International Journal of Modern Anthropology
Int. J. Mod. Anthrop. (2018) Vol: 2, Issue No: 11, pp: 14 - 46
Available online at: www.ata.org.tn ; DOI: http://dx.doi.org/10.4314/ijma.v2i11.1

Original Synthesis Article

New insights into human early embryo development: a particular theoretical study

Hassen Chaabani

Laboratory of Human Genetics and Anthropology, Faculty of Pharmacy, University of Monastir, 5000 Monastir, Tunisia. E.mail: hassenchaabani@gmail.com

*(**Received** 18 January 2018; **Accepted** 5 Mars 2018; **Published** 5 May 2018)*

Abstract – The experimental research on the subject of human early embryo development has been remained insufficient because of ethical norms and legal constraints. In this context, the carrying out of theoretical studies could speed up the slow knowledge progression on this subject. Thus, I present here a particular model of theoretical study based on a synthesis of selected published experimental results combined with what has been provided from my interpretation of scientific signs masked in some Qur'an verses. In the obtained detailed scenario, I consider that the third cleavage, resulting in 8 blastomeres, is coupled to a particular rearrangement in which 2 daughter cells seem move down and 2 others move up; while the 4 remaining cells seem stay at their initial position (I called them "4 HI cells"). Nevertheless, I consider that the fourth cleavage, resulting in 16 blastomeres, is coupled to a rearrangement that gives the impression of a harmonious descent: in fact, one of each two daughter cells seems pushed down. This descent materializes a morula top–bottom axis, which will go to coincide with the embryo-abembryo axis of the blastocyst. Just after this fourth cleavage, during a polarization process, the nucleuses of the entire 16 cells move towards a basal region. I consider the polarized 16 cells as the precursors of all the Troph-Ectoderm (TE cells), whilst acknowledging that the 4 HI cells are at once precursors of TE cells and the Inner Cell Mass (ICM). Moreover, in this study I evoke, for the first time, the possible contribution of the microvilli of some outer cell surfaces to the guidance and move of the early human embryo all along the oviduct and during the initiate steps of its implantation in the endometrium. At the end I contribute to the classification of the concept of knowledge and I show how this study represents a model of fruitful exchanges between philosophy, science and religion.

Key words: Human early embryo development - Troph-Ectoderm (TE cells) - 16 blastomere stage - Morula / blastocyst axis - Microvilli - Early embryo transport - Initiation of implantation - Knowledge definition - Qur'an scientific signs - Philosophy, science and religion – Dynamism of Holy Qur'an.

Introduction

Generally human fertilization occurs when a man's sperm, or spermatozoon, combines with a woman's egg (secondary oöcyte), inside a woman's uterine tube (usually in the outer third of the uterine tube). This combination leads to the mixing of the 23 male and 23 female chromosomes in a single-cell embryo called a zygote, which like the ovum, remains enclosed by the strong membrane of glycoproteins designated zona pellucida. Thus human zygote is the first diploid cell formed following fertilization able to give rise to all of the specialized cells engaged in the constitution of a new human being.

About a day after fertilization a first division of the zygote forms 2 cells with no cytoplasm synthesis. After this division (cleavage), series of other cleavages take place decreasing cell size with each subsequent division. The dividing cells are called blastomeres and remain enclosed within the zona pellucida. At the 8 cell stage, blastomeres are undifferentiated and aggregated into a sphere (see Brison et al. 2014).

By about 3 days after fertilization, while still in the uterine tube, the embryo contains 16 to 32 cells configured as solid ball of cells is called a "morula" because it looks somewhat like a mulberry. At this stage the cells start to bind firmly together in a process called compaction, and cleavage continues as cellular differentiation begins (Boklage 2009). After about 4 days (during the 5th and 6th days) the embryo contains 32 to 64 cells which appeared differentiate in a small group of internal cells surrounded by a larger group of outer cells. The latter give rise to the trophoblast, also designated Troph-Ectoderm (TE), while the inner cells become the Inner Cell Mass (ICM). The outer TE cells secrete fluid to form a cavity into the centre of the morula, creating a hollow blastocyst. The latter enters the uterus, and must "hatch" from the zona pellucida before its fixing to the uterine wall (Fleming 1987). In fact the ICM will give rise to all parts of the embryo and some extra-embryonic mesoderm such as amnion and the allantois (a structure that will later develop into the umbilical cord). On the other hand, the TE cells do not contribute to the embryo proper, but they participate in the other extra-embryonic structures particularly those involved in placenta formation and implantation.

This distinction between TE cells and ICM is the first differentiation event in human and other mammalian development. As it was proposed by Tarkowski and Wroblewska (1967) this lineage segregation is directed by the position of the cell, namely cells on the inside and cells on the outside are exposed to distinct environments and to different amounts of cell contact, resulting in distinct fates. Because all cells so organized in blastocyst have only a small amount of yolk, they require implantation onto the uterine wall in order to receive nutrients. Just before this implantation, the ICM further diverges into early epiblast (EPI), consisted of pluripotent cells that are able to give all the tissues of the fetus, and an extraembryonic lineage called primitive endoderm (PrE) (Gardner 1998; Niakan et al. 2012; Saiz and Plusa, 2013).

As shows this overview, although the principal events of early human embryo development are known innumerable related details and mechanisms are not yet revealed. Even if some of them are already provided in mouse, we could not allocate them automatically to human: in fact, although this development shares some similar morphological characteristics between these two species several details differ such as the timing of events and global gene expression pattern (Kan et al. 2010; Wong et al. 2010). Thus to reveal all human-specificities of this early embryonic development, researchers must intensify their experimentation on human embryo material; but, this is not possible owing to ethical norms and legal constraints. For that reason, I present here a theoretical study based on a synthesis of fragmentary existing knowledge combined with assumptions deduced from my interpretation of Qur'an scientific signs. These assumptions can be classed within what I call "preliminary knowledge". The latter would become a "ready knowledge" if it is supported by empirical findings. Revising the historic relationship between philosophy, science and religion, I show through my present study a model of their fruitful exchanges.

Polarity of human zygote

The sexual reproduction in animals is characterized by the formation of a zygote (egg) the cell mass of which is generally not uniformly distributed, but it exhibits significant differences. In order to describe this polarity, the terms animal pole and vegetal pole were invented to describe the two opposite poles of the egg. Due to gravitational forces, the yolk within settles to the bottom of the egg and forms the vegetal pole;

consequently, the polarity becomes more apparent when more yolk is present in the egg. But, in human the zygote is very small (only 100 μm in diameter) and has sparse, equally spaced yolk; thus we cannot speak about a real polarity in its general convention. However, in some mammals, some asymmetry is represented by the polar bodies that, extruded during meiosis, are located very likely in a region that could be considered as within the animal pole, but it is not demonstrated in human.

At the molecular scale, as indicate above, during the 2- and 4-cell stages, the human embryonic genome activation (EGA) is yet absent or minor. Thus, maternally derived gene products, mostly RNA molecules, could be already present in the zygote and are responsible, among other things, for the development of these two first cleavages. In the following I show that the possibility of an unequal distribution of maternally derived gene products in the zygote could not be supported.

Characteristics of the three first human embryo cleavages

Each of the two resulting cells from the first cleavage of the zygote is totipotent (defined as the ability to contribute to all embryonic and extra-embryonic lineages). This is demonstrated in the case of their separation by accident: each has the ability to develop into a new organism. But usually they remain together to co-operate in the development of just one new individual. In this usual case, the human zygote undergoes series of cleavage divisions in which the net size of the embryo remains the same. In other words, this cleavage represents a form of mitotic cell division in which the cell divides but the total volume remains unchanged.

As the one of other Mammals the human zygote has sparse, equally spaced yolk and is thus isolecithal (Greek, “equal yolk”). The cleavage of the human zygote is holoblastic (Greek holos, “complete”) meaning that the cleavage furrow extends through the entire cell. In sharp contrast to most animals this cleavage is relatively slow in mammals; it is about 1/day (one cleavage during 12 to 24 hours) in humans. In addition, as in Mammals, this cleavage is asynchronous, namely human blastomeres do not all divide at the same time. So embryos could contain odd numbers of cells (Gilbert 2000).

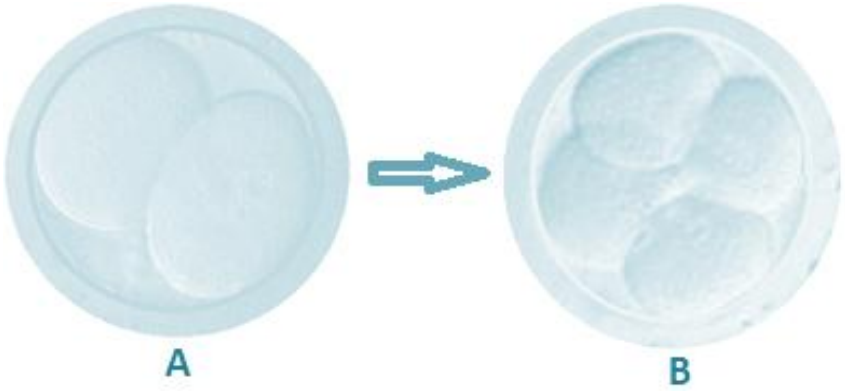
The first two cleavages

According to Gulyas (1975), the holoblastic cleavage of human zygote would be rotational: it involves a normal first division along the meridional axis (vegetal-animal

axis if we consider the region of polar bodies as an animal pole) giving rise to two daughter cells; one of these two cells divides meridionally, and the other divides equatorially. However, the recent work of Doronin et al. (2016) showed that all 4-cell human embryos have four developmental variants that are based on the sequence of appearance and orientation of cleavage planes during embryo cleavage from 2 to 4 blastomeres. In any case, I think that we would not give importance to the two first cleavage planes because, first the vegetal-animal axis mainly determined by the location of polar bodies in a region that could be considered as within the animal pole was not demonstrated in human embryo and the cluster of cells during the 2 first cleavages have no particular plan. In other words this 'polar body' region, if exists, seems to exert any or little control over the destiny of the resulting 4 cells. Second the 4 first cells seem do not keep their resulting position but they move following unfocused rearrangement within the zona pellucida (see Fig. 1, A and B).

