Stem Cell Research: The IMANA Perspective

By

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Stem cell research is a relatively new field of medicine that has great promise but has led to confrontation with established religious and moral values. It has already generated heated debate about what are the boundaries of scientific research that it should not cross.¹

Most of the ongoing research has been utilizing embryonic stem cells (ESCs). These are derived from the embryonic inner cell mass and kept growing in tissue culture. Most of the studies were made on murine ESCs but also there has been great demand for human ESCs (hESCs) because they are believed to be much more promising in search for cures of human disease. Human embryos have been created by In Vitro Fertilization (IVF) specifically for stem cell research but more commonly human embryos used for stem cell research were supernumerary embryos left over from IVF done for reproductive purposes and donated by the couples concerned. Attempts have also been made to use spontaneously aborted fetuses but mostly these cells fail to grow in culture. Also cloned embryos have been developed through the procedure of somatic cell nuclear transfer (SCNT) which is sometimes called therapeutic cloning.²

There have been realized benefits of stem cell research the best known of which is the successful treatment of leukemia and many other hematologic disorders by bone marrow transplants and more recently by using umbilical cord blood (UCB) stem cells. However, the real promise of stem cell research is the potential development of a new field of medicine what has been called “Regenerative medicine.”³ This aims at growing tailor made human tissues or organs to be used to colonize or to replace damaged tissues/organs to recover their lost function. Progenitor cells have been developed that can be made to differentiate into myocardial cells, neurons, hepatocytes and pancreatic cells as well as other types of cells. These cells can potentially be used to treat Parkinson’s disease, Alzheimer Disease, and patients with spinal cord injury. It is speculated that they will

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**Realized and Potential Benefits of Stem Cell Research**

There have been realized benefits of stem cell research the best known of which is the successful treatment of leukemia and many other hematologic disorders by bone marrow transplants and more recently by using umbilical cord blood (UCB) stem cells. However, the real promise of stem cell research is the potential development of a new field of medicine what has been called “Regenerative medicine.”³ This aims at growing tailor made human tissues or organs to be used to colonize or to replace damaged tissues/organs to recover their lost function. Progenitor cells have been developed that can be made to differentiate into myocardial cells, neurons, hepatocytes and pancreatic cells as well as other types of cells. These cells can potentially be used to treat Parkinson’s disease, Alzheimer Disease, and patients with spinal cord injury. It is speculated that they will
also be used in the treatment of type I diabetes, myocardial infarction as well as other conditions. Another important potential benefit is in the field of pharmacology, pharmacotoxicology and specially embryotoxicology.\textsuperscript{3} When testing medications in growing cultures of ESCs becomes practical, it will eliminate the need for the use of experimental animals which has been plagued by the problem of interspecies variation.

**Potential Problems with Stem Cell-Based Therapies**

The multitude of cell divisions that will have to be part of the process of stem cell based therapies may add up to significant genetic mutations that may cause serious health problems. In addition, epigenetic modifications such as DNA mutation may also occur. Another serious consideration is that the stem cells are programmed to divide and if this division continues uncontrollably it may lead to tumourogenesis. Also implanted ESCs are going to be immunogenic and graft rejection is a real possibility. Along with the pursuit of stem cell research applications for therapy, strategies to produce techniques that enhance the possibility of reversibility should be developed as well before stem cell research enters into the clinical realm.\textsuperscript{3} So at this stage it behooves scientists while emphasizing potential benefits of stem cell therapy they should not exaggerate these benefits.\textsuperscript{5}

**Somatic Cell Nuclear Transfer (SCNT)**

In this procedure,\textsuperscript{3} a somatic cell is obtained (by biopsy) from an individual. A human oocyte is obtained from an egg donor. The oocyte is enucleated and then fused with the biopsied cell transferring its nucleus to the new cell which is then induced to develop into an embryo in a process akin to that used in cloning (hence therapeutic cloning). As the blastocyst forms, the inner cell mass is isolated and cultivated to produce ESCs which are then induced to differentiate into various cell types eventually producing a tissue to be used as an autologous tissue graft to the original person form whom the somatic cell was obtained. If the procedure is successful then it can be used clinically. For example, a somatic cell is derived from a diabetic
patient, and, using SCNT technology, pancreatic cells are generated and transplanted into that person. If these transplanted cells function properly, the person will be cured of diabetes. The new transplanted pancreatic tissue will have the sick person’s DNA and antigens. There will be no need for immunosuppression. There will be no danger of organ/tissue rejection.

