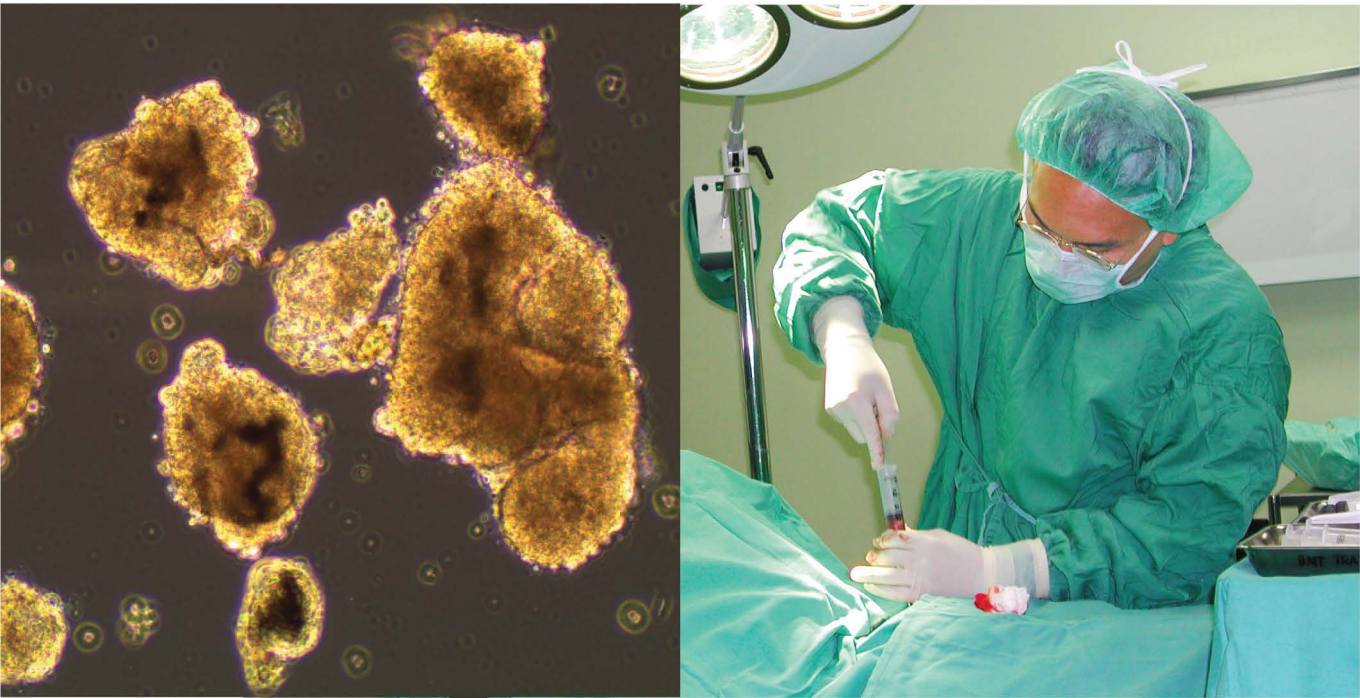


GUIDELINES FOR STEM CELL RESEARCH AND THERAPY



The Guidelines For Stem Cell Research and Therapy was prepared by
Stem Cell Research and Ethics Subcommittee of National Stem Cell Committee in
collaboration with the Obstetric & Gynaecological and Paediatric Services Unit of the
Medical Services Development Section, Medical Development Division, Ministry of
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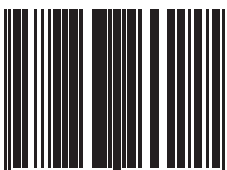
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FOREWORD

DIRECTOR GENERAL OF HEALTH MALAYSIA



The 2nd edition of the National Guidelines for Stem Cell Research and Therapy, prepared by the Medical Development Division of the Ministry of Health, has comprehensively revised the first edition of the same book to facilitate researchers and clinicians involved in stem cell research and therapy.

Stem cells have a tremendous potential in terms of therapy. However, many of these therapies, especially those involving replacement and repair of tissues and organs, are still experimental in nature. Despite the obvious enthusiasm, there is still a lot of scientific research that needs to be done before such therapies can be endorsed by the Ministry of Health. Most importantly, differentiated cells derived from stem cells must be tested comprehensively in terms of safety, quality and efficacy before they can be used in humans. There is certainly no short cut to this.

There is also the big ethical issue on the use of embryonic stem cells derived from leftover human embryos from IVF procedures. The committee has looked into this matter comprehensively and obtained valuable input from key opinion leaders. The fatwa from the Muslim jurists has also been sought. The use of embryonic stem cells is addressed comprehensively in this document.

There are already some approved indications for stem cell therapy e.g. in the setting of bone marrow or peripheral blood stem cell transplantation for the treatment of leukaemias and certain malignancies. However, for some others, the indications are still experimental in nature. Xenotransplantation, for example, is still considered experimental in nature and it is important for clinicians and the public to be aware of this.

