

Human and Animal Cloning: Boon and Bane in the Light of Islam and Ethics

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ABSTRACT

The advantages and disadvantages of human and animal cloning are reviewed. However, cloning is not a creation per se. Creation is proper to the Creator (Koran, Pilgrimage, 73): ...Those, on whom, besides Allah, ye call, cannot create (even) a fly, if they all met together for the purpose!...

Animal cloning permissibility in Islam is conditioned by no causing of harm to animals and the domination of advantages. Cloning of whole human body is forbidden, even if it were for treatment purposes. Reasons are discussed (Contradiction with diversity, social and legal problems...). Islam preserves the society nucleus (the family) and dignity; therefore, it prohibits the implication of a third party in the reproduction process.

However, therapeutic cloning can be permitted and even rewarded by God. The embryo stage at which it can be manipulated raises important questions of ethical, legal and religious order and, therefore, needs jurisprudence (Fatwa). Up to what fetal developmental stage can an embryo be manipulated (e. g. extraction of stem cells)? Is it permissible before acquiring the spirit (40 or 120 days)?

Human being is not authorized to spoil on Earth even if he has a kind of superiority over other creatures which are communities like us (Koran, Livestock: 38)

Superiority is not absolute and based on responsibility (stewardship). Awareness and precautions are necessary before drawbacks are irreversible.

Keywords: Animal and Human Cloning, Ethics, Islam, Pharmaceuticals, Reproduction.

INTRODUCTION

Cloning is derived from the Greek word "twig or branch" meaning the process leading to production of a complete plant from a branch. Cloning now means production of multiple identical copies at the level of DNA (molecular cloning), cells (cell cloning), or organisms. This paper, however, focuses on the latter type of cloning. The principle of cloning of organisms is, therefore, applied on Earth since the beginning of life! Prokaryotes, many plants, insects and some animals reproduce asexually and beget "identical" copies. Monozygotic twins in many animals and in human are clones. However this paper focuses on animal and human cloning by manipulation.

It's commonly known that the first animal to be cloned was Dolly the sheep in 1996 but announced in 1997 (Wilmut et al., 1997). Surprisingly, in 1952, the laboratory toad, *Xenopus* was cloned by a technique similar to that used today (Briggs and King, 1952). However, Dolly was the first organism ever to be cloned from adult cells.

A cloning strategy used today for cloning by nuclear transfer consists of injecting a diploid cell from the morula between the zona pellucida and the plasma membrane of an enucleated oocyte, electrically favoring fusion of the plasma membranes of the cell and the oocyte. Actually the electrical field used favors formation of pores in the oocyte membrane followed by uptake of calcium ions. This mimics what's happening in the natural fertilization where sperm not only donates its genome to the oocyte but also induces the uptake of calcium ions by the oocyte. The success rate using this protocol is 1%. Other protocols were used to increase the

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efficiency of cloning. One of these protocols is based on the synchronization between the donor cells and the recipient oocytes, so that the chromosomes are delivered in an appropriate configuration. Classically, cells are synchronized by depleting the culture medium of serum and growth factors. This leads to stopping growth and entering in G₀ phase. As most cells cannot survive for long time under these conditions they enter apoptosis. However, addition of serum and growth factors reinitiate growth and all cells are synchronized. They can be used as donor cells. It was initially believed that G₀ phase is the most appropriate phase for the donation of nuclei. However, G₁ rather than G₀ was more efficient in cloning of cows (Kasinathan et al., 2001).

Following Dolly, many other species were cloned like cows (Vignon et al., 1998), mice (Wakayama et al., 1998, 2000, Rideout, 2000), cattle (Kato, 1998; Renard, 1999; Wells, 1999; Kubota, 2000), pigs (Polejaeva, 2000; Betthausen, 2000; Onishi, 2000), goats (Baguisi, 1999), cats (Braun, 2002)...

When looking for religious jurisprudence (Fatwa) concerning cloning, it's important to bear in mind that this new technology is after all a matter of manipulation of preexisting cells (e.g. donor cells, oocytes). It is not a creation *per se* which is proper to the creator. This helps avoiding misleading conclusions as cloning is manipulating what God created and not creating. Creation is too much complex to be just determined by the DNA sequences. It's a challenge issue of the extra power of God Who is unique in His capacity to create!

Koran, The Bee: 17 :

17

Is then He Who creates like one that creates not? Will ye not receive admonition?

The challenge of creation includes creatures less complex than human (e.g. flies)

Koran, Pilgrimage: 73 :

O men! Here is a parable set forth! Listen to it! Those, on whom, besides Allah, ye call, cannot create (even) a fly, if they all met together for the purpose! And if the fly should snatch away anything from them, they would have no power to release it from the fly. Feeble are those who petition and those whom they petition!

Koran, The Criterion: 2-3 :

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2. He to whom belongs the dominion of the heavens and the earth: no son has He begotten, nor has He a partner in His dominion: it is He who created all things, and ordered them in due proportions.

3. Yet have they taken, besides him, gods that can create nothing but are themselves created; that have no control of hurt or good to themselves; nor can they control death nor life nor resurrection.

Furthermore, it is evident that each clone will definitely have a separate and unique soul. This can be indicated by the observation that they do not have the same exact life span. Actually the spirit is out of the reach of human and is exclusively attributed to God.

