Stem Cell Research

An evaluation of Stem Cells and their potential application to medicine

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‘We are like dwarfs on the shoulders of giants, so that we can see more than they.’
—Bernard of Chartres, 12th century

Abstract

Stem cell research is a pioneering area of scientific study, with the potential to initiate an unprecedented expansion in man’s medical capabilities. Stem cells may have the ability to alleviate sufferers of currently incurable diseases, and could revolutionise the way in which we address pathological issues. Although stem cell research is still in its early phases, it is already being heralded by some as the ‘holy grail’ of medicine, and by others as the first scientific intrusion into fundamental ethical principles. Yet regardless of moral perspective, this innovative new technique is likely to become the centre point of scientific development in the 21st century.

Introduction

What is a Stem Cell?

Stem cells are capable of continuous replication, and self-renewal, and have the ability to produce daughter cells that are more specialised than the initial parent cell. As a stem cell divides, it has the capability of becoming more specialised, known as the process of differentiation. The extent to which a parent stem cell can produce a potential variety of different specialised cells, known as its plasticity, differs depending on the type of the initial cell. Indeed differentiation can occur in many different forms, ranging from progenitor cells that produce only one cell type, to multipotent cells that can produce a limited selection of offspring similar to the parent cells. At the opposite side of the differential spectrum are totipotent cells that are capable of producing any type of cell in the known biological repertoire, and can potentially form an entire organism.

There are two distinct categories of stem cells, adult stem cells (ASCs) and embryonic stem cells (ESCs), which both have different properties and ethical concerns.

Adult Stem Cells

ASCs are stem cells that are obtained from the human body. Their biological function is to assist with cell repair and regeneration, and they are used to replace damaged cells, usually of a particular type. As a result their plasticity is fairly limited. Consistent with all stem cells, ASCs are capable of sustained replication, throughout the life of the host organism. ASCs can be divided into several sub-categories, depending on their role and function in the body.

ASCs exist to replace damaged or ineffective cells within the body, and operate within different organs and biological systems. Despite their essential function within the body, ASCs are scarce, and as a result research into them is often ambiguous and speculative. Their methods of differentiation differ, both between different types of ASC, and also within the cells themselves.
Embryonic Stem Cells

Unlike ASCs, embryonic stem cells (ESCs) have remained until recently a relatively unexplored area of science. Instead of being obtained from the human body, ESCs are harvested from developing embryos, which contain stem cells of significantly enhanced plasticity. Following fertilisation, a human egg will develop into a blastocyst after 5-6 days. This contains two distinctive layers, an outer layer that will later form the placenta, and the inner layer that will mature into the fetus. At this early stage of development, the inner layer cells are almost entirely undifferentiated, and are temporarily pluripotent (i.e. They have the ability to differentiate into any cell except totipotent stem cells). These cells are extracted from the blastocyst and cultured *in vitro*, thus isolating ESCs of near-limitless differential potential. A diagram of this can be viewed below:

However, the diagram illustrates a refined, hypothetical method of collecting and utilising stem cells, which has not currently been achieved. Instead it offers a speculative technique, which may well prove feasible once scientific understanding of stem cells has been broadened.
After 14-16 days, the embryo develops into a gastrula, which contains three distinct embryonic germ layers. Each layer contains stem cells that will form specific areas of the body. As a result, the stem cells within each of these layers will have lost their pluripotent ability. Throughout subsequent embryonic divisions, the ESCs will become increasingly specialised, thus maturing into a fetus.

Consequently, the earlier that ESCs are collected from the embryo, the greater their plasticity. However, although ESCs cultured \textit{in vitro} have the potential to differentiate into any cell type, the precise stimuli that determine the nature of the cell produced has not yet been established. Although current research shows progression in this area, ESCs remain somewhat unpredictable, and cannot be integrated into clinical medicine until their apparent irrational nature is understood, and controlled.

\section*{Discussion}

\subsection*{Evaluation of Stem Cell Types}

The regenerative properties of stem cells give them unparalleled potential for application to medicine. Although ASCs are already being used in modern treatments for immunodeficiency diseases, their limited plasticity restricts their uses to a limited field. However, stem cells with a higher plasticity can potentially be applied to a variety of diseases, thus providing a universal treatment to many conditions, which is ultimately the aim of stem cell research. The plasticity of many stem cell types allow them to be of use anywhere in the body, thus have the ability to treat a wide variety of conditions. Yet this requires the use of ESCs, which provokes more ethical concerns.

