Stem Cells and Their Potential Role in Treating Parkinson's Disease

by

Simon C. Maxwell

Supervised by

Dr. Karen Marshall

Abstract

Parkinson's Disease (PD) is a chronic neurodegenerative disease for which there is no current effective treatment or cure. Stem cell therapy is a new type of medical treatment that is being considered as a possible way to replace damaged cells and restore functionality with promising but so far limited results. This paper provides basic information about stem cells and explores the role stem cells are playing in the search for effective treatment and considers the medical potential stem cells may hold in developing a cure for Parkinson's disease.

Stem Cell Role & Parkinson's Disease

On March 9, 2009, President Obama signed executive order, "Removing Barriers to Responsible Scientific Research Involving Human Stem Cells" and revoked the previous presidential order which, since August 9, 2001, has limited federal funding for embryonic stem cell research (Obama 2009). According to Andres, Meyer, Ducray and Widmer (2008), there are already early clinical trials that support the potential for stem cell therapies for devastating neurodegenerative disorders with significant impact on a patient's quality of life:

> Due to increasing life expectancy and a higher prevalence of neurodegenerative and neurovascular pathologies in the elderly population, these disorders will become even more important for our society in the future and there is need for the development of new, adequate treatment options (Andres et al. 2008).

Today, donated organs and tissues are often used to replace ailing or destroyed tissue, but the need for graftable or transplantable tissues far outweigh the available supply (Stem 2009). Stem cells offer the possibility of a renewable source of replacement cells and tissues. To achieve the highest potential for stem-cell based therapies, scientists must be able to understand and

manipulate stem cells for successful differentiation, transplantation and engraftment (Stem 2009).

This paper explores current research in restorative stem cell therapies with respect to the neurodegenerative disease known as Parkinson's Disease (PD). Foundational information will be presented about PD followed by a concise discussion on stem cell characteristics, clinical studies and current research. This information will be considered with regard to the potential of stem cell therapies as they relate to providing treatment for PD patients. Finally, a discussion will conclude noting existing limitations while presenting the opinion that there is sufficient evidence to support stem cell therapies as a potentially viable option for future PD treatments.

Parkinson's Disease

Parkinson's Disease is a progressive neurodegenerative disorder affecting millions of people worldwide. Andres et al., (2008) in union with Geraerts, Krylyshkina, Debyser and Baekelandt (2007) list PD as the second most common neurodegenerative disorder affecting more than 1% of all individuals over the age of fifty years with a lifetime risk of 2% for men and 1.3% for women. According to Geraerts et al. (2007), Parkinson's Disease is caused by a profound and progressive loss of dopaminergic neurons in the nigrostriatal pathway, which leads to symptoms such as resting tremor, bradykinesia, rigidity and postural imbalance. Symptoms do not appear until the striatal dopamine levels have decreased by more than 70% (Geraerts et al., 2007) which implies that many different compensatory mechanisms must be present in the cell types. Further, motor complications (dyskinesias) and other side effects (e.g., mood disorders and sleep disturbances) appear after chronic treatment (Geraerts et al., 2007.).

While there are currently some effective treatments for patients with PD, treatment strategies are mainly symptomatic and aimed at increasing dopamine levels in the degenerating

nigrostriatal system (Lee and Park, 2009). Existing drugs are limited in their relief and decrease in effectiveness as PD progresses. Nevertheless, Lee et al. (2009) explains that these treatments do not halt the progressive nature of PD and are ineffective against gait freezing and postural instability, which are more disabling than tremors and rigidity. Lee, et al. further explains that as PD progresses, drug-induced motor complications, such as "wearing off" and dyskinesia appear and notes that PD dementia is not responsive to dopaminergic therapy and is considered the most important factor influencing the daily activities and survival of Parkinson's patients.

Stem Cell Properties

The National Institutes of Health's (NIH) website for Stem Cell Information is a source designed for the non-scientific community to begin to understand stem cells and their early research development: (http://stemcells.nih.gov/index.asp). As described, stem cells are undeveloped cells without mature, tissue-specific characteristics that are able to proliferate, to reproduce themselves and to produce generations of progenitor cells, which can differentiate into one or more specialized cell types. Stem cells can be embryonic (ESC) which are derived from an *in vitro* blastocyst or non-embryonic (non-ESC) which are derived from somatic/adult stem cells that include (but are not limited to) neural stem cells, bone marrow or mesenchymal stem cells (MSCs), umbilical cord blood stem cells, and a new type of stem cell that has been genetically reprogrammed to create an induced pluripotent stem cell (Tuch, 2006).

