Links:

Citrobacter rodentium
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=genomeprj&cmd=Retrieve&dopt=Overview&list_uids=13422

Cryptococcus neoformans
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=genomeprj&cmd=Retrieve&dopt=Overview&list_uids=9581

HOST IMMUNE RESPONSE

Bacteria provide a breath of fresh air

The outcome of infection with a particular pathogen is increasingly thought to depend on an individual's history of infection, not only with the same or similar pathogens (which might elicit a memory immune response) but also with unrelated pathogens. Accordingly, the immune response induced by one pathogen in the lungs has been shown to alter the response to subsequent pulmonary infection with an unrelated pathogen. Now, reporting in *The Journal of Infectious Diseases*, Tracy Hussell and colleagues show that infection with a gut-restricted bacterium modifies the immune response to pulmonary infection with a fungus, indicating that such immune modulation can occur not only within a single mucosal site but also following infection at a distal mucosal site.

Immune interaction is known to occur between mucosal sites, but the extent of this interaction between distant sites has not yet been determined. So, the authors set out to investigate how infection of the gut might affect subsequent infection of the lungs. They used a model in which mice were intragastrically infected with the gut-restricted bacterium *Citrobacter rodentium* and then, 14 days later, intranasally infected with the fungus *Cryptococcus neoformans*. Using histological analysis of tissue samples and flow-cytometric analysis of bronchoalveolar lavage fluid, mice that had been infected with *C. rodentium* were found to have a significantly lower load of *C. neoformans* and fewer infiltrating lymphocytes and eosinophils in the lungs than mice that had not been infected with *C. rodentium*.

To analyse further the extent of this immune modulation, the authors examined the T-cell subsets that were present in the lungs after *C. neoformans* infection. Previous infection with *C. rodentium* was found to result in a reduction in the number of activated $CD4^+$ T cells (also known as T helper (T_H) cells) but not activated $CD8^+$ T cells. Because eosinophilia is driven by T_H2 cells (one of the two main subsets of T_H cells), the authors then assessed the cytokine-expression profiles of the pulmonary $CD4^+$ T cells. Previous infection with *C. rodentium* was found to increase the number

of $CD4^+$ T cells expressing tumour-necrosis factor (a T_H1-cell cytokine) and decrease the number expressing interleukin-4 (a T_H2-cell cytokine), thereby shifting the balance of the immune response from a T_H2-cell-biased response to a T_H1-cell-biased response.

The finding that an intestinal bacterial infection can modulate T_H2-cell-driven pulmonary immunopathology contributes to our understanding of the 'hygiene hypothesis', which states that, in Western society, the increasing incidence of atopic diseases (such as hay fever and allergic asthma; which are T_H2-cell mediated) is associated with lack of exposure to T_H1-cell-inducing infectious agents in childhood.

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ORIGINAL RESEARCH PAPER Williams, A. E., Edwards, L. & Hussell, T. Colonic bacterial infection abrogates eosinophilic pulmonary disease. *J. Infect. Dis.* **11**, 223–230 (2006)