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The Power of Stem Cells

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Review Article

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ABSTRACT

Stem Cells are precursor cells that can give rise to multiple tissue types. The benefits to individuals and to society gained by the introduction of new drugs or medical technologies are difficult to estimate. The introduction of antibiotics and immunizations (vaccines), for instance, have significantly expanded life compasses and enhanced the wellbeing of individuals everywhere throughout the world. In spite of these different advances in the counteractive action and treatment of human diseases, devasting illnesses, for example, coronary disease, diabetes, tumor, and different neural diseases, for example, Alzheimer's disease present proceeding with difficulties to the wellbeing and prosperity of individuals all around. The science prompting the advancement of system and techniques for culturing human stem cells could prompt exceptional medicines and even cures for these and different diseases.

INTRODUCTION

Information about undifferentiated (stem) cell science and its potential applications has been aggregating for over 30 years. The study of stem cells dates to the mid-1960s, and numerous papers have been published on the isolation and lab manipulation of stem cells from animal models. While these models are blemished, they are acknowledged and valued in the scientific community as good initial predictors of what happens in human beings. The science of stem cell research, possibly as essential as alternate advances, is going to enter a stage improvement that could prompt phenomenal cures and palliative medications [1].

Human stem cell research holds colossal potential for contributing to our understanding of key human science research. The present excitement over potential stem cell treatments and therapies exudes from new understandings of hereditary qualities and formative science. In spite of the fact that it is unrealistic to anticipate the results from basic examination, such studies will offer the genuine probability for medications and ultimately for cures for many diseases for which sufficient treatments don't exist.

In the 1960s, it was perceived that certain mouse cells had the ability to shape different tissue types, and the discovery of bona fide stem cells from mice happened in 1971.

It has been recently found out that researchers have comprehended stem cells well enough to consider the potential outcomes of developing undifferentiated organisms outside the body for long periods of time. With that progress, thorough tests can be led, and the likelihood of manipulating these cells in such a way, to the point that particular tissue can be developed in real. It is difficult to venture or

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project out when real medicines or cures may rise up out of such research, yet the paths this examination may take and potential applications have been abundantly examined.

Depending on how many different paths stem cells can follow in their development and to what portion of a functioning organism they can contribute, they have distinctions-

Totipotent stem cells

Totipotent stem cells are one of the most important stem cells type because they have the ability to progress into any cell found in the human organization. In human development, the egg cell in a woman and the sperm cell from a man fuse together to form a single cell called the zygote. The zygote divides several times and forms cells that are the precursors to the trillions of cells that will ultimately organize the human body.

Pluripotent stem cells

Pluripotent stem cells are often termed 'true' stem cells because they have the potential to differentiate into almost any cell in the body. This means that under the right circumstances, a stem cell that is isolated from an embryo can produce almost all of the cells in the body [2]. Yet after this embryonic development stage is over, the stem cells no longer have this unlimited potential to develop into all cell types. Their pluripotency is thus lost and they can only become certain types of cells [3-5] (Figure 1).

