

# The biological status of the early human embryo. When does human life begins?

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ABORTION / ABORTION PILL RU-486 / ASSISTED REPRODUCTION AND IVF / BIOETHICS / CLONING / EMBRYONIC STEM CELLS / EMERGENCY CONTRACEPTION / ETHICS OF SCIENTIFIC RESEARCH / GENETICS AND GENOMICS / MEDICAL DEONTOLOGY / SPECIAL REPORTS

*“Those who argue that that embryo can be destroyed with impunity will have to prove that this newly created life is not human. And no-one, to the best of our knowledge, has yet been able to do so.”*

## Introduction

In order to determine the nature of the human embryo, we need to know its biological, anthropological, philosophical, and even its legal reality. In our opinion, however, the anthropological, philosophical and legal reality of the embryo — the basis of its human rights — must be built upon *its biological reality* (see also [HERE](#)).

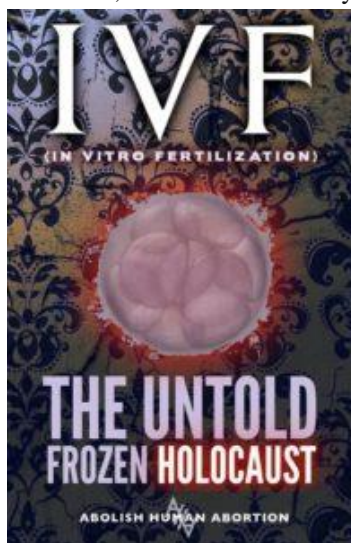
Consequently, one of the most widely debated topics in the field of bioethics is to determine when human life begins, and particularly to define the biological status of the human embryo, particularly the early embryo, i.e. from impregnation of the egg by the sperm until its implantation in the maternal endometrium.



Irrespective of this, though, this need to define when human life begins is also due to the fact that during the early stages of human life — approximately during its first 14 days — this young embryo is subject to extensive and diverse threats that, in many cases, lead to its destruction (see [HERE](#)).

These threats affect embryos created naturally, mainly through the use of drugs or technical procedures used in the control of human fertility that act via an *anti-implantation mechanism*, especially intrauterine devices (as DIU); this is also the case of drugs used in emergency contraception, such as levonorgestrel or ulipristal-based drugs (see [HERE](#)), because both act via an anti-implantation mechanism in most of the time.<sup>(1)</sup>

<sup>(2)(3)</sup> However, it also affects embryos created by in vitro fertilisation – IVF (see [HERE](#) IVF remains), which are manipulated or even disposed off when techniques such as pre-implantation genetic diagnosis – PGD are used to select healthy embryos and their subsequent gestation, to select children in parents with hereditary or genetic diseases, or to create embryos and later children in order to use their haematopoietic material to treat a sibling with a hereditary or genetic condition (see [HERE](#) embryos discarded by this technique). This practice is accompanied by a high loss of human embryos, given the low efficacy of the technique, which is less than 3%, which are manipulated or even disposed off when techniques such as pre-implantation genetic diagnosis (PGD) are used to select healthy embryos and their subsequent gestation, to select children in parents with hereditary or genetic diseases, or to create embryos and later children in order to use their haematopoietic material to treat a sibling with a hereditary or genetic condition (see [HERE](#) medicine babies techniques) .<sup>(4)</sup> In particular, though, this threat can come from the *manipulation of embryos left over from IVF*, as a result of the



freezing and thawing processes to which they are subjected for possible subsequent use for reproductive or experimental purposes, or even for intended therapeutic ends. There are currently more than **200,000 frozen embryos in Spain and 1.5 million worldwide**, not to mention the high loss of embryos entailed in the use of IVF.<sup>(5)</sup>

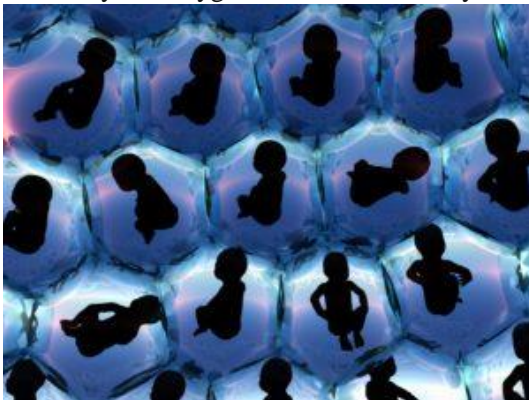
Finally, this threat also extends to embryos produced by **cloning** and **parthenogenesis**, which can then be used for presumably therapeutic and, in particular, experimental ends, mainly to obtain embryonic cell lines that can then be used for biomedical experiments, leading to the inevitable destruction of the embryos created (see **HERE**).

A critical point in the current bioethical debate is, therefore, **to establish the biological nature** of the human embryo, because of the ethical classification that its manipulation merits will depend on the category to which it is attributed (See **Human embryo. Which biological entity is required?**)

### Different positions on early embryo biological nature

There are generally said to be four positions on its biological nature:

