Stem Cell Treatment Applied to Genetic Disorders.

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ABSTRACT

Stem cell research is an area which potentially holds the answer to many genetic deficiencies and currently incurable diseases. And whereas current means of treatment have proved to cause bodily rejecting complications (as will be discussed), the very nature of stem cells suggests that such problems would be eradicated if they are used as an alternative in medicine. Stem cell research is a new phenomenon within medical advances, and yet at this early stage of development already the possibilities seem bounteous and exciting proposals seem to prove accurate when practical work is carried out. Medicine is an area of advanced technology, enough to detect a genetic disorder at a prenatal stage. In many cases, the foetus is left to develop and treatment can only commence at a post natal stage. Therefore this report focuses on the possibilities of embryonic stem cell research and its potential to treat genetic disorders at a prenatal stage encouraging the prospect of reducing the effects that a genetic disorder can cause as the child develops.

INTRODUCTION

So what are embryonic stem cells and how are they different to adult stem cells? The idea to cure diseases with the body’s own devices has been around for a long time for instance in the treatment of bone marrow transplants in the cure for cancers. The first attempts at bone marrow transplant go back to the 19th century, when people first realised that problems with blood diseases stemmed from the bone marrow.

However it was pathologist Rudolf Virchow in the 1800’s who pioneered the idea that diseases start at a cellular level. The body has many devices such as the immune system to restore cells to a functioning state after ‘attack’ of invading pathogens. Therefore the immense complexity of the human body implies that it also has the ability to self restore when certain cells or tissues cease to function correctly e.g. in the case of motor neurone disease when nerve cells in the brain degenerate. Therefore it is logical to suggest that if damage occurred to functioning cells, the body would have a natural restoring system. It seems that stem cells could be the answer.

Stem cells which are found in multiple areas such as the blood, the skin, the brain, differ from other kinds of cells in the body. All stem cells, regardless of their source, have three general properties:

1) they are capable of dividing and renewing themselves for long periods;
2) they are unspecialized;
3) and they can give rise to specialized cell types.

For these reasons stem cells seem to be the body’s natural restoration mechanism.

Why are embryonic stem cells favoured over adult stem cells? Primarily stem cells are required in large quantities if a large sample of tissue is to be cultured in a small time period (it is vital that tissue can be cultured quickly in order to meet the demands of the patient whose deterioration rate may be rapid). Adult stem cells are scarcer to locate and harder to culture. Secondly embryonic stem cells (derived from embryos that develop from eggs that have been fertilized and then donated for research purposes) can proliferate for a year or more in the laboratory without differentiating, but most adult stem cells cannot.
Therefore future research is needed to discover what are the factors in living organisms that normally regulate stem cell proliferation and self-renewal.

They lack tissue-specific structure and are capable of dividing and renewing themselves for long periods of time. For these reasons the possibilities for embryonic stem cell research are widespread and bounteous.

It is clear to see that stem cells could be the answer to diseases such as motor neuron disease, it could be the future treatment of Parkinson’s disease, a common neurogenerative disorder, and the end of organ transplantation.

Whereas current organ transplantations in most cases are successful, evidently there is a shortage of donors. Also the transplant patient must endure in some cases a lifetime of drug intake in order to suppress the immune system. The body’s natural response cannot have effect and consequently reject the new tissue. This is not ideal as the inhibition of the immune system leaves the body susceptible to attack from other diseases. Thus culturing the body’s own tissue cells eliminates the possibility of bodily rejection and also deals with the problem of donor shortages.

In people who suffer from type I diabetes, the cells of the pancreas that normally produce insulin are destroyed by the patient's own immune system. New studies indicate that it may be possible to direct the differentiation of human embryonic stem cells in cell culture to form insulin-producing cells that eventually could be used in transplantation therapy for diabetics.

For incurable diseases such as motor neuron disease, the prospect of the body’s own stem cells morphing into neurons could be a successful treatment. I cannot commit to the idea that this will be a successful cure since there is an issue with genetic disorders that the faulty gene (which is always different for different disorders) could continue to cause the ‘new’ implanted neurons (cultured from embryonic stem cells) also to degenerate. Obviously, in such genetic disorders, embryonic stem cells can compensate for the loss or damage of body cells however genetic technology (possibly implantation and acceptance of foreign functioning genes) is also needed for a conclusive cure.

Stem cell implantation has already proven a success. Many laboratories have already successfully developed methods to induce embryonic stem cells to differentiate into many different cell types. One study attempts to reproduce the specific neuron (DA neurons) which produce dopamine for the cure of Parkinson’s disease. The progressive degeneration of these DA neurons leads to tremor, often associated with the disease. It is thought Parkinson’s disease could be the first disease to be amenable to stem cell transplantation.

