

Embryonic Stem Cells  
to cure currently  
Incurable diseases and  
Problems of implantation of stem cells



**By**  
**Dorothy Cheng**  
**Tanuka Palit**  
**PASS WITH MERIT**

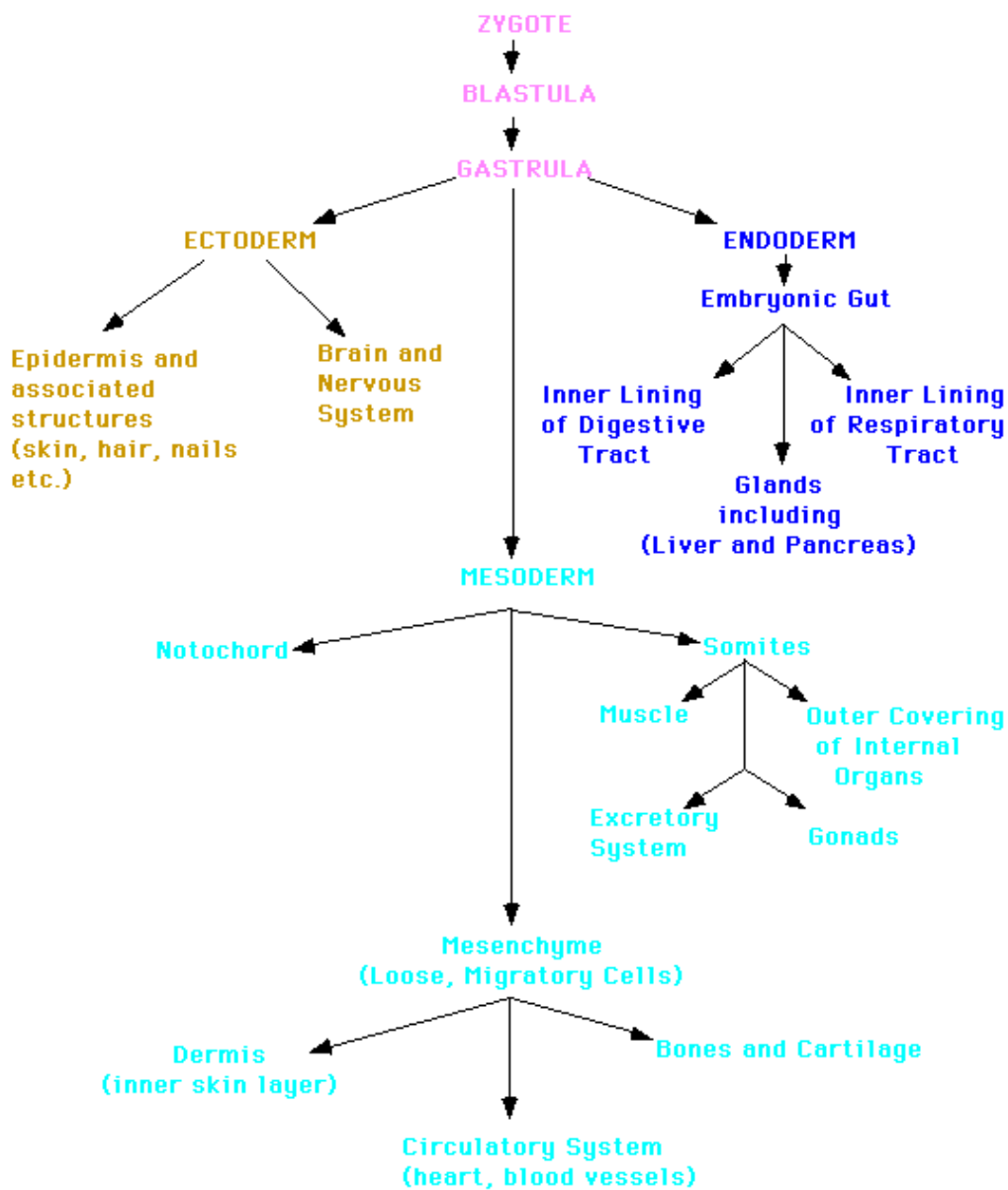
Research Paper  
Based on  
Pathology Lectures  
At Medlink 2008

Abstract

As adult stem cells do not offer a wide potential to researchers as embryonic stem cells do, this report will therefore concentrate on embryonic stem cells. Embryonic stem cells could bring great benefits in that it might lead to the development of transplantable tissues as therapies for a wide range of human illnesses which are currently considered difficult or impossible to treat such as spinal cord injuries, the danger of stem cell rejection, the replication of stem cells leading to form tumours and blindness.