Koran, Isra', The Night Journey, Children Of Israel:

85 :

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85. They ask thee concerning the Spirit (of inspiration). Say: "The Spirit (cometh) by command of my Lord: of knowledge it is only a little that is communicated to you, (O men!)"

Islam opines that the laws of God are immutable and dominant in the nature and that human beings can never willfully create "unless God, the Lord of all Beings, wills" (Koran:29)

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The will of God in the Koran could be understood as the "processes of nature" under the ultimate control of God. The attitude vis-à-vis these processes should be limited by the Islamic rules, not every natural process can be admitted automatically by Islam. Let's take the example of improving the chances of fertility for a married couple. It's regarded as an act of faith in the ultimate will of God as the Giver of all life that Islam does not oppose. Human cloning is a more debatable issue.

Finally, according to the Islamic famous scholar, Prof. Yousuf Al-Qaradawi, cloning makes it materially easier to imagine the idea of resurrection. If man was able to replicate animals and even humans using simple protocols, then resurrection will be imaginable even for non believers. Re-giving life for creatures by Almighty became materially understandable even if the Almighty does not need our protocols to make whatever He wants. Himself, he creates procedures and laws in this life and afterwards!

Koran, The Romans, The Byzantines:27 :

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“He it is who produces creation then reproduces it and it is easier for Him. His is the Sublime Similitude in the heavens and in the earth. He is the Mighty, the Wise”

AIMS OF THE STUDY

- (1) Understanding the cloning biotechnology because coping up with technology is a duty.
- (2) Demonstrating that copying by cloning does not produce real identical individuals!
- (3) Reviewing the expected advantages, disadvantages in the light of ethical and Islamic considerations.
- (4) Demonstrating the scientists and public's duties and responsibilities toward these emergent biotechnologies and taking the necessary precautions before it's too late to repair possible devastating drawbacks.

METHODOLOGY

The methodology of this research is based on the principle that scientific advances should have a main objective, the welfare of the human being and his environment. This is an ethical attitude supported by logic and Islam. In this context, the advantages and disadvantages of animal and human cloning are reviewed in this paper. They are weighed in the light of common ethical principles and Islamic holy and authentic texts (which are influencing factors in our life) in order to reach a coherent and responsible conclusion vis-à-vis this revolutionary biotechnology.

Boon and Bane:

People are divided into opponents and proponents in their regard to cloning. Opponents in general base their skepticism on misinformed decisions. Man fears the unknown and is wary of new technologies. As the Earth lived for trillions of years without cloning, why attempting to disturb nature now? Why exposing the environment and its equilibrium to unexpected and possibly irreversible drawbacks or even destruction? Humans fear production of monster animals for aesthetical, ethical and religious reasons. Eugenics (controlled human breeding based on notions of desirable and undesirable human traits) represents a main and

historical point in the rejection of cloning by the public mind.

Proponents base their claims on the need for revolutionary and efficient means mainly in animal production and health domains. Cloning can accelerate and intensify genetic breeding. It can complement the transgenesis with all its advantages. Cloning of transgenic animals of special added value can multiply the advantages of transgenesis especially in the domain of production of pharmaceuticals. If we want to simplify by extrapolation, cloning takes place since the beginning of life but using natural means (asexual reproduction in case of many plants and even some animals as well as the so called identical twins or more precisely monozygotic twins).

In the following sections, advantages as well as drawbacks of the cloning biotechnology will be further detailed and linked to limits and ethics:

Applications of Cloning:

The abrupt emergence of cloning lead to an inability of most people to evaluate its advantages as well as its risks. The incomprehension was enhanced illogically in the public mind by non correlated issues like contaminated human blood, dangerous animal diseases like the mad cow, global warming etc. Furthermore, the mal coverage of biotechnological applications issues in the media enhanced furthermore the fear of the unknown in the public culture. However, this paper will review the applications of cloning with appropriate links to the religious texts:

(A) Basic Research:

Cloning is based on obtaining totipotent cells from fully differentiated cells. Cloning, therefore, provides an attractive opportunity for studying differentiation and re-differentiation mechanisms. A striking phenomenon was remarked in cloned animals after birth: they suffered from repeated syndromes, some of which, interestingly, are similar to certain human development diseases. Consequently, cloned animals can be used as animal models for the human diseases. Many cloned animals are even unable to survive (Reviewed by Houdebine, 2003). Cloned animals can be used to study ageing as it was found that such animals have shorter lifespan than the normal animals (Parry and Wakayama, 2002; Ogonuki et al., 2002). This might be due to loss of some of their biological functions. In addition, cloned animals suffer

from diseases that were not experienced by their progenitors. Dolly died suffering from an early arthritis which was not contracted by its progenitor. Is there a correlation between this disease and shortening of telomeres? Interestingly, the analysis of telomere length and telomerase activity in cloned pigs demonstrated that telomere length in cloned piglets was rebuilt or elongated with the use of cultured donor fetal fibroblasts. This was paralleled by an increase in the activity of telomerase (Jeon et al., 2005).

The classical dogma of irreversible differentiation is no longer valid. Mouse nerve stem cells were transplanted in the mouse bone marrow which was irradiated to eliminate the original haematopoietic stem cells. Astonishingly, an important part of the transplanted nerve cells were transformed into haematopoietic stem cells capable of producing red and white blood cells.

