

# Stem cell therapy: a possible cure for amyotrophic lateral sclerosis?

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## INTRODUCTION

Imagine yourself at the peak of adulthood, running, swimming, enjoying all aspects of life to the fullest, and being diagnosed with a fatal disease. Like a bird that soars the skies and gets shot down, that is the feeling that a person diagnosed with Amyotrophic Lateral Sclerosis must feel because to date, it is practically a death sentence. Amyotrophic Lateral Sclerosis (ALS) is a neurodegenerative disease that progressively affects motor neurons causing the loss of almost all voluntary movement. First described by Jean-Martin Charcot, ALS became known in the United States as Lou Gehrig's disease in honor of the great baseball player who developed the disease in the 1930s. Two of my personal heroes, the Nobel Prize winning astrophysicist Stephen Hawking and guitar virtuoso Jason Becker, suffer from the disease and despite the nearly complete paralysis of their arms, legs and the muscles necessary for speech, there is no cognitive impairment, allowing them to still excel in their respective fields. Knowing these facts, it was inspirational for me to see these individuals persevere and triumph in the face of adversity and I started reading about ALS. Being a biotechnology student researching in a neuroscience laboratory, it is of interest to investigate the causes of neuronal disease and when I found out that ALS was incurable with no determined cause, I really reflected on the matter and saw the applications of biotechnology, cell culture and stem cell research in finding the causes and a cure. Novel stem cell therapies are currently being tested and developed for amyotrophic lateral sclerosis presenting a possible cure for this horrible disease and I wanted to find out if these treatments are in fact capable of curing ALS.

In this reading process, I learned that ALS is generally fatal within 1-5 years with a prevalence of 2-3 per 100,000 people. The causes of almost all occurrences of the disease remain unknown, where between 5-10% of cases the disease is inherited in a dominant manner and an astonishing 90-95% of instances, there is no apparent genetic linkage. Both forms show progressive muscle weakness, atrophy and spasticity, each of which reflects the degeneration and death of upper or lower motor neurons in the brain and spinal cord. Weakening of the respiratory muscles and diaphragm is generally the fatal occurrence. To date, several theories have been proposed where one or more of these mechanisms may interact and lead to motor neuron death. The mechanisms of neuronal death in ALS include defective glutamate metabolism, free radical injury, mitochondrial dysfunction, gene defects, apoptosis, autoimmune dysfunction, and viral infections. These proposed mechanisms have provided targets for drug treatments, but to date there is no effective treatment against ALS. Is stem cell treatment a good candidate for curing ALS? This is a question I wanted to answer and a more profound research allowed me to do this.

In this research I found out that stem cells are biological cells that are found in all multicellular organisms and have the ability to divide through mitosis and differentiate into diverse cell types. In humans, there are two types of stem cells: adult stem cells, found in various tissues, and embryonic stem cells, isolated from the inner cell mass of blastocysts. Also from the different classes in biotechnology I have taken, it was shown that stem cells can now be artificially grown and transformed into specialized cell types with characteristics consistent with cells of various tissues. In recent times,

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researchers have used various types of stem cells to develop an effective treatment against ALS including: autologous, allogeneic, adult, fetal, mesenchymal, umbilical cord blood, hematopoietic and amniotic. Autologous stem cells are found in most adult tissues, such as bone, skin and blood, and which are also present in placentas and umbilical cords. I think that the therapy using autologous stem cells is a good candidate because of the potential to differentiate into specialized cells and shows no risk of rejection by the patient. Letizia Mazzini and colleagues (2003) injected autologous bone marrow derived stem cells into the spinal cord of seven ALS patients and reported that the procedure had a reasonable margin of clinical safety. Also in 2008, John T. Dimos successfully generated induced pluripotent stem cells from an 82-year-old woman with familial ALS and differentiated them to motor neurons. Another type of cells used is allogeneic stem cells that are derived from a healthy donor and transplanted into the patient. In contrast to using autologous cells, using these donated cells show a risk of rejection and in my opinion, is a liability treating ALS patients. Another type currently tested for ALS is mesenchymal stem cells. These are of particular interest because they have the capacity to differentiate into a variety of tissues, including fat, cartilage, bone, tendon, ligaments, muscle, skin and nerve cells. One advent of these stem cells is that they can be obtained and propagated in culture for long periods of time without losing their capabilities to self-renew and differentiate. This is another example of a type of stem cell that can be used in ALS patients without the risk of rejection. Cheng Zhang and colleges (2009) successfully made multiple transplantations of human marrow stem cells through the central nervous system improving motor

