

## RESEARCH HIGHLIGHTS

## CHEMISTRY

## Express delivery

*Org. Biomol. Chem.* doi:10.1039/b504988a (2005)  
It is difficult to design drugs that can cross the blood–brain barrier. But a team led by Jean Louis Kraus of the Mediterranean University in Marseilles, France, has found that ascorbic acid can act as a delivery vehicle.

Ascorbic acid is actively transported from the blood to the brain, where it has a protective function. The researchers showed that attaching ascorbic acid to a drug called DAPT, used to treat Alzheimer's disease, dramatically increased DAPT uptake into the brains of live mice. Furthermore, the drug's activity *in vitro* was increased by linking it to ascorbic acid.

## EARTH SCIENCE

## Taking the strain

*Earth Planet. Sci. Lett.* 234, 421–435 (2005)  
Monitoring barely perceptible tremors could reveal whether geological slip faults are likely to spawn larger earthquakes, propose Rocco Malservisi, now at the Ludwig Maximilian University of Munich, and his colleagues.

The researchers studied the Hayward fault, which is part of the San Andreas fault system in California. The build-up of strain along this slip fault is gently released as segments of rock creep past each other. But jammed regions have triggered significant earthquakes in the past. Modelling the 'microquakes' allowed the researchers to map the jammed areas far below the surface.

## STEM CELLS

## Cancer source

*Cell* 121, 823–835 (2005)  
The starting point for some lung cancers (pictured right) may be a newly discovered type of stem cell, according to Tyler Jacks's team at the Massachusetts Institute of Technology in Cambridge.

The team discovered a population of stem cells that produce some of the lung's specialized cells — both Clara and alveolar epithelium cells. Experiments in a mouse model for lung cancer implicated these stem cells in the formation of tumours. The *K-Ras* cancer gene that initiates tumours in mice was shown to drive proliferation of the stem cells, and tumours developed in regions where stem cells were found. Lung injuries that increased the incidence of tumours also boosted the number of stem cells, suggesting that these cells explain the link between tissue damage and lung cancer.

## Bad vibrations

*Anim. Behav.* doi:10.1016/j.anbehav.2004.09.019 (2005)  
Tree-frog embryos have a remarkable ability to hatch early when their eggs are attacked by snakes. This depends on sophisticated sensing of vibrational cues, reports Karen Warkentin of Boston University, Massachusetts.

Eggs of the red-eyed tree frog, *Agalychnis callidryas*, usually hatch after seven days, but the embryos can emerge up to 30% earlier to escape a predator's attack. Warkentin shows that eggs are more likely to hatch when exposed to vibrations recorded from a snake attack than when exposed to recordings of the vibrations caused by heavy rain. The embryos must therefore be able to distinguish between these different kinds of motion.



K. M. WARKENTIN

## GENETICS

## Muffled mice

*Proc. Natl Acad. Sci. USA*  
doi:10.1073/pnas.0503739102 (2005)  
The *Foxp2* gene has previously been associated with speech and language in people, and with song learning in zebra finches and canaries. By engineering mice with one or two disrupted copies of *Foxp2*, a group led by Joseph Buxbaum of the Mount Sinai School of Medicine in New York has now shown that disrupting even a single copy of the gene impedes the ability of baby mice to call out to their mother.

If confirmed, the link between *Foxp2* and

communication in mice could make the mouse brain a useful model for addressing questions about the control of speech and articulation in humans.

## CELL BIOLOGY

## Disentangling DNA

*Nature Struct. Mol. Biol.* doi:10.1038/nsmb953 (2005)  
Mutations in the *BRCA1* gene are associated with breast cancer, and it is well known that the protein produced by this gene is important for tumour suppression and the repair of damaged DNA.

Researchers led by Junjie Chen at the Mayo Clinic in Rochester have identified a new role for the BRCA1 protein in maintaining the integrity of DNA in normal cells. They show that the BRCA1 protein binds to and enhances the activity of the topoisomerase II enzyme that helps untangle DNA and segregate chromosomes when cells are replicating their DNA.

## COSMOLOGY

## Ripples in space

*Phys. Rev. Lett.* (in the press)  
Preprint astro-ph/0412066 at <http://arxiv.org> (2004)  
Microwave radiation left over from the Big Bang, known as the cosmic microwave background, contains ripples that reflect the

IMAGE  
UNAVAILABLE  
FOR COPYRIGHT  
REASONS

distribution of matter in the 300,000-year-old Universe.

Roberto Trotta from the University of Oxford and Alessandro Melchiorri of the University of Rome 'La Sapienza' claim they can detect fluctuations in this radiation caused by the distribution of neutrinos — weakly interacting particles that formed in the first minutes of the Universe. Trotta and Melchiorri base this claim on data collected by the space-based Wilkinson Microwave Anisotropy Probe during its first year in orbit. Their find seems consistent with the standard model of cosmology, but further data are needed to strengthen their assertion.

## BACTERIOLOGY

### Deadly mix up

*J. Exp. Med.* doi:10.1084/jem.20050112 (2005)

Cerebrospinal meningitis can strike swiftly and fatally, which is surprising because the bacteria that cause it, *Neisseria meningitidis*, normally reside benignly in the nose.

