Debate on Ethical Issue in Human Stem cell Research

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A meaningful debate on ethical issues in human stem cell research (1) one will need to clearly understand the terminology used, the sources and its classification of currently available stem cells in Biomedical Research. Also he should be aware of the promise that such research could possibly bring to human being as well as what conflicts will encountered to the principle of biomedical ethics today.

I、 DEFINITION AND TERMINOLOGY

A stem cell is a unique and essential cell type found in mammals that possess the ability to divide for infinite periods in culture and can give rise to many different specialized cell of that particular species of animals or human being. Consequently, it becomes the most important research subject and competitive field in biomedical research of today.

A fertilized egg is "Totipotent", meaning that its potential is total. In the first 24 hours after fertilization, two pairs of 23 chromosome, from egg and sperm met and mixed. The new cell now has 46 chromosome, is called a "zygote". This cell then divided into two identical totipotent cells. This means that either one of these two cell if placed into a woman uterus, has the potential to develop into "fetus". In fact, identical twins develop when two totipotent cells separated and developed into two individual genetically identical human beings. The cells continue to divide from 2 to 4 to 8, and 16...they are "blastomeres". About 4 days after fertilization and after several cycles at cell division, these totipotent cells begin to specialise and forming a hollow sphere of cell mass called "Blastocyst". The blastocyst has an outer layers of cells and inner cluster of cell mass toward one end. These cells are "pluri-potent stem cell", can give rise to many type of cells but not all types of cell nessary for the development of fetus in uterus. The blastocyst then will take 48 hours to migrate from fallopian tube to uterus. At about 6 to 9 days after fertilization, the blastocyst reaches to uterus for the implantation. The outer layers of cell will go on to embed itself into uterine wall and formed placenta, amniotic sac and other supportive tissue, needed for the "fetus" development. The inner cell mass will go on to form virtually

all type of cells and tissue of human being. These Pluri-potent inner cells, however, can not give rise to form placenta tissue. At about 14 days after fertilization, the inner cell mass started to form a linear thickening structure — the primitive streak. Up to this point in time the development is called "pre-embryonic period" and the entity is called "pre-embryo". From 14 days to 56 days is called "the embryonic period" in which the primitive streak further develops to form organs and tissue of the embryo. From 56 days or 8 weeks and thereafter, the development of "embryo" became a fetus. This period of time is called "fetal period"(2).

The pluri-potent stem cell undergo further specialization into stem cells that are committed to give rise to cell lines that have a particular function, such as blood stem cell, skin stem cell, or mesenchymal stem cell that developed into mesenchymal tissues. These, more specialized stem cells have less potential than pluri-potent stem cell, yet they still able to differentiated into several cell types, hence, are multi-potent. The multipotent stem cell can be found in bone marrow, skin, liver, brain of children and adult, cord blood of the new born which are now generally classified as non-embryonic stem cells. Contrarily, the stem cell which taken out from embryo is called embryonic stem cell.

II、SOURCES OF HUMAN STEM CELL IN RESEARCH

At the present time, human stem cells can be derived from the following sources:

1、 Human fetal tissue following therapeutic abortion: Cells isolated from the premodial reproductive region of the fetus. These cells called embryonic germ cell which are cultured to grow into pluri-potent stem cell.

2、 Human embryos that are created by in-vitro fertilization (IVF) that are no longer needed by couples being treated for infertility: Cells can be isolated directly from the inner cell mass at the blastocyst stage of development at pre-embryonic period. Those cells are pluri-potent.

3、 Human embryo that are created by IVF with gametes donated for the sole purpose of providing research material: The same pluri-potent stem cell can be isolated in blastocyst at pre-embryonic stage of development.

4、 Human embryo, can potentially generated asexually by "somatic cell nuclear transfer (SCNT)" similar to cloning technique in animal, in which the nucleus of an adult human cell (somatic cell) is introduced into an enucleated human egg i.e.: The fusion of two cells will create a new cell that similar to a fertilized egg, which is totipotent, and can develop into embryo.

