STEM CELL RESEARCH IN THE TREATMENT OF EYE DISORDERS

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ABSTRACT

Stem cell research is one of the most controversial areas of medical research and one that has polarised opinions. This paper will address the basic science of stem cells, the different methods of isolating these cells and the potential therapeutic applications. It will discuss the controversies and the moral and religious objections to this research as well as the position adopted by different authorities, advisory and expert committees. There is always a balance between the needs for developments and research to provide and improve medical treatments and what is considered acceptable and ethical by the society.

INTRODUCTION

Definition of a stem cell

A stem cell is an undifferentiated cell of a multicellular organism which is capable of giving rise to an unlimited supply of cells and also has the ability to differentiate into other types of cells such as skin cells, muscle cells, and nerve cells.

Due to their ability to provide different types of cells they offer us the prospect of new and effective treatments for degenerative conditions and illness that affect all of us, including macular degeneration or cerebrovascular accidents.

Types of stem cells:

Mouse Embryonic Stem Cells (mESCs):

Mouse embryonic stem cells are the first type of stem cell to be identified. Martin Evans, at Cardiff University, was the first to identify them. Embryonic stem cells are derived from early embryos, therefore in theory have the ability turn into other types of cells in the body.
Embryonic Stem Cells (ESCs)

Cells derived from early embryos have the potential for limitless reproduction and can potentially provide different types of cells. Embryonic stem cells are obtained from the cell mass blastocyst. In 1988 James Thomson successfully isolated embryonic stem cells and grew them in the laboratory. These cells have been obtained from embryos produced by in-vitro fertilisation (IVF) that would have otherwise been discarded and destroyed. It is also possible to produce embryos specifically for extracting stem cells.

To induce the embryonic stem cells to undergo differentiation, certain conditions are needed. Scientists alter the chemicals in the culture medium or alter the cells by the insertion of genes. The cells can differentiate spontaneously once they have developed into embryoid bodies but the scientists need to direct this process so that a specific type of cell is produced.

![Embryoid Bodies Diagram]

Figure 1 shows the differentiation of mESCs

Adult Stem Cells:

Adult stem cells are cells that are derived from mature differentiated tissues and can be used therapeutically for the replacement of injured or diseased tissues like muscle. They
can only be used in the treatment of that specific indication, as they do not have the potential to differentiate to other types of cells. An example would be the liver; adult stem cells from the liver can only produce more liver cells. Adult stem cells are used in a variety of treatments for example bone marrow cell transplantation.

**Induced Pluripotent Stem Cells (iPSCs):**

Induced pluripotent stem cells are cells that have been modified by researchers to mimic embryonic stem cells. Induced pluripotent stem cells have the potential to differentiate into different types of cells, tissue and organs, and they can therefore be employed in the treatment of patients and for further research.

**Cord Blood Stem Cells:**

These cells are obtained from the blood in the umbilicus. They have unlimited ability to reproduce and have great potential for use in the treatment of a number of diseases, especially haematological disorders as well as diseases such as diabetes, leukaemia and various other forms of cancer.

**DISCUSSION**

**Structure of eye**

Figure 2 shows the structure of the human eye.
Details of certain structures

Macula:

The Macula is yellow in colour; it absorbs excess blue and ultraviolet light that enters the eye. The macula has structures that are specialised for high-acuity vision. The macula is the central region of the retina located at the back of the eye, between the superior and inferior temporal arteries. It is the part of the retina, which is responsible for central vision and for the detection and appreciation of fine details such as reading and close intricate work. The macula is 5.5 mm in diameter.

![Figure 3 shows the structure of the macula.](image)

Cornea:

Accounts for two-thirds of the eyes total optical power. It is the outermost layer of the eye, which is clear, dome-shaped. It receives its nourishments from the tears and aqueous humour that fills the chamber behind it.

Retina:

The retina is the light sensitive layer of tissue at the back of the inner eye which acts like a camera. The retina converts images to electric signals that are transferred to the brain.