1. The first position is that of those who consider that the human embryo, in its first days of life, is a cell cluster with no biological structure, i.e. an unorganised cluster of cells and, accordingly, with no biological or ontological value. While *this approach seems anachronistic in the light of current biomedical knowledge*, this is not the case, as reflected for example in Spanish Law 14/2006 on Human Assisted Reproduction Techniques (22 May 2006),<sup>(6)</sup> which in Article 1.2 states that, “a pre-embryo is understood as the embryo constituted in vitro, formed by a group of cells resulting from the progressive division of the oocyte from its fertilisation until 14 days thereafter”. In other words, this law accepts the obsolete theory that identifies the human embryo as a cluster of cells.
2. The second position is that of those who believe that the human zygote obtained by somatic cell nuclear transfer (SCNT) (cloning) is a different biological entity to the zygote obtained naturally (see our ethical assessment **HERE**). This has even been given its own unique name, “clonote”, with a value less than the zygote obtained by the fusion of human gametes, whether naturally or using human assisted reproduction techniques.
3. The third position is that of those who consider that the single-cell, polarised, asymmetrical human embryo, the zygote, obtained naturally or artificially, is a living being of our species, bearer therefore of

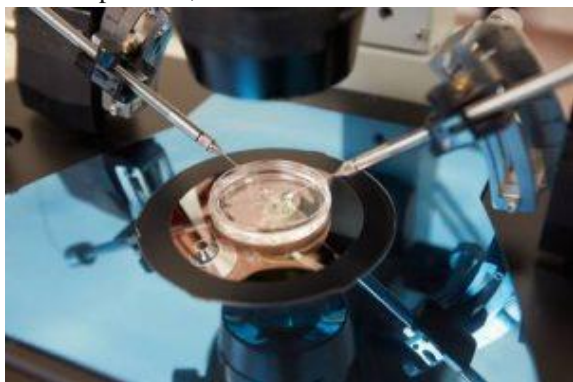


the dignity that all human beings intrinsically possess, and consequently worthy of being treated in accordance with that dignity.

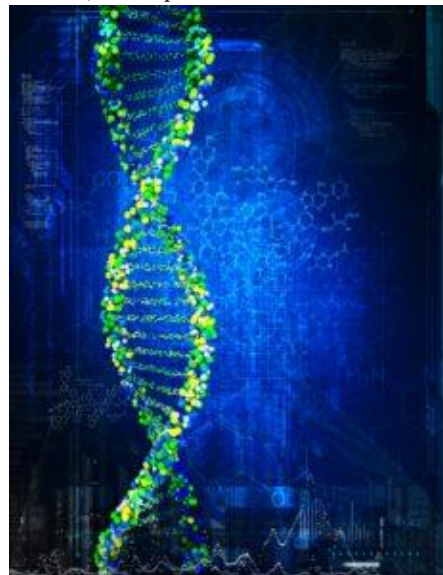
4. There is even a fourth group, which are those researchers or clinicians who circumvent the problem, and who neither affirm nor deny the human identity of the embryo; they simply state that only the scientific aspect concerns them and that discussing the human nature of that biological entity that they use does not affect their job (See **HERE**). But **can a scientist set out his experimental objectives without assessing their ethical consequences?** Considering scientific research as another human act, it is not illogical to say that, as in any other

activity of man, in his research, the scientist cannot fail to take into account the ethical side of his work. For that reason, this aspect should unfailingly be included in the development and assessment of his experimental protocols. A scientist can never stop responding ethically to the acts that he carries out.

As a result of the above, it can generally be said that, from a bioethical point of view, for those who defend the first position, i.e. those who maintain that the early embryo is a cell cluster, there would be no ethical



difficulty in *using it as a source of stem cells or experimental material* (see Report, *Genetics engineering of human*



*embryos*), because even though this will entail its destruction, it would be destroying something with no biological or ontological value, never a living human being. However, for those who defend the third position — and I count myself among them — any manipulation of that *emerging being would have to be done based on its biological and ontological reality of human embryo, that is, a living human being* (see [HERE](#)).

It is, therefore, essential to establish the biological nature of the early human embryo, in order to be able to delve further into *the open bioethical debate on the use of those early embryos for biomedical experiments or intended therapeutic goals*.

## Is early human embryo a living being of our species?

In this report, our aim is to try to establish that the early human embryo is a living being of our species, a human individual, and thus deserving of the highest respect. If we can do so, the first hypothesis could be ruled out, i.e. the theory that the human embryo is a cell cluster not organised as a living individual. In relation to the second position, that of those who argue that the single-cell embryo obtained by SCNT (clonation) or *parthenogenesis* is substantially different from the naturally-obtained zygote, which would allow it to be used in some circumstances, we shall return to that later. We shall, therefore, pause to assess whether the human embryo is a living being of our species, an individual human being.

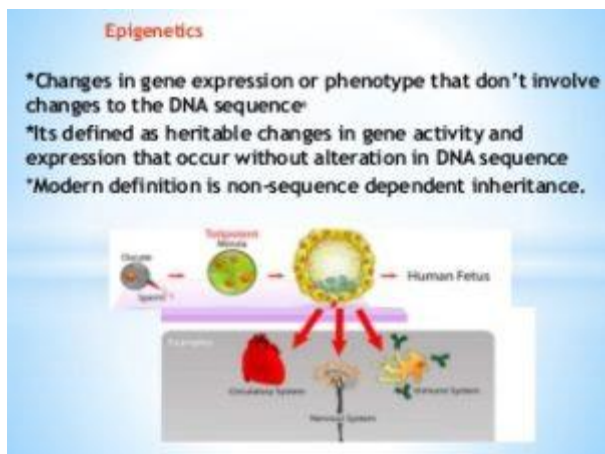
There are *numerous biological and genetic arguments to establish that the early human embryo is a living being of our species* and not a cell cluster. We shall refer to some of them

### 1. Genetic identity of the embryo

A traditionally used argument in defence of the human nature of the early embryo states that *the genome of the zygote already contains all the genetic information necessary for that new being to develop into a state of adulthood*. In other words, the genetic identity of the new individual and his membership of a particular species have already been determined in the genome. If nothing organic from outside modifies the genomic content of that emerging biological individual — since it only receives messages that help to regulate its own development from the surrounding world — it is difficult, if not impossible, to establish any leap during the evolution of its life that could mark the start of a genomic reality different from the previous. The evolution of that being is a continuous biological process giving rise to the different phenotypic realities of its development, within the living unit that identifies it as a *unique living human being*, from the impregnation of the egg by the sperm until its natural death.

