IκB kinase 2 is essential for IgE-induced mast cell de novo cytokine production but not for degranulation.

The immunoglobulin E (IgE)-mediated mast cell (MC) response is central to the pathogenesis of type I allergy and asthma. IκB kinase 2 (IKK2) was reported to couple IgE-induced signals to MC degranulation by phosphorylating the SNARE protein SNAP23. We investigated MC responses in mice with MC-specific inactivation of IKK2 or NF-κB essential modulator (NEMO), or animals with MC-specific expression of a mutant, constitutively active IKK2. We show that the IgE-induced late-phase cytokine response is reduced in mice lacking IKK2 or NEMO in MCs. However, anaphylactic in vivo responses of these animals are not different from those of control mice, and in vitro IKK2-deficient MCs readily phosphorylate SNAP23 and degranulate similarly to control cells in response to allergen or calcium ionophore. Constitutive overactivation of the NF-κB pathway has only slight effects on allergen-triggered MC responses. Thus, IKK2 is dispensable for MC degranulation, and the important question how IgE-induced signals trigger MC vesicle fusion remains open.