Pmepa1 expressed in osteoclasts is specifically induced by bone components and regulates bone resorption

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論 文 名　：**Pmepa1 expressed in osteoclasts is specifically induced by bone components and regulates bone resorption**

（Pmepa1 は Bone コンポーネントによって破骨細胞で発現が誘導され、骨吸収を制御する）

区　　分　：甲

論 文 内 容 の 要 旨

Osteoclasts are bone-resorbing multinucleated cells differentiated form hematopoietic stem cells. During bone resorption, osteoclasts are polarlized to form ruffled border to degrade bone by secretion of H^+ proton and acid proteases. Here Prostate transmembrane protein androgen induced-1 (Pmepa1) was found that modulating bone resorption by regulating secretion in osteoclasts. Pmepa1 was induced by RANKL and specially expressed in preosteoclasts *in vitro*, but also expressed in osteoclasts present in bone tissue of adjuvant arthritis rats and in osteoclasts formed on dentine. Expression of Pmepa1 was increased by treatment of calcium ionophore A23187, TGF-β and osteopontin, and was also correlated with bone resorption activity. In this study, knockdown of Pmepa1 decreased bone resorption activity by regulating secretion of cathepsin K and proton to extracelluar space. In addition, the localization of cathepsin K was impaired in Pmepa1-deficient osteoclasts. Pmepa1 protein was localized to lysosome and early endosome and also colocalized with LC3 and Nedd4 in osteoclasts. Knockdown of Pmepa1 decreased the expression of E3 ubiquitin ligase Nedd4 and increased Pten protein, which was related to cell proliferation and apoptosis. These results suggested that Pmepa1 specifically expressed in active osteoclasts, and regulated bone resorption by regulating secretion of proton and cathepsin K to extracelluar space.