THE USE OF STEM CELLS IN
THE TREATMENT OF
DEGENERATIVE EYE DISEASES AND
POSSIBLE FUTURE DEVELOPMENTS
IN THE USES OF STEM CELLS IN THE
TREATMENT OF EYE DISEASE AND INJURIES

BY
REBECCA LAND
EMMA SIMS
Pass with Merit

RESEARCH PAPER
BASED ON
PATHOLOGY LECTURES
AT MEDLINK 2011
ABSTRACT

In this paper we will discuss the current research about the use of stem cells in the treatment of degenerative eye diseases and eye injury. It will offer information about previous research and ongoing research around the topic and suggest possible future developments in treatments and cures. As well as giving brief scientific information on the science behind the use of stem cells, we will also discuss moral issues that affect the use of stem cells – especially when taken from embryos. In conclusion, we believe that in the future, scientists will be able to grow completely new eye tissue using stem cells from the patient. This would therefore prevent problems associated with rejection and could be used to treat both eye disease and injury.

Introduction

There are three types of stem cell – embryonic, somatic (adult) and foetal (including cord blood). Embryonic stem cells are the most versatile as well as being the most controversial – coming from ‘spare embryos’ grown in the lab. The earliest cells after fertilisation are totipotent, which means they can develop into any cell type in the body including extra-embryonic tissues. These develop into pluripotent cells (as shown in figure 1) that can develop into all body cell types excluding extra-embryonic tissue such as the placenta. This means with pluripotent cells alone, we would be unable to create a human.

However, stem cell research didn’t start here. Since 1956, when the first bone marrow transplant was performed, stem cell research has progressed greatly. From investigating bone marrow, scientists discovered that bone marrow contains at least two kinds of multipotent stem cells. Multipotent stem cells only have the ability to develop into a limited variety of cells. In the marrow there were haematopoietic stem cells that could form differing types of blood cell, and stromal stem cells that can form bone, cartilage, fat and connective tissue. In 1978, British scientist Robert Edwards and Dr. Patrick Steptoe were the first to successfully create a ‘test tube’ baby. Obviously it was a huge development in the fertility industry, however, this also meant that scientists could now have a living sample of cells with the ability to create human life, accessible to them within a lab. This kick-started a large amount of research into the pluripotent cells of the embryo. In the nineties, pluripotent stem cells were isolated from embryos and scientists investigated their properties. After experimentation, they discovered that when exposed to certain proteins, these cells differentiated into various cell types.
After the discovery made by James Thompson, in 1999, researchers determined that stem cells can be made to differentiate into different cell types by human intervention.\[2\] This was a great finding that would potentially mean that scientists could create any cell type that they needed to. This would mean that new organs could be made from stem cells to be transplanted into patients with diseased or non-functioning organs. However, currently scientists are still experimenting on differentiating stem cells into various cell types. Some require proteins to be added to them, whilst others require genes to be added to the cells.\[4\]

Scientists need to be sure that the cells are fully differentiated, because if they are grown whilst not fully differentiated, this could cause deformations in the genetics of the new cells and could potentially cause cancer.\[4\]

As well as this, in 2006, researchers at Kyoto University in Japan identified conditions in which specialized, differentiated cells from an adult could be taken back to their original stem cell form.\[7\] This would mean creating stem cells that can replace the use of embryonic stem cells, and could be used to create any cell type in the adult body. To do this, they ‘reprogram’ a cell back to its original state. Despite several seemingly successful experiments, these induced pluripotent stem cells have been found to not be exactly like the original embryonic pluripotent stem cells.\[8\]

Scientists found that the induced pluripotent stem cells (iPSC) had many slight genetic differences to embryonic stem cells. They also found out that when re-differentiated, these iPSC created differentiated cells that shared these genetic differences to naturally formed cells.\[8\] This could have a large effect on the function of the cells and therefore scientists have to continue to research reprogramming cells so that they can be sure that the new cells will develop normally.

Then in 2011, new research was carried out as to whether embryonic stem cells can restore vision in humans.\[9\] Embryonic stem cells were taken, then induced to form iPSC’s, otherwise known as induced pluripotent cells, and manipulated into forming the cells found lining the back of the eye. 50,000 retinal pigment epithelium cells were then injected into the retinas of two patients. The retina is the light-sensitive layer of tissue at the back of the inner eye that sends the image to the brain, as shown in figure 2\[12\] –

![Fig. 2 -](image)