Practitioners and scientists involved in stem cell research and therapy must adhere to these guidelines to ensure that no harm is done to the patients. Failure to do so may result in repercussions which may put the practitioners or scientists in a difficult position especially if they are proven to be unethical in their practice or research with regards to the use of stem cells. We all have the responsibility to uphold the highest standards in medical care and medical ethics.

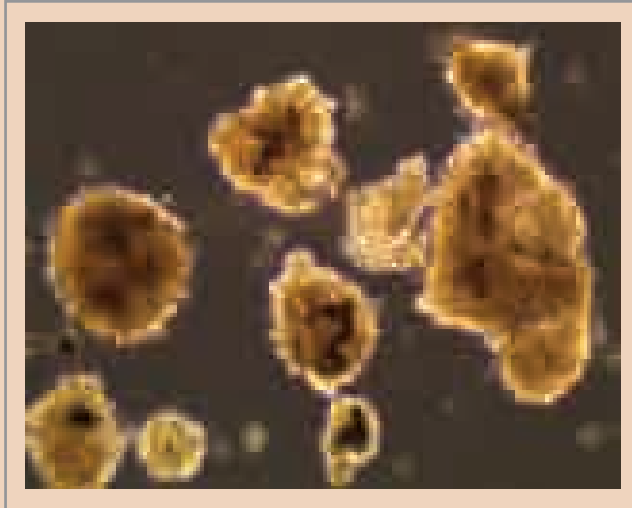
I hope this guideline will be a valuable reference document to clinicians, researchers, institutional research and ethics committee as well as the public.



TAN SRI DATO' SERI DR. HJ. MOHD ISMAIL MERICAN

Director General of Health Malaysia

Ministry of Health Malaysia



Undifferentiated hESC colonies grown on low attachment plate
(without feeder layer) (phase contrast 10X)



Undifferentiated hESC colony on low attachment plate
(without feeder layer) (phase contrast 20X)

(Source : Institute for Medical Research, 2008)

1.0 Introduction

Although there are many controversies surrounding stem cell research, the Ministry of Health recognises that it is crucial for local scientists and clinicians to be involved in stem cell research provided that these conform to ethical guidelines. It is vital for medical scientists to keep abreast of current advances in science, especially when there is an enormous potential of revolutionizing therapy in the form of cell replacement therapy. Hence the Ministry of Health has set up a task force to readdress essential issues in stem cell research and consider the evolution of emerging therapies in this update of the guidelines.

2.0 The Status Of Stem Cell Research In Malaysia

Stem cell research is relatively new in Malaysia. Most of the work thus far has involved haemopoietic stem cells (bone marrow, peripheral blood and cord blood). As these are from adult tissues, ethical concerns may be minimal since they are being used in the setting of haemopoietic stem cell transplantation. The use of sources of cells other than the adult stem cells e.g. cell lines or fertilized embryos is a major concern as it is likely that our local researchers will be conducting research in this area.

3.0 Background On Stem Cells

Stem cells as the name implies are cells capable of developing into other types of cells and tissues; for this reason they are often referred to as 'pluripotential' cells. Historically, stem cells have

been viewed within the context of the embryo because it is within these early stages that we see the dramatic transitions of stem cells forming a range of tissues and organ systems. For example in the early trilaminar embryo, we see ectoderm cells giving rise to the outer epidermis and central nervous system, mesoderm cells giving rise to the cardiovascular system as well as bones and muscle, and endoderm cells forming the early gastrointestinal tract plus various accessory organs like the lungs and liver. Much of the proposed research on stem cells centers upon the early human embryo.

Alternatively, there have been promising studies with adult tissues where so-called 'stem-cell' activity has been demonstrated. For example under certain growth and hormonal conditions skin cells have been successfully transformed into bone or muscle cells. In other studies, bone marrow cells have been reprogrammed into heart muscle cells. Studies with adult tissue as potential sources of stem cells are starting, but there is a significant potential for using adult tissue in future treatment of human diseases.

Whether stem cells prove to be ‘the treatment of the future’ will depend on continued research and exploration. However, with current scientific, ethical, moral, and political questions yet to be resolved, stem cell therapy has yet to be seen and proven safe.

4.0 What Are Stem Cells?

Stem cell research exploded to the scientific scene in 1998 when researchers first reported that they had successfully isolated human embryonic stem cells. Unique properties of stems include that they are unspecialized, or they have the potential to make many different types of cells, are capable of dividing and renewing themselves for long periods of time, and they can also turn into specialized cells. Unspecialized cells transform into specialized cells such as neurons, muscle cells, or red blood cells through a process known as differentiation. Stem cells are either harvested from adults or embryos, and growing these cells outside the body requires the right mix of nutrients, hormones, growth factors,

and blood serums. Undifferentiated cells are considered pluripotent when they have the potential to become any type of cell provided the condition is right. Once researchers isolate stem cells and allow for them to proliferate in a culture for six months without differentiating, a stem cell line has been created.