Additional potential benefits of SCNT are the ability to study the pathogenics of genetic diseases and ultimately correcting the gene defect by drugs or by correcting/ replacing the defective gene.4

**Umbilical Cord Blood as Source of Stem Cells**

Umbilical cord blood (UCB) is a valuable source of hematopoetic stem cells.6 Its major advantage is that it is less immunogenic and is associated with a lower incidence of acute graft versus host reaction. However, the cell dose is approximately 10% of adult bone marrow donor unit, so it can only be used in children or “small” adults.

UCB is collected at delivery. Stem cells are separated, cryopreserved and stored for future use. Cord blood transplant has been used successfully in the treatment of oncologic, hematologic, immunologic and metabolic diseases.6 Its use is rapidly expanding into new areas including regenerative medicine e.g. the treatment of diabetes7 and other conditions.8

**Adult Stem Cells**

Few stem cells are found in many adult tissues. These cells from different tissues can be coaxed to differentiate into many other types of cells to be used in regenerative medicine.8 The main advantage of ASCs is that they will not provoke immune system rejection and that they should not become cancerous. On the other hand, the transdifferentiation potential for most ASC is probably limited compared to the unlimited transdifferentiation potential of the pluripotent hESCs. Further, ASC(s)1,2 are rare compared to the abundant hESCs that can be obtained and they are hard to grow in vitro.9
The use of UCB or ASCs does not raise moral/ethical objections other than the usual issues related to assessment of benefit / risk, privacy and informed consent. On the other hand, the use of hESCs while holding the greatest promise is the one that has created the greatest controversy. Embryonic stem cell research brings into conflict two moral principles:

1) The duty to respect human life.
2) The duty to reduce human suffering.

The question is whether we as a society can agree on which of these two principles ought to be given precedence or whether we can agree that there is a time in the development of the embryo that it is not be considered “human” worthy of “full” protection accorded a fetus or a live born infant?

The question then evolves on what is the moral status of the human embryo. There are three positions:

1) The fertilized egg (zygote) has a full moral status.
2) While the fertilized egg has a moral status but it only becomes deserving of protection at a later stage. The moral status increases as the fertilized egg becomes more human-like.
3) The embryo is an organic material with a moral status no different from any other body part.

Those who believe that the fertilized egg has a full moral status argue that there is no nonarbitrary, morally significant dividing line in the continuum of physical growth between an embryo and a developed human. Therefore the embryo is a potential person from fertilization. Their point is that while it is true that an embryo does not exhibit the properties of personhood, it will if allowed to develop and fulfill its potential.

The proponents of the second opinion agree that the fertilized egg is potentially a person but they argue that there are degrees of value of a life depending on the stage of this life.
Consequently, there are degrees of respect that ought to be shown to that life. They define these following stages:

a) Fertilization to implantation at the 6th day.
b) From the sixth day (implantation) to the appearance of the primitive streak at the end of the second week.
c) From the second week until viability which has traditionally been set at 24 weeks.

They argue that the rights of the human embryo/fetus increases as it goes from one of these stages to the next.

The third group argues that fertilized human eggs and embryos are merely parts of other peoples’ bodies. They claim that for a “being” to be destroyed, that being should have an interest that is defeated. They further argue that for a being to have an “interest,” this being must have beliefs, desires, expectations, aims and purposes and the embryo has none of these.16

Many ethicists have taken a reasonable middle ground view. They point out that before implantation (6-7 days after fertilization), the blastocysts cannot grow independently. A stage in the development of the embryo that is up to the end of the second week (after fertilization), at which time the primitive streak appears, can be defined. The primitive streak defines the head-tail and right-left orientation of the embryo and along which the major tissues and organs begin to develop. This stage has been called the pre-embryo. The pre-embryo has no nervous system and can not be considered sensate.17 Also at the end of the second week there is no more possibility of twinning.15 At that time, the pre-embryo becomes an embryo and acquires a unique personhood. In this view, the early human embryo has an “intermediate” moral status. Thus, the pre-embryo and particularly before implantation, the blastocyst can be used for experimentation i.e. stem cell research. However, special respect needs to be given to the blastocysts to be manifested by a) limiting their use to important human purposes. b) establishing guidelines for the research. c) establishing procedures to ensure that these guidelines are followed.
They support their argument with the observation that in natural reproduction, many fertilized eggs either stop developing or fail to implant and are “lost”.\textsuperscript{14}

**Sources of Human Embryos for Stem Cell Research**

In IVF procedures performed in the course of fertility treatment many generated embryos are found to be “nonviable” (unsuitable for implantation) and will be discarded while they could be used for research.

Further, in these procedures there are always excess (supernumerary) fertilized eggs produced. These are commonly cryopreserved for possible future use by the couples who produced them but often they are never used and can be an adequate source for stem cell research. Fresh fertilized eggs would be a much more efficient source of stem cells. They have to be donated by the couple undergoing IVF after obtaining a thorough informed consent.