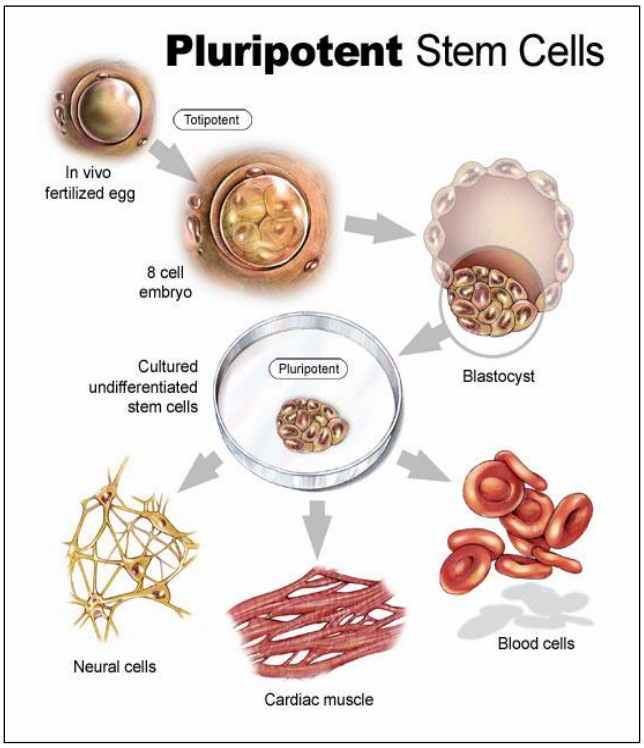

Figure 1: Pluripotent stem cells.

Multipotent stem cells

Multipotent stem cells have the same essential elements of all stem cells. Similarly as with all stem cells multipotent stem cells are unspecialized cells that can: Self-renew for long periods of time and differentiate into specific cells with particular functions. A multipotent stem cell can give rise to other types of cells however it is constrained in its capacity to differentiate [5] (Figure 2).

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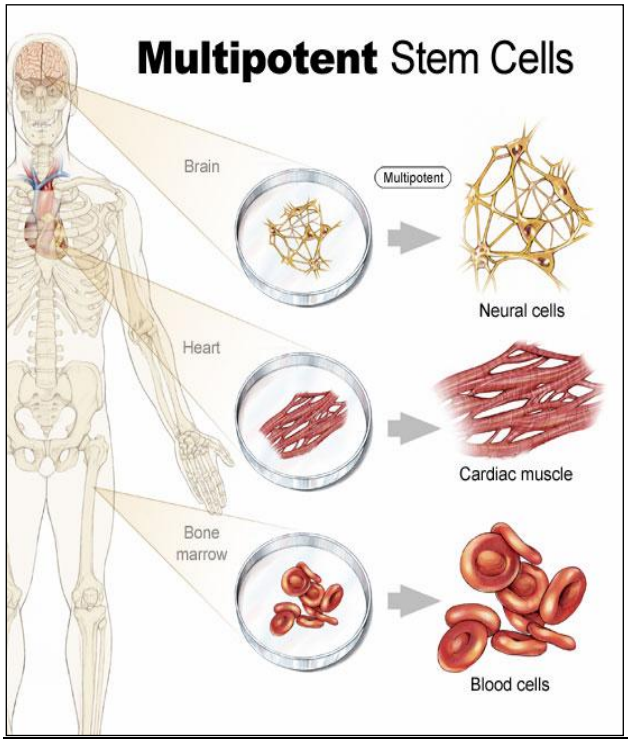

Figure 2: Multipotent stem cells.

Types of Stem cells

In mammals, there are two wide types of stem cells: embryonic stem cells, which are isolated from the internal cell mass of blastocysts, and adult stem cells, which are found in different tissues. Along with these two stem cells, Hematopoietic stem cells also play a very crucial role in the disease prevention.

Embryonic Stem Cells (ES): Embryonic immature microorganisms are derived from the internal cell mass of a blastocyst (an early fetus) and Embryonic germ cells are gathered from fetal tissue at a to some degree later phase of development (from an area called the gonadal ridge), and the cell types that they can form into may be somewhat limited.

Human ES cells allow scientists to investigate-

- how early human cells become committed to the major lineages of the body;
- how these lineages lay down the rudiments of the body's tissues and organs [6,7];
- how cells within these rudiments differentiate to form the myriad functional cell types which underlie normal function in the adult. The knowledge gained will impact many fields.

For example,

- Cancer biology will reap an especially large reward because it is now understood that many cancers arise by perturbations of normal developmental processes.
- The availability of human ES cells will also greatly accelerate the understanding of the causes of birth defects and thus lead directly to their possible prevention.

