

Triggering of the High-Affinity IgE Receptor in an Aggregation- Independent Manner

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The high-affinity IgE receptor, FcεR1, is responsible for the sensitization of mast cells and basophils to IgE-targeted antigens. The current model of FcεR1 triggering rests on the principle of aggregation-driven phosphorylation, yet several recent observations have indicated that this is incomplete. Here we re-examine the minimal requirements for FcεR1 triggering and observe that it is induced without receptor aggregation by surface-associated antigen in a size-dependent manner. Using confocal microscopy and fluorescence correlation spectroscopy we determine that this is driven by exclusion of the large inhibitory phosphatase CD45 from the receptor-antigen contact, abrogation of which inhibits triggering. Such kinetic segregation (KS) of CD45 and FcεR1 also occurs in triggering-deficient cells and basophil-derived giant plasma membrane vesicles, and hence is a passive, steric process. Partial KS also occurs in cells forming surface contacts in the absence of FcεR1 ligand, leading to ligand-independent triggering that is responsible for the conventional morphology of basophilic cell lines in culture. The potential for both aggregation and KS mechanisms broadens the range of antigen capable of inducing triggering, and so affords the system substantially increased versatility.