AAO Foundation Award Final Report

Principal Investigator	Yang, Wuchen
Co-Investigator	NA
Secondary Investigators	NA
Award Type	Research Aid Award
Project Title	Role and Mechanism of Bone Morphogenitic Protein 2 Action in Cementogenesis
Project Year	Y2013-2014
Institution	University of Connecticut Health Center
Summary/Abstract (250 word maximum)	Please see the attached.
Were the original, specific aims of the proposal realized?	Both specific Aims have been realized. The role of BMP2 in cementogenesis was investigated using an in vivo loss-of-function study (Aim 1). Signature expression in cementogenesis was profiled using micrarray approach (Aim 2). The gene expression profile of Bmp2-cKO^{CB} cementoblasts has not been completed due to a low production of B2ckO mice during breeding.
Were the results published? If not, are there plans to publish? If not, why not?	1. Rakian A‡, Yang W‡, Gluhak-Heinrich J, Cui Y, Harris MA, Villarreal D, Feng JQ, Macdougall M, Harris SE. Bone morphogenetic protein-2 gene controls tooth root development in coordination with formation of the periodontium. Int J Oral Sci. 2013;5(2):75-84. (‡ Authors contributed equally to this study) 2. Roguljic H, Matthews BG, Yang W, Cvija H, Mina M, Kalajzic I. In vivo identification of periodontal progenitor cells. J Dent Res. 2013;92(8):709-15.
Have the results of this proposal been presented? If so, when and where? If not, are there plans to do so? If not, why not?	Investigator presented her research results on 2013 IADR in Seattle, Washington and on 2014 AADR/CADR in Charlotte, North Carolina. *In vivo Role of BMP2 in Regulating Cellular Cementogenesis. Yang W, Gluhak-Heinrich J, Cui Y, Rakian A, Kalajzic Z, Nanda R and Kalajzic I. J Dent Res 92(A): 3344, 2013* *Optimization of Bioactive Polymer-Ceramic Nanocomposite Scaffolds for Bone Regenerative Engineering. Yang W, Shalumon K, Tang X, Laurencin C.T., Kumbar S.G. J Dent Res 93(A): 593, 2014*
To what extent have you used, or how do you intend to use, AAOF funding to further your career?	The outcomes generated through the support of this one year RAA award will be used as the preliminary data for a further extensive proposal that will be submitted for NIDCR career development funding to continue study on mechanisms of periodontium healing.

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Summary/abstract (250 words maximum):

Bone Morphogenetic Protein 2 (BMP2) is suggested to be capable to drive dental follicle cells towards cementoblasts and alveolar osteoblasts, and is currently being tested as a potent molecule for periodontium reconstruction. However, the fundamental role of endogenous BMP2 action in dentinogenesis is still unknown.

Using an in vivo loss-of-function mouse model to specifically delete Bmp2 in mesenchyme-derived cell population (Bmp2-cKO^{CB}), the unknown role of endogenous BMP2 action in cementogenesis and root development is investigated.

Bmp2-cKO^{CB} mice display hypomineralized cementum with a reduction in thickness in radiograph observation. By Hematoxylin-Eosin staining and histomorphometric measurement, reduced cementum volume was further confirmed. Decreased cementum formation rate was observed in Bmp2-cKO^{CB}. Furthermore by immunohistochemistry, we detected downregulation of cementogenesis regulators such as BSP and OPN in cellular cementum and a subset of PDL cells. These data show deletion of BMP2 in cementoblasts postnatally interrupts normal cementoblast development to a functional matrix secretion stage leading to a reduction of cementoid production. Thus, BMP2 is proved to be necessary for proper cementum formation by regulating mesenchyme derived cells, and continues to play a crucial signaling role in the process of cellular cementogenesis throughout late age.

In preparation to evaluate the gene expression in Bmp2-cKO^{CB} cementoblasts, gene expression was profiled in isolated primary cementoblasts. 320 Signature genes were identified when profiles of cementoblasts were compared to that of calvaria osteoblasts. Known and novel genes and signaling pathways specifically in cementogenesis are thus suggested to give insights to further investigation on the development of cementoblasts.