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

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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.