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DMP1 - a key regulator in mineralized matrix formation

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Dentin matrix protein 1 (DMP1) is a non-collagenous extracellular matrix protein that has been implicated to have a regulatory function during mineralized matrix formation¹⁻⁵. Analysis of the protein sequence of DMP1 showed three important facts: (a) The entire secreted protein is hydrophilic and exists as a random coil; (b) DMP1 contains a large number of acidic domains with two or more consecutive aspartic acid or glutamic residues, and these domains frequently contain one or more serines; and (c) Many of these serines could be phosphorylated by messenger independent kinases. A published report demonstrates that DMP1 could undergo proteolytic cleavage into an N-terminal and a C-terminal domain⁶. We have shown that the C-DMP1 can nucleate hydroxyapatite in the presence of type I collagen⁷. During the nucleation and growth process, the initially formed metastable amorphous calcium phosphate phase, transformed into thermodynamically stable crystalline hydroxyapatite in a precisely controlled manner. These events were confirmed by X-ray diffraction (XRD), Selected area electron diffraction pattern (SAED), Raman spectroscopy and elemental analysis. However, the N-terminal domain of DMP1 inhibited HAP formation and stabilized the amorphous phase that was formed.

To investigate the role of DMP1 during calcified tissue formation, transgenic mice overexpressing DMP1 under the control of the CMV promoter was generated. The skeletal and dental tissues of the transgenic mice were characterized by histology, histomorphometry and immunostaining. Histological and histomorphometrical analysis indicated that non-targeted overexpression of DMP1 accelerated dentinogenesis, endochondral and intramembranous ossification processes when compared with the wild type. In addition, enhanced terminal differentiation of the epiphyseal growth plate chondrocytes was also observed. Immunostaining analysis of the dental tissue showed accelerated expression of the key dentin matrix pro-

teins namely; dentin matrix protein 2 and dentin sialoprotein.

Together, these data demonstrate that DMP1 is a key regulatory protein that is required for normal growth and development of bone, cartilage and dentin.

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The authors have no conflict of interest.

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