But while neglecting the effect of plane orientation of the first two cleavages, one cannot exclude the possibility of an unequal distribution of maternally derived gene products in the zygote. Taking into account this eventuality and the fact that the blastomeres of a 4-cell stage human embryo are, very likely, potentially totipotent (flexible and able to develop into blastocysts with ICM and TE) (Van de Velde et al. 2008), it is reasonable to consider that the first two cleavages were done in such a way that each of the 4 resulting cells bring together all types of maternally derived gene products initially present in the zygote.

Fig. 1 : A. First cleavage of human zygote (*The 2 cells are totipotent)*
B. Second cleavage of human zygote (*The 4 cells undergo an unfocused rearrangement)*



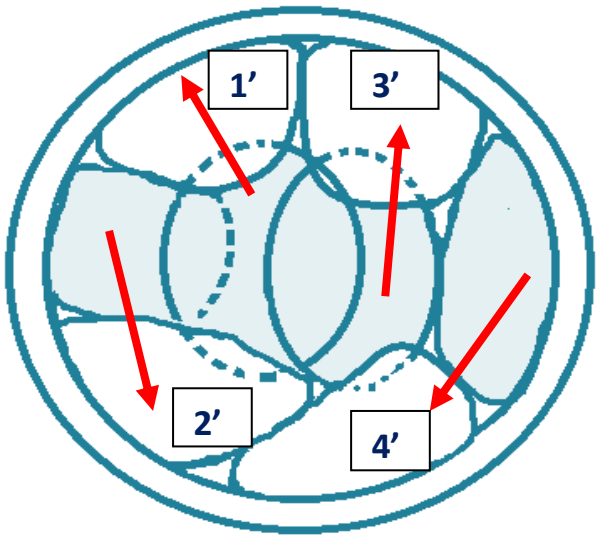
The third cleavage

I propose some new details concerning the third cleavage as follows: I consider that the first 4 cells (1, 2, 3, and 4) undergo a third cleavage coupled to a particular rearrangement, which gives the impression that two daughter cells (2' and 4') move down, and two others (1' and 3') move up for starting the coverage of the 4 remaining cells (*colored cells*, Fig. 2). The latter seem stay at their initial position: they try to keep a relatively 'High' position with a tendency to be in 'Internal' position during the future divisions and, consequently I call them "4 H I Cells". I have established this new consideration as been the most suitable background that goes with what concerns the next cleavage according to my Qur'an verse interpretation.

Moreover, it may be noted that the resulting 8 cells, having approximately the same size, undergo some changes already described previously:

- An evident beginning of the embryonic genome activation (EGA) (Dobson et al., 2004; Vassena et al., 2011); while in the mouse, a zygotic gene activation (ZGA) is initiated during the 1- to 2-cell stage (Wang et al., 2004).
- Blastomeres start to bind together but only the presence of primitive intercellular junctions at this 8-cell stage were observed (Pereda and Croxatto 1978; Mottla et al. 1995),

Fig. 2 : Diagram of the third cleavage of human zygote (8 cell stage)
The 4 HI cells are colored; arrows indicate directions of a particular cell rearrangement coupled to this third cleavage



Characteristics of the fourth and fifth cleavages

Several details relating to the 8-16 and 16-32 divisions of human embryos have not yet been identified. However, my interpretation to the Qur'an verse n° 6 of Sourat Azomor among those of several other verses related to the human creation (Chaabani 2006) has revealed concealed Qur'an signs that could concern some of these unknown details. In this verse God said what means "*He created you from a single identity, then made from it a pair and takes down for you eight pairs of cattle (Anaam), He creates you in your mothers' abdomen following successive creation stages underneath three darks. That is "Allah", your unique true God who has the universe possession, how do you remote from faith in Him*". As I have noted previously (Chaabani 2006), the verses on scientific subjects generally would have a simple apparent meaning and another independent scientific one wherein hided scientific signs could be revealed. I have nominated this situation among others "Integration of multiple meanings for the same Qur'an verse". Here I present only my scientific interpretation of this verse:

- First, I consider that the terms "a single identity" concerns what we name nowadays "Zygote". In fact the latter has not any meaning towards current common languages, but it is mainly derived from Greek zygótos "joined" or "yoked". Thus, this name is as those of the majority of "International scientific vocabulary" that has been made by taking a word with a general simple meaning from one of the languages of antiquity, often Latin and Greek. Hence these scientific names used since the first steps of the development of different scientific fields, keep on to be without any change; while major scientific characteristics of the named things have been revealed in modern times. In other words, such stagnant scientific terminology stay without any meaning that could reflect the current state of knowledge. However God "Allah", since about 12 centuries, had given real scientific names that reflect the current state of knowledge (and even the future one) such as in the present case He consider what we name our "zygote" as our "single identity". In fact each person begins as a **single** cell in which all his characteristics are stored in genetic materials included in this cell and consequently the person himself or rather his **identity** is potentially present in it. Hence, what we name human **zygote** represents a real **single identity** from which human being could be created.

- Second, Allah said that our creation following "successive creation stages". This is proved by scientists and called nowadays "the successive stages of human embryogenesis".

- Third, the meaning of "**three** darks", although seems at the beginning somewhat unclear, it represents a very accurate scientific sign that would concern the **three** main walls that shield the embryo situated in the deeper (darker) center of the lower part of the mother abdomen: (1) the abdominal wall, (2) the uterus wall, and (3) the extra-embryonic wall. Even each of these three walls is composed of **three** secondary structures: - The abdominal wall is mainly composed of three layers of muscles: they are, from the outside to the inside: external oblique, internal oblique, and transverse abdominal; - The uterus wall is composed of three coats: an external or serous, a middle or muscular, and an internal or mucous; and - The extra-embryonic wall is composed of three principal membranes: the amnion, the yolk sac (that develops into the allantis) and the chorion.

- Fourth, the term "*Anaam*", Arabic name in the plural means cattle (camels, sheep, horses …….), seems incompatible with the denotation that could be given to all the verse. So, I consider that the intended meaning of *Anaam* is the Troph-Ectoderm (TE) cells: namely this term is used in this verse as a metaphor whereby TE cells are like *Anaam* (cattle) on the grounds of the shared roles towards humans. In fact they play an important part in the transport, nutrition and body protection of humans after their birth. The same contribution is carried out by TE cells to humans before their birth (during their embryologic and fetal stages).

On the basis of these considerations, the first part (relating to our subject) of this Qur'an verse would give us three important scientific details:

1. The number of precursors of all TE cells is 8 pairs of cells (16 cells)
2. The emergence of these 8 pairs of cells (precursors) is coupled to a descent (*He takes down for us eight pairs of TE cells*): combined this information with scientific data, I propose two moves downwards that could be happened at the emergence of 16 cell stage:

- A first descent proposed for the first time (Fig. 3, A): the 8-16 plane divisions (very likely more and less perpendicular to an apical-basal axis) are positioned in such a way that the resulting cells undergo immediate rearrangement giving the impression of a harmonious descent: in fact, one of each two daughter cells seems pushed down. This

permits the 4 HI Cells (*colored ones*) (Fig. 3, A), already covered by only one cell layer at the top, to continue to keep a relatively high position.

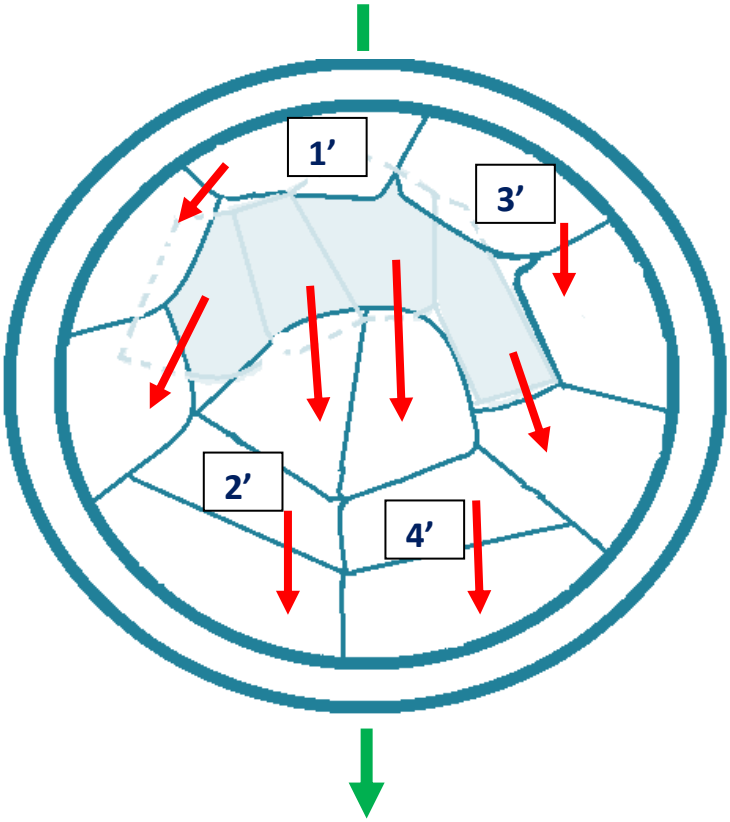
- A second descent (Fig. 3, B): just at the emergence of 16 cells, all their nucleuses moves towards a basal region (second descent). This nucleus descent is not yet proved experimentally in human, but it is demonstrated in mouse (Reeve and Kelly 1983; Ajduk et al. 2014). It represents a part of the polarization process which is also characterized, among other things, by the fact that the surface microvilli, almost homogeneously distributed on the first blastomeres, become restricted to an externally facing apical pole (over the free surface) (Reeve and Zionek 1981; Dale et al. 1995; Nikas et al. 1996). Thus, I consider that in human the polarization process would be similar to that in mice with some human particularities such as it occurs at the 16 cell stage and not at 8 cell stage. The polarity in the next divisions is mainly maintained thanks to specialized junctions (compaction process), which, as noted by Lopata et al. (1983), appeared in complete organization at this 16 cell stage.