**Ethical Considerations with Somatic Cell Nuclear Transfer (SCNT)**

One misconception about SCNT resulted from the more popular nomenclature that has been given to the procedure i.e. “therapeutic cloning”. SCNT is not reproductive cloning. Its opponents argue that this is a first step along a slippery slope that would conclude in accepting reproductive cloning.

Another ethical concern is the source of the donated human eggs (ova) used for SCNT. These need to be donated by healthy women. The concern is that for this research to continue there will be a surge in the need for donor women and this will substantially increase if SCNT is developed - as it is hoped - into a therapeutic modality. The concern then is that there will be the potential for exploitation of women to satisfy the increasing demand for procurement of human eggs.\textsuperscript{1,18} Egg donation involves the use of hormones to stimulate egg production and an invasive procedure to retrieve the eggs. Donors are usually compensated. It is generally permissible to substitute for lost wages, expenses for the procedure and the inconveniences
encountered during the invasive procedure and possible side effects from the use of hormones to cause superovulation with the major risk, though rare, of ovarian hyperstimulation.1,18 The question is how much these are worth and would money be the reason for volunteering or would it be pure altruism. In any case, a thorough informed consent must be obtained.18

Religion and Stem Cell Research

Christianity

Broadly speaking Catholics, Orthodox (Greek/Coptic) and conservative Protestant churches have similar views on this topic which is that the human embryo is an individual from the moment of fertilization, and that it has the right to its own life. They further believe that every intervention not in favor of the embryo is a violation of its right and that no good end justifies the destruction of an embryo.19,20 On the other hand, “less conservative” Protestant churches teach that the embryo has potential human status but the life of the embryo has to be weighed against the possible benefit that may result from scientific research. They believe that while the life of an embryo is sacred from the time of fertilization, embryo research may be permitted prior to the primitive streak stage.10

Judaism

Judaism is also nonmonolithic. There are several subgroups. The main groups are Orthodox, conservative and reform. Broadly speaking, there are some principles in Judaism that pertain to this discussion. These include: a) healing is a required obligation,21 b) any activity that contributes to advancement in the world can not be considered contradicting God’s orders,22 c) God is the one who gave us the power to create new technology, and then we can use it,12 d) each activity which has no reason to be prohibited is permitted without having to find a reason for its permissibility,22 e) the human fetus < 40 days of age and certainly the preimplantation embryo does not have full human status.21
Islam

Islam is usually defined as submission to Allah’s (God) will. Muslims believe that Islam controls their actions in material as well as spiritual matters. Islam is commonly described as a way of life. So a Muslim in performing any act should ask himself whether this act is permissible or not. One has to find if there is a Quranic injunction on that matter and if not then one has to find out if there is a Hadith (saying) of Prophet Muhammad ﷺ and if not then one has to resort to the opinion of Islamic jurists (fuqahā’) who use ijtihād (independent judgment) and put concerted effort to come up with a new ruling.23

The most important consideration in the topic under discussion is when life starts. There is no specific definition of the beginning of life either in the Quran or the Hadith. It is generally agreed that ensoulment i.e. the breathing of Allah’s rūh into the fetus differentiates biological life which starts at the time of fertilization from human life.24 There is a difference of opinion between scholars whether ensoulment occurs at 40 or 120 days,24-26 depending on a varied interpretation of a hadith narrated on the authority of Ibn Mas‘ūd.

Verily, the creation of each one of you is brought together in his mother’s belly for 40 days. Then it remains there as a leech-like structure for a similar [period]. Then it remains there as a lump of chewed flesh for a similar [period]. Then an angel is sent and it blows into him the spirit ...27

All scholars agree that life is entitled to respect even before ensoulment but becomes more so after it occurs.28 The following are Islamic principles that may apply to stem cell research:
a) Islam has always encouraged humans to contemplate and explore new horizons.\textsuperscript{29-31}

\textit{إِنَّمَا يَخْشَى اللَّهُ مِنْ عِبَادِهِ الْعَلِيمَاءُ}

... Those (who) truly fear Allah, among His Servants, (are those) who have knowledge ...\textsuperscript{29}

\textit{قُلُ سَيْرُوا فِي الْأَرْضِ فَانظُرُوا كَيْفًا بَداً الْخَلْقُ}

Say: "Travel through the earth and see how Allah did originate creation..."\textsuperscript{30}

\textit{أُوَلَمْ يَنظُرُوا فِي مَلْكُوتِ السَّماوَاتِ وَالْأَرْضِ وَمَا خَلَقَ اللَّهُ مِنْ شَيْءٍ}

Do they see nothing in the dominion of the heavens and the earth and all that Allah hath created?\textsuperscript{31}

b) The Messenger \textit{ﷺ} ordered us to seek cure for disease: Allah created disease and treatment, and He made for each disease a treatment. So seek treatment but do not use \textit{ḥarām} (forbidden things).\textsuperscript{32}

