Stem Cell: Definitions, Treatment And Evidence

Introduction

Definition of stem cells

Stem cells are undifferentiated cells that can be found in the human anatomy and are capable to differentiate into many various forms of different cells which serve various functions in different sections of the human anatomy. It is not necessary that the stem cell must be differentiated into another cell when a it is dividing. When a stem cell is divided, it can still be a stem cell. During embryonic development and in the adult body, stem cells are found. Stem cells from embryonic development are referred as embryonic stem cells whereas those found in the adult body are known as adult stem cells.

Sources of stem cells

There are four sources of stem cells, adult stem cells, embryonic stem cells, induced pluripotent stem cells (iPSCs), and mesenchymal stem cells (MSCs). However, during this research, we only look at three main sources of stem cells which are adult stem cells, embryonic stem cells, and induced pluripotent stem cells (iPSCs).

Embryonic stem cells

The first origin of stem cells is known as embryonic stem cells. Embryonic stem cells are obtained from human embryos as a product of the in-vitro fertilization (IVF) procedure. These stem cells are donated for science. This procedure is the process of fertilizing an embryo in a laboratory dish rather than in the body of a woman. Furthermore, embryonic stem cells can differentiate and develop into more than 200 forms of adult cells. Besides, embryonic stem cells are able to propagate themselves indefinitely under defined conditions. Finally, they can be referred to as pluripotent stem cells.

Adult stem cells

Adult stem cells are cells that are undifferentiated and distributed all over the body. They divide and rejuvenate impaired tissues to replenish dying cells. They are formed from tissues and organs in the body that are already developed. Unlike pluripotent stem cells, adult stem cells are not able to distinguish into as many other forms of cells. Adult stem cells are also referred as somatic stem cells.

Induced pluripotent stem cells (iPSCs)

iPSCs are somatic stem cells that are turned into embryonic stem cells. These cells can be distinguished between all types of body-specific cells and they can potentially create new cells for any type of tissue or organ. In order to create iPSCs that function just like embryonic stem cells, scientists have genetically reprogrammed somatic stem cells to act like pluripotent stem

cells. For instance, adult stem cells are forced to express factors and genes related to the preservation of embryonic stem cell defining properties. While the cells follow the distinguishing benchmark for pluripotent stem cells, it is not known whether there are clinically significant discrepancies between embryonic stem cells and iPSCs.

Stem Cell Treatment

There are many studies that has been conducted on stem cells to aid in treating injuries or diseases in which many are still undergoing further research. One of the most familiar stem cell therapy is the replacement of damaged bone marrow by transplanting blood stem cells into the bloodstream of the patients. However, in this report, we will be focusing on stem cell therapy of the cornea and the spinal cord respectively.

Stem Cell Treatment for Eye (Currently Used)

We as a group have conducted research on stem cell therapy, specifically, for the cornea. The cornea is a transparent, protective outer eye surface that plays a major part in vision and helps to determine how well the eye can fixate on close-up and distant objects. If a disease, infection, or injury damages the cornea, the resulting wounds can impair the vision of an individual.

How is the cornea damaged?

There are many ways the cornea can be damaged. One reason how cornea impairment can occur is because of ulcers in the cornea. A corneal ulcer usually occurs with mild to serious eye discharge and weakened vision as a painful, red-eye. Most cases of corneal ulcers are caused by a bacterial infection that invades the cornea, and most of the time followed by eye injury or other damage. Furthermore, the cornea can also be damaged because of inherited eye diseases, such as Keratoconus and Fuch’s Dystrophy. Keratoconus is a genetic disorder that causes the cornea to be in the shape of a cone instead of dome-shaped. For individuals with certain medical problems, including certain allergic diseases, Keratoconus develops more quickly. Fuch’s Dystrophy on the other hand, is a genetic disease where the cells in the inner surface of the cornea cannot work productively and can lead to cloudy vision, glare and eye discomfort. Moreover, the cornea can be damaged because of swelling, thinning and clouding of cornea. This occurs because of inflammation on the outermost layer of the eye. Last but not least, scarring of the cornea because of an injury or infection is also another reason why cornea damage can happen. The causes of damage to the cornea will lead to the decrease of limbal stem cells.

How is a damaged cornea being treated now?

There are two procedures that are being used currently, to transplant the cornea. The first method is known as Endothelial Keratoplasty (EK). The Endothelial Keratoplasty treatment removes diseased tissues from the back corneal layers. Two ways of treatment are available, Descemet Membrane Endothelial Keratoplasty (DMEK) and Descemet Stripping Endothelial Keratoplasty (DSEK) specifically. DSEK is the most common procedure where it uses donor tissues to remove roughly one-third of the cornea. DMEK on the other hand uses a much thinner donor tissue layer. Due to the immensely thin and fragile tissue used in DMEK, this technique is more difficult and challenging compared to DSEK and thus, it is not commonly

used.