Adult stem cells are undifferentiated cells found among differentiated tissue or organs, and they have the potential to renew itself or differentiate into major specialized cell types. The role of adult stem cells in the body is to maintain and repair the tissues in which they are found. Adult stem cells are thought to reside in a specific area of each tissue where they remain quiescent, or non-dividing, for years until they are activated by either disease or tissue injury. Tissues that house stem cells include brain, bone marrow, peripheral blood, blood vessels, muscles, skin and liver. Adult stem cells are generally tissue specific, for instance, haemopoietic stem cells are blood-forming cells that are found in bone marrow. While adult stem cells have the potential to differentiate into mature tissue when isolated from the body,

they are extremely difficult to divide in the laboratory. Scientists believed that adult stem cells from one type of tissue can only yield that same type of tissues when cultured; but recent experiments have raised the possibility that stem cells from one tissue may be able to create cell types of completely different tissue types, also known as plasticity. While adult stem cells are free of ethical concerns, they are facing numerous scientific challenges.

Human embryonic stem cells have the potential to develop into essentially any type of cell in the human body. In theory, scientists believe that embryonic stem cells have the potential to theoretically divide without limit to replenish or create other cells. Embryonic stem cells also have the potential to either remain a stem cell or to develop into a specialized cell such as a red blood cell or a muscle cell. Embryonic stem cells are primarily obtained from frozen embryos that are donated through *in vitro* fertilization programs from extra embryos that were created for infertile couples to use during fertility treatments. A

surplus of embryos are usually created and kept frozen for future use by the couple. When couples no longer need their frozen embryos for reproductive purposes, depending on the laws of that particular country, the embryos are used for stem cell research. Cell lines are grown by isolating human embryonic stem cells from the inner mass of a human blastocyst, or a 5-day embryo. With the help of fibroblast feeder layers, embryonic stem cells can be cultured indefinitely.

Human embryonic stem cells (hESC) can also be obtained by a method referred to as somatic cell nuclear transfer (SCNT), or therapeutic cloning. During SCNT, a nucleus is removed; removing the nuclear genome of an oocyte, and it is replaced with the nucleus of an adult cell. The egg is then activated to form a blastocyst, containing fewer than 100 cells, which contains genetic material identical to the adult donor cell. Scientist can either remove stem cells from the blastocyst or place the blastocyst into a uterus where it would have the potential to develop into a fetus. By using SCNT, researchers are able to

control the genotype of hESCs which eliminates the probability of tissue rejection. While a cloned animal is abnormal, cloned stem cells are perfectly normal. If a gene is active in a fertilized stem cell, it is also active in a cloned stem cell at the same activity level. Research shows that there is no significant molecular difference between cloned and non-cloned stem cells.

While embryonic stem cells and adult stem cells are both sources of undifferentiated cells, they both have several differences. Because embryonic stem cells are pluripotent, they have the ability to become all types of cells whereas adult stem cells are limited to developing into two cell types of the tissue or organ that they originated from. Another difference between the two cells is the ease of growth in a culture. It is relatively easy for researchers to grow a large number of embryonic stem cells in culture compared to adult stem cells which are relatively rare and have no methods for greatly expanding the number in cultures. Finally, if a patient's own cells are used to create adult stem cells, there is little risk that they would be rejected by the individual's

immune system, but because hESC clinical trials have not been conducted, scientist are unsure of the risk of rejection in the use of embryonic stem cells.

Scientist believe that stem cell research is important to the future of medicine because with adequate and appropriate research, stem cells have the potential to treat disease by transplanting human stem cells into patients suffering from degenerative diseases such as Parkinson's disease, diabetes, traumatic spinal cord injury, Purkinje cell degeneration, Duchenne's muscular dystrophy, heart disease, and hearing and vision loss. With gene therapy, a genetic defect would be corrected by giving a healthy version of the gene to a patient. A physician would isolate stem cells from the patient and introduce a harmless virus into the stem cells that express the correct version of the mutated gene and re-administer the stem cells back to the specific disorders. By using SCNT, scientists may also be able to change diseased cells to their primordial form and then monitor them to determine how and why abnormalities develop. Once scientists have understanding of

diseased cells, they will be more successful in creating treatment options.

While the untapped possibilities leave many members of the medical research community excited, there are numerous obstacles that may impede human stem cell research. Issues such as morality, funding, and national regulations impede scientists across the world from pursuing research possibilities related to gene therapy and stem cell research.

