New target discovered for food allergy treatment

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Researchers at National Jewish Health have discovered a novel target for the treatment of food allergies. Erwin Gelfand, MD, and his colleagues report in the October 2012 issue of the *Journal of Allergy and Clinical Immunology* that levels of the enzyme Pim 1 kinase rise in the small intestines of peanut-allergic mice. Inhibiting activity of Pim 1 markedly reduced the allergic response to peanuts.

"Pim 1, and its associated transcription factor, Runx3, play a crucial role in allergic reactions to peanuts," said Dr. Gelfand, senior author and chair of pediatrics at National Jewish Health. "As such, they offer promising new targets for the treatment of allergic reactions to peanuts, and possibly other foods." Pim1 kinase is involved in many signaling pathways and is expressed in T cells and eosinophils, cell types linked to allergic diseases. Runx3 is a transcription factor associated with the regulation of T cells.

In a mouse model of food allergy, the researchers found that Pim1 kinase levels increased in the intestines of allergic mice that had been fed peanuts, as did various inflammatory cells and levels of cytokine molecules associated with allergies. Levels of Runx3 mRNA, however, dropped significantly in the allergic mice. When researchers administered a small molecule that inhibits the activity of Pim 1 kinase, mice no longer experienced diarrhea and other symptoms associated with their peanut allergy.

Plasma levels of histamine, a potent cause of allergy symptoms, dropped

to almost baseline levels after administration of AR460770, which is produced by Array Biopharma. Inflammatory mast cells, eosinophils, and CD4 and CD8 T cells all increased only slightly in response to peanuts. Levels of several cytokine signaling molecules associated with allergies, IL-4, IL-6 and IL-13, also dropped after treatment with the Pim 1 inhibitor. Runx3 mRNA, rose back to near baseline levels.

"Our data identified for the first time that Pim1 kinase contributes in important ways to the development of peanut-induced allergic responses, " said Dr. Gelfand. "Targeting this novel regulatory axis involving Pim 1 kinase and Runx3 offers new therapeutic opportunities for the control of food-induced allergic reactions."

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