5、 Non-embryonic stem cells, which obtained from cord blood, bone marrow, skin, liver, pancreas and brain etc. These stem cells, however, are multipotent.

III、THE PROMISE OF HUMAN STEM CELL RESEARCH

There are two levels of important reason, why human stem cell research is essential. The first level is fundamental understanding in biological science of cell specialization. The second level of promise is to advance in health care of human being in the long run.

Science and Fundamental level of understanding:

1、Pluri-potent stem cell could help us to understand the complex events that take places during human development.

2、Understanding of factor or factors involved in decision making process that results in cell specialization.

3、We know that turning gene "on and off " is central to the process of cellular decision-making. But we do not know much about these "decision-making" gene or what turns them on or off.

4、The fundamental errors that cause the cell lost control of its own growth and became cancer, or the point of specialization arrest that cause birth defect.

Clinical and practical level in Health Care:

Stem cell research can provide:

1、 Dramatically change the way of drugs development and testing (Toxicology) by using available human cell lines, to replace phase II, III time consuming clinical trials.

2、 Tissue or cell therapy: If pluri-potent stem cell can be stimulate to develop into special cell and tissue that can offer the possibility of a renewable source of replacement of cell to treat a myriad of ailments such as Diabetes Mellitus, Parkinson disease, ALS, Alzheimer disease and A replacement of tissue to treat many diseases such as spinal cord injury, stroke, burn, heart disease, osteoarthritis or organs for transplantation and so on.

IV、ETHICAL ISSUES IN HUMAN STEM CELL RESEARCH

◆ General consideration：

The scientific advance of the successful isolation and culture of embryonic stem cell and embryonic germ cell have renewed a longstanding controversy about the ethics of research involving human embryo and cadaveric fetal tissue. Although we believe most would agree that human embryos deserve respect as a form of human life, disagreement arise regarding both what form such respect should take place and what level of protection is required at the different stages of embryonic development.

Since the embryo research that is not therapeutic to the embryo itself. It is bound to raise serious concern between two important ethical commitments: to cure disease and to protect human life. For those who believe that the embryo has the moral status of a person from the moment of conception, research that would destroy the embryo is considered wrong and should not take place. For those Utilitarians who believe otherwise may arrive at an ethically acceptable policy and to balance a number of ethical concerns.

There are also distinctive different opinions on moral issue and long ethical debates regarding elective abortion on the use of embryos for research purpose. Yet, so far the research on non-embryonic stem cell are spared and immune from this hot debate; because they are cellular element obtained from a living person that "Do no Harm" (principle of non-maleficence) to the donor, and do not involved in a destruction of life and can provide potentially great benefit (principle of beneficence) to human being. The same principle can be applied in the research of pluri-potent stem sell if its harvest would not cause the destruction of the "pre-embryo".

◆ Status of Pre-embryo Research

In May 4, 1979 report, Ethics Advisory Board (EAB in US). Agreed that "the human embryo is entitled to profound respect, but this respect does not necessarily encompass the full legal and moral rights attribute to person". The EAB statement supported research on the safety and efficacy of IVF and embryo transfer techniques to be used for the treatment of infertility. American Fertility Society (AFS) committee on ethics, in its 1986, 1990 reports recommended that human pre-embryos not to be maintained for research beyond 14^{th} days after fertilization. The 14^{th} days limit was also recognized by EAB in 1979, the Waller Commission Report (Australia) in 1984, and Warnode Committee Report (Great Britain) in 1984.

ACOG committee on ethics takes the position that human pre-embryo research can be justified under certain conditions. ACOG recognizes the value of the pre-embryo as relative, in the sense that it does not require the degree of protection and absolute respects that accorded to human person. But the pre-embryo is "human" – not simply like other human tissue (for its genetically unique and has human potential).... It is not a "human person" and does not as yet have within itself a determinate potential to become an individual "human person". There are 10 conditions (guidelines) research on human pre-embryo should be conducted: (3)

◆ Ethical Relevance of 14 Days Limit on "Pre-embryo" Research:

A：Lack of individuation and singleness of the developing entity

1) Fertilization is not a momentary but a 2 days process.