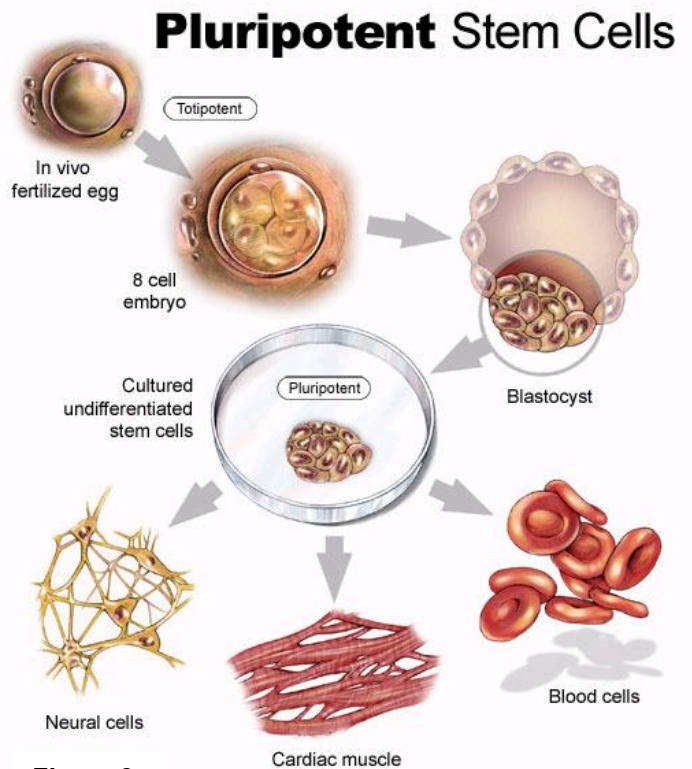
Introduction

Embryonic stem cells are derived from a four or five-day old human embryo that is in the blastocyst phase of development, donated through IVF treatment. One embryo can provide a limitless supply of stem cells. Embryonic stem cells have an ability to turn into any of the body's two hundred cell types as they are pluripotent, meaning they are able to differentiate into all derivatives of the three primary germ layers: ectoderm, endoderm and mesoderm (see figure 1 below).



**Figure 1**  
*Diagram showing all three germ layers that Embryonic stem cells can differentiate into*

There is a great interest in stem cells as they can serve any function after they are instructed to specialize. Every cell in the body is derived from the first few stem cells formed in the early stages of embryological development. Therefore, stem cells extracted from embryos can be made to become any desired cell type making them powerful enough to have the potential to treat cancer, spinal cord injuries, muscle damage, regenerate damaged tissue and organs and even cure many diseases that are currently incurable. For example, stem cells that lie beneath the skin (the ectoderm) have been used to create new skin tissue that can be grafted on to burn victims. Replacement cells and tissues can be used for treating brain diseases such as Parkinson's and Alzheimer's by replenishing the damaged part of the brain so that the specialized brain cells that keep unneeded muscles from moving are brought back. Recently embryonic stem cells have been directed to differentiate into these types of cells. They could also be used for cell deficiency therapy, for example developing healthy heart cells that could be transplanted into patients with heart disease so that the damaged part of the heart can be repaired with new healthy heart muscle cells. This type of therapy can also help people with type 1 diabetes by injecting new pancreatic cells in their pancreas to replace the insulin-producing cells that have been lost or destroyed by the patient's own immune system. This is extremely useful as the only current therapy is unlikely to occur due to the lack of supply of pancreases available for pancreatic transplant.



