



AMERICAN JOURNAL OF ADVANCES IN NURSING RESEARCH

Journal homepage: www.mcmed.us/journal/ajanr



STEM CELL THERAPY

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Article Info

Received 24/01/2017

Revised 29/01/2017

Accepted 31/01/2017

Key word: Stem cell, Germ cell, somatic gene, mutation, bone marrow and umbilical cord blood.

ABSTRACT

Stem cell therapy is a set of experimental techniques which involves introducing a healthy copy of the new gene for correcting defective gene or inactivating the improperly functioning mutated gene or replacing a mutated gene that are responsible for causing diseases. The purposes of this therapy is to correcting defecting gene, Inactivating improperly functioning mutated gene and replacing a improperly functioning mutated gene (most common type). Diseases like Haemophilia, leukemia, aplastic anaemia, burns (new skin cell grafting) Parkinson's disease, Amyotrophic lateral sclerosis, Alzheimer, Stroke etc can be treated with stem cell therapy Germ line gene therapy somatic gene therapy, adult stem cell transplants using bone marrow stem cells, adult stem cell transplants using peripheral stem cells, (Now most commonly used), stem cell transplants using umbilical cord blood, and therapeutic cloning.

INTRODUCTION

During 1990 the concept of stem cell therapy was introduced. Blood stem cells were the first stem cells to be identified. Their discovery in the 1960s marked the beginning of stem cell research. Stem cell therapy is likely to have the greatest success with diseases that are caused by single gene defects. Only genetic diseases caused by errors in a single recessive gene are being considered for treatment, since the insertion of a normal dominant gene should override the effect of the abnormal gene [1].

Definition of stem cell therapy

Stem cell therapy is a set of experimental techniques which involves introducing a healthy copy of the new gene for correcting defective gene or inactivating the improperly functioning mutated gene or replacing a mutated gene that are responsible for causing diseases [2].

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Purposes of stem cell therapy

- Stem cell therapy for correcting defecting gene,
- Stem cell therapy Inactivating or knocking out improperly functioning mutated gene
- Stem cell therapy replacing a improperly functioning mutated gene [3].

The goal of stem cell therapy

- To replace unhealthy cells with healthy ones and to do so efficiently,
- Allowing proper cell functioning in the human body

Diseases on which research studies are undertaken for evaluation of stem cell therapy includes

Haemophilia, leukemia, aplastic anaemia, burns(new skin cell grafting) Parkinson's disease, Amyotrophic lateral sclerosis, Alzheimer, Stroke, Spinal Cord Injury, retinal diseases, Multiple Sclerosis, Radiation Induced Intestinal Injury, Inflammatory Bowel Disease, Liver Disease, Duchenne Muscular Dystrophy, Diabetes, Heart Disease, Severe combined immune deficiencies Bone Disease, Renal Disease,



Chronic Wounds, Graft-Versus-Host Disease, Sepsis and Respiratory diseases [4].

Types of Stem Cell Therapy

There are a number of stem cell therapies that are currently being investigated or used to treat a range of diseases. These are:

Germ line gene therapy

Germ line gene therapy involves the modification of germ cells (gametes) that will pass the change on to the next generation. Gives permanent changes and eliminating some diseases from a particular family with germ line therapy genes could be corrected in the egg or the sperm that is being used to conceive. The child that results would be spared certain genetic problems that might otherwise have occurred [5]

Steps of procedure

1. Remove the man's sperm producing cells that contain a defective gene.
2. A healthy gene is added to each cell to replace the defective gene
3. The cells are put into mouse testes
4. They mature inside the mouse and start producing healthy human sperms
5. Those sperms once tested are used to fertilize women's eggs in a laboratory dish.
6. The resulting embryos are placed in a women's womb.
7. She gives birth to a child whose genes are free from the father's disease [6].

Somatic gene therapy

Somatic cell gene therapy changes/fixes/replaces genes in just one person. The targeted cells are the only ones affected; the changes are not passed on to that person's offspring. Short lived because the cells of the most tissues ultimately die and are replaced by new cells. It has two types includes *invivo* (genes are changed in the cells when cells are still inside the body), *exvivo* (cells are modified outside the body and then transplanted back again) [7, 8]

Steps of procedure for *exvivo*

1. Cells are removed from the patient
2. In the laboratory a virus is altered so that it can't reproduce.
3. A gene is inserted in to the virus
4. The altered virus is mixed with cells from the patient
5. The cells from the patient are genetically altered.
6. The altered cells is injected into the patient
7. The genetically altered cells produce the desired protein or hormones.

Adult stem cell transplants using bone marrow stem cells

A bone marrow stem cell transplant uses stem cells derived from bone marrow to provide a fresh and healthy source of new blood cells which in turn, allows for a patient to receive higher doses of chemotherapy to treat certain types of cancer such as leukaemia. The bone marrow stem cells may be allogeneic and therefore donated by a family member or stranger, or they may be autologous, which utilizes a patient's own stem cells.

