RESEARCH HIGHLIGHTS

Venom not a *digestif*

J. Exp. Zool. doi:10.1002/jez.411 (2007)

The presence of digestive enzymes in snakes' venom has prompted scientists to propose that their venom evolved to help them consume their prey. Experiments carried out by Marshall McCue at the University of Arkansas in Fayetteville suggest that this is not the case.

McCue found that western diamondback rattlesnakes (*Crotalus atrox*, pictured) digested mice no faster when the mice had been injected with venom than when they had not. The diamondback's venom is among the richest in digestive enzymes, so this result lends support to theories that snakes evolved venom for some other purpose — such as hunting or defence.

J. VAN DYKE

PALAEONTOLOGY

Climate for change

Geology **35,** 831–834 (2007)

Mineral deposits from caves in southern Israel (pictured below) point to increased rainfall in this now inhospitable region between 140,000 and 110,000 years ago, researchers report.

The timing coincides with the dates of early human sites in northern Israel. This supports the idea that climatic changes helped modern humans to migrate from Africa by making the deserts suitable for human settlement and passage.

There was already evidence for parts of the Saharan desert being wetter during this period, but the new data, from Anton Vaks at the Geological Survey of Israel and the Hebrew University of Jerusalem, Israel, and his colleagues, covers the 'bottleneck' region of the Sinai-Negev Desert, which connects Africa to Asia. A subsequent return to arid conditions in this region may have spurred further northward migration.

A. VAKS

GENETICS

Indicators of asthma

Am. J. Hum. Genet. doi:10.1086/521200 (2007)

Researchers in the United States have shown how a difference in one genetic base, or single nucleotide polymorphism (SNP), may influence a person's risk of developing asthma.

Several SNPs found in non-coding regions near the gene *HLA-G* have been associated with asthma risk. Zheng Tan at the University of Chicago, Illinois, and his team looked in these regions for docking sites for genetic regulators known as microRNAs. The group found one docking site that comes in two versions, differing in a SNP dubbed +3142C/G. One version binds microRNAs better than the other. Tan's group showed that this SNP, which is situated close to those previously associated with asthma, also influences asthma risk, probably through effects on microRNA binding. The effect depends on maternal asthma status, which suggests that differences in microRNA regulation begin in the womb.

CELL BIOLOGY

Transformers

Cell **130,** 678–690 (2007)

Centrioles are the 'Transformers' of the cell: in one guise, these organelles form structures known as centrosomes that help organize chromosomes during cell division; in another, they seed the formation of cilia and flagella.

Brian Dynlacht and his colleagues at the New York University School of Medicine have now identified two proteins that may help centrioles switch between these roles.

Cells have only one pair of centrioles, so they cannot have cilia and divide at the same time. The team found that boosting cells' levels of a protein called CP110, known to have a role in the centrosome cycle, suppressed cilia formation. The researchers also showed that cells lacking either CP110 or Cep97, which they characterize as recruiting CP110 to centrosomes, grew extra cilia.

MICROBIOLOGY

A light touch

Science **317,** 1090–1093 (2007)

A light-sensing enzyme that helps plants turn to face the Sun has been found in four species of bacteria, including a human pathogen. The enzyme, a histidine kinase, is kicked into action by blue light.

Roberto Bogomolni, at the University of California, Santa Cruz, and his colleagues scanned bacterial genomes for similar enzymes and identified contenders in a marine bacterium, a plant pathogen and in two species of *Brucella* — a pathogen of cows and humans.

Brucella that lack the enzyme or that have been kept in the dark are more likely to be killed by immune cells than normal *Brucella*. The benefit to the bacterium of linking its virulence to light remains unclear.

BIOTECHNOLOGY

Seeing red

Nature Methods doi:10.1038/nmeth1083 (2007)

An engineered protein should offer biologists images of deep tissues in live animals better than any they can produce today.

Animal tissues are most transparent to light from the far-red end of the visible spectrum but, unfortunately for scientists

seeking to light creatures up from the inside, no natural proteins fluoresce very well at these wavelengths. Dmitriy Chudakov of the Shemiakin-Ovchinnikov Insititute of Bioorganic Chemistry in Moscow, Russia, and his colleagues created and tested more than 100,000 mutant forms of a red sea anemone protein to find one with a longer-wavelength glow. This protein, dubbed Katushka, was brighter than two existing far-red fluorescent proteins in tests with transgenic frogs. The researchers have also made a monomeric version of the protein, mKate, to use as a tag on other proteins.

PHYSIOLOGY

An eye on the time

Cell **130,** 730–741 (2007)

Switching off the eye's circadian 'clock' disrupts visual processing in mice, researchers have found. Many organs of the body have such clocks, but their function has been unclear.

Charles Weitz at Harvard Medical School and his colleagues deleted a circadian control gene, *Bmal1*, in the retina of mice. They noted that this disturbed the normal night and day cycle of retinal electrical activity.