However, identifying the individuality of that emerging human being by its genome is a limited and even erroneous concept. Indeed, every day there are more biological arguments to support that a human individual is something more — certainly much more — than its **genetic code**. In this respect, we have an

increasing amount of information on non-genetic mechanisms, the so-called *epigenetic mechanisms*, that have a major effect on embryo development. These are becoming better understood each day. In fact, biology has reached a clear understanding of the life processes, understanding them as a dynamic



collaboration of genes and environment that gives rise to regulated gene expression during the constitution and development of a new being. (7) We thus believe that DNA is necessary, but not sufficient, to identify a human individual. Not everything is in the genome; instead, the genetic information grows with the expression of the genes contained within it, which requires the activation and emission of its specific development program. This program is activated as the life cycle of that individual progress, enabling the new being to initiate the complete and orderly emission of the genetic messages necessary for its development to take place in an orderly and complete manner. For this reason, increasing importance is being given to

epigenetic factors, which cause minor modifications in the genome but do *not affect its nucleotide sequence*. These include DNA cytosine methylation, chromatin remodelling through histone acetylation, methylation and phosphorylation, or so called “**imprinting**“, which refers to the *ability to impede the expression of some genes in the early stages of embryonic life, especially through selective silencing, depending on whether they come from the male or female gamete*.

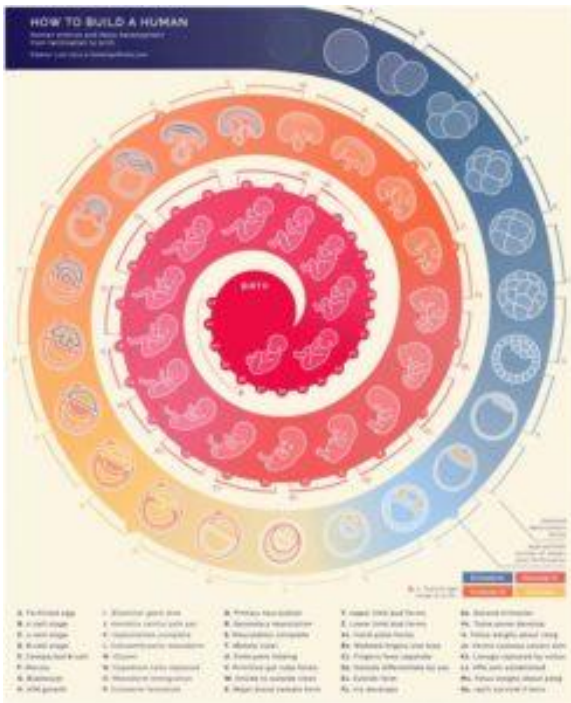
That is to say, during the development of the living being, *new genetic information not expressed directly in the primitive genome emerges as a result of the interaction of the genome with its environment*. This information is what is known as *epigenetic information*. Therefore, any phenotypic expression of a living being is the result of the gene content of their genome and the epigenetic information that is generated throughout its evolution, as a fundamental consequence of the interaction of the genome with its environment.

## 2. Is the early embryo an organised and living human being?

In addition, though, there are other reasons that support the position that the early human embryo cannot be considered a simple cell cluster, but an organised and living human being. These most notably include:

- a better understanding of the mechanisms that regulate the emission of the embryo development program;
- everything relative to so-called “position information”, i.e. *the information necessary for embryo development depends on the interactions between its own cells and the interactions of these cells with the cell niche that they occupy*;
- the role that fusion of the cell membranes of both gametes, male and female, plays in the start-up of the embryo development process and new knowledge on the mechanisms that determine the asymmetry and polarity of the zygote, and how this influences the assignment of functions for each of its cells, as well as the spatial asymmetry of the various organs in the embryo body;
- various biochemical factors, mainly intra and extracellular calcium levels, which may directly affect embryonic development
- genetic regulation of cell differentiation mechanisms;
- control of **telomerase function**;
- the biochemical dialogue established between the embryo during its stay the Fallopian tube and its mother, and the related inhibition of the mother’s immune response, which allows the embryo to implant in her uterus without being rejected (see new findings of this dialogue [HERE](#))

*Briefly review of these biological processes*



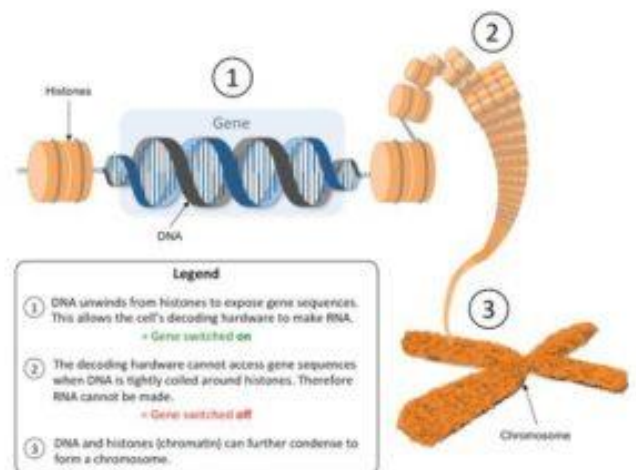
We will briefly review each of these biological processes, which as a whole and from the harmonious sequence of their actions, seem clearly inconsistent with the hypothesis that that primordial embryonic being is a cell cluster and not an organised living being.