3. As demonstrated in the Figure 3 (A and B) the two descents imply that, since the 16 cell stage, the global embryo ball (morula) moves mainly in determined position according to a top-bottom axis which coincide with a general apical–basal axis. However, each cell has its proper apical-basal axis, which according to its position is almost parallel to the general one or slightly deviated from it. During the next stage, blastocyst stage, this top-bottom axis of the global morula goes to coincide with the embryo-abembryo axis of the blastocyst (embryo at the top part).

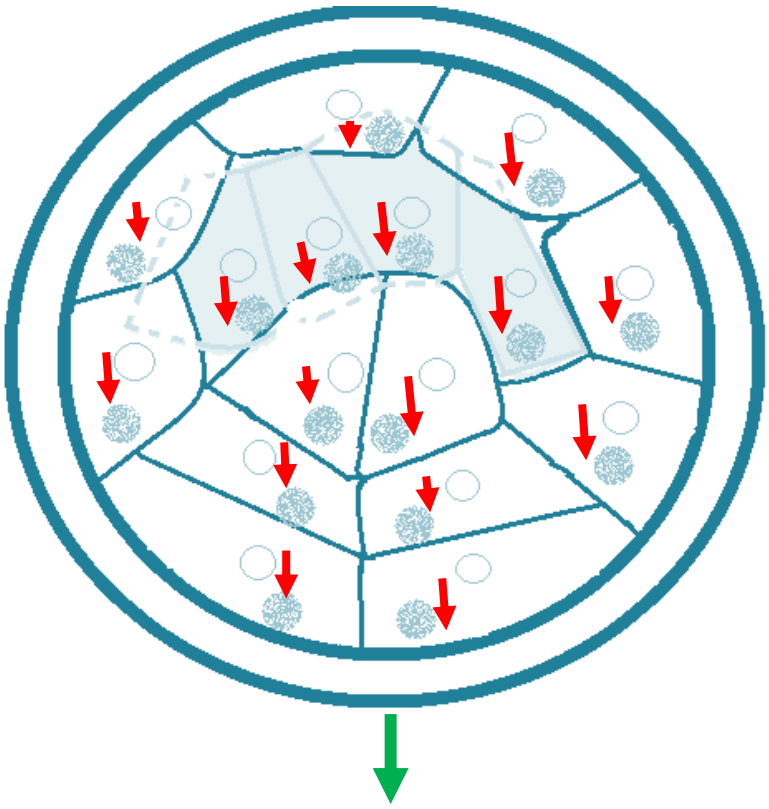
4. Finally I could extend the first deduction as follows: the 16 (eight pairs) polarized cells represent the precursors of all the TE cells, whilst acknowledging that the 4 HI cells are at once precursors of the TE cells and the Inner Cell Mass (ICM). In fact, during the fifth cleavage, these 4 HI cells undergoes an asymmetric division giving rise to 4 polar outer cells (TE cell), and 4 apolar cells (ICM cells) that keeps their initial position; while the other 12 cells undergoes a symmetric division given rise to similar polar outer cells (TE cells). Hence the fifth cleavage in the human embryo leads to the emergence of a morula of 32 cells differentiated in two subpopulations of cells that differ in their properties and position: 28 outer cells (TE) and 4 inner cell mass (ICM). During the sixth cleavage only symmetric divisions would occur giving a blastocyst of 64 cells (56 TE and 8 ICM). In mouse these two models of divisions were already proposed, but in different stages (from the 8 cell stage) and different portions of cells involved in each of the two models of division (Chrode et al. 2013).

Fig. 3 : Diagram of the fourth cleavage (16 cell stage)

A. The first descent: *The 4 HI cells are colored; these cells and their daughters (1', 2', 3', and 4') undergo a fourth cleavage coupled to a rearrangement downwards (red arrows indicate the directions); green arrow represents the top- bottom axis of the morula*



B. The second descent: *The 4 HI cells are colored; red arrows indicate the movement of all nucleuses towards a basal region; green arrow represents the top- bottom axis of the morula*



Do TE cells contribute to the transport of early human embryo?

It is known that *Anaam* (cattle) take part in our nutrition (we eat their meat) and indirectly in our body protection particularly from cold (for example some of our clothes are made from their wool and / or leather). Figuratively, the TE cells, take part in our nutrition and protection before our birth: they become structures, called membranes, a part of which develop into a large portion called placenta that permits the embryo / fetus to be nourished (contribution of oxygen and nutrients) by the mother. In fact, this placenta grows after implantation into the wall of the uterus and is joined to the embryo / fetus by the umbilical cord. However the other part of these membranes shares in the formation of the outermost (around the embryo / foetus) membrane "chorion", which with the "amnion" (filled with an amniotic fluid) contribute to the protection of the embryo / foetus.

Moreover this metaphor provided in my interpretation of the Qur'an verse (n° 6 of "Sourat Azomor") could intend that TE cells, in addition of their contribution in nutrition and protection of human embryo, contribute to its transport. In other words, as some *Anaam* (cattle), particularly camels and horses, contribute to our transport; some TE cells would contribute to the transport of our early embryo all along the oviduct until the uterus. To my knowledge, this eventuality is not evoked and the move of the early human embryo is not yet deeply studied. I believe that it may be as complex as the sperm cells travel, in which several factors are involved. A brief presentation of these factors could give idea on those involved in the move of our early embryo.

The sperm cells travel

Human sperm cells can "smell" chemicals given off by the egg that may attract them when they are in close proximity (Spehr et al. 2003). But before this "chemotaxis", dominated only near the egg, sperm cell must navigate a distance that is thousands of times longer than its length passing through the diverse environments of the cervix, the uterus and, finally, the oviduct. During this relatively long travel; evidence suggests that contractions of the cervix and uterus help to pump sperm cells along the first part of their travel. However, in the oviduct, sperm cells move against the flow of uterine mucus, and for accomplish this swimming against a current, mechanisms range from peristaltic pumping to temperature sensing and response to fluid flow variations "rheotaxis" were proposed. In this way, the study of Kantsler et al. (2014) shows that

sperm cells use head-on currents to guide themselves up fallopian tubes toward an egg particularly by moving upstream along the walls of the channels in a spiral movement that, moreover, increases the chances of meeting the egg. Thus I can sum up these data by classing what are involved in the sperm cell travel in intrinsic and extrinsic factors:

- as intrinsic factors, the sperm cell, due to its long flagellum, (1) has the ability to move properly, (2) has the ability to accomplish a particular spiraling movement within a complex reothaxis permitting a swimming against a current, and (3) has the ability to "smell" chemicals given off by the egg.
- as extrinsic factors, (1) contractions of the cervix and uterus would help the accomplishment of the first stage of sperm cell travel, and (2) egg (secondary oöcyte) secretes chemicals that may guide sperm cells to it when they are in close proximity.

The transport of the human pre-implantation embryo

The fertilization of the human egg takes place at the ampulla (distal third part of the fallopian tube "oviduct"). Once fertilized, the resulting cell "zygote" begins to develop in embryo, which spends about 5 days traveling into the remaining oviduct parts until it reaches the uterus, where it finally implants. It is considered that this embryo transportation occurred thanks to the movement of the epithelium cilia of the oviduct and its rhythmic muscular contractions. This oviduct role appears to be preferentially regulated by hormones that cause a distinct regionalization of activities depending on the day in the female reproductive cycle (Pulkkinen 1995).

Some unclear points let think that the pre-implantation embryo move seems more complex than to be accomplished thanks to only the two considered extrinsic factors, for example:

- These two extrinsic factor concern only the travel all along the oviduct; while at its arrival in the uterus the embryo ball (blastocyst) must be (1) attracted towards the endometrium (orientation), then (2) it must be hatched and (3) it must adjust itself in such a way that the embryonic pole faces the endometrial surface (apposition).
- The defect of the move of pre-implantation embryo leads to procreation problems such as the possibility of implantation outside the uterine cavity (ectopic pregnancy). The consideration of oviduct cilia dysfunction as the main cause of this defect is questionable. For example, only about 50% of women with Kartanger syndrome (due to impaired cilia motility) have procreation problem. This could be explained as follows: one possibility is that some women having this syndrome would have oviduct cilia

motility more and less normal. Another possibility is that their cilia motility is defected, but the embryo movement was accomplished thanks to the contribution of other factor (s) that has balanced the cilia dysfunction.

From these two examples of problematic points and what I have inspired with the case of sperm cells, I propose, for the first time, the involvement of intrinsic factor beside the two known extrinsic factors in the move of the pre-implantation human embryo. According to what is deduced from my interpretation of the Qur'an verse presented above, this intrinsic factor would concern the TE cells and their precursors. But how these cells could intervene in the guidance and the move of the early human embryo? In fact microvilli carried by human egg continue to be present after fertilization and on resulting cells of zygote divisions. Moreover, as stated above, the surface microvilli, almost homogeneously distributed on the first blastomeres, become from the 16 cell stage restricted to externally facing apical regions. I consider that outer early embryo cells (TE cells or their precursors) through external exposed microvilli surfaces represent the intrinsic factor that contributes to the guidance and the move of the early human embryo. Before presenting related explanations and mechanisms, I prefer, for a better comprehension, to review briefly the present state of knowledge on microvilli functions.