Adult Stem Cells: Adult stem cells are derived from mature tissue. Indeed, even after complete maturation of an organism, cells need to be replaced (a great example is blood, however this is valid for muscle and other connective tissue also, and may be true for at least some nervous system cells). Adult stem cells are multipotent; the quantity of tissues that they can recover contrasts inadequately with the pluripotency of embryonic stem cells and embryonic germ cells. Their utilization for bone and cartilage

replacement is undergoing FDA-approved clinical trials at the present time. Adult-derived stem cell therapies will supplement, however can't supplant, therapies that may be in the end acquired from ES cells [8,9]. They do have some advantages.

For example,

- Adult stem cells offer the chance to use little examples of adult tissues to obtain an initial culture of a patient's own cells for expansion and resulting implantation (this is called an autologous transplant). This process avoids any moral, ethical or legal issues concerning wellspring of stem cell, furthermore shields the patient from viral, bacterial, or other contamination from another person.
- With proper manufacturing quality controls and testing, allogeneic adult stem (cells from a benefactor) may be useful practically also.

Hematopoietic Stem Cells: Already in clinical utilization are autologous and allogeneic transplants of hematopoietic stem cells that are isolated from mobilized peripheral blood or from bone marrow by positive choice with antibodies in commercial devices [10-12].

- In general, there is less moral and ethical concern over their introductory source.
- Additionally, since they regularly differentiate into a narrower set of cell types, guiding them to a craved destiny is clearer.

APPLICATIONS OF STEM CELLS

Stem cells are already in use to cure ailments like

- Acute Leukaemia, Chronic Leukemia [13],
- Myelodysplastic Syndromes,
- Stem Cell Disorders,
- Myelo-proliferative Disorders,
- Lympho-proliferative Disorders,
- Phagocyte Disorders,
- *Inherited Disorders* like Osteoporosis, B-Thalassemia [14],
- Inherited metabolic disorders.
- *Inherited Erythrocyte Abnormalities* like Beta Thalassemia and Sickle cell disease, and other Malignancies like Multiple Myeloma, Plasma Cell Leukaemia, Renal Cell Carcinoma and Retinoblastoma [15,16;37]. Trials are currently on the way for the proper treatment of Cardiac Diseases, Diabetes, Multiple Sclerosis, Muscular Dystrophy, Parkinson's disease, Spinal Cord Injury and Stroke [17;38-41].

Researchers are hoping of further and vastly improved stem cell applications in Alzheimer's disease, Lupus and Rheumatoid Arthritis in future [18]. Last year more than 6,800 cases were reported globally where stem cell transplants have been successful.

PRACTICAL APPROACHES OF STEM CELLS

Master cardiac stem cell discovered by Harvard scientists: Studying with human embryonic stem cells Harvard University scientists were able to discover a master heart stem cell, which can provide new fast and authentic ways for drug development [19-20].

Stem cells with platelet rich plasma help produce hyaline-like tissue in injured area: Study shows higher relation between collagen I and II after autologous stem cell treatment. Collagen is the main

supportive protein of cartilage, connective tissue, tendon, skin, and bone. It is a fibrous insoluble protein which consists of bundles of tiny reticular fibrils that combine to form the white gleaming inelastic fibers of the tendons, the ligaments, and the fascia [21].

Method To Neutralize Tumor Growth In Embryonic Stem Cell Therapy Discovered- ScienceDaily (May 7, 2009): Scientists at the Hebrew University of Jerusalem have found a system to possibly eliminate out the tumor-danger factor using human embryonic stem cells. Their work makes ready for further advance in the promising field of stem cell therapy.

Stem cell therapy can help dental implants by growing sufficient periodontal tissue: A new study which was published in the Journal of Oral Implantology, claims that stem cell procedure can really help in dental implantations by renewing enough tissues around it.

Embryonic muscle stem cell creating genes are not required to regenerate injured muscles: As per Science Daily it's a stem cell surprise, and its being such a surprise that would divert the whole global stem cell thoughts and would overturn the previous stem cell researches.

