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Regenerative Therapy of the Central Nervous System

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Editorial Note

The central nervous system (CNS) has a limited capacity to spontaneously regenerate following traumatic injury or disease, requiring innovative strategies to promote tissue and functional repair. Tissue regeneration strategies, like cell and/or drug delivery, have demonstrated promising leads to experimental animal models, but are difficult to translate clinically. The efficacy of cell therapy, which involves somatic cell transplantation into the CNS to exchange damaged tissue, has been limited thanks to low cell survival and integration upon transplantation, while delivery of therapeutic molecules to the CNS using conventional methods, like oral and intravenous administration, are limited by diffusion across the blood–brain/spinal cord-barrier. The use of biomaterials to market graft survival and integration also as localized and sustained delivery of biologics to CNS injury sites is actively being pursued. This review will highlight recent advances using biomaterials as cell- and drug-delivery vehicles for CNS repair.

Successful therapeutic strategies have been difficult to achieve due to the complexity of the CNS and an inhospitable environment in and around the lesion site for cell transplantation. Limited diffusion of drugs/biologics across the blood–brain barrier (BBB) further restricts the utility of common delivery methods (ie, oral and intravenous). This review will focus primarily on regenerative medicine strategies—that is cell transplantation and endogenous cell stimulation—with particular focus on the role of biomaterials to promote recovery following traumatic brain and spinal cord injuries, and degenerative diseases, such as AMD and RP, which cause degeneration of the photoreceptors and the retinal pigment epithelium (RPE).

Cells and their extracellular matrix (ECM) define the cellular microenvironment in terms of chemical, physical and mechanical properties.

The CNS ECM comprises proteoglycans like chondroitin sulfate proteoglycans (CSPGs), glycosaminoglycans like hyaluronan (HA), and proteins like laminin, collagen, and fibronectin.

A commonly used hydrogel is Matrigel; however, because it springs from a mouse sarcoma, its composition is complex and variable; making well-defined studies difficult to realize and reproduce so as to mimic the native ECM, a hydrogel that gives a blank palette on which biomolecules are often painted is usually wont to promote specific cell–substrate interactions. Recent advances on neural cell–biomaterial interactions are highlighted below, including chemical signals (the role of cell-adhesive molecules, growth factors and other cells); mechanical cues; and physical cues (ie, architecture of the biomaterial) on neural cellular response).

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