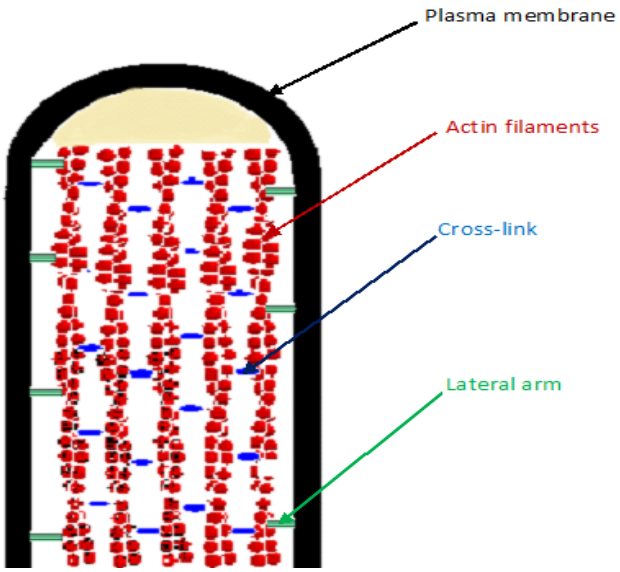


Fig. 4 : A schematic presentation of upper portion of a microvillus

Microvilli are cell surface thin protrusions, composed of cytoplasmic membrane and parallel bundles of actin filaments. In each bundle actin filaments held together by cross-linking proteins; while lateral arms link the actin filament bundle to the plasma membrane (Fig. 4). Microvilli are most recognized in epithelial cells of intestinal and renal brush borders and functions of such microvilli include expansion of cell surface area for absorption and molecule presentation and inhibition of cell adhesion (Chhabra and Higgs 2007). But microvilli are present on the surface of numerous other differentiated cells and show other specific important functions such as those of microvilli in sensory receptor cells for sound, light, and odor perception (for review see Lange 2011). However, in the case of immune cell microvilli, although that several functions have been proposed only some have been demonstrated particularly that of the leukocyte capture to blood vessel walls (Muller et al. 2006) or that they represent distinct inducible membrane domains that can regulate direct cell-cell interactions via grouping and three-dimensional presentation of cell-surface receptors (Greicius et al. 2004). Moreover, other functions specific to oocyte microvilli, which could act as a platform to concentrate adhesion / fusion proteins and / or to provide a membrane protrusion with a low radius of curvature. They may also have a dynamic interaction with the sperm that serves to capture the sperm cell and bring it into close contact with the oocyte plasma membrane (Rung et al. 2007).

I believe that these examples of different types of cell microvilli show only a part of their real functional competence, because the pointed out functions are not yet enough studied at the molecular level and recent molecular studies begin to show the complexity of these functions wherein several related unknown mechanisms would be revealed. In addition numerous other specific cell microvilli are not yet studied and their roles are still a mystery as is the case here of the microvilli found mainly on external exposed surfaces of early human embryo cells. Thus I get back to my hypothesis that these microvilli would contribute to the guidance and the move of the early human embryo. As I have only explained how I have deduced and established this assumption, in the following I will show at what degree it could be compatible with related empirical knowledge trying, at the same time, to propose preliminary possible mechanism(s). To do this, I will be good to begin to split this possible combined function into two abilities: Ability of

sense and guidance, and that of the move itself. This, only permit to propose the mechanism(s) proper to each of the two abilities without deny their evident interconnection.

- Ability of sense and guidance:

Generally, it is accepted that cells sense their physical environment. For example various cell types, such as cells of the intestinal epithelia, proximal tubule of the kidney, nasal epithelia and placental syncytium, can through their microvillar surfaces sense and interact with the fluid environment (for review see Miura et al 2015). Here I propose that external exposed microvillar surfaces of the early human embryo cells can sense and interact with environment inside the oviduct and the uterus. But how this could be done while early embryo cells are covered by the Zona Pellucida (ZP)? In fact the latter when it is observed through sophisticated techniques, it shows a delicate meshwork of thin interconnected filaments, in a regular alternating pattern of wide and tight meshes. Namely from the zygote stage, ZP represents some alteration and the wide meshes correspond to "pores" of the "spongy" ZP, whereas the tight meshes correspond to the compact parts of the ZP surrounding the pores (Familliari et al. 2006). Thus through these pores microvilli can be in contact with the surrounding fluid environment and therefore, all along the oviduct, they could guide the movement of the embryonic ball and even sense when it is jammed to get going again by reacting suitable move. Moreover, arriving in the uterus microvilli TE cells could intervene in the first steps of the initiation of the implantation process.

In fact this ability allowing cells to adapt to their physical environment represents a phenomenon called mechanotransduction, which is an integral part of cellular physiology and would consist of translating mechanical forces and deformations into biochemical signals such as changes in intracellular calcium concentration or activation of diverse signaling pathways. Extensive research over the last decades has identified several molecular players; however, many components, and especially the identity of the primary mechanosensor(s), remain incompletely defined (Jaalouk and Lammerding 2009, Miura et al. 2015). Following a different research track, other authors suggested that the structural mechanotransduction pathway is rather a physical connection between extracellular environment and the genome (Wang et al.2009; Tamiello et al. 2016).

- Ability of move:

As stated above, I consider that the move of the early human embryo would be accomplished thanks to combined extrinsic factors (the movement of the epithelium cilia of the oviduct and its rhythmic muscular contractions) and an intrinsic factor carried out by the external exposed microvilli surface cells of the embryo itself. But how these microvilli surfaces can intervene in this physical exertion? On the basis of reasoning and intuition guided by the current knowledge on microvilli, I propose the following simple preliminary mechanism:

Concentrated at several clusters of external exposed surfaces, microvilli would be able to start series of activation / deactivation. In a given situation, this activation concerns one or some cluster(s) of microvilli (over a surface or some surfaces). I consider that the activation state is associated to the fact that microvilli become longer "elongation", while when they return to their initial size "reduction", they are deactivated (deactivation state). The elongation of a cluster of united microvilli at the same time and towards the same direction will generate mechanical force (Fig. 5). The latter is exerted against the Zona Pellucida (ZP) leading to an imbalance of the embryo ball from the top-bottom (vertical) axis. This activation of microvilli is followed by a deactivation (return to their small size) leading to a return of the embryo ball to a top-bottom axis in a more advanced vertical position (Fig. 5 and 6). Hence, this repeated alternation of activation / deactivation of microvilli of determined exposed surfaces helps the embryonic bull to move forwards in corresponding determined direction. When the situation needs some change of the direction, the alternant activation / deactivation process passes to other microvilli cluster (s) on other surface (s), which can guide the move towards the left, the right, the top or the bottom following the requisite direction.

Following the same principle of this mechanism, the embryo ball can move more rapidly and powerfully by rotating around itself in any direction (see Fig. 7). This could be done particularly to get going again when accidentally the embryo ball is jammed within the internal oviduct wall. This rotational mechanism is similar to that of a water walking ball: in the latter the ball turns thanks to the pressure putted by the person through his hands and/or his feet against the internal side of this ball; while in the case of the embryo ball, it turns thanks to the pressure putted by TE cells through their microvilli cluster(s) against the internal side of the ZP (Fig. 7).

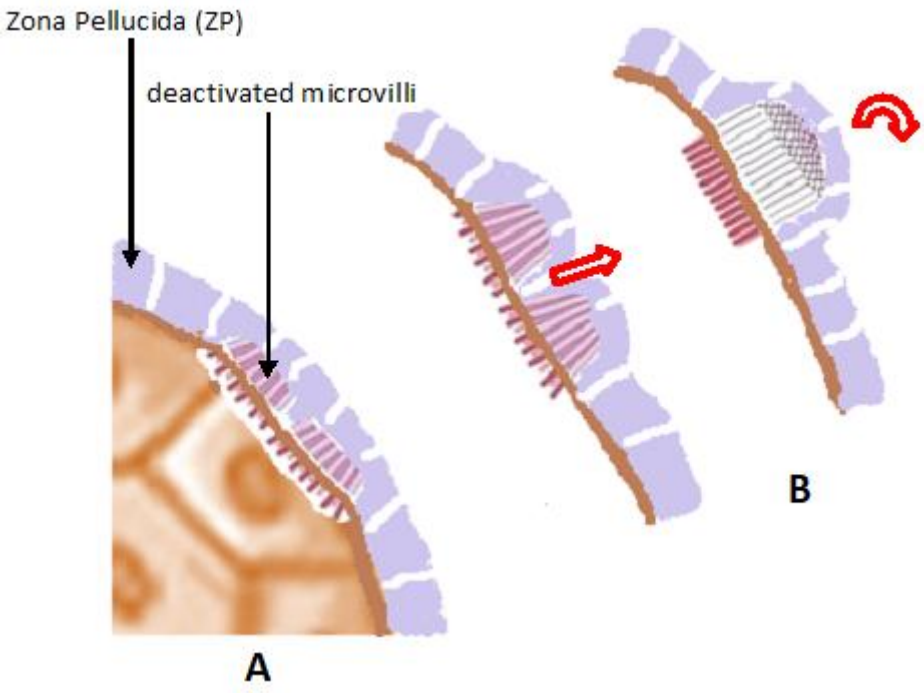


Fig. 5 : A schematic presentation of the microvilli dynamism:
- A: deactivation state **- B:** activation (elongation) state
The elongation of microvilli is coupled to a possible intermicrovillar adhesion and clustering and consolidation of two or more clusters in a robust one permitting an improved force (represented by the red arrows)