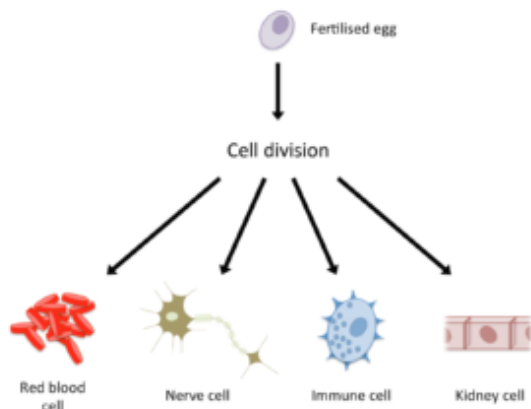
2.1. As already mentioned, in order for human life to begin, it requires not only the existence of a certain human genome, but also **activation of a development program, information contained in the genome itself**, which emits the instructions necessary for the life of that embryo to begin. (7) In sexual fertilisation, activation of the development program commences at a very early stage of embryonic life, namely the moment at which fusion of the membranes of the male and female gametes begins. It has even been suggested that it can start with the fusion of their pronuclei, which is already complete at the first cell division. Indeed, during the hours of fertilisation, the DNA of both progenitors fuses to achieve the structure and pattern of the new individual.

At the same time, however, there is a “switching on” at fertilisation, a start-up, of the expression of the information in the genes. The new fusion of the gametes, insofar as they are carriers of half the genetic inheritance, is not enough but requires that this genome interacts with its environment in order for the so-called epigenetic process to commence. This switches on the motor of embryonic development with which a new human life begins. (7)

How, though, is the development program activated? It is known that immediately after fertilisation, a DNA cytosine demethylation process begins, which is the specific trigger for initiating expression of the genome development program. Indeed, today we know that methylation of the cytosines of certain genes favours their repression, i.e. they cannot express their activity: the coding of a specific protein. Therefore, if these genes are activated as a result of a demethylation process, regulated by certain demethylases, the development program that these genes regulate is activated accordingly. That is, cytosine methylation and histone acetylation and deacetylation, determine epigenetic patterns that differ from one cell type to another and from one moment to another in the life process of the same individual. This delicately regulated mechanism is the first and fundamental step to begin the development of a new human life.

When the zygote is generated by SNCT (cloning), in order for an embryo to be produced, the genetic information contained in the somatic donor cell nucleus must be reprogrammed, i.e. the cell must be dedifferentiated. This action is due to reprogramming factors contained in the cytoplasm of the oocyte receiving the somatic nucleus, returning its genome to a genomic situation similar to that of the embryonic cells. This is when the nucleus of the transferred cell can express the orders necessary for the life of that new individual to begin.

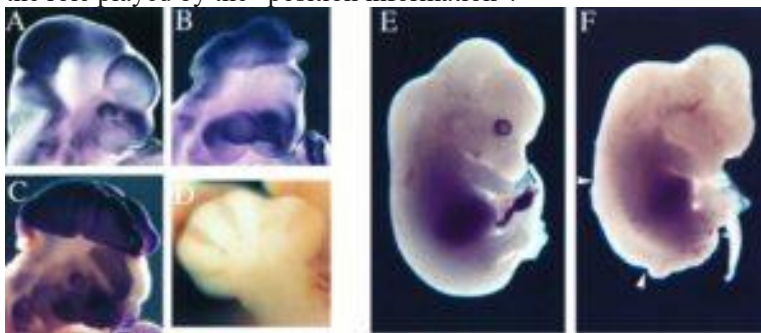




2.2. Another aspect to consider in the development of the early embryo that, in our view, means that it cannot be considered as a simple cell cluster, is ***the precise mechanisms that regulate the multiplication and differentiation of its cells***, part of these dependent on the interactions established between the embryonic cells themselves and of these with those of their cell niche.

In fact, as cell development advances — and from the first division of the zygote — an active exchange of information is established between its cells and between these and their environment, especially represented by the cell niche in which each blastomere (cell from an embryo of fewer than 8 to 16

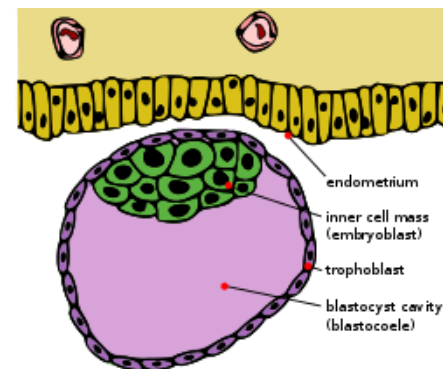
cells) is located. These orders help to ***activate the differentiation mechanisms of the embryonic cells themselves***, mechanisms regulated, among other things, through the expression of new genes, which they only do at certain times in their evolution, as a result of the aforementioned cellular interactions. That is, the behaviour of a cell, as regards principally its biological evolution, does not depend solely on the genetic information contained within its genome, but also on the information exchanged through its own cell surface; this depends first of all on the blastomeres to which it relates, and later the place that that cell occupies in the biological unit that contains it. This is what is called “position information”. That is, the development of a living being does not depend only on its genome, but also on other mechanisms that regulate the functional expression of its genes. This is conditioned, among other things, by the interactions between its own cells and the spatial situation of those cells, and by the site in which each of these is located. This regulation determines where, when and for what purpose a cell has to divide in accordance with a unitary and harmonious development. This cell differentiation towards a specific cell phenotype also occurs in adulthood and becomes particularly obvious when an undifferentiated adult stem cell, for example, a bone marrow mesenchymal cell, reaches a certain tissue. There, it is incorporated in a specific cell niche that determines that that undifferentiated cell differentiates towards the specific cells of that particular tissue. This differentiation mechanism is especially dependent on the instructions that the cells in the cellular environment send to the undifferentiated cell incorporated in that cell niche, a clear example of the role played by the “position information”.