**Figure 2**

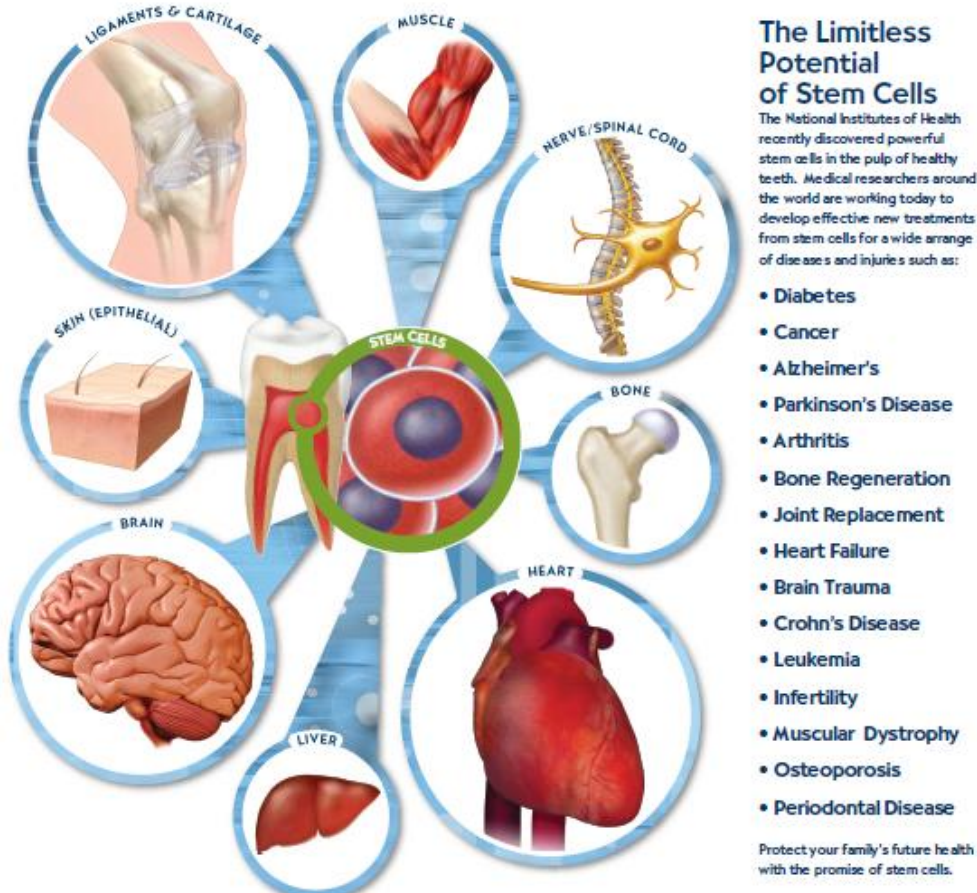
It is also said that the use of embryonic stem cells 'may be a first step toward methods for treating osteoarthritis, and other diseases, by producing replacement cells unlikely to trigger immune-system rejection.' (From the 2004 AAAS (American Association for the Advancement of Science Annual Meeting) Annual Meeting)

Recently, in the last month, we are told that there are possibilities that stem cells may turn cancerous and researchers have found that viruses and other disease-causing agents can be passed during stem cell therapy to the people who receive cell transplants. This evidence was found from the case where a boy treated with Embryonic Stem Cells for Ataxia Telangiectasia (a rare genetic disease that attacks the brain region controlling movement and speech) developed two tumours- one in his spine and one in his brain at the same sites at which he received three courses of Embryonic Stem Cells injections to the brain and fluid surrounding the spine. Below, we have decided to research into ways to stop these embryonic stem cells from replicating uncontrollably and causing tumours, whilst looking at ways to cure spinal injury, blindness and cancers.

## Discussion

In 2008 researchers found that dental pulp stem cells stimulated growth of new neural cells, many forming neurons after placing dental pulp stem cells from the tooth of a monkey ( a rhesus macaque) into the hippocampal areas (a brain structure located inside the medial temporal lobe of the cerebral cortex) of mice. This shows that there is a specific therapeutic potential of dental pulp stem cells and the patient's own stem cells can be used for therapy, greatly decreasing the risk of cell rejection, which is now a major problem in transplant medicine. A rich supply of stem cells can also be found in the dental pulp in 'baby' teeth (deciduous teeth) that children begin losing around their sixth birthday. According to the scientists that made this discovery, they have the potential to induce the formation of specialized dentin, bone, and neuronal cells, meaning that they could possibly be manipulated to repair damaged teeth, regeneration of bone and to treat neural injury. These cells can be stored for long periods of time and still retain their multipotency and tissue-producing capacity. Collecting stem cells from dental pulp is a non-invasive practice that can be performed in the adult during life and the young after surgical extraction of wisdom teeth. Tissue sacrifice is very low when collecting the dental pulp stem cells the transplantation of new-formed bone tissue obtained from dental pulp stem cells leads to the formation of vascularized adult bone and integration between the graft and the surrounding host blood supply.

Figure 3



To treat spinal cord injuries, the damage to oligodendrocytes first needs to be reversed; they are cells that insulate nerve fibres with myelin so that signals can be transmitted to and from the brain. Embryonic stem cells could be used to be converted into oligodendrocyte progenitor cells that could replace myelin-forming cells which have died as a result of the spinal cord injury and so regenerate the myelin sheath on surviving axons. These progenitor cells could then be injected at the site of injury. However it is known that pure embryonic stem cells tend to grow into tumours.

