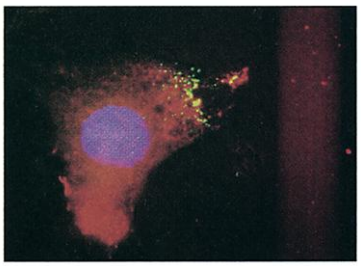
EDITORS' CHOICE

edited by Stella Hurtley

CELL BIOLOGY

A Quick Fix



Resealed fibroblast (red) binds antibodies against a lysosomal glycoprotein (green).

For an animal cell, rupture of the plasma membrane would be thought to imply certain death. However, in some instances repair is possible. Indeed it appears that mechanisms for rapid repair exist in most cell types.

Reddy *et al.* examined the process of plasma membrane repair in tissue culture cells wounded by scraping. Surprisingly, the repair process involved fusion of the cell's degradative organelles, the lysosomes, with the cell surface. Upon wounding, lysosomes fused with the plasma membrane, rapidly sealing the cell in a Ca^{2+}-triggered process. The mechanism of fusion involved the lysosomal form of synaptotagmin, SytVII, and could be inhibited by expressing the cytoplasmic C2A domain of Syt VII involved in Ca^{2+} sensing. In primary skin fibroblasts wounded by the contraction of their supporting collagen matrix, lysosomal exocytosis was also responsible for cell resealing. Thus, in addition to degrading ingested proteins, lysosomes also play a key role in plasma membrane repair by acting as Ca^{2+}-regulated secretory vesicles. — SMH

Cell **106**, 157 (2001).

MOLECULAR BIOLOGY

Remodeling p53

About half of all human cancers contain mutations in the *p53* tumor suppressor gene. In response to certain forms of cellular stress, the p53 protein induces cell cycle arrest by sequence-specific DNA binding and transcriptional activation of key target genes. Previous studies used purified DNA consensus sequences to produce a model in which p53 acquires DNA binding activity only after its carboxyl-terminal region is modified.

Using a chromatin-based assay that may better mimic the substrates p53 encounters in the cell nucleus, Espinosa and Emerson arrive at a very different model of how p53 regulates transcription. Studying the chromatin-assembled *p21/WAF1* promoter, they find that unmodified p53 does bind DNA/chromatin and requires the same carboxyl-terminal region that was previously thought to repress DNA binding. The chromatin-bound p53 recruits a histone acetyltransferase (p300) to the promoter, which then acetylates the p53-bound nucleosomes, perhaps facilitating interaction with other components of the transcriptional machinery. Whether p53 uses the same or different mechanisms to regulate expression of its many other target genes is an important question that remains to be investigated. — PAK

Mol. Cell **8**, 57 (2001).

GEOPHYSICS

Not Giving Physics the Slip

Great earthquakes (magnitude > 8) rupture over large distances in such a way that the amount of horizontal displacement (rupture length) between the two sides of the fault can be greater than the amount of vertical displacement (rupture width). Essentially, the rupture width cannot go any deeper than the base of the brittle crust, but the rupture length seems to be unlimited. This observation seems to defy physical principles of fracture mechanics observed in the laboratory.

Now, a study by Shaw and Scholz may resolve this apparent inconsistency. They modeled a great earthquake rupture in three dimensions with two layers of different frictional strength. Friction helps to determine how far a fault will slip; when friction decreases with increasing slip or slip rate, a fault will stick and slip to produce an earthquake, but if friction increases with increasing slip or slip rate, a fault will simply creep along. In simulations, the rupture length is related to a kinetic effect; slip pulses take a long time to build to their maximum intensity and then take a long time to dissipate. Thus, for a great earthquake, the slip pulses can move over long distances, and the maximum slip can occur far from the epicenter. Thus there is nothing fundamentally different about the physics of a small-to-large earthquake as compared with great earthquakes. — LR

Geophys. Res. Lett. **28**, 2991 (2001).

MICROBIOLOGY

Instant Death

Bacteriophages produce small proteins called holins, which, at a defined point in the infection cycle, punch holes in bacterial cell membranes. After the accumulation of a critical number of holin molecules in the cell membrane, oligomerization is triggered, causing cell lysis. Bacteria can be tethered to a substrate by antibodies directed against their flagella, and their cell bodies will then rotate. The rate of this rotation is proportional to the proton motif force (pmf) of the bacterial cell membrane and is a measure of membrane integrity.

Gruendling *et al.* saw that in phage-infected bacteria, rotation stops abruptly a few seconds before catastrophic cell lysis. Apparently, the pmf keeps the holins apart until the threshold concentration is reached, when they instantaneously clump to form a weak patch in the membrane. This collapses the pmf and causes membrane rupture. However, the holin's target in the membrane remains unknown, and the mechanism of action of these hugely diverse and ancient clock-like proteins remains elusive. — CA

Proc. Natl. Acad. Sci. U.S.A. **98**, 9348 (2001).

