# Research News

## Immunoregulation of diabetes

By manipulating the cells that suppress the immune response, researchers have developed a new approach to preventing diabetes in mice. Type 1 diabetes occurs when the immune system attacks healthy insulin-producing cells in the pancreas. In the 20 November issue of the *Proceedings of the National Academy of Sciences*, Naumov *et al.* report that CD1d-restricted invariant natural killer T (iNKT) cells prevent diabetes in mice. iNKT cells regulate the immune response to ensure that only diseased tissue is targeted for attack. The authors found that the relative numbers of iNKT cells from the pancreatic islets decrease at the time of conversion from periinsulitis to invasive insulitis in the NOD mouse model of diabetes. Conversely, NOD mice that had a low incidence of diabetes had an increased number of iNKT cells. iNKT cells are activated by the lipid α-galactosylceramide, which is presented to them by CD1d on the surface of dendritic cells. Administration of α-galactosylceramide prevented diabetes in NOD female mice, and also led to accumulation of iNKT cells and dendritic cells in pancreatic lymph nodes. They suggest that administration of α-galactosylceramide or other means of activating NKT cells could be preventive for people with a genetic risk of developing diabetes.

## Creutzfeldt–Jakob gene

People who lack a specific immune response gene may be three times more likely to suffer new-variant Creutzfeldt–Jakob disease (CJD), according to a study published in the 15 November issue of *Nature*. CJD is fatal neurodegenerative disease thought to develop in people exposed to the infective bovine spongiform encephalopathy agent from 'mad' cows. However, little is known about whether there is a genetic predisposition for contacting CJD. Collinge and colleagues performed a genetic analysis of 50 patients with vCJD—approximately half the population known to have the disease. They found that almost one-third fewer patients carried the *DQ7* gene, compared to the rest of the population. The *DQ7* gene encodes a member of the HLA complex that is involved in immune activation. However, the gene does not seem to offer protection against the sporadic form of the disease, in which infectious prions are thought to form spontaneously in the brain instead of through ingestion of contaminated meat products.

## Antibiotic sweat


AP Photo/Tina Fineberg

Most people don't associate sweat with disease resistance, but a recent report suggests sweating can actually help fight infection. In the December issue of *Nature Immunology*, Schittek *et al.* show that human sweat contains an antimicrobial peptide that is active against a wide spectrum of pathogenic microorganisms, including *E. coli*, *E. faecalis*, *S. aureus* and *C. albicans*. Dermicidin is a 47-amino-acid peptide produced in the sweat glands and secreted into sweat. A proteolytically processed form of the protein is then transported to the skin surface. The authors report that the peptide was found to maintain its activity in the acidic, high-salt concentration conditions characteristic of sweat. Two other antimicrobial peptides, cathelicidins and β-defensins, have been previously found to be expressed by skin cells. Dermicidin joins immunoglobulin A, interleukins-1, -6 and -8, and tumor necrosis factor-α as immunoproteins detected in human sweat. The peptide may provide one of the first lines of defense against invading microorganisms.

## Nano-nukers

Scientists have created a molecule-sized atomic generator that can enter cancer cells and emit a single high-linear-energy α-particle that destroys the tumor. In the 16 November issue of *Science*, McDevitt *et al.* report the use of these 'nanogenerators' to kill leukemia, lymphoma, breast, ovarian, neuroblastoma and prostate cancer cells *in vitro*. The generator consists of actinium-225 coupled to a monoclonal antibody against a tumor antigen. Actinium-225 has a 10-day half-life, and as it decays, it emits high-energy cytotoxic α-particles. The authors injected the nanogenerators into mice bearing prostate or lymphoma xenografts, and report reduced tumor growth and increased survival times. Because the generators are highly potent, only small amounts of radioactivity need be administered therapeutically, and the treatment was non-toxic to normal cells. Actinium-225 has a relatively long half-life, allowing the nanogenerators to have better penetration of large tumors than previously tested α-emitting radionuclides. The long half-life also makes it possible for these generators to be produced at a central radiopharmacy and shipped throughout the world.

## Hypertrophy prevention

Although statin drugs are best known for their ability to block cholesterol biosynthesis, they also have a variety of other biological effects. Statins are widely prescribed to people with high serum cholesterol and are at risk of developing atherosclerosis. In the 14 November issue of the *Journal of Clinical Investigation*, Takemoto *et al.* report that these drugs might also be useful in treating a different cardiovascular condition—cardiac hypertrophy. Cardiac hypertrophy is a result of the adaptive response to increases in blood pressure. This causes cardiac myocytes to undergo changes in cell size and contractility that can lead to congestive heart failure. The Rho family of small GTP-binding proteins, which have been previously associated with cytoskeletal regulation and with cardiac hypertrophy, are regulated by a lipid modification known as isoprenylation. Statins, which block mevalonate biosynthesis, prevent formation of a variety of lipid metabolites, so the authors tested to see if they inhibited activation of Rho proteins. They found that statin treatment prevented Rho activation in cardiac myocytes, and also prevented cardiac hypertrophy in rats. The anti-hypertrophic effect occurred even when cholesterol was restored to the cells, suggesting that statins' clinical benefits extend beyond prevention of cholesterol synthesis.

**By Kristine Novak**