EDITORS' CHOICE

edited by Gilbert Chin

CELL BIOLOGY

An Unfolding Story

The unfolded protein response (UPR) is an intracellular signaling pathway that regulates protein folding. Through this pathway, the cell senses when unfolded proteins accumulate in the endoplasmic reticulum (ER) and responds by activating transcription of genes encoding proteins involved in folding, such as chaperones. A key player in this pathway is Ire1p, an ER transmembrane protein with endonuclease and kinase activities. Upon induction of the UPR, Ire1p translocates from the ER to the nucleus, where it initiates the splicing of a messenger RNA specifying a transcription factor that activates UPR target genes.

The mechanism of translocation has now been clarified by Niwa *et al.*, who show that Ire1p is proteolytically severed from the ER membrane, producing a soluble, enzymatically active fragment which then enters the nucleus. In an intriguing twist to this story, both Niwa *et al.* and Katayama *et al.* show that nuclear localization of Ire1p and UPR induction are impaired in cells lacking or defective in presenilin-1, a protease linked to the aberrant production of amyloid deposits in Alzheimer's disease (AD), suggesting that defects in UPR may play a role in the pathogenesis of AD. — PAK

Cell **99**, 691 (1999); *Nature Cell Biol.* **1**, 479 (1999).

ECOLOGY

Tropical Tree Communities

Conservation of biodiversity depends on, among other things, a knowledge of the distribution and abundance of the target organisms. For many large organisms of the temperate zone we have reasonably accurate distribution maps, but for tropical trees there are few, if any, species that have been mapped at the scale that matters — that of the sustainable population. Pitman and colleagues present the results of a survey of more than 800 tree species in the western Amazonian forests of the Manu National Park, Peru, using a network of forest plots of various sizes distributed over a total area of 400 km^2. They show that most species are, not surprisingly, rare in most locations, but the data are sufficiently detailed to reveal different forms of rarity.

Live from the rainforest.

Building on a scheme developed in the 1980s by Deborah Rabinowitz, Pitman *et al.* classify tree species according to their habitat specificity, geographic range, and local and regional population size. They find that most species are extensively distributed across western Amazonia and grow in a range of different forest types. At large spatial scales, such species can therefore be abundant. Fewer than 20% of species are restricted to a small number of forest types, and none of the species is endemic to the Manu park (*i.e.*, not found elsewhere). Reassuring as this picture might seem for the conservation of lowland tropical forest trees, these results in fact underscore the need for the protection of very large areas of forest if viable populations are to be maintained. — AMS

Ecology **80**, 2651 (1999).

OCEANOGRAPHY

Tracking Down a CO_2 Source

The carbonate ion content of seawater influences many important properties of the atmosphere and ocean, such as the atmospheric concentration of CO_2 and the preservation of calcium carbonate shells on the sea floor. Broecker *et al.* have compared the size distribution of calcium carbonate grains in marine sediments from a site on the Ontong Java Plateau in the western equatorial Pacific to similar measurements made in the Equatorial Atlantic to determine whether the world ocean experienced a decrease in carbonate ion concentration during the past 8000 years. Their results from both sites are consistent with a decline large enough to account for the ~22 parts per million increase in the atmospheric concentration of CO_2 that occurred over the same interval. In contrast, Indermühle *et al.* recently have suggested that this CO_2 increase was due to a large decrease in terrestrial biomass. — HJS

Paleoceanography **14**, 744 (1999); *Nature* **398**, 121 (1999).

APPLIED PHYSICS

An Atom Slalom

Atoms cooled in vacuum to near absolute zero display wavelike properties that allow experiments to be performed that are analogous to those for photons, such as interferometric measurements, and assemblies of cold atoms in Bose-Einstein condensates can act as atom lasers. More complex "atom optics" will require the equivalent of optical waveguides, which guide a light beam precisely to a desired point.

Müller *et al.* have now steered laser-cooled rubidium atoms from source to end-point along a 10-cm channel that contains three curves (right-left-right), each with a 15-cm radius of curvature. The atoms are confined by the magnetic field set up by two parallel wires carrying electrical current in the same direction. The rectangular wires, patterned by photolithography on a glass substrate, are 100 μm apart and have a cross section of 100 μm by 100 μm. The magnetic field off-center increases linearly with applied current, so the low-field–seeking rubidium atoms are confined to the central region. With a 3-ampere current flowing in the wires, they can achieve a flux of 2 x 10^6 atoms per second. — ISO

Phys. Rev. Lett. **83**, 5194 (1999).

