

Somatic Cell Nuclear Transfer and Human Embryo Controversy: An Update

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La transferencia nuclear y la polémica sobre el embrión humano: una actualización del debate

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ABSTRACT: It is usually the consensus that a new biotechnology might raise ethical questions, which must be faced on the basis of the existing ethical and legal paradigms. However, sometimes it may be precisely those paradigms (and the presuppositions they are built on) what should be revisited after its advent. The aim of this paper is to show how the appearance of somatic cell nuclear transfer technology caused a Copernican turn in some of our current ethical paradigms as well as induced a radical change in the way concepts such as embryo or human being were defined in our legal systems.

RESUMEN: Habitualmente pensamos que las nuevas biotecnologías pueden crear problemas éticos, que deben ser resueltos sobre la base de los paradigmas éticos y legales que existen en cada momento. Sin embargo, algunas veces son precisamente esos paradigmas (y los presupuestos que los fundamentan) lo que deben cuestionarse a raíz de los avances tecno-científicos. El propósito de este texto es mostrar cómo la aparición de la tecnología de transferencia de núcleos celulares causó un giro copernicano en algunos de nuestros paradigmas éticos, a la par que introducía modificaciones sustanciales en la forma en que nuestros ordenamientos jurídicos abordaban conceptos como el de embrión o ser humano.

KEYWORDS: somatic cell nuclear transfer, human embryo, ethics, law

PALABRAS-CLAVE: transferencia de núcleos celulares, embrión humano, ética, derecho

Introduction

When the notion of somatic cell nuclear transfer comes to our mind we usually associate it with cloning or the creation of human stem cells. In fact, in the last years, this biotechnology has been the subject of a hard ethical discussion, where different ideological trends have been opposed in an attempt to ban it, or to promote it. As commonly occurs, this discussion never reached a consensus. In fact, it has remained more than less the same for a number of years now. However, this does not mean that we cannot learn from this debate. In a quite unexpected way, what this discussion has demonstrated is that some of our legal and ethical axes were not really aligned properly. Indeed, we have learned that we can modify some of our shared knowledge so that our ethics and laws can be improved in the near future. Regarding the law, these changes have already been included in the legislations of a number of countries. Regarding ethics, it will probably take much longer to find out what has been the real impact of these new circumstances; surely, they will eventually result in some of our most beloved beliefs being revoked.

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In the following pages I will try to explain all these circumstances in further detail. For this, I will start with the legal framework, which is much easier to analyze and subsequently, I will discuss the ethical issues.

The legal framework

Twenty years ago, all the regulatory frameworks referred to the concept of a human embryo as a human being in its first stages of life¹. Keeping in mind that the human being could perfectly be defined as the result of the fecundation of a human egg by a human sperm, it is quite easy to conclude that the human embryo was defined as "*the immediate result of the fecundation of a human egg by a human sperm*"². However, these statements did not really reflect facts, as far as fertilization is an extremely complex process, being so that its final result can be seriously unlike: a fertilization may create a being capable of evolving in a balanced manner until becoming an adult individual of the specie to which it belongs, but can also originate a nearly aberrant creature³. Of course, law was not indifferent to these scientific evidences. Consequently, embryos were usually divided into two different categories, *viable embryos* (that according to the common legal definition are capable of developing into a person, that is, a born human being) and *non-viable embryos* (which are those embryos that are unable to do so). The legal status and the pool of rights associated with these embryos were completely different in most of the regulations that addressed this issue.

Nowadays, the situation has varied substantially. Most of the bills passed in the last fifteen years do not define the human embryo on the basis of its origin, but according to its potentiality. In The Netherlands, the Act dated 20 June 2002, which contains rules relating to the use of gametes and embryos (Embryos Act), states that an embryo is a cell or a complex of cells with the capacity to develop into a human being, whereas an embryo in the human body (*in vivo*) is referred to as a fetus (Article 1 (c-d)). Germany's Embryo Protection Act of 1990 defines an embryo as a "*fertilized human egg capable of developing from the time of fusion of the nuclei, and each totipotent cell removed from an embryo that is capable of dividing or developing into an individual human being if the necessary conditions prevail*". Outside Europe, in Japan, the Law Concerning Regulation Relating to Human Cloning

Techniques and Other Similar Techniques dated June 2001 defines the embryo as "a cell (except for a germ cell) or cells which has/have potential to grow into an individual through the process of development in utero of a human or an animal and has/have not yet begun formation of a placenta"⁴.