Nerve growth factors (see fig 4) could possibly be used to grow the axons as they are small secreted vertebrate protein which begins the differentiation and survival of particular neurons. Nerve growth factors are critical for the survival and maintenance of sympathetic and sensory neurons.

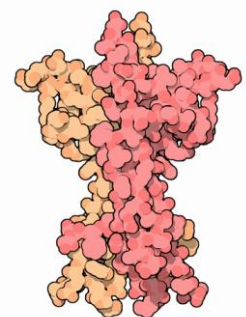


Figure 4 Nerve growth factor, beta polypeptide

Therefore by injecting nerve growth factors with neuron cells extracted from stem cells in dental pulp or embryonic stem cells into the site of the spinal injury there could be a possibility of improved function after spinal cord injury. Another method that could possibly cure spinal cord injury could be a spinal cord decompression surgery with autologous bone marrow stem cells applied directly to the injury site. As spinal cord injury creates a cavity at the injury site, a supportive surface or substrate through which nerves could grow is needed for a successful spinal cord strategy. The surviving nerve cell bodies, both above and below the injury site must also be stimulated to regrow their axons which are where nerve growth factors could be used. Taking cells from patients themselves to build a graft into the injury site would mean that the implanted cells would not be subject to immune rejection.

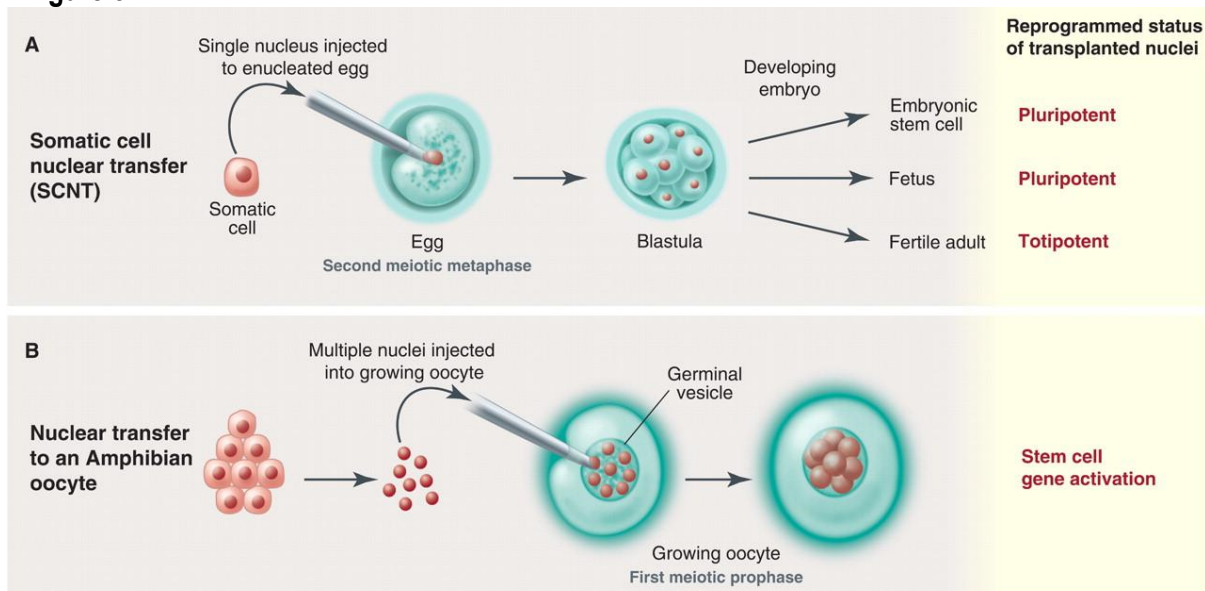
There is a danger of using embryonic stem cells as they would continuously replicate eventually forming a tumour. Our stem cells become less able to divide as they age. Recent research done in mice shows that compounds that suppress stem cells can be found in the blood in the aged. Knowing this, young blood and old blood could be blended in different ratios. A growth hormone and insulin-like growth factor (IGF-1) could be increased as IGF-1 is an important blood-borne factor that increases cell growth so by increasing the level of IGF-1, stem cells may be able to stop replicating and consequently forming tumours. Nevertheless IGF-1 prevents cell death and has been proposed to be a factor of the initiation of cancer, but drugs in the somatostatin class are currently available to suppress growth hormone and IGF-1 in people. So to prevent tumours from forming due to the replication of stem cells, growth hormones and IGF-1 and the patient's own blood, containing compounds that suppress stem cells, could be injected some time after the stem cells have been injected to the injury site in order for the stem cells to grow older and stop replicating. After a certain amount of time monitoring the growth of the stem cells regularly, as the stem cells have replaced the damaged site halfway, drugs in the somatostatin class can also be injected in the same site in order to suppress IGF-1, which initiates cancer.

