Angiogenic potential of dental pulp stem cell for neurovascular diseases

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Introduction

Dental pulp stem cells (DPSCs) have perivascular characteristics suggestive of potential application of DPSCs as perivascular cell source. In this study, we investigated whether DPSCs had angiogenic capacity by co-injection with human umbilical vein endothelial cells (HUVECs) in vivo; in addition, we determined the role of stromal cell-derived factor 1-a (SDF-1a) and C-X-C chemokine receptor type 4 (CXCR4) axis in the mutual interaction between DPSCs and HUVECs.

Methods

DPSCs were primarily isolated and cultured for 3 passages. To characterize the stemness of DPSCs, immunophenotypes and differentiation were determined. The angiogenic potential of DPSCs was assessed by in vivo Matrigel plug assay. The involvement of SDF-1a/CXCR4 axis was verified using AMD3100, an antagonist of CXCR4.

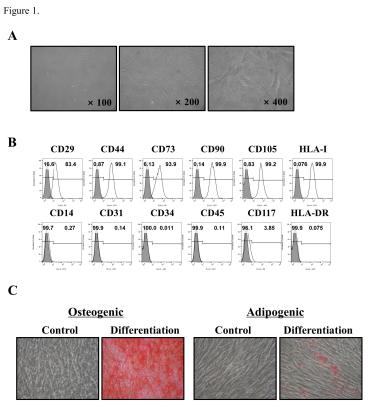
Results

DPSCs showed typical mesenchymal stem cell-like characteristics which included the expression of surface markers and in vitro differentiation potentials (osteogenesis, adipogenesis, and chondrogenesis). When DPSCs were co-injected with human umbilical vein endothelial cells (HUVECs) in in vivo Matrigel, enough number of microvessel-like structures was observed. However, DPSCs alone or HUVECs alone could not make microvessel-like structures significantly. When AMD3100 was co-injected with DPSCs and HUVECs, there was no microvessel-like structure in vivo.

Conclusions

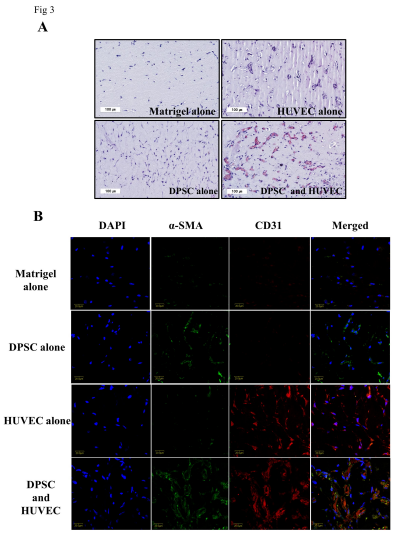
In conclusion, DPSCs might have perivascular characteristics that could contribute to in vivo angiogenesis. This study suggests potential application of DPSCs for neovascularization of engineered tissues and neurovascular diseases.

Figure 1. Primary isolation and characterization of DPSCs



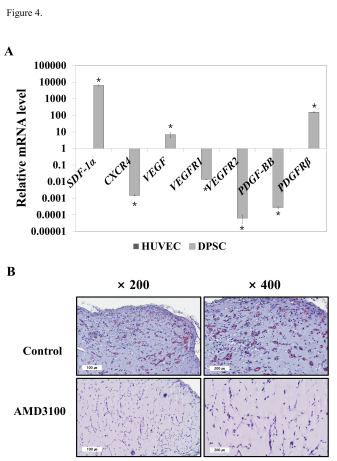
DPSCs showed MSC-like characteristics including morphology (A), surface markers (B), and differentiation potential (C).

Figure 2. In vivo angiogenic potential of DPSCs



(A) In the results of DPSCs alone or HUVEC alone, no obvious microvessel-like structures were observed. However, when DPSCs and HUVECs were co-injected, microvessel-like structures were formed and red blood cells were observed in the lumen. (B) Immunofluorescent staining by CD31 and -SMA showed that microvessel-like structures were stained on co-injection with DPSCs and HUVECs subcutaneously.

Figure 3. The involvement of SDF-1 and CXCR4 axis in in vivo angiogenesis by DPSCs and HUVECs



The expression of angiogenic factors and receptors was verified by qPCR. (A) The expression of SDF-1, PDGFR, and VEGF was higher in DPSCs than HUVECs. On the contrary, the expression of CXCR4, PDGF-BB, VEGFR1, and VEGFR2 was higher in HUVECs than DPSCs. *P < 0.05. (B) To confirm the functional involvement of SDF-1 and CXCR4 axis in in vivo angiogenesis, AMD3100, an antagonist of CXCR4, was mixed with Matrigel plug. After 7 days post-injection, there was no microvessel-like structures in the AMD3100 treatment group, as compared to control group, no AMD3100 treatment group.