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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 comes 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, scaffolds, tissue engineering

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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 fallowing 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 by replacing the lost glial and neurons cells and by mediating remyelination and trophic actions.[3] Using of stem cells lonely for the cure of this degeneration is not very effective because of there is any appropriate microenvironments in the site of the defect.[4,5] For this reason, recently nerve tissue engineering by using of scaffold and stem cells opens a novel aspect for the treatment of nervous system defects.[6,7] In this study, we showed that scaffolds could support stem cells for curing of neurodegenerative disease.

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. Inside 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 sub ventricular 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

i. modulating the bioactivities of growth factors and cytokines

ii. sequestering growth factors, or

iii. 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]

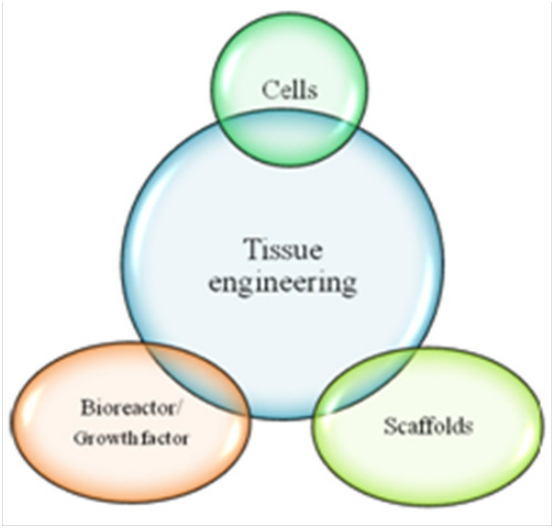

Figure 1 Principles of tissue engineering.

Biomaterials

Typically, three individual groups of biomaterials such as ceramics, synthetic polymers, and natural polymers are used as scaffolds fundamentals in tissue engineering. Several synthetic polymers have been used in the attempt to produce scaffolds including poly-l-lactic acid (PLLA), poly-dl-lactic-co-glycolic acid (PLGA), polycaprolactone (PCL) polyglycolic acid (PGA), and polyvinyl alcohol (PVA).[21,23] Though these polymers have shown much success as they can be manufactured with a tailored architecture, they have downsides including the risk of rejection due to reduced bioactivity. In addition, concerns exist about the degradation process of PGA and PLLA by carbon dioxide as the degradation product that lowering the local pH which can result in cell and finally tissue necrosis.[24,25]

Biomaterials for instance chitosan, gelatin, alginate-based substrates, and collagen have all been used in the production of scaffolds. Unlike synthetic polymer-based scaffolds, natural polymers are biologically active and support excellent cell adhesion and growth. Moreover, they are also biodegradable and so allow host cells, over time, to produce their own extracellular matrix and replace the degraded scaffold. However, the natural scaffolds have poor mechanical properties, which limit their use in some tissue like bone. To solve this problem, scaffolds were manufactured with a combination of the synthetic and natural materials or occasionally by ceramics like hydroxy apatite.[26,27]

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 scaffolds 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.

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Conflict of interest

Author declares that there is no conflict of interest.

References

1. Lunn JS, Sakowski SA, Hur J, et al. Stem Cell Technology for Neurodegenerative Diseases. *Ann Neurol*. 2011;70(3):353–361.
2. Lindvall O. Cell replacement therapies for central nervous system disorders. *Nat Neurosci*. 2000;3(6):537–544.
3. Lindvall O, Kokaia Z. Stem cells in human neurodegenerative disorders -time for clinical translation? *J Clin Invest*. 2010;120(1):29–40.
4. Srikanth P, Young-pearse TL. Stem Cells on the Brain : Modeling Neuro developmental and Neuro degenerative diseases using human induced pluripotent stem cells. *J Neurogenet*. 2014;28(1–2):5–29.