Another major problem that must be solved before we can start using stem cells on a wide basis is the threat of rejection. When stem cells are placed in the body, the immune system recognizes them as foreign and so this prevents the stem cells taking effect in treatments.

Over the years, people have found ways to stop these immunological problems by using immunosuppressive agents to soften the patient's immune response. This has helped in organ therapies. Also there are many "immunologically privileged sites" such as the eye, brain and some have argued that embryonic stem cells also have an immune privilege.

Furthermore, it is common for someone to use their healthy tissue to use in cell-replacement therapies. However for such examples as replacing a damaged cornea is hard to fix as stem cells from a donor may cause risk of rejection. It seems now that scientists are set on using the controversial method of somatic cell transfer to stop this rejection.

**Figure 5**



In this diagram we see that a somatic cell e.g. a skin cell's nucleus can be removed and put into an egg without its nucleus. This will then turn into a blastocyst and cultured to form embryonic stem cells. The theory behind this is that as the stem cell has the nucleus of the donor, it will not be recognized as foreign by the immune system. However this process is said to be less efficient.

Another method of insuring no cell rejection is placing multiple nuclei into a germline vesicle of an oocyte (female germline cells) and produce a stem cell that way. The oocyte is directly reprogrammed to have stem cells marker genes that can be altered to cause differentiation. Oocytes explore the reprogramming of eggs. Eggs are easy to reprogram as they can reprogram specialized nuclei with a lot of efficiency.

Another nuclear reprogramming method is by creating induced pluripotent cells. Research carried out by Takayashi and Yamanaka in 2006 found that when inserting four genes into adult mouse fibroblasts they led to the appearance of some cells with embryonic stem cell characteristics. When adding further genes to it, the stem cells could enter all cell lineages. Also when they were transplanted into "immune privileged" hosts they became pluripotent (formation of some cell types) and therefore were given the term induce pluripotent stem cells. So stem cells can be produced from many other methods and give better advantages such as no stem cell rejection and better efficiency.

In the future, it seems scientists will be carrying on with the idea of nuclear reprogramming so solve stem cell rejection. Nuclear reprogramming will have many other advantages as well. Firstly it will help in cell-replacement therapy. And also in the future hopefully we will be able to produce cultured lineages from diseased tissues. This could help us find out more about disease.

For example, stem cell scientists from UCLA have derived from induce pluripotent stem cells, motor neurons that are electrically active. They also supported that iPS cells had similar properties to embryonic stem cells. William Lowry, a stem cell scientist has said that "It is clear from the literature that you can make at least immature versions of many different kinds of cells from human iPS cells." The next step seems to be looking in more depth to these induced pluripotent cells and seeing if they make them more useful for specific purposes e.g. spinal injury. As pluripotency is turning into some cell types, it is maybe best to try and achieve unipotency that generates to one cell type. This usage of stem cells can be much more specific and more useful towards the patient. Also it is a much safer method to use. So the goal should be developing somatic stem cells through nuclear reprogramming that would be best in treatment. Efficiency, techniques and potency must be taken into account.

Also animal eggs from those such as cows and rabbits can be used to produce ES stem cells from somatic nuclei in the human. But so far embryonic stem cells cannot be obtained from animal relatives, for example inserting human nuclei in a monkey. This could also be developed which may solve some of the ethical concerns that people have. Although embryonic stem cells may be derive from the embryo at the pre-implantation stage of the development. The extraction procedure will end the ability of that particular embryo to develop through implantation in the uterus. This removal brings the existence of the embryo to an end. Therefore, the embryo-derived cells are not in themselves an embryo as they cannot develop into a human being; they are therefore just like any other human tissue.

## **Eyes**

Embryonic stem cells have also done wonders to treat eye diseases. Most diseases in the eye are to do with the retina or cornea and stem cells provide us with a wide variety of autologous corneal epithelial or retinal cells used for transplantation. ESC's are needed especially for such repair as bilateral corneas that have been damaged, which is not possible at present. The possible developments of this will be discussed later.