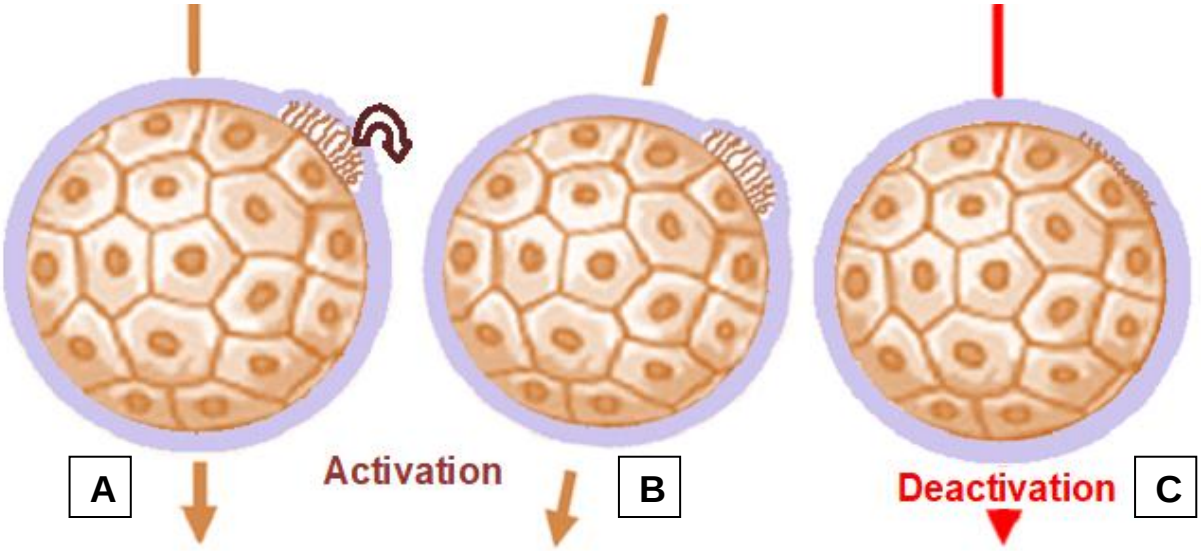


Fig. 6 : Simplified mechanism of the move of the embryo thanks to microvilli
The elongation of microvilli exerts a force against the Zona Pellucida (ZP)(position A) leading to an imbalance of the embryo ball from the top-bottom (vertical) axis (position B). This activation of microvilli is followed by a deactivation (return to their small size) leading to a return of the embryo ball to a top-bottom axis in a more advanced vertical position (position C).

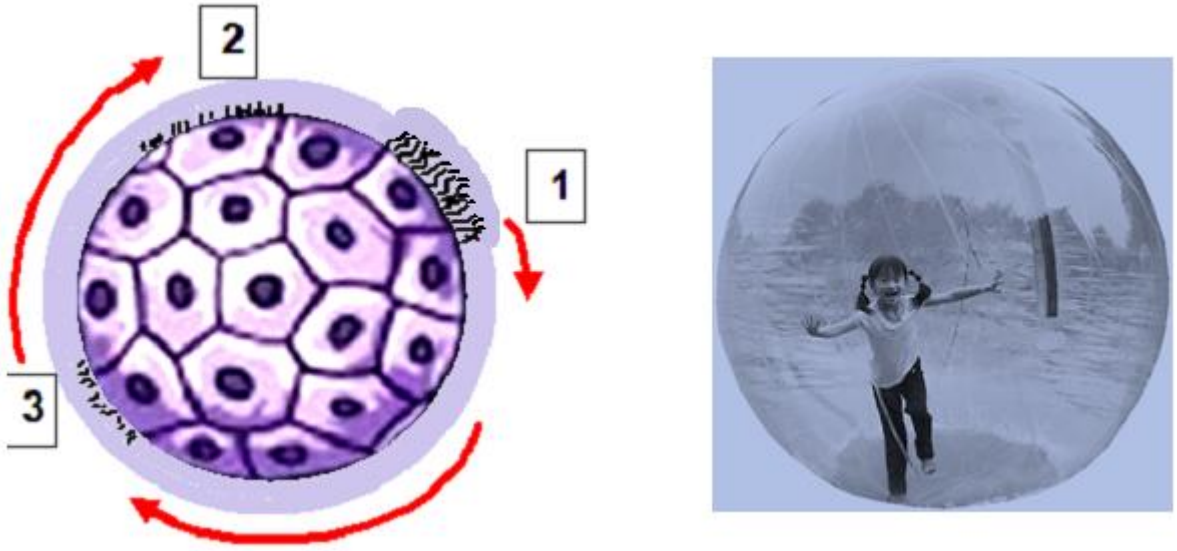


Fig. 7 Rotation of the embryo ball around itself (a striking resemblance with a water walking ball)

The embryo ball can move more rapidly and powerfully by rotating around itself in any direction. This could be done particularly to get going again when the embryo ball accidentally is jammed within the internal oviduct wall. As showed in this figure each rotation needs that microvilli at the position **1** *are activated and initiate the move, then microvilli of the initial position* **2** *arriving to the position* **1** *become activated and so on). This rotational mechanism is similar to that of a water walking ball: in the latter the ball turns thanks to the pressure putted by the person through his hands and / or his feet against the internal side of this ball; while in the case of the embryo ball, it turns thanks to the pressure putted by TE cells through their microvilli cluster(s) against the internal side of the ZP.*

This preliminary mechanism just proposed does not show any discordance with empirical data on microvilli. In fact, microvilli are highly dynamic and can grow and shrink (McConnell et al. 2009) and their development "elongation" would be mainly the consequence of the polymerization of actin filaments. Accordingly, what I have proposed as activation/ deactivation of microvilli, associated to the elongation / reduction of their size, is also associated to polymerization / depolymerization of actin filaments. Although the starting and the regulation of such activation seems complex and it is far from being fully revealed, some molecular factors such as members of the ezrin-radixin-moesin (ERM) protein family and some of their interaction partners would play a key role in the organization microvilli development in various types of epithelial cells (Fehon et al., 2010). In the same way, it was noted that microvilli abundance

and/or length correlate well with the extent of ezrin phosphorylation, and several kinases have been implicated in the direct T567 phosphorylation of ezrin in intestinal epithelial cells, including protein kinase B2/Akt2 (Shiue et al., 2005). However, it was demonstrated that polymerization and depolymerization of actin filaments can generate significant forces for cell movements in the absence of any associated molecular motors (for review see Dogterom 2005).

Finally I want to point out an artistic vision on the move of the early embryo ball thanks to microvilli. As stated above, the proposed first mechanism is described as a repetitive alternation of activation / deactivation of microvilli: activation that leads to an imbalance of the embryo ball from the top-bottom (vertical) axis, followed by deactivation that leads to a return of the embryo ball to a top-bottom axis. This regular rhythmic move seems similar to that of a floating boat or rather to the rocking (forwards and backwards) of a camel rider due to the slow regular steps of the camel. This artistic nice similarity comes to support my explanation of the cited Qur'an verse showing that the metaphor concerning the transport of early human embryo is in double aspects: In addition to the fact that the TE cells would contribute to our transport before our birth (during the pre-implantation stage) as do *Anaam* (camels and horses) after our birth, the rhythm of this transport is similar to the rocking of a rider of one of *Anaam* categories "the camel" (this nice similarity is turned into picture: Fig. 8).

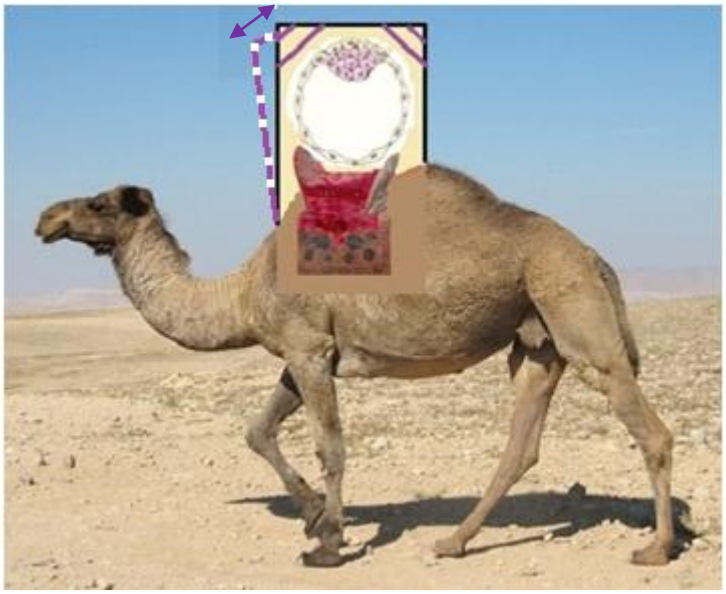


Fig. 8. Artistic vision of a nice similarity
(Arrow indicates the repetitive regular rocking forwards and backwards)

Contribution of TE cell microvilli to the initiation of the implantation process

Arriving in the uterus cavity, TE cells microvilli of the blastocyst, would contribute in the initiate phases (orientation, hatching and apposition) of the implantation. In fact, these phases are not yet clearly described in human. However, it would be considered as somewhat similar to those observed in placental mammals, particularly rhesus monkeys (Enders et al. 1986):

