Synopsis of Original Research Paper

The Role of Glycosaminoglycan on Vasculogenesis

Jun-Ichi Sasaki

Department of Biomaterials Science, Osaka University Graduate School of Dentistry

Vasculogenesis is referred to as the assembling of stem cells and endothelial progenitor cells into endothelium and subsequent formation of nascent capillaries. The elucidation of vasculogenesis of stem cells will facilitate control of neovascularization and further development of novel cosmetics as well as tissue regenerative therapies. Heparan sulfate (HS) proteoglycans, which are composed of HS glycosaminoglycan chains and covalently attached core protein, are a widely distributed constituent of extracellular matrices in all mammalian tissues. HS could enhance the binding affinity between growth factors and related receptors to modulate a variety of biological activities, however little is known about the role of HS in endothelial differentiation and neovascularization of mesenchymal cells. Dental pulp stem cells (DPSCs), which are classified as mesenchymal stem cells, are highly proliferative and exhibit a multipotent differentiation ability. Notably, owing to constitutive expression of vascular endothelial growth factor receptor 1, DPSCs more readily differentiate into vascular endothelial lineages compared with other mesenchymal cells. In this study, we hypothesized that HS highly orchestrates vasculogenesis of mesenchymal stem cells and the role of HS on endothelial differentiation was investigated by using DPSCs. It was revealed that an HS antagonist suppressed the sprouting ability and endothelial differentiation of DPSCs. Silencing of *exostosin-1* (*EXT1*), a crucial glycosyltransferase for HS biosynthesis, in DPSCs significantly altered their gene expression profile. In addition, EXT1-silenced DPSCs expressed lower levels of endothelial differentiation markers and displayed a reduced vascular formation capacity compared with control DPSCs transduced with scrambled sequences. Collectively, these findings indicate the crucial role of HS on endothelial differentiation and vasculogenesis of mesenchymal stem cells, opening new perspectives for the application of HS to novel cosmetics and regenerative medicine.