Stem cell transplant help diabetics skip insulin jabs for 4 years: US scientists confirmed through week's Journal of the American Medical Association, that stem cell transplant could help diabetes type I patients to get rid of daily insulin jabs for as long as four years [42].

Stem cell treatment may put an end to Tennis Elbow: August 29th, 2008 Alan Mishra, the professor of orthopedic surgery at Stanford University Medical Center, has developed an experimental treatment that encourages the body to heal wounds quickly and effectively. The experiment, if successful, can bring an end to the very common and devastating problem especially in life of a sportsman, tennis elbow.

Stem cells and extracts of bone marrow both can improve post heart attack cardiac disorders: A new study conducted on mice by scientists from University of California, San Francisco (UCFS) has identified that an extract derived from bone marrow cells can effectively improve cardiac function after heart attack as bone marrow stem cells do accordingly [22-23].

Stem cells can reverse spinal cord injuries in animals: January 28th, 2009 LONDON - Stem cells from spinal cord lining, transplanted into animals with spinal injury, regenerated 10 times faster in recipients than similar cells derived from healthy control animals. The findings show that transplanted cells, known as ependymal stem cells, were found to proliferate after spinal cord injury and were recruited by the specific injured area.

Stem Cell-Rich Umbilical Cord Blood is a Life Saver: June 26th, 2006 Brandyn Orr, 12, of Mesa was diagnosed with leukemia when he was 2 years old and relapsed when he was 6. He was treated with an umbilical cord blood transplant using the blood collected during the birth of his brother Devyn, 7.

Stem cell functions may help scientists find early development of Mascular Dystrophy: Researchers from University of Birmingham, UK, claimed that they have able to identified key factors that could hopefully presume the chances of Mascular Dystrophy(DM)at the most primary stage.

Esophagus stem cell in mice able to grow into tissue-like structures: December 17th, 2008 In yet another success in stem cell research, University of Pennsylvania scientists have found stem cell in the esophagus of mice are able to grow into tissue-like structures and when placed into immune-deficient mice were able to form parts of an esophagus lining. The researchers set out to identify and characterize potential stem cells--those with the ability to self-renew-in the esophagus to understand normal biology and how injured cells may one day be repaired.

LifeCell India plans to collect stem cells from umbilical cord tissue: March 25th, 2009, Better late than never, Indian scientists plans not to throw away the umbilical cord tissue which is enrich with

valuable Mesenchymal stem cells, that help to form bone, cartilage, tendon, ligament cell etc. Mesenchymal stem cells are adult stem cells and are found in the bone marrow as well [24,25,43].

The probability of umbilical cord stem cell matching with anyone in the world is larger than that of a bone marrow stem cell matching. Out of the many cases of stem cell transplants that were done last year to cure various malignant and non-malignant diseases, more than 300 cases were done from the stem cells collected from umbilical cords. NIH announces opening of new bone marrow center for treating diseases without surgery September 27th, 2008. As a way to regrow injured muscles, tendons, and bones without resorting to surgery, NIH today announces to open a new bone marrow center which will specially reside within the treatment for Arthritis, Musculoskeletal and Skin Diseases. The main aim of the NIH scientists is to make an Institute were they will be able to do research on the diseases like arthritis and Musculoskeletal diseases using autologous stem cells (from a patient's own body).

STEM CELL RESEARCH IN INDIA

Major research leads in India:

- Use of limbal stem cells to repair corneal surface disorders caused by limbal stem cell deficiencies. So far, more than 300 patients have been treated at LV Prasad Eye Institute (LVPEI), Hyderabad [26].
- A technology has been established at Christian Medical College (CMC), Vellore for collection, isolation and purification of HSCs for haplo-identical haematopoietic stem cell transplantation.
- Banana lectins have been isolated and purified showing stem cell preservation activities.
- Indigenous human embryonic stem cell lines are being generated at few institutions in the country.

