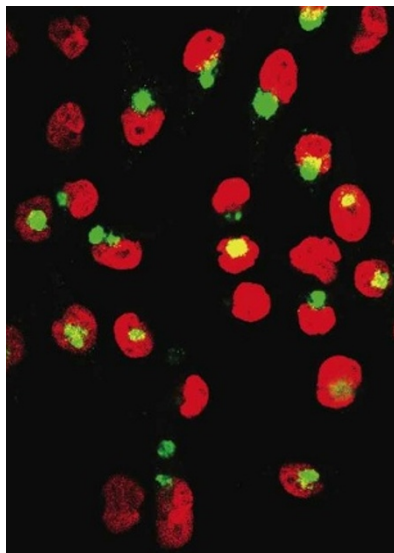


RESEARCH HIGHLIGHTS



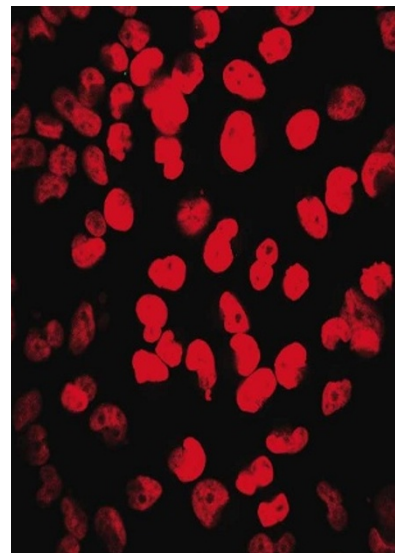
Casting anchor

Science **320**, 520–523 (2008)

A potential drug target for Alzheimer's disease may be more tractable now that scientists in Germany have discovered how to tether compounds that block a crucial enzyme to the cellular compartment in which the enzyme does its deadly work.

This enzyme, β -secretase, cleaves the protein APP (labelled green, left) to make amyloid- β peptide, which causes the plaques that contribute to neurodegeneration, in a compartment called the endosome. But soluble inhibitors do not reach this area when tested in cell cultures.

Kai Simons from the Max Planck Institute of Molecular Cell Biology and Genetics in Dresden and his colleagues chemically modified one inhibitor by linking it to a fat-soluble sterol group. The resulting compound could anchor itself inside an endosome and efficiently block amyloid- β generation there (pictured right). It also stopped the development of plaques when injected into a mouse model of Alzheimer's disease.



L. RAJENDRAN

NEUROBIOLOGY

Pecking order

Neuron **58**, 273–283 (2008)

Social hierarchy is a major determinant of health and mortality, yet how the brain processes group position has been shrouded in mystery. By monitoring blood flow in gamers' brains, Caroline Zink, Andreas Meyer-Lindenberg and their colleagues at the US National Institute of Mental Health in Bethesda, Maryland, have revealed distinct brain activity patterns that form in response to status cues.

The researchers set artificial hierarchies by assigning 72 volunteers a skill rank in a computer game that flagged onscreen opponents as superior or inferior players. But the opponents were really computers, and the games and ranks were rigged so that status was only perceived. One of the authors' discoveries is that brain regions associated with emotion or pain become busier when gamers are losing to inferior opponents.

HUMAN BIOLOGY

Boy appétit

Proc. R. Soc. B. doi:10.1098/rspb.2008.0105 (2008)

Pregnant women who munch through a lot of calories around the time they conceive may be more likely to bear boys than girls.

Fiona Mathews of the University of Exeter, UK, and her colleagues divided 740 British women into three groups according to what they remembered eating in early pregnancy and around the time they conceived. Only 45% of those in the group with the lowest energy intake carried boys, compared with 56% of women in the highest-calorie group.

These data support the Trivers–Willard hypothesis, say the authors, which predicts that females in good condition will have more male offspring.

CHEMICAL BIOLOGY

Dope hope

Nature Chem. Biol. doi:10.1038/nchembio.86 (2008)

Marijuana calms people down and relieves pain, but also has the negative effect of promoting memory loss. By blocking the breakdown of two naturally occurring compounds that bind to the same brain receptor as cannabis, scientists in California have found a way to boost the positive effects associated with cannabis use.

THC, the marijuana plant's psychoactive component, binds to a receptor called CB₁, as do the brain's own cannabinoids 2-AG and

anandamide. John Casida of the University of California, Berkeley, and his colleagues used organophosphorus nerve agents to inhibit the enzymes that catalyse the destruction of these two compounds. Adding one particular nerve agent caused a more than tenfold increase in the levels of these chemicals in the brain. The finding could help pharmacologists design new drugs that relieve pain.

ASTRONOMY

Galactic beginnings

Astronom. J. **135**, 1968–1981 (2008)

It is the ultimate chicken and egg problem: Which came first, galaxies' stars or the black holes at their centres? David Alexander from Durham University, UK, and his collaborators are putting their money on the stars.

The group surveyed six young galaxies more than 10 billion light years away and found that their black holes were between sixty million and one hundred million times more massive than our Sun.

That may be huge, but given the number of stars in each galaxy and current models of how galaxies grow, the findings suggest that these black holes appeared after the stars started multiplying. The stars probably helped the black holes grow by feeding them gases leftover from the stars' own birth.

ANIMAL BEHAVIOUR

A reassuring tune

Curr. Biol. **18**, 576–579 (2008)

Zoologists have debated whether birds that look out for predators while the rest of their flock feeds are behaving selfishly or cooperatively. But few have asked why these



PIXLAND/PHOTOLIBRARY.COM

winged watchmen draw attention to themselves by making particular calls.

