学位の種類	博士（医学）
報告番号	甲第１３９５号
学位記番号	第１０００号
氏名	中口 加奈子
授与年月日	平成 26 年 3 月 25 日
学位論文の題名	Growth factors released from gelatin hydrogel microspheres increase new neurons in the adult mouse brain (マウス成体脳における細胞成長因子徐放化製剤のニューロン新生促進効果) Stem Cells International Vol.2012 Article ID 915160 7 pages, 2012
論文審査担当者	主査： 飛田 秀樹 副査： 浅井 清文, 澤本 和延

Abstract

Recent studies have shown that new neurons are continuously generated by endogenous neural stem cells in the subventricular zone (SVZ) of the adult mammalian brain. Some of these new neurons migrate to injured brain tissues and differentiate into mature neurons, suggesting that such new neurons may be able to replace neurons lost to degenerative disease or injury and improve or repair neurological deficits.

Various proteins, including neurotrophic factors and paracrine signaling molecules, are reported to enhance neurogenesis in the SVZ. However, one limitation of using these factors in the treatment of brain diseases is the lack of appropriate delivery systems. It is difficult to engineer systemically administered proteins to cross the blood-brain barrier, and such proteins can cause systemic toxicity at high concentrations. On the other hand, a single local injection of liquid drugs into the brain parenchyma, using a cannula, is invasive, and this strategy may not enhance neuronal regeneration effectively, given the limited volume and persistence of substances administered in this way. Therefore, for clinical applications, safe and effective methods for the sustained delivery of neurogenesis-enhancing factors to the SVZ or injured neural tissues must be developed.

Here, we tested whether delivering growth factors via gelatin hydrogel microspheres would support neurogenesis in the SVZ. Insulin-like growth factor-1 (IGF-1)-containing microspheres increased the number of new neurons in the SVZ. Hepatocyte growth factor (HGF)-containing microspheres increased the number of new neurons migrating from the SVZ towards the injured striatum in a stroke model in mouse. These results suggest that the strategy of using gelatin hydrogel microspheres to achieve the sustained release of growth factors holds promise for the clinical regeneration of damaged brain tissues from endogenous neural stem cells in the adult SVZ.