Clinical research system established: Clinical research is an integral part of stem cell science:

- “Human Studies Committee” for evaluation and guidance for clinical research particularly for development of clinical research protocols;
- “National Bioethics Committee” to ascertain rigid ethical guidelines being followed while conducting research on human beings;
- “Task Force on Stem Cells and Regenerative Medicine” to evaluate basic research and also recommend funding for clinical research based on the evaluation of the above committees and
- “Programme Advisory Committee” to consider the proposals of Centre of Excellence and infrastructure.

INITIATIVES TAKEN IN INDIA TOWARDS APPLICATION OF STEM CELLS

LifeCell, in collaboration with CRYO-CELL International, USA facilitates the cryogenic preservation of stem cells at its unique facility in Chennai. LifeCell has set up a 21,000 sq ft laboratory at the cost of Rs 14 crore on the outskirts of Chennai city.

The storage of stem cells is done at -196 Centigrade under liquid nitrogen. LifeCell has only a private stem cell bank currently, but now for the first time in the country, they are planning to have a public stem cell bank also.

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STEM CELL THERAPIES IN INDIA

Several major institutes in India are engaged in stem cell research, with most focusing on using stem cells to regenerate nerve, heart and adult muscle cells, and repair damaged bone tissue.

- The L. V. Prasad Eye Institute, for example, has treated blindness using stem cells derived from the eye.
- Similarly, the Christian Medical College, in Vellore, plans to use stem cells derived from bone marrow to treat chronic liver failure and to regenerate tissue to treat heart disease, traumatic brain injury and Crohn's disease- a form of inflammatory bowel disease whose incidence is rising worldwide.
- Other centres for stem cell research include the National Centre for Cell Sciences in Pune and the National Brain Research Centre at Manesar near Delhi.
- India also has a successful "In Vitro Fertilisation (IVF) Industry that regularly uses blastocysts -the initial cell mass formed when human eggs are fertilised -which are a source of stem cells. [Indian] IVF clinics are already donating blastocysts for stem cell research.

However, India has some disadvantages too. Groups working in the area are fragmented and there are insufficient resources for large-scale experiments.

In August 2004, an Indian parliamentary committee recommended the Department of Biotechnology place greater emphasis on wider applications of stem cells to treat genetic disorders.

"CMC-DBT Center for Stem Cell Research" at CMC, Vellore to do fundamental and translational undeveloped cell research. This Centre is under development and will be practically functional soon. It was further understood that just a "Centre" may not be adequate for stem cell research in the nation like India. It was felt that there is a requirement for a full-fledged establishment for stem cell research in the country. In such manner, a proposition to build up an "Institute for Stem Cells and Regenerative Medicine" is under thought.

Limited types of stem cell therapies are already in use-

- The most well-known therapy is the *stem cell transplant (a form of a bone marrow transplant) for cancer patients*. In this therapy, stem cells that can give rise to blood cells (red and white cells, and platelets) are given to patients to restore tissue destroyed by high dose chemotherapy or radiation therapy.
- *The Institute of Kidney Disease and Research Centre (IKDRC) at Ahmedabad*, claims to have pioneered stem cell therapy for the first time on patients suffering from acute and chronic nephritis which may end in kidney failure. "Nephritis is an early kidney disease which in many cases is chronic and becomes resistant to drugs. The disease may lead to kidney failure. Since we are doing stem cell therapy for kidney transplant patients, we decided we should also try using it to prevent kidney failure as well," said IKDRC director, Dr HL Trivedi.
- *Stem cell experimental therapy by nichi-in Centre for Regenerative Medicine, India* - Though stem cells are available in Embryo, Umbilical Cord Blood, Wharton's jelly etc., at NCRM ONLY the autologous (patient's own) cells taken from bone marrow or other parts (depending upon the condition) are used at the moment for several illnesses for which strong scientific evidences are available as well as similar treatment has been reported in the peer reviewed scientific journals with an acceptable outcome [27].

