Seeing Into The Future:
The Potential of Embryonic Stem Cells
As a Cure for Progressive Retinal Atrophy in Canines

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Word count: Approx 2400

Grade awarded June 2006: PASS WITH DISTINCTION

Research Paper based on
Pathology Lectures at Vetsix 2005
ABSTRACT

In the Pathology and Parasitology lectures at Vetsix 2005, we were given a background on Embryonic Stem Cells. Currently a very controversial scientific area, stem cells have great potential in many aspects of both Human and Veterinary Medicine. Embryonic Stem Cells are already being used to some extent for disorders such as spinal injuries and neurodegenerative diseases. However, there are problems; scientists have not yet discovered how to cause these cells to differentiate into a certain type of cell e.g. a red blood cell versus any other human cell.

Having a particular interest in Veterinary Medicine, I have decided to focus my research paper on the uses of Stem Cells to cure blindness in animals, in particular Progressive Retinal Atrophy (PRA) in canines. While loss of sight is extremely distressing in a family pet, it can signal the end of the career of a valuable working animal, for example a sheepdog or a guide dog.

INTRODUCTION

Embryonic stem cells can be defined as ‘cells derived from early embryos that can replicate indefinitely and differentiate into many cell types. Stem cells serve as a continuous source of new cells’ (Hall and Horton, 1997). Embryonic stem cells are undifferentiated – they do not resemble any specific adult cell, and are pluripotent – they can develop into any type of adult cell under the correct circumstances. Adult stem cells are more specialized, and much more difficult to discover in the body.

First successfully isolated and cultured by James Madison and his team of developmental biologists at the University of Wisconsin in November 1998, embryonic stem cells are taken from fertilised embryos at the blastocyst stage (around 4-5 days after fertilisation). The embryos can be sourced from in vitro fertilisation (IVF) clinics, where surplus embryos are often discarded. The cells can then be cultured, where they will proliferate, remaining undifferentiated for prolonged periods of time. However, these cells retain their ability to develop into specific types of cell, some examples of which include gut, neural, bone, cartilage and muscle cells. It is this pluripotency that causes embryonic stem cells to be of such great interest to Medicine and Science.

Many people have rested their hopes on stem cell therapy; Phillips (2000) reports on the PersonalMD health website; ‘stem cells have the potential to revolutionize the practice of medicine and improve the quality and length of life’. Stem cells could be extremely useful, and not only for mere transplantation of new cells into organs. Stem cells could be used in drug testing and studying development, as well as to treat or cure a wide range of conditions such as diabetes, cardiac disease, strokes, burns and diseases such as Parkinson’s and Alzheimer’s, often through replacing damaged cells with new ones.

One of the first widespread uses of human embryonic stem cells could be in the field of drug testing and discovery. From embryonic stem cells, uncontaminated populations of a specific cell type could be used to measure cell response to different chemicals, ‘permitting the rapid screening of hundreds of thousands of chemicals that must now be tested through much more time-consuming processes’ (University of Wisconsin-Madison, 2005). This could have particular relevance in reference to diseases that involve specific cell types, or cases where the effect of chemicals on cells is unknown e.g. as yet unrecognised carcinogens.

The uses of stem cells for transplantation are endless; according to the University of Wisconsin-Madison ‘In theory, if stem cells can be grown and their development directed in culture, it would be possible to grow cells of medical importance such as bone marrow, neural tissue or muscle.’ (University of Wisconsin-Madison, 2005)

Blindess is one such condition that can potentially be treated using stem cell therapy. The following discussion will use Progressive Retinal Atrophy in canines as an example of blindness in order to demonstrate how stem cells could be potentially used.
Progressive Retinal Atrophy (PRA) is a hereditary retinal disease affecting the photoreceptor cells, eventually leading to blindness. The term PRA covers several types of degeneration, one sub-classification of which is late onset photoreceptor degeneration, also known as progressive rod-cone degeneration, where the dog does not begin to lose sight until after 1 year of age. There is currently no pharmacological or surgical treatment or cure.

Late-onset PRA occurs when photoreceptor cells, more specifically; ‘rod’ and ‘cone’ cells on the retina deteriorate (see figures 1 and 2). The retina is the lining at the back of the eye, the cells of which receive light stimuli from the environment and transmit the information to the brain (via the optic nerve) where it is interpreted to become vision. Rod cells begin to degenerate first, causing night blindness (rod cells are responsible for vision at low light levels) and loss of peripheral vision, as they are more thinly spread towards the outside of the eye (death of a just a few cells in this area will cause narrowing of vision). Cone cells then degenerate, causing complete loss of vision.

According to Acland and Aguirre (2005); ‘With one exception, PRA in all breeds so far studied is an autosomal recessive disorder. That means that to be affected a pup has to receive one copy of the defective gene from both parents’. Therefore, both parents of an affected dog must be either affected or carriers (see figure 3). The disease is known to be a mutation in a newly identified gene, known as prcd, and a DNA test is available to detect the presence of this gene.

Late-onset PRA tends to appear in working dogs primarily, including several breeds of Spaniels, Sheepdogs, Collies, Retrievers, Hounds, Terriers, as well as a small number of miniature breeds. This disease could have a massive effect on both dog and handler, in terms of quality of life, time invested, and cost.