- Just prior to implantation, the blastocyst comes near the endometrium (orientation), I propose that this attraction happens thanks to the ability of TE cell microvilli to smell a molecular factor probably secreted by the endometrial epithelium and reacts by suitable move provided by microvilli following the general principle of the mechanism just described.
- Then the zona pellucid (ZP) is shed and the blastocyst appears hatched. On the basis of the fact that the ZP remains intact if an unfertilized egg is placed in the uterus under the same conditions (Walter and Boulpaep 2014) I consider that this "Hatching" process would be mainly occurred thanks to an intrinsic factor from the blastocyst itself very likely at the outer cells (TE cells) level that through their microvilli could secrete a particular substance and / or exercise a pushed force leading to the "Hatching" process.
- I have already considered that, in human, morula keep a global top-bottom axis (see Fig. 3), which will go to coincide with the embryo-abembryo axis of the blastocyst (embryo at the top part). Arriving near the endometrial epithelium in this situation the uncovered blastocyst ball acquires a particular position "apposition": It must rotate around its center through about 90° until the top of the ball (the embryonic pole: taken by the inner cell mass (ICM)), becomes more and less in equatorial position for oppose the endometrial surface (Fig. 9, C). In other words, the blastocyst must adjust itself in such a way that the embryonic pole faces the endometrial surface. I propose that TE cell microvilli contribute in carrying out this dynamic process "apposition" thanks to the activation of a suitable microvilli cluster (s) leading to its slight rotation in only one direction (Fig. 9). Moreover, as the embryo ball is already uncovered (elimination of the ZP) TE cell microvilli, more developed at the embryonic pole, found themselves in a direct contact with the endometrial surface able to smell molecular factors that, secreted at the endometrial surface, help the carrying out of the following steps of the implantation. In fact some studies are noted some aspect of this molecular dialogue between the blastocyst and endometrium by reveling some possible mediators such as

cytokines and chemokines acting (Bentin-Ley et al., 2000) or MUC1, a transmembrane glycoprotein, expressed at the apical surface of endometrial epithelial cells (Margarit et al. 2010). In fact, the global process of implantation in human is controlled by a complex and sophisticated interaction between embryo and endometrium, which begins at the early stages of oocyte maturation (Emiliani et al. 2005). Several hormones and factors involved in this dialogue enable synchronous development of the oocyte and maturation of the endometrium (for review see Teh et al. 2016).

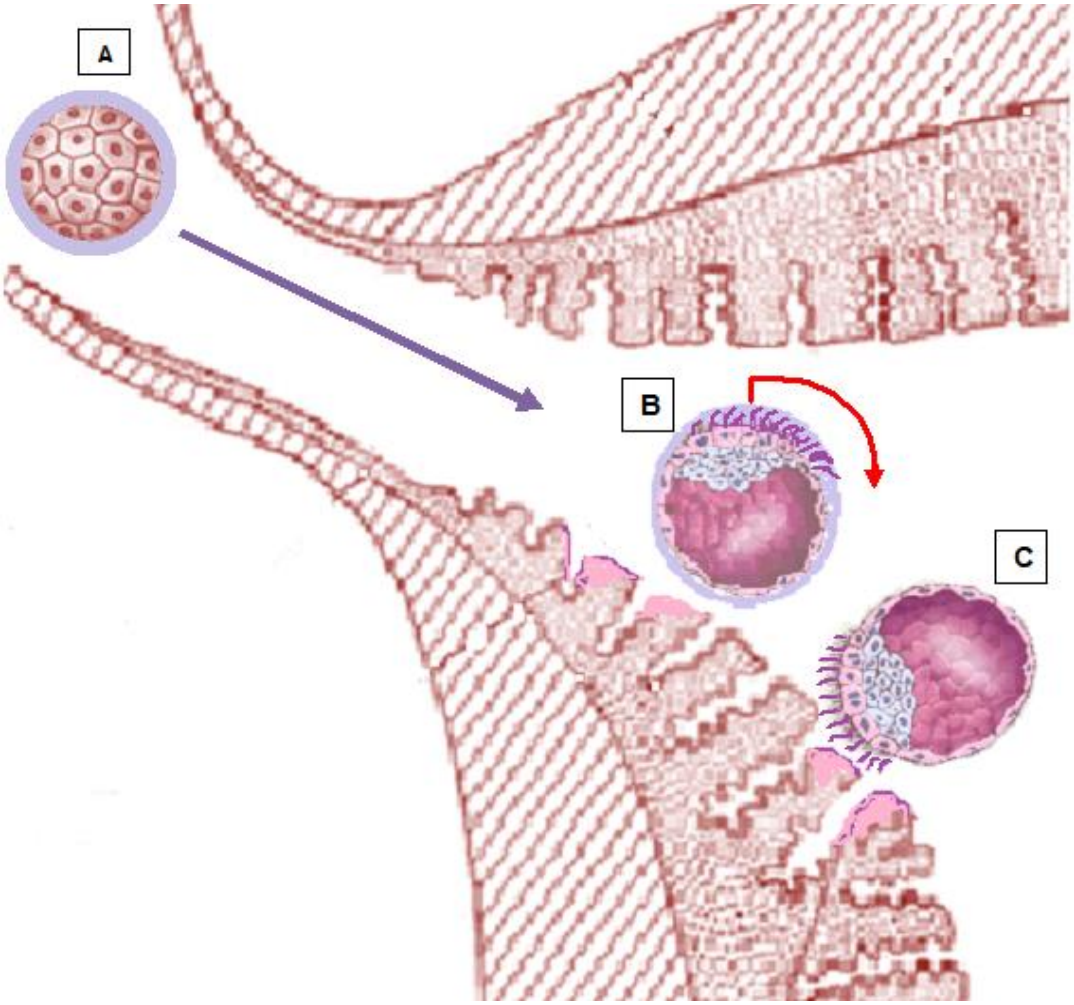


Fig. 9. A schematic presentation of the possible contribution of the TE cell microvilli in the "apposition" phase of the implantation process.

***B**: blastocyste in its usual position (top-bottom axis: embryo at the top part). **C**: arriving near the endometrial epithelium, it becomes hatched and, thanks to the activation of microvilli cluster(s), rotes around its center through about 90° aiming to adjust itself in such a way that the embryonic pole faces the endometrial surface.*

Particularities of the present theoretical study:

To ensure a good understanding of such particularities, two points should be reviewed before: the relationship between philosophy, science and religion, and the classification of the concept of knowledge, which represents one of the issues of what we call nowadays theoretical philosophy.

Relationship between philosophy, science and religion:

Science was born and developed for a long period in the bosom of philosophy. In fact, in ancient times, writings were mainly theoretical and what is known today as philosophy included all sciences, humanities and arts. During the Golden age of Muslim civilization (from about CE 850 to 1400), eminent scholars are, in the majority, at the same time philosophers and scientists. For example Ibn Rushd, better known as Averroes (CE 1126-1198), he was a Spanish-Arabic philosopher, physician, lawyer and polymath. While, Al-Ghazali (CE 1058 –1111), although he was essentially a theologian, a mystic and a jurist, he had well taken cognizance of philosophy and sciences of his epoch making for the first time a real clear distinction between philosophy and sciences such as mathematics and medicine (see Al-Ghazali). From this time the separation of sciences from philosophy began gradually for reached an evident independence during the Renaissance: The 'Rebirth' of Science & Culture (refers to a period in European history approximately between the 14th and 16th century CE), then the Enlightenment (a European intellectual movement of the 17th and 18th centuries).

Particularly from the Golden age of Muslim civilization another problem emerged: it concerns the questionable relationship between religion and philosophy. Although several theologians were against philosophy particularly when it is used falsely to lead to the atheism, the great philosopher Averroes, showed that there is no conflict between religion and philosophy, believing rather that they were just different ways of reaching the same truth, and consequently, there is no incompatibility between religion and philosophy when both are properly understood (see Averroes). When the sciences are more developed and completely separated from the philosophy, the debate turn out to be between Science and religion and has been somewhat persist until nowadays and often studied within the field of philosophy itself in an interdisciplinary field of “science and religion” (also called “theology and science”). The conflict

between science and religion, influenced by variable socio-cultural conditions, has had its ups and downs over the past centuries. Concerning the three monotheist religions (Judaism, Christianity, and Islam) the last peak period occurred in the nineteenth century. I believe that the conflict between these three monotheist religions and science represents a false problem. However, I consider that the real problem is in a general misunderstanding of these religions: First, the Holy text of these religions are often misinterpreted and / or, except for the case of Holy Qur'an (unique Islam book), are subject of some changes. Second innumerable things were falsely allocated to each of these religions and their accumulation during the past centuries given a distorted picture more and less different from the real one.

According to my consideration some contemporary scientists have shown that there is any discordance between science and Holy Qur'an wherein God "Allah" encourages all peoples to seek knowledge and look for the mysteries of His universe and creatures included humankind. Moreover, He evoke several principal scientific subjects and provide signs compatible with scientific facts unknown in the area of Qur'an descent (in the seventh century) and have only been discovered in modern times (e.g. see Chaabani 2006; Bucaille 2011; Chaabani 2011, 2015).

To get back to the connection between Philosophy and sciences, I would note that even in a complete autonomous, sciences have kept until now a mutual profound interaction with philosophy. In fact philosophers, particularly the renowned ones, have a deeply scientific thought. Moreover, without following sciences progress they cannot continue to more understanding traditional philosophic problems and try to clarify and / or resolve modern ones. Mutually, the true scientific researcher must have a powerful theoretical / philosophical understanding that contributes to pave the way for discovering the important empirical findings in different hard science fields. In this context, the four classic theoretical branches of philosophy (metaphysics, epistemology, axiology, and logic), has been developed within another possible classification in theoretical philosophy and applied philosophy (such as Ethics and Political philosophy). Nowadays, some philosophers continue to make stronger the link between sciences and philosophy such as the case of the philosopher Joshua Knobe (2008, 2014) who has outlined an "Experimental philosophy" as a new movement that seeks to return the discipline of philosophy to a focus on questions about how people actually think and feel.

Review of the definition and the classification of knowledge

Several similar definitions were given to the word “Knowledge” (e.g., Ackoff 1989). I think that although these definitions are correct and complementary they seem quite general to such an extent that they could lead to confusions or false problems. Here I will review the definition of knowledge by classing it, for the first time, in only two major classes: “Preliminary Knowledge” and “Ready Knowledge”. Before this, I must present in brief the two components - data and information- that our brains use to make knowledge.

