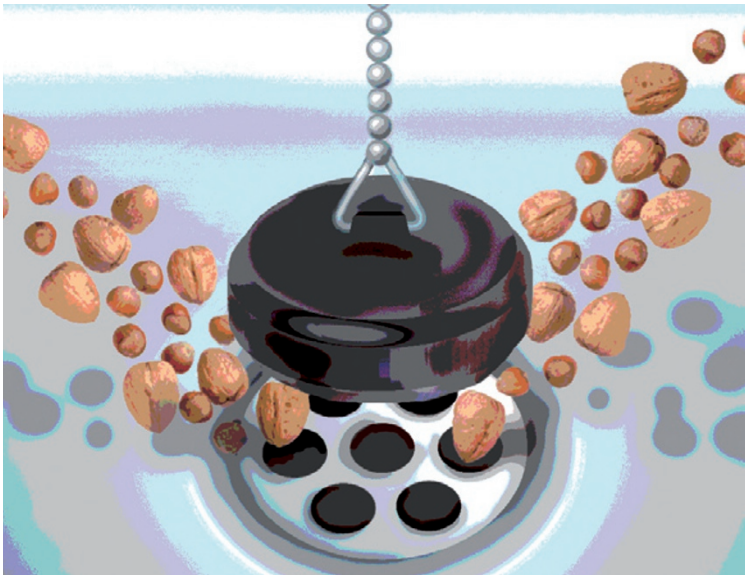
MAST CELLS

Food allergy unplugged

The prevalence of food allergy is on the increase. Yet how susceptible individuals become sensitized to food antigens remains poorly understood. Now, a report in *The Journal of Experimental Medicine* shows an important role for interleukin-9 (IL-9) and mast-cell-mediated gut leakiness in the induction of oral antigen hypersensitivity in mice.



IL-9 has previously been implicated in T helper 2 (T_H2)-cell driven allergic reactions in the airways, in which it has an important role in IgE production and mast-cell activation. So, Forbes *et al*. looked to see whether IL-9 might be similarly involved in allergic reactions in the gut induced by sensitization with ovalbumin (OVA) and subsequent oral challenge with OVA. Indeed, *Il9* mRNA levels in the small intestine were found to increase in wild-type mice with oral-antigen-induced intestinal anaphylaxis. Moreover, the intestinal anaphylaxis, characterized by mastocytosis, mast-cell activation and diarrhoea, was attenuated in IL-9-deficient mice. This attenuated phenotype was associated with fewer intestinal mast cells and lower levels of mast-cell protease 1 but not with a diminished T_H2-type response.

The role of IL-9 in increasing intestinal mast-cell numbers was confirmed using mice that overexpressed IL-9 specifically in the enterocytes of the small intestine. A comparison of the genes expressed in the intestine of these IL-9-overexpressing mice and of wild-type mice with oral-antigen-induced intestinal anaphylaxis revealed a similar profile, suggesting that IL-9 overexpression in the intestine is sufficient to promote an intestinal anaphylaxis-like phenotype. Interestingly, a prominent feature in both groups of mice was increased permeability of the intestine ('leaky gut'), a factor thought to predispose to gastrointestinal disease in humans. Consistent with this being a susceptibility factor, mice overexpressing IL-9 in the gut were more susceptible to oral-antigen-induced intestinal anaphylaxis, such that prior sensitization with OVA was not necessary for the induction of allergic disease following oral OVA challenge. Finally, a link between the leaky gut phenotype and mast cells was confirmed, by showing that mast-cell depletion abrogated the increased intestinal permeability in IL-9-overexpressing mice.

So, together these observations support a mechanism whereby IL-9 overexpression predisposes mice to oral antigen hypersensitivity by acting as a potent inducer of mastocytosis, which in turn increases intestinal permeability.

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ORIGINAL RESEARCH PAPER Forbes, E. E. *et al.* IL-9- and mast cell-mediated intestinal permeability predisposes to oral antigen hypersensitivity. *J. Exp. Med.* 31 March 2008 (doi:10.1084/jem.20071046)