As is evident, the prospects of embryonic stem cells research for the use of tissue repair and regeneration is endless.
DISCUSSION

A substantial problem which arises from stem cell transplantation is the bodily acceptance of foreign embryonic stem cells. It is impossible to retrieve one’s own embryonic cells. Similar to current organ and tissue transplantation, a patient’s body can reject the tissue containing disimilar genetic information.

If adult stem cells are used, when possible, the patient’s own stem cells would ensure a perfect match, or if an identical twin were to donate stem cells. However, the first successful cord blood stem cell transplant (one type of cell called amniotic epithelial cells in the human placenta has characteristics that are strikingly similar to embryonic stem cells in their ability to regenerate a wide variety of tissues) was performed in 1988 in Paris, France and it was a success. To date, more than 6,000 cord blood stem cell transplants from unrelated donors and several hundred from sibling donors have been performed worldwide. This tells me that there is a high rate of bodily acceptance for cord blood stem cells deriving from a donor. This is a very new process and with the first case only 17 years ago it is difficult to predict the ultimate outcome of this form of transplantation however since cord and embryonic stem cells are able to divide and renew over long periods it is likely that the stem cells now implanted and differentiated into different tissue cells will prove a success.

My main topic of interest relates to the transplantation of embryonic stem cells (or cord blood stem cells) at a prenatal stage when a foetus is diagnosed with a genetic disorder.

As previously mentioned, some genetic diseases can be aided but not cured by stem cell transplantation. For instance if a foetus was diagnosed with having Osteogenesis Imperfecta, (a brittle bone disease, caused by a genetic defect that impairs the body's production of a protein called collagen) then a transplant of bone marrow stem cells to produce new collagen can help. As previously mentioned, stem cells that are unmatched could be used without rejection. However stem cell therapy is not a cure. To fully cure genetic disorders, it would require the collaboration of genetic technology with stem cell treatment. Scientists have yet to discover how to turn genes ‘on’ and ‘off’. Genes influence the differentiation of stem cells therefore if the defect in the patient’s DNA is not corrected, this will affect the functioning of the new tissue. This form of transplantation would be a suitable treatment for diabetes where insulin levels can be restored with the transplantation of cells which secrete insulin (differentiated from embryonic stem cells) freeing them from the lifelong necessity of daily insulin. In each case, the patient’s genetic code is not altered, so consequently they still suffer from the genetic disorder, however with the transplantation of such cells which are able to produce the supplement that their body naturally lacks, the patient is able to lead a life in the absence of insulin supplements (diabetes) or regular fractures (Osteogeneisis Imperfecta). If these cells were to be transplanted, it could be detectable whether the stem cell therapy was a permanent or temporary cure. To use Osteogenesis Imperfecta as my example, mutated genes will still exist within the patient DNA, implantation of collagen producing cells will control the symptoms, however since it is not know how to inhibit the mutated genes, they have the ability to influence the renewal of these specialised cells and consequently alter the functioning.
of these cells. If a method of gene inhibitory action were devised, along with the implantation of supplements that the patient naturally lacks (stem cell transplantation) then a cure for such diseases as Osteogenesis Imperfecta would be possible. I proposed that a prenatal insemination of differentiated stem cells is a suitable stage since it is when vital development occurs. In the case of diabetes, a lack of insulin will reduce the foetus’ healthy development due to the lack of ability to store glucose resulting in persistent high blood glucose levels. In such cases, the sooner a disorder is treated, the less long term damage is caused. The method of transplantation for a foetus would be similar to that of an adult, where stem cells would be taken into the bloodstream.

Another problem arises in that if stem cell research proves to be a great success in later development, stem cells will need to be cultured at faster rates. For this scientists must discover what it is in our genetic information that controls the rate of stem cell differentiation. Only once this is established can they discover how to increase that rate. Also, donors from other species. It is evident that unmatched stem cells are successfully accepted by another body, so it is likely that unlike organ transplantation where experimentation shows humans have rejected organs from another species, it is possible stem cells do not share this same property.

The permanent cures achievable by stem cell research at the moment seem to be the culturing of tissue in order to replace non-functioning tissue such as diseased organs, or complete organ transplantation (although the formation of a new organ from stem cells may still take years), the replacement of cartilage for arthritis sufferers, (Professor Anthony Hollander 2005); non genetic disorders.

**Ethical issues**

Embryonic stem cell research seems a fantastic and fast developing field within research with its endless possibilities. However the use of experimentation on embryonic cells can be seen as destroying a potential life in attempts to rescue a living being. Such a proposal causes widespread controversy. These gametes which are infrequently donated could be used for artificial insemination with the increasing demand for IVF treatment. Yet in response to the objection towards embryos taking part in stem cell research, research is necessary for medical advances to occur, and most significantly, the women who donated those eggs did so in full awareness and accordance that the fertilised eggs could be used for embryonic stem cell research.