performance and prolonging the life of superoxide dismutase (SOD1) transgenic mice. SOD1 is a gene that encodes for the enzyme superoxide dismutase involved in the protection of cells against free radical injury. Also Albert Clement and colleagues (2003) showed that in SOD1G93A chimeric mice, motorneuron degeneration requires damage from mutant SOD1 acting in non-neuronal cells. Wild-type nonneuronal cells could delay degeneration and extend survival of mutant-expressing motorneurons. Hematopoietic stem cells are adult cells obtained from a patient's own blood, are frequently used to treat life threatening and are now being clinically tested for treatment of ALS. These are cells that can be isolated from the blood or bone marrow and differentiated into a variety of specialized cells. This procedure also yields greater numbers and better quality cells for transplantation. More recent research by Dr. Hector R. Martinez (2009), where he transplanted autologous CD133+ stem cells into the frontal motor cortex in ALS patients, clearly revealed the capability for therapy. This is one of the most promising because it was demonstrated that is a safe and well-tolerated procedure. Embryonic stem cells are totipotent cells capable of differentiating into any type of cells, including motor neurons, one target for curing ALS. These cells are obtained from embryos that are 4 to 5 days old. Thanks to the versatility of these cells for regenerating or repairing diseased or injured tissue in human beings they hold great promises. The downside of this is that these cells must be guided into becoming the needed cell type because if there is a dormant cancer tumor somewhere in the body, an embryonic stem cell is just as likely to energize that cancer if it is not properly guided through the differentiation process. An alternative I found for this is using amniotic fluid.

The use of this fluid produces multi-potent stem cells that are extremely active and not tumorigenic. Research at this time is in the earliest of stages and is not considered a replacement for human embryonic stem cell research, but I think it holds great promises because they can differentiate and not produce cancer.

The other aspect of the treatment process with stem cells for amyotrophic lateral sclerosis is the transplantation. For ALS patients, the objective is to replace and repair damaged and deceased neurons in the brain and spinal cord. These are painful and dangerous surgical procedures that require careful scrutiny because of the fragility of ALS patients. Because of respiration difficulties, heavy sedation could prove fatal and this is a challenge for health professionals because minimally invasive clinical and surgical procedures need to be used for the safety of the patient. Adult and fetal stem cells have been transplanted into the brain in clinical trials of ALS and other conditions for some time now. Surprisingly, this type of brain surgery can be performed with a minimum use of sedation. Current clinical trials utilize peripheral blood-derived hematopoietic stem cells and incorporate minimally invasive brain surgery in the attempt to repair or replace damaged neurons to manage the symptoms of ALS, with impressive results to date. A problem with brain transplantations is the obstacle of the blood brain barrier (BBB). The BBB protects the brain from invasion and delivering cells to the brain is a challenge, but research with a mouse model for ALS done by Zhang (2009) demonstrated how this obstacle can be bypassed. Another method is to transplant cells derived from the spinal cords of human fetuses into the lumbar part of the spinal cord of ALS

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patients. This is a risky procedure because ALS patients are extremely fragile and to me is not as safe as transplantation to the brain. The problem is that to reach the lower motor neurons one has to transplant as close as possible to the spinal area. Other methods involve intravenous and intramuscular stem cell injections appear promising only when used in conjunction with other forms of delivery, but in my opinion, brain and spinal cord injection of stem cells are the best way to deliver treatment and with the invention of new medical instruments, the room for complications diminishes.

All the scientific data points to stem cells as capable of slowing the progression of amyotrophic lateral sclerosis, but none have proven it can cure it. The biochemical evidence to date clearly indicates that the process of motor neuron degeneration in ALS is complex and not clearly elucidated. Genetic understanding of familial ALS is relatively well advanced, but less so in sporadic disease. The advent of technology and the falling costs of genotyping will enable researchers to reveal the genetic roots of ALS. Given the fact that 90 % of ALS cases are sporadic, much work is needed to find the missing link between familial and sporadic ALS. The use of mice models for ALS is extremely important in finding therapies because it mimics the disease and provides a template for human therapy. As showed by Ripps (1995), a mouse model for ALS was produced and proved that the gene characteristics of the disease are present. Mice models are great for testing, but the problem is that to prove stem cells are effective on humans with ALS one has to test it on actual patients. Currently the Food and Drug Administration (FDA) approved tests with stem cells on humans with ALS, but they are in the early stages of trials with no definitive results. Also the <https://assignbuster.com/stem-cell-therapy-a-possible-cure-for-amyotrophic-lateral-sclerosis/>

retrieval and use of human embryonic stem cells has been under the radar of ethical groups for years. Their argument stands on the fact that to obtain the cells one has to kill a living undeveloped human being. This raises ethical problems and government approval can be tedious because of the public pressure involving this matter. Stem cell research is an emerging field with lots of applications and the pursuit of novel therapeutic methods on diseases like ALS is just becoming apparent. I think that stem cell therapy could hold the key in curing ALS, but more extensive research is necessary. With my experience in neuroprotection and biotechnology, I hope in the future to contribute in the search for a cure for ALS not for personal gain, but for all those people in the world living with this condition who never gave up hope.

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