Reconstruction of the cornea was first carried out on mice using mouse embryonic stem cells. When this was first carried out, there was some corneal restoration but some tumours (teratomas) were found. Furthermore, an interesting study carried out with human embryonic stem cells was carried out by a scientist named Howard Green. Full differentiated human squamous epithelium was generated and found in 50% of the cell culture. This study therefore showed that it can apply to corneal restoration as it also is squamous. So embryonic stem cells hold promise for repairing corneal tissue.

## Conclusion

Stem cells are swiftly becoming the central focus to curing the dangerous diseases that affect our global population. Through careful research we have found out about treating spinal injury and eye diseases such as corneal restoration. When looking in the media, we have found many cases of stem cells being used. There have been people cured of blindness and birth defects such as Optic Nerve Hypoplasia that people all thought was incurable is now treatable. However there are still problems to fix before stem cells can be widely used in medicine. Such stories as the seventeen year old boy developing benign tumours in his spine and brain from stem cells show that it is not safe yet for stem cells to be used on a wider basis. Also we can't stop our immune system from recognizing some stem cells as "foreign" and rejecting them. We have researched ideas of nuclear reprogramming that could solve this stem cell rejection and somatic cell transfer seems to be the technique that everyone is using. We have also suggested that the next step forward is to produce somatic stem cells that are more specific to the injury being treated, so that embryonic stem cells have more of a unipotency characteristic than pluripotency which is more efficient for medical processes. And there are ways this cannot be seen as practical as we may want cells to have a pluripotent quality to be able to differentiate again in the future. Also the ethical concerns about using embryonic stem cells from an embryo may be revised as somatic cell transfer would not mean we are actually destroying an embryo. However the ethical concerns about stem cells still remain. This research paper has shown that stem cells have come a long way since the time they were discovered in the small University of Wisconsin in 1998. However the more and more scientists discover about these unique cells, the more problems arise. It is clear that in the future, doctors will be using stem cell treatments a lot more frequently as they have the potential to work miracles in the medical world.

## References

- [http://www.sciencemag.org/content/vol322/issue5909/images/large/322\\_1811\\_F1.jpeg](http://www.sciencemag.org/content/vol322/issue5909/images/large/322_1811_F1.jpeg)
- K Takahashi, S Yamanaka, Cell 126, 663 (2006)
- <http://newsroom.ucla.edu/portal/ucla/ucla-stem-cells-scientists-make-82872.aspx>
- [http://www.sciencedirect.com/science?\\_ob=ArticleURL&\\_udi=B6W7H-4MFK446-2&\\_user=10&\\_rdoc=1&\\_fmt=&\\_orig=search&\\_sort=d&\\_view=c&\\_acct=C000050221&\\_version=1&\\_urlVersion=0&\\_urlserid=10&md5=401de1bc9c7fb41033af54ae4e80ab6f](http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6W7H-4MFK446-2&_user=10&_rdoc=1&_fmt=&_orig=search&_sort=d&_view=c&_acct=C000050221&_version=1&_urlVersion=0&_urlserid=10&md5=401de1bc9c7fb41033af54ae4e80ab6f)
- A Vugler et al (2007). Embryonic Stem Cells and Retinal Repair. *Mechanisms of Development* 124(11-12); 807-829
- R Homma et al (2004). Induction of epithelial progenitors in vitro from mouse embryonic stem cells and application for reconstruction of damaged cornea in mice, *Investigative Ophthalmology and Visual Science*
- [www.stemcellschina.com](http://www.stemcellschina.com)
- [http://www.curemedical.com/spinal\\_injury.html](http://www.curemedical.com/spinal_injury.html)
- <http://www.apparelyzed.com/embryonic-stem-cell-therapy.html>
- Science Daily (Nov 12 2008) on stem cells from monkey teeth can stimulate growth and generation of brain cells <http://www.sciencedaily.com/releases/2008/11/081111142606.htm>
- Press release on the 2004 AAAS Annual meeting [http://www.eurekalert.org/pub\\_releases/2004-02/aaft-hes020504.php](http://www.eurekalert.org/pub_releases/2004-02/aaft-hes020504.php)
- Potential for use of Adult, Embryonic stem cells for tissue regeneration <http://www.medicalnewstoday.com/articles/128516.php>
- Information on stem cells [http://www.medicalnewstoday.com/info/stem\\_cell/whatarestemcells.php](http://www.medicalnewstoday.com/info/stem_cell/whatarestemcells.php)