# RESEARCH HIGHLIGHTS

## What makes a queen?

*PLoS One* **2,** e509 (2007)

What makes a queen a queen, and a worker a worker? For honey bees (*Apis mellifera*) the answer is now clear: an enzyme called target of rapamycin (TOR) helps to create the sharp division between castes. TOR is involved in nutrient-sensing and growth control.

Gro Amdam of Arizona State University in Tempe and her colleagues found that expression of the gene that encodes for TOR was higher in honey-bee larvae destined to become queens than in those destined to be workers. Moreover, when TOR was blocked chemically or genetically, larvae developed traits of worker bees.

K. WOTH/PHOTOLIBRARY.COM

PHYSIOLOGY

## Itching for relief

*Science* **316,** 1494–1497 (2007)

For some it's a chance encounter with poison ivy; for others it's an ongoing struggle with latex sensitivity. Whatever the source, the itchy agony of contact dermatitis is a familiar ailment. Now, researchers suggest that relief could come from the compounds, called cannabinoids, that give marijuana its mind-altering properties.

Thomas Tüting and Andreas Zimmer of the University of Bonn in Germany and their team showed that inhibiting cannabinoid receptors — either genetically or chemically — enhances skin hypersensitivity to allergens in mice. Applying topical cannabinoids or inhibiting an enzyme that degrades endogenous cannabinoids relieves the inflammation associated with allergic dermatitis.

METABOLISM

## Hunger linked to fidgeting

*Cell Metab.* **5,** 450–463 (2007)

Scientists have identified a molecular link between feeling hungry and fidgetiness: a transcription factor known as Bsx. This could be a target for combating obesity, they say.

Mathias Treier from the European Molecular Biology Laboratory in Heidelberg, Germany, and his colleagues showed that Bsx regulates in mice both the level of spontaneous physical activity and two brain peptides that regulate how much the mice eat. Mice lacking Bsx moved less and showed different eating behaviours.

The *Bsx* gene is conserved across species, so may also be involved in energy balance in humans. The scientists speculate that mutations in *Bsx* may explain why some over-eaters become obese whereas others do not: people with normal copies of the gene may be better at matching their activity levels to their food intake.

VIROLOGY

## Stowaway

*PloS Pathog.* **3,** e75 (2007)

A genetic study suggests that the yellow fever virus reached South America from western Africa some 300 to 400 years ago, probably in ships carrying slaves.

Juliet Bryant and Alan Barrett of the University of Texas in Galveston and their colleague analysed 133 samples of yellow fever virus, taken from 22 countries over 76 years.

By comparing the viruses' RNA sequences, the team showed that South American strains are more closely related to those in western Africa than either group is to those in eastern Africa. The viruses can be traced back to an ancestral strain that existed in Africa within the past 1,500 years.

BETTMANN/CORBIS

CLIMATE SCIENCE

## Precarious on reflection

*Proc. Natl Acad. Sci. USA* **104,** 9949–9954 (2007)

A world in which greenhouse warming was offset by human interventions could end up a drier, more precarious place, models predict.

H. Damon Matthews and Ken Caldeira at the Carnegie Institution in Stanford, California, modelled changes in climate due to increased greenhouse gases with and without 'geoengineering' interventions, such as the addition of dust to the stratosphere to reflect sunlight back into space. The models show that geoengineering could prevent the world's average temperature from rising, but it would produce drier continents than seen today or in models with no such intervention.

If geoengineering efforts were started but then failed or were abandoned, and carbon dioxide emissions had continued throughout, climate shifts could be abrupt and severe, with warming taking place at up to 4 °C per decade.

CANCER BIOLOGY

## Deactivate to defend

*Cell* **129,** 969–982 (2007)

Researchers have found that PP2A proteins defend against cancer by turning down the activity of a cancer-promoting enzyme.

Many tumours have mutated forms of proteins from the PP2A family, which regulate other proteins by removing phosphate groups. Some of the cancer-linked mutations are in a particular part of PP2A (the Aβ subunit), the role of which in cancer wasn't understood.

William Hahn's group at the Dana-Farber Cancer Institute in Boston, Massachusetts, used RNA silencing to prove that cells with the mutated subunit became cancerous. They next used mass spectrometry to identify which cellular proteins bind only to this subunit. One protein did: the enzyme GTPase RalA, which has already been linked to cancer. The team then found evidence that the Aβ subunit deactivates the enzyme, implying that the subunit is a bona fide tumour suppressor.

MATERIALS SCIENCE

## Let's twist again

*Angew. Chem. Int. Edn* doi:10.1002/anie.200700708 (2007)

Researchers in Japan have introduced a new twist, quite literally, to the control of light.

Masaki Horie of the RIKEN Institute of Physical and Chemical Research in Saitama, Kohtaro Osakada of the Tokyo Institute of Technology and their colleagues made a molecular crystal from rotaxanes, which consist of molecular chains threaded through hoops.