Another procedure that is being used currently is Anterior Lamellar Keratoplasty (ALK). During the ALK process, diseased tissues are discarded from the front corneal layers. These front corneal layers include the epithelium and stroma. There are two types of ALK as well and they are Superficial Anterior Lamellar Keratoplasty (SALK) and Deep Anterior Lamellar Keratoplasty (DALK). SALK leaves the endothelium intact and only reinstates the front layers of the cornea. However, DALK is a technique that is used when the damage in the cornea extends far into the stroma. In DALK, a small incision is made on the side of the eyeball so that the intermediate and front layers of the cornea can be removed without damaging the back layers. Healthy donor tissue is then grafted to replace the section removed.

Limbal stem cells

Limbus can be found at the edge of the cornea. This edge contains stem cells known as limbal stem cells. These limbal stem cells are essential in making new corneal cells to replace the damaged corneal cells. Without these limbal stem cells, there will be no repairing of corneal cells. This will affect the capacity of light entering the eyes and will slowly lead to loss of vision. Limbal stem cells can also be referred as corneal stem cells.

How can stem cells repair the cornea?

We have found two methods of repairing the cornea with stem cells. One is already proven whereas the other must undergo further research. The two ways we found were discovered in Europe and Japan respectively.

The method from Europe is known as the Holoclar treatment. In this treatment, limbal stem cells are obtained from the patient themselves or from a donor. If one of the eyes of the patient is not damaged, these limbal stem cells can be collected from the eye which is in good condition. However, if none of the eyes of the patient is healthy or undamaged, the limbal stem cells must be obtained from a donor. The Holoclar treatment works by obtaining limbal stem cells from an undamaged limbus of a donor or maybe the patient themselves. These limbal stem cells are then set in a petri dish to be grown in the laboratory using cell culture techniques. This step, it will produce thin sheets of corneal cells. These thin sheets of corneal cells will then be implanted into the eyes of the patient. This treatment can be used on patients with intermediate to extreme limbal stem cell deficiency.

The second method is where corneal cells can be created by using iPSCs. The procedure begins with obtaining somatic stem cells from the patients themselves. These adult stem cells are then reprogrammed into iPSCs. Thin sheets of iPSCs will then be implanted into the eyes of the patient. Corneal cells will then be created from these thin sheets of iPSCs.

Evidence

As the Holoclar treatment was proven to be efficacious in replacing the lack of limbal stem cells in the cornea and improving vision, the Agency’s Committee for Medicinal Products for Human Use (CHMP) thus validates the treatment. Despite having some side effects from the Holoclar treatment, these side effects are still controllable. Also, because moderate to a severe loss of

limbal stem cells are serious conditions and if were to remain untreated, can lead to the reduction or complete loss of eye vision. Hence, the Committee believes that the benefits far outweigh the risks, and thus approves the use of Holoclar treatment in the European Union.

For the Japanese's method of using induced pluripotent stem cells, it was first tested successfully on an animal model. This then led to the Japanese health ministry giving Kohji Nishida, an ophthalmologist from Osaka University, permission to conduct this procedure on four patients. As of the time being, results from the first treatment have appeared to be successful. The four patients whereby this procedure was conducted on reported that their eye vision has improved since the operation. The second procedure for this treatment is planned to be carried out later this year. The ophthalmologist, Kohji Nishida is optimistic that more people will be able to seek this treatment within 5 years.

Our Opinions

Our opinion on both these treatments is that the Japanese should continue researching more on using iPSCs to repair the cornea. This is because adult stem cells collected from the patients themselves are reprogrammed into iPSCs. Hence, there will be a lower chance of transplant rejection. As for Europe's method, the Holoclar treatment, to procure the limbal stem cells from either the donor's or the patient's eyes, surgery must be performed. As the surgery of obtaining the limbal stem cells is quite complex, there is a certain risk that may be faced by the donor or the patient. Besides, limbal stem cells that are donated may not necessarily be transplanted successfully into the patient's eye as there is a higher chance of transplant rejection. Lastly, if both eyes of the patient are damaged, it will be a lengthy process to wait for a donor to donate their limbal stem cells.

Stem Cell Treatment for Injuries in the Spinal Cord (Ongoing Research)

Causes of spinal cord damage

There are various reasons that contribute to spinal cord injury. An awful spinal cord injury might be a consequence of an abrupt, traumatic or a high impact blow to the spine. All of these may cause damage to the vertebrae in the form of dislocation, fractures, or compressing of the vertebrae.

The dominant factor of traumatic spinal cord damage is due to motor vehicle damage that accounts for approximately half of all spinal cord injuries. Next, another major factor for spinal cord injury is by slipping or falling. This is more prevalent among the elderly. Sports or high-impact activities can also cause spinal cord injuries. One well-known victim of spinal cord damage is Christopher Reeves who injured his spinal cord while horseback riding.