Lens:

The lens focuses the light rays, which pass through it to create a clear image of an object.
Current research into the treatment of eye disorders:

**Macular Degeneration (MD):**

1) **Age Related**

Age related macular degeneration (AMD) is a painless eye condition that typically leads to the gradual loss of central vision, however it can sometimes cause a rapid reduction in vision. The symptoms of AMD include: difficulty in reading because the text appears blurry, less vibrant colours and difficulty in recognising faces. There are two types of AMD: dry AMD and wet AMD. Dry AMD develops when the cells of the macula become damaged due to an accumulation of drusen, which is a waste product. Dry AMD is the most common type and the least serious. Wet AMD develops when abnormal blood vessels form underneath the macula and cause damage to its cells. This type of AMD is also referred to as neo-vascular AMD. It is more serious and, if left untreated, can cause vision to deteriorate within days.

2) **Stargardt’s Macular Dystrophy**

Figure 4 shows the difference between a normal macula, a macula affected by dry AMD and a macula affected by wet AMD.
Stargardt’s macular dystrophy, sometimes referred to as Stargardt’s disease, is an inherited condition and is the most prevalent form of juvenile macular dystrophy, affecting around one in 10,000 children. The disease affects the macular, and therefore results in loss of acuity and difficulty in reading or performing fine intricate tasks.

**Stem cells and degenerative eye conditions**

A trial in London in 2011 used retinal cells derived from human embryonic stem cells, which were injected into the retina of people suffering from Stargardt’s macular dystrophy. The trial was carried out at Moorfields Eye Hospital. Twelve patients had the cells injected into their eyes. Due to the fact that the cells are human embryonic stem cells, there have been some criticisms and ethical objections. Josephine Quintaville from ‘Comment on Reproductive Ethics’ said that she believes that vulnerable patients were used in these experimental treatments and went on to say that although we should continue to look for cures for degenerative eye diseases this should not use treatment that involves destroying viable human embryos.

**Glaucoma**

Stem cells are currently being considered as a treatment for glaucoma. There are two main types, open-angle and closed-angle glaucoma. The underlying cause is an increase in the fluid pressure in the eye. Glaucoma can result in loss of vision due to the progressive death of retinal ganglion cells in the eye resulting in the irreversible loss of vision. Open-angle glaucoma is the commoner form of glaucoma: it is a chronic condition that tends to develop slowly and is usually asymptomatic till the late stages of the disease. Closed-angle glaucoma usually presents acutely with a painful red eye sometimes accompanied by nausea and vomiting. It is treated as a medical emergency. Both types of glaucoma can result in deterioration and ultimately loss of vision. Current treatments with medications and surgery are designed to lower the intraocular pressure and to reduce the risk of further loss of vision. There are currently no reliable treatments that result in recovery of lost vision. Stem cell therapy offers the prospect of reducing and possibly reversing some of this visual loss.
Keratoconus

Keratoconus is a non-degenerative, non-inflammatory disorder of the eye. This disorder affects around 1 in a 1000 individuals. The cornea become stretched and thins at the centre resulting in bulging, making the vision more short sighted and irregular. As a result the vision is distorted. Unfortunately Keratoconus can be difficult to diagnose because it usually develops rather slowly, however some patients may experience headaches, increased light sensitivity, distorted and/or blurred vision. Stem cells may help in the regeneration of the cornea and repair of he damage caused by Keratoconus.

Figure 5 shows the structure of the eye.

Figure 6 shows a normal eye against an eye affected by Keratoconus
**Stem Cells Timeline:**

**1981, Mouse beginnings**
*Martin Evans* who did his research at Cardiff University and continued at the University of Cambridge, was the first individual to identify ESCs in mice.

**1998, Human Stem Cells**
Research was undertaken at the University of Wisconsin, Madison by James Thomson. He also worked alongside John Gearhart from Johns Hopkins University, Baltimore, successfully isolated hESCs and grew them in a lab.

**2001, Bush controversy**
George Bush restricted federal funding for the research on human embryonic stem cells as it was considered unethical.