Moreover, the Opinion Statement of the Advocate General of the European Court of Justice, related to the Case 34/10, *Oliver Brüstle vs. Greenpeace eV*, stated in its point 91 that "I consider, moreover, that every totipotent cell, whatever the means by which it has been obtained, is an embryo and that any patentability must be excluded. (36) This definition therefore covers unfertilised ova into which a cell nucleus from a mature cell has been transplanted and unfertilised ova whose division has been stimulated by parthenogenesis in so far as, according to the written observations submitted to the Court, totipotent cells would be obtained in that way"⁵. This opinion obviously influenced the Court's sentence, when stating that "any human ovum after fertilisation, any non-fertilised human ovum into which the cell nucleus from a mature human cell has been transplanted and any non-fertilised human ovum whose division and further development have been stimulated by parthenogenesis constitute a 'human embryo' within the meaning of Article 6(2)(c) of the Directive", due to the fact that "Although those organisms have not, strictly speaking, been the object of fertilisation, due to the effect of the technique used to obtain them they are, as is apparent from the written observations presented to the Court, capable of commencing the process of development of a human being just as an embryo created by fertilisation of an ovum can do so (point 36)"⁶.

As might be deduced, all of these definitions share a common approach that is strictly linked with the idea of potentiality (no matter where this potentiality comes from, if a fecundation or a nuclear transfer); this is radically different from the traditional one, based on the concept of fecundation. In my opinion, the only possible explanation to this change relies on the emergence of a new framework associated to that new biotechnology called somatic cell nuclear transfer. Even though it was developed a long time ago, this technology became popular when Ian Wilmut's team created the first cloned mammal in history, which they named Dolly in 1996⁷. The impact of Dolly's birth can hardly be described. It not only demonstrated that Weismann's barrier might be wrong⁸, but, together with Thomson's findings⁹, it also opened the doors to an impressive enforcement of regenerative medicine through the development of what was quite incorrectly called therapeutic cloning¹⁰. Last but not least, the existence

of Dolly and the subsequent creation of hundreds of clones from different mammal species, finally including the human being¹¹, made us aware that human cloning was a real threat, evidence which raised a huge ethical discussion¹².

Keeping this in mind, the evolution of the legal concept of an embryo makes real sense. From the moment it was suspected that nuclear transfer may create a human being, lawyers were forced to choose between two options. First, they could keep the traditional definition of embryo intact, sustaining that a human being could only be created through fecundation. However, this option included several serious flaws. The most astonishing of them all was that it made it impossible to ban human cloning if created through nuclear transfer. From a legal point of view, in a framework as such it would have been very easy for those creating the clone to reply to those trying to accuse them that they had never performed a fertilization and, therefore, no human embryo (and consequently, no human being) would have been created at all.

The difficulties associated with assuming that kind of results made it unavoidable to address the second option, which was to design a new paradigm where the human embryo would be characterized exclusively by its potentiality, as the examples exposed show. In this new framework, concepts such as viable/non-viable embryo will obviously disappear. The first, because of its redundancy (only a cell or group of cells capable to develop onto a born human being, that is, a viable cell, would be considered an embryo) and the second because of its inadequacy (a non-viable embryo would never exist in a world where viability is the condition that must be met for it to be considered an embryo)¹³.

Therefore, the conclusion I will arrive to in the first part of this paper is that the appearance of a new biotechnology in mammals such as somatic cell nuclear transfer lead us to a huge shift in our legal framework. Moreover, this change involved a substantial improvement in the way law defined the legal status of the embryo. In the past, the idea of a person and that of an embryo appeared as completely independent in most of the European legal systems. The embryo was defined as the result of a fecundation and a person was defined as a human being, to which the law assigned a charter of fundamental rights. Thanks to this shift, the concepts of an embryo and a person have been linked; nowadays, an embryo is an entity that is able to develop onto a person, which makes the legal construction much more coherent. Finally, this approach enables us to ban any method of clone creation,

regardless of how they may be created, while avoiding general bans of a specific biotechnology, which is something that makes no real sense (let us think about the irrationality of banning IPS creation biotechnology only for the simple reason that they may be used to clone human beings). Thanks to this huge shift we are able to maintain that it is not the technology but the finality it is used for and the final result of its application which makes an act an offence, which is a great improvement provided by the new framework in comparison with the old one.