One patient was in her 70’s and had age related macular degeneration whilst the other patient was in her 50’s and had Stargardt’s disease; both were registered blind. After the injection of approximately 50,000 retinal pigment epithelium, the cells attached to the membrane at the back of the eye and survived the next 16 weeks of study. The experiment was not designed to see if stem cell therapy in the eye worked, it was to see if the injection was safe and whether there would be any spontaneous cell replication. However, an improvement in vision was noted.\[9\] This trial gave hope that degenerative diseases may be curable in the future.
In late 2011/early 2012, model Katie Piper underwent stem cell treatment for one of her eyes. Her eye had been left completely blind after acid was thrown in her face. Katie had the procedure done at Queen Victoria Hospital, in East Grinstead, England. Doctors took stem cells and tissue from a donor bank, grew them, and then implanted them into the eye. The main aim was for the donor cells to stimulate the production of Katie’s own multipotent cells in her eye. From only being able to see light, after the treatment Katie was able to recognise objects and shapes and could count how many fingers doctors held up.\textsuperscript{[13]}

**Discussion**

As mentioned before, stem cell research is extremely controversial. From the beginnings of research, scientists were destroying many ‘spare’ embryos from fertility clinics for their experiments.\textsuperscript{[14]}

Many anti-abortion and religious groups are totally against the use of embryos in stem cell research. In a statement released by the National Right to Life Committee, they said they opposed the use of embryonic stem cells, and instead suggested putting more money into research about adult stem cells, where no lives are harmed.\textsuperscript{[5]} The main reason for the controversy is the argument of when life begins. Some religious groups and pro-life groups believe that life begins as soon as the egg is fertilised.

In The Catechism of the Catholic Church, paragraph #2322 states that “from its conception, the child has the right to life. Direct abortion . . . is a criminal practice, gravely contrary to the moral law. The Church imposes the canonical penalty of excommunication for this crime against human life.”\textsuperscript{[10]} In this case, if life begins as soon as the egg is fertilised, by killing the cells during research scientists are committing murder. This has caused many religious groups to protest against stem cell research. People in these pro-life groups generally agree that an embryo at any stage should still be considered as a person.\textsuperscript{[10]} This could then mean that they should be entitled to human rights.

Totipotent cells taken from embryos could be used to generate a supply of eye cells for emergency use by many different people, however there is a risk that the cells may be rejected or have no effect at all as they do not have the same DNA as the receiver. If you were to take the donors cells at birth from the placenta and induce them to form totipotent cells, you could then use these cells in an emergency with a reduced risk of rejection as they would have the same deoxyribonucleic acid as the cells were originally theirs. This would also mean that no embryos would be harmed and would satisfy the pro-life and Christian groups.

In people with diseases of the eye, pluripotent stem cells can be induced to form many cells that are needed in the eye. Stem cells that have been injected into the eye have shown that they replace older and injured cells.\textsuperscript{[9]} If they could have injections into the eye on a yearly basis, the chances of the eye repairing itself increases greatly as a single application may not contain enough stem cells to form a new layer of retinal pigment epithelium cells that will work to repair the vision of the eye. In spite of this, this method would only help people with diseases that affect the retina. Other diseases or injuries may affect another part of the eye. Many injuries to the eye affect the cornea. The cornea is the transparent window on the surface of the eye.\textsuperscript{[14]} As it is
exposed to the environment, it is very easy to injure it and although most minor injuries repair themselves, when the injury goes deep into the cornea it can cause scarring and loss of vision.[14]

To avoid using embryonic cells, it may be possible to take any type of cell from the patient and induce or ‘reprogram’ the cell into a pluripotent cell. Scientists have already had some success with this process, and if they could create reprogrammed stem cells from specialised adult cells, it would offer endless possibilities for treatments. As research has shown, stem cells can be made to differentiate into a specialised cell by using proteins or other DNA. If scientists were able to isolate the process that caused stem cells to develop into specialised cornea cells for example, then maybe they could grow them into a completely new cornea. If they could do this, they would avoid the problems of rejection from corneal transplants and patients would no longer need to take anti-rejection drugs for the rest of their life.

Firstly, scientists would have to remove the problems with the iPSC’s. Currently there are problems with differences between iPSC’s and embryonic stem cells protein markers. This may affect the development of a new cornea, so would have to be resolved. However, if they managed to grow a new cornea from the patient’s cells, it would share their DNA and could be transplanted into the patient with minimal problems or risks.

Any part of the eye can be affected by degenerative diseases. Many of these diseases can’t be cured at the moment but with advancements in the use of stem cells, it may be possible to grow other parts of the eye such as the retina or optical nerve. Even if not all specialised cells could be turned into eye cells, it may be slightly easier to use specialised cells from different parts of the eye.