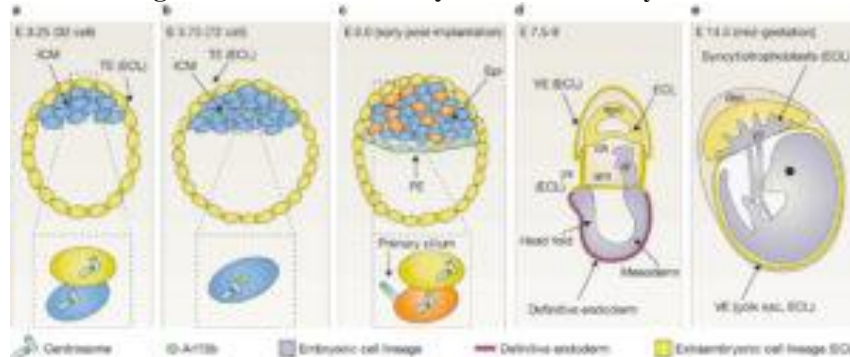
2.3. Another important aspect to consider in this single-cell human embryo and the ***embryonic phenotypes subsequently generated***, as an organised living unit, is everything related to the role that the cell membranes of the gametes play, and the asymmetric structuring of that first two-cell embryo. This is fundamentally determined by the dividing line (polarisation plane) that

is established between the point at which the sperm penetrates the zona pellucida of the egg to fertilise it and the polar nucleus of the egg itself. This cellular asymmetry, determined by the polarisation plane of the zygote, is an important factor for organisation of the embryo into cellular structures with different, precise, well-determined functions, giving rise to two unequal blastomeres with different destinies in the embryo. The blastomere with the cellular material that includes the sperm entry point is divided equatorially and asymmetrically, before the other blastomere. *These two initial asymmetric cells of the embryo are those that will give rise first to the inner cell mass (ICM), and then to the body of the embryo.* The other blastomere then divides, in this case symmetrically, thus giving rise to the 4-cell embryo. The trophoblast and the placenta are generated from the latter two cells. As well as the cellular asymmetry of the first blastomeres,

these also possess different cellular biochemical components with particular and different functions, especially related to the specific development and biological function of each of the cells. In fact, the two cells resulting from this first cell division have a different calcium concentration, which helps to regulate the genetic expression of their genome and the kinetics of their cell division. The cell with the highest calcium ion concentration divides earliest, thereby generating the 3-cell embryo. This division takes place on an equatorial plane, then the other is divided along a meridional plane. At around 24 hours of life, the embryo already has four cells. As already mentioned, the first two calcium-rich cells will give rise to the ICM and, subsequently, the body of the embryo, while the two cells with the lowest calcium ion concentration will give rise to the extraembryonic trophoblast, from which the placenta will be formed.



All of the above, aimed at demonstrating *the organisation of the human embryo in its early stages of life, and that each of the cells has a specific defined function*, has been corroborated by simple, demonstrative experiments by Zernicka-Goetz's group (see [HERE](#)),<sup>(8)(9)</sup> in which the authors labelled the first two cells of a rat embryo with different colours (one red and the other blue). From the red-stained cell arose the ICM of the blastocyst, which, as mentioned, will give rise to the body of the embryo; the extraembryonic trophoblast was derived from the other, the blue-stained cell, which in turn will give rise to the placenta and the tissues that sustain it. That is, the functional identity of the first two cells of the embryo is determined by the first cell division, with each cell already having a specific role in embryo development. This led Helen Pearson to comment, in an article published in Nature,<sup>(10)</sup> that **the biological identity of the human being is established from day one of the embryo's life.**



**Early embryo has its own cell lineage, timing, and architecture from the beginning**

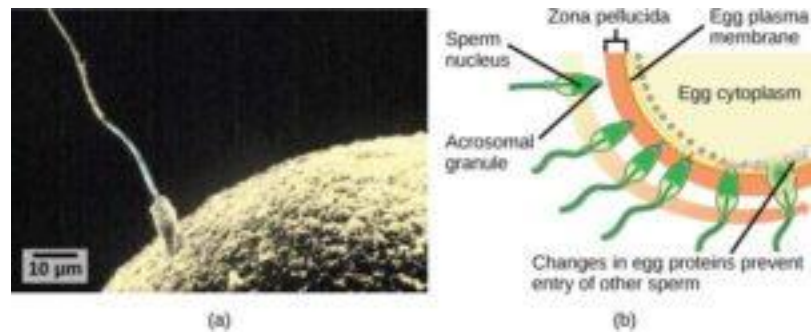
A new research from scientists at [The Rockefeller University](#) shows, for the first time, molecular and cellular processes in human development that occur up to day 14 after fertilization. "We had seen self-

organization using this system in the mouse embryo, and also in human embryonic stem cells, but we did not anticipate we'd see self-organization in the context of a whole human embryo," says Brivanlou, one of the authors of the research, together with Zernicka-Goetz. "Amazingly, at least up to the first 12 days, development occurred normally in our system in the complete absence of maternal input... We unveil the self-organizing abilities and autonomy of in vitro attached human embryos. **We find human-specific molecular signatures of early cell lineage, timing, and architecture.** Embryos display key landmarks of normal development, including epiblast expansion, lineage segregation, bilaminar disc formation, amniotic and yolk sac cavitation, and trophoblast diversification. (11)

