

photomicrographs in the article are striking and clearly visualize the effects of this innate immune mechanism. Interestingly, other studies have shown that this same molecule is also expressed in the airways and has antibacterial functions in the respiratory tract. Understanding the regulation and function of RegIII $\gamma$  may lead to new insights into the pathogenesis and treatment of inflammatory and infectious diseases in both anatomic locations.

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James E. Gern, MD  
Madison, WI

### **Galectin-9 Induced by Dietary Synbiotics Is Involved in Suppression of Allergic Symptoms in Mice and Humans**

de Kivit S, Saeland E, Kraneveld AD, et al. *Allergy*. 2012;67(3):343-352

**PURPOSE OF THE STUDY.** To investigate whether galectin-9 has a role in the mechanism of suppression of allergic skin reactions and mast cell degranulation induced by dietary synbiotics.

**STUDY POPULATION.** Three-week-old specific pathogen-free C3H/HeOuj mice were studied in a cow's milk allergy model with or without a probiotic or prebiotic. Ninety human infants with atopic dermatitis were studied in a double-blind, placebo-controlled multicenter trial in which they received a hydrolyzed formula with or without synbiotics.

**METHODS.** Mice were sensitized orally to whey while being fed a diet containing a specific prebiotic (9:1 mixture of short-chain galacto-oligosaccharides and long-chain fructo-oligosaccharides), a specific probiotic (*Bifidobacterium breve* M-16V), a combination of both, or a control diet (4 groups). Galectin-9 expression was determined by immunohistochemistry in the intestine and measured in the serum by enzyme-linked immunosorbent assay. T-cell differentiation was determined in the mesenteric lymph nodes as well as in galectin-9-exposed peripheral blood mononuclear cell cultures via expression of transcription factors T-bet, GATA-3, ROR $\gamma$ T, and Foxp3 along with cytokine production assays. Sera from mice were studied for the capacity to suppress mast cell degranulation. Sera from the 90 human infants were evaluated for galectin-9 levels.

**RESULTS.** Galectin-9 expression by intestinal epithelial cells as well as serum galectin-9 levels were increased in mice and humans after dietary intervention with the symbiotic combination (pre- and probiotic together). In mice, the levels correlated with reduced acute allergic skin reaction and reduced mast cell degranulation. In addition, the dietary synbiotics resulted in enhanced Th1- and T<sub>reg</sub>-cell differentiation in lymph nodes and

in peripheral blood mononuclear cell cultures exposed to galectin-9.

**CONCLUSIONS.** Dietary supplementation with a synbiotic (prebiotic short-chain galacto-oligosaccharides/long-chain fructo-oligosaccharides + probiotic *Bifidobacterium breve* M-16V) enhances serum galectin-9 levels which is associated with the prevention of expression of components of allergic responses.

**REVIEWER COMMENTS.** The results of this study show galectin-9, an epithelial product expressed in mucosal surfaces during inflammatory responses, is a significant component of the protective anti-allergy effect of synbiotic treatment. This effect is supported by data showing modulation of Th1- and T<sub>reg</sub>-cell polarization as well as immunoglobulin E sequestration (another study has shown strong binding of galectin-9 to immunoglobulin E) resulting in the reduced mast cell degranulation observed. Galectin-9 may be an important marker for the suppression of food allergy and further studies are warranted.

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Stuart L. Abramson, MD, PhD  
San Angelo, TX

### **TSLP Promotes Interleukin-3-independent Basophil Haematopoiesis and Type 2 Inflammation**

Siracusa MC, Saenz SA, Hill DA, et al. *Nature*. 2011;477(7363):229-233

**PURPOSE OF THE STUDY.** Allergic diseases involve epithelial surfaces, and the epithelial cytokine thymic stromal lymphopoietin (TSLP) has been described as the "master switch" for allergic inflammation. The purpose of this study was to determine how TSLP contributes to allergic disease pathogenesis.

**STUDY POPULATION.** Most studies were performed in mice. Human studies were performed with the use of basophils from patients with eosinophilic esophagitis or from healthy controls.

**METHODS.** TSLP-treated mice were evaluated for changes in circulating immune cells and cytokine secretion. The effect of tissue-specific TSLP production was determined by using transgenic mice overexpressing TSLP in the lung, or an atopic dermatitis model. Bone marrow cells were cultured with either TSLP or interleukin (IL)-3, and basophil differentiation was assessed. Characterization of TSLP-induced basophils from mice or humans was performed by the use of gene expression analysis and immune phenotyping.

**RESULTS.** Mice injected with TSLP had increased numbers of IL-4-secreting basophils in the spleen, as well as increased plasma levels of the pro-allergic T-helper type 2 (TH2) cytokines IL-4, IL-5, and IL-13. Endogenous

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Stuart L. Abramson

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