5.0 Ethical Issues Of Stem Cell Research

Many difficult questions engulf the morality of destroying embryos or using remnants of aborted fetuses to improve the medical wellbeing of other human beings. Opponents of embryonic stem cell research argue that human life begins when an egg is fertilized; therefore, a human embryo is equivalent to a human being. Proponents of embryonic stem cell research argue

that during the natural reproductive process human eggs often fertilize, but fail to implant in the uterus. While a fertilized egg has the potential to form a human life, it is not equal to a human being until it has at least successfully implanted in a woman's uterus. IVF clinics often create more embryos than needed over the course of fertility treatments and the excess frozen embryos are discarded. Opponents state that research on these embryos still condones the destruction of embryos, while proponents believe that it is morally permissible to use these embryos for potentially life saving biomedical research.

6.0 International Legislation On Human Embryonic Stem Cell Research

The policies on human embryonic stem cell (hESC) research used by different countries vary tremendously and change frequently. The basis for the regulation of stem cell research includes the source of the stem cell, objective of research, and the symbolic

moral right of the embryo. There are four statuses of regulation on human embryonic research worldwide as shown in Table 1.

Table 1: Global Status of Regulation of Human Embryonic Research

Status of Regulation	Countries
Regulated by law	Australia, Belgium, China, Denmark, Finland, Hungary, India, Israel, Japan, Singapore, Spain, South Korea, Sweden, United Kingdom.
Law in preparation	Brazil, Canada, France, Iran, Netherlands, South Africa, Portugal, Spain, Taiwan
Prohibited	Austria, France, , Germany, Ireland, Italy, Netherlands, Norway
No law yet	Africa, Belgium, Czech Republic, Greece, Italy, Poland, Slovenia, Switzerland, Turkey

7.0 Potential Impact On Health

Stem cell research is important to the future of medicine because with adequate research, stem cells have the potential to treat degenerative conditions by transplanting human stem cells into patients. Presently, many of these chronic conditions have no cure and are managed by treating the symptoms. While the initial cost of receiving stem cell therapy may be high, it has the potential to outweigh the life long costs incurred through daily medications and hospitalizations. By making disease management easier, the quality of life for those diagnosed with these diseases and their family members would be greatly increased. With sufficient development of stem cell therapy, chronic diseases such as diabetes, heart disease, and Parkinson's disease may be more effectively managed. To realize the promise of novel cell-based therapies for such pervasive and debilitating diseases, scientists must be able to easily and reproducibly manipulate stem cells so that they possess the necessary characteristics for successful

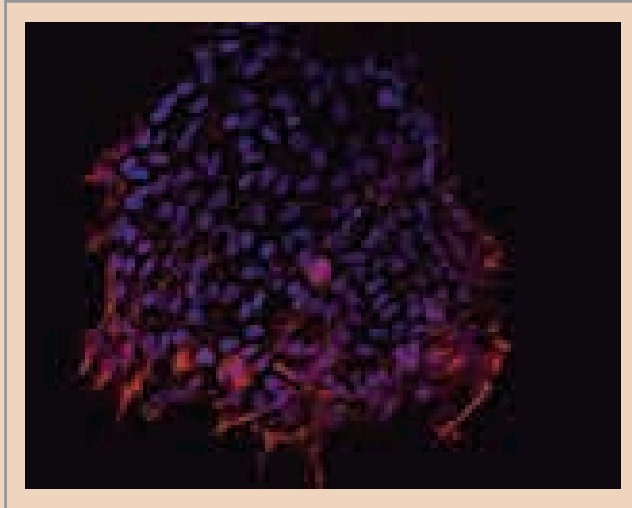
differentiation, transplantation and engraftment. The following is a list of steps in successful cell-based treatments that scientists will have to learn to precisely control to bring such treatments to the clinic. To be useful for transplant purposes, stem cells must be reproducibly made to:

- Proliferate extensively and generate sufficient quantities of tissue.
- Differentiate into the desired cell type(s).
- Survive in the recipient after transplantation.
- Integrate into the surrounding tissue after transplantation.
- Function appropriately for the duration of the recipient's life.
- Avoid harming the recipient in any way.

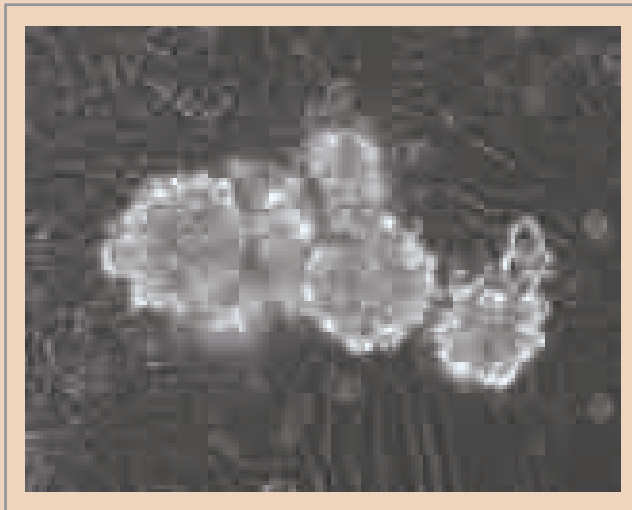
Also, to avoid the problem of immune rejection, scientists are experimenting with different research strategies to generate tissues that will not be rejected.