The ethical framework

If changes in the legal area have been relevant, it is in the ethical arena where they have had the greatest impact. Leaving apart for a moment the most pure utilitarian approaches (that is, those which make no distinctions between all the sentient beings), ethical paradigms regarding human beings may be divided into two different categories; those which consider the concept of a human being as the keystone of all ethical constructions and those which let the concept of person play that role. For the first stream, which we will call "conservative paradigm" for the purpose of simplifying the debate, the human being or every single human being should equally be considered morally relevant as long as we all share the same human dignity, a concept that could be defined as the special value of a human being, no matter where it stems from¹⁴. Instead, in the second paradigm, which we will call "liberal paradigm", only persons, that is, beings who posse a specific quality or pool of qualities which are considered morally relevant, regardless of whether or not human beings, should be the subject of an ethical debate; that is, *digna*.

The effect of Dolly's upraising was completely different in both paradigms. For the liberal paradigm, the rising of new biotechnologies that are capable of creating human clones did not suppose a great challenge. From their point of view, the solution to the ethical problems involved in a clone was quite simple; if the clone was created and it happened to share the quality or pool of qualities that are linked to the concept of person, it would be considered a person and treated as such. In that sense, this ethical approach seems to be perfectly capable of handling these situations.

However, the conservative paradigm will never be able to solve the ethical issues raised by cloning in such a simple way. Let me explain why. As previously stated,

this paradigm is based on the idea that the concept of a human being plays a key role in ethics. For this reason, it seems reasonable to suppose that a clear definition of human being becomes extremely relevant, due to the importance of the concept. The conservative paradigm has traditionally made a great effort in that sense, and, until the rising of Dolly it seemed that its results could be acceptable. That is the reason why it makes a sense to stop for a moment in the analysis of the possible ways to define a human being.

A human being may be defined in several ways. Initially, it may be described as a member of the human species. However, this makes it absolutely necessary to define the concept of species and human species, which has been traditionally considered as extremely difficult to accomplish (especially after new discoveries have proven our genetic links with Neanderthals, for instance¹⁵). This is why it is much more common to define the human species from the human being concept (in other words, as the conjunct of all human beings) than the opposite and this is probably why the conservative paradigm adopted this view.

However, there might be a second way of defining human beings that seems much more plausible. As commonly known, it was in the sixth century when Boecio defined the person as "*individual substance of a rational nature*" (*Naturæ rationalis individua substantia*)¹⁶. Thus, we might be tempted to strictly refer to it and forget about these issues. However, this second attempt would not solve our problems either. In fact, we must keep in mind that Boecio's definition is related to the concept of a person, not to that of a human being. Only if we consider that both terms share the same meaning we can apply this to the concept of a human being and this is precisely what is discussed here. Furthermore, even if we consider these concepts as synonyms, Boecio's definition will never allow us to determine if a specific offspring is or is not a human being unless we do not arrive at a previous conclusion about its human nature. In this sense, nature is usually defined as that which makes a being part of humankind and so it seems that we have arrived at a dead end (how can we determine its human nature if we have not previously defined "*human nature*"?).

In a third approach, the relevance of the aforementioned difficulties obliged those defending the conservative paradigm to build a concept of human being that was linked directly to some biological facts considered essential for describing it. As previously stated, a human being was defined as the being created through the

fecundation of a human egg by a human sperm. The qualities we usually associate to human beings (such as rationality, for instance) are the consequence of being human, not its condition. Therefore, we could say that human beings (considering as such whatever may come from a fecundation) are digna because they all share a common human nature, which is what determines the qualities of a concrete being and not the opposite (this is the idea involved in the classic formulation *agere sequitur esse*¹⁷, which is essential to this paradigm).