- Data is considered as a fact or statement of event of the world, but without relation to other things. We can perceive it with our senses. It is always correct but it varies over time.
- Information is considered as a collected and processed data about someone or something. It is faced with the way data is related. In other words, information is composed of data arranged in useful and noteworthy form. It can be correct or wrong. For it we do not need a real use of our cognitive ability.

Concerning the definition of knowledge, if we try to present a short definition it would seem unclear and / or incomplete therefore it leads to confusions; while if we try to present a definition as comprehensive and complete as possible, it would seem quite long and therefore I could dissect it through two major points as follows:

- How making knowledge? As stated above when data is collected and processed about someone or something, it becomes information. However, when information is filtered in useful one that concerns a determined subject, it becomes knowledge. The latter is formed in our brain thanks to cognitive and analytic ability, which rise as well as knowledge, acquired through learning and experience, becomes more and more abundant.
- Knowledge has a very vast meaning, thus we must try to put its limits and to make clearer its heterogeneity. Nowadays knowledge is much diversified; it concerns all what have been presented in all specialties and subspecialties of hard sciences, social sciences and humanities at the educative and research levels as well as all related popular know-how, justified ideas and beliefs, and hypotheses or theses. Different types of knowledge are proposed such as those proposed by philosophers - logical, semantic, systemic, and empirical -. But these types seem quite detailed and complex and stay important at a specific academic context. Here I propose only two general types in which we can easily class any knowledge and that will resolve some false problems such as if

opinions, ideas, beliefs and hypotheses belonged or not to knowledge. In fact all these different expressions are constructed in our brains from information and / or acquired knowledge, therefore, on the basis of what presented above it is not reasonable to get them away from knowledge. But the real problem that these brain products can be true or false; while knowledge, particularly at the learning level, is often considered as composed by facts and principles known as true. Hence, this problem can be resolved if we class knowledge in two major classes "preliminary knowledge" and "ready knowledge".

* Ready knowledge: is all the facts and principles that are considered as true and therefore accepted and shared by all as a common universal entity. It pile up in the course of time and it could be acquired mainly by learning.

* Preliminary knowledge: This includes, all justified ideas, conclusions, suggestions, hypotheses, theses, theories provided in published research academic works. It includes also personal reasonable ideas and beliefs that according to their significance and usefulness arrive to be spread (directly from a person to others or via books or communication media). In fact all these coherent brain expressions cannot be considered as true. But they represent the buds of the knowledge: they can wither and disappear or they can blossom and develop to finish by being proved with evidence and shared by all to reach the level of "ready knowledge". For example Newton's Universal Law of Gravitation is founded from the idea that all the particles of matter in the universe attract each other through the force of gravity. Thus, Newton is above all a great thinker and owing to his ideas that the modern physics was developed. Another example can be found in my present study wherein the formulated assumptions (hypotheses or educated guesses) represent a concrete new "preliminary knowledge", which would turn progressively into "ready knowledge" if it is supported experimentally.

Particularities of the present theoretical study:

In this study, I have agreed to the general major components of theoretical studies: - make out the objective of the study, - make a literature review, - develop a framework, and - construct a suitable work-plan. In the following I try to point out the most important particularities of this study and show, at the same time, how it represents a model of fruitful exchanges between science, philosophy and religion.

1. The subject of this study concerns the early human embryo development: although the principal events of this development are observed and determinate several related details are yet unknown. For this reason, the principal objective of this study is to look for these details in order to fill the knowledge gaps. As ethical norms and legal constraints have put limitations on empirical studies of human embryo, the carrying out of theoretical studies could speed up the knowledge progression in this subject by guiding the future empirical works to the best and shorter research way and by providing assumptions that could be adopted after positive experimental tests. For this reason, the present theoretical study represents a productive grounding for future empirical works.

2. In this study the literature review represents a particular synthesis of qualitative data on the early human embryo development. In fact, the empirical data (ready knowledge) on this subject are scarce, fragmentary, sparse, and sometimes confused with those observed in other mammals. Therefore the present synthesis comes to get together the selected suitable empirical data into a whole, but as the latter presents several knowledge gaps, I have filled them by "preliminary knowledge" deduced from my explanation of some Holly Qur'an verses. So in this particular synthesis chosen empirical data (ready knowledge) and assumptions (preliminary knowledge) were combined, using intuitive reasoning, to reach a more complete scenario on the early human embryo development.

3. I have previously explained (in my book in Arabic, Chaabani 2006, and in some papers in English such as Chaabani 2011; 2015) how some Qur'an signs relating to scientific concepts are masked within Arabic rhetorical modes, which reache unusual creativity summit by presenting at least two possible meanings: a provisory superficial meaning and a real scientific meaning. The revelation of the latter could be possible generally from the time of the discovery of the corresponding scientific facts. However, I have also showed that from some scientific Qur'an signs it would be possible to deduce assumptions related to some unknown scientific details (not yet revealed by scientists). Thus these deduced new details could be considered as hypotheses or educated guess (preliminary knowledge) as long as they are not proved experimentally.

But if they agree with what will be obtained by empirical methods they become scientific details (ready knowledge).

Several examples of such educated guesses have been signaled in my book (in Arabic Chaabani 2006). A first example on the position of women ovary was published after a deeper study (in English, Chaabani 2013); while I present here a second example on another subject: the early human embryo development. But one can ask why I have considered such deductions as hypothetic while Qur'an is the real truth? As a part of my answer I would inform the reader that within the Qur'an text we can distinguish two principal types of verses:

- Decisive verses (in Arabic *Muhkamet*). Each has only one clear meaning, intended for all peoples, they represent together the basis of the Qur'an.
- Allergorical ones (in Arabic *Mutashabihet*) that could have two or more meanings. Only the real great minds, who are firmly rooted in knowledge, can try to reach the corresponding true interpretation that only Allah know it.

Underlining these two kind of verses "Allah" (God) said what means "*It is He Who has revealed the Book (Qur'an) to you; some of its verses are decisive, they are the basis of the Book, and others are allegorical; then as for those in whose hearts there is perversity they follow the part of it which is allegorical, seeking to mislead and seeking to give it (their own) interpretation, but none knows its interpretation except Allah and those who are firmly rooted in knowledge (they) say: We believe in it, it is all from our Lord; and none remembers except the real great minds"*[Qur'an :7].

To get back to the question, the answer is that scientific signs are present within allegorical verses, so whatever my degree of knowledge, objectivity and wisdom, I cannot say that my interpretation represents the real true one; but compared with previous ones one can says that this interpretation is more founded and more acceptable and therefore it could be closer to the real true one known only by Allah. Hence my scientific information deduced from my interpretation to some allegorical Qur'an verses could not exceed the hypothetic level. But if it is supported by experimentation it will be considered as successful interpretation that has the merit of becoming a "ready knowledge".

I believe that allegorical Qur'an verses represent the main enigma relating to the fact that Islam is a dynamic, progressive religion that stays worthwhile at anytime and anywhere. This type of verses concerns two major circumstances: (1) in the case of verses wherein information relating to some complex or delicate subjects, they seem not

quite clear and incomplete or with more than one meaning. In fact this gap of details or absence of a firm commandment is very likely intentional aiming to offer Muslims the right to establish and choice corresponding rules and / or complementary details, which agree with the good of humankind at the individual and social levels in a given era and place, and (2) in the case of verses, which contains hidden scientific signs, could stay during many centuries with a simple apparent meaning until the corresponding scientific discovery occurs. It is only from the 20th century that some scientific signs in some allegorical verses have become comprehensible. Scholars in different scientific specialties (Physics, Biology ….) would continue to reveal other Qur'an signs related to scientific concepts or details already known or until now unknown by scientists as in the present case.

Conflicts of Interest: The author declares no conflict of interest.

References

Ajduk A., Biswas Shivhare S., Zernicka-Goetz M. 2014. The basal position of nuclei is one pre-requisite for asymmetric cell divisions in the early mouse embryo. *Developmental Biology* 392 (2): 133–140.

Al-Ghazali A.H. Ihya Ulum-Id-Din. Dar Abou Hazm. Beirut, Lebanon.
Averroès A.I.W. Incohérence de l'Incohérence (Tahafut al-Tahafut) Le Caire, Al-Matbaa Al-Ilamiya.

Bentin-Ley U., Sjogren A., Nilsson L., Hamberger L., Larsen J.F., Horn T. (2000). Relevance of endometrial pinopodes for human blastocyst implantation. *Hum Reprod Suppl* 6: 67-73

Boklage CE. 2009. How new humans are made. World Scientific. (ISBN 978-981-283-513-0)

Brison D.R., Sturmey R.G., Leese H.J. 2014. Metabolic heterogeneity during preimplantation development: the missing link? *Human Reproduction Update* 20 (5): 632–640.

Bucaille M. 2011. Le Coran la Bible et la science, Paris, Pocket, coll. « Evolution » (ISBN 978-2266131032)

Chaabani H. (2006). Laws of the Human Creation under the lights of Sciences and holy Qur'an " (in Arabic: Sounanou khalq al-Inssan tahta adhoua'i al-Ilm oua nour al-Qur'an). Les Imprimeries Reunies, Tunis, Tunisia (ISBN: 978-9973-61-201-4).

Chaabani H. (2011). Compatibility of the holy Qur'an with sciences: anthropological concepts as an example. *International Journal of Modern Anthropology*. 1(4): 78 – 84.