All of the above problems could be erased using stem cells; in order to treat PRA, stem cells could potentially be collected and cultured. Then, it would be possible to cause these cells to turn into ‘rod’ and ‘cone’ retinal cells; ‘stem cells might be very handy, because some of them do have the capacity to divide and form new photoreceptors’ (Pathmanaban and Marshall, 2005). The cells could then be surgically transplanted onto the retina. Once in the retina, the cells should

In late-onset PRA, the owner/handler will not notice any loss of sight until 1 to 5 years of age, although defects in the retina can be detected using an electoretinogram. The animal will then begin to show signs of night blindness (impaired vision where there is restricted light), and within a year will have progressed to total blindness, with peripheral vision being lost first. This type of PRA bears similarities to retinitis pigmentosa in humans; therefore, a cure for PRA could carve the way for advances in human medicine also.
incorporate within the existing tissue, with the help of the retina, which emits signals in the eye to indicate the presence of damaged cells.

In relation to the research that has already been conducted, there are positive and negative aspects. PRA can be easily diagnosed; Optigen has already developed a DNA test for PRA. Also, progress has been made in the use of adult stem cells in order to cure neural diseases in mice (Coghlan, 2003). Legally, ethics for research are not as restricted in animals e.g. ‘British law requires that any new drug must be tested on at least two different species of live mammal. One must be a large non-rodent’ (Anon, 2004). However, it can also be argued that human ophthalmology is more advanced than canine ophthalmology, and that there is little or no proof that cells could be transplanted onto the retina (Pathmanaban and Marshall, 2005).

The cost implications of this treatment should also be considered; as well as the considerable expense for the owner, the sheer amount of research needed would require millions of pounds worth of funding. The potential cost of treatment needs to be balanced out against the sum any owner would be willing to spend on alleviating a non life-threatening condition, or the economy of treating a working dog.

Although a discussion of the ethics of embryonic stem cells can be seen below, it is important to consider the ethics of this particular example of use for embryonic stem cells- treating blindness in canines. It can be argued that to treat blindness, in particular in a working dog, would dramatically improve its quality and length of career, and therefore life. Also, transplantation of stem cells would probably be a one-off surgical procedure, and would cause no more distress to the animal than any other routine procedure. However, experiences of owners of blind dogs show that they can adapt quickly to loss of sight, especially in a degenerative disease that progresses slowly such as PRA; ‘The large majority of dogs still lead a decent, happy life’ says Dr Eric Smith (Vogel, 2000), showing that a cure for blindness is not necessary. One could also argue that stem cells may only return partial sight to the dog, making the expense of treatment unjustifiable.

There are also ethics that need to be taken into account when considering Stem Cell research as a whole; it must be remembered that general public may identify any advances in Veterinary Medicine as potential advantages or disadvantages for human medicine but with added emotional issues. These factors will be discussed in the following section.

While stem cells, embryonic or otherwise, could bring about miraculous improvements in the everyday lives of millions around the world, and ‘existing federal regulatory and professional control mechanisms, combined with informed public dialogue, provide a sufficient framework for oversight of human stem cell research’ (Chapman et al, 1999), there is a potential that stem cell technology could be abused, exploited, or even used to harm others. Currently, in several countries, stem cell research is legal within limits, causing stem cells to become a subject of political competition between countries. An example of this is Korean scientist Dr. Woo Suk Hwang ‘once regarded as the world’s leading stem cell pioneer’ (Sample, 2006) who has fabricated stem cell research, making severe ethical lapses in the process, including allegedly using eggs donated by female lab staff.

This draws attention to the fact that the sources of stem cells should be carefully regulated. The AAAS states that ‘Embryonic stem cells should be obtained from embryos remaining from infertility procedures after the embryo’s progenitors have made a decision that they do not wish to preserve them. This decision should be explicitly renewed prior to securing the progenitors’ consent to use the embryos in ES cell research’ (Chapman et al, 1999). Some extreme groups even argue that IVF procedures are unethical, because surplus embryos have the potential to become human beings, and because to ‘artificially’ create a human being can be argued to be ‘playing God’, which leads on the debate of ‘when does a human life begin?’

Currently, there are two alternative methods of procuring stem cells. Adult stem cells can be found in tissues or organs, and lie dormant until injury or illness occurs. Although some can
differentiate into various cells (e.g. a brain stem cell may be able to become one of several types of neural tissue), and could potentially come from the patient themselves, adult stem cells are extremely difficult to locate, and their differentiation is limited (as yet, there is no way to cause the same brain stem cell to become a piece of skin tissue). The other alternative is the use of umbilical cord blood; which can be collected from the umbilical cord and placenta at birth and stored commercially (there are already companies offering this service). In fact, cord blood stem cell transfusions are already being used e.g. for conditions such as leukaemia, as the cells in this blood are more immature and less likely to be rejected.

Therefore, stem cells certainly have vast potential to cure conditions such as blindness, in particular PRA. However, many research and ethical issues remain to be resolved before a practical cure is attained.

CONCLUSION

To conclude, PRA is a condition that could have a severe effect on the quality of life of a dog, in particular a working dog. In the future, there is potential for treatment, even a cure for this condition, using stem cells.

Stem cells could be taken from a source, as yet unknown, cultured, and then surgically transplanted onto the retina of the affected animal. This should greatly improve vision, potentially eradicating the need for euthanasia.

Aside from ethical issues with this procedure, there are currently many technical problems that need to be researched and resolved before a cure for PRA is practical and cost effective. I believe that further research into stem cells will eradicate many current problems e.g. causing cells to differentiate into ‘rod’ and ‘cone’ cells, and that deeper knowledge of the canine eye and ophthalmologic surgery will help with others. Over time, as stem cells are more widely used, treatment will become decreasingly expensive and therefore more accessible to the average owner.

It is impossible to know the full potential of stem cells, and although the idea of using stem cell treatments as everyday veterinary procedures seems far-fetched, it may well be that animal treatments will eventually pave the way for significant developments in human medicine.
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(As per Harvard referencing system)


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