The treatment protocols are submitted to the ethics committee and approved before treatment is started and the prime concern is here is "Prium Non Nocere", which means "Not to harm", as the treatment of any disease should not be more harmful than when leaving it untreated.

They DO NOT USE Embryonic Stem Cells or Umbilical Cord Blood Cells or any other material from either other human beings or animal source.

At present moment following diseases/conditions are dealt with:

- Critical limb ischemia/ischemic ulcer of the leg, foot especially in diabetic patients untreatable with conventional treatments such as bypass surgery
- Ischemic heart diseases and cardiomyopathy untreatable with conventional treatments such as angioplasty, stents or bypass surgery
- Spinal cord injury and neurological trauma where the patient has no conventional treatment available and left paraplegic [28-30;44]
- Cirrhosis of Liver
- Oral Submucal Fibrosis

DRAWBACKS OF STEM CELL APPLICATIONS

- A major drawback to the use of stem cells is that after nearly ten years of research, there are no approved treatments or human trials using embryonic stem cells.
- ES cells, being totipotent cells, require specific signals for correct differentiation - if injected directly into another body, ES cells will differentiate into many different types of cells, causing a teratoma(a tumor). The development of tumors from embryonic stem cells is especially puzzling given that these cells start out as completely normal cells. Because of their combined abilities of unlimited expansion and pluripotency, embryonic stem cells remain a theoretically potential source for regenerative medicine and tissue replacement after injury or disease.
- Differentiating ES cells into usable cells while avoiding transplant rejection are just a few of the hurdles that embryonic stem cell researchers still face. Many nations currently have moratoria on either ES cell research or the production of new ES cell lines.
- A case report published in PLoS Medicine, describes a rare side effect of human fetal stem cell therapy.

Ninette Amariglio and Gideon Rechavi from the Sheba Medical Center, Tel Aviv, Israel, and colleagues report the case of a boy with a rare genetic disease, Ataxia Telangiectasia, who underwent human fetal stem cell therapy at an unrelated clinic in Moscow and who, four years after the therapy began, was shown to have abnormal growths in his brain and spinal cord [31-32].

Although such reports show the requirement for alert in stem cell therapy, the researchers still infer that their discoveries "don't suggest that the exploration into the biology of stem cell therapy ought to be abondoned. They do, however, recommend that extensive research into the science of stem cells and in-depth preclinical studies, particularly of security, should be pursued so as to boost the potential advantages and benefits of regenerative drug while minimizing the risks" [33].

While embryonic stem cell potential remains untested, adult stem cell treatments have been successfully used for many years to treat leukemia and related bone/blood cancers through bone marrow transplants [34-35]. Adult stem cells are also used in veterinary medicine to treat tendon and ligament injuries in horses.

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CONCLUSION

The interest and creation of knowledge through scientific research is an endeavor that offers gigantic scholarly rewards for researchers while also performing an imperative social function. The advancement of science has changed our lives in ways that would have been unusual and unpredictable only a half-century prior. In spite of the fact that it is difficult to predict the results, researchers and general society will increase colossal new learning in the science of human improvement that will probably hold surprising potential for treatments and cures and the guarantee is great to the point that it appears to be savvy to consider truly how best to further stem cell research in a way that is sensitive to open sensibilities and convey out approaches to widen out the stem cell applications.

We perceive that science does not exist in segregation from the bigger group that feels its effects, whether saw as good or bad. The work of researchers is, and ought to be, adapted and coordinated by thought of more extensive human qualities. This implies that the advancement of open arrangement, particularly where exceptionally highly controversial matters are included, must consider every single intrigued part of general society. It is just through broad based participation that the estimations of all partners in the research endeavor can be precisely considered and weighed.

However, there still exists a great deal of social and scientific uncertainty surrounding stem cell research, which could possibly be overcome through public debate and future research, and further education of the public.

Stem cells, however, are already used extensively in research, and scientists do not see cell therapy as the first goal of the research, but see the investigation and application of stem cells as a goal worthy in itself.

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