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Neural Stem Cell : A Review

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ABSTRACT *The discovery of stem cells that can generate neural tissue has raised new possibilities for repairing the nervous system.Stem cells are defined as cells that have the ability to renew themselves continuously and possess pluripotent ability to differentiate into many cell types. Neural stem cells (NSCs) offer a unique and powerful tool for basic research and regenerative medicine. However, the challenges that scientists face in the comprehension of the biology and physiological function of these cells arestill many. In this review, we focus on the biological properties of NSCs and discuss how these cells may be exploited for a better medical use. We also review and discuss ongoing NSC-based research for few diseases and challenges we are are facing along with future research require in NSCs.*

INTRODUCTION

Neural stem cells (NSCs) are self-renewing multipotent cells that generate the main phenotype of the nervous system. Stem cell are characterized by their capability to differentiate into multiple cell types via exogenous stimuli from their environment[1]. They undergo asymmetric cell division into two daughter cells, one non-specialized and one specialized. NSCs primarily differentiate into neurons, astrocytes, and oligodendrocytes[2]. Neural progenitor and stem cells have been isolated from various areas of the adult brain, including non-neurogenic areaas, such as the spinal cord, and from various species including humans[3]. NSCs are immature cells present in the developing and adult Central Nervous System (CNS). Typically, NSCs are defined by three cardinal characteristics: self-renewal potential, neural tripotency (i.e., the capability to give rise to all of the major neural lineages: neurons, astrocytes and oligodendrocytes) and competence for in vivo regeneration. They are being studied for treatment of various diseases.

ORIGIN, DEVELOPMENT AND COMMUNICATION

The origin, development and communication of NSCs is a very complex procedure and there is lot that is needed to be learn about it, but present research has shed some light on how these NSCs develop and communicate among themselves. Decoding these factor will play a important role in research of NSCs in curing many disease.

NSCs are are limited in their capability to differentiate and hence they are considered adult stem cells. Neurogenesis is the process by which NSCs are generated throughout an adult's life[4]. NSCs can be differentiated to replace lost or injured neurons or in many cases even glial cells[2] because neurons are not capable of dividing within the central nervous system (CNS). NSCs are differentiated into new neurons within the SVZ of lateral ventricles, a remnant of the embryonic germinal neuroepithelium, as well as the dentate gyrus of the hippocampus.

Adult NSCs were first isolated from mouse striatum in the early 1990s. When cultured in vitro they are capable of forming multipotent neurospheres. Neurospheres can produce self-renewing and proliferating specialized cells. These neurospheres can differentiate to form the specified neurons, glial cells, and oligodendrocytes [2] [4]. Further studies have shown that cultured neurospheres have been transplanted into the brains of immunodeficient neonatal mice and have shown engraftment, proliferation, and neural differentiation[4].

NSCs are stimulated to begin differentiation via exogenous cues from the microenvironment, or stem cell niche. Some neural cells are migrated from the SVZ along the rostral migratory stream which contains a marrow-like structure with ependymal cells and astrocytes when stimulated. The ependymal cells and astrocytes form glial tubes used by migrating neuroblasts. The support for the migrating cells as well as insulation from electrical and chemical signals released from surrounding cells is provided by astrocytes in the tubes. The primary precursors for rapid cell amplification are astrocytes. To repair or replace neural cells the neuroblasts form tight chains and migrate towards the specified site of cell damage [5].

Neural stem cell proliferation declines as a consequence of aging. Various approaches have been taken to counteract this age-related decline[6]. FOXO proteins regulate neural stem cell homeostasis, Wnt signaling is inhibited by FOXO protein to protect neural stem cell[7].

FUNCTIONS

NSCs perform vital function in the body specially in central nervous system. Studies have shown that NSCs perform essential role in mice as well as in human being and these functions cannot be performed by any other Adult stem cells.

NSCs play an important role during development producing the enormous diversity of neurons, astrocytes and oligodendrocytes in the developing CNS. They also have important role in adult animals, for instance in learning and hippocampal plasticity in the adult mice in addition to supplying neurons to the olfactory bulb in mice. Neural stem cells have been shown to engage in migration and replacement of dying neurons[16].