The possibility of cloning a human being using nuclear transfer seriously challenged this framework. In fact, after Dolly, the conservative paradigm had only two options. The first was to affirm that a human clone could never be a human being because there was no fertilization involved in the process and, therefore, we could not consider the result of a somatic cell nuclear transfer a human embryo (that is, a human being). However, not even the most fanatic representative of this paradigm supported this logical conclusion. Instead, most of them denounced that biotechnology as an efficient tool for creating a human being¹⁸. However, it is impossible not to arrive at the conclusion that, while doing so, they were destroying the basis of their own paradigm: if a human being is considered something or someone that has not been created by means of fecundation, it is absolutely necessary to substitute their definition of human being for a different one that does not necessarily involve the concept of fecundation. But this implies using a definition of an embryo that is completely different to the earlier one and that could be summarized in the following: an embryo is a "*X being that has enough potentiality to develop onto a Y being*"¹⁹.

This change, directly related to what happened in the legal arena, resulted in a Copernican turn in the conservative framework, regardless of whether it was noticed or not. Firstly, this option certainly allowed us to uphold that there might be embryos that proceeded from alternative sources to that of fertilization, but only at the expense of having to admit the contrary, that is, that there might be fertilized ovules who may be not-embryos due to a lack of this potentiality, something that the conservative paradigm had usually rejected. However, its implications are even stronger than these: if we are to characterize an embryo for its potential for creating a human being, then we logically need to define the concept of a human being prior to that of an embryo. If we define embryo as an X that is able to develop onto Y, we need to know what Y means prior to determining if A is X or not. In other words, the possibility of defining a human being as the result of a biological fact can no longer

be used, and if this is not possible, then how will this paradigm define the concept of human being in the future? Using a specific quality or pool of qualities? But if this were the case, wouldn't it require recognizing that the alternative proposal is better than that defended by the conservative paradigm? An urgent answer to these questions is needed. Recent attempts to face this issue, such as the DIANA criteria introduced by Suarez Lang and Huarte²⁰ and adhered, for instance, by Patrick Lee²¹ do not seem to be convincing enough as to consider it solved.

The conclusion I would like to highlight is: the conservative paradigm has to face a terrible dilemma: if it clings to its traditional definition of embryo, it will have to conclude that a human clone is not a human being; however, if it denounces cloning as an unmoral way of creating a human being, it will be recognizing that its traditional definition of human embryo is not functional any more. As far as this definition is its basis for defining what a human being is, the whole paradigm may be under serious problems.

Notes

1. Some examples are listed below:

- United Kingdom. The Human Fertilisation and Embryology Act 1990 defined an embryo as "a live human embryo where fertilisation is complete".
- South Africa. The National Health Act, (December 2003) states that "a human embryo is a human offspring in the first eight weeks from conception"
- Spain. The Law 14/2007, of 3 July, on Biomedical Research defines embryo as "a phase of embryonic development from the moment in which the fertilised ovocyte is found in the uterus of a woman until the beginning of organogenesis and which ends 56 days from the moment of fertilisation, with the exception of the computation of those days in which the development could have been stopped" (art. 3.1).

2. The Free Dictionary defines it as " the young from the moment of fertilization until it has become structurally complete and able to survive as a separate organism"

3. For example, among these we can find the chimeras or the mosaicisms, that is, cells whose DNA is altered in such a manner that they will never be able to adequately develop. All things considered, this matter is neither as spectacular nor worrying as that of the moles, which are a concoction of cells that fostered by an erratic DNA, systematically multiply, truly becoming cancers that must be extirpated from the body of a woman in order to avoid her death. The aforementioned cases are certainly not exceptional. In fact, and being optimists, data reveal that more than half of the fertilised ovules have anomalies that are so serious that they will never be used for implantation, either by the aforementioned circumstances or by some failure in any of the genes involved in the process of development, such as the OCT4 or the CDX2, without looking any further.

