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# Stem Cells – A Promise to Elixir

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## Abstract

Stem cells are pluripotent cells which are having properties to differentiate into different lineages of cells types. Recently stem cells have been doubted in regards of their curative abilities of several diseases. The increasing number of difficulties to treat diseases versus the wait for promising cures creates restlessness among clinicians and patients. However we need to envisage the fact that stem cell research is bound by many ethical concerns and other limitations and, despite of its boundaries, staggering achievements have been made in this field of regenerative medicine. Evidential results have been obtained for treatment of cancer, organogenesis, cardiology, neurological disorders, genetical disorders, HIV, diabetes, obesity, vision impairment and even cosmetic applications. Many of these health conditions do not have a cure till date due to the intricacy in understanding their causes. The ones which have a cure have to bear considerable side effects during the course of medical treatments. Stem cell therapy is riveting because of its ability to cure complicated diseases rather than just controlling the health condition of the patients. It has not only shown promising curative possibilities but also proven itself with many successful cases, some of which have been discussed. Upon regular establishment of this therapy a lot of medical limitations will be resolved. Patients which are underage, overage or suboptimal for other tortuous medical treatments could also benefit from such simpler cures. They are a natural cure and can be practiced with fundamental techniques. This editorial emphasises on such marvels of stem cell therapy which show the brighter side of this dilemma.

**Keywords:** Stem cells; Induced pluripotent stem cell; Regenerative medicine; Stem cell therapy; Cancer; Molecular markers

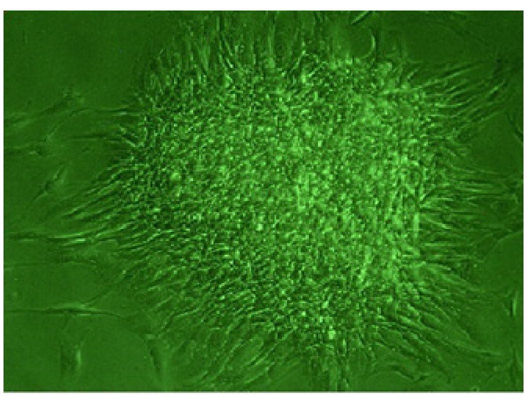
## Introduction

Stem cells (SCs) are basically unspecified type of cells which can be embryonic or somatic in origin. They can remain dormant for long durations and upon induction can differentiate to give tissue/organ specific cells [1]. Induced pluripotent stem cells (iPSC) are stem cells which have been induced in a way to achieve desired type of cells upon differentiation. Because of their "magical" properties they have been magnetising research all over the world bewitching enormous scientists all this while. Since 1970s when transplantable SCs were first discovered, corking amount of research has been done giving possibilities of understanding causes of certain incurable diseases to finding their cures, regenerating tissues and organs, growing fresh organs, reversing age and much more. But despite of all the glamour they have achieved, time has come where people are beginning to question that whether stem cells really have the kind of curative potential they have been vouching for all this while or is it just much ado about nothing? The entire wait since the time we've been hearing about their splendid powers and then added on with some false claims by some scientists has shaken people's trust in this scientific community. However we must understand that, the research is still in its infancy and, it will be too early for any judgemental statements. This article is an attempt to compile the real-time wonderments of stem cells research which will once again resurrect the hope in those who had started to think otherwise.

## Stem Cells for Cancer

While it is still under question that whether all cancer tumours contain stem cells, majority of the scientists believe in their existence and use them as potential targets in drug therapy (Figure 1). Many laboratories are now targeting cancer stem cells rather than just cancer cells. It has also been proven that there is existence of heterogeneity in these stem cell populations. This opens a new boulevard for targeting the different sub-clonal populations in tumours and hence, assuring complete eradication. This is a new concept of identifying and characterizing circulating tumour cells (CTC). Such targeted therapies will lead to a much more sophisticated era of patient-customised treatments with replete cytogenic response.

