International Journal Of Bilogical Sciences

Osterix Controls Cementoblast Differentiation through Downregulation of Wnt-signaling via Enhancing DKK1 Expression

Zhengguo Cao1,2, , Rubing Liu1, Hua Zhang3, Haiqing Liao1, Yufeng Zhang1, Robert J. Hinton3, and Jian Q. Feng3

1. The State Key Laboratory Breeding Base of Basic Science of Stomatology (Hubei-MOST KLOS) & Key Laboratory for Oral Biomedical Engineering of Ministry of Education(KLOBME), School & Hospital of Stomatology, Wuhan University, Wuhan, China 2. Department of Periodontology, School & Hospital of Stomatology, Wuhan University, Wuhan, China 3. Texas A&M University, Baylor College of Dentistry, 3302 Gaston Avenue, Dallas, TX, USA Both authors equally contribute to this work. Corresponding author: Correspondence should be addressed to Zhengguo Cao. Tel: +86-27-87686212, E-mail: jery7677@hotmail.com

Abstarc :

Osterix (Osx), a transcriptional factor essential for osteogenesis, is also critical for in vivo cellular cementum formation. However, the molecular mechanism by which Osx regulates cementoblasts is largely unknown. In this study, we initially demonstrated that overexpression of Osx in a cementoblast cell line upregulated the expression of markers vital to cementogenesis such as osteopontin (OPN), osteocalcin (OCN), and bone sialoprotein (BSP) at both mRNA and protein levels, and enhanced alkaline phosphatase (ALP) activity. Unexpectedly, we demonstrated a sharp increase in the expression of DKK1 (a potent canonical Wnt antagonist), and a great reduction in protein levels of ?-catenin and its nuclear translocation by overexpression of Osx. Further, transient transfection of Osx reduced protein levels of TCF1 (a target transcription factor of ?-catenin), which were partially reversed by an addition of DKK1. We also demonstrated that activation of canonical Wnt signaling by LiCl or Wnt3a significantly enhanced levels of TCF1 and suppressed the expression of OPN, OCN, and BSP, as well as ALP activity and formation of extracellular mineralized nodules. Importantly, we confirmed that there were a sharp reduction in DKK1 and a concurrent increase in ?-catenin in Osx cKO mice (crossing between the Osx loxP and 2.3 Col 1-Cre lines), in agreement with the in vitro data. Thus, we conclude that the key role of Osx in control of cementoblast proliferation and differentiation is to maintain a low level of Wnt-?-catenin via direct up-regulation of DKK1.

Key Word :
cementum; Osterix; DKK1; cementoblast differentiation; Wnt signaling

Volume 11, Number 3, - 2015 , ISSN 1449-2288