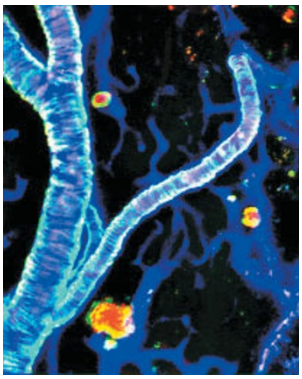
Visualizing amyloid plaques



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The only sure diagnosis for Alzheimer disease comes after death, when the telltale signs of β-amyloid plaques and tangles can finally be revealed. The quest to develop tests for Alzheimer disease has focused in large part on developing compounds that recognize signs of illness in the brain by techniques such as positron emission tomography (PET).

In the 26 September online edition of *PNAS*, Brian Backsai *et al.* tested the visual boundaries of Pittsburgh compound B (PIB), a fluorescent compound that binds to amyloid plaques. By inserting a glass coverslip into skulls of the mice, they were able to trace the path of the compound using a specialized type of microscopy called multiphoton microscopy. PIB quickly entered the brain, and within minutes the compound labeled amyloid deposits in transgenic animal models of Alzheimer disease. The nonspecific binding cleared quickly (blue pseudocolor indicates distribution of the biomarker immediately after i.v. injection, green 5 minutes later, and red 20 minutes later). PET scanning produces images distinct from those revealed by multiphoton microscopy, but the new results bode well for gearing up to visualization methods more applicable in humans.

Building a 'magic bullet'

Researchers have built a protective shell around a cytokine, increasing its half-life and targeting it directly to sites of inflammation, according to a report in the November *Nature Biotechnology*.

Gill Adams *et al.* took interferon-β (IFN-β), a cytokine with modest therapeutic effect in some autoimmune diseases, and built it a shell using a fragment of transforming growth factor-β. The shell was attached to the cytokine by domains specifically cleaved by matrix metalloproteinases (MMPs), enzymes concentrated in areas of inflammation or tissue remodeling. The shell sterically hindered the interaction of IFN-β with its receptors, boosted its half-life to 55 hours and restricted its activation to areas expressing MMPs.

The authors found that fluid from the joints and spinal cords of rheumatoid arthritis patients and monkeys with experimental autoimmune encephalomyelitis specifically activated the protected cytokine. Injection of a plasmid expressing the engineered cytokine also inhibited paw swelling and other clinical symptoms in a mouse model of arthritis.

The investigators suggest that the redesigned cytokine could work more effectively and cheaply than the currently used form of IFN-β, which is prescribed for some autoimmune diseases, including multiple sclerosis. The new cytokine could be effective in a variety of illnesses in which MMPs are expressed, including osteoarthritis, rheumatoid arthritis, multiple sclerosis and cancer.

Written by Charlotte Schubert and Pierrette Lo

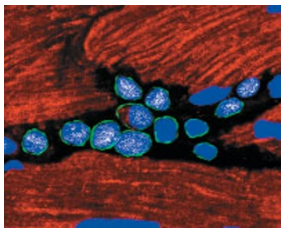
Hope for hepatitis C

The results of a small but dramatic clinical trial raise hope for an effective drug against the hepatitis C virus (HCV), which infects over 170 million individuals worldwide. In the 26 October online edition of *Nature*, Daniel Lamarre *et al.* examined a protease inhibitor specifically designed to inhibit the viral NS3 protease, essential for viral survival. The drug, BILN 2061, passed all preclinical hurdles and was tested in a group of 10 patients with HCV. Administration of the drug resulted in substantial reduction of HCV plasma RNA after only one or two days, reaching undetectable levels within 24–28 hours in some patients. No serious side effects occurred, and liver function appeared normal. The investigators note that protease inhibition, in addition to stopping the virus itself, might also lead to restoration of an antiviral response mediated by IFN regulatory factor-3. Longer clinical trials are pending.

Beyond nerves

It's not the nerves, but the cells around them that seem to cause an inherited form of amyotrophic lateral sclerosis (ALS), according to a report in the 3 October *Science*. Most cases of ALS arise spontaneously, but about 2% are caused by inherited mutations in the gene for superoxide dismutase (SOD-1). SOD-1 mops up free radicals, and defective SOD-1 is toxic to cells in culture. But researchers have been puzzled by results in whole animals: mice overexpressing SOD-1 only in neurons seem quite healthy. Albrecht Clement *et al.* created SOD-1 chimeric mice with both normal cells and cells overexpressing a defective SOD-1 polypeptide. The investigators found that normal motor neurons in the chimeric mice developed aspects of ALS pathology. Non-neuronal cells that did not express SOD-1 delayed degeneration and extended survival of mutant SOD-1–expressing motor neurons. The authors concluded that cellular context is key.

Cardiac stem cells



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The human heart does not bounce back well after myocardial infarction or other types of damage. Now, a report in the 19 September *Cell* uncovers a hidden population of cardiac stem cells, raising hopes for future regenerative therapies. To date, much of that hope has focused on stem cells in the bone marrow, which seem to have some ability to contribute to heart tissue. Antonio Beltrami *et al.* found that the newly identified cells appear distinct from these marrow cells in several ways, including the expression of the cell surface protein c-Kit (green; stem cell DNA, blue; α-sarcomeric actin, red). The cardiac stem cells, isolated from older rats, were expandable indefinitely in culture and gave rise to multiple types of cardiac tissue. What's more, the cells were able to repair damage when injected into rats after myocardial infarction. The very existence of the cells unveils another mystery: if these cells lie dormant in the heart, why do they not activate and divide in response to injury?