**2006, Cells reprogrammed**
*In Japan; Shinya Yamanaka* of Kyoto University identified a method of producing
embryonic-like cells from adult cells – without the use of an embryo. The researchers reprogrammed ordinary adult cells by inserting four key genes forming "induced pluripotent stem cells".

**2007, Nobel Prize**
Evans was awarded a Nobel Prize for medicine along with Mario Capecchi and Oliver Smithies for their work on genetics and research into embryonic stem cells and their therapeutic potential.

**2012, Blindness treated**
ESCs were used in a trial that investigated blindness and the result was encouraging.

**2014, Human trials**
Masayo Takahashi at the Riken centre, Kobe is in the process of selecting individuals for a potential treatment in treating age-related blindness.

This timeline shows that stem cells have been researched for over 30 years and that there is a good prospect of further advances and the adoption of these new treatment modalities into clinical practice.

**Ethical considerations**

Stem cell research promises to revolutionise the treatment of many conditions that are currently associated with poor outlook. Medical advances are usually welcomed by the general public who share the enthusiasm of the researchers in finding treatment that can improve the prognosis of the patients and reduce their suffering. However, stem cell research has been mired with controversy and opposition. Some have even expressed their fear that this research may ultimately lead to human cloning and that research in this field is a violation of the sanctity of life.

I have researched this and I would like to present my understanding of these issues. Although there are some who oppose any work in this field regardless of the origin of cells used, the majority of opponents reserve their strongest opposition to research using cells derived from embryos. The objection is that the process destroys these embryos that have the potential to grow to an independent human being.

Research and treatments that are currently in use such as in-vitro fertilisation produce excess number of embryos that are subsequently destroyed. I think that provided that the donors provide valid consent, the use of these 'unwanted embryos' to produce cells and
tissues that can provide treatment for diseases, such as degenerative illnesses is commendable and in my view ethical. I can well understand that some find the use of embryos that have been specifically created for this research objectionable, but I think that making use of excess embryos that are a by-product of the treatment of infertility should not be discredited.

Stem cells derived from blood obtained from the umbilical cord or from adult tissues are viewed as a more acceptable source. The Baptist and the Catholic Churches for example maintain that new life begins at the point of conception and therefore they oppose the use of cells derived from embryos but do not object to the use of cells derived from umbilical blood. Judaism and Islam emphasize the importance of helping others and permit some research on early embryos.

The Warnock Committee advised the United Kingdom government that no research should be permitted on embryos beyond 14 days, as around this time the primitive streak appears which will subsequently develop into the nervous system. There is also concern about pharmaceutical companies applying for patents on cell lines for future commercial considerations and whether it can be ethical or indeed in the public interest to allow this.

**Conclusion**

Although the prospects of effective treatments using stem cells may seem exciting there are still many technical difficulties with this treatment as well as the ethical and moral issues. The most useful and arguably the most important type of stem cells is the embryonic stem cells. These cells can differentiate into various types of cells in the body, including muscle and nerve cells. Embryonic stem cells can be grown relatively easily in the laboratory, which is a pre-requisite for treatments that requires a large quantity of cells.

Macular degeneration is just one area in which human embryonic stem cells are being used. We are in the early stages of the development of this treatment and more research and development is needed. The early results are very promising and no significant adverse side effects have been seen. This treatment would need to be assessed in a well-controlled clinical trial looking at the benefits and the short and long-term side effects before it is finally adopted as beneficial and cost effective treatment.

There are many ethical considerations and difficulties that need to be addressed. Some individuals, especially those with strong religious beliefs maintain that an embryo has rights as it has the potential of developing into an independent human being. Some fundamentalists argue that researchers are interfering in the work of God and may be
accomplices in the murder of embryos who are prevented from achieving their potential of developing into a new life.

The adoption of these new treatments has been slow due to the understandable legislative and ethical considerations. Other sources of stem cells such as blood from the umbilical cord cause fewer objections and may allow a more rapid application of stem cell treatments.

Scientists and medical researchers should take the lead in explaining the great promise of these treatments and also in allaying the fears and objections, which are largely based on the limited understanding of these techniques.

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