8.0 Conclusion

While the benefits of stem cell research may seem to be out of reach for the immediate future, with continued research, stem cell therapies are predicted to become common treatment for degenerative diseases. To be successful, researchers must collaborate and share limited resources.



Immunofluorescence staining of hESC for detection of embryonic surface marker. Nestin/RRX-DAPI (20X)



Undifferentiated hESC colonies grown in mouse feeder layer (phase contrast 10X)

(Source : Institute for Medical Research, 2008)

GUIDELINES FOR STEM CELL RESEARCH AND THERAPY

Guidelines For Stem Cell Research

1. The Ministry of Health will undertake to encourage and promote stem cell research in Malaysia.
2. All stem cell research and applications must be reviewed by the respective Institutional Review Board (IRB) and/or the Institutional Ethics Committee (IEB) for approval to ensure ethical research and use of stem cells. The IRB and IEC must strictly adhere to the National Guidelines for Stem Cell Research and Therapy.
3. A copy of all research proposals must be submitted to the National Stem Cell Research and Ethics Subcommittee which shall retain the rights to review any research proposal as and when required.

4. All experiments and clinical trials involving stem cells must be based on a solid foundation of basic scientific and animal experimentation and carried out with the highest medical and ethical standards.
5. Research on human adult stem cells is allowed.
6. Research on stem cells derived from foetal tissues from legally performed termination of pregnancy is allowed.
7. Research on non-human stem cells is allowed.
8. Use of embryonic stem cell lines for research purposes is allowed.

9. Research on embryonic stem cells derived from surplus embryos is allowed. (Please refer to the *Keputusan Muzakarah Jawatankuasa Fatwa Majlis Kebangsaan Bagi Hal Ehwal Agama Islam Malaysia berkaitan Pengklonan dan ART* dated 22 February 2005)
10. The creation of human embryos by any means including but not limited to assisted reproductive technology (ART) or somatic cell nuclear transfer (SCNT) specifically for the purpose of scientific research is prohibited.
11. To facilitate autonomous choice and avoid conflict of interest, decisions related to the production of embryos for infertility treatment should be free of the influence of investigators who propose to derive or use hES cells in research. Whenever it is practicable, the attending physician responsible for the infertility treatment and the investigator deriving or proposing to use hES cells should not be the same person.

12. No cash or in-kind payment may be provided for donating blastocysts in excess of clinical need for research purposes.
13. Consent for blastocyst donation should be obtained from each donor at the time of donation. Donors who have given prior indication of their intent to donate for research any excess blastocysts that remain after clinical care should nonetheless give informed consent again when any specific research is being considered. Donors should be informed that they retain the right to withdraw consent until the blastocysts are actually used in cell line derivation.
14. In the context of donation of gametes or blastocysts for human embryonic stem (hES) cell research, the informed consent process should include the following information:-
 - (a) A statement that the blastocysts or gametes will be used to derive hES cells for research that may include research on human transplantation.

- (b) A statement that the donation is made without any restriction or direction regarding who may be the recipient of transplants of the cells derived, except in the case of autologous donation.
- (c) A statement as to whether the identities of the donors will be readily ascertainable to those who derive or work with the resulting hES cell lines.
- (d) If the identities of the donors are retained (even if coded), a statement as to whether donors wish to be contacted in the future to receive information obtained through studies of the cell lines.
- (e) An assurance that participants in research projects will follow applicable and appropriate best practices for donation, procurement, culture, and storage of cells and tissues to ensure, in particular, the traceability of the stem cells. (Traceable information, however, must be secured to ensure confidentiality)

- (f) A statement that derived hES cells and/or cells lines might be kept for many years.
- (g) A statement that the research is not intended to provide direct medical benefit to the donor(s) except in the case of autologous donation.
- (h) A statement that embryos will be destroyed in the process of deriving hES cells.
- (i) A statement that neither consenting nor refusing to donate embryos for research will affect the quality of any future care provided to potential donors.
- (j) A statement of risks involved to the donor.

15. Research that should not be permitted at this time:

- (a) Research involving *in vitro* culture of any intact human embryo, regardless of derivation method, for longer than 14 days or until formation of the primitive streak begins, whichever occurs first.
- (b) Research in which HES cells are introduced into non-human primate blastocysts or in which any ES cells are introduced into human blastocysts.
- (c) No animal into which HES cells have been introduced at any stage of development should be allowed to breed.
- (d) Fusion of human stem cell or other cells of pluripotent nature with cells of non-human origin, shall not be permitted to develop beyond 14 days, or until the formation of the primitive streak begins, whichever occurs first.

