The Use of Hair Follicle Stem Cells in the Repair of Sciatic Nerves

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Word Count: Approx 2000

Grade Awarded June 2006: PASS WITH MERIT

Research Paper
Based On
Pathology Lectures
At Medlink 2005
Abstract

Hair follicles are found at the base of each hair of the body. They contain a small area known as the bulge, this area contains an easily accessible source of pluripotent adult stem cells (stem cells which can develop into any of the three major tissue types: endoderm (interior gut lining), mesoderm (muscle, bone, blood), and ectoderm (epidermal tissues and nervous system)). This paper is mainly focused on the differentiation of these stem cells into Schwann cells; these are the cells which support the peripheral nervous system, each cell forming a segment of myelin sheath around the nerve axons. Schwann cells aid in the regeneration of the nerve axon. This process could provide many possibilities for future medical advances, which will be discussed in more detail in this paper.

Introduction

Stem cells are undifferentiated cells, found all over the body, which retain the ability to divide and differentiate into different cell types. Stem cells are essential to the body, as this ability to divide and differentiate replenishes and replaces cells which are damaged. Stem cells are categorised according to their differential potential; totipotent stem cells have the ability to divide into any type of cell in the body, the cells produced by the first few divisions of a fertilised egg produce totipotent stem cells. Pluripotent stem cells have the ability to divide into any type of cell, except totipotent stem cells, from which they derive. Multipotent stem cells can only produce cells of a closely related nature, for example red blood cells, white blood cells and platelets. Unipotent stem cells can only divide to form one type of cell, but have the property of self-renewal which distinguishes them from non-stem cells.

Many medical researchers believe that stem cell research has the potential to change the face of medicine with possibilities of repairing specific tissues or even growing organs. Embryonic stem cell research was started in 1998 in America when James Thomson, of the University of Wisconsin, Madison, was the first person to successfully remove cells from embryos. This was the world’s first embryonic stem cell line. This marked a huge breakthrough in medical research and has led the way for major future developments.

Embryonic stem cells are cultured cells obtained from the undifferentiated inner mass of an early-staged embryo (this is sometimes referred to as a blastocyst, an embryo with between 50 and 150 cells). Embryonic stem cells are thought to have a much greater development potential than adult stem cells, due to their totipotent nature, they are able to differentiate into each of the three major tissue types; endoderm, mesoderm and ectoderm.

Embryonic stem cell researchers are currently attempting to grow embryonic stem cells in vitro, beyond the first stages of cell development. It is of paramount importance to make sure the embryonic stem cells are fully differentiated into the desired cell type before they are transplanted into the patient. This is because undifferentiated embryonic stem cells may develop into a tumour after transplantation. Currently, scientists are trying to develop techniques to prevent rejection of implanted cells by the patient.

One of the possibilities to prevent rejection is to create embryonic stem cell clones that are genetically identical to the patient. This can be achieved by fusing an egg cell, from which the nucleus is removed, with a patient's cell. The fused cell produced now only contains the DNA of the patient and is allowed to grow to the blastocyst
stage of development, and stem cells are then extracted, and because the stem cells are genetically identical to the patient, the patient's immune system will not reject differentiated cells derived from these embryonic stem cells. However, this raises even more ethical issues regarding the obtainment of the egg (further reading: http://en.wikipedia.org/wiki/Embryonic_stem_cells)

As an alternative to this, hair follicle stem cells have pluripotent potential, and eliminate the ethical problems associated with embryonic stem cells whilst overcoming the problem of rejection, and thus we will discuss this idea further.

**Discussion**

In this section we will discuss the recent developments and possibilities for the future of hair follicle stem cells. Researchers at AntiCancer, Inc. in California have discovered that stem cells from hair follicles of mice can be used to rejoin severed nerves in mouse models.

Hair follicle stem cells are easily accessible and normally function to form the hair follicle, in turn forming the growing hair in all mammals, including humans. Hair follicle stem cells have shown great potential to produce nerve cells, amongst others, due to their pluripotent nature.

Human embryonic stem cells are known to be capable of differentiating into almost all tissue cells, but have aroused ethical debates in many countries. Scientists have also come across problems such as rejection of the implanted cells by the patient’s immune system. As a direct result of this, many recent studies have focused on using adult stem cells for future medical applications.

Researchers in both America and Japan have shown hair follicles to be a highly promising source of relatively abundant and accessible, active, pluripotent adult stem cells. In previous studies, a team led by Robert Hoffman, a professor at the University of California, have induced hair follicle stem cells to differentiate into blood vessels and neurons. The researchers have said that these studies have suggested the potential of hair follicle stem cells to form diverse cell types. The research team have now successfully induced hair follicle stem cells to develop into Schwann cells.