A "correct copy" of stem cells can themselves serve as a potential therapy. Many trials are carried out all over the world using autogenic as well as allogeneic stem cell transplantation (SCT) to cure people from this dreadful ailment. It has been well established that bone marrow stem cell transplantation is a suitable cure for blood cancer [2,3]. We can derive stem cells even from peripheral blood or umbilical cord for therapeutic uses. Since 1957, after the first stem cell transplantation, the process has undergone spectacular optimisations. Today we have professionals which can carry out this therapy with a much reduced impact of treatment toxicity or graft rejections or graft versus host reactions. The future is even more promising as therapies continue to improve. A study was carried out in our lab on peripheral blood derived stem cells from chronic myelogenous leukemia (CML) patients testing bcr-abl positive. The cells were allowed to grow and were observed from time to time for phenotypic and genotypic changes. The most interesting results came from bcr-abl profiling where the cells originally testing bcr-abl rearrangement positive transformed and tested bcr-abl rearrangement negative. It indicates the existence of clonal Ph-negative stage in at least some cases of CML Ph-positive leukaemia. Establishment of a method which could develop such transformed myeloblasts testing Ph-negative would be a boon to the future of CML [4] treatment. Autologous SCT will eliminate the fear of mortality, graft-host reactions and other common problems associated with regular treatments and hence become suitable for a wider category of patients. Calling for more research, autologous SCT could become the preferred second line treatment after failure of first line TKI treatments [5].



*Cells of CML Patients forming a clone*

Figure 1. Clone of stem cells grown in lab

## Stem Cells for Heart and Other Organs

A new epoch has begun where we are not just imagining the day when the *in vitro* transformed cells will actually take 3D functional forms of organs *in vivo*. We now near to that future where shortage of donor organs for transplants we be overtaken by supply of "fresh made" partial or entire organs. Also the need for immune suppression and the graft-host rejection reactions would be eliminated as the stem cells would belong to the patient himself. Apart from generating fully formed organs, this area of research also focuses on making tissue chips which can be tested for treatment toxicity and other reactions.

We are now talking from dishes to bodies. Scientists all over the world have come up with many approaches for development of organs which can be created *in vitro* and retain their functionality *in vivo*. Successful results were obtained through isolation of a subpopulation $Lin^-CD29^{hi}CD24^+$ in mice which were enriched in mammary stem cells [6]. A single cell marked with LacZ gene was able to reconstitute a complete mammary gland in vivo. Similarly another single stem cell $Lin\text{-}Sca^-1^+CD133^+CD44^+CD117^+$ was able to generate entire prostrate *in vivo* after transplantation using adult stem cells [7]. Embryonic stem cells have proven their ability to generate organs like kidney [8] and pancreas [9] previously, whereas a stem cell cocktail has been reported to produce liver in mouse models [10]. Also, there are reports where miniature humanoid organs have been created using stem cells. Due to ethical concerns and other scientific guidelines humans might have a wait a little more before we can get these techniques in regular practice. Meanwhile some researchers have developed simpler organs through tissue engineering [12]. Dental pulp stem cells have shown extensive differentiation abilities and also have been used to demonstrate *in vivo* construction of adult human bones with Haver's canals. This is achieved with the help of improvised scaffolds [13] which can be used to generate entire or partial tissues usable for transplants. Tissue engineering can be done by isolating stem cell and culturing them on nanofibre scaffolds till the time they achieve sizable and functional growth. After which they can be implanted in the patient to repair or reconstruct the damaged organ. Success has been achieved using specialized and improved scaffolds for replacing wind pipes, blood vessels, nose, ears, cartilage repair knee caps and more [14-17]. Newer age tissue engineering involves process of whole organ decellularization (which may not even be of human origin) can be used as a perfect scaffold for human organogenesis [18]. The organ if first drained off the living cells, leaving behind only the extra cellular matrix (ECM). This ECM can now used as a scaffold as it serves the purpose greatly (Figure 2). It is induced with patient's stem cells to generate functional organs. Here, Dr. Dorris Taylor (Director of regenerative medicine research at Texas heart institute) rightly states that, "Give nature its tools and get out of the way". Stem cells for tissue/organ repair/transplant could hence burst out with revolutionary news anytime sooner or later, changing the face of transplantation industry.

