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HYPOTHESIS

The Possibility of Differentiation of Human Endometrial Stem Cells into Neural Cells

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Abstract

In the last few decades, the idea of being able to repair the brain by introducing new cells to repair the damaged areas has become an accepted potential treatment for neurodegenerative diseases. The stromal cell fraction of many tissues and organs has shown in vitro neurogenic differentiation; however, these cell types are limited by availability, invasiveness of extraction and in some cases limited proliferative capacity. Human endometrial adult stem cells have many clinical advantages over the other stem cells. Here, we propose the hypothesis that endometrial adult stem cells may be induced into neural cells.

Keywords: Endometrial stem cell; Differentiation; Neural cell

Introduction

Human neurodegenerative disorders such as stroke, Parkinson and Alzheimer diseases, amyotrophic lateral sclerosis, epilepsy, trauma, and intoxications are all characterized by neuronal cell loss, associated with consequent loss of functions and disabilities.[1] Cell replacement is a potential strategy for treatment of such diseases. The use of primary fetal brain cells has allowed proof-of-principle of the validity of this approach in small clinical studies.[2] The limited availability of the primary fetal cells, together with the isolation and culture of precursor cells in the adult brain capable of differentiating into the neurons has led to a surge of interest in identifying a renewable source of cells suitable for the wide-scale application of transplantation therapy in the CNS. Positive results of cell replacement therapy have also been reported following immature neural cell grafting in Huntington's disease and experimental animal models of stroke.[1-3] It was shown that various stem cells such as mesenchymal stem cells/ marrow stromal stem cells (MSC), hematopoietic stem cells (HSC), multipotent adult progenitor stem cells (MAPCs), umbilical cord blood stem cells (UCBSC), and embryonic stem cells (ESC) have the potential to differentiate into the neural cells.[4-8] However, these cell types are limited by availability, invasiveness of extraction and in some cases limited proliferative capacity. Also, MSCs from older patients failed to expand in culture and one might speculate that this is an indication that their effectiveness in general might be diminished.[9,10]

The human endometrium is a dynamic tissue, which undergoes cycles of growth and regression with each menstrual cycle. Endometrial regeneration also follows parturition and extensive resection and occurs in postmenopausal women taking estrogen replacement therapy. It is likely that adult stem/progenitor cells are responsible for this remarkable regenerative capacity.[11,12] It was demonstrated that human endometrium contains a low number of endometrial stem cells which seem to belong to the family of the mesenchymal stem cells. These cells are engaged in the monthly restructuring and remodeling of human endometrium.[13-16] Previous studies have shown the potential differentiation of the endometrial

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stem cells into chondrogenic and osteoblastic lineages when cultured in appropriate induction medium.[14,17-19] In addition, other studies have shown that stromal cells from endometrial explants can proliferate and then generate new vessels.[20,21] It demonstrates the multipotency of menstrual blood stem cells (MenSCs) by directionally differentiating MSCs into chondrogenic, adipogenic, osteogenic, neurogenic, and cardiogenic cell lineages.[14,15]

Since endometrial stromal cells are easy to isolate, expand rapidly from patients without leading to major ethical and technical problems, and produce a higher overall clonogenicity, they have a great potential as therapeutic agents as autologus. Therefore, endometrium may be an alternative source of MSC-like cells for tissue engineering purposes, obtainable with no extra morbidity than that required for other sources of stem cells.[22]

Hypothesis

Stem cell therapy has been suggested as a novel treatment for the management of neurodegenerative diseases. The previous studies demonstrated that the pluripotent embryonic stem cells and adult stem cells are capable of differentiating into neural cell types which express neural-related proteins.[23] Recently, stem cells were isolated from human endometrium, using co-expression of two perivascular cell markers, CD146 and PDGF-receptor β (PDGF-Rβ).[22] Herein, we postulate that because of the outcome and complication of the other sources of stem cells, stem cell therapy through application of endometrial stem cells can open a new horizon for the treatment of neurodegenerative disorders with lesser degree of complications and better efficacy and outcome.[24]

Evaluation of the Hypothesis

The hypothesis can be evaluated by using flow cytometery for detection of stem cell markers such as CD146, CD90 in the isolated endometrial stem cells. Also, isolated stromal cells will be examined to be free from hematopoietic cells using CD34 staining. The next step is to investigate the ability of human endometrial adult stem cells to differentiate into the neural cells showing characteristics of neural-like cells. For this purpose, the endometrial stem cells will be induced by neuroogenic medium. Subsequently, immunocytochemistry will be used for the confirmation of neuronal markers expression such as Nestin and Map2 in the differentiated cells.

Discussion

Surgical repair of the peripheral nerve injuries is a frequent clinical problem. For larger nerve defects, transplantation of a nerve graft is often necessary to facilitate nerve regeneration and functional improvement. Alternatives to conventional autografts have long been sought because of some problems associated with autografts, and the emergence of tissue engineering has greatly stimulated the development of the artificial nerve grafts.

It was indicated that the endometrial stem cells displaying excellent pluripotency potential[25] also exist in the basal layer of endometrium of menopausal women.[26] Previous studies concerning long-term follow-up of animals treated with endometrial regenerative cells, and the karyotypic normality of these cells after extended passage (68 doublings) confirmed lack of tumorigenicity.[24] However, the baseline colony-forming ability of the endometrial stromal cells is comparable to most enriched bone marrow MSC populations.[27-29]

It may be concluded that the endometrial stem cells in the treatment of neuronal disorders are more convenient than other sources of stem cells due to the following properties. First, obtaining bone marrow stem cells in the clinic is not easy, because of the requirement for anesthesia. Second, endometrial stromal cells produce a higher overall clonogenicity of 1.25% in comparison to the clonogenic activity of stromal cells in bone marrow. Third, bone marrow MSCs are not perfect seeding cells for the elderly patients since these cells lose their differentiation capacity significantly with increased donor age. Fourth, endometrial stromal cells can be obtained by a simple, safe and painless procedure such as Pop smears, in contrast to bone marrow aspiration. Fifth, karyotypic normality of the endometrial stromal cells after extended passage (68 doublings) demonstrates lack of tumorigenicity. Endometrial stromal cells represent a unique population and their proliferation rate is approximately once every 19 hours.

Conclusion

In the past few years, research on the stem cells has exploded as a means to build up probable therapies

for treatment of inoperable neurodegenerative diseases. In spite of the promising results, significant restraints hinder the use of different sources of stem cells for transplantation in humans. Besides ethical concerns, the viability, purity, carcinogenic potency, and final destiny of the cells have not been completely defined. A highly promising source of relatively abundant and accessible, active, pluripotent adult stem cells is afforded by human endometrium. Consequently, we speculate that endometrial adult stem cells can differentiate into neural cells when they are exposed to specific microenvironment. These stem cells are an attractive alternative candidate for nervous system regeneration, because they exhibit several important and potential advantages over other stem cells.

Conflict of interest: None declared.

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