Another concern surrounding the use of ESCs, is the undesirable consequence of immune rejection. The genetic discrepancies between a patient treated with ESCs, and the initial embryonic donor may result in the patient’s body rejecting the stem cells. In order to overcome this, immunosuppressive drug may have to be administered. However as outlined by the House of Lords report into stem cell research, published in 2002, ‘they are not always effective; they must normally be taken over the lifetime of the patient; and they leave the patient open to infection.’ \cite{1} However, the report continues to explain that this concern may be overcome by tissue matching through the establishment of ‘stem cell banks of sufficient size to comprise stem cells with a reasonable (though never perfect) match to the majority of individuals in the population.’

\section*{1. How can Stem Cell research be applied to Medicine}

Stem cell research has the ability to enhance and transform all aspects of medicine. According to a recent article published in the Pharmaceutical Journal on 3 December 2005, ‘Stem cells have the potential to revolutionise current medical practice by a variety of methods.’\cite{3} Some of which are described below.

\subsection*{Cell Therapy}

Cell therapy involves the regeneration of damaged tissue inside the body, through use of stem cells. This can be achieved via two different approaches. Firstly, stem cells can be implanted directly into a damaged or diseased area of the body, where they are subsequently stimulated, either naturally or artificially, to differentiate into functional cells of the damaged tissue.
A second approach is to culture stem cells and allow them to differentiate \textit{in vivo} to form cells of the desired type, before transplanting them into the patient. The obvious restriction to this procedure is the lack of current understanding concerning the differential stimuli of different stem cells. However assuming that this limitation is overcome, then ESCs of high plasticity could provide an unlimited reserve of all tissue types, and theoretically there is no integral reason that might prevent this currently speculative notion becoming reality.

**Tissue Engineering**

Tissue engineering has the prospects of becoming one of the most indispensable areas of modern medicine, as it offers both patient and administrative benefits. In this procedure stem cells are used to create entire organs or tissue structures, that can be grown \textit{in vitro} before be transplanted into the patient. However, such intrusive treatment is highly susceptible to immune rejection, due to any genetic discrepancies between the transplanted organ and the patient. Consequently measures need to be undertaken to overcome this problem for the treatment can be utilised safely and effectively. The refinement of such a method would defeat the present issue of transplant waiting lists, as it eliminates the scarcity of donor organs, thus allowing patients to receive immediate treatment, instead of traumatic periods of waiting.

**Stem Cell Activation**

An alternate method of utilising stem cells involves the activation of a patient’s own cells. As current research progresses, scientists will become more able to produce and control finite stem cell stimuli. This knowledge can be adapted to a patient, as certain chemical signals may stimulate an individual’s own stem cells into enhanced activity, thus regenerating any damaged tissue and removing the need for donor cells. Although this treatment in its active form does not require the use of embryonic stem cells, and eliminates the need for laboratory grown cells, ESCs will undoubtedly have to be used in order to research the complex notion of chemical stimuli, and as result this procedure is not entirely exempt from ethical constraints.

2. **Areas of Potential Stem Cell Application**

**Auto Immune Diseases**

Stem cell treatment can be applied to auto-immune diseases through a variety of methods. In diseases such as SCID (Severe Combine Immunodeficiency), significant defects exist in the T and B-lymphocytes, which are used to defend the body from pathogenic intrusions. Consequently the body cannot present any effective defence against infections, leaving the sufferer highly vulnerable to diseases such as pneumonia or meningitis, which can prove life threatening. However, it is believed that the approach of stem cell activation has the potential not only to alleviate, but also to cure such diseases. In this hypothetical treatment, patients would undergo ‘autologous hematopoietic stem cell transplantation.’ Firstly a growth factor would be administered to the patients to trigger a rapid production of HSCs, which would then be isolated and cultured in vitro. Once sufficient HSCs had been collected, the patient would receive radiation therapy in order to destroy the existing ineffective immune system. Following this the isolated HSCs would be subsequently transplanted...
back into the body where they would differentiate into functioning T and B-lymphocytes. Such a treatment would prove both ethically viable, as well as clinically possible, as the stem cells used are derived entirely from the patient, thus overcoming the dubious morality of utilising ESCs, and the biological limitation of immune rejection.

**Diabetes**

Type 1 diabetes occurs as a result of the body’s inability to manufacture insulin, the hormone that determines the rate that glucose is removed from the blood. In sufferers of type 1 diabetes, the body’s own immune system destroys the insulin-producing pancreatic cells, thus blood glucose levels are permitted to rise to dangerously high levels. The implications of constantly high blood glucose concentrations can lead to heart disease, blindness and kidney failure. Currently treatment only extends to manual administration of insulin supplements, or an entire pancreas transplant. The latter however, although theoretically viable carries significant surgical risks, especially through the necessary use of immunosuppressive drugs, which is exacerbated by the severe shortage of donor organs.

