genetic Diagnosis. *Human Reproduction* 2014; 29(8):1610-1617.
13. Damian BB, Bonetti TC, Horovitz DD. Practices and Ethical Concerns Regarding Preimplantation Diagnosis. Who Regulates Preimplantation Genetic Diagnosis in Brazil? *Braz J Med Biol Res*. 2015; 48(1): 25-33.
14. Ventura-Junca P, Santos MJ. The Beginning of Life of a New Human Being From the Scientific Perspective and its Bioethical Implications. *Biol. Res.* 2011; 44: 201-207.
15. Santos MJ, Ventura-Juncá P. El inicio de la vida de un nuevo ser humano desde la perspectiva científica biológica. En Rodríguez Á, (ed.). *Aborto y anticoncepción de emergencia: aspectos antropológicos, éticos y jurídicos*. Ecuador: Ediciones del Centro de Bioética de la Universidad Técnica Particular de Loja; 2013: 35-46.
16. Evans JP, Florman HM. The State of the Union: The Cell Biology of Fertilization. *Nat Cell Biol.* 2002; 4 Suppl: s57-63.
17. Sutovsky P. Sperm-Egg Adhesion and Fusion in Mammals. *Expert Rev. Molec. Med.* 2009; 11(e11):1-12.
18. Daniels R, Lowell S, Bolton V, Monk M. Transcription of Tissue-Specific Genes in Human Preimplantation Embryos. *Human Reproduction* 2997; 12(10): 2251-2256.
19. Ikegami K, Ohgane J, Tanaka S, Yagi S, Shiota K. Interplay Between DNA Methylation, Histone Modification and Chromatin Remodelling in Stem Cells and During Development. *Int. J. Dev. Biol*. 2009; 53: 203-214.
20. Santos MJ, Ventura-Junca P. Bioethical Aspects of Basic Research and Medical Applications of Human Stem Cells. *Biol Res* 2012; 45: 317-326.
21. Smith B, Brogaard B. Sixteen Days. *J. Med. Philos*. 2003; 28: 45-78
22. Cimadomo D, Capalbo A, Ubaldi FM, et al. The Impact of Biopsy on Human Embryo Developmental Potential during Preimplantation Genetic Diagnosis. *BioMed Res Int*. 2016; Article ID 7193075. DOI: http://dx.doi.org/10.1155/2016/7193075
23. Chen CK, Yu HT, Soong YK, Lee CL. New Perspectives on Preimplantation Genetic Diagnosis and Preimplantation Genetic Screening. *J Obstet Gynecol.* 2014; 53(2): 146-150.
24. Klitzman R, Abbate KJ, Chung WK, et al. Views of Preimplantation Genetic Diagnosis Among Psychiatrists and Neurologists. *J Reprod Med* 2014; 59(7-8): 385-392.
25. Tur-Kaspa I, Jeelani R, Doraiswamy PM. Preimplantation Genetic Diagnosis for Inherited Neurological Disorders. *Nat Rev Neurol.* 2014; 10(7): 417-424.
26. Yan L, Wei Y, Huang J, Zhu X, et al. Advances in Preimplantation Genetic Diagnosis/Screening. *Sci China Life Sci.* 2014; 57(7): 665-671.
27. Handyside AH, Kontogianni EH, Hardy K, Winston RML. Pregnancies from Biopsied Human Preimplantation Embryos Sexed by Y-specific DNA Amplification. *Nature* 1990; 344, 768-770.
28. Brezina PR, Brezina DS, Kearns WG. Preimplantation Genetic Testing. *BMJ* 2012; 18(345): e5908. DOI: 10.1136/bmj.e5908.
29. Zhang S, Tan K, Gong F, et al. Blastocysts can be Rebiopsied for Preimplantation Genetic Diagnosis and Screening". *Fertil Steril.* 2014; 102(6): 1641-1645.
30. Scott KL, Hong KH, Scott RT Jr. Selecting the Optimal Time to Perform Biopsy for Preimplantation Genetic Testing. *Fertil Steril.* 2013; 100(3): 608-614.
31. Collins SC. Preimplantation Genetic Diagnosis: Technical Advances and Expanding Applications. *Curr Opin Obstet Gynecol*. 2013; 25(3): 201-206.
32. Martín J, Cervero A, Mir P, Martinez-Conejero JA, Pellicer A, Simón C. The Impact of Next-Generation Sequencing Technology on Preimplantation Genetic Diagnosis and Screening. *Fertil Steril.* 2013; 99(4): 1054-1061.