In a similar manner, transplantation of an organ stem cell into another, switches these stem cells into stem cells capable of dividing into various organ stem cells. This is called transdifferentiation, it seems to be a widely occurring and a tissue regeneration mechanisms (Reviewed by Houdebine, 2003). Stem cells are defined as being capable of giving rise to one stem cell and another differentiated cell upon division. Most stem cells give rise to several cell types. Stem cells are found in the blastocyst (called embryonic stem or ES cells) and also can be found in a limited number of organs (bone marrow, skin, hair, eyes, dental pulp and even in the brain, to the surprise of many, where they continue to produce certain kinds of nerve cells...). However, the culture of embryonic stem cells is easier than the organ stem cells. Injecting lines of organ stem cells into damaged organs to regenerate them and permit their reconstruction is promising but not yet set up as a therapy. It's vital to understand the nature and composition of the armada of inducers that trigger the phenomenon of transdifferentiation (Lemischka, 2002).

(B) Biotechnological Applications of Human and Animal Cloning:

(1) Animal Reproduction:

Using cloning, elite and precious animals can be propagated for their own high value as well as for use as progenitors. This can accelerate and intensify genetic selection. Racing horses present a demonstrating example for high value animals: using cloning, a champion horse

can be used produce champions rapidly in comparison to the classical breeding. In addition, cloning can intensify the efficiency of transgenesis through the rapid propagation and crossing of genetically modified animals rather than waiting long time in the classical breeding.

The beloved house pets (cats...) can be cloned for a kind of continuity even after their death! People like to continue their favorite relationships even with animals even if they can be disappointed or even bitterly disappointed by some phenotypic change in the copies of their beloved original pets.

Reproducing individuals of species threatened by extinction is an important application of animal cloning. An important trial was the cloning of the gaur, a rare wild ruminant using cow oocytes as recipients. It can be an efficient method to save endangered species that became no longer able to propagate independently and efficiently. Unfortunately, the one animals issued from this cloning did not survive. The idea was reapplied on mouflons: cells were taken from mouflons found dead in the pasture. Their nuclei were implanted into enucleated sheep oocytes and gave rise to one viable offspring apparently normal (Loi et al., 2001). Other attempts can be done but need suitable ecological, ethical and financial commitments.

According to a "Fatwa" issued by the Islamic scholar Prof. Yusuf Al-Qaradawi, animal cloning permissibility is conditioned by: no causing of harm or torture to animals and in any case benefits to people must be greater than the possible and tolerable harm. Again it's of capital importance to make a logical and ethical compromise between being dependent on animals for nutrition and avoiding harming them! (See Cloning and Animal Welfare in the following sections)

(2) Propagation of Transgenic Animals:

Multiplication of transgenic animals represents a main and realistic application of cloning. Rather than continuous DNA microinjection into pronuclei in animals, it's easier to clone and multiply the interesting modified animals obtained once by transgenesis. In other word, transgenic founders of high value can, be propagated by cloning and therefore, introgression of the genetic modification into herds can be highly accelerated (Reviewed by Houdebine, 2003).

Propagation of animal models for human diseases that were created by transgenesis is an important application of cloning. Many examples of animal models for human

diseases can be cited as for example muscular dystrophy syndrome. Animal models for this disease were created through knocking out of the LAM2 gene coding for laminin isoform. Furthermore, transfer of agrin gene restores muscle function by formation of neuromuscular junctions (reviewed by Houdebine, 2003). Transfer of a different gene suppresses the pathology (Moll et al., 2001). Cloning can be helpful in the multiplication of animal models created by transgenesis for the following diseases: HIV infection (Dunn et al., 1995; Cohen, 2001), the human papilloma virus (Souders et al., 2007), prion diseases (Moore and Melton, 1997), atherosclerosis (Iritani et al., reviewed by Houdebine, 2003), oncogenes and cancer (Bartek and Lukas, 2001), mammary tumors (Schwertfeger et al., 2001), Alzheimer's disease (Chapman et al., 2001),...etc.

Similarly, cloning is a precious tool to propagate the so called "pharm animals" genetically engineered to produce pharmaceuticals, many examples can be cited as for the production of industrial quantities of human growth hormone (Goeddel et al., 1979), enzymes (Van den Hout et al., 2001), blood factors (Wood et al., 1984), vaccines (Davis et al., 2001), antibodies (Hotta, 2004; Holliger and Hudson, 2005), structural proteins (Heine and Boyle, 1993) etc. Kues and Niemann, 2004 summarized the contribution of "pharm" animals to human health, covering the production of antimicrobial peptides, dietary supplements or functional foods, animals used as disease models and the contribution of animals to solving urgent environmental problems and challenges in medicine such as the shortage of human cells, tissues and organs and therapeutic proteins. Some of these areas have already reached the level of preclinical testing or commercial application, others will be further advanced only when the genomes of the animals concerned have been sequenced and annotated.

In addition of propagating transgenic animals by cloning, it can also be used to create genetically modified from genetically modified cells. Genetic modification of cells, whether by transfection, homologous recombination or any other technique can, therefore, be followed by cloning. Homologous recombination was successfully used for gene replacement in sheep (McCreath et al., 2000), pigs (Dai et al., 2002; Platt, 2002; Lai et al, 2002). In an elegant experiment, cells were taken from an adult mice suffering from a genetic disease. These cells were genetically modified by transfer of the normal non mutated allele. These modified cells were used as donors

to create cloned mice by nuclear transfer. The cloned mice were healthy (Rideout et al., 2000).

