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BRAIN RESEARCH

Research Report

Myelin-forming ability of Schwann cell-like cells induced from rat adipose-derived stem cells in vitro

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ARTICLE INFO

Article history:
Accepted 28 August 2008
Available online 11 September 2008

Keywords:
Adipose-derived stem cell
Schwann cell
Myelin

ABSTRACT

Although Schwann cell (SC) transplantation can enhance peripheral and central nerve repair experimentally, it is difficult to generate sufficient SC quickly for clinical application. So alternative cell systems for SC are desired. SC-like cells induced from adipose-derived stem cells (ADSC) may be one of the ideal alternative cell systems for SC. However, myelin-forming ability, which is the most important characteristics and function of SC, has not been investigated in SC-like cells from ADSC up to now. In this experiment, ADSC were harvested from rat inguinal fat pad. Rat ADSC were fibroblast-like in shape, almost all the cells expressed mesodermal marker fibronectin, and only few cells expressed neural stem cell marker nestin. A mixture of glial growth factors (Heregulin, bFGF, PDGF and forskolin) could induce rat ADSC into SC-like cells. SC-like cells were spindle-like in shape and expressed glial markers GFAP and S100, similar to genuine SC. When intracellular cAMP was increased, SC-like cells could express myelin protein p0. More importantly, when co-cultured with rat pheochromocytoma cell line (PC12 cells), SC-like cells could induce the differentiation of PC12 cells rapidly and form myelin structures with PC12 cells in vitro. Our data further demonstrated that SC-like cells from ADSC were able to form myelins and these cells may benefit the treatment of peripheral and central nerve injuries.

1. Introduction

Schwann cells (SC) which are myelinating cells of peripheral nervous system (PNS) play a central role in neurodegenerative and regenerative processes of PNS. Transplanted cultured SC can also enhance axonal regeneration across nerve gaps (Mosahebi et al., 2001). Although the environment in the central nervous system (CNS) is unfavourable for the re-growth of nerve fibers, it is reported that SC can promote axonal regeneration of lesioned adult rat spinal cord (Takami

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Abbreviations: ADSC, adipose-derived stem cells; SC, Schwann cells; PNS, peripheral nervous system; CNS, central nervous system; MSCs, bone marrow stromal cells

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doi:10.1016/j.brainres.2008.08.088

et al., 2002). Transplanted SC can remyelinate demyelinated axons of CNS and restore the normal conduction properties (Honmou et al., 1996). Another advantage of SC is that SC could be harvested from nerve biopsies for autologous transplantation. However, the clinical application of SC is limited. For example, one or more functional nerves have to be sacrificed, and additional morbidity would be caused; cultured SC have restricted mitotic activity in vitro, so the time required to expand the cells would delay treatment. So, alternative cell systems are desirable.

Bone marrow stromal cells (MSCs) may be an ideal alternative cell system for SC, since MSCs can be accessed easily and expanded rapidly in culture conditions for autologous transplantation, and some groups reported that MSCs can transdifferentiate into SC-like cells in vitro (Caddick et al., 2006; Dezawa et al., 2001) and in vivo (Dezawa et al., 2001). However, MSCs harvest procedure is painful, and the frequency of MSCs in bone marrow is relatively low (Zuk et al., 2001).

Recently, it is reported that adipose-derived stem cells (ADSC) could be isolated from adipose tissue (Zuk et al., 2002). Both ADSC and MSCs are derived from embryonic mesoderm; ADSC and MSCs have similar phenotype and gene expression profiles (De Ugarte et al., 2003a,b); and both of them can differentiate along several mesenchymal tissue lineages, including adipocytes, osteoblasts, chondrocytes, myocytes, and so on (Gimble et al., 2007; Zuk et al., 2002). ADSC can also proliferate rapidly in culture for a long time (Zuk et al., 2002). However, ADSC have some unique advantages: human