Chaabani H. 2013. A theoretical ovary position in link with the global anatomical structure of each human female body. *International Journal of Modern Anthropology* 1(6): 78 – 84

Chaabani H. (2015). Man creation had begun since the creation of the first biological material very likely in Clay. *International Journal of Modern Anthropology*. 1(8): 49 – 65

Chhabra ES, Higgs HN. 2007. The many faces of actin: matching assembly factors with cellular structures. *Nat Cell Biol*. 9:1110–1121

Dale B., Tosti E., laccarino M. 1995. Is the plasma membrane of the human oocyte reorganized following fertilization and early cleavage?
Zygote 3:31-36.

Dobson A. T., Raja R., Abeyta M.J., Taylor T., Shen S., Haqq C. and Reijo Pera R.A. 2004. The unique transcriptome through day 3 of human preimplantation development. *Hum Mol Genet* 13: 1461-1470.

Dogterom M1, Kerssemakers JW, Romet-Lemonne G, Janson ME. 2005. Force generation by dynamic microtubules. *Curr Opin Cell Biol*. 17(1):67-74.

Doronin Yu.K., Senechkin I.V., Hilkevich L.V., and Kurcer M.A. 2016. Cleavage of Human Embryos: Options and Diversity. *Acta Naturae* 8(3): 88–96.

Emiliani S, Delbaere A, Devreker F, Englert Y. 2005. Embryo-maternal interactive factors regulating the implantation process: implications in assisted reproductive. *Reprod Biomed Online* 10: 527-540.

Enders AC, Schlafke S, Hendrickx AG. 1986. Differentiation of the embryonic disc, amnion, and yolk sac in the rhesus monkey.
Am J Anat 177: 161-185

Familiari G., Relucenti M., Heyn R., Micara G., Correr S. 2006. Three-dimensional structure of the zona pellucida at ovulation.
Microsc Res Tech 69 (6): 415-426.

Fehon R. G., McClatchey A. I. and Bretscher A. 2010. Organizing the cell cortex: the role of ERM proteins. *Nat. Rev. Mol. Cell Biol.* 11, 276-287.

Fleming T.P. 1987. A quantitative analysis of cell allocation to trophectoderm and inner cell mass in the mouse blastocyst. *Dev Biol* 119: 520–531.

Gardner RL. 1998. Contributions of blastocyst micromanipulation to the study of mammalian development. *Bioessays* 20:168–180.

Gilbert S.F. 2000. Developmental Biology. 6th edition. Sunderland (MA): Sinauer Associates.

Greicius G1, Westerberg L, Davey EJ, Buentke E, Scheynius A, Thyberg J, Severinson E. 2004. Microvilli structures on B lymphocytes: inducible functional domains?
Int Immunol. 16(2):353-64.

Gulyas B.J. 1975. A re-examination of cleavage patterns in eutherian mammalian eggs: rotation of blastomere pairs during second cleavage of the rabbit.
J Exp Zool 193: 235–248.

Jax C. How to Form a Theoretical Study of a Dissertation
https://classroom.synonym.com/form-theoretical-study-dissertation-12142.html

Kan He, Hongbo Zhao, Qishan Wang, Yuchun Pan. 2010. A comparative genome analysis of gene expression reveals different regulatory mechanisms between mouse and human embryo pre-implantation development.
Reprod Biol Endocrinol 8:41

Kantsler V., Dunkel J., Blayney M. Goldstein R.E. 2014. Rheotaxis facilitates upstream navigation of mammalian sperm cells.
eLife 3:e02403

Knobe, J. & Nichols, S. (2008). Experimental Philosophy. New York: Oxford University Press.

Knobe, J. & Nichols, S. (2014). Experimental Philosophy, Volume 2. New York: Oxford University Press

Lange K. 2011 Fundamental role of microvilli in the main functions of differentiated cells: Outline of an universal regulating and signaling system at the cell periphery.
J Cell Physiol 226(4):896-927.

Lopata A., Kohlman D., and Johnton I. 1983. The fine structure of normal and abnormal human embryos developed in culture, in: Fertilization of the human egg in vitro (H.M. Beier, and H.R. Linder, eds), Springer-Verlag, Berlin.

Margarit, L.; Taylor, A.; Roberts, M. H.; Hopkins, L.; Davies, C.; Brenton, A. G.; Conlan, R. S.; Bunkheila, A.; Joels, L.; White, J. O.; Gonzalez, D. 2010. MUC1 as a Discriminator between Endometrium from Fertile and Infertile Patients with PCOS and Endometriosis.
The Journal of Clinical Endocrinology & Metabolism. 95 (12): 5320–5329.

Maro B., Johnson M.H., Pickering S.J., and Louvard D. 1985. Changes in the distribution of membraneous organelles during mouse early development.
J Embryol exp Morph 90: 287-309.

McConnell R.E., Higginbotham J.N., Shifrin D.A. , Tabb J.D.L., Coffey R.J., and Tyska M.J. 2009. The enterocyte microvillus is a vesicle-generating organelle
J Cell Biol. 185(7): 1285–1298.

Miura S., Sato K., Kato-Negishi M., Teshima T., Takeuchi S. 2015. Fluid shear triggers microvilli formation via mechanosensitive activation of TRPV6
Nature Communications . 6 (8871)

Mottla G.L., Adelman M.R., Hall J.L., Gindoff P.R., Stillman R.J., Johnson K.E. 1995. Lineage tracing demonstrates that the blastomeres of early cleavage stage human pre-embryos contribute to both trophectoderm and inner cell mass.
Hum Reprod 10: 384-391.

Niakan K.K., Han J., Pederson R.A., Simon C., and Reijo Pera R.A. 2012. Human pre-implantation embryo development.
Development 139(5): 829–841.

Nikas G., Asangla Ao, Robert M.L. Winston R.M.L., and Handyside A.H. 1996. Compaction and Surface Polarity in the Human Embryo In Vitro
Biology of Reproduction 55: 32-37.

Pereda J., Croxatto H.B. 1978. Ultrastructure of a seven-cell human embryo.
Biol Reprod 18:481-489.

Pulkkinen MO. 1995. Oviductal function is critical for very early human life. *Ann Med* 27: 307

Reeve W., and Ziomek C. 1981. Distribution of microvilli on dissociated blastomeres from mouse embryos: evidence for surface polarization at compaction. *J Embryol Exp Morphol* 62:339-350.

Reeve W.J. and Kelly F.P. 1983. Nuclear position in the cells of the mouse early embryo *J Embryol Exp Morphol* 75: 117–139.

Runge K.E., Evans J.E., He Z.Y., Gupta S., Mc Donald K.L., Stahlberg H., Primakoff P., Myles D.G. 2007. Oocyte CD9 is enriched on the microvillar membrane and required for normal microvillar shape and distribution. *Dev. Biol*. 304(1):317-25.

Saiz N, Plusa B. 2013. Early cell fate decisions in the mouse embryo. *Reproduction* 145:65–80.

Schrode N., Xenopoulos P., Piliszek A., Frankenberg S., Plusa B., and Hadjantonakis A-K. 2013. Anatomy of a blastocyst: cell behaviors driving cell fate choice and morphogenesis in the early mouse embryo. *Genesis* 51(4): 219-233.

Shiue, H., Musch, M. W., Wang, Y., Chang, E. B. and Turner, J. R. 2005. Akt2 phosphorylates ezrin to trigger NHE3 translocation and activation. *J. Biol. Chem*. 280: 1688–1695.

Spehr M., Gisselmann G., Poplawski A., Riffell J. A., Wetzel C. H., et al. 2003. Identification of a testicular odorant receptor mediating human sperm chemotaxis. *Science* 299: 2054–2058.

Tamiello C., Buskermolen A.B.C., Baaijens F.P.T., Broers J.L.V., Bouten C.V.C. 2016. Heading in the Right Direction: Understanding Cellular Orientation Responses to Complex Biophysical Environments. *Cell Mol Bioeng*. 9: 12–37

Tarkowski AK, Wroblewska J. 1967. Development of blastomeres of mouse eggs isolated at the 4- and 8-cell stage. *J Embryol Exp Morphol* 18:155–180.

Teh W-T., McBain J., Rogers P. 2016. What is the contribution of embryo-endometrial asynchrony to implantation failure? *J Assist Reprod Genet* 3(11): 1419–1430.

Van de Velde H., Cauffman G., Tournaye H., Devroey P., Liebaers I. 2008. The four blastomeres of a 4-cell stage human embryo are able to develop individually into blastocysts with inner cell mass and trophectoderm. *Human Reproduction*, 23 (8): 1742–1747.

Vassena R., Boué S., González-Roca E., Aran B., Auer H., Veiga A., Belmonte J. 2011. Waves of early transcriptional activation and pluripotency program initiation during human preimplantation development.
Development 138, 3699–37

Walter B.; Boulpaep E. 2004. Medical Physiology: A Cellular And Molecular Approaoch. Oxford: Elsevier

Wang N, Tytell JD, Ingber DE. 2009. Mechanotransduction at a distance: mechanically coupling the extracellular matrix with the nucleus. *Nat. Rev. Mol. Cell Biol*. 10:75–82.

Wang Q., Piotrowska K., Ciemerych M.A., Milenkovic L., Scott M.P., Davis R.W. and Zernicka-Goetz M. 2004. A genome-wide study of gene activity reveals developmental signaling pathways in the preimplantation mouse embryo. *Dev Cell* 6 : 133-144.

Wong CC1, Loewke KE, Bossert NL, Behr B, De Jonge CJ, Baer TM, Reijo Pera RA. 2010. Non-invasive imaging of human embryos before embryonic genome activation predicts development to the blastocyst stage. *Nat Biotechnol*. 28(10):1115-21.

To cite this article:
Hassen Chaabani 2018. New insights into human early embryonic development: a particular theoretical study.
International Journal of Modern Anthropology. 2 (11): 14 – 47
DOI: http://dx.doi.org/10.4314/ijma.v2i11.1