33. Scott RT, Upham KM, Forman EJ, et al. Cleavage-Stage Biopsy Significantly Impairs Human Embryonic Implantation Potential While Blastocyst Biopsy Does Not: A Randomized and Paired Clinical Trial. *Fertil Steril* 2013; 100(3): 624-630. DOI: 10.1016/j.fertnstert.2013.04.039.
34. Simpson JL. Preimplantation Genetic Diagnosis at 20 Years. *Prenat Diagn*. 2010; 30(7): 682-695.

35. Zernicka-Goetz M. Cleavage Pattern and Emerging Asymmetry of the Mouse Embryo. *Nat Rev Mol Cell Biol.* 2005; 6: 919-928.
36. Liss J, Chromik I, Szczyglińska J, Jagiełło M, Łukaszuk A, Łukaszuk K. Current Methods for Preimplantation Genetic Diagnosis. *Ginekol Pol.* 2016; 87(7): 522-526. DOI: 10.5603/GP.2016.0037.
37. Baart EB. Preimplantation Genetic Screening Reveals a High Incidence of Aneuploidy and Mosaicism in Embryos from Young Women Undergoing IVF. *Human Reproduction* 2005.
38. Lee E, Illingworth P, Wilton L, Chambers GM. The Clinical Effectiveness of Preimplantation Genetic Diagnosis for Aneuploidy in all 24 Chromosomes (PGD-A): Systematic Review. *Human Reproduction* 2014; pii: deu303. [Epub ahead of print].
39. Mitalipov S, Amato P, Parry S, Falk MJ. Limitations of Preimplantation Genetic Diagnosis for Mitochondrial DNA Diseases. *Cell Rep.* 2014; 7(4): 935-937.
40. Sampino S, Zacchini F, Swiergiel AH, et al. Effects of Blastomere Biopsy on Post-Natal Growth and Behavior in Mice". *Human Reproduction* 2014; 29(9): 1875-1883.
41. Eldar-Geva T, Srebnik N, Altarescu G, et al. Neonatal Outcome After Preimplantation Genetic Diagnosis". *Fertil Steril.* 2014; 102(4): 1016-1021.
42. Winter C, Van Acker F, Bonduelle M, Desmyttere S, De Schrijver F, Nekkebroeck J. Cognitive and Psychomotor Development of 5- to 6-Year-Old Singletons Born After PGD: A Prospective Case-Controlled Matched Study. *Human Reproduction* 2014; 29(9): 1968-1977.
43. Zakharova EE, Zaletova VV, Krivokharchenko AS. Biopsy of Human Morula-Stage Embryos: Outcome of 215 IVF/ICSI Cycles with PGS. *PLoS One.* 2014; 9(9): e106433. DOI: 10.1371/journal.pone.0106433.
44. Beaudet AL. Preimplantation Genetic Screens. *Science Translational Medicine* 2015; 349(6255), 1423. DOI: 10.1126/science.aad4803.
45. Locke J. *An Essay Concerning Human Understanding*. Edited with an Introduction by Peter H. Nidditch. Oxford: Clarendon Press, 1975 (1694).
46. Martin R, Barresi J. (eds.). *Personal Identity*. Oxford: Blackwell; 2003.
47. Perry J, (ed.). *Personal Identity*. Berkeley: University of California Press; 2008.
48. Tooley M. Abortion and Infanticide. *Philosophy and Public Affairs* 1972; 2, 37-65.
49. Singer P. *Practical Ethics*. Cambridge: Cambridge University Press; 1993.
50. Kaczor Ch. *The Ethics of Abortion. Women's Rights, Human Life, and the Question of Justice*. London: Routledge; 2011.
51. Boonin D. *A Defense of Abortion.* Cambridge: Cambridge University Press; 2003.
52. Martin R, Barresi J. Introduction. Personal Identity and What Matters in Survival: An Historical Overview. In Martin R, Barresi J. (eds.). *Personal Identity*. Oxford: Blackwell; 2003: 1-74.
53. Olson E. *The Human Animal. Personal Identity Without Psychology*. New York: Oxford University Press; 1997.
54. Olson E. An Argument for Animalism. In Martin R, Barresi J. (eds.). *Personal Identity*. Oxford: Blackwell; 2003: 318-334.
55. Olson E. *What Are We? A Study in Personal Ontology*. Oxford: Oxford University Press; 2007.
56. Snowdon PF. *Persons, Animals, Ourselves*. Oxford: Oxford University Press; 2014.

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