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MAST CELLS' RESPONSES TO ALLERGEN CHALLENGE AND THEIR MODULATION

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The quest for novel therapeutic interventions becomes important due to increase in allergic and inflammatory disorders worldwide including developing countries like India. Allergic reactions predominantly are mediated by activation and degranulation of mast cells through cross-linking of their high affinity surface receptors FcεRI on binding of IgE and allergen. Mast cell activation leads to release of early phase pre-stored mediators and late phase newly synthesized cytokines. We explored if mast cells can be trained to become tolerant of allergen. RBL-2H3 mast cell line and primary bone marrow mast cells were used to study mast cell secondary responses to allergens and their modulation. For this study, cells were first sensitized with DNP-BSA specific IgE and treated with different combinations of DNP-BSA to mimic allergen challenge *in vitro*. Cells were further sensitized and treated with IgE and DNP-BSA for a secondary challenge. β-hexosaminidase release and cytokine expression was analysed after each allergen challenge. Surface receptor expression was also analysed. The β-hexosaminidase release was significantly decreased after secondary challenge. Secondary challenge also resulted in reduced pro-inflammatory cytokine expression at mRNA level. Further, use of inhibitors revealed that various signalling pathways and histone modifications are involved in such modulations. Our study revealed the mast cell responses can be modulated in vitro after a primary challenge, to become tolerant or less responsive to the next allergen challenge.

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