International Journal Of Bilogical Sciences

TGF-?-Operated Growth Inhibition and Translineage Commitment into Smooth Muscle Cells of Periodontal Ligament-Derived Endothelial Progenitor Cells through Smad- and p38 MAPK-Dependent Signals

Mariko Yoshida1#, Naoto Okubo1#, Naoyuki Chosa1, Tomokazu Hasegawa2, Miho Ibi1, Masaharu Kamo1, Seiko Kyakumoto1, Akira Ishisaki1?

1. Division of Cellular Biosignal Sciences, Department of Biochemistry, Iwate Medical University, 2-1-1 Nishitokuta, Yahaba-cho, Shiwa-gun, Iwate 028-3694, Japan 2. Department of Pediatric Dentistry, Tokushima University Hospital, Kuramoto-cho, Tokushima 770-8504, Japan

Abstarc :

The periodontal ligament (PDL) is a fibrous connective tissue that attaches the tooth to the alveolar bone. We previously demonstrated the ability of PDL fibroblast-like cells to construct an endothelial cell (EC) marker-positive blood vessel-like structure, indicating the potential of fibroblastic lineage cells in PDL tissue as precursors of endothelial progenitor cells (EPCs) to facilitate the construction of a vascular system around damaged PDL tissue. A vascular regeneration around PDL tissue needs proliferation of vascular progenitor cells and the subsequent differentiation of the cells. Transforming growth factor-? (TGF-?) is known as an inducer of endothelial-mesenchymal transition (EndMT), however, it remains to be clarified what kinds of TGF-? signals affect growth and mesenchymal differentiation of PDL-derived EPC-like fibroblastic cells. Here, we demonstrated that TGF-?1 not only suppressed the proliferation of the PDL-derived EPC-like fibroblastic cells, but also induced smooth muscle cell (SMC) markers expression in the cells. On the other hand, TGF-?1 stimulation suppressed EC marker expression. Intriguingly, overexpression of Smad7, an inhibitor for TGF-?-induced Smad-dependent signaling, suppressed the TGF-?1-induced growth inhibition and SMC markers expression, but did not the TGF-?1-induced downregulation of EC marker expression. In contrast, p38 mitogen-activated protein kinase (MAPK) inhibitor SB 203580 suppressed the TGF-?1-induced downregulation of EC marker expression. In addition, the TGF-?1-induced SMC markers expression of the PDL-derived cells was reversed upon stimulation with fibroblast growth factor (FGF), suggesting that the TGF-?1 might not induce terminal SMC differentiation of the EPC-like fibroblastic cells. Thus, TGF-?1 not only negatively controls the growth of PDL-derived EPC-like fibroblastic cells via a Smad-dependent manner but also positively controls the SMC-differentiation of the cells possibly at the early stage of the translineage commitment via Smad- and p38 MAPK-dependent manners.

Key Word :
Ligament, TGF-?, Differentiation, Endothelial Cell, Smooth Muscle Cell

Volume 8, Number 7, - 2012 , ISSN 1545-1003