The new discovery of amniotic epithelial cells found in the placenta, only discovered within the last decade to have the same long lasting renewal effect of embryonic stem cells, can be seen as an alternative to the use of embryonic stem cells. Unlike embryonic stem cells, which are obtained only by destroying human embryos, these cells can be extracted from the same placentas that now are routinely discarded after birth. They thus could be a non-controversial alternative to embryonic stem cells. Also, since successful transplantation has occurred between non genetically similar donor and patient, this eliminates the necessity for stem cells to derive from the placenta of a sibling who is likely to have similar genetic make-up. This prevents controversy from ‘designer babies’ that might be conceived with the purpose of donating cord blood stem cells to a sibling in need of cultured cells.
However, as with other forms of human donations e.g. blood, organs, the health care system frequently encounters shortages. Cord blood stem cells are a very new discovery and because of this it is likely that many women may be reluctant to donate the placenta after childbirth since this new research may be unknown to them. New discoveries show that the human testicle may provide a less controversial source of cells for stem cell research. The German scientists who confirmed their radical findings already knew certain cells in the testes of newborn mice were able, like embryonic stem cells, to generate numerous different tissue types. The researchers believe similar cells could also be extracted from humans. But until now they had not been able to show the same cells existed in adults. This enlightens the future of stem cell research for many reasons. For instance this ultra new discovery proposes the possibility that there are many more bodily regions and in both genders that also produce stem cells with this same property. These areas merely haven’t been discovered yet. This discovery could eliminate any problems relating to donor shortages because in most circumstances, each human should carry their own accessible supply of stem cells with that same characteristic of embryonic stem cells. Embryonic stem cell research would no longer cause an ethical issue (in the field of stem cell research) since there would be no need to use embryonic stem cells for tissue culture or formation of new cells.

CONCLUSION

Conclusively, my theory show how at this stage of medical development, stem cell transplantation can be assist treatment for genetic disorders but not permanently cure them. This is possible due to the ability of stem cells to differentiate into cells that are absent from the patient due to their genetic disorder. Evidently these cells have a vital purpose within the complex human system thus by restoring them by culturing (from stem cells) and then implanting them, the cells are able to carry out their intended function. My theory is based upon the idea that stem cells can restore the cells that are naturally absent due to a genetic disorder, however not all genetic disorders involve the absence of a specific cell and for these genetic disorders, my method would be insufficient.

I cannot commit to the fact that my theory is a cure for genetic disorders. As discussed this is because the mutated genes would still exist. If scientists could discover how to inhibit the effects of these mutated genes or even culture and then transplant functioning genes, in collaboration with stem cell transplantation, then a possible cure for a genetic disorder may arise. However genetic disorders are each so unique that it is inaccurate to suggest that this method could cure all genetic disorders. I believe that only when the genetic code is amended can there be a cure because although the stem cell transplantation will restore a function such as the production of insulin, (transplantation of pancreatic cells that secrete insulin, cultured from cord blood stem cells) the mutated gene will still exist and can influence the differentiation of stem cells possibly causing them to malfunction. It is this response that needs to be inhibited and can be established through future developments.
It is also difficult to commit to the success of cord blood stem cell implantation for the cure of genetic disorders since the first implantation only occurred 17 years ago and although currently proving a success, the long term effect of stem cell transplantation is obviously inconclusive. However, it is suggested that it will be a long term success due to the very nature of cord blood cells and our knowledge that they can renew over long time periods.

Although initially a problem seems to be the immune system’s responsive rejection of foreign cells, numerous accounts of successful implantation prove that initially the body accepts donor cells with alternative genetic information. It is likely that this initial bodily acceptance will continue throughout the patient’s life since an immune response is immediate. However since this is such a new development, the conclusions are yet to be discovered. This versatile quality suggests that in the future stem cell implantation will be a leading treatment since it eliminates the need for any immunosuppressant drugs. Once tissue culture develops into full organ formation using this method, I believe this treatment will eradicate the need for organ donation and consequently demands for organ transplantation will be met more rapidly due to the accessibility of stem cells, since every human has them.

I feel it is vital that future research should involve locating other body regions (such as the testes) containing stem cells with the same properties as cord blood stem cells, thus ensuring every individual has their own supply of stem cells with the ability to renew over long periods. This way they are accessible when needed or can be donated in order to maximise the rate of culturing tissues for those in need. Finally, this discovery overrides the potential problems that may arise due to a shortage of placenta donations.
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