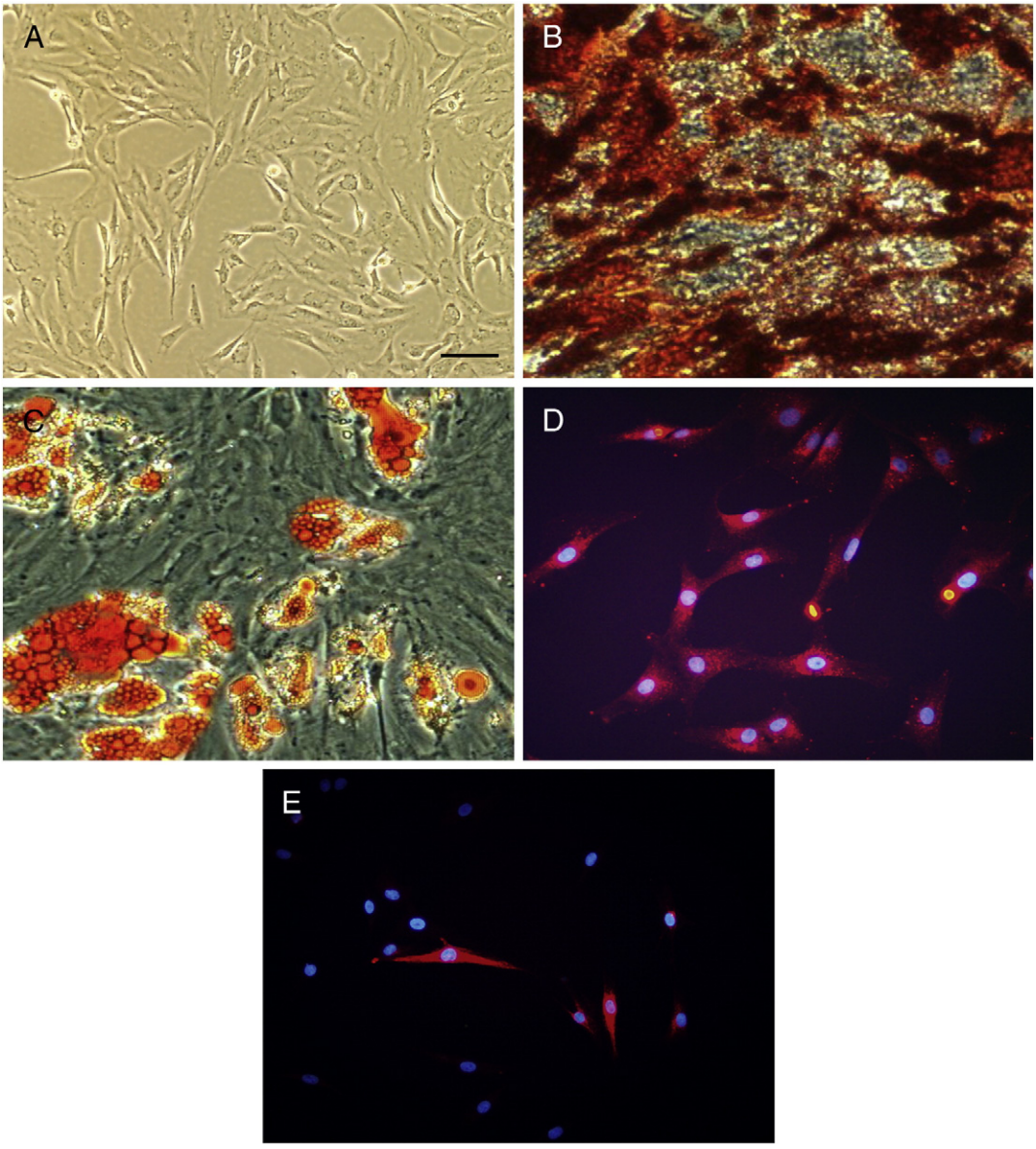

Fig. 1 – Characterization of rat ADSC. Rat ADSC of 3–5 passages were used for our experiments. (A) Rat ADSC of 3–5 passages are a mono-layer of large and flat cells under phase contrast. (B, C) Rat ADSC could undergo osteogenic (B) and adipogenic (C) differentiation when cultured in lineage-specific differentiation culture medium. (D, E) Immunocytochemistry of rat ADSC shows that almost all of rat ADSC express mesodermal marker fibronectin (D), only few cells express neural stem cell marker nestin (E). Nuclei are labeled with DAPI (blue). Bar, A: 100 μm; B–E: 50 μm.