However, in other animals like pigs, rabbits and rats, microinjection is still easier than cloning. But, there is an important disadvantage in microinjection: that is obtaining of mosaic animals (30% of animals) in contrary to cloning where all the organisms cell harbor the same genetic material. In addition, animals are different in function of the integration of the foreign DNA upon microinjection (Reviewed by Houdebine, 2003).

(3) Human Reproduction:

Technically speaking, human cloning is possible even if the efficiency is poor and it was announced that human embryos were obtained by cloning in USA and Korea and rapidly stopped (Cibelli et al., 2001). The ethical issue is of utmost importance, this is the reason for the great impact of the cloning of Dolly on the public opinion. Ethics concerning this important issue will be discussed later in this paper.

It is useful to distinguish between reproductive cloning in case of animals and human, the first might be justified in contrary to the second.

However, whole human body human cloning is prohibited in Islam, even if it were for treatment purposes, according to Prof Yusuf Al-Qaradawi in an on-line article entitled " ". Prohibition is due to the following reasons: Contradiction with diversity in creation, the confusing matter of social and legal relationships between the clone and the progenitor: will the copy be brother, son of "his or her" progenitor? Or would it be himself or herself? The divine pattern of creating things in pairs is clearly opposed by this pattern of reproduction. However, cloning can be permitted, furthermore, recommended and rewarded by Allah, if cloning goes into cloning specific parts of the human body for treatment purposes as for example heart and kidney

(http://www.qaradawi.net/site/topics/printArticle.asp?cu_no=2&item_no=2940&version=1&template_id=130&parent_id=17).

Even though an influencing scholar, Sheikh Wahbeh Az-Zoheily in Damascas, considered in 1998 that reproductive cloning can be permissible "in the frame of family", human reproductive cloning is rather prohibited in Islam notably outside the "family arena" according to the Azhar scholar Mohammad Sayyed Tantawi.

Reproductive cloning issues children via an abnormal

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Interestingly, the Roman Catholic Church, under the papacy of Benedict XVI, has similar attitude vis-à-vis of cloning as the Islamic one detailed above. The Roman Catholic Church considered the human cloning as being condemned and as a grave offense to the dignity of that person as well as to the fundamental equality of all people (Stein and Boorstein, 2008).

(4) Therapeutic Cloning:

Stem cells are rare, and under the available techniques, difficult to be cultured. Stem cells can be obtained from adult organs, but this source is limited. Blood from the umbilical cord provides a valuable source of pluripotent stem cells or organ stem cells. ES lines could be established in the late eighties from mouse blastocysts and also could be obtained from spare animal or human embryos resulting from in vitro fertilization (Thomson et al., 1998). Such embryos can also be obtained by nuclear transfer using donor cells from the patient. In the latter case, the pluripotent and differentiated cells that could be taken from the cloned embryos have no histoincompatibility problems with the patient, compatibility is inherent. The pluripotent stem cells can be harvested from the mentioned embryos. These stem cells can differentiate in vitro into specialized cells like neurons...Therapeutic cloning consists of grafting such differentiated cells into patients to restore a damaged organ (Griffith and Naughton, 2002). Attempts to graft pancreatic human cells into diabetics have been

done and were unsuccessful for technical reasons. Similar trials were done with limited but promising success for implantation of human hepatic cells to cure fulminant hepatitis.

It was demonstrated that human neuron precursors could differentiate from stem ES cells and could colonize the mouse brain as normal neurons (Studer, 2001). Such ES cells, under the effect of different combinations of inducers, gave rise to red blood cells producing hemoglobin, nervous cells synthesizing dopamine, lymphocytes producing antibodies, muscle cells, cardiac cells etc.

Pluripotent embryonic stem cells can also be obtained by parthenogenesis. In a certain number of species, oocytes can develop without fertilization into diploid embryos and normal animals. This is extrapolated to mammals but is strictly limited and under experimental conditions. In mice, rabbits and other species including monkeys, parthenogenesis could be induced by chemicals. Inomycin, by induction of calcium flux into oocytes, and rosovitine by inhibiting the maturation promoting factor (MPF) were found to induce parthenogenesis in rhesus monkeys oocytes (Mitalipov, Nusser and Wolf, 2001). This approach was used successfully in another primate, *Macaca fascicularis*, and is expected to succeed also in human being (Reviewed by Houdebine, 2003). Parthenogenesis raises limited ethical rejection but more studies are needed to validate it as source for embryonic stem cells.

Reprogramming of differentiated cells into another on demand can also provide a valuable tool for therapy in general and can be considered as therapeutic cloning if the cells to be reprogrammed are obtained from cloned embryos. A promising approach of skeleton muscle cells grafting could lead to partial regeneration into cardiac muscle (Reviewed by Houdebine, 2003). It was demonstrated that neurons derived from reprogrammed fibroblasts functionally integrate into the fetal brain and improve symptoms of rats with Parkinson's disease (Wernig et al., 2008). Adipose cells could also be reprogrammed into cardiomyocytes following transient exposure to a rat cardiomyocyte extract. This study suggests that alteration of cell fate using cellular extracts may be applied to multiple cell types (Gaustad et al., 2004).

It is important to make a clear distinction between human reproductive cloning and human therapeutic cloning. The latter is ethically accepted in contrary to the

former. That is why "nuclear transplantation" was suggested to replace the therapeutic cloning (Vogstein, Alberts and Shine, 2002). In the nuclear transplantation therapy, viable embryos are created only for obtaining stem cells. At the blastocyst stage their development is interrupted. The established cell lines from these embryos can be used to cure human diseases. This can be ethically accepted.