Andrew Radford at the University of Bristol, UK, and his colleagues observed groups of pied babblers (*Turdoides bicolor*; pictured right) in the Kalahari in Africa, and recorded the sentinels' sounds. Playing the calls back, they found that the group ate more when a watchman sang; the flock also spread out more and looked up less often.

Because the foraging gains of other birds seem to explain the behaviour, the authors argue that it is an example of cooperation. The close kinship between guard and guarded suggests that sentinel duty is a means by which individuals increase their genetic contribution to future generations.



reversibly with temperature.

The same process could cause an electrostatic attraction between icy grains exposed to cosmic rays in space, promoting their aggregation into proto-planetary lumps.

VIROLOGY

Rubbish imitation

Science **320**, 531–535 (2008)

The vaccinia virus had a dirty secret.

Researchers in Switzerland have revealed that it dupes cells into taking it in by mimicking the detritus that many types of cell would normally mop up.

The work is important because vaccinia typifies pox viruses such as smallpox. Jason Mercer and Ari Helenius of ETH Zurich watched fluorescently labelled virus particles trigger the membranes of their target cells to develop a spherical bulge called a 'bleb'. Blebbing proved crucial for infection, and a fat molecule called phosphatidylserine in the viral membrane proved crucial for virus-induced blebbing. Because the process normally deals with 'rubbish' in healthy cells, it flies under the radar of the immune system and thus enables pox viruses to evade detection as they spread between cells.

ATMOSPHERIC SCIENCE

Jetting away

Geophys. Res. Lett. **35**, L08803 (2008)

Three bands of fast-moving wind — known as jet streams — have shifted position in recent decades, according to a new analysis of weather data that were collected between 1979 and 2001.

Shifts in the jet streams are expected in a changing climate, and the work by Cristina Archer and Ken Caldeira, of the Carnegie Institution of Washington in Stanford, California, looked at observational records for any

such effects. They report that the northern jet stream weakened, and that one of the southern jet streams weakened whereas the other strengthened. All three jet streams moved higher in altitude and closer to the poles, by about 19 kilometres per decade.

NEUROSCIENCE

Algal vision

Nature Neurosci. doi:10.1038/nn2117 (2008)

Blind mice that had lost all the light receptors in their retinæ have had their vision partly restored thanks to a light-sensitive ion channel from a green alga, *Chlamydomonas reinhardtii*.

Botond Roska of the Friedrich Miescher Institute for Biomedical Research in Basel, Switzerland, and his colleagues inserted the gene for this ion channel into the DNA of specific mouse retinal cells, the ON bipolar cells. Formerly blind mice with these cells gained rudimentary sight because light opened algal ion channels in the modified retinal neurons, allowing positively charged ions to flood in and a signal to be sent to the visual region of the brain. The mice fled from strong light and responded to moving grid patterns.

MOLECULAR PHYSICS

Slicing the ice

J. Phys. Chem. B doi:10.1021/jp073870c (2008)

Ice can generate a voltage when heated or cooled, say Richard Bell at Pennsylvania State University in Altoona, James Cowin of Pacific Northwest National Laboratory in Richland, Washington, and their co-workers. The trick is to deposit ions at $-113\text{ }^{\circ}\text{C}$ onto a 1-micrometre-thick ice film, thereby charging the surface of the film and rotating its water molecules, which become locked in position when the film is later cooled.

Normally, water molecules are randomly oriented in ice. Each one has an asymmetrical distribution of positive and negative charge that could create a voltage were many water molecules to become frozen in alignment. Cowin's team's method achieves a voltage as large as those generated by commercial materials and that varies steeply and

JOURNAL CLUB

Kristi Anseth

University of Colorado, Boulder

A biologist looks to 'click chemistry' for better three-dimensional tissue models.

A hot topic in organic chemistry is the development of ways to neatly home in on a particular chemical group and cause a reaction to proceed extremely efficiently under mild conditions. Such highly optimized reactions have been grouped under the term 'click chemistry'. A commonly

cited example involves functional groups called azides and alkynes, which react to form triazoles with the aid of a copper catalyst.

Click chemistry has all sorts of uses, although few are in biology because the technique relies on toxic metal catalysts. However, Carolyn Bertozzi and her colleagues at the University of California, Berkeley, and the nearby Lawrence Berkeley National Laboratory recently demonstrated copper-free click chemistry in a living system (*J. M. Baskin et al. Proc. Natl Acad. Sci. USA* **104**, 16793–16797; 2007). These authors selectively — and

rapidly — labelled cell-surface polysaccharides with with triazole bound to a fluorescent probe. The technique allows real-time imaging of cell surface molecules that are otherwise impossible to achieve.

This research throws open the door for a host of new applications for click chemistry. As a tissue engineer, I am particularly excited about exploiting it to make better gels for three-dimensional cell culture.

Physiological processes are routinely guided by interactions between cells and their tissue environment. Thus, a major hurdle

in tissue regeneration is knowing which biochemical signals must be recapitulated in cell culture, and how to present them at the appropriate time and place. Copper-free click chemistry could allow scientists to synthesize materials that deliver these signals at times that are governed by the physiological conditions in which the material resides. Next on my wish list is the ability to control the spatial organization of these reactions.

Discuss this paper at <http://blogs.nature.com/nature/journalclub>