

Mesenchymal Stem Cells in Regenerative Therapy of the Nervous System

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### **Abstract**

Mesenchymal stem cells (MSCs) are a form of stem cell found in bone marrow and can help aid with neurological damages. Not much is known about it in terms of risks but it has been found to renew damaged cells by replacing them with new ones in both central and peripheral nervous systems. Studies have been conducted on rats that have suffered cerebral ischemia which is lack of blood flow to the brain. Only those that contained a high rating of cerebral ischemia such as being brain dead were excluded in the experiment to ensure proper results. It was found that rats with the disease that suffered minor damages were able to repair their neurons with MSCs therapy. Rats that were not brain dead but suffered extreme brain damage unfortunately were not able to properly regenerate neurological damage done. MSCs contain potential in becoming a beneficial and new form of regenerative medicine to help aid with neurological damage caused by diseases.

### **Introduction/Background**

Eukaryotic cells are composed of membrane-bound organelles and a nucleus. They are important for the growth of human life and reproduction. These cells undergo two types of division; mitosis and meiosis. Mitosis is a process part of the cell cycle responsible for the replication of chromosomes and cells whereas meiosis is a process of cell division that halves chromosome numbers resulting in four haploid cells. Both functions are important to human life, however mitosis serves an even a more importance in the study of stem cells.

Stem cells are currently researched and investigated to identify potential risks and health factors that arise from the use of them. An example is stem cells use in the nervous system. Unlike other cells in the body that undergo mitosis to repair damaged cells, the nervous system is not capable of repairing its cells because each neuron in the human body has a specific job. The

replication of these cells would do more harm than good if neurons had the ability to replicate because it would affect the connections already made between each other.

Specific stem cells currently researched are mesenchymal stem cells (MSC). MSCs are stromal cells meaning that they are connective tissues. These stem cells can differentiate into different cells because of their capacity of renewing themselves as other cells. Due to this reason, MSCs contain therapeutic properties for renewal of tissue. MSCs are being looked at today to help repair damage cells caused in the nervous system from diseases.

Treatments have been successful in studies, however there have been some limitations to the practice of using stem cells for therapy.

Since stem cells have the ability to on take the role of a cell, it must be regulated and monitored. According to Nayoun, "Despite the considerable progress

that has been made in the development of MSC therapy for various diseases, studies have produced mixed results regarding their therapeutic efficacy” (2015). One of the results is the rate in which stem cells divide

since it is very important to the patients' health and how it affects them because it can cause an excess amount of division resulting in a tumor. The results are not specifically directed to MSCs but stem cell as a whole.

### **Mesenchymal Stem Cells in the Nervous System**

Many neurological diseases affect the brain by damaging neurons and tissues that are part of the central nervous system. Cerebral ischemia is a disease caused by insufficient blood flow to the brain resulting to cerebral hypoxia or a limited supply of oxygen. As a result, it can lead to the death of tissue in the brain or cause a stroke. Mesenchymal stem cells have been observed to help aid in the replacement of damaged neurological tissue lost from minimal blood flow to the brain. MSCs from bone marrow “selectively targeted injured brain tissue and promoted functional recovery via various cell delivery routes” (2014) proving to be beneficial in aiding the effects caused by cerebral ischemia, however they still need to be clarified.

What is understood by MSCs are that they are immunosuppressive and anti-inflammatory when injected into an area resulting in a better immune response. The immune system is familiar with cells all around a person's body because of the DNA coding and recognition. When a foreign cell enters the body, in this case stem cells, the immune system responds by attacking the cell because it is seen as a potential threat to the body. For MSCs, they do not trigger any response of the immune system making it a better choice as a form of therapy.

Mesenchymal cells have been able to also help damaged cells caused in the peripheral nervous system. Commonly, nerve injuries occur in the peripheral nervous system specifically Schwann cells. Injuries to these cells can also result in a form of ischemia. Schwann cells are important in neurons because they help regenerate damaged myelin sheath in cells. The myelin sheath is a protective coat around that axon of a neuron that provides insulation allowing the cell to transmit electrical signals. When these areas are damaged, inflammatory changes occur resulting in leukocytes, or white blood cells and Schwann cells to clear the body of myelin debris. However, when intervention of these damaged areas are delayed, Schwann cells begin to die off diminishing the potential of repair.

