Dynamin and PTP-PEST cooperatively regulate Pyk2 dephosphorylation in osteoclasts

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Abstract:

Bone loss is caused by the dysregulated activity of osteoclasts which degrade the extracellular bone matrix. The tyrosine kinase Pyk2 is highly expressed in osteoclasts, and mice lacking Pyk2 exhibit an increase in bone mass, in part due to impairment of osteoclast function. Pyk2 is activated by phosphorylation at Y402 following integrin activation, but the mechanisms leading to Pyk2 dephosphorylation are poorly understood. In the current study, we examined the mechanism of action of the dynamin GTPase on Pyk2 dephosphorylation. Our studies reveal a novel mechanism for the interaction of Pyk2 with dynamin, which involves the binding of Pyk2's FERM domain with dynamin's plextrin homology domain. In addition, we demonstrate that the dephosphorylation of Pyk2 requires dynamin's GTPase activity and is mediated by the tyrosine phosphatase PTP-PEST. The dephosphorylation of Pyk2 by dynamin and PTP-PEST may be critical for terminating outside-in integrin signaling, and for stabilizing cytoskeletal reorganization during osteoclast bone resorption.

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