ESCs can differentiate into cells of all three lineages (ectoderm, mesoderm and endoderm) but are currently burdened by ethical and other legal restrictions (Tuch, 2006) whereby non-ESCs are generally committed to one lineage. In compromise, MSCs are becoming more attractive for their unencumbered ethical status and their multipotent ability to differentiate under appropriate conditions (Lee et al., 2009).

Park, Borlongan, Eve and Sanberg (2008) rank stem cell transplants in the following descending order of preference: bone marrow-derived cells, neural stem cells, umbilical cord blood cells, embryonic stem cells, and myoblasts. Although ESCs have been used exclusively in the field of neuroscience, bone marrow-derived cells are most commonly used for transplantation in the neuroscience fields with neural or progenitor cells being the second choice (Park et al., 2008). This ranking should not imply best clinical practices as legal and ethical issues are considered in the ranking and selection process.

Medical Potential of Stem Cells to Treat Parkinson's Disease

Geraerts et al. (2007) considers PD as a particularly favorable candidate for stem cell therapies because PD represents a selective degenerative process of predominately dopaminergic neurons of the nigrostriatal pathway. Lee et al. (2009) concurs with Geraerts et al. and regards PD as the best candidate for cell therapy because it is uniquely selective in its destruction of dopaminergic neurons.

Early proof-of-concept cell-based therapies for PD patients were achieved with the transplantation of MSCs which are rich in dopaminergic neurons (Geraerts et al., 2007). Clinical outcome was encouraging in some patients up to 10 years after transplantation, despite the progression of the PD process. However, Geraerts et al. (2007) offset this early success by presenting two controlled trials where transplantation did not prove beneficial, perhaps because of the disease state, immunological problems, or low graft survival.

Andres et al. (2008) sites a trial evidencing stem cell grafts surviving and reinnervating the host striatum of a PD patient resulting in significant increased flurodopa with long-term graft survival 6 and 12 years after surgery. Notably, Andres et al. (2008) discloses that less than 20%

of the transplanted dopaminergic cells survive and that positive results are only achieved after significant amounts of cell tissue is grafted.

With mixed success, few if any cell transplantations have been carried out in PD patients in the last few years. Nevertheless, these stem cell studies were important as the first experimental cell-based treatment strategies and, according to Geraerts et al. (2007), they proved the revolutionary usefulness of cell-based approaches in the treatment of neurodegenerative disorders. To date, the optimal approach for endogenous stem cell therapy is not known (Geraerts et al., 2007).

Discussion

Current enthusiasm for effective stem cell treatments for Parkinson's Disease is tempered by Andres' et al. (2008) recommendation for a better understanding of the basic disorder to aid in the development of effective stem cell strategies to overcome side effects such as dyskinesias with the foremost problem being the missing knowledge of how transplanted cells differentiate, which includes uncontrolled growth or tumor formation. Further research is needed to determine the number and types of adult stem cells that exist and in which tissues, how they evolve and remain in undifferentiated states, their capacity to relocate and how science can duplicate this process for therapeutic resolution (Stem, 2009). These answers must be found if restorative neuroscience is to consider harvesting a patient's own neural stem cells (Andres et al., 2008).

It is important to note that the usage of ESCs has raised several ethical concerns not addressed in this paper which may hamper basic research and the selection of certain stem cells. As well, research and experimentation with xenotransplantion (tissue transplanted across the species barrier) remains outside the scope of this paper.

The findings reported from clinical studies examined in this paper demonstrate that stem cell replacement strategies have the potential to become effective therapeutic approaches for treating Parkinson's Disease. The results of experimental therapies based on dopamin-rich fetal cell grafts encourage future cell-based strategies for PD patients (Geraerts et al., (2007).

The management of PD should be designed to control symptoms, slow progression of the disease and prevent levodopa-related complications. As scientists achieve a better understanding of neurodegeneration, more effective therapeutic strategies will probably become available. This would require an understanding of developmental biology which researchers throughout the world are trying to fully acquire (Tuch, 2006).

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