Mesenchymal stem cells were found to have successful results in the repair of the lost Schwann cells in the nervous system. As stated, “Mesenchymal stromal cells (MSC) are a type of multipotent somatic stem cell originating from a non-hematopoietic predecessor found in the bone marrow and are capable of differentiating into neural phenotypes, mesodermal cell lineages, and Schwann-like cells” (2016) making them an ideal use in repairing damaged cells.

### **Methods/Research**

To examine how mesenchymal stem cells function inside the human central nervous system, rats were experimented on to see the beneficial outcomes or risks that may occur from the transplantation of stem cells to a host. In the study, “A total of 90 healthy adult male Sprague-Dawley (SD) rats weighing 220-280 g, and 15 healthy adult male SD rats weighing 80-120 g, were obtained from the Experimental Animal Center of the Second Affiliated Hospital of Harbin Medical University (Harbin, China). The rats were maintained in a room at  $23\pm 1^{\circ}\text{C}$  under a 12-h light/dark cycle with ad libitum access to food and water. All experiments were performed with approval from the Ethics Committee of Harbin Medical University” (2016). The rats were then set up for preparation to suffer neurological deficiency by reducing the rats blood flow to the brain to replicate the

Mesenchymal stem cells have a lot of potential in aiding those with neurological problems because they are able to renew themselves to produce new existing cells. It was found that the majority of rats that were tested on were able to regenerate their neurons with little to no problems, the few that were unable to regenerate their cells were those with extremely damaged tissues that were unable to make a full recover. Damaged tissue in rats were commonly seen in those that

effects of cerebral ischemia. The rats were then rate on a 5-point scale (5 being the highest) to categorize them on severity of the neurological issues they suffered. Unfortunately, rats that were scaled 4 or 5 were not suitable for the experiment because they lacked consciousness.

From the 15 healthy rats, MSCs were taken from fresh bone marrows rats sacrificed to receive efficient MSC cells. Once extracted, the cells were incubated and cultured in preparation of transplanting them to the rats affected by neurological damages. The rats were kept in their initial state with stem cells injected inside them for approximately 3 day. Ten rats were then again sacrificed in which their brains were stored in liquid nitrogen to preserve and prepared for evaluation.

### **Results**

couldn't walk (different from rats that were brain dead).

MSCs have unique qualities yet they are not well established for treatments. The Safety and risk factors are the limitations that surround MSCs because not much is found about the harm that these cells may cause when transplanted into a host. The research of the cells is current and ongoing. MSCs are able to provide a new treatment and approach promising potential benefits in repairing neurons of the human brain.

### **Conclusion**

Mesenchymal stem cells are can be beneficial in neurological repair because they contain properties in cellular repair. It is found to be a new approach for regenerative medicine because MSCs can renew themselves to take the form of other cells. For those that suffer cerebral ischemia, MSCs have been a potential form of therapy to help regenerate neurons lost from a lack of blood flow in those that suffered cerebral ischemia.

Cells in the nervous system are unable to reproduce because it can affect the wiring of the brain that controls the different parts of the body. After research of stem cells, scientists have found the potential of MSCs and what they can due for neurological repair. Since MSCs are derived from bone marrow, they can target tissue injured in the brain and promote recovery, however it is still an area of open research due to the

lack of information surrounding MSCs.

Furthermore, MSCs have been found to help aid the repair of most neurological damage cause from cerebral ischemia besides those that had extreme damages. MSCs therapy is still under research and not much yet is known about it in terms of risks or damages it may have on the recipient who has had MSCs transplanted into them. Due to this reason, MSCs have a lot of research currently being done to ensure the safety of these therapeutic procedures.

Once enough research is found surrounding MSCs, it is possible that this form of therapy can help aid many neurological diseases that has affected people. Mesenchymal stem cells have a lot of potential in regenerative medicine and can help treat those suffering from neurological diseases in the future.

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