MEDICINE

Breathing More Easily

It has been estimated that worldwide 150 million people suffer from asthma, and the prevalence is increasing in most countries. Although the condition can be controlled in most cases by treatment with corticosteroids, the side effects of long-term administration have created the impetus for finding new therapies. As the allergic reaction that leads to asthma is mediated by immunoglobulin E (IgE), one approach has been the blockade of IgE and subsequent release of histamine.

Milgrom *et al.* conducted a clinical trial of a mouse-derived monoclonal antibody (rhuMAb-E25), which recognizes IgE; to minimize adverse reactions, critical amino acids in the variable region of the mouse immunoglobulin were placed within the background of human immunoglobulin G. In a group of 317 patients with moderate to severe asthma,

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high or low doses of the antibody (or doses of a placebo) were administered by injection. Relative to the placebo controls, who also were closely monitored and received counseling about treatment adherence, individuals treated with rhuMAb-E25 exhibited dramatic decreases in plasma IgE levels and fewer symptoms, and they reported a higher quality of life. There was a small increase in lung function, as measured by expiratory flow rate, and patients had fewer severe episodes that required the use of bronchodilators. — BJ

N. Engl. J. Med. **341**, 1966 (1999).

CHEMISTRY

Extending the Genetic Code

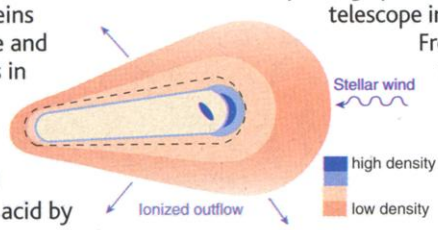
The genetic code maps the set of 64 three-base codons onto the canonical set of 20 amino acids. The incorporation of unnatural amino acids into proteins has been used to study structure and function, and to modify proteins in ways not accessible via enzymatic post-translational modification. In earlier work, a stop codon was re-programmed to add a single unnatural amino acid by using an amber suppressor transfer RNA (tRNA). More recently, a four-base codon and a frameshift suppressor tRNA (a chemically acylated version of yeast $tRNA^{Phe}$) were utilized in similar fashion. Hohsaka *et al.* now report that different unnatural amino acids can be incorporated into the same protein, streptavidin, at two positions with the four-base codons AGGT and CGGG. Ribosomal synthesis of the full-length protein containing the two derivatized residues required both modified tRNAs; the omission of either resulted in a frameshift reversion to the three-base codon (either AGG or CGG) and premature termination at a nearby stop codon. — PDS

J. Am. Chem. Soc. **121**, 12194 (1999).

ASTRONOMY

Disappearing Proplyds

Proplyds are low-mass young stars that are surrounded by disks of circumstellar material, which is photoionized by hydrogen gas from nearby stars into a teardrop shape. Proplyds reveal details about the early life of young stars; planet formation can occur within the circumstellar disks if they survive long enough. The Orion nebula is a rich region for star formation and contains many bright proplyds. Henney and O'Dell obtained high-resolution spectra of four proplyds in the Orion nebula with the HIRES spectrograph on the Keck I telescope in Hawaii. From these data, they were able to model several increasingly dense ionized layers on the head of the proplyd (the side exposed to bombardment by ionizing stellar radiation) and a narrow tail on the shielded side. From this model they extracted a mass loss rate from a typical proplyd disk of 0.4×10^{6} solar masses per year, which is extremely rapid and inconsistent with the predicted lifetimes of the proplyds, suggesting that either the masses of the circumstellar disks have been underestimated or another process maintains these fragile disks. — LR



Model of Proplyd Photoevaporation

CREDIT: MODIFIED FROM HENNEY & O'DELL

Astronomical J. **118**, 2350 (1999).

Science's stke

Dispatched Sends Hedgehog On Its Way

Developmental patterning of the *Drosophila* wing requires the morphogen Hedgehog (Hh), which is secreted by posterior (P) compartment cells and acts at short range on a narrow strip of anterior (A) cells at the A/P border. Binding of released Hh to Patched (Ptc) serves to sequester Hh at the A/P border and to trigger subsequent signaling steps which are transduced by Smoothened. The appropriate localization of Hh also requires a post-translational modification in which cholesterol is covalently attached to the protein.

Burke *et al.* report that release of cholesterol-modified Hh is mediated by a protein called Dispatched (Disp). Like Ptc, Disp is a transmembrane protein containing a sterol-sensing domain, a motif found in proteins that regulate cholesterol metabolism. How Disp liberates Hh from P cells is not clear, but it appears to be specific for the cholesterol-tagged form of Hh because an artificial Hh construct containing a different membrane anchor was not released. Although Ptc and Disp are structurally similar, they perform seemingly opposite tasks in that the former sequesters Hh while the latter is required to release the morphogen. — LDC

Cell **99**, 803 (1999).