16. Laboratory requirements :

- (a) Laboratories conducting stem cell research shall conform to required guidelines for good laboratory practices.
- (b) All laboratories conducting stem cell research for the purpose of clinical trials shall be GMP compliant as required by the National Pharmaceutical Control Board (NPCB)
- (c) All laboratories producing stem cells or tissue products for commercial/manufacturing purposes shall be certified as GMP compliant by the NPCB.

17. All imported stem cells/tissue products for use in clinical trials and therapy shall be GMP certified and registered by the NPCB.

18. Procurement, management, storage and disposal of stem cells and tissues used in research and clinical trials must be in accordance with the national guidelines.

19. Therapeutic outcomes, adverse effects and tissue integration shall be documented or reported to the National Stem Cell Research and Ethics Sub-committee.

Guidelines For Stem Cell Therapy

Background

Haemopoietic stem cell and umbilical cord stem cell transplantations are the most established form of stem cell therapy. The use of other stem cells including hES and somatic stem cells is considered experimental. Xenotransplantation or therapy involving the use of animal stem cells or animal cells are currently prohibited.

Indications for stem cell/ cell-based therapies

1. Standard/established

- (a) The current indications for HSC therapy (HSCT) are listed in the National Guidelines for Haemopoietic Stem Cell Therapy.

2. Potential/development/experimental

The following applications shall either be at the in vitro, animal studies or clinical trial settings:-

- (a) The use of HSC, HSC-derived cells and umbilical cord stem cells in tissue repair, regeneration and vascularisation shall be considered developmental.
- (b) MSC has shown potential in chronic inflammatory diseases, graft rejection and graft versus host disease (GVHD) and shall be done in research settings.
- (c) The use of other types of stem cells e.g. neural stem cells in Parkinson's disease, cardiac stem cells, hepatic stem cells, pancreatic stem cells, skeletal-muscle stem cell, stem cells of skin, lungs, retinal and intestinal epithelium as well as inducible pluripotent stem cells are still experimental.

- (d) Cell-based therapies e.g. antigen-specific T- cells and dendritic cells shall be done in research settings.
- (e) Gene therapy to correct genetic disorder e.g. subacute combined immune deficiency disorders (SCID) and thalassaemia is still in developmental phase. The use of lentiviral shall be carried out in a P3 laboratory.
- (f) All other indications not listed in as standard or established shall be considered experimental and must first be approved by the institutional review board (IRB) and/or institutional ethics committee. Copies of the proposal must also be submitted to the NSCRE sub-committee.

3. Therapy using human embryonic stem cells

- (a) The use of hESC for therapy shall be considered experimental.

4. Xenotransplantation

- (a) Xenotransplantation involving stem cells/cells e.g. islet cells for tissue repair and regeneration shall not be performed until more scientific and clinical evidence (Phase 3) is obtained.
- (b) Rejection and the risks of transmission of infectious diseases have not been adequately dealt with.
- (c) Clinical trials shall occur only when there are preclinical data indicating a high probability of benefit to the recipients and data on safety.

- (d) Any clinical xenotransplantation shall only be approved by the NSCRE sub-committee.

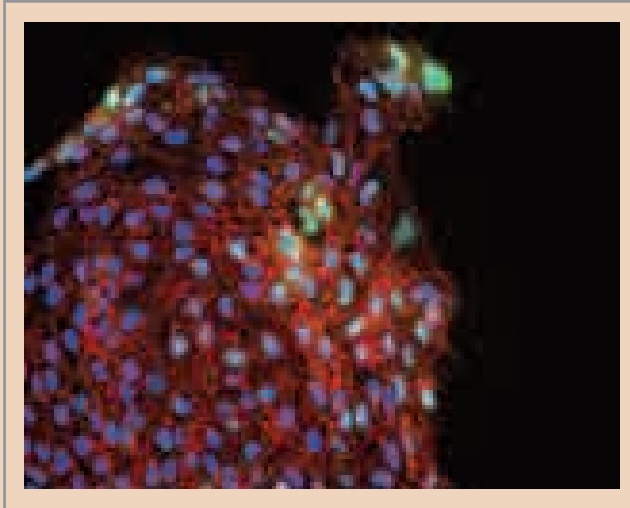
5. Patient evaluation

Please refer to the National Guidelines for Haemopoietic Stem Cell Therapy.

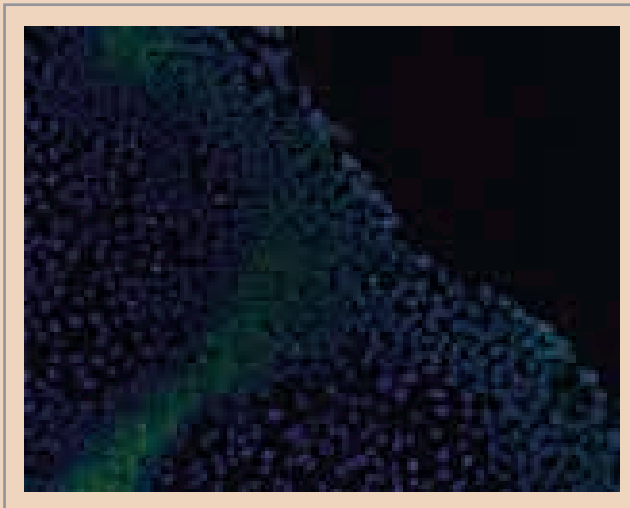
6. Regulation and Standards

- (a) Private healthcare facilities and services intending to perform or performing stem cell or cell based therapies shall be licensed under the Private Healthcare Facility and Services Act 1998.
- (b) It is recommended that these centres perform internal and external audits to ensure quality, viability, purity, safety, reproducibility and efficacy of the end-products.