The stage of the embryo at which such cells can be harvested is of capital importance. It raises questions of ethical, legal and religious order. It was approved by some countries (e. g. UK) to manipulate human embryos up to 14 days (blastocyst stage). An Islamic point of view on this matter needs a "Fatwa". The basis for any ethical assessment of human embryo manipulation is the following: Is the human embryo a human since the first day? On the other extremity, is it a matter of aggregate of cells until a project is formulated by its parents? Is it something in between? The later compromise should consider scientific, social and religious contexts. We are instructed by the authentic Prophetic Saying reported by Muslim [2645] that a differentiation breakthrough happens at 42 days after fertilization. In addition, another authentic Prophetic Saying reported also by Muslim [2643] implies that the spirit is acquired by the fetus at 120 days of the fetal development. Another interpretation considers, surprisingly that the spirit is acquired at 40 days and that mentioning 40 for 3 successive times in the Prophetic means the same interval. This revolutionary interpretation is based on the breakthrough of differentiation that appears at 42 days of the fetal life (Muslim Hadith 2645). In the Prophetic Saying reported by Muslim (Muslim Hadith 2643), the breakthrough in differentiation takes place at the end of the "traditionally-understood three successive intervals of 40 days". It's not impossible; from both Hadiths, that what is traditionally considered as 120 days for acquiring spirit is just 40 days. In addition, Muslim Hadith 2645 talks about "appearance" of sight, vision, skin, muscles and bones at 42 days. Muslim Hadith 2643 talks about just "Modgha", a morsel of flesh" (Pilgrimage; Alhaj, verse no 5) is undoubtedly not differentiated. By combining the two Hadiths, we find it possible that spirit is acquired at the end of 40 days during the fetal life (e. g. 42 days). This needs of course further discussion and approval by the Islamic references. Furthermore, in Muslim Hadith 2645, sight, vision, skin, muscles and bones appear at 42 days and in Muslim Hadith 2643, just a morsel of flesh

appears at the "traditionally understood 120 days". It is no surprising, again that the three intervals of 40 days are in fact the same period (e. g. 40 days).

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If forty-two nights have passed over the embryo, God sends an angel to it, who shapes it and creates its hearing, vision, skin, flesh, and bones... Hadith no. 2645 (translation from <http://www.islam-guide.com/ch1-1-h.htm#footnote3>)

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Abdullah (b. Mas'ud) reported that Allah's Messenger (may peace be upon him) who is the most truthful (of the human beings) and his being truthful (is a fact) said: Verily your creation is on this wise. The constituents of one of you are collected for forty days in his mother's womb in the form of blood, after which it becomes a clot of blood in another period of forty days. Then it becomes a lump of flesh and forty days later Allah sends His angel to it with instructions concerning four things, so the angel writes down his livelihood, his death, his deeds, his fortune and misfortune. By Him, besides Whom there is no god, that one amongst you acts like the people deserving Paradise until between him and Paradise there remains but the distance of a cubit, when suddenly the writing of destiny overcomes him and he begins to act like the denizens of Hell and thus enters Hell, and another one acts in the way of the denizens of Hell, until there remains between him and Hell a distance of a cubit that the writing of destiny overcomes him and then he begins to act like the people of Paradise and enters Paradise (translation from http://www.iiu.edu.my/deed/hadith/muslim/033_smt.html#001_b33).

Do the previous sections mean that it could be authorized to manipulate zygotes during the first 120 (or 40) days of conception? Religious and scientific references should convene to provide answers or at least

jurisprudence on this current issue.

Creation is a matter of challenge and consequently was employed in Koran as an evidence for the Resurrection. This creation should, therefore, be respected and honored, not abused or exposed to useless human manipulations:

Koran, Pilgrimage: 5 :

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5. O mankind! if ye have a doubt about the Resurrection, (consider) that We created you out of dust, then out of sperm, then out of a leech-like clot, then out of a morsel of flesh, partly formed and partly unformed, in order that We may manifest (our power) to you; and We cause whom We will to rest in the wombs for an appointed term, then do We bring you out as babes, then (foster you) that ye may reach your age of full strength; and some of you are called to die, and some are sent back to the feeblest old age, so that they know nothing after having known (much), and (further), thou seest the earth barren and lifeless, but when We pour down rain on it, it is stirred (to life), it swells, and it puts forth every kind of beautiful growth (in pairs).

All efforts should be given to preserve the integrity and dignity of human beings. Ethically accepted alternatives for manipulation of human embryos are a subject of intensive research efforts. In 2006, it was demonstrated that pluripotent stem cells can be induced from mouse embryonic or adult fibroblasts (fully differentiated cells) by introducing only a few defined transcription factors (Oct3/4, Sox2, c-Myc, and Klf4) under ES cell culture conditions. When these induced pluripotent stem (iPS) cells were subcutaneously transplanted into nude mice, they resulted in tumors containing a variety of tissues. The iPS cells participated in embryonic development when injected into blastocysts. These data demonstrate that pluripotent stem cells can be directly generated from fibroblast cultures (Takahashi and Yamanaka, 2006). Subsequently human iPS cells were also induced from dermal fibroblasts under the induction of the previously mentioned four factors, Oct3/4, Sox2, c-Myc, and Klf4. These iPS cells were similar to human embryonic stem (ES) cells in morphology, proliferation, surface antigens, gene expression, epigenetic status of pluripotent cell-specific genes, and telomerase activity.

