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Src-dependent and independent multinucleation of osteoclasts

Jiro Takito
Showa University, Japan

Abstract

Osteoclasts are multinucleated cells responsible for bone resorption. Multinucleation enhances the resorbing efficiency of osteoclasts. Aberration of multinucleation or size control of osteoclasts is seen in some bone diseases such as Paget's disease of bone and Cherubism of bone. The mechanism of size control of osteoclasts has been elusive. We have previously reported that the actin-rich superstructure, called a zipper-like structure specifically appeared during the cell fusion of large osteoclasts. Because the zipper-like structure is a derivative of the podosome belt, reagents that affect the structure or the function of podosome belt should produce smaller osteoclasts. The organization of podosome belt is regulated by a proto-oncogene; Src interacted with dynamin, an endocytic GTPase. We, here, examined the effect of pharmacological reagents on the multinucleation of osteoclasts differentiated from RAW 264.7 cells. A Src inhibitor, SU6656, inhibited the maintenance of the podosome belt and the zipper-like structure. SU6656 inhibited the formation of large osteoclast, but increased the number of small osteoclasts. Dynasore, an inhibitor of dynamin showed the similar effects. Furthermore, a stabilizer of actin stress fibers, jasplakinolide caused the osteoclasts smaller, suggesting the involvement of actin dynamics in the fusion of osteoclast. Taken together, the dynamic reorganization of actin filaments maintained via Src/dynamin signaling is involved in the hypermultinucleation of osteoclast. Because bone remodeling is regulated by nutritional factors, we will discuss the nutritional intervention for the size control of osteoclast.

Biography

Jiro Takito has completed his Ph.D. at the age of 28 years from Tohoku University and postdoctoral studies from Mitsubishi Kasei Institute for Life Sciences. He is the assistant professor of Showa University and the affiliate associate professor of Tohoku University. He has published more than 38 papers in reputed journals.