2012

Stem Cell Therapy

Macy Reedy Physiology major Department of Microbiology and Molecular Genetics, Oklahoma State University, Stillwater, OK 74078, USA

Key Words: Stem cell, transcription factors, mesenchymal, stem cell therapy

Stem cells are defined as cells that can practice self-renewal and differentiation. For these reasons, more and more people are conducting experiments with stem cell therapies in order to treat and find a cure for today's diseases. These cells are the ideal ones to use because they adapt to any cell type and are able to reproduce in high numbers. They also can be derived from patients' own cells which allow the fears of immune system rejection to be avoided. The four articles mentioned below are all different examples of experiments where stem cells were used to test the effiency and outcomes of stem cell therapies and compare them to the outcomes of other, more practical treatments. These experiments prove that stem cell therapy is a far superior way to treat diseases, and the need for organ, tissue, and cell donation will definitely decrease with a sure way to reproduce cells without a donor. One article discusses beta cell replication from stem cells, one discusses making heart tissue grafts from stem cells, one discusses using stem cells to repair injured nerves in mice and restore function, and one discusses reprogramming adult somatic cells into pluripotent stem cells for myocardial stem cell therapies.

Introduction

"Stem cell" is a term used to describe a cell that is capable of performing both differentiation and self-renewal. Differentiation is the ability of a less specialized cell to become a more specialized cell, and self-renewal is the ability of a cell to replicate itself. According to Robin Lovell-Badge, embryonic stem cells are able to provide a potential supply of cells for cell-based therapies for some human diseases (88-91). There have already been many examples of stem cell use from bone marrow and skin in therapies for treatment of Parkinson's disease and diabetes. Lovell-Badge believes that humans have not discovered the true potential of stem cells and that if stem cells are in any shape or form able to help cure diseases, that people have an obligation to continue studying and experimenting with them to find these cures. However, despite the possibility of curing many of the diseases that people are suffering today, many people have ethical issues with the use of stem cells and believe that they should not be used in this manner (88-91).

Recent Progress

One specific example of stem cell therapy in humans was seen in people with diabetes; type 1 and 2 (Shroeder 490-498). One of the side effects of diabetes is beta cell loss in patients, and many believe that the only way to find a cure for diabetes would be to replace those beta cells. Because organ donation is an unreliable option for cell replacement, the use of pluripotent stem cells and embryonic stem cells offer another option to provide beta cells without the hassle of waiting for a donor. Embryonic stem cells are considered a great option to produce a different source of transplantable cells that both secrete insulin and react to glucose because they are able to generate high numbers of cells and are able to differentiate into any type of cell in the human body (Shroeder 490-498). For the pluripotent stem cells to be considered as beta cell replacements, they have to show therapeutic potential. This means that they have to reproduce a high number of mature offspring and make homogenous populations of the wanted cell type. Additionally, in the Shroeder article, the in vitro produced pancreatic cells have to be able to survive in vivo for long periods of time. Shroeder states that if no side effects are seen within the immune system and the patients are still genetically stable, that this method of beta cell replication involving stem cells should be considered far better than any other antidiabetic treatments today (490-498).

Another application of stem cell therapy was seen in an experiment that included transfers of human stem cell derived cardiomyocites into the injured hearts of mice and rats. The experimenters made a model of a guinea pig heart with injuries to show that these stem cells were able to protect against heart arrhythmias. The stem cell grafts that were conducted were able to contract normally along with the host's heart muscles, and there was even evidence that showed that there were a reduced number of cases of ventricular tachycardia. The presence of both coupled and uncoupled graft regions in the hearts which suggested true heart regeneration were also important. The steps of this experiment included expanding undifferentiated human stem cells by using a medium infused with a growth factor, and then the human stem cells were differentiated into cardiomyocytes by serial application of specific proteins. Then, they were preserved for 16-18 days. The cultures were heatshocked day before collection one and then cryopreserved. Cells were thawed before transplantation and then suspended into a growth serum. Because the results of this experiment included improvement in the motor function of the heart, it supported further experimentation into the field of stem cell cardiac therapies (Shiba 322-325).

A third example of stem cell therapy has to do with the interworkings of the nervous system. Usually, peripheral nerves are repaired by regeneration of axons. However, the outcomes using this technique are not always so great. The most promising cell type for this would be human mesenchymal stem cells, which are derived from embryonic stem cells. They are able to produce a usable amount of cells and are known to be effective in repairing injured hearts (Lee 7039-7046). Despite the fact that these human mesenchymal stem cells have great regenerative abilities, there is still sometimes an issue with poor engraftments after some transplants. So, to reduce this, a sphere was produced from human mesenchymal stem cells to reinstate cell to cell relations without the addition of anything else. This would lead to better engraftment conditions after transplants and the overall therapeutic effect would also be greater. In the study, the experimenters tested whether the human mesenchymal stem cells could regenerate the damaged peripheral nerves. This began with cells being removed from feeder cells and put into Petri dishes for incubation for 14 days. This would determine the embryonic body. The human mesenchymal cells were tested for differentiation potency towards certain types of cells, and then expanded in a specific type of media. Then, the cells were cultured in suspension in a dish that contained sphere medium and incubated. Spheres of culture

