Engineering bioactive materials for cell-directed therapeutics

by

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ABSTRACT

Stem cells offer great potential to treat various diseases. Stem cells that can be directed to differentiate into specialized nerve cells could be used to repair injured spinal cord. Directed differentiation of stem cells into muscle cells could facilitate repair of an injured heart after cardiac infarct; stem cells differentiated into insulin producing cells could treat patients with diabetes. The recent focus has been to use neural stem cells (NSCs) to treat genetic and acquired diseases of the CNS. For this goal to be feasible, NSCs used therapeutically must demonstrate the ability to differentiate along specific lineages, to migrate long distances, and to survive in the milieu of the injured brain.

In this work, we describe studies of the proliferation and differentiation of neural stem cells (NSCs) encapsulated within three-dimensional scaffolds – alginate hydrogels – whose elastic moduli were varied over two orders of magnitude. The rate of proliferation of neural stem cells decreased with increase in the modulus of the hydrogels. Moreover, we observed the greatest enhancement in expression of the neuronal marker β-tubulin III within the softest hydrogels, which had an elastic modulus comparable to that of brain tissues. We have also designed poly (D, L-lactic-co-glycolic acid) (PLGA)-based drug delivery systems to release therapeutic molecules of interest such as Shh, FGF-2 and hyaluronidase that are known to control stem cell fate, with the aim of treating various disorders such as spinal cord injury. Transplantation of Shh-releasing microspheres or a combination of Shh-treated spinal cord neural stem cells with Shh-releasing microspheres resulted in motor recovery in spinal cord injured mice. Such scaffolds that control stem cell fate would be broadly useful for applications in regenerative medicine and tissue engineering. We also describe our preliminary attempts to design bioactive materials such as polyvalent aptamers and shRNA that can help prevent HIV and influenza infection and its transmission.