NEWS UPDATES

Hydrogen sulfide freezes mice

Mice exposed to hydrogen sulfide (H_2S) in their oxygen (O_2) supply fall into a state of suspended animation reminiscent of hibernation, according to a new study. If the gas affects humans similarly, it could someday become a lifesaving treatment with a wide range of applications, from heart attacks to organ transplantation.

Hydrogen sulfide is a colorless, noxious gas with the offensive stench of rotten eggs. There is evidence that H_2S, which is produced by the human body, competes with O_2 in mitochondria, suggesting that it may reduce metabolic rate in mammals. To test this hypothesis, a team of researchers at the University of Washington, Seattle, and the Fred Hutchinson Cancer Research Center (Seattle, WA) exposed mice to air containing 80 p.p.m. of H_2S. Within 5 min the mice fell into a deep sleep; by the 6th hour of H_2S exposure, the animals' metabolic rate had dropped by ~90% and the average core body temperature had been reduced from 37 °C to a minimum of 11 °C. In addition, CO_2 output and O_2 consumption dropped to ~10% of normal, with the mice taking fewer than 10 breaths/min, compared with 120 breaths/min when exposed to normal air (*Science*, 22 April).

When returned to normal air, the animals woke up and their metabolic rate and core body temperature returned to normal. The researchers submitted the mice to behavioral and functional testing and found no adverse effects to the H_2S-exposed mice. If H_2S proves to produce an equally extreme metabolic slowing effect in humans, potential applications could include preservation of organs for transplant and reduction of bleeding in trauma victims.

Gene therapy stops the bleeding

Using gene therapy, researchers have corrected hemophilia A (HA) in dogs and mice, potentially paving the way to a cure for the oldest known hereditary bleeding disorder in humans.

Hemophilia A is an X-linked bleeding disorder characterized by a deficiency in clotting Factor VIII (FVIII). About 1 in 5,000 males are born with HA, which ranges widely in severity. The usual treatment of HA with FVIII injections can be expensive and inconvenient; in addition, up to one-third of patients develop antibodies to the injected protein. Previous attempts at correcting HA in large animals using gene therapy have produced unsatisfactory results.

Now, a group led by Katherine P. Ponder of the Washington University School of Medicine (St. Louis, MO) reports success in using gene therapy to correct HA in dogs and mice. Because the liver is a site of FVIII production in nonhemophiliacs, the team used a retroviral vector to deliver a truncated version of the FVIII gene with a liver-specific promoter to the livers of neonatal HA dogs and mice. The treated animals churned out therapeutic levels of FVIII (*Proc. Natl. Acad. Sci. USA*, 26 April), and none of the animals had mounted an immune response to the FVIII as of 1.5 years after treatment. If this gene therapy approach proves reasonably safe, with a low risk of side effects such as insertional mutagenesis, its use could one day cure humans with HA.

Tracking down the source of HDL

Most of the 'good' cholesterol produced in the body is synthesized in the liver, according to a new study in mice.

A person's blood concentration of high-density lipoprotein (HDL) is inversely proportional to his or her risk of cardiovascular disease, but the site of HDL biogenesis has been unclear. Knowing that Tangier's disease, which is characterized by extremely low HDL levels, develops when a mutation in the *ABCA1* gene is present, John S. Parks of Wake Forest University School of Medicine (Winston-Salem, NC) and his colleagues created a strain of mice in which they specifically knocked out the *Abca1* gene in the liver. These mice produced 80% less HDL than their wild-type littermates, suggesting that the liver is the most important source of plasma HDL (*J. Clin. Invest.*, May). This new understanding of HDL production may help researchers develop ways to increase HDL levels in patients at risk for atherosclerosis.