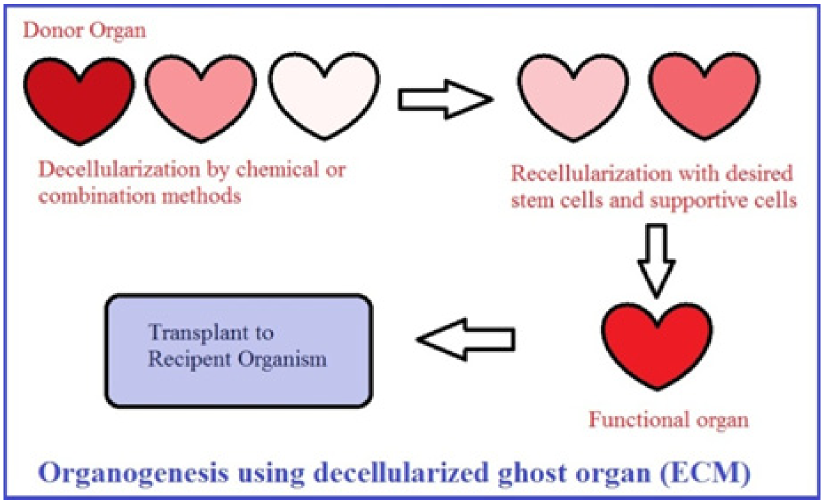



Figure 2. Decellularization for making heart and other organs

## Stem Cells for Neurological Disorders

For decades we have been discussing about several neurological disorders like Alzheimer's disease, Parkinson's disease, Huntington's disease, cerebral palsy, multiple sclerosis, motor neuron disease, spinal cord injury and other complications. Till date we haven't been able to achieve success in fully curing them. The existing drugs only aid in controlling the symptoms to some extent. Reports open greener avenues on stem cell therapy for neurological disorders. Animal models have shown formation of differentiated and functional neurons *in vivo*. With the help of certain drugs and genetic engineering, stem cells can be "reprogrammed" to express growth factors in the brain. Such an approach warrants intensive research as it holds potentials to cure Alzheimer's and other neurodegenerative disorders [19]. In another research on Parkinson's, scientists were successful in obtaining fully differentiated dopamine (DA) neurons from undifferentiated embryonic stem cells [20]. These neurons showed a stable restoration of normal behaviour in animal models. Researchers are investing efforts in studying characters of different types of stem cells that might be selectively suitable for different types of neurological disorders like Parkinson's and Huntington's [21]. This will ensure that the transplant gets suitable environment to grow, repair, regenerate and sustain long term survivals. Where other therapies are mostly targeting on controlling symptoms, stem cells exhort hope of best possible recuperation. If not immediately; stem cells at least evince ability to develop full cure for these diseases in future.

## Stem Cells for HIV Infection

The well known auto immune deficiency syndrome has concerned the world over the past many decades as the disease still awaits a cure. The number of HIV positive people is alarming high and so the death poll. Most of the drugs available in the market are only for controlling the symptoms. Meanwhile there are reports which show evidence of cure of HIV with the help of stem cell transplantation. Scientists have taken efforts to recognise stem cells which are homozygous for CCR5Δ32/Δ32. These cells lack the receptor CCR5 which is essential for the HIV cells' entry into CD4+ immune cells. Such cells are not infected by the virus and hence can used for treatment. In a study, this therapy was used and the patient's CD4+ cells resumed to normal constitution in the largest immunologic organs. The HIV RNA & DNA remained undetected in long term follow up study. The patient was declared cured for the disease without the need of any additional antiretroviral therapy [22]. Sooner with more studies on larger cohorts and variegated patient samples, we will be able to use this kind of a therapy for permanent cure of the diseases. Also unlike other therapies this is a one-time treatment rather than lifetime continuation of various drugs.