\textit{إِنَّ اللَّهَ تُعَالِي أَنْزِلَ الدَّاءُ وَالْدِّوَاءُ وَجَعِلَ لِكُلِّ دَاءٍ دَوَاءً فَتَدَاوَوا وَلَا تَدَاوَوا بِحَرَامٍ}


c) All actions are in principle permissible as long as they are not categorically prohibited.

d) In matters in which other invocations are silent then the concept of \textit{maṣlaḥa} (a public interest) applies: "where the welfare of people resides, there resides the statue of God."\textsuperscript{28}
Abdulaziz Sachedina, a Muslim Professor of Religious Studies at the University of Virginia, stated “Research on stem cells made possible by biotechnical intervention is regarded as an act of faith in the ultimate will of God as the Giver of all life as long as such an intervention is undertaken with the purpose of improving human health.”

There has been several published reports on the Islamic perspective of stem cell research by both non-Muslims and Muslims. These authors conclude that Islam permits stem cell research in principle.

The Muslim World League’s Islamic Jurisprudence Council conference in December 2003 held in Mecca, Saudi Arabia issued this fatwā (religious opinion):

It is permissible to use stem cells for either legitimate scientific research or for therapy as long as its sources are legitimate for example, adults if they give permission as long as it does not inflict harm on them; children with their guardian’s permission for a legal benefit without inflicting harm on them; placenta or umbilical cord blood with the permission of the parents; spontaneously aborted embryos or those aborted for a legally acceptable cause and with the permission of the parents; excess fertilized eggs produced during the course of IVF and donated by the parents with assurance that they are not to be used to produce an illegal pregnancy. It is forbidden to obtain or use stem cells if its source is illegitimate as, for example, intentionally aborted fetuses (abortion without a legal medical reason); intentional fertilization between a donated ovum and sperm; and therapeutic cloning.

This last point is unclear. Although it seems to prohibit therapeutic cloning completely, it may be that the prohibition is meant if the procedure is performed to create an embryo to be a stem cell donor. It may be that the prohibition does not apply to the actual SCNT to generate a tissue that will be transplanted in the donor of the somatic cell or to diagnose and study the treat-
ment of a genetic disease in that donor.

Yusuf al-Qaradawi, a well-known contemporary Islamic scholar, stated that if it becomes possible through research to clone organs e.g. heart, liver and kidney, it will be permissible and it may become mandatory to pursue such endeavors. All Shia scholars agree that therapeutic cloning is permissible.

Somatic cell nuclear transfer using a somatic cell from a person and fusing it with an enucleated human ovum thus producing a human embryonic clone is a promising form of “therapeutic cloning.” There is no resolution that specifically addresses the permissibility of the technique of somatic cell nuclear transfer in humans because it is still in the theoretical phase.

**Summary**

There is general agreement among Muslim scholars that stem cell research using adult stem cells e.g. bone marrow, peripheral blood or umbilical cord blood, is permissible. On the other hand, the use of human embryonic stem cells (hESCs) in research has not been universally accepted by Muslim scholars. Scholars realize the great potential of stem cell research in curing so far incurable human diseases and that embryonic stem cells have more potential than adult stem cells. The majority of contemporary scholars does not consider the fertilized egg as an embryo in the legalistic sense and support both stem cell research and preimplantation genetic diagnosis (PGD). They opined that embryonic stem cell research using surplus pre-embryos produced during the course of IVF performed for infertility patients is permissible with the consent of the couple. All agreed that it is prohibited to create these pre-embryos for the sole purpose of research. This was expressed in many resolutions, including that of the First International Conference in Bioethics in the Muslim World, Cairo, 12/10-13, 1991, the Fiqh Council of North America, International Institute of Islamic Thought, USA, Islamic Organization of Medical Sciences (IOMS), the Society of Islamic Medical Sciences of the Syndicate of Jordanian Physicians Conference of September 2000 and the Muslim World League’s Islamic Fiqh Council.
**Conclusion**
The Ethics Committee of IMANA thus believes that:

1. In principle, stem cell research, including the use of hESCs and SCNT, is acceptable due to its therapeutic potential.
2. Fertilized eggs before implantation are not considered fully human because without implantation they can not survive and develop into a human being.
3. The supernumerary embryos produced during IVF can not be donated to other couples and if they will not be used by the same couple, they will have to be destroyed or left to die. Using them for stem cell research in this case is, at a minimum, acceptable and may even be preferred over their destruction.
4. Islamic scholars agree that creating human embryos for the sole purpose of research is prohibited.

Allah ﷻ knows best.

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