"More recently, new mechanisms have been described that regulate embryonic cell differentiation towards different lineages. Thus, Plachta et al.<sup>(12)</sup> found that the capacity of the cells of the 4-8 blastomere embryo to differentiate depends not only on the concentration of Oct 4, as we will discuss later but also on the kinetics of this factor between the embryonic cells. This supports the idea that the embryonic cells, in their initial stages of development, present molecular differences that directly affect their biological destiny.

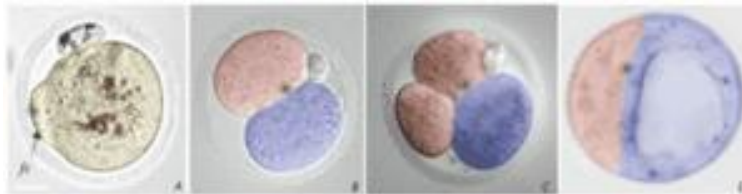
2.4. Another aspect of interest, which also supports the organisation of the human embryo in the early stages of its life, is that *small variations in the concentration and diffusion of calcium ions in the zona pellucida of the egg where the sperm penetrates seems to play an active role in the processes of division and organisation of its first cell*

Indeed, in order for the sperm to penetrate the egg, two things are basically required: first that it is activated by a glycoprotein from the zona pellucida of the egg, fertilizing, and second, the existence of signals that determine the site where the sperm must penetrate the egg, which appears to be conditioned by the increase in calcium ion levels in that zone.



A recent study provides new findings on *the mechanism by which the sperm and egg can recognise each other in the fertilisation process*, permitting the adhesion and penetration of the sperm through the membrane of the egg, as a previous step for the chromosomal crossover of both gametes and the generation of a new human being. In it, the authors described the three-dimensional chemical structure of an egg membrane receptor called Juno,<sup>(13)</sup> which advances our understanding of how this receptor interacts with the corresponding membrane protein of the sperm, called Izumo1, in the manner of a lock and key.

Furthermore, it seems that the increase in calcium ions at the sperm entry point also helps to regulate the mechanisms responsible for the first cell division of the zygote, while the calcium ion concentration may affect the spatial distribution of the embryonic cells. In fact, from the point at which the sperm reaches the egg, there is a release of calcium ions, which diffuse like a wave towards the opposite zone; at this point the dorso-ventral axis of the embryonic body is fixed. Perpendicular to it, the head-tail axis is established, in the absence of determining which pole will be the cephalic and which the caudal; this will happen in the second week of embryonic development, with which the right-left axis of the embryo body will be fixed.<sup>(7)</sup> It is also known that the extracellular calcium concentration also affects the spatial distribution of the embryonic cells, so that whether a cell is located to the left or right of the embryonic body depends on whether a gene, called the nodal gene, is expressed (left) or not (right), which depends on the calcium levels in each of these parts.



More is now known about *the asymmetric division of the zygote*, since according to a report in *Investigación y Ciencia*,<sup>(14)</sup> “an essential aspect of the development of multicellular organisms is the generation of multiple and very varied

types of cells from a single cell. In certain cases, this is achieved by asymmetric cell divisions, so called because the two resulting daughter cells receive different combinations of factors that determine their cellular destiny, i.e. the molecules that determine the type of cell that each of them will become”. In this study, the author makes reference to another study, by Derivery et al,<sup>(15)</sup> who studied the division of cells that organise the sensory organs of the fruit fly, *Drosophila melanogaster*, demonstrating a *complex and well-programmed system of divisions* that essentially consists of two phases. In the first, it was found that, towards the end of cell division, a structure composed of microtubules is assembled in the center of the cell and moves equally towards both sides of the plane that will cleave the cell in two. After this, the endosomes (molecular vesicles) are distributed homogeneously on this structure, moving in both directions along the microtubules forming it. In the second phase, just before the cell divides, the microtubules are destabilised to one side, with the result that the endosomes will spend more time on that side and will end up accumulating in it. As González, the author of the study says, “Taking into account the ubiquitous nature and high degree of evolutionary conservation of the components involved, the mechanism described herein could be operational in other species and cell types in which asymmetric distribution of a load — vesicular or another type — transported by proteins that move along an asymmetric bundle of microtubules”. This could provide important clues to understand the functioning of fundamental biological processes in higher organisms and among them, why not in the asymmetric division of the zygote? This would undoubtedly confirm that the human embryo from the **zygote phase is a living being that controls its development with very specific biological mechanisms, which could in no way occur in random cell clusters.**

2.5. Another aspect to consider, which decidedly goes against considering the early embryo as a simple cell cluster, is *the genetic regulation of the mechanisms of cell differentiation, which points towards specifically determined epigenetic control*. Indeed, it is known that, as cell division progresses, the cells of



the embryo lose plasticity, i.e. they gradually lose the potential to give rise to different cell types. This mechanism arises and is partly regulated, by the expression of different genes, especially Oct-4 (see [HERE](#)), which already exists in the first embryonic blastomeres, and even in the egg. It codes for a transcription factor, which is necessary in order for each blastomere to *maintain its totipotency*, by slowing down the differentiation impulses from the cells in its environment. In fact, each of the cells of a 3-5 day embryo maintains its ability to differentiate into cells of all types of tissues through the action of Oct-4. However, as embryo development continues, its cells lose Oct-4 activity and consequently the mechanism they have to remain undifferentiated. When they become differentiated adult cells, the Oct-4 activity has almost disappeared; in contrast, when these differentiated cells are dedifferentiated to return to their embryonic state, in cell reprogramming processes, the Oct-4 levels are recovered. There are other genes that also help these cells to remain undifferentiated, the most significant among them being Nanog.