4. At: http://www.dnapolicy.org/policy.international.php?action=detail&laws_id=28#
5. At: <http://curia.europa.eu/jurisp/cgi-bin/...>
6. See: Oliver Brüstle vs Greenpeace, Case C-34/10, available at: <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX%3A62010CJ0034%3AEN%3AHTML>
7. The existence of the offspring was published in February 2007, but it was born in 1996. See: I. WILMUT, E. SCHNIEKE, et al., "Viable offspring derived from fetal and adult mammalian cells", *Nature*, 385 (1997), 810-813.
8. The Weismann barrier is the principle that hereditary information moves only from genes to body cells, and never in reverse. In more precise terminology hereditary information moves only from germline cells to somatic cells (that is, soma to germline feedback is impossible).
9. The following year Thomson's work on stem cells confirmed the plasticity of cells, confirming general thoughts on it. See: THOMSON, J. A., J. ITSKOVITZ-ELDOR, S. S. SHAPIRO et al., "Embryonic stem cells lines derived from human blastocysts", *Science*, 282, (1998), 1145-1147.
10. See: I. DE MIGUEL BERIAIN, "Cell Nuclear Transfer and yod cloning: a necessary identification?" in VV. AA., *Bioethics. Global and societal aspects* (European Association of Global Bioethics, 2009).
11. Masahito Tachibana, Paula Amato, et als, "Human Embryonic Stem Cells Derived by Somatic Cell Nuclear Transfer", *Cell*, Volume 153, Issue 6, p1228-1238, 6 June 2013.
12. See, for instance: I. DE MIGUEL BERIAIN, *Bioética y nuevas biotecnologías en salud humana*. (Gijón: Junta General del Principado de Asturias. Sociedad Internacional de Bioética, 2009). Published also in English as: *Bioethics and new Biotechnologies in Human Health*. International Prize "House of Representatives of the Principality of Asturias-International Society of Bioethics (SIBI)"; ROMEO CASABONA, C. M., "La cuestión jurídica de la obtención de células troncales embrionarias humanas con fines de investigación biomédica. Consideraciones de política legislativa", *Revista de Derecho y Genoma Humano*, 24 (2006), pp. 75-125.
13. This way it would be easy to provide a solution to the debate on whether a concrete cell that is created through a procedure that would not be fertilization would be an embryo or not: it would be enough for us to know if it had reasonable probabilities of development in the aforementioned sense. This certainly would not be too complex in practice. Nowadays we already have available indicators that are sufficiently precise to be able to know when we are facing a human blastocyst and what its characteristics are. Morphological analyses as well as the contrast of the information that is provided by some of its genes are more than enough to discard any possibility of development in many of the cells that up until today we call embryos. Obviously, there will always be cases in which there will exist a certain interval of doubt, but for those there would always remain the option to trace a presumption of potentiality, without changing at all the fundamental design, a presumption that in any case would always be *iuris tantum* and not *iuris de iure*.
14. In fact, most of those who embrace this paradigm associate the idea of human dignity with the belief in a common rational nature shared by all human beings, no matter what their real capabilities might be. See, for instance: ORDERBERG, D, *Applied Ethics*, Oxford: Blackwell, 2000, pp. 31-41; LEE, P., "The pro-life argument from substantial identity: a defense", *Bioethics*, 18, pp. 249-263. .
15. See: R. E. GREEN, J. KRAUSE et als, "A Draft Sequence of the Neandertal Genome", *Science*, Vol. 328, no. 5979 (2010), 710-722
16. The definition is given in Boethius's *Liber de Persona et Duabus Naturis*, ch. 3.
17. See: D. L. SCHINDLER, "Agere Sequitur Esse: What does it mean? A Reply to Father Austriaco", *Communio*, 32 (2005) pp. 795-824

18. In regards to this matter, we deem convenient at this point to make a reminder that almost the totality of those who oppose the (wrongly called) therapeutic cloning do so because they believe that the cells obtained through these procedures are embryos.
19. See: I. DE MIGUEL BERIAIN, "The human embryo: a concept that needs updating", *Perspectivas en Derecho y Genoma Humano*. Number 7, July 2006. pp. 1 y 2.
20. Antoine SUAREZ, Matthias LANG, Joachim HUARTE, "DIANA Anomalies: Criteria for Generating Human Pluripotent Stem Cells Without Embryos", *The National Catholic Bioethics Quarterly*, vol. 7, n.2 (2007), pp. 315-336.
21. Patrick Lee, "Distinguishing Embryos from Non-embryos", in Antoine SUAREZ and Joachim HUARTE (Eds), *Is this Cell a Human Being?*, Springer, 77-95