These cells could also differentiate into cell types of the three germ layers in vitro (Takahashi et al., 2007). iPS cells represent an ethically acceptable alternative to embryonic stem cells.

Limits and Risks of Human and Animal Cloning:

(1) Cloning and Animal Welfare:

In addition of causing animal suffering by collection of oocytes and the subsequent manipulation of animals, cloned animals suffer from diseases unprecedented in their progenitors. There were early claims that Dolly the Sheep had pathologies resembling accelerated aging and shortening of life span. She died when she was six much less than her progenitor. Scientists speculated that Dolly's death in 2002 was related to the shortening of telomeres, DNA-protein complexes that protect the end of linear chromosomes. However, other researchers, including Ian Wilmut who led the team that successfully cloned Dolly, argue that Dolly's early death due to respiratory infection was unrelated to deficiencies with the cloning process. The life span of the cloned animals is less than controls (Ogonuki et al., 2002). Cloned mice also suffered from obesity. However, this phenotype was not transmitted to the progeny which is an indicator of epigenetic inheritance and erased by the sexual reproduction and production of gametes (Tamashiro et al., 2002). Furthermore, many phenomena are remarked after cloning: large numbers of late abortions, deaths of newborns, several abnormalities as large offspring with an underdeveloped placenta, thymic aplasia, kidney atrophy, fluctuations of the body temperature, liver or heart hypertrophy, high leptin concentration, partial immuno suppression etc. In general, long term cultures of cells (e. g. few days) in addition to embryo manipulation are correlated with these phenomena (reviewed by Houdebine, 2003). Surprisingly, and for unknown reasons, goats seem to be refractory to these phenomena (Reggio et al., 2001). Experiments were conducted by real-time quantitative reverse transcription-polymerase chain reaction to examine expression patterns of eight developmentally important genes in cloned bovines. Results suggest an aberrant gene expression occurring in most tissues of cloned bovines that died soon after birth. For each of the genes studied, aberrant expression resulting from nuclear transfer was tissue-specific. Because these genes play important roles in embryo

development and organogenesis, the aberrant transcription patterns detected in these clones may contribute to the defects of organs reported in neonatal death of clones (Li et al., 2005).

In order to limit animal suffering, the “3-R precautionary rule” was proposed: reducing numbers of experimental animals, refining experimental protocols and replacing animals, whenever possible, by cell cultures and in vitro tests. A growing list of alternatives to the use of experimental animals is, fortunately, available, e. g. use of animal cell cultures...(Moore, 2001).

Bitterly, not to fall under hypocrisy and from a practical, moral and religious point of view, we are animal consumers and we cannot eliminate animal suffering unless we all become pure vegetarians. A trial to “resolve” this dilemma is by admitting that humans are superior over the other creatures in this world. These creatures have been created for the service of mankind:

13: Koran, The Kneeling:

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The Night Journey 70 :

70

70. We have honored the sons of Adam; provided them with transport on land and sea; given them for sustenance things good and pure; and conferred on them special favors, above a great part of our creation.

However, being superior over other organisms does not authorize human being to degrade and spoil on Earth. Man should have a full respect for God’s creatures, which are communities like us! In this way, man respects himself.

Livestock 38 :

38

38. There is not an animal (that lives) on the earth, nor a being that flies on its wings, but (forms part of) communities like you. Nothing have we omitted from the Book, and they (all) shall be gathered to their Lord in the end.

It’s, unfortunately, evident that eating animals and talking about animal suffering profoundly raises a flagrant conflict. As most people are not pure vegetarians, we should at least look for a compromise and minimize animal's suffering. Actually, at the same time that man is superior in this world, him, and only him; among the

other living organisms has an outstanding duty on Earth, that is the stewardship (Khilafa). This stewardship implies getting benefit from World without an absolute domination and abuse, neither degradation nor spoiling. In the following Prophetic Sayings “we are instructed by Allah to behave in complete beneficence and kindness in everything. If we should kill, then with kindness, if we slaughter, then with kindness. We should sharpen knives and restfully positioning the animal”:

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To reduce animal suffering from cloning of transgenic animals, it is promising to use alternatives of animal transgenesis. As mentioned earlier (in the section of biotechnological applications of cloning), multiplication of transgenic animals represents a main biotechnological application of cloning. This strategy (of alternatives) is in complete harmony with the point "replacing animals" in the “3-R precautionary rule” discussed above (in the section of Limits and Risks of Human and Animal Cloning). Besides the use of classical ethically-accepted alternatives like cell cultures, the use of plants is also ethically accepted for production of pharmaceuticals (Miao et al., 2008; Ferrante et al., 2001; Fieldler and Conrad, 1995).

(2) Identity and Dignity Problems:

This issue is most evident in the case of human cloning. Having the same genetic identity by the clone and the progenitor might give rise to an unpleasant feeling in both of them. Each one might be disappointed of his genetic replicate! More importantly, what would be the social, economical and legal relationships between these individuals? For example, would the insurance societies be affected by the health status of progenitor to deprive the clone? Would the employers do so? What is the legal relationship between those individuals? Is it a matter of father with his son? Or an original and copy? This would undoubtedly raise problems in the social and legal relationships and rights between people (e.g. heritage...). Such rights should be preserved. All these possible negative drawbacks lead to condemning and refusing human cloning according to Yusuf Al-Qaradawi in an on-line article entitled " " .