appeared 24 hours later. Sciatic nerve defects were created in male mice by making incisions into the right back leg, exposing the sciatic nerve and cutting into the nerve in the central area underneath the gluteus maximus (Lee 7039-7046). The human mesenchymal cells were transplanted into the damaged nerve and the mice were closed up. Eight weeks after this procedure, a dissection and biopsy both were conducted on the regenerated nerves. Electrophysiological examinations, or nerve conduction tests, were done on the mice to measure action potentials of the sciatic nerve, and results showed that they had increased greatly. A walking-foot-print analysis was also conducted to test the visibility of the digits on the feet of the mice. Mice with a damaged sciatic nerve will have foot-prints that show no detail of their digits. Results showed great detail of the digits on the paws. The next test was a nerve simulation test. Nerves were stimulated in order to test the voltage needed to induce muscle contractions in the mice. Results showed very low voltages that were very near numbers that normal mice would exhibit. (Lee 7039-7046).

Another example of stem cell therapy also revolves around heart conditions and involves reprogramming adult somatic cells into pluripotent stem cells. The goal of this reprogramming is to encourage their differentiation into working cardiomyocytes. Heart failure is one of the leading causes of death in the United States, and one of its major causes is cell loss and deterioration after heart attacks and strokes. Cell loss and scar formation lead to a loss of contractile function of the heart muscles. Once again, human embryonic stem cells were chosen to replace cardiac cells because of their ability to differentiate in many different cell lineages (Zwi-Dantsis 3285-3299). However, because of fear of rejection from the immune system, something else must be done with the stem cells first. The use of transcription factors was able to reprogram somatic cells into stem cell to make patient and disease specific cells. The primary aim of cardiovascular regenerative medicine is to produce a fully operating cardiac tissue that works well the myocardium of the host. The experiment conducted with the guinea pig hearts not only showed the versatility of human stem cells, but also proved that the stem cells have true potential to help improve the health of many lives. Stem cells' abilities to differentiate and adapt proves that they could provide endless opportunities to improve the lives of people. This trial contained evidence that cardiomyocites made from human stem cells are able to assimilate into the adult heart. With results like these, more and more people will be far more likely to adopt stem cell replacement therapies for heart disease and other diseases as well.

The results of the peripheral nerve regeneration experiment introduce a more efficient cell source for regenerative medicine. Because they are easily expanded and maintained, they are a much more stable cell supply. Human mesenchymal cells can be derived from human embryonic stem cells and therefore offer up a much higher potential for regeneration. This experiment concluded that it is possible to repair the injured sciatic nerves of mice with transplanted human mesenchymal stem cells that were produced from human embryonic stem cells.

The experiment that included reprogramming somatic cells into stem cells is a great, recent advancement in regenerative medicine because it has the ability to make patient-specific pluripotent stem cells that could possibly elude the immune system. Eluding the immune system would completely bypass the fear of rejection of the new cells in the body.

Discussion

Stem cell therapy in diabetic patients presents a way to help restore homeostasis inside the bodies of the patients. Normal function of organs such as the pancreas should go back to normal, and so should insulin secretion. If this is true, it should cause type 2 diabetes patients to have less dependence on insulin shots or completely terminate the need for them.

The experimenters claim that there are three main events that occur after peripheral nerve regeneration after an injury and they are: Wallerian degeneration, axon regeneration and growth, and nerve reinnervation. These all explain the processes behind the experiments with the mice. Wallerian degeneration refers to the actual cutting of the mices' nerves, and the axon is actually separated from the neuron cell body and degenerates (Lee 7039-7046). After that, it is all about reinnervating the tissue for growth. The experimenters state that because healing of peripheral nerves after injury is still imperfect, people are testing ways to make it better, including them.

The idea of being able to repair an injured heart with tissue grafts made from human stem cells provides amazing opportunities to both the field of science and patients. If an injured heart could be repaired and full function could be restored fully without the need of an organ donation, people would not need to wait for help from organ donors. There would be a lot less suffering for the patients. As for scientists, if hearts can be repaired in this way, then who is to say that this could not be continued in the future to ultimately find a cure for heart disease or diabetes.

The new technology in the experiment soothes a lot of ethical conflicts surrounding the use of stem cells. Reprogramming somatic cells into stem cells completely bypasses the issue while still being able to conduct stem cell research (Zwi-Dantsis 3285-3299). Also important, this technology provides an endless amount of personalized cell for patients, which optimizes personalized medicine. Patients' results will be better and their overall health will improve.

References

- Lee, et al. "Regeneration of Peripheral Nerves by Transplanted Sphere of Human Mesenchymal Stem Cells Derived from Embryonic Stem Cells." Biomaterials. 33 (2012): 7039-7046.
- Lovell-Badge, Robin. "The Future for Stem Cell Research." Nature. 414 (2001): 88-91.
- Shiba, et al. "Human ES-Cell-Derived Cardiomyocytes Electrically Couple and Suppress Arrhythmias in Injured Hearts." Nature. 489 (2012): 322-325.
- Shroeder, Insa S. "Potential of Pluripotent Stem Cells for Diabetes Therapy". Current Diabetes Reports. 5 (2012): 490-498.
- Zwi- Dantsis, Limor, and Lior Gepstein. "Induced Pluripotent Stem Cells for Cardiac Repair." Cellular and Molecular Life Sciences. 69 (2012): 3285-3299.