Heart sealant

A molecular 'glue' counteracts heart failure in a mouse model of Duchenne muscular dystrophy, report Soichiro Yasuda *et al.* in *Nature* (doi:10.1038/nature03844).

Heart failure is the second most common cause of death among people with this disease, which is due to a deficiency in the protein dystrophin. But exactly what is wrong with the cells in the heart has been unclear.

The researchers found that heart muscle cells in dystrophin-deficient mice did not stretch well. The cells tended to break under strain, causing calcium ions to flood the cell through small tears in the membrane, suggest the researchers. That influx would result in hypercontraction and cell death.

The researchers asked whether repairing the tears could counteract pathology. They patched the tears with poloxamer 188, a drug that slips into lipid layers and repairs biological membranes. The drug was able to restore stretch to heart muscle cells and alleviate symptoms of heart failure in dystrophin-deficient mice.

Poloxamer 188 is in phase 3 trials for short-term use in individuals with sickle-cell anemia. But another study investigating its long-term use ended early because of muscle pain, so hurdles remain before the drug might be used in muscular dystrophies. —*JB*

Protect the matrix

A drug that helps prevent breakdown of the extracellular matrix counteracts brain damage in a mouse model of stroke, report Zezong Gu *et al.* in the 6 July *Journal of Neuroscience* (25, 6401–6408). The drug takes aim at specific protein in of the matrix metalloproteinase (MMP) family.

Previous work has found that MMPs, in particular MMP-9, operate in a range of neurological conditions, including stroke. In mouse models of ischemic stroke, for instance, MMP-9 levels spike—this drives neuronal cell death, presumably because cells have lost life-giving contact with the extracelluar matrix. Compounds that inhibit MMPs can counteract the effects of stroke in animal models, but such drugs have fallen from favor because they target a range of MMPs and have multiple side effects.

Enter SB-3CT. Gu *et al.* found that this MMP-9 inhibitor reduced the size of brain damage to about one-third of that of the untreated mice when injected 2 hours after ischemic stroke. The researchers found that the drug interferes with the ability of MMP-9 to degrade the extracelluar matrix component laminin.—*CS*

Guts of the hygiene hypothesis

Bacteria that live in the gut may protect against the development of allergies, suggests a study in the 15 July *Cell* (**122**, 107–118).

Previous studies have shown that mice housed in germ-free environments had systemic immune defects. Sarkis Mazmanian *et al.* also found this to be the case, reporting that germ-free mice had fewer T cells and underdeveloped spleens compared to mice that had a normal assembly of microflora. The investigators could trace the protective effect to a single type of sugar molecule, polysaccharide A (PSA), on the surface of an abundant gut bacterium, *Bacteroides fragilis*. They found that colonization of the gut with only this bacterium restored the health of the spleen and the number of immune cells. What's more, purified PSA alone could rescue the immune defects, whereas *B. fragilis* lacking PSA could not.

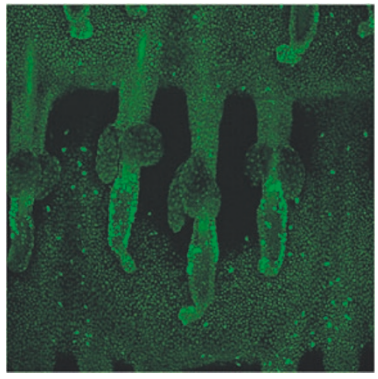
Written by Allison Alcivar, Jasmine Bhatia and Charlotte Schubert.

Mazmanian *et al.* provide evidence that gut bacteria help maintain the balance of T helper (T_H) cell subsets. Germ-free mice mostly secreted T_H2 cytokines, which mediate allergic responses, whereas colonization of the gut with bacteria promoted the expression of T_H1 cytokines, which stimulate T-cell proliferation. In line with that, the investigators found in cell culture that PSA-presenting dendritic cells caused T-cell proliferation and induced secretion of T_H1 cytokines.

The researchers believe these results bolster the 'hygiene hypothesis,' which holds that increased antibiotic use and better sanitation has fostered the rise in allergies seen in developed countries. —*AA*

Mass immobilization

Stem cells in the skin misbehave in mice with shortened telomeres according to a study in the 21 July *Science* (doi:10.1126/science.1115025).



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Stem cells cluster in a region of the hair follicles in skin (four follicles shown, BRDU-labelled cells in green).

Normally, adult stem cells can proliferate, and their progeny leave the stem cell 'niche'—a process called mobilization. Ignacio Flores *et al.* found that in mice with shorter telomeres, the stem cells seemed to hide out in their niche, responding poorly to signals to proliferate and mobilize.

The authors next examined mice that overexpressed telomerase, an enzyme that puts telomeres on the ends of chromosomes. These mice had low numbers of stem cells in the niche due to increased mobilization. Normally these mice have increased susceptibility to cancer. The results suggest that there may be a relationship between telomere length and health of stem cells, thought to give rise to cancers.

Aberrant stem cell function may also underlie aging, according to some theories. But whether there is a direct relationship between telomere length and stem-cell mobilization with age remains to be seen. —*CS*

Rickets revealed

Rickets, once a common scourge because of vitamin D deficiency, is not conquered. The disease also occurs in many hereditary disorders, including those associated with reduced phosphate levels. The exact molecular events behind rickets have been unclear and in the 5 July *Proceedings of the National Academy of Sciences*, Yves Sabbagh *et al.* outline a mechanism (**102**, 9637–9642).

During normal bone development, bone-forming cells called chondrocytes, cells that secrete cartilage, proliferate and then eventually die by apoptosis. In rickets, this cell death is impaired.

The researchers examined mouse models of rachitic disorders and found that the lack of phosphate seemed to underlie the persistence of chondrocytes. The results suggest that during normal bone development, circulating phosphate promotes chondrocyte apoptosis and holds rickets at bay—all downstream of vitamin D. The investigators next plan to find the phosphate sensor or transporter on chondrocytes responsible for mediating cell death. —*CS*