Quiescent stem cells are Type B that are able to remain in the quiescent state due to the renewable tissue provided by the specific niches composed of blood vessels, astrocytes, microglia, ependymal cells, and extracellular matrix present within the brain. These niches provide nourishment, structural support, and protection for the stem cells until they are activated by external stimuli[15]. Once

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activated, the Type B cells develop into Type C cells, active proliferating intermediate cells, which then divide into neuroblasts consisting of Type A cells. The undifferentiated neuroblasts form chains that migrate and develop into mature neurons.

POTENTIAL APPLICATIONS

Neural Stem Cell have the potential to be used in curing many disease like Parkinson's disease , Huntinton's disease, Stroke, Lysosome storage disease, Alzheimer's disease, Multiple Sclerosis Spinal cord Injury and Brian tumour. These all application are in research phase and a lot of work is needed to be done before moving to clinical phase.

Parkinson's disease

The requirement is to generate cells that synthesize and release dopamine for implantation into the dopaminedepleted striatum[8]. For this method to be effective, it is not yet known whether these cells must also mature into projection neurons with synaptic host connections, a process that is required for optimal effects of embryonic nigral grafts.[9]

Huntington's disease

If we can control differentiation into mature neuronal phenotypes then many other diseases that involve loss of specific neuronal types, such as the striatal medium spiny projection neurons lost in Huntington's disease[10], might be suitable for transplantation of neurons expanded from stem cell sources[11].

Stroke

In spite of rather limited evidence from animal studies, clinical trials are already underway for this strategy by migrating stem cells and immortalized precursors through central nervous system and repopulating sites of ischaemia[12].

Multiple sclerosis

Oligodendrocyte lineages are better characterized than neuron lineages, and oligodendrocyte precursors can differentiate and provide a functional remyelination of axons after focal experimental demyelination. The main problem in application for multiple sclerosis is how to stimulate the migration of such cells to diverse sites of demyelination that occur sporadically in the human disease. Not withstanding the potential applications of oligodendrocyte lineages in several diseases, many key technical problems remain to be resolved[13].

CHALLENGES

It is still uncertain what kind of stem cells would be an ideal source for cellular grafts. We need to better understand the mechanism by which transplantation of stem cells leads to an enhanced functional recovery and structural reorganization. Before envisaging any therapeutic application of such cells , we need to confront several, and still unsolved, problems like the ideal stem cell source for transplantation in each specific disease context, the appropriate number of cells to transplant, a clinically applicable transplantation strategy[14], the right disease stage for cell transplantation and finally the most appropriate in vivo and/or in vitro manipulations to obtain the proper cells to be transplanted. Hence all these challenges must be met before we can move on to the clinical applications to cure various diseases.

FUTHER RESEARCH

As regions of the embryo are patterned and development unfolds, neural stem cells may be an essential mediator of developmental signals, acquiring a changing repertoire of gene expression, morphology and behaviour. Despite differences in the properties of stem cells isolated from different regions and at different times, they still selfrenew. Self-renewal can therefore be considered as the propagation of stem cells, rather than the production of exactly the same type of cell. It will be important to examine how developmental signals, both spatial and temporal, specify changes in neural stem cells. Markers for neural stem cells will allow their selection from different stages and regions to examine their potential after transplantation into the embryo or adult, and a comparison of their gene expression. Such explorations will help identify essential mediators of stem cell self-renewal, and genes that determine production of different types of progeny. Markers will also help solve the tantalizing issue of which cells in vivo are stem cells.

CONCLUSION

There are still many obstacles to be overcome before clinical application of cell therapy in neurological disease patients is adopted. Steady and solid progress in stem cell research in both basic and preclinical settings should support the hope for development of stem cell-based cell therapies for neurological diseases. The growing interest and participation in stem cell therapies of big pharmaceutical companies and their collaborating partners worldwide will represent an important step in order to increase the number of new well-defined clinical trials in the next few years.

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