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5. Mckay R. Stem Cells in the Central Nervous System. *Science*.1997;276(5309):66–71.
6. Ghasemi-mobarakeh L, Prabhakaran MP, Morshed M, et al. Application of conductive polymers, scaffolds and electrical stimulation for nerve tissue engineering. *J Tissue Eng Regen Med.* 2011;5(4):e17–35.
7. Martino S, D'Angelo F, Armentano I, et al. Stem cell-biomaterial interactions for regenerative medicine. Biotechnol Adv. 2012;30(1):338–351.
8. Sylvester KG, Longaker MT. Stem cells: review and update. Arch Surg. 2004;139(1):93–99.
9. Short B, Brouard N, Occhiodoro-scott T, et al. Mesenchymal Stem Cells. 2004;34(2003):565–71.
10. Tachibana M, Amato P, Sparman M, et al. Human embryonic stem cells derived by somatic cell nuclear transfer. *Cell*. 2013;153(6):1228–1238.
11. Rezza A, Sennett R, Rendl M. Adult stem cell niches: cellular and molecular components. *Curr Top Dev Biol*. 2014;107:333–372.
12. Macneil S. Biomaterials for tissue. 2008;11(5):26–35.
13. Han D, Cheung KC. Biodegradable Cell-Seeded Nanofiber Scaffolds for Neural Repair. *Polymers (Basel)*. 2011;3(4):1684–1733.
14. Vunjak-Novakovic G, Scadden DT. Biomimetic platforms for human stem cell research. *Cell Stem Cell*. 2011;8(3):252–261.
15. Srouji S, Kizhner T, Suss-Tobi E, et al. 3-D Nanofibrous electrospun multilayered construct is an alternative ECM mimicking scaffold. *J Mater Sci Mater Med*. 2008;19(3):1249–1255.
16. Khan N. Applications of electrospun nanofibers in the biomedical field. *SURG*. 2012;5(2):63–73.
17. Baniasadi H, Ramazani SAA, Mashayekhan S. Fabrication and characterization of conductive chitosan/gelatin-based scaffolds for nerve tissue engineering. *Int J Biol Macromol*. 2015;74:360–366.
18. Yang F, Murugan R, Wang S, et al. Electrospinning of nano/micro scale poly(l-lactic acid) aligned fibers and their potential in neural tissue engineering. *Biomaterials*. 2005;26(15):2603–2610.
19. Ichihara S, Inada Y, Nakamura T. Artificial nerve tubes and their application for repair of peripheral nerve injury: an update of current concepts. *Injury*. 2008;39 Suppl 4:29–39.
20. Biazar E, Khorasani MT, Zaeifi D. Nanotechnology for peripheral nerve regeneration. *Int J Nano Dim*. 2010;1(1):1–23.
21. Temenoff JS, Mikos AG. *Biomaterials: the intersection of biology and materials science*. Pearson; 2008.
22. Croisier F, Jérôme C. Chitosan-based biomaterials for tissue engineering. *Eur Polym J*. 2013;49(4):780–792.
23. Shi D. *Biomaterials and tissue engineering*. Springer Science & Business Media; 2013.
24. Rasal RM, Janorkar AV, Hirt DE. Poly(lactic acid) modifications. *Prog Polym Sci.* 2010;35(3):338–356.
25. Gómez-Pachón EY, Vera-Graziano R, Campos RM. Structure of poly(lactic-acid) PLA nanofibers scaffolds prepared by electrospinning. *IOP Conf Ser Mater Sci Eng*. 2014;59(1):012003.
26. Cui W, Zhou Y, Chang J. Electrospun nanofibrous materials for tissue engineering and drug delivery. *Sci Technol Adv Mater*. 2010;11(1):014108.
27. Kordestani SS. Wound Care: Natural BioPolymer Applications. *In: Encyclopedia of Biomedical Polymers and Polymeric Biomaterials*. Taylor & Francis; 2016. p. 8245–8257.
28. Sun J, Tan H. Alginate-Based Biomaterials for Regenerative Medicine Applications. *Materials (Basel)*. 2013;6(4):1285–1309.
29. Kim MS, Kim G. Three-dimensional electrospun polycaprolactone (PCL)/alginate hybrid composite scaffolds. *Carbohydr Polym*. 2014;114:213–221.
30. Furth ME, Atala A. *Tissue Engineering*. In: Principles of Tissue Engineering. Elsevier; 2014. p. 83–123.
31. Vasita R, Katti DS. Nanofibers and their applications in tissue engineering. *Int J Nanomedicine*. 2006;1(1):15–30.
32. Huang Z, Zhang Y, Ramakrishna S, et al. Electrospinning and mechanical characterization of gelatin nanofibers. *Polymer*. 2004;45(15):5361–5368.
33. Williams SF. *Bioabsorbable, biocompatible polymers for tissue engineering*. Google Patents; 2003.
34. Albanna MZ, Bou-Akl TH, Blowytsky O, et al. Chitosan fibers with improved biological and mechanical properties for tissue engineering applications. *J Mech Behav Biomed Mater*. 2013;20:217–226.

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