Intestinal Expression of Interleukin-9 Induces Mastocytosis and Mast Cell Activation

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Background: Clinical and experimental investigations have demonstrated a link between Th2 intestinal inflammation, antigen-specific IgE, and mast cell derived secondary mediators including histamine, serotonin, and platelet-activating factor (PAF) in the effector phase of food-induced anaphylaxis. The Th2-cytokine IL-9 is thought to play a central role in mastocytosis and mast cell activation.

Hypothesis: Overexpression of IL-9 in the intestine induces intestinal mastocytosis and also induces the expression of mast cell genes including mast cell protease (MCP) -1, -2, -4, and -5, and also the high affinity IgE receptor FCεR1α.

Methods: Jejunum segments were obtained from wild-type (WT) and IL-9 transgenic (TG) mice. Intestinal mast cell levels were determined by staining for chloroacetate estrase activity. cDNA was generated from jejunum RNA using standard techniques. Quantitative RT-PCR was performed on cDNA using primers specific for mouse mast cell protease 1, 2, 4, and 5, and also FCεR1α, the high affinity IgE receptor, and the housekeeping gene GAPDH.

Results: Ectopic overexpression of IL-9 in the intestine was associated with intestinal mastocytosis (12.63 $\pm$ 2.80 vs. 0.48 $\pm$ 0.24 mast cells/hpf, iFABPp-IL-9TG vs WT mice; $p < 0.05$). Levels of mMCP-1 (34.47-fold increase, $p=0.005$), mMCP-2 (97.12-fold increase, $p < 0.005$) mMCP-4 (10.09-fold increase, $p < 0.05$) and FCεR1α (4.57-fold increase, $p < 0.05$) expression in the jejunum of IL-9 TG mice was significantly elevated as compared to WT mice. In contrast, no significant difference in intestinal expression of mMCP-5 (1.5-fold increase, $p=1.0$) was observed in IL-9 TG mice as compared to WT mice.

Conclusions: These data establish that intestinal expression of IL-9 induces mastocytosis and the expression of the mast cell related genes, mMCP-1, -2, -4 and FCεR1α. These studies suggest that IL-9 may play an important role in food-induced intestinal anaphylaxis.