- (c) The procurement and processing of stem cells shall comply with the National Standards of Procurement and Processing of stem cells.
- (d) Laboratories performing gene therapy research involving the use of viral vectors shall comply with the Biosafety Level 3.
- (e) Personnel performing stem cell transplants shall be adequately trained and proficient and shall acquire privileging status from the respective institutions.



Immunofluorescence staining of hESC for detection of embryonic surface marker. Brachyury/Cy2-SSEA-4/RRX-DAPI (20X)



Immunofluorescence staining of hESC for detection of embryonic surface marker. Nanog/Cy2-DAPI (20X)

(Source : Institute for Medical Research, 2008)

**Keputusan Muzakarah
Jawatankuasa Fatwa Majlis Kebangsaan
Bagi HAL Ehwal Agama Islam Malaysia
berkaitan Pengklonan dan ART
(Assisted Reproductive Technology)**

**1. Hukum Pengklonan Terapeutik dan Penyelidikan
Sel Stem (Stem Cell)**

Bil : MFK Kali ke-66

Tarikh : 22 Februari 2005

Keputusan :

- 1.1 Pengklonan terapeutik untuk tujuan rawatan perubatan seperti mencipta sel-sel tertentu atau menggantikan organ yang telah rosak dengan mengambil kira langkah-langkah sempadan yang dibenarkan oleh syarak adalah diharuskan.**

- 1.2 Harus menggunakan embrio yang disimpanbeku atau lebih embrio dari proses persenyawaan di luar rahim (IVF) untuk tujuan penyelidikan dengan syarat mendapat persetujuan pasangan suami isteri yang menerima rawatan dan kajian tersebut dilakukan sebelum mencapai tahap 'alaqah' (*blastocyst*).
- 1.3 Penyelidikan ke atas pra-embrio selain dari untuk tujuan terapeutik hendaklah mendapat kebenaran daripada pasangan suami isteri dan pra-embrio hasil penyelidikan ini, tidak boleh sama sekali ditanam dalam rahim isteri atau mana-mana wanita yang lain.
- 1.4 Harus melakukan penyelidikan ke atas pra-embrio untuk mengetahui penyakit genetik bagi pasangan yang berisiko tinggi dan hanya embrio yang dikenalpasti bebas dari penyakit sahaja boleh ditanam dalam rahim ibunya dalam tempoh perkahwinan yang sah.

- 1.5 Rawatan kejuruteraan genetik ke atas pra-embrio yang melibatkan pengubahsuaian sifat semulajadi seperti rambut, warna rambut, kebijaksanaan, ketinggian dsd termasuk memilih jantina adalah haram. Bagaimanapun pemilihan jantina diharuskan sekiranya faktor jantina menatijahkan suatu penyakit genetik yang serius yang boleh membawa kematian.
- 1.6 Sebarang penyelidikan yang berunsurkan komersial atau yang tiada kaitan dengan kesihatan ibu atau janin adalah tidak dibenarkan.
- 1.7 Penyelidikan hendaklah dijalankan secara sah dan proposal penyelidikan mestilah jelas, saintifik dan dikendalikan oleh penyelidikan yang benar-benar mempunyai kemahiran, amanah dan bertanggungjawab.

- 1.8 Sel stem daripada sumber-sumber adalah **harus** digunakan untuk tujuan rawatan perubatan dan kaji selidik :
- i. Daripada seorang dewasa (sel stem dewasa) dengan izin dan prosedurnya tidak mengakibatkan mudarat;
 - ii. Daripada seorang kanak-kanak dengan keizinan ibu bapanya dan prosedurnya tidak mengakibatkan mudarat;
 - iii. Daripada uri dan darah tali pusat bayi dengan keizinan ibubapanya;
 - iv. Daripada janin yang gugur secara spontan atau keguguran akibat daripada rawatan perubatan yang dibenarkan syarak dengan syarat mendapat keizinan ibubapanya, bukan janin yang digugurkan secara sengaja atau digugurkan tanpa sebab-sebab perubatan yang dibenarkan oleh syarak;

- v. Daripada lebih embrio (*excess embryos*) yang disimpan beku daripada teknologi bantuan kesuburan IVF dengan syarat mendapat keizinan daripada ibubapanya. Sel stem daripada embrio yang dihasilkan secara sengaja (*created embryo*) dengan teknologi *Somatic Cell Nuclear Transfer (SCNT)* adalah tidak dibenarkan berdasarkan kaedah sad al-zaraie' (menutup pintu keburukan).

