› NEWS UPDATES

NO treatment for septic shock

Septic shock occurs when acute inflammation, low blood pressure and blood clotting cause blood delivery to the organs to slow dangerously, resulting in lack of oxygen followed by progressive organ failure. Septic shock is the leading cause of death in intensive care units; mortality rates may exceed 70%. The mechanisms underlying development of septic shock are not completely understood. Nitric oxide (NO) is thought to contribute to the hypotension component, but past attempts to inhibit NO production in animal models and human patients with septic shock resulted in more organ damage and higher mortality rates. New research from Anje Cauwels, Peter Brouckaert (Ghent University, Belgium) and colleagues now suggests that NO may protect against organ damage and mortality from septic shock.

Cauwels and Brouckaert used mouse models of septic shock and treated these mice with nitrite, which can be reduced to NO in the body. Mice that received nitrite experienced less hypothermia, mitochondrial damage, oxidative stress tissue infarction and mortality than did the mice that received no nitrite (*J. Exp. Med.* **206**, 2915–2924; 2009).

How exactly NO exerts its protective effects will be the subject of future research. For now, these results suggest that reinforcing rather than blocking the effects of NO may be a more successful treatment for septic shock.

Internal clock helps regulate blood pressure

Mice lacking a functional circadian clock have salt-sensitive hypertension, researchers report (*Nat. Med.* published online 13 December 2009; doi:10.1038/nm.2061). These *Cry*-null mice lack the Cry1 and Cry2 proteins that are essential for keeping the self-sustained daily rhythm of the circadian clock going.

Hitoshi Okamura of Kyoto University (Japan) and colleagues sampled plasma concentrations of the hormone aldosterone, which promotes salt and water retention, from *Cry*-null mice and wild-type control mice that were kept in constant darkness. The *Cry*-null mice had consistently elevated aldosterone levels that, unlike the levels in the control mice, exhibited no circadian fluctuation. Further analysis showed the adrenal glands of the *Cry*-null mice hyperexpressed the gene *Hsd3b6*, which led to increased aldosterone production.

The researchers also compared the blood pressures of the *Cry*-null and control mice. The *Cry*-null mice exhibited none of the circadian variation in blood pressure shown by the control mice. Since aldosterone-dependent hypertension might be related to sodium intake, the researchers also studied the sensitivity of the blood pressure of the mice to salt intake. On the high-salt diet, the *Cry*-null mice developed elevated blood pressure, whereas the blood pressure of the control mice was unaffected. Future research will focus on whether the gene *HSD3B1* expressed in human adrenal glands, which is similar to *Hsd3b6*, has a role in salt-sensitive hypertension.

Producing iPS cells more efficiently

Since Shinya Yamanaka and his colleagues produced the first induced pluripotent stem (iPS) cells from adult mouse cells in 2006, researchers have been developing more efficient methods to reprogram somatic cells into an embryonic-like state. Now, two teams of researchers have shown that they can reprogram adult mouse cells into iPS cells by using only one genetic insertion (*Nat. Methods* published online 13 December 2009; doi:10.1038/nmeth.1409 and 10.1038/nmeth.1410).

These methods, developed by Konrad Hochedlinger of Harvard University, Rudolf Jaenisch of the Massachusetts Institute of Technology (Cambridge, Massachusetts) and colleagues, improve upon previous procedures that required multiple genetic insertions. The research teams combined the four reprogramming genes required for iPS cell production (*Oct4*, *Klf*, *Sox2* and *c-Myc*) onto a piece of DNA. They then inserted this piece of DNA into one locus in the mouse genome and bred the mice. To activate the expression of the reprogramming genes, the researchers fed the mice the antibiotic doxycycline.

The research teams were able to easily breed and maintain these 'reprogrammable mice'. These new methods simplify the iPS production process and will allow researchers to produce iPS cells that they can compare with genetically identical embryonic stem cells.