ALLERGY

Eliminating E from the class

What causes the all-too-familiar symptoms of sneezing or itchy eyes? Serum immunoglobulin (Ig) E, produced by antibody-secreting B cells, is the culprit. For most of us, IgE levels are kept low, but for an unfortunate few, IgE concentration becomes inappropriately elevated, giving rise to the activation of inflammatory cells and to the classic symptoms of allergy. In the January issue of *Nature Immunology*, Shimizu and colleagues elucidate the molecular mechanism that suppresses IgE production at the level of transcription, which makes this pathway a potential target for therapy.

Antibodies come in a five flavours, or isotypes, each of which has a distinct constant region in its heavy chains encoded by a specific gene. During an immune response, B cells begin by producing antibodies of the isotype IgM, and then a process called class switching — a molecular heavy-chain mix-and-match — permits the secretion of different antibody isotypes. This process, which occurs by transcriptionally regulated region-specific recombination involving deletion of the intervening DNA, does not markedly affect antibody specificity, but alters and diversifies the effector functions of the antibody.

The starting point for understanding the pathway to IgE class switching came from the demonstration that mice deficient in Id2 — a negative regulator of transcription — are impaired in specific aspects of immune function, and secrete large amounts of serum IgE. Shimizu and colleagues showed that there is a dramatic increase in the number of IgE+ B cells produced in response to immunization and that this reflects class switching to the E isotype. Id2 acts as a negative regulator of class switching by binding the E2A transcription factor, which promotes transcription at the E switch region. Not surprisingly, Id2-deficient B cells have increased E2A activity. Further studies showed that Id2 is regulated by the cytokine transforming growth factor (TGF) β1; the addition of the cytokine to wild-type B cells increased the levels of Id2 and suppressed class switching to IgE.

These results are exciting because the class-switching functions described for Id2 are very specific. Although IgE antibodies provide protection against a limited spectrum of parasites, other than that, would we really miss them?

Melanie Brazil

References and links

ORIGINAL RESEARCH PAPER Sugai, M. *et al.* Essential role of Id2 in negative regulation of IgE class switching. *Nature Immunol.* **4**, 25–30 (2003)
FURTHER READING Valenta, R. The future of antigen-specific immunotherapy of allergy. *Nature Rev. Immunol.* **2**, 446–453 (2002) | Kawakami, T. & Galli, S. J. Regulation of mast-cell and basophil funtion and survival by IgE. *Nature Rev. Immunol.* **2** 773–786 (2002)
WEB SITE
Encyclopedia of Life Sciences:
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Antibody classes | atopy and asthma

IN BRIEF

NEURODEGENERATIVE DISEASES

Novel therapeutic approach for the treatment of Alzheimer's disease by peripheral administration of agents with an affinity to β-amyloid.

Matsuoka, Y. *et al. J. Neurosci.* **23**, 29–33 (2003)

Plaques containing β-amyloid (Aβ) are one of the hallmarks of Alzheimer's disease, and so reducing levels of Aβ is thought to be a promising therapeutic strategy. Matsuoka *et al.* show that peripheral treatment with gelsolin, a protein that has high affinity for Aβ, reduced the level of Aβ in the brains of mice, which should encourage the development of novel agents to sequester plasma Aβ that are not limited by the need to penetrate the brain or evoke an immune response.

ANTI-MIGRAINE DRUGS

Prophylactic treatment of migraine with an angiotensin II receptor blocker: a randomized controlled trial.

Tronvik, E. *et al. JAMA* **289**, 65–69 (2003)

Currently available drugs to protect migraine sufferers from attacks have limited efficacy, and can cause adverse effects that are incompatible with long-term use. Tronvik *et al.* found that the angiotensin II type I receptor blocker candesartan, which is widely used as an antihypertensive drug, provided effective protection against migraine attacks without significant side effects.

OBESITY

C. elegans: a model for exploring the genetics of fat storage.

McKay, R. M. *et al. Dev. Cell* **4**, 131–142 (2003)

McKay *et al.* generated nematode worms (*Caenorhabditis elegans*) that lacked two genes crucial for fat formation in mammals, and found that worms deficient in either gene displayed a lipid-depleted phenotype. On the basis of this phenotype, further genes involved in worm lipid storage could be identified, indicating that *C. elegans* could be a valuable model to study the biology of fat accumulation, and hence aid the identification of potential therapeutic targets for obesity.

AUTOIMMUNE DISEASES

Leptin surge precedes onset of autoimmune encephalomyelitis and correlates with development of pathogenic T cell responses.

Sanna, V. *et al. J. Clin. Invest.* **111**, 241–250 (2003)

Sanna *et al.* show that the hormone leptin, which is well-known for its role in regulating food intake, but which also has effects on autoimmunity, actively contributes to the pathogenesis of experimental autoimmune encephalomyelitis — a model of multiple sclerosis (MS) — influencing its onset and severity. Their findings suggest that modulating leptin concentration through dietary approaches, and/or the administration of drugs that interfere with the leptin pathway, might be useful in the treatment of MS and other autoimmune diseases.