IN BRIEF

ASTHMA

CD4+ invariant T-cell–receptor+ natural killer T cells in bronchial asthma.

Akbari, O. *et al. N. Engl. J. Med.* **354**, 1117–1129 (2006)

Recent studies in mice by Akbari and colleagues have shown that a newly identified subgroup of T cells, the CD1d-restricted natural killer T cells, contribute to allergen-induced airway hyperreactivity. The same authors now provide evidence of the pathogenic role of this subset of cells in humans. They found that 60% of the pulmonary $CD4^+CD3^+$ cells in patients with moderate-to-severe asthma were natural killer T cells expressing an invariant T-cell receptor, Vα24Vβ11. Targeting these cells might therefore be a potential new strategy against asthma.

DRUG DELIVERY

Chronic, programmed polypeptide delivery from an implanted, multireservoir microchip device.

Prescott, J. H. *et al. Nature Biotechnol.* 12 March 2006 (doi:10.1038/nbt1199)

Implantable drug delivery devices are often limited by poor dosing flexibility. Prescott and colleagues report the successful programmed delivery of a nonapeptide, leuprolide, over 6 months from a microchip implanted in dogs. The microchip, measuring 15 × 15 × 1 mm, contains 100 reservoirs individually controlled by electrothermal activation. The chip can be used with both solution- and solid-phase drugs, and was able to sustain consistent pharmacokinetics and bioavailability measurements over the 6-month period.

DRUG DESIGN

Kinase patent space visualization using chemical replacements.

Southall, N. T. & Ajay. *J. Med. Chem.* **49**, 2103–2109 (2006)

Southall and Ajay describe an approach to searching patented chemical space that enables chemists to understand how compound series relate to one another. They catalogued chemical replacements (patterns of regular chemical substitution into a chemical series) and present results for a set of kinase inhibitors that uncovered chemical themes that others have used to design patents within this chemical space. The strategy could be extended to searching for toxicophores or for characterizing the SARs of patented chemical series.

ALZHEIMER'S DISEASE

Early onset behavioral and synaptic deficits in a mouse model of Alzheimer's disease.

Jacobsen, J. S. *et al. Proc. Natl Acad. Sci. USA* **103**, 5161–5166 (2006)

Evidence suggests that neuronal dysfunction in Alzheimer's disease (AD) might occur before the accumulation of β-amyloid (Aβ) plaques and neurodegeneration. Jacobsen and colleagues looked at morphological, functional and behavioural parameters in the Tg2576 mouse model of AD and found that neuronal deficits could be temporally clustered; for example, 4–5-month-old mice had decreased dendritic spine density, impaired long-term potentiation, memory loss and increased fraction of Aβ42. The reduction in spine density as an early indicator of pathology has potential as a biomarker for AD drug development.