Research news

A new HIV hideout

A recent study challenges the commonly held belief that the first cells to be infected by sexually transmitted SIV and HIV are dendritic cells and macrophages. Zhang *et al*. report in the 12 November issue of *Science* that after intravaginal SIV inoculation or sexual transmission of HIV, $CD4^+$ T cells were the main sites of retroviral replication. Even more unexpectedly, it was not only activated T cells that became infected, but also resting T cells. Low-level but consistent viral replication was detectable in $CD4^+$ cells lacking the activation markers HLA-DR, Ki67, CD25, and the proliferation-related antigens cyclin D3, cdk6 and PCNA. During treatment with anti-retroviral therapy, the number of active $CD4^+$ T cells carrying viral RNA decreased rapidly, but the number of resting $CD4^+$ cells containing viral RNA remained about the same. Thus the resting T-cell compartment may be an ideal HIV hideaway—a finding that may explain viral persistence after highly active antiretroviral therapy.

E2F decoys for vein-grafts

A recent double-blind clinical trial has shown that intraoperative gene therapy with E2F 'decoys' safely and effectively prevents vein graft failure. Vascular proliferative disorders, such as restenosis after angioplasty, bypass-graft failure and atherosclerosis are complications that frequently arise after vascular bypass surgery. Current experimental approaches to inhibit neointimal hyperplasia and graft atherosclerosis include blockade of the cell cycle transcription factor E2F by *ex-vivo* gene therapy, an approach that has proven successful in rabbits receiving experimental vein grafts. In the 30 October issue of *The Lancet*, Mann *et al.* report that E2F blockade with a double-stranded decoy oligodeoxynucleotide inhibits cell cycle progression and cell proliferation in the grafted tissue. Intraoperative treatment of 17 patients with the E2F 'decoy' was associated with fewer graft occlusions, revisions or critical stenoses for up to 12 months, and the absence of postoperative complications associated with gene therapy. Future large-scale clinical trials are required, however, to determine the efficacy of this approach in the routine prevention of vascular bypass complications

Chromosome 22 sequencing completed

The human genome project has reached a major milestone, reporting the first complete sequence of a human chomosome. Using the 'clone-by-clone' strategy, an international consortium led by the Sanger Center sequenced chromosome 22, and are publishing the results in the 2 December issue of *Nature*. Chromosome 22 is the second-smallest of the human autosomes and constitutes 1.6–1.8% of the human genome. This gene-rich chromosome encodes at least 545 genes, a third of which are of unknown function. Chromosome 22 also contains a high number of pseudogenes (134), and about 40% of the chromosome is composed of repetitive sequences. Much of the chromosome had already been mapped before the human genome project began, as deletions and translocations in chromosome 22 have been associated with a wide variety of disorders. These include chronic myelogenous leukemia, breast cancer, immunoglobulin deficiencies, Ewing's sarcoma, DiGeorge Syndrome, spinocerebellar ataxia, meningioma, neurofibroblastoma, and cat-eye sydrome. The complete sequence and analysis are available at http://www.sanger.ac.uk/HGP/Chr22 and http://www.genome.ou.edu/Chr22.html.

Oral defense with cathepsin C

Regular brushing, flossing and swilling of mouthwash make for good dental hygiene, but warding off infection by the billions of microbes in our oral cavity also depends on the immune system. In the December issue of *Nature Genetics*, Nalin Thakker and colleagues report that cathepsin C is an essential factor in defending against peridontal infection. The authors show that *CTSC*, encoding cathepsin C, is mutated in people with Papillon-Lefevre syndrome (PLS), a hereditary disorder characterized by severe and early-onset periodontitis, which causes premature tooth loss. Cytotoxic T lymphocytes and natural killer cells require cathepsin C to produce granzymes A and B, the secreted proteases that destroy infected cells as well as the cellular mediators of the inflammatory response. In PLS, loss of cathepsin C function probably renders the oral epithelium susceptible to invading bacteria and the damaging effects of inflammation. Cathepsin C may also be involved in processing specific types of keratin that maintain the structural organization of the oral epithelium that forms a mechanical barrier to bacteria. *CTSC* mutations that cause partial loss of cathepsin C activity might be associated with common late-onset forms of periodontitis, and future studies of cathepsin could reveal ways of preventing and treating gum disease.

Bone marrow donation of asthma

In addition to histocompatability matching, the allergenic status of bone marrow donors should be a matter for consideration, according to data presented last month at the 65th annual American College of Chest Physicians meeting. In a study of whether IgE-mediated hypersensitivity can be transferred by B lymphocytes during bone marrow transplantation, Anthony Gal's team at Emory University School of Medicine (Atlanta, Georigia) found a high prevalence (73%) of allergen sensitivity transfer from a positive donor to a negative recipient. This is compared with an only 2.3% chance of an allergy developing when both donor and recipient test negative for allergic reactions. In two cases of sensitivity transfer, bone marrow recipients who did not have a history of asthma subsequently developed the allergic condition, which was controlled with anti-asthma medication, one year after transplantation from an asthmatic sibling. These findings add to a growing body of evidence showing that diseases can be transmitted after organ transplantation. Cases of viral infections, certain malignancies and dermatitis being transferred during organ transplantation have been documented since the mid-1980s.

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