## Stem Cells for other Human Disorders

AMD or Stargardt's disease leads to severe vision impairment. Engineered stem cells targeted to recharge the quiescent population of rods and cones by acting as retinal pigment epithelium, were injected into the patient's eye and followed up for almost 2 years. More than 50% of the participants experienced improved vision and reading ability without any immune rejections [23].

Stem cells have also made advances in curing other common disorders. Pre diabetic mice were used to isolate pancreatic stem cells which were induced in lab to produce functional islets with α, β and δ cells. Regeneration of such functional β cells can be a potential cure for type I diabetes [24].

Stem cells also have commoving news for those suffering from one of the most common problem of obesity. Zeve et al. [25] has very well reviewed the importance of adipocyte derived stem cells for therapeutic use in treating obesity and, sequentially helping in curing associated diseases like diabetes and hyperlipidemia. There are two types of adipocytes viz. Brown Adipocytes (BAT) and White Adipocytes (WAT). BAT are fewer in number and contain lot of mitochondria to generate energy by burning calories whereas, WAT are abundantly present and have the function of calorific storage and release it in times of need. Under certain triggers, adipose tissue derived stem cells can be worked upon to attain WAT to BAT transformation. However, the exact mechanism of this transformation from WAT to BAT is not well understood and is under rigorous studies [25].

## Induced Pluripotent Stem Cells (iPSC) as Drug Delivery Vehicles for Various Disorders

Although viral vectors have been well established in drug delivery systems, they still hold a chance a being oncogenic [26]. Shinya Yamanaka (Kyoto, Japan) was awarded the 2012 Nobel Prize along with Sir John Gurdon for setting a landmark by successfully reprogramming stem cells. If iPSCs are used instead of these vectors, we could achieve better target delivery with non-immunogenic vehicles. They are well known for their migratory properties. iPSCs have already proven to produce proteins, repair organs and differentiate as desired and are the best candidates for this routine [27]. Therefore, research for delivering iPSCs from somatic cells for cure of various diseases is under progress in many laboratories all over the world.

iPSCs behave similar to embryonic stem cells in their properties. Hence they hold the promise to find cures for many diseases which the world is suffering since many ages. Patient's own iPSCs can be used for treatment. They can be repaired for the given genetic aberrations and then re-induced in the patients to achieve treatment. Scientists have developed many tools and methods with the help of which this technology can be brought to use [28].

## Stem Cells for Beauty and Cosmetic Applications

Apart from the disease troubled world, there are problems which equally worry everyone on this globe. Problems associated with aging like dullness of skin, wrinkles and patches, lack of glow, hair fall, baldness and such. Stem cells save the day once again with their astounding properties to reverse skin aging, restore its natural healthy balance, re-grow hair, grow hair follicles on bald animal models and more such wonders. Stem cell therapy for treating baldness is gaining wide acceptance and establishing itself speedily with continual improvisation. Reports say that percent inclusion of certain plant stem cells (like apples) in vehicle creams can be used as a premium product which is emollient, antioxidant and reduces wrinkles and inflammation, enhances glow and fights the free radicals which cause skin aging [29]. We can soon expect stem cell induced products in the market for combating these common issues.

## Conclusion

Walking through the timeline and the leaps achieved, stem cells have undergone a seemingly amazing journey all these years. Embryonic, adult or induced; stem cells behold a far more assured future than we can imagine. They are the next generation of medical treatments with nature's own device. They are our hope to all those diseases which seem incurable in the present date. They are the future of non-invasive treatments. Whether it is some haematological or neurological problem, whether we are dealing with organ specific disorders or damage repairs, whether it is some dreadful infection or some toxicity, all of these problems will be solved by stem cells in the coming time. They are the next level of cures science patiently awaits and such findings can rescue the world from common ailments which create problems in a healthy lifestyle. All of the above and much more than what can be included in an editorial, can only suggest that stem cells are many things but, not a mere hype. It is time we embrace these magical bodies of nature and look forward to the day when they take over most of the health issues faced by the world and become an elixir!

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