Treatment of Neurodegenerative Diseases with Using of Stem Cells/Scaffolds

Abstract

Over the two decades, stem cell technologies have become an increasingly attractive option to treat neurodegenerative diseases. However, this approach has been limited due to transplanted cell death because of the unsuitable microenvironment. Tissue engineering by using of stem cells, scaffolds and growth factors come to improve the chance of regeneration. In the current mini-review, we discuss the advantages of synthetic extra cellular matrix for stem cell-based therapies in patients suffering from neurodegenerative diseases. Hence, explained about biological and mechanical properties of scaffolds in nerve engineered tissues. There is growing public hope with a greater understanding of the capacity of stem cell technologies that regenerative medicine will continue to progress into effective treatments for neurodegenerative diseases.

Keywords: Neurodegenerative diseases; Stem cells; Scaffold; Tissue engineering

Abbreviations: HD: Huntington Disease; PD: Parkinson Disease; ALS: Amyotrophic Lateral Sclerosis; SMA: Spinal Muscular Atrophy

Introduction

Neurodegenerative diseases are developed by the damage of neurons and other neural cells in nervous systems. This matter may occur following up acute and chronic neurodegeneration such as stroke, trauma or the loss of a particular neuronal subtype over a long period [1]. These diseases in the brain are known as Alzheimer disease (AD), Huntington disease (HD) and Parkinson disease (PD). In the brainstem and spinal cord, spinal muscular atrophy (SMA) and amyotrophic lateral sclerosis (ALS) are the other types of degeneration [2]. Treatment of these degenerations are pretty difficult because of healing time of neural cells are too slowly to occur. About two last decades, stem cell–based approaches come to restore function in neurodegenerative disease. Definitely, transplantation of stem cells in models of neurodegenerative diseases in animals can improve function over a long period [1]. These diseases in the brain are known as Alzheimer disease (AD), Huntington disease (HD) and Parkinson disease (PD). In the brainstem and spinal cord, spinal muscular atrophy (SMA) and amyotrophic lateral sclerosis (ALS) are the other types of degeneration [2]. Treatment of these degenerations are pretty difficult because of healing time of neural cells are too slowly to occur. About two last decades, stem cell–based approaches come to restore function in neurodegenerative disease. Definitely, transplantation of stem cells in models of neurodegenerative diseases in animals can improve function over a long period [1].

Types of stem cells

Cell source is the main issue for tissue engineering and regenerative medicine. Somatic and stem cells are two suitable sources for regeneration of tissue. Stem cells have the capacity to proliferate and differentiate into various cellular lineages [8,9]. There are different classifications of stem cells which embryonic stem cells (ESCs) and adult stem cells (ASCs) are two types of these cells. ESCs are totipotent cells with practically unlimited self-renewal and differentiation capacity that be derived from the inner cell mass of a blastocyst during gastrulation [10]. Adult stem cells (ASCs) are the other source of stem cells compare to ESCs, exhibit similar self-renewal capacity but show a more limited differentiation potential that gives rise to a specialized tissue-specific cell line. This restricted potential could be related to the niche of the ASCs that were maintained the characteristics of their embryonic layer of origin [7,11].

Extra cellular matrix (ECM)

Stem cell self-renewal is the result of cell division that takes place within the microenvironment (niche). Generally, the stem cell niche consists of a definite space within the tissue. In the niche, the stem cell number is maintained constant by balancing inactive and activated cells [12,13]. In the adult mammalian brain, stem cell niches are retained in the subventricular zone (SVZ) of the lateral ventricles and in the sub granular zone (SGZ) of the hippocampal dentate gyrus. In the niche, stem cells are likely exposed controlled biochemical mixtures of soluble cytokines, chemokines, growth factors and also insoluble transmembrane receptor ligands and extracellular matrix molecules [14]. The ECM greatly influences cell adhesion, proliferation, migration, differentiation, and survival by

a. modulating the bioactivities of growth factors and cytokines
b. sequestering growth factors, or
c. directly affecting receptor activities.

Topographical structures of ECM have the potential to influence cell behavior by altering morphology, proliferation, adhesion, motility, protein abundance, and gene regulation [15,16].

Nerve tissue engineering

Tissue engineering provides a different medical therapy, which regulates the cell behavior through the development and design of synthetic ECM to support three-dimensional (3D) cell culture and tissue regeneration. The essential approach in neural
tissue engineering involves the production of scaffolds and merging with stem cells to produce a suitable functional tissue for implantation (Figure 1). In recent years, fibrous scaffolds have been extensively studied as a material for nerve repair; due to their structural similar have been manufactured to meet special property requirements for nerve tissue regeneration [17-19]. When stem cells transplant into injury site without any matrixes, this cell dies or migrate to another site of the nervous system. In order to solve these problems, isolated stem cells from the body should support by a scaffold which could mimic function and structure of ECM [20].

Scaffold necessities

Abundant scaffolds produced from various biomaterials and many techniques to regenerate different tissues and organs in the body. Regardless of the tissue type, several key considerations are important when designing or determining the suitability of a scaffold for use in tissue engineering [29-32].

Biodegradability: Scaffolds must be biodegradable so as to allow cells to make their own extracellular matrix. Also, these degradation products should be non-toxic and able to excrete the body without interference with other tissues and organs.

Biocompatibility: The very vital principle of any scaffold for tissue engineering is that it must be biocompatible; cells must adhere and migrate through the scaffold and begin to proliferate before laying down new matrix. When implantation, tissue engineered construct must elicit an insignificant immune reaction in order to prevent it causing such a severe inflammatory response that it might reduce regenerating or cause rejection by the body [33].

Scaffold architecture: The design of scaffolds used for tissue engineering is of critical importance. Scaffolds should have a high porosity structure to ensure cellular penetration and adequate diffusion of nutrients to cells within the construct and to the extracellular matrix formed by these cells. Moreover, a porous interconnected structure is required to let diffusion of waste products out of the scaffold, and the products of scaffold degradation should be able to eliminate the body without interference with other organs. Another key factor is the mean pore size of the scaffold. The pores need to be large enough to allow cells to migrate into the structure, where they finally attach to the ligands within the scaffold, but small enough to create a sufficiently high specific surface, leading to a minimal ligand density to allow efficient binding of a critical number of cells to the scaffold. Then, for any scaffold, a specific range of pore sizes existed.

Mechanical properties: Ideally the scaffold should have mechanical properties constant with the anatomical site into which it is to be implanted. It must be strong enough to allow surgical handling during implantation [34]. It is clear that a balance between porous architecture and mechanical properties sufficient to allow cell infiltration and vascularization is key to the success of any scaffold. Numerous materials for nerve defect have been produced with appropriate mechanical properties that used for different parts of the nervous system to improve injury.

Conclusion

Stem cell is not lonely enough for curing of neural system defects due to there is not a good substrate for attachment of cells. Then, the regenerative medicine by using scaffolds and stem cells comes to help the healing of nerve injury and neurodegenerative diseases as a novel. For this reason, an ideal artificial ECM should manufacture that can mimic nervous system ECM at the first. Next, a good source of cells such as differentiated cells or stem cells should be selected according to injury zone and seeded on synthetic fabrics until implant in the site of defect.
References


