Mast cells are essential effector cells in IgE-associated immune responses. The major receptor for mast cell activation is the high affinity IgE receptor Fc epsilon RI. Fc epsilon RI crosslinking induces mast cell degranulation and de novo synthesis of potent proinflammatory mediators. Recent work identified Bcl10 and Malt1 as central regulators of a specific signaling pathway that controls NF-kappaB activation and proinflammatory cytokine production upon Fc epsilon RI ligation on mast cells. Bcl10 and Malt1 cooperate for the activation of this signaling cascade and selectively function downstream of PKC isoforms. However, Bcl10 and Malt1 are not involved in Fc epsilon RI- or PKC-induced signaling events that control degranulation or leukotriene synthesis. Thus, the Bcl10/Malt1 complex specifically uncouples the pathway for cytokine production from degranulation events. This review will summarize our current knowledge of the regulation of Fc epsilon RI-induced NF-kappaB activation in mast cells and discuss potential implications for allergic inflammatory diseases.