By contrast, disrupting the central circadian clock in the brains of wild-type mice did not significantly affect the rhythm of the retinal impulses. This suggests the retinal circadian clock has an autonomous role in visual processing. Extensive changes in light-dependent gene expression are thought to be associated with the effect.

OPTICS

Stuck in a loop

Phys. Rev. A **76,** 023816 (2007)

Light ricocheting around inside a silica sphere like sound in a whispering gallery can be brought to a stop, researchers have shown.

Anatoliy Savchenkov and his colleagues at the Jet Propulsion Laboratory in Pasadena, California, calculated that a series of pulses of light entering a 'whispering-gallery-mode' resonator — a device that accepts only certain wavelengths of light — can end up with a zero 'group velocity'. This theoretical prediction runs against general expectations, but the team confirmed it through experiments.

Researchers have proposed using other systems that slow light for information storage. Savchenkov says it should be possible to build a resonator memory, although the stopped light in the resonator as configured in these experiments could hold no information.

STEM CELLS

Hope for the broken-hearted

Nature Biotechnol. doi:10.1038/nbt1327 (2007)

Poets tell us that, once broken, the heart does not readily heal. But progress in repairing damaged rat hearts with human embryonic stem cells raises hopes that such treatments may one day work for humans.

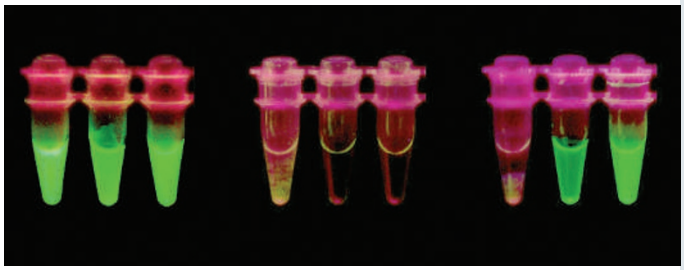
Charles Murry at the University of Washington in Seattle and his colleagues report that human embryonic stem cells treated with two proteins, activin A and bone morphogenic protein 4, develop into heart cells more efficiently than those treated with current methods. They also concocted a 'prosurvival cocktail' that blocked potential cell-death pathways, improving the survival of stem-cell derived heart cells when they were transplanted into rats. In rats that had had a heart attack, these cells replaced dead tissue, and prevented deterioration of heart function.

CHEMICAL BIOLOGY

Unscrambling the egg

J. Am. Chem. Soc. **129,** 10110–10112 (2007)

Anyone who has boiled an egg will have noticed the solidification that occurs as heat causes proteins to unfold then aggregate. Such aggregation can be a problem for the therapeutic use of proteins, so scientists are interested in schemes that might prevent it.



AM. CHEM. SOC.

David Liu and his colleagues at Harvard University, have found a way to make various proteins resistant to aggregation. They 'supercharge' the protein surfaces by substituting amino acids that appear on the outside surface of the folded protein with amino acids that can be ionized. Surprisingly, this does not seem to interfere with the protein's structure or function — but it keeps the molecules soluble after boiling, whereas unmutated forms aggregate.

The picture (above) shows solutions of the biochemical marker green fluorescent protein before (left) and immediately after boiling (centre), and after cooling (right). The leftmost vial in each set contains the standard protein, the other two contain supercharged forms.

JOURNAL CLUB

Joe F. Costello
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To an epigeneticist, cancer is encrypted in genes and their packaging.

Early in my career I had the good fortune to study epigenetics in a lab focused on the molecular genetics of cancer. At the time, geneticists typically thought that in cancer, epigenetic changes — which affect regulation of the genome but not the genome's sequence — were epiphenomena less worthy of study.

This might have made the experience akin to being a Republican mayoral candidate in left-leaning San Francisco; instead it was positively transforming.

As my own research group took shape, I began to integrate genetic and epigenetic theories of malignant transformation. Now, hereditary human cancers and genetically engineered mice once held up as evidence for genetic models also provide evidence for epigenetic models, and we study the interactions of the two mechanisms.

In this light, a recent paper (G. G. Wang *et al. Nature Cell Biol.* **9,** 804–812; 2007) captured my attention because it dissects how one genetic change leads to epigenetic changes that ultimately cause leukaemia.

The work focuses on an abnormal fusion protein — produced after part of one gene fused, or translocated, with part of another — and narrows down its cancer-causing properties to a particular region of the protein. This region mediates an epigenetic change: it adds a methyl group to one amino acid of a histone, part of a gene's packaging in the nucleus.

The team found that the fusion protein misdirects its methylation to the histones that package *HoxA* genes, triggering further miscoding of the histones. This activates the genes, which promote self-renewal of blood-cell precursors, contributing to leukaemia.

I wonder if the interactions could be traced back even further. Given the role of epigenetics in stabilizing chromosomes; might it have been epigenetic miscoding that made the gene susceptible to translocation in the first place?

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