**2.6. *The enzyme telomerase is also a fundamental factor in the regulation of the life cycle of embryonic cells.*** Telomerase determines that the telomeres (terminal part of the DNA chains that protects the chromosomes from degradation) do not become smaller with each cell division, which prolongs their life cycle. The size of the telomeres decreases with each cell division, causing the cell to age. Embryonic stem cells and tumour cells therefore contain high levels of telomerase that prevent the telomeres from shortening, favouring the indefinite proliferation of these cells. That is, it seems that the aging mechanisms of the first embryonic cells are finely regulated, which we believe can only occur in well-structured biological entities and never in a cell cluster.

2.7. Another biological fact that objectively suggests that the human embryo is an organised living being is ***the peculiar biochemical dialogue established between the embryo and its mother*** (see [HERE](#) our article), which starts from the embryo, and which, in some way, helps to regulate its evolutionary dynamics through the Fallopian tube. In effect, *during its journey through the tubes, the early embryo sends specific molecular messages to both the tube and its mother, to which both respond to others*. As mentioned, this biochemical dialogue between mother, tube and child allows the embryo to move forward at the right speed to be able to access the uterus at the precise time for its proper implantation.<sup>(16)</sup>

Recently, a further step has been taken in the ***dialogue between the mother and the embryo, her child, during its passage through the Fallopian tube and implantation in the maternal endometrium***. The maternal endometrium produces and secretes other compounds in the endometrial fluid in which the embryo is enclosed, which are fundamental for its implantation; these include several integrins ( $\beta 3$ ,  $\alpha 4$  and  $\alpha 1$ ) and interleukins (such as interleukin-1), as well as chemokines (IL8, MCP-1), leptin and human chorionic gonadotrophin.

Now, however, with the publication of an article in *Development* (see [HERE](#)),<sup>(17)</sup> which we will discuss here, that ***biochemical and immunological dialogue has been extended to the genetic field*** (see our article [HERE](#)), after investigators found that elements in the fluid secreted by the endometrium, and which the child absorbs during the implantation process, may modify the gene expression of the child.

This has major biomedical and bioethical consequences. From a biomedical point of view, this genetic interaction could predispose the embryo to both metabolic and genetic disorders, i.e. it could increase the child's risk of some diseases, such as type 2 diabetes.

This interrelationship between mother and child could also occur in **“in vitro” fertilisation** when donor eggs (i.e. not from the mother) or surrogate mothers are used. In the first case, in the implanted embryos from fertilisation of donor eggs, the genetic expression of its genome could be modified by the influence of the maternal messages. In other words, information would be incorporated into the child's genome from the maternal endometrium, so that somehow (and very partially), it would come to constitute an ***embryo genetically modified by the influence of the biological mother***.

Moreover, in the case of surrogacy, ***the surrogate mother could also influence the child's genome***, i.e. biological links could be established with the child carried, beyond those created by the pregnancy.

In both circumstances, by modifying the expression of the child's genome, the relationship between the egg donor or surrogate mother and the child born would be substantially implemented, which could undoubtedly create more biological and social problems than these practices currently entail.

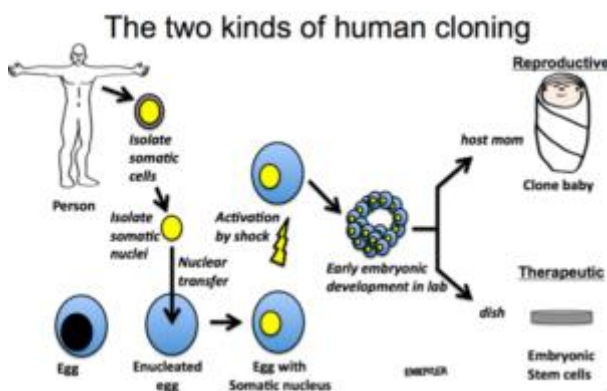
This is, therefore, a very interesting paper that, in our view, supports the human nature of that biological entity that is the early human embryo, and which adds fresh insights, especially in the field of IVF and surrogate motherhood.

Related to the biochemical dialogue discussed above, the phenomenon of “maternal-fetal immunotolerance” is particularly significant.

All biological systems have a particular function, aimed at fulfilling a specific purpose in order to facilitate the development and maintenance of the living being that incorporates them. In relation to this, the immune system has the critical purpose of fighting the entry of foreign elements into a living body, so they fulfil a fundamental physiological function, which is to prevent infections; on the other hand, however, they can also give rise to autoimmune processes through which the body attacks itself, causing various major diseases.

However, there is one circumstance — in our opinion unique in the immune system of mammals — which is that *the immune system can be inhibited in the mother to allow a foreign body, namely her child, to be implanted in her body without being rejected* (it must be remembered that 50% of the child’s genetic endowment comes from the father and consequently is foreign to the mother). This is what happens with a so-called immune tolerance between mother and embryo (see [HERE](#)).