(http://www.qaradawi.net/site/topics/printArticle.asp?cu_no=2&item_no=2940&version=1&template_id=130&parent_id=17).

(3) Limited Justifiability of Reproductive Cloning:

Reproductive cloning is supported by limited justifications, medically speaking. In fact, sterility can be overcome by several approaches like in vitro fertilization. In Islam, however, these techniques are admitted and considered as an aid to fertility, but strictly within the bounds of marriage. In addition, using a female other than the one's wife as a surrogate mother is prohibited in Islam. The intervention of surrogate mothers might worsen things as they might reclaim "their" babies. Surrogate mothers are not just neutral recipients. However, some of the legitimate fears of human reproductive cloning are: procreation of incestuous and adulterous innocent children, possibly without known parents. Creation of human whole organisms and or parts can become companies profit work. Islam takes the precautionary measures to preserve the human personality, dignity and honor. The family, the nucleus of the society is of capital importance and should be preserved. That's why Islam prohibits the implication of a third party in the reproduction process, whether this third party be a sperm, an ovule, a uterus or a donor cell for cloning according to the following on-line Fatwas:

<http://www.islamset.com/arabic/abioethics/koling/clone1.html>

http://mdarik.islamonline.net/servlet/Satellite?c=Article_A_C&pagename=Zone-Arabic-Mdarik/MDALayout&cid=1175010081783#ixzz21Ewja7. UD

(4) Risks of Transgenesis Can be Extended to Cloning:

As cloning can be used to propagate genetically modified animals of special added value, the drawbacks of transgenesis can also, unfortunately be applicable on cloning. The drawbacks are discussed by Ghareeb, 2009. These include altering the nutritional properties and safety of the human food, possible toxicity and allergenicity of the foreign gene, emergence of animal virus favored by transgenes is also a possible danger of transgenesis, ecological risks (propagation of transgenic plants and animals, effects on biological equilibrium, horizontal transfer of DNA, potential selective advantage etc (Reviewed by Houdebine, 2003).

(5) Low Efficiency:

The low efficiency is issued from the fact that cloning takes place through an artificial physiological situation even if mimics nature. Actually, this biotechnology is quite empirical and expected to stay this way for long time (Western and Surani, 2002). In the case of cloning Dolly the sheep, the rate of success was very low. Among the 277 oocytes used, only 29 gave rise to embryos only 3 of which were born and one of these could survive. Two researchers working at the same time, in the same laboratory and under the same conditions obtain, astonishingly, cloning results quite different from each other (Perry and Wakayama, 2002). Different numbers of clones are obtained, depending on the culture conditions of cells used as nuclear donors. Pretending being able to clone humans can be done by those who don't realize the state of art in this field, or by imposters who are en quite of glory or money! (Jaenisch and Wilmut, 2001). The efficiency of cloning is highly dependent on the state of the donor cells. It was found that cells from the same fetus but cultured under slightly different conditions show different capacities for generation clones (Renard et al., 2002).

Of the possible reasons for the low efficiency of cloning the fact that dividing cells loose and restore sequences of their telomeres. However, the balance becomes negative as the cells age. Dolly had shortened telomeres even if other cloned animals had normal telomeres or longer than normal. Astonishingly, the two lambs born to Dolly after a natural fertilization have normal telomeres. It seems that gametogenesis restores the damaged telomeres (reviewed by Houdebine, 2003). This suggests that shortening of telomeres is not due to cloning per se. However, it seems that the nature of the donor cells (notably their age) determines the length of telomeres in the cloned animal. In case of Dolly, the donor cells were taken from a six-year-old sheep and more importantly, cells were cultured for a long time. More than one hypothesis can be postulated to explain those phenomena: one hypothesis is of genetic order: the genotype of each donor cell is unknown. Cells used for cloning can seem normal even though they harbor mutations than do not affect the life cycle of the cell but affect negatively the embryonic development.

Another hypothesis explaining the failure in animal cloning is based on epigenetics: In fact, it should be undrelined that our fate is NOT entirely determined by

our genome! Epigenetic variations might help explain why one "identical twin" acquires a genetically based disease, such as schizophrenia, but the other does not, despite their identical genomes!

Genome reprogramming by DNA methylation represents one of the mechanisms of epigenetics. It was found that the DNA in cloned animals is strikingly more methylated in the somatic cells and ES cells. This results from incomplete demethylation and from premature remethylation. This might inhibit expression of genes necessary for the embryo development. For example the gene of the growth factor IGF II which is necessary for the embryonic development was found to be heavily methylated in fetuses whose development was interrupted (Reik et al., 2001; Rideout et al., 2001; Dean et al., 2001). In a later study this gene was found to be differentially methylated in bovine oocyte and sperm DNA (Gebert et al., 2006). Developmental potential and reprogramming efficiency was demonstrated in bovine embryos cloned with adult fibroblasts treated by a demethylating agent, S-adenosyl-homocysteine (Jeon et al., 2006). In cloned cattle, DNA methylation at IGF II receptor gene was markedly altered in comparison with normal fetus and disrupted and not completely reprogrammed after nuclear transfer (Long and Cai, 2007). Strategies for dissecting epigenetic mechanisms in the mouse are reviewed (Mager and Bartholomei, 2005).