Adult stem cell transplants using peripheral stem cells (Now most commonly used)

A peripheral blood stem cell harvest is a technique used to restore a person's blood cells after they have been damaged by chemotherapy or radiation. Peripheral stem cell may be Autologous or Allogeneic or Syngeneic: a patient receives stem cells from an identical twin.

Steps of procedure

1. One week before a donor receives drugs to increase the number of stem cells in his or her bloodstream
2. The donor's blood is removed,
3. it flows through a machine that removes the stem cells.
4. The blood then flows back to the donor
5. The extracted stem cells are then frozen until they are transferred to the recipient.
6. After the stem cells are transplanted into the patient, they move from the bloodstream to the bone marrow.
7. It is here that they produce healthy white blood cells, red blood cells and platelets. (Engraftment)
8. Engraftment generally occurs over the two to four weeks following stem cell transplantation.

Stem cell transplants using umbilical cord blood

After a baby is born, cord blood is left in the umbilical cord and placenta. It is relatively easy to collect, with no risk to the mother or baby. It contains haematopoietic (blood) stem cells: rare cells normally found in the bone marrow. Is used to treat children with leukaemia, or genetic blood diseases like Fanconi anaemia. The cord blood is transplanted into the patient, where the HSCs can make new, healthy blood cells to replace those damaged by the patient's disease or by a medical treatment such as chemotherapy for cancer.

Therapeutic cloning

Therapeutic cloning is another phrase for a procedure known as somatic cell nuclear transfer. A major benefit of therapeutic cloning is that the cells removed are pluripotent. Pluripotent Cells can give rise to all cells in the body with the exception of the embryo.



This means that pluripotent cells can potentially treat diseases in any body organ or tissue by replacing damaged and dysfunctional cells. Another distinct advantage to this type of therapy is that the risk of immunological rejection is alleviated because the patient's own genetic material is used

Steps of procedure

1. A scientist extracts the nucleus from an egg
2. The nucleus holds the genetic material for a human or laboratory animal
3. The scientist then takes a somatic cell from a patient, which is any body cell other than an egg or sperm, and also extract the nucleus from this cell
4. The nucleus that is extracted from the somatic cell in the patient is then inserted into the egg, which had its nucleus previously removed
5. In a very basic sense, it's a procedure of substitution. The egg now contains the patient's genetic material, or instructions
6. It is stimulated to divide and shortly thereafter forms a cluster of cells known as a blastocyst
7. This blastocyst has both an outer and inner layer of cells and it is the inner layer, called the inner cell mass that is rich in stem cells.
8. The cells in the inner cell mass are isolated and then utilised to create embryonic stem cell lines.

Which are infused into the patient where they are ideally integrated into the tissues, imparting structure and function as needed.

To design and carry out a stem cell therapy treatment, a researcher must:

1. Identify the gene(s) responsible for the disorder.
2. Make copies of the normal gene.

3. Insert the copies into vectors.
4. "Infect" the affected cells with the vectors.
5. Activate the gene so that transcription and translation take place.

Challenges of Stem Cell Therapy

1. Identifying stem cells within an actual tissue culture
2. Isolating specific cell types from tissue culture
3. Finding appropriate solutions to trigger these cells to grow into the desired cell types.
4. Acceptance of implanted stem cell with native body cell of the patient. For example, if cardiac cells are implanted, they must be able to beat in sync with the patient's own heart cells.
5. Triggering of an immune reaction that result in rejection of the new cells.
6. Finding a balance between directing cell growth into specialized tissues that can replace damaged ones, and also ensuring that cells don't excessively grow and become cancer cells.

Risk of stem cell therapy

- Damage to organs or blood vessels
- Graft versus host disease
- Death
- Risk of abortion if prenatal test regarding baby with genetic diseases.

Stem cell Therapy Disappointments

- In 1999 a boy died due to an immune response to an adenovirus gene therapy vector.
 - Four children have developed cancer due to a retrovirus gene therapy vector
- The cost is very high

Table 1. A tool used to deliver a genetic material into the cells includes

Viral method (transduction)	Non viral method
<p>Adenovirus Infects many cell types Does not integrate into host genome and can be lost.</p> <p>Retrovirus Integrates into host genome and cannot be lost Integrates into host genome and can cause cancer</p> <p>Adeno-Associated Virus (AAV) Integrates into host genome and cannot be lost Difficult to work with.</p> <p>Herpes Simplex Virus (HSV) DNA stays in nucleus without integrating into host genome. Only infects cells of the nervous system.</p>	<p>Physical method (carrier free gene deliver) Employs a physical force that permits the cell membrane and facilitates intracellular gene transfer</p> <ul style="list-style-type: none"> • Needle injection • Electroporation • gene gun • Ultrasound • hydrodynamic delivery <p>Chemical method: (synthetic vector based gene delivery) DNA must be protected from damage and its entry into the cell by covering the plasmid DNA with lipid.</p> <ul style="list-style-type: none"> • Lipoplexes • Polyplexes



ACKNOWLEDGEMENT: None

CONFLICT OF INTEREST:

The authors declare that they have no conflict of interest.

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