Schwann cells are named after the German physiologist Theodor Schwann. These cells are a type of neuroglia (cells that provide support and nutrition to the neurons) that mainly provide myelin insulation to axons in the peripheral nervous system (the part of the nervous system that is outside the central nervous system and comprises the cranial nerves excepting the optic nerve, the spinal nerves, and the autonomic nervous system). The nervous system relies heavily upon this myelin sheath for insulation and as a method of maintaining levels of electric charge in the axon. Non-myelinating Schwann cells are involved in the maintainance of the axons and are crucial for neuronal survival. Schwann cells outnumber neurons by 50 to 1.
Schwann cells, the supporting cells of the peripheral nervous system, form a myelin sheath around the axon of the nerve, this is shown in figure 1, the dark circles are Schwann cells which are surrounding the axons forming the myelin sheath. As well as this, they also aid in cleaning up peripheral nervous system debris and guide the re-growth of the axons. To do this Schwann cells arrange themselves in a series of cylinders which serve as a guide for sprouts of regenerating axons.

The research project mentioned above, written M. Hoffman, carried out experiments on mice. These experiments showed that stem cells extracted from hair follicles could recover damaged sciatic nerves. When the Schwann cells, which were cultured from stem cells extracted from hair follicles, were transplanted into the site of the sciatic nerve of the anaesthetised mice, the nerve healed much faster, than if no treatment had been given, and also fully. Figure 2 shows the strength of contraction of the gastrocnemius muscle in mice with transplanted hair follicle stem cells as well as mice without treatment. After 4 weeks, the mice with transplanted stem cells have a higher strength of contraction of the gastrocnemius than the untransplanted control mice by approximately 90%. After a further 4 weeks, both the control mice and the mice with transplanted stem cells show an improvement in the strength of contraction, but the mice with transplanted stem cells show more improvement than the control mice by approximately 80%. After a period of time, the mice with transplanted hair follicle stem cells recover the functionality of the sciatic nerve, this then results in these mice being able to walk again.

This research shows that hair follicle stem cells, if stimulated correctly, can be used in the future to treat injured nervous systems in not just mice, but other mammalian species, including humans. If applied to human patients, the use of a patient’s own hair follicle stem cells could potentially heal any part of the peripheral nervous system within a relatively short period of time. This treatment could therefore have the potential to help patients with damaged sciatic nerves, which would affect their ability to walk, due to an inability to contract the gastrocnemius muscle, so therefore this treatment can cure these problems and restoring the patient’s ability to walk. This treatment is carried out by stimulating stem cells isolated from the vibrissa follicle bulge area to develop into Schwann cells. These cells then form a myelin sheath around the axon of the neuron and guide the re-growth of the axons. This gradual
process reforms the nerves which would otherwise not heal completely. The reparation of the sciatic nerve allows the gastrocnemius muscle to contract, enabling the patient to walk again. This idea can be applied to every nerve which is part of the peripheral nervous system.

There are also other potential applications of hair follicle stem cells which, although not life-saving, will improve the quality of life for people. One such example of this is the use of a patient’s own hair follicle stem cells to treat baldness. Firstly, the stem cells are extracted from the hair follicles, then they are surrounded by skin cells and transplanted into the skin, the stem cells then develop into all of the cells along which make up the hair follicle. This development provides hair growth in places where hair loss has occurred. However, this has so far only been achieved in experiments on mice, but this marks a possibility for future developments and Professor George Cotsarelis, who led the research at the University of Pennsylvania School of Medicine, said "I think this or something like it will be available in the next five to 10 years."

Although hair follicle stem cells circumvent almost all of the ethical issues surrounding embryonic stem cell research, there are still some ethical concerns which must be taken into consideration. One of these issues is how far researchers should take stem cell technologies; just because something can be done, should it be? Although research can be carried out on mice and other animals, should this be done? And who should fund this research? These are questions that many people feel must be answered; many different people will have strong but differing viewpoints on these matters. People who may have strong views on these ethical issues are; people suffering from medical conditions which may benefit from stem cell therapies in the future, research scientists, religious followers and the policy makers involved in making laws. Is there a correct answer in response to these issues?

**Conclusion**

We believe that, although embryonic stem cells provide a large amount of potential to overcome future medical obstacles, the ethical issues which they raise are inhibitive, as there are legal, ethical and social issues which need to be addressed. In light of this, we have come to the conclusion that adult stem cells provide a much more ethically viable alternative. In particular hair follicle stem cells, which, due to their pluripotent nature, present many of the benefits which embryonic stem cells provide.

Hair follicles produce a lot of potential, for example, they provide many opportunities to improve people’s quality of life, through cosmetical treatments such as that for hair loss. However, there are also many more medically beneficial treatments which may be available in the future, such as the re-growth of damaged nerves of the peripheral nervous system, as discussed above.

Undoubtedly the future will reveal many more possibilities of uses of hair follicle stem cells, ranging from the repair of skeletal muscles, to providing replacement tissues or organs grown from these cells to patients in need of them. The main benefit of all of this however, is not just the ability of these cells to do this, as there are alternative stem cell sources. The major benefit that will be gained from this is the elimination of the ever worrying problem of immuno-rejection of transplanted tissues.
or organs. This problem can be solved by extracting the required stem cells from the patient’s own hair follicles, due to these cells being 100% genetically identical to the patient.

Finally, we believe that hair follicle stem cells are the way forwards in the research of stem cells.
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