As the DNA methylation is not a strictly defined mechanism and can be influenced by the environmental conditions, it is conceivable why culture conditions influence the viability and consequently the efficiency of cloning. Therefore, it can be hypothesized that drugs which can reduce methylation or induce demethylation can be used to solve this problem. Such drugs can be added in the culture medium of cells used in cloning. In additions, drugs that induce acetylation (e. g. Trichostatin A, TSA, a histone deacetylase inhibitor) can be used to increase blastocyst development compared to controls. The erasure of preexisting epigenetic marks of donor cells improves subsequent in vitro development of cloned embryos by providing donor cells with similar epigenetic characteristics as in vivo embryos (Enright et al., 2003; Enright et al., 2005).

Adjustment of the other conditions like temperature, oxygen concentration, and composition of the medium can help to optimize conditions for donor cells used in cloning (Reviewed by Houdebine, 2003). It is clear from this explanation that the cellular nuclei of cloned animals

are genetically identical to the donor cells. However, cloned animals are phenotypically different from the donor cells as they are epigenetically not identical. A same phenomenon is found even in the so called "identical" twins! The epigenetic reprogramming of the transferred somatic cell nucleus with emphasis on DNA methylation, imprinting, X-chromosome inactivation and telomere length restoration in bovine development were reviewed by Niemann et al., 2008; Bao et al., 2005; Beaujean et al., 2004). Obtaining completely genetically identical clones is conditioned by using recipient oocytes and donor nuclei from the same female. Otherwise, the mitochondrial genome (exclusively maternal) can make difference in case of use of different oocytes.

Nevertheless, technical progress should not change the ethical attitude concerning human cloning. For animal cloning, however, such progress can alleviate suffering and possibly reduce negative drawbacks besides reducing costs, but should be conducted within the ethical and religious restrictions discussed throughout this paper.

International Regulations:

Muslims should follow divine instructions (inspired from Koran and Sunnah) notably in the basic issues like the one evoked in this paper. However, Muslims should also be aware of the international context. Concerning cloning, a consensus international attitude is found from the following quick overview. In general, animal cloning is authorized with restrictions (a growing list of cloned animals is publicly published as detailed in the Introduction). Reproductive human cloning is prohibited while human cloning for therapeutic objectives is a debate subject:

Australia: in this country, human cloning is prohibited, though since 2006, therapeutic cloning (within regulatory limits and legislations) and the creation of human embryos for stem cell research passed the House of Representatives.

European Union: Human cloning is prohibited though none binding with no legal standing. The related protocol was ratified only by Greece, Spain and Portugal. The suggested Treaty of Lisbon tries, however, to ratify the protocol to become legally binding in EU.

UK: Human reproductive cloning is prohibited while the therapeutic cloning of embryos is not, but within the first 14 days of the fetal life. Genetically identical embryos can be created from which stem cells can be

taken for research into many diseases like Alzheimer's, cancer, diabetes and Parkinson's (Pattinson, 2006; BBC News. 15 November 2001).

UN: in 2005 a non-binding United Nations Declaration on Human Cloning was adopted. An Ad Hoc Committee on an International Convention against the Reproductive Cloning of Human Beings was formed (United Nations. <http://www.un.org/law/cloning/>. Retrieved on 2007-01-28).

USA: Banning of all forms of cloning was voted in 1998, 2001, 2004 and 2007 at the U.S. House of Representatives. Some of states prohibit both reproductive and therapeutic cloning while others outlaw only the former one. Federal funding is prohibited for research in this domain. However, there is, currently, no absolute banning of cloning in US by federal laws. Such laws would raise difficult constitutional questions. The present US president (Barak Obama) suggests legitimization of therapeutic cloning.

CONCLUSIONS AND RECOMMENDATIONS

Our stewardship on Earth implies advancing science and its application for the service of humanity with a full respect of all creatures and ecology. Weighing risks and taking precautions are vital before the drawbacks are irreparable or irreversible. Serving human being without harming the other creatures is what can be understood from the following verses, so that we should not belong to those who "slit the ears of cattle, and to deface the (fair) nature created by Allah".

Koran, The Women:: 116-121

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REFERENCES

.1995
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 .2000

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116. Surely Allah does not forgive that anything should be associated with Him, and He forgives what is besides this to whom He pleases; and whoever associates anything with Allah, he indeed strays off into a remote error.

117. (The Pagans), leaving Him, call but upon female deities: They call but upon Satan the persistent rebel!

118. Allah did curse him, but he said: "I will take of Thy servants a portion Marked off;

119. "I will mislead them, and I will create in them false desires; I will order them to slit the ears of cattle, and to deface the (fair) nature created by Allah." Whoever, forsaking Allah, takes Satan for a friend, hath of a surety suffered a loss that is manifest.

120. Satan makes them promises, and creates in them false desires; but Satan's promises are nothing but deception.

121. They (his dupes) will have their dwelling in Hell, and from it they will find no way of escape.

Muslim countries are requested to formulate specialized committees to set up the ethics of biological research and adopt protocols for study and research. Of the important tasks of such committees is preparation of a document on fetal rights. Cloning of animals could be authorized under suitable restrictions, while that of human for reproductive purposes to be prohibited. As for therapeutic human cloning, more thorough study and cooperative work is needed between Islamic scholars and scientists to take a responsible decision.

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