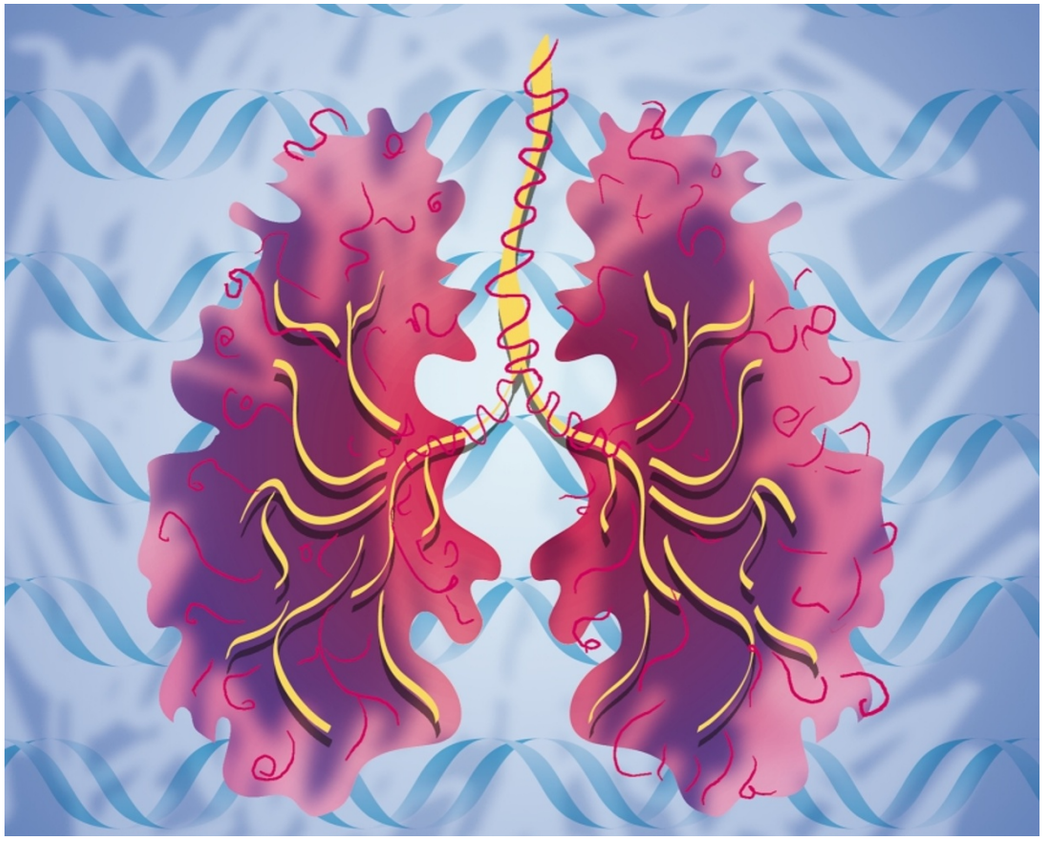

ALLERGY AND ASTHMA

New family ties to asthma

In addition to environmental factors, asthma has a strong genetic component, and several chromosomal regions are linked with susceptibility to asthma and allergy. Pinpointing actual genes within these regions is no easy task. By taking advantage of the similarities between mouse and human genomes, Jennifer McIntire and co-workers, reporting in *Nature Immunology*, have identified a new family of candidate asthma-susceptibility genes.

Asthma is a chronic debilitating disease that is characterized by airway hyperreactivity and inflammation. Allergic asthma is the most common form of the disease and is thought to result from immune responses to normally harmless inhaled antigens. This leads to the accumulation of effector cells, such as mast cells and eosinophils, and the release of inflammatory mediators. T-helper type 2 (T_H2) responses underpin the development of allergic responses. In this respect, it is intriguing that a region of human chromosome 5 associated with susceptibility to asthma (5q23–35) contains many genes that regulate T_H2-cell development — including the interleukins *IL4*, *IL5*, *IL13*, *IL9* and *IL12p40* — but none of these has yet been proven to be an asthma-susceptibility gene.

In this study, a classic genetic approach was used to investigate the effects of individual asthma-susceptibility loci in isolation from the influence of other traits. Allergen-induced airway hyperreactivity (AHR) in mice is an experimental model of asthma. Congenic mice strains were generated in which AHR-susceptible BALB/c mice carry small segments of chromosomes from resistant DBA/2 mice. The congenic mouse strains were then screened for reduced IL-4 production and resistance to AHR. This approach identified a susceptibility locus which is homologous with human 5q33, and has been named *Tapr* (T cell and airway phenotype regulator).

Fine mapping of the locus shows that *Tapr* is distinct from the *IL4* gene cluster, *IL12p40*, and other candidate genes found in the syntenic region of human chromosome 5. Positional cloning of *Tapr* uncovered a new family of three genes that are named *Tim*. Tim1, Tim2 and Tim3 are transmembrane proteins with extracellular immunoglobulin-like and mucin-like domains, and an intracellular tail with tyrosine phosphorylation sites. The human homologue of Tim1 is the hepatitis A virus receptor (HAVR), which might explain the inverse relationship between HAV infection and allergic diseases.

Sequencing of *Tim1* and *Tim3* showed major polymorphisms between the susceptible and resistant mouse strains. But how might Tim variants influence T_H2 development? The mechanism is not clear, but it seems that Tim expression by activated T cells early in activation might be crucial in controlling the polarization of T cells for T_H2-cytokine secretion.

Jennifer Bell

References and links

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ENCYCLOPEDIA OF LIFE SCIENCES Atopy and asthma

WEB SITE

The Umetsu lab: http://www.stanford.edu/~umetsu/

IN THE NEWS

Vaccine news from different worlds

It seems that vaccine development has never had such a high profile. With vaccines available against smallpox and anthrax, how exactly they should be used to combat the threat of bioterrorism has been a subject of debate in the US press. A feature in *The Washington Post* pointed out that existing vaccines to potential bioterrorism agents were "developed decades ago and can cause severe side effects or even death" and advised its readers against investing in vaccine development.

Although acknowledging the risks, Warren Leary, writing in *The New York Times*, advocated voluntary vaccination against smallpox — "even if only part of the population were vaccinated, the bang for the terrorist's buck could be drastically curtailed".

Meanwhile, ongoing efforts to develop vaccines for the big killers — HIV, malaria and tuberculosis — have not hit the headlines. Although the *BBC World Service* did report on a "promising" new malaria vaccine undergoing clinical trial in the Gambia. The low-key tone was perhaps appropriate given that the vaccine only protected 47% of individuals. Another report from the *BBC News* provided a timely warning that "Weak vaccines strengthen disease". This story covered the predictions of Edinburgh-based epidemiologists (originally published in *Nature* 13 December 2001) that, in the case of chronic diseases, such as malaria, vaccines that are less than 100% effective have the potential to do more harm than good. Specifically, vaccines that only protect a proportion of the population could lead to outbreaks of more virulent forms of disease and the news article claims that this "could kill more people that any vaccination programme would save".

Jennifer Bell