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 DMP1 and Phosphate Regulation (Session Summary)

# Dentin Matrix Protein 1 (DMP1)

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Dentin matrix protein 1 (DMP1) is a member of the Small Integrin-Binding Ligand N-linked Glycoprotein (SIBLING) family. Some other proteins in this family are osteopontin (OPN), matrix extracellular phosphoglycoprotein (MEPE), bone sialoprotein (BSP), and dentin sialophosphoprotein (DSPP). Each of these is a secreted protein associated with mineralization in dentin and bone. DMP1 was first cloned by Anne George<sup>1</sup> and was shown to be expressed mostly by osteocytes and odontoblasts<sup>1,2</sup>. It plays an important role in mineralization of bone and dentin<sup>3</sup>. DMP1-null mice have been helpful in deciphering the functions of this protein. The mice have defects in dentin development, hypomineralization and rickets<sup>4</sup>, as well as an apparent chondrodysplasia<sup>5</sup>. These mice also had very low levels of phosphate in their blood coupled with abnormally high levels of fibroblast growth factor 23 (FGF23)<sup>6</sup>.

FGF23 is a phosphate regulating hormone that blocks reabsorption of phosphate in the renal tubules<sup>7</sup>. FGF23 is secreted by several cell types but the majority is produced in bone and dentin tissues. In addition to lowering serum phosphate levels, FGF23 blocks the conversion of 25(OH) Vitamin D<sub>3</sub> to 1,25(OH)<sub>2</sub> Vitamin D<sub>3</sub> by suppressing the activity of 1-alpha-hydroxylase in the kidney<sup>8</sup>. The interaction between DMP1 and FGF23 is not well understood yet we know that both proteins are produced mostly by osteocytes and odontoblasts. DMP1 integrates into the matrix surrounding osteocytes and most likely affects osteocyte function. It is therefore possible that DMP1 is a component of the phosphate sensor in osteocytes that acts as a local regulator of FGF23 secretion. Of course, this is merely speculation since the phosphate sensor has not yet been identified.

However it is interesting to note that individuals with inactivating mutations of DMP1 have hypophosphatemia and rickets, symptoms that mirror those in subjects with activating mutations of FGF23. The former genetic disorder is called autosomal recessive hypophosphatemic rickets (ARHR)<sup>6</sup> and the latter is called autosomal dominant hypophosphatemic rickets (ADHR)<sup>9</sup>.

Our current concept of DMP1 is of a matrix protein that regulates mineralization and the production of the bone-derived hormone FGF23. Interesting, there is growing evidence suggesting that DMP1 production is regulated by local mechanical perturbations. Mechanical loading increased DMP1 expression in alveolar bone<sup>10</sup> and long bone<sup>11</sup>. One might expect that local changes in DMP1 caused by mechanical loading could affect tissue mineralization but this connection has not yet been demonstrated. At present, the biological significance of mechanical regulation of DMP1 is not known.

## References

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