2) "Zygote" is an entity with new genotype but incapable of expression at its earliest stage. (being regulate instead by information from oocyte)

3) Relevant animal research demonstrated one or more blastomeres can be removed from the aggregated inner cell mass, the remainder can still produce a complete adult, and individual blastomere can be removed and develop into a complete individual, further more, cell derived from two "pre-embryos" of different genetic origin can aggregate into one large mass and develop into one individual call "Chimera"

4) From the earliest stage of cell division all the way to the complete formation of the "Primitive Streak". The pre-embryo is capable of dividing into more than one entity.

This can yield a conclusion that the human pre-embryo does not possess the biological individuality (singleness) necessary for a concrete potentiality to become a human person, even though it does possess a unique human genotype.

B : High Rate of Spontaneous Early Pre-embryo Loss

Data based on the use of highly sensitive assays for human chorionic gonadotrophin indicate that a significant number (60%) loss of pre-embryo spontaneously. Whatever the reason, natural reproduction occurs in such a way that over half (may as high as 78%) of fertilization do not result in live birth. This may undergird the conclusion that moral status of pre-embryos is to be differentiated from that of embryos.

◆ Ethical Debates on each specific Source of Human Embryonic Stem Cell

At the present time, Human embryonic stem cell (germ cell) research should be limited to two sources 1) and 2) but not others.

1) From cadaveric fetal tissue obtained from therapeutic abortion: Research that uses tissue from aborted fetus is analogue to use of fetal tissue in transplantation to treat disease like Parkinson. There are considerable agreements throughout the world. The precaution should take, however, is to prevent fetal tissue donation from influencing the abortion decision, particularly when the issue of abortion still under contentions debate.

2) From embryos remaining after infertility treatments:

The potential donors of embryos for embryonic stem research must be able to make voluntary and informed consent and

①Disclosure that embryonic cell research is not intended to provide medical benefit to embryo donors.
②Make clear that consenting or refusing to donate embryos to research will not affect the quilting of any future care provided to prospective donor.
③Describe to the potential donor, the general area of the research to be carried out with the embryos and the specific research protocol if knows.

④Disclosure of the source of funding and expected commercial benefits of the research with embryos, if knows.
⑤Make clear that embryos used in research will not be transferred to any woman's uterus.
⑥Make clear that the research will involve the destruction of the embryos.

3) From embryos made solely for research purpose using IVF :

Human embryos that created by IVF, with gametes donated for the sole purpose of providing research is known as "Research Embryo". The primary objection is that there is a morally relevant difference between generating an embryo for the sole purpose of creating a child and producing an embryo with no such goal. The objection for creating a "Research Embryo" is about respecting human dignity, by avoid instrumental use of human embryos. It does not treat them (embryos) with appropriate respect or concern as a form of human life.

4) From embryos made using somatic cell nuclear transfer into oocyte:

The creation of a human organism using this technique raise question similar to those raised by the creation of research embryos through IVF for solely instrumental use only, and irrespective of human dignity. Besides, the unknown risks and "Creation of new life" has been great concerns among ethicist. Particularly, never will they (embryos) be treated with appropriate respect as a form of human life.

CONCLUSION

So far there are sufficient 60 some human embryonic cell lines is currently available for research in U.S.A. They obtained primarily from two less controversial sources. Cadaveric fetal tissue and embryos remaining are after infertility treatment. But researchers still fear inadequate source of the material to be competitive internationally. The Federal Government policy is, however, restrict to use public (Federal) funding to other sources such as "Research Embryo" and somatic cell nuclear transfer (SCNT). Perhaps, hopefully, someday, the pluri-potent embryonic stem cell — one or two of the blastomere, can be taken out (donate) without do any harm or sacrifice the "Pre-embryo" and to culture it to become a cell line for research purpose, like has been safely and successfully done in animal model, this will be much less in ethical conflict.

REFERENCES

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