Effect of Compound48/80 on antigen dependent degranulation in BMMC

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Mast cells (MCs) recognize antigens (Ag) via IgE-bound high affinity IgE receptors (Fc ε RI) and trigger type I allergic reactions. The MC activation by Ag is regulated by various bioactive substances such as PGE_2 and ATP. Recently, mas-related G protein-coupled receptor B2(MrgprB2) was identified as the Gi-coupled receptor for basic secretagogues, such as compound 48/80 (C48/80). Gi-coupled receptor signals are well known to up-regulate the Ag-induced MC activation. In this study, we examined the effect of C48/80 on Ag-dependent and independent degranulation in bone marrow-derived mast cells (BMMC). Stimulation of BMMC with Ag, high concentrations of ATP (hATP) or ionomycin triggered degranulation. These responses were enhanced by co-stimulation with PGE_2 via Gi-coupled EP3 receptor activation. In contrast, C48/80 unexpectedly suppressed Ag-induced degranulation without affecting the responses induced by hATP or ionomycin. The inhibitory action of C48/80 on Ag-induced degranulation was insensitive to pertussis toxin treatment. Although C48/80 did not affect Ag-induced increase in intracellular Ca^{2+} concentration, it suppressed Ag-induced phosphorylation of various proteins such as Syk and LAT. These results suggest that C48/80 selectively suppresses the Ag-induced degranulation in a manner independent of MrgprB2.