This may be easier as generally adult multipotent cells can develop into a limited number of cells that are usually related in some way. For example, bone marrow multipotent cells can produce many different types of blood cell. If scientists could isolate the patient’s adult multipotent cells from their eye, then possibly these could be used to form other parts of the eye. Multipotent cells have already been found in the optic cup of the eye within birds, which scientists believe develop into retinal neurons as well as other eye cells.[11]

If a similar thing happened in humans, then maybe these cells could be harvested from the eye and grow in a lab to produce a new retina for the patient that shared the patient’s DNA. However, if this process did occur in humans then maybe it would be right to assume the human retina would’ve been able to repair itself without any intervention – which of course hasn’t been seen in major eye injuries. A reason for this may be that the eye can only produce a certain amount of cells, or the cells may only be produced for minor injuries and wear and tear. In this case, it may be possible to only take a few cells from the eye but to then grow a large enough number to create the retina in a lab.

One problem is that in severely injured eyes or eyes that are completely blind, there are sometimes no stem cells to harvest, as production has been ceased due to the trauma to the eye. This happened with Katie Piper,[13] as told in the introduction, which is why the doctors used cells from a cell bank. This may sometimes raise
ethical issues with religions, as you are using cells from other people. Strict religious
groups may believe this is ‘unnatural’ - although any scientific intervention would be
considered so.

It is possible to skirt around the moral roadblock of using all embryonic stem cells in
the embryo, which results in death of the embryo. Some scientists have managed to
just remove one stem cell from the embryo, and then induce it to make more stem
cells. Scientists have even been able to remove a small group of cells at the 16-30
cells stage without doing any apparent harm to the development of the embryo. This
method leaves the embryo to develop normally whilst providing a good supply of
other stem cells. [4] This could be the method used as not only would it make the
doctors feel less guilty about using embryonic stem cells, the recipient would also be
more willing to undergo the operation, and governments would also be more lenient
on funding. Funding is vital part of research, as without it scientists would be unable
to complete any major research.

There have been some investigations into whether the removal of a single or small
group of cells may affect the development of the child. But if scientists used this
technique on a large scale, and then had a surge of children born with deformities or
disabilities, there would be many ethical consequences and the scientists would have a
lot to answer to. Around 2,500 children have had one or two cells removed at the 8-10
cell stage, and none showed any signs of any deformities. [16] But this does not mean
that they will not develop deformities in the future, nor does it mean that there is no
increased risk in a child being born with a deformity.

**Conclusion**

In conclusion, we believe in the future it may be possible to use alternative methods
of obtaining embryonic stem cells on a large scale without destroying embryos. This
would have a large impact on the view of stem cell research as scientists will no
longer be ending potential lives by carrying out their research. Before using these
methods, they would need to be sure that removing cells from an embryo will not
affect the development of the child in any way.

At the moment, much of the funding for stem cell research is going into investigating
adult somatic stem cells. This completely eradicates the use of embryos which is a
great thing when it comes to the beliefs of religious groups. Hopefully in the future,
scientists will be able to create completely pluripotent stem cells by reprogramming
specialised cells. To do this, scientists must first remove any marker differences
between iPSC’s and embryonic stem cells to reduce any risk of developmental or
cancer problems.

If scientists are able to do this, then these specialised cells from the patient needing
stem cell treatment can be taken back to pluripotent stem cells and used to grow or
repair the patients affected organ. In the future this may be a better option than
transplantation, as it requires no anti-rejection treatments as the implanted tissue is a
perfect match to the patient.

Therefore these lab grown organs and tissues could be used to cure many
degenerative diseases and injuries by simply replacing the diseased or damaged tissue.
This sort of treatment would be especially beneficial to diseases such as age-related macular degeneration, which is one of the main causes of blindness, as it only affects a small part of the retina. The retina could be replaced by one grown using the patient's own cells, and the condition could therefore be treated. Some variations of age-related macular degeneration are completely incurable, so any improvement in sight from stem cell treatment would be beneficial.

As far injury treatment, doctors already use corneal transplants and these have been successful for years. However, these require rejection drugs to be taken for the rest of the recipient’s life. If a cornea could be grown using any of the methods discussed, this would avoid the use of anti-rejection drugs, which are an inconvenience to the patient and can have side effects such as abnormal hair growth, high blood pressure and a lower resistance to infection.[15]

Therefore, overall we believe the development and research in association with stem cells will eventually lead to much more efficient treatments of both eye disease and injury, maybe including the use of lab grown tissue. However, due to the morals and ethics of stem cell research, this point may be a long way away.

References –

Note – All references with a stated author are listed alphabetically -


‘When Does Human Life Begin? Conception And Ensoinment’ Lindsey Disney, Updated December 27, 2010


Web references without stated author in order of appearance -