There is also non-traumatic spinal cord damage that is caused by inflammation, cancer or genetic diseases, like hereditary spastic paraplegia. Paraplegia refers to paralysis in the lower half of the body and both legs.

How do stem cells help with spinal cord repair?

There are a few ways as to how stem cells aid in repairing spinal cord repair. Firstly, the nerve cells will be differentiated from stem cells to restore those that have died due to injury or damage of the spinal cord. Secondly, the myelin sheath of the damaged nerve cells is rebuilt thanks to new supporting cells generated by the stem cells. This encourages the repair and re-growth of impaired axons. Stem cells help prevent additional damage to the nerve cell by releasing protective and useful substances like growth factors and taking in harmful toxins such as free radicals. Stem cells also help prevent the spread of injury by reducing inflammation that may take place after an injury.

Process of stem cells repairing the spinal cord

Several clinical trials are testing the prospects of allogeneic neural stem cells from a single donor in treating spinal cord injury or damage.

A serum is made consisting of allogeneic stem cells, scaffoldings, and growth factors to aid in stimulating growth. Scaffoldings are tiny structures that are made of micro-polymers which help to keep the spine in place as well as protect the newly implanted stem cells. This serum is then injected into the spinal cord's damaged area.

During the healing process, some of the connections between neurons are restored by the stem cells. Stem cells also aid in creating the cells that are needed to support the new and old neurons.

Evidence

In December of 2010, Stemcells Inc. held a phase I and phase II clinical experiment on incurable spinal cord damage.

These trials were held at Balgrist University Hospital at Zurich, Switzerland. The trial utilized stem cells obtained from brain tissues from human beings, which can also be referred as neural stem cells (NSCs). Three main types of neural cells located in the central nervous system can be differentiated from NSCs. The trial was initiated and dependent on preliminary clinical evidence that oligodendrocytes (a form of neuroglia) were restored after human NSCs were implanted into a particular rodent model to test for spinal cord injuries.

For the trial, 12 patients with incurable thoracic spinal cord injuries had their spinal cord injected with human NSCs. In 2014, an additional clinical trial was initiated to ensure the safety and effectiveness of transplanting NSCs on cervical spinal cord damages. In total, 43 patients had undergone the stem cell treatment and had no reported side effects. However, Stemcells Inc. abruptly terminated its stem cell program as it was not as effective as the company has expected it to be.

Our Opinions

Stemcells Inc. revealed no significant adverse side effects on the patients. However, Stemcells Inc. ended the research program because the outcomes were not as successful as they had in mind. It was effective, but not up to the company’s standards.

In our opinion, we think that instead of terminating the project, they should work on the results that they have to produce a more effective cure.? For example, the company could have tried using different types of stem cells or had another trial.

Enrichment Topic

Characteristics of Stem Cells

Stem cells have properties that them apart from the other cells in the body. The properties are self-renewal, potency and their ability to regenerate tissue. Self-renewal is the capability of stem cells to remain in their undifferentiated state despite having to undergo numerous cycles of cell division. Secondly, potency is how stem cells can transform into various forms of cells needed by the body. For example, a stem cell can differentiate into various cells like epithelial cells and sex cells. Lastly, stem cells can also form tissues for regeneration.

Ethical Concerns Surrounding Stem Cells

There are several ethical concerns surrounding stem cells in recent years especially on the ways embryonic stem cells are acquired. This is because the embryo is destroyed during the procedure of harvesting the embryonic stem cells. The killing of a fertilized embryo is thought to be morally wrong. Another ethical concern surrounding stem cells is the inquiry on when does life starts? Advocates of stem cell research believe that embryos are still not considered as living human beings. However, those who are against studies on stem cells strongly believes that embryos are already considered as living human being and that it is morally wrong to destroy it when harvesting stem cells. Lastly, breakthroughs of iPSCs have also raised ethical concerns. With the breakthrough and development of iPSCs, there really is not much of a need to harvest or use embryonic stem cells anymore. However, this breakthrough can lead to another ethical concern whereby these iPSCs are reprogrammed to function as embryonic stem cell. With this, researchers can theoretically create a clone of the donor. This will then become another ethical issue on its own as many countries have already forbid human cloning.

Further studies needed on stem cells

Further studies are needed on stem cells specifically on adult stem cells and embryonic stem cells. This is because biological differences exist between adult stem cells and embryonic stem cells and among adult stem cells that are found in various types of tissues. As biological differences of embryonic stem cells and adult stem cells are still not distinguished, there may be some therapeutic implications. Thus, to get additional scientific data on these cells, more studies must be conducted on adult stem cells and embryonic stem cells. Further studies on adult stem cells and embryonic stem cells may lead to the advancement of regenerative medicine and therapeutic potential.

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