The crystal's colour switched from green to orange when its temperature was pushed above 128 °C, accompanied by a change in the way the crystal rotates polarized light. The team attributes this to a phenyl group on the end of each rotaxane's chain that twists out of alignment with phenyls on its hoop.

NEUROBIOLOGY

## Brain tangle

*Neuron* **54,** 713–720 (2007)

By combing through the genomes of 1,411 people, researchers have identified a gene that influences an individual's risk of developing late-onset Alzheimer's disease.

One version of the gene — which encodes the protein Gab2 — is protective; another boosts risk of the disease. The gene plays a role only in people who already have an elevated risk of Alzheimer's because they carry a particular form of another gene, known as *APOE*.

Eric Reiman of the Banner Alzheimer's Institute and Dietrich Stephan of the Translational Genomics Research Institute, both in Phoenix, Arizona, and their colleagues also show that Gab2 is expressed in brain regions that are susceptible to the neuronal tangles characteristic of Alzheimer's. They propose that Gab2 normally protects against tangles, and that the risky version of the gene produces a dysfunctional form of the protein.

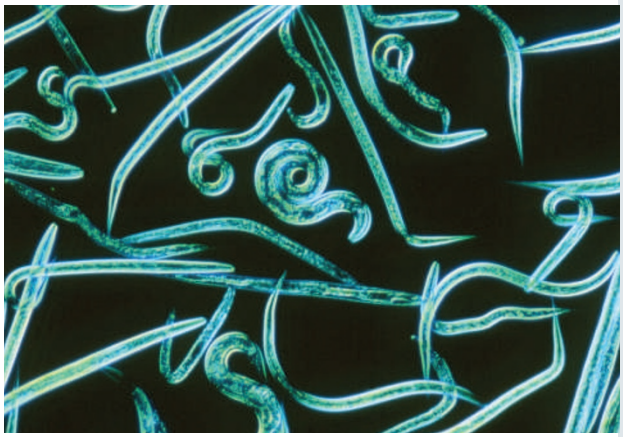
DEVELOPMENTAL BIOLOGY

## Worms' talk

*Nature Chem. Biol.* doi:10.1038/nchembio.2007.3 (2007)

When food runs low or life gets too crowded, the nematode worm *Caenorhabditis elegans* (pictured below) signals to its neighbours that it's time to slow down. The chemical signal — known as the 'dauer' pheromone — causes the worms to stop moving and subsist on stored fat until conditions improve.

Researchers had previously identified one component of the pheromone cocktail, but it did not seem strong enough to trigger the dauer response on its own. Now, Jon Clardy and his colleagues at Harvard Medical School in Boston, Massachusetts, report the isolation of two related compounds. All three are members of a class of sugars called ascarosides, but the most recent pair are about 100 times more effective at triggering the dauer response than the first one found.



S. STAMMERS/SPL

NANOTECHNOLOGY

## Miniature painting

*Nano Lett.* doi:10.1021/nl070462b (2007)

How does one apply a layer of paint one molecule thick to the inside of a tiny hole?

Amit Meller and Meni Wanunu of Boston University, Massachusetts, wanted to do this to turn their nanopores — tiny holes drilled through a sheet of silicon — into smart sensors for detecting single molecules or pH. The coated pores work as sensors because the pore's conductance changes when molecules or ions enter inside and interact with the paint.

For pores with a diameter greater than 10 nanometres, simply dipping the device into a solution of organosilane molecules did the trick, creating a neat and durable layer of organosilanes. The researchers managed to paint smaller pores too, by driving the solution through the hole to prevent clogging.

## JOURNAL CLUB

**Robert Langer**
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**A bioengineer sees a future for safe gene-silencing therapies.**

The possibility of treating genetic disorders by modifying gene expression has been an attractive yet elusive goal for decades. Problems with the safety and efficacy of various types of gene therapy have held back progress. In particular, there have been some high-profile failures, including a number of deaths during clinical trials.

But seminal studies reported by Andrew Fire and Craig Mello in 1998 led to a potentially new class of therapeutic agent. These researchers, who went on to share a Nobel prize for their work, found that small pieces of RNA, dubbed siRNAs, can silence genes.

Although switching off genes may have fewer complications than adding new ones, the safe and effective delivery of genetic agents remains a critical challenge. I was therefore pleased to see a recent paper reporting tests of an siRNA-delivery system in monkeys (J. Heidel *et al. Proc. Natl Acad. Sci. USA* **104,** 5715–5721; 2007), suggesting that safe, repeated systemic administration of siRNAs is possible.

Mark Davis of the California Institute of Technology in Pasadena and his colleagues created nanoparticles composed of siRNAs and a novel polymer based on the sugar cyclodextrin. These particles were injected into the monkeys and their health was monitored. The monkeys tolerated multiple doses of siRNA of increasing amounts.

This paper was of interest to me not only because my group works on lipid formations that might serve as delivery systems for siRNA or other genetic agents, but also because I was pleased to see a former student doing well. Jeremy, the first author, once worked in my lab as an undergraduate.

Studies such as this one are bringing back to the field the excitement that surrounded gene therapies in the 1980s.

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