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Biopolymer-Cell implants and injectable gels for CNS repair

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No effective treatment is currently available for repair and regeneration of injured tissues of the central nervous system (CNS), i.e. the brain, spinal cord, and retina. Recent research has focused on cell/tissue transplantation and various related tissue engineering approaches. Discussed here is research aimed at development of biopolymer implants and injectable gel compositions containing viable microglia which are designed to create a neurotrophic environment for scar free neuroregenerative wound healing. Because the wound healing process for CNS trauma, i.e. spinal cord injury, normally results in central gray matter necrosis, scarring, and cavitation, there is a need to prevent these adverse events and provide a physical scaffold or bridge to support the regeneration of functional neural tissue within and across the lesion. Our research has shown that porous biopolymer matrices containing viable microglial cells, especially compositions with phospholipid nanosurface modification, can afford a highly favorable terrain for regrowth of functional neural tissues. For example, microporous gels derived from alginate and hyaluronic acid, and seeded with primary microglia, were evaluated as composite cell-biopolymer implants in Wistar rats with induced spinal cord injuries. Porous gels were prepared by a casting-lyophilisation process. For some compositions, pore surfaces were also modified by a novel gamma radiation surface graft technique with 2-methacryloyloxyethyl phosphorylcholine (MPC), a vinyl functional polymerizable phospholipid. For functional evaluation, microglial cells from perinatal rat brains were seeded into the biopolymer matrix and 8-12mm implants were placed at the site of a right side spinal injury at the C4/C5 level in the rat model. Weekly MRIs indicated the absence of cystic cavitation compared to controls. At 6-12 months, biopolymer-cell implanted animals had restored neuromuscular function as shown by vertical exploration limb use. Phospholipid modification appeared beneficial. Post-mortem histology confirmed significant neural tissue regrowth. These results suggest that the study of biopolymer implants containing cells which naturally release neurotrophic growth factors, i.e. microglial, Schwann, and stem cells, represents a fertile field for development of clinical procedures for repair of damaged CNS tissues.

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