

## Using Biomaterial Factors to Control Neural Stem Cell Destiny for the Regeneration of Damaged Brain

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### Abstract

The identification of neural stem cells (NSCs), which have the capacity for self-renewal and differentiation into a wide range of neural lineages, offers hope for the future treatment of brain neurological disorders like stroke/cerebral ischemia, traumatic brain injury, and neurodegenerative diseases. However, due to tissue inflammation or blood-brain barrier, only a few numbers of NSCs were able to survive or reproduce. To direct stem cell destiny and behaviour for nerve regeneration, a suitable culture environment that closely resembles the natural NSC niche must be created. When creating functionalized scaffolds, which could be used as more than just delivery systems, it is important to take into account the topology, mechanical characteristics, bioactive chemicals, and their spatial and temporal presentations of the NSC niche. Axon growth at the site of the injured brain, support endogenous or exogenous cells proliferation, migration, and homing, and stimulate particular cellular responses at the molecular level. This review aims to describe the many types of biomaterial.

**Keywords:** NSCs niche; Biomaterial design; Brain tissue engineering; Nerve regeneration

### Introduction

Due to the significant loss of cerebral parenchyma in recent years, effective treatments for brain neurological illnesses, such as stroke/cerebral ischemia, traumatic brain injury (TBI), and neurodegenerative diseases, have been lacking. Transplantation of stem cells has recently gained importance as a method for regenerating damaged brain tissue [1-4]. With the ability to differentiate into all different types of neural cell types, including neurons, astrocytes, and oligodendrocytes, neural stem cells (NSCs), which have been isolated from various areas of the developing and adult nervous system, offer promising prospects for the treatment of brain disorders. The blood-brain barrier, however, makes it difficult to deliver neurotropic chemicals into the brain by the usual oral or intravenous methods, making stem-cell therapy for illnesses of the central nervous system (CNS) challenging. Furthermore, the because to inflammation, glial scar formation, the release of inhibitory chemicals, and the lack of growth-promoting astrocytes, the lesion brain cannot provide a favourable milieu for NSCs regeneration [5].

### Material Syntheses and Processing Techniques

Therefore, in order to enhance NSC proliferation without sacrificing "stamens" or causing undesirable differentiations, sophisticated biomaterials generating bioactive artificial microenvironments must be created. Physically present within informative local tissue niches that support and control stem cells' fate are stem-cell populations in the body. A variety of signals that address the biologically significant sequence of events leading to stem cell lineage commitment can be incorporated into an artificial microenvironment of NSCs using innovative material syntheses and processing techniques. In order to give trophic factors, nourish residual neurons around the site of the lesion, maintain replacement cells, offer contact guidance for directed axonal outgrowth, and reduce adverse inflammatory reactions, biomaterials may potentially be employed as delivery vehicles for NSC transplantation. We could better understand the mechanisms governing NSC fate specification and self-renewal through the investigation of NSC-biomaterial interactions [6].

The thoughtful creation of new scaffolding that support NSC integration and survival in sick or damaged areas of the central

nervous system. Changes to one or more parameters during the early stages of cell culture may ultimately affect gene expression and long-term functional differentiation. In order to control NSC fate for brain tissue engineering, this research examined current advancements in the studies of biomaterials as artificial habitats for NSCs. In order to create a strong conceptual foundation for the construction of artificial niches, we first listed the elements of the natural NSCs niche. Then, we discussed numerous biomaterial factors that affect NSC fate in vitro in terms of both biophysical and biochemical factors, as well as functionalized scaffolds that make it possible to transplant NSCs for brain regeneration in vivo. The adult nervous system contains neural stem cells, which ended the myth that the brain is a dormant organ incapable of regeneration. NSCs for stem cell-based therapeutics have so received a lot of attention recently in the context of adult brain regeneration. Careful management of the cellular behaviour would be necessary for the therapeutic application of NSCs therapies to be successful [7].