ABBREVIATION

GMP	-	Good manufacturing practice
GVHD	-	Graft rejection and graft versus host disease
hESC	-	Human embryonic stem cells.
HSC	-	Haematopoietic stem cells
IRB	-	Institutional review board
IVF	-	In vitro fertilization
NSCRE	-	National stem cell research and ethics.
SCNT	-	Somatic cell nuclear transfer
SCID	-	Subacute combined immune deficiency disorders

GLOSSARY

Adult stem cell - An undifferentiated cell found in a differentiated tissue that can renew itself and (with certain limitations) differentiate to yield all the specialized cell types of the tissue from which it originated. (NIH)

Blastocyst - A preimplantation embryo of 30-150 cells, is a hollow sphere made up of an outer layer of cells (trophectoderm), a fluid-filled cavity (blastocoel), and a cluster of cells on the interior (inner cell mass).

Cell lines - Cultures of disaggregated tissue that can be maintained and propagated for use in research. The length of time cells will survive in culture varies. Some cell lines are immortalized; that is, they can be maintained essentially indefinitely, for one of a variety reasons. Embryonic stem cells

and embryonic germ cells are immortal because they express telomerase, one of the factors necessary for cells to propagate normally.

Ectoderm - The outermost of the three primary layers of an embryo; produces the nervous system, the epidermis and epidermal derivatives, and the lining of various body cavities such as the mouth.

Embryo - (a) In humans, the developing organism from the time of fertilization until the end of the eighth week of the gestation, when it becomes known as a foetus. (NIH)

(b) The developing organism from the time of fertilization until significant differentiation has occurred, when the organism becomes known as a foetus. An organism in the early stages of development. (CR)

Endoderm - One of the three primary layers of an embryo; it is the source of the digestive tract and other internal organs.

Foetus - A developing human from usually two months after conception to birth. (NIH)

Fibroblast - A stellate or spindle-shaped cell with cytoplasmic processes present in connective tissue, capable of forming collagen fibers; an inactive fibroblast is sometimes called a fibrocyte. (SMD)

Gene - A functional unit of heredity that is a segment of DNA located in a specific site on a chromosome. A gene directs the formation of an enzyme or other protein. (NIH)

Gene therapy - The use of genetic material, usually DNA, to correct inherited or accumulated genetic damage.

Genome - The complete genetic code for any individual or species.

Genotype - The genetic constitution of an organism or a group of organisms. (SMD)

Haemopoietic stem cells - A stem cell that gives rise to all red and white blood cells and platelets. (NIH)

Human embryonic stem cells, hESC - A type of pluripotent stem cell derived from the inner cell mass (ICM) of the blastocyst. (NIH)

In vitro - Refers to processes taking place in test tubes or similar container. In vitro fertilization, IVF - A technique that unites the egg and sperm in a laboratory instead of inside the female body. (NIH)

Mesoderm - Middle layer of a group of cells derived from the inner cell mass of the blastocyst; it gives rise to bone, muscle, connective tissue, kidneys, and related structures. (NIH)

Pluripotent - Having the ability to give rise to all of the various cell types of the body. Pluripotent cells cannot make extra-embryonic tissues such as the amnion, chorion, and other components of the placenta. Scientists demonstrate pluripotency by providing evidence of stable developmental potential, even after prolonged culture, to form derivatives of all three embryonic germ layers from the progeny of a single cell and to generate a teratoma after injection into an immunosuppressed mouse. (NIH)

Stem cell - Undifferentiated multipotent precursor cells that are capable both of perpetuating themselves as stem cells and of undergoing differentiation into one or more specialized types of cells. (CR)

Somatic cell nuclear transfer, SCNT - A technique that combines an enucleated egg and the nucleus of a somatic cell to make an embryo. SCNT can be used for therapeutic or reproductive purposes, but the initial stage that combines an enucleated egg and a somatic cell nucleus is the same. See also therapeutic cloning and reproductive cloning (NIH).

Xenotransplantation - Xenotransplantation or Xenografting is the transplantation between different species of organ, tissue, or cells.

Note :

- Definition marked “(CR)” are from the Council’s report on human cloning (*Human Cloning and Human Dignity: An Ethical Inquiry*, Washington, D.C.: Government Printing Office, 2002).
- Definition marked “(NIH)” are from the National Institutes of Health online stem cell glossary at <http://stemcells.nih.gov> (accessed April 22, 2009).
- Definitions marked “(NRC)” are from the National Research Council Report, *Stem Cell Research and the Future of Regenerative Medicine* (Washington, D.C.: National Research Council, 2001).
- Definitions marked “(SMD)” are from Stedman’s Medical Dictionary.

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