

OSTEOSCOOP

News on current events in osteoporosis and rheumatology

MEPE is a new bone renal hormone and vascularization modulator

N°131 – May 2010

MEPE (Matrix Extracellular Phosphoglycoprotein) is a protein secreted by osteoblasts and osteocytes. Its synthesis is increased in several phosphate and bone-mineral metabolic disorders such as hypophosphatemic rickets and oncogenic hypophosphatemic osteomalacia. Under normal circumstances, MEPE is cleaved to release a peptide which acts as an inhibitor of bone mineralization. MEPE may be a substrate for an enzyme called PHEX, and PHEX may prevent proteolysis of MEPE and release of the peptide which inhibits bone mineralization. In patients with X-linked hypophosphatemic rickets (XLH) and in mice with the Hyp mutation, PHEX is mutated and therefore cannot bind to MEPE. This results in the release of MEPE into the circulation, thereby causing hypophosphatemia and renal Pi wasting. To elucidate the causative role of MEPE in these disorders, the authors of a recent study [1] created a murine model overexpressing MEPE protein in bone.

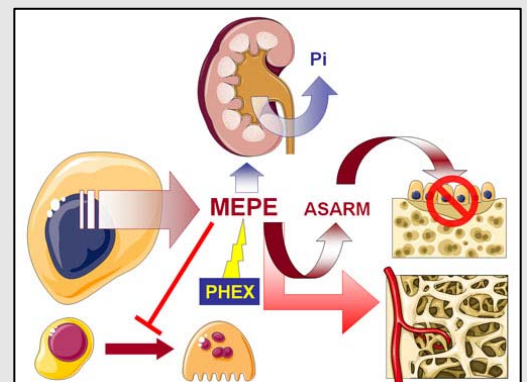
MEPE transgenic mice displayed a growth and mineralization defect with altered bone-renal vascularization that persisted to adulthood. The growth mineralization defect was due to a decrease in bone remodeling and MEPE transgenic mice were resistant to diet induced renal calcifications. Osteoblastic cells displayed reduced activity but normal differentiation. Osteoclastic precursors were unable to differentiate in the presence of osteoblasts. In the kidney, NPT2a upregulation induced an increase in phosphate renal reabsorption, leading to hyperphosphatemia.

In conclusion, MEPE is an important component to an age-diet dependent pathway that regulates bone turnover, mineralization and suppresses renal calcification. This novel pathway also modulates bone-renal vascularization and bone turnover.

1. David V et al. *Endocrinology*. 2009;doi:10.1210/en.2009-0216.

MEPE is a new bone renal hormone and vascularization modulator

MEPE is a protein secreted by osteoblasts and osteocytes. MEPE is cleaved by an enzyme, PHEX, to release peptides (ASARM) which inhibit mineralization in bone and possibly in other tissues. Overexpression of MEPE leads to a growth and mineralization defect and bone vascularization is impaired. Osteoclast differentiation is reduced. In the kidney, MEPE increases phosphate reabsorption, leading to hyperphosphatemia, and prevent diet-induced calcifications.



PROTELOS[®]
Treatment of postmenopausal osteoporosis to reduce the risk of hip and vertebral fractures