Therefore, a great deal of research was done on the NSCs' microenvironment, also known as their niche. As two of the primary sources of NSCs in vivo, the sub ventricular zone (SVZ) of the forebrain and the sub granular zone (SGZ) of the hippocampus serve as in vivo NSCs niches, which physically locate NSCs and maintain their stem-cell fate. The niche could generally support the following NSC functions: First of all, the niche keeps NSCs in to avoid being drained by ageing; it must be in a quiescent, undifferentiated state. NSCs transplanted outside of the niche are very likely to develop into glial cells; hence the niche should offer a neurogenic environment for NSCs [8]. Third, and the niche must be designed so that the type and

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**Received:** 14-Sep-2022, Manuscript No. jbtbm-22-81008; **Editor assigned:** 17-Sep-2022, Pre-QC No. jbtbm-22-81008 (PQ); **Reviewed:** 03-Oct-2022, QC No. jbtbm-22-81008; **Revised:** 10-Oct-2022, Manuscript No. jbtbm-22-81008 (R); **Published:** 17-Oct-2022, DOI: 10.4172/2155-952X.1000302

**Citation:** Wang L, Mashad Y (2022) Using Biomaterial Factors to Control Neural Stem Cell Destiny for the Regeneration of Damaged Brain. J Biotechnol Biomater, 12: 302.

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quantity are both. The SVZ of the adult mammalian brain is made up of a variety of cell types, including astrocytes, NSCs, transit-amplifying cells, neural progenitors (neuroblasts), and a monolayer of ependymal cells lining the ventricle. All cell types are interconnected rather than being separate from one another. The NSCs are relatively dormant cells that exhibit glial fibrillary acidic protein and markers resembling embryonic radial precursors. Neuroblasts are produced as a result of the transit amplifying cells that the NSCs produce [9].

The neuroblasts go to the olfactory bulb through glial tubes, where they produce neurons that are integrated into the neural network. And studies revealed that in the SVZ, a dense plexus of blood capillaries snakes along and within neuroblasts chains. A few of the transit-amplifying cells and NSCs are so closely linked to blood vessels that the vasculature could provide them with important signals. The ECM is the most significant non-cellular component of the neural stem cell niche and has the ability to control the concentration and presentation of signalling molecules as well as act as an anchor for NSC adherence. The interstitial matrix and basement membrane, which comprise sticky glycoproteins, glycosaminoglycans, and ions, are the two main structural components of the ECM [10, 11].

## Discussion

The ternary network of brevican, aggrecan, neurocan, and vertical proteoglycans, as well as interspersed link proteins of tenancies linking to cell surfaces, makes up the interstitial matrix of the brain's extracellular matrix (ECM). Tenascins and proteoglycans would interact with hyaluronic acid (HA), which serves as the brain's "backbone," to create an ordered HA-proteoglycan network around the embedded cells. Laminins (LNs), which make up the majority of the A set of heterotrimeric proteins known as the basement membrane makes up the niche in NSCs and has five a, three b, and three g genetic variations, respectively. LNs provide a variety of purposes in the signal transit in addition to serving as an essential structural component. For instance, basal lamina processes known as fractones reach out from blood vessels to make contact with each stem cell in the niche [12, 13].

As a result, each stem cell receives LN signals from at least three different sources: contacting fractones, interstitial laminins, and their processes linked to blood arteries. Additionally, crucial roles are played by other ECM components like the glycoprotein tenascin C (TnC), chondroitin sulphate proteoglycans (CSPG), and heparin sulphate proteoglycans (HSPG). As previously mentioned, the SVZ was abundant with blood arteries that snaked along, and NSCs were closely positioned in opposition to the extracellular matrix (ECM) encircling vascular endothelial cells [14, 15].

It was established that normal SVZ cells in vivo have a propensity to grow close to blood arteries because endothelial cells have the ability to promote NSC self-renewal and expansion by secreting soluble substances.

## Conclusion

In the SVZ niche, the activated NSCs produce transit amplifying

cells, which in turn produce neuroblasts. NSCs that have undergone differentiation into neuroblasts may migrate away from the niches and then undergo differentiation into particular lineages at a particular location. It has been noted that even in the adult brain, neuronal migration took a complicated and extensive shape. From the lateral ventricle walls, neuroblasts go to the olfactory bulb, where they develop into neighbourhood interneurons. Although it is unclear what is causing neuroblasts to migrate away from the SVZ. The ependymal flow caused by the development of chemo repulsive gradients in the SVZ is one of the potential causes.

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