It is believed that stem cells could be used to regenerate the damaged pancreatic cells, thus restoring the regular production of insulin. Experiments have shown that this is possible through the use of ASCs. However, initial evidence suggests the therapeutic effects of ASC treatments are limited, and that the differentiated islet (insulin-producing) cells that result demonstrate an impaired ability to manufacture insulin, which proves insufficient compared to the natural insulin production of an unaffected individual. The alternative is the use of ESCs, which produce higher yielding islet cells, and seem less susceptible to immune rejection. This approach is, however, more ethically provocative.

**Heart Disease**

Coronary heart disease is the most prominent cause of premature death in the UK, and therefore any possible treatment for the condition will have significant implications on the quality of many individual lives, as well as the nation’s collective health. At present major surgery is often the only option for sufferers of myocardial infarction, which proves both intrusive, potential dangerous and also expensive. Coupled with the current shortage of donor hearts, this process is becoming too ill resourced to be sustainable. Stem cells offer a less traumatic and economically feasible method of treatment. Research has proved that under certain conditions stem cells can differentiate into specific heart components, such as cardiomyocyte cells (which form the contracting muscle of the heart). Consequently, tissue damaged from the effects of CHD can be replaced as required, allowing treatment to be coordinated closer to the individual needs of the patient, offering many advantages over open heart surgery, or heart transplants.

Recent experiment proves this is possible using ASCs, as shown in the diagram below:
However, again the most promising areas of treatment arise from the application of ESCs, which provide higher plasticity, thus a greater ability to regenerate a maximum number of cell types within a damaged vicinity of the heart.

**Neurodegenerative Disorders**

Neurodegenerative diseases are yet another area that can benefit from stem cell application. Parkinson’s disease occurs when a high proportion of the brain’s dopamine producing cells die, thus inhibiting the overall abundance of dopamine in the body. Production can be stimulated through the use of L-Dopa, yet constant exposure to this drug causes it to become progressively ineffective. To date, it has been recognised that the stimulation of dopamine production will reverse the symptoms of Parkinson’s, yet attempts to achieve this, including the transplant of adrenal glands and other dopamine-producing organs, have proved largely unsuccessful. Yet again, the regenerative properties of stem cells may be able to repair cells damaged by the disease, thus overcoming its symptoms. A diagram illustrating this procedure can be viewed below:
Such application demonstrates another pathological barrier, impassable by current medicine, but easily traversable by the development and refinement of stem cell treatment.

**The Ethical Debate**

Despite their potential medical benefits, there exists considerable opposition into stem cell, in particular ESC, research. Although at the time of extraction, the embryo exists only in the form of approximately 50 cells, it is still argued that this early blastocyst should be entitled to fundamental human rights. Many people believe that life begins at the moment of conception, and therefore the developing embryo should be regarded in the same esteem as a developed human.

It is also believed that following the integration of stem cell research into society, women may be pressurised by the medical community to donate embryos. There are also concerns that an accumulation of donated embryos may lead to embryo stockpiling, which may in turn result in surplus embryos being used for more cosmetic purposes.

Conversely, embryonic stem cell research has the potential to save, preserve and enhance existing lives, and it can be considered as ‘the lesser of two evils.’ Currently embryos that are unused during IVF treatment are discarded, without ethical objections. ESC research would exist to provide an alternate use for otherwise redundant embryos. Also under current government legislation, subsequent research will be strictly controlled and monitored.
Conclusion

The two different types of stem cells possess many unique characteristics, and serve distinctly different purposes; from repairing the human body, to creating and developing a human embryo. Their potential for application remains unprecedented, although greater ethical sensitivity surrounds methods with higher medical prospects. Stem cell research has the ability to overcome many prominent issues in the health service today, primarily the volatile and unpredictable nature of organ transplant lists. However, essentially the greatest asset of stem cell research is the prospect of significantly enhanced patient treatment, and future developments may benefit every recipient of health care in this country and across the world. Stem cells also enable the medical profession to approach and treat patients through a protocol of systematic and progressive methods, tailored to the requirements of the individual. This will inevitably help medicine move away from the shackles of statistical concern and economic priorities, and overcome the dated approach of generic patient treatment, according to finite and often inflexible guidelines and procedures. Not only can stem cell research revolutionise patient treatment, it can also transform the universal interaction between patient and Doctor, which will have profound implications across the globe.

Undoubtedly stem cell research will remain an exciting area of scientific development in the future, but whether it can overcome moral objections remains yet to be seen.
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