## Sema4D/Plexin-B1 Signaling Regulates Osteo/Odontogenic Differentiation of Dental Pulp Stem Cells

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Abstract: Objectives: The purpose of this study was to investigate the role of Semaphorin 4D (Sema4D)/Plexin-B1 signaling on osteo/odontogenic differentiation of human dental pulp stem cells (DPSCs) and uncover its molecular mechanism. Methods: DPSCs were cultured in osteo/odontogenic medium. After treatment with Sema4D (10µg/mL), osteo/odontogenic differentiation and mineralization was evaluated by measuring alkaline phosphatase (ALP) activity and alizarin red S staining respectively. The expression of osteo/odontogenic genes (ALP, Col1A1, BSP, and Runx2) was determined by real-time polymerase chain reaction. p-Plexin-B1, Plexin-B1, Col1A1, RhoA, and ErbB2 were analyzed by western. Results: ALP activity and mineralization formation of DPSCs were significantly decreased after treatment with Sema4D (P<0.05). Sema4D significantly down-regulated osteo/odontogenic-related genes expression (ALP, Col1A1, BSP, and Runx2). p-Plexin-B1, Plexin-B1 and RhoA protein expression levels increased after stimulated with Sema4D, while the expression of Col1A1 decreased. Pretreatment with Plexin-B1 antibody blocked Sema4D induced p-Plexin-B1 expression. Conclusion: Sema4D suppressed osteo/odontogenic differentiation of DPSCs via RhoA-mediated pathways.

Keywords: Sema4D/Plexin-B1, dental pulp stem cells, osteo/odontogenic differentiation, alkaline phosphatase (ALP)

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