As a result of the above, we believe that the complex organisation of that living being, the pre-implantation human embryo, responsible for the aforementioned biological processes, is inconsistent with being an unorganised cluster of cells. In other words, that the human embryo is a living being of our species appears to be beyond any reasonable biological doubt.



### 3. Nature of the human embryo obtained by somatic cell nuclear transfer (cloning) or parthenogenesis

As mentioned previously, among the different positions on the biological nature of the human embryo is that of those who consider that the human embryo obtained by SCNT (cloning) or parthenogenesis (see [HERE](#) our medical and ethical assesmet) has a different biological nature to that of the zygote naturally obtained by fusion of the egg and sperm. In fact, it even has a different name: clonote or parthenote. This biological difference is

based fundamentally on the fact that the clonote and parthenote lack the genetic information contributed by the fusion of the egg and sperm, as well as the male genome, information that they consider necessary for that clonote and parthenote to develop into a healthy adult human being. This theory is supported by the biological fact that, until now, it has not been possible to generate human individuals by these techniques, <sup>(18)</sup> although other types of mammals have been cloned, the first being Dolly the sheep.

If this hypothesis were true — given that a living adult human being cannot be generated from a clonote and parthenote — that could be used as a source of biological material, especially stem cells, for biomedical experiments. This could be done with no additional ethical difficulties because although it would have to be destroyed to obtain the aforementioned biological material, a biological entity that could never develop into an adult individual would be destroyed. That is, we would not be talking about a human embryo, but rather an embryoid body. However, if the blastocysts produced by cloning or [parthenogenesis](#) could continue developing into an adult being, something hitherto unknown, it would be risky to say that the clonotes and parthenotes could be used for biomedical experiments with no ethical difficulties, since the dignity of human nature is not determined by the mechanism used to generate the embryo, but by the nature of the adult individual produced, a nature that, in our opinion, is difficult to argue is not that of a being of our species.

#### 4. Arguments against the position that the zygote is a human individual

For some, however, there are arguments against the classification of the zygote as a biologically defined human individual. Among these, it is the problem of the uniqueness and indivisibility of the zygote, essentially derived from the fact of its possible twinning until 14 days of development, that which arouses most controversy. Those who defend this position argue that if the embryo can divide, it would not be an individual. Against this argument, it could be said that the embryo, in its early stage of life, is unique but divisible; later, as its life cycle advances, it will become a being, equally unique, but indivisible. It should be clarified that individuality and indivisibility are different concepts. The fact that a biological individual can be divided is not contrary to its individuality, just as the fact that they can divide is not contrary to the uniqueness of simpler animals, especially single-celled organisms. This is especially true for those animals that reproduce parthenogenetically. I do not believe that any biomedical expert would dare to say that these animals are not individuals of their species, before dividing, and that those that emerge from that division are not different individuals of the same species. In summary, the biological concept of the individual does not mean that it cannot be divided, but that there is an organised living structure within it with the characteristics typical of individuals of its species. The concept of individual in biology does not refer so much to the inability to divide, as to the fact that there is a real organisation that endows that particular individual with the biological category of living.



Others maintain that human life begins with the pregnancy, i.e. that it begins with the implantation of the embryo in the mother's uterus, and that therefore any manipulation of that biological being before the pregnancy begins (in other words, before implantation) is ethically acceptable, because they would not be acting on a developing human being, but on what they call a "pre-embryo". In our opinion, it is an elementary mistake to confuse viability with living being. Viability requires the previous existence of a living being that can later be eradicated. Furthermore, some of the supporters of this theory contend that, in order to guarantee its viability, it is essential that the embryo can feed

itself, something that would not be accomplished, according to them, until it consolidates its implantation in the maternal endometrium. However, these people should be reminded that the embryo already feeds itself with material provided by its mother before implantation, since from the impregnation of the egg by the sperm until its implantation, i.e. during the passage of the zygote/embryo through the Fallopian tube (approximately 5 days) until its definitive accommodation in the mother's womb, the new being feeds itself with the material contained in the cytoplasm of the egg itself, which, of course, has been provided by its mother.

The idea that embryonic life begins with implantation, that is, from day 14 post-fertilisation, was proposed in 1979 by the United States Ethics Advisory Board. This notion was later endorsed by the Australian Waller commission and especially the Warnock Commission, who also in 1984 started to use the term "pre-embryo" to describe the pre-implantation embryo.

In relation to the position that human life begins with the consolidation of implantation, a recent article<sup>(19)</sup> is very illustrative. The article reports that 57% of American gynaecologists believe that gestation, and therefore human life (because if there is no living being, it can hardly be gestated) begins at fertilisation, and that only 28% believe that it begins with implantation of the embryo in its mother. This decidedly supports the position that human life does not begin with the pregnancy, but at fertilisation.

#### 5. Final consideration

In light of the above, we believe that we can safely say that the life of a human being clearly begins with the fusion of the pronuclei, male and female, i.e. at fertilisation, and that this primitive embryo is therefore

deserving of the respect owed to all adult humans, which will consequently condition that any manipulation of the early human embryo, not intended for its own good, and especially its destruction, is ethically unacceptable.

In our opinion, however, there is another, possibly more definitive, argument for defending the inviolability of the early human embryo, which is that human life possesses such dignity, a direct consequence of its own nature that doubts that *the newly generated biological entity, the embryo, might be a human being should be sufficient for it to be respected unconditionally*. In other words, it would not even be necessary for those of us who say that human life begins at fertilisation to prove it — something I believe we have done — but those who argue that that embryo can be destroyed with impunity will have to prove that this newly created life is not human. And no-one, to the best of our knowledge, has yet been able to do so.

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