ASTROPHYSICS

Early Metal Production in the Universe

To understand the chemical evolution of the universe, astronomers use spectroscopy and photometry to determine the abundances of heavier elements (metals). Metals are created by stellar nucleosynthesis and supernovae, and their abundances can be used to estimate the amount and rate of star formation. Co, for example, is overabundant relative to Fe in metal-poor systems, such as Galactic bulge and thick-disk stars, that may have formed early in the universe. This overabundance may be produced by the fastest evolving stars.

Given the implications about star formation rates suggested by the overabundance of Co, Ellison *et al.* measured Co in damped Lyman alpha systems (DLAs). A DLA is a region of high hydrogen density that lies between a very distant bright quasar and the observer. In these very distant regions, Co is overabundant relative to Fe. Thus, this Co signature suggests that star forma-

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SOURCE: (IMAGE) NORMA ANDREWS, YALE

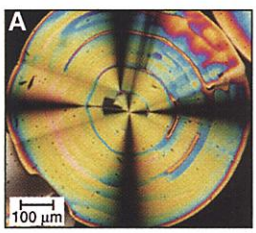
tion was probably rapid in the early universe and would also be consistent with the Co-overabundant metal-poor systems being formed at about the same time, confirming that Galactic bulge and thick-disk stars are old. — LR

Mon. Not. R. Astron. Soc. **326**, 628 (2001).

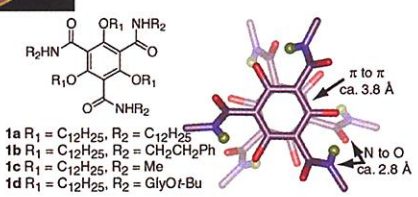
CHEMISTRY

Stacking Them High

Molecular-scale wires have many potential applications in nanotechnology. Such wires may be assembled from molecular units by exploiting intermolecular interactions, such as metal-ligand bonds or hydrogen bonds. Benzene rings may also stack up to form the conductive backbone of a molecular-scale wire; substituents may then form an insulating sheath around this core. Unfortunately, the interactions between the benzene rings are relatively weak, and the resulting columnar structures are not very stable.



Columnar stacks lead to ordering that can be seen under polarized light.



Bushey *et al.* have synthesized benzene rings with three amide substituents in alternate positions on the ring; the remaining three positions are taken up by various ether substituents. The resulting molecules form columnar structures that are stabilized by hydrogen bonds between the amide nitrogens and the ether oxygens of alternating rings in the column. The approach is versatile in that other functional groups could be placed on the outside of the column. Furthermore, the dipole moment should be amplified in the columnar stacks, which should prove useful in electro-optical and other applications. — JU

J. Am. Chem. Soc., 10.1021/ja0104148.

APPLIED PHYSICS

One... Two... Three... Push

How hard can you push on one corner of a table placed on a rug before the leg bends as much as it can, and the table starts to shuffle across the floor? Moresco *et al.* have looked at this type of problem, but on the molecular scale, by prodding a molecule with a scanning tunneling microscope (STM) under high vacuum. Four substituents on a Cu porphyrin complex act as legs, both supporting it and anchoring it above a flat copper (100) surface. Previous studies at room temperature showed that the legs are not square to the surface but tilt by 10° to 20°. Using the STM in constant-height mode at much lower temperature (12 K), they pushed on one of the legs and recorded changes in current with displacement. By comparing these measurements to calculations, they determined that the leg tilted an additional 20° and that the other three legs tilted by about 10°. Once the legs were sufficiently deformed, the molecule had enough internal energy to overcome the surface barriers, and it shuffled across the copper surface. — MSL

Phys. Rev. Lett., 10.1103/PhysRevLett.87.088302.

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Specific Splice Signals

The generation of different proteins from a single gene by alternative splicing is regulated in a time- and tissue-specific manner. Although initiated by extracellular signals, transmission of such information from the cell surface to nuclear splicing machinery is not fully understood.

Now Weg-Remers *et al.* have made some progress by looking at the expression of variant isoforms of CD44 on the surface of T cells. Activation of primary T cells initiated the ERK, JNK, and p38 MAP kinase signaling cascades. However, only activation of the Ras-ERK pathway was needed to generate a mature form of CD44 that included a particular exon. Mutation of the splice-responsive elements within this exon reduced expression of the CD44 isoform in response to ERK activation. Splicing did not depend on protein synthesis, suggesting that posttranslational modification of regulatory splice factors, possibly by phosphorylation, may regulate splicing. The specificity of exon selection could thus be determined in part by the activation of distinct signaling pathways. — LC

EMBO J. **20**, 4194 (2001).

CREDITS: BUSHEY ET AL., J. AM. CHEM. SOC. 33, 8157 (2001)