Researchers led by Xavier Nassif of the National Institute for Health and Medical Research in Paris have shown that a phage — a virus that invades bacteria — may participate in this apparently unpredictable switch to infectiousness.

The researchers compared the genomes of different strains taken from a large epidemiological collection in the Czech Republic. A particular gene cluster was detected in all the strains isolated from patients with disease, but in only 10% of the non-pathogenic strains. This cluster was identified as phage DNA.

## BIOTECHNOLOGY

### Muscle booster

*Nature Biotechnol.* doi: 10.1038/nbt1109 (2005)

Engineered muscle can now be grown *in vitro* with ready-made blood vessels, thanks to a technique developed by Robert Langer of the Massachusetts Institute of Technology and his colleagues. This should make it possible to grow thicker tissue samples for transplants, because the vessels supply nutrients to cells deep within the sample.

Langer's approach is surprisingly simple. His team mixed endothelial cells and precursors of mural cells — the cells that form blood vessels — into a culture of muscle precursor cells, known as myoblasts. The endothelial and mural cells self-assembled into a vascular network as the muscle tissue grew. When the muscle was transplanted into mice, the vessels grown *in vitro* hooked up with the animal's existing vessels, improving the implant's survival.

## CANCER

### Skin deep

*Nature Genet.* doi:10.1038/ng1586 (2005)

A mouse model of human skin cancer has been created by Paul Khavari's group at Stanford University, California, allowing the researchers to investigate the genetic mutations that underpin the disease.

Although many genes have been linked to tumours known as melanomas, it is not known which mutations have an active role in initiating tumour development. The team engineered human cells from the base of the skin's surface layer to express some of these mutations. They added these cells into human skin tissue grown on mice. The progress of the disease revealed the potency of the selected mutations, validating an approach that might now be applied to other human tumours.

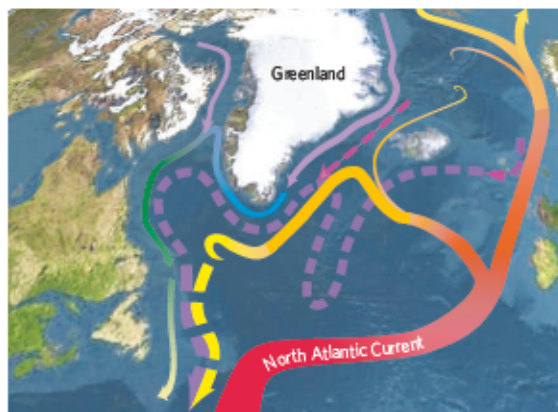
## CLIMATE CHANGE

### Watery world

*Science* 308, 1772–1774 (2005)

The volume of fresh water that has flooded into the North Atlantic Ocean since 1965 has been quantified for the first time, providing hints for how climate change may affect ocean currents (pictured).

Ruth Curry from the Woods Hole Oceanographic Institution in Massachusetts and Cecilie Mauritzen from Oslo's



Norwegian Meteorological Institute calculate that a torrent of fresh water caused a famous 'salinity anomaly' in the 1960s, but had little effect on ocean currents because it mostly ended up in remote subpolar basins. Since then, an average of 100 cubic kilometres of fresh water from rain, rivers and melting ice has diluted the upper layers of the Nordic seas each year, affecting the water density. Within a century, the seas' decreasing salinity could weaken the Atlantic circulation that takes cold, dense water southwards and brings vital, warm water northwards.

## JOURNAL CLUB

Christopher Miller  
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**A biochemist whose expertise lies in observing ion channels spots parallels in the study of protein synthesis.**

"What walks on four legs at dawn, two at noon and three at sunset?" asked the Sphinx. Oedipus' correct answer was "Man, who crawls as an infant, strides as an adult, and hobbles with a stick in old age." But I would say that techniques in science follow the same trajectory.

I first witnessed this three decades ago, when electrophysiological recording made it possible to see single molecules in cells' ion channels. The method's morning was characterized by 'spot-the-blip' papers, whose results simply said: Look at me, I'm a protein! Only later, as noon approached, did the method allow us to explore mechanisms.

Now I am watching the exceptionally sexy techniques of single-molecule fluorescence travel the same path. An initial flurry of papers simply described using a light microscope to see single macromolecules. But researchers have started to address mechanistic questions, as in Scott Blanchard's paper last year (S. C. Blanchard *et al. Nature Struct. Mol. Biol.* 11, 1008–1014; 2004).

This paper attacks a central question concerning the birth of bonds in proteins. The authors track fluorescent versions of molecules called transfer RNAs, which carry the first amino acids of a protein chain into the cell's translation machinery. They clearly see the transfer RNAs going through two stages of checks before allowing the bond between the amino acids to form, some 100 milliseconds later. Such processes have never before been observed directly.

From my own ion-channel experience, I anticipate a long and mechanistically informative midday for the single-molecule fluorescence field, before the inevitable methodological decrepitude of evening sets in.