

Calcium/calmodulin-dependent regulation of Rac1 and Rac2 GTPases in histamine-induced chemotaxis of mouse mast cells

Nishio Yusuke, Inui Makoto, Kuramasu Atsuo

Dept. Pharmacology, Yamaguchi Univ. Grad. Sch. Med.

Histamine induces chemotaxis of mast cells through the histamine H4 receptor. This process involves activation of the small GTPases, Rac1 and Rac2, and phospholipase C-mediated calcium mobilization. However, it is not clear whether these two pathways interact. In this study, we showed that histamine-induced activation of Rac1 and Rac2 was mediated by calcium/calmodulin in mouse mast cells. The phospholipase C inhibitor, U73122, the intracellular calcium chelator, BAPTA-AM, and the calmodulin antagonist, W-7, significantly suppressed histamine-induced chemotaxis and Rac activation. The phosphatidylinositol-4,5-bisphosphate 3-kinase (PI3K) inhibitor, LY294002 failed to diminish ionomycin-induced Rac activation and extracellular signal-regulated kinase (ERK) phosphorylation whereas histamine-induced activation of Rac and ERK was sensitive to LY294002, suggesting that the calcium/calmodulin-dependent pathway bypasses PI3K activation. These results indicate two distinct pathways that lead to the activation of Rac1 and Rac2 GTPases in histamine-induced chemotaxis of mouse mast cells.