Abstract

Engineering a multifunctional scaffold for spinal cord repair

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Spinal cord injury (SCI) affects approximately 10,000 individuals in the United States every year. SCI occurs most commonly in young adults, leaving them seriously disabled for the remainder of their lives. Several potentially useful therapeutic strategies have emerged over the last decade including the use of scaffolds and bridges, delivery of neurotrophic factors, other therapeutic peptides and use of marrow stromal cells to promote neuronal regeneration and functional recovery. However, none of the current strategies have shown enough effect to move to clinical trials and no major efforts have been undertaken to test a combination of these strategies, which can potentially be synergistic, and lead to greater therapeutic effect. Therefore, a need exists to develop a multifunctional construct which can integrate multiple, promising therapeutic strategies. We propose to develop a novel, injectable scaffold containing stem cells (either adult messenchymal lineage or fetal neural lineage) and neurotrophic factors. The polymeric scaffold is a branched copolymer of poly (N-isopropylacrilamide) and poly(ethylene glycol) (PNIPAAm-PEG), which exhibits a phase transition typically between 29-320C. We hypothesize that localized, sustained, simultaneous delivery of multiple therapeutic proteins into the CNS along with an injectable polymeric-cellular scaffold creates a synergistic effect by synchronously modulating the injured environment and activating different signaling pathways. The delivery of nuerotrophic factors (specifically, NT-3 and BDNF) can be controlled by encapsulating them within biodegradable microparticles

made from poly-lactic acid (PLA). By engineering this injectable hydrogel and cellular based scaffold to mimic the host tissues we can create a novel platform technology with applications in treatment of SCI and other tissue engineering applications.