

DEVELOPMENT

## Sharpening Boundaries

Gradients of morphogen concentration have been postulated to inform cells of their relative positions within a developing organism in order to adopt the appropriate fates, but do they offer enough information to support a robust formation of developmental patterns? Piddini and Vincent explored the development of the wing in *Drosophila*, which depends on a gradient of the morphogen Wingless (Wg). They progressively depleted Wg-expressing cells in the developing wing and found that the wings looked nearly normal and that expression of the *distal-less* (*dll*) and *vestigial* (*vg*) genes (enhanced by low concentrations of Wg) persisted. In flies in which small patches of mutant cells that could not transduce Wg signals were interspersed with normal cells, the expression of *dll* and *vg* did require continuous signaling by Wg. Apparently, cells only needed the continued presence of Wg when surrounded by wild-type cells, indicating that cells receiving Wg signals were themselves producing a signal that inhibited Wg signaling in their neighbors—a process known as lateral inhibition, which can enhance contrast at the edges of regions of cells immersed in a signal gradient. The inhibitory effect required the presence of Notum (also called Wingful), an inhibitor of Wg signaling that is known to be produced in cells near the source of Wg production. — LBR

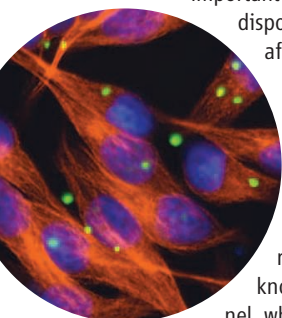
*Cell* **136**, 296 (2009).

CELL BIOLOGY

## Cleaning House

In preparation for cell division, proliferating cells assemble protein complexes to ensure the faithful duplication of cellular components; equally important are the disassembly and disposal of these structures afterward. Many proteins are hydrolyzed in the cytosol by the proteasome, but others are digested within lysosomes. During the last moments of cell division, the two daughter cells remain joined by a bridge known as the midbody channel, which contains the midbody and a large structure known as the midbody ring. As the two daughter cells separate, the midbody ring moves into one of the daughter cells, whence it eventually disappears. Pohl and Jentsch find that the midbody ring is cleared away via autophagy—a lysosome-based degradatory pathway that recycles cellular organelles during starvation. The authors showed that autophagy accessory factors associate with the midbody ring during abscission, suggesting that the two processes may be coupled. Rings (shown at left, green) accumulated when lysosomal function was inhibited and also in cells of patients with lysosomal storage disorders. — HP\*

\*Helen Pickersgill is a locum editor in *Science's* editorial department.



ECONOMICS

## Keeping Track of Risk

The global financial events of the past year have brought home to many individuals the ineluctable tradeoff between reward and risk in which investments placed in an asset class with higher returns—for instance, equities—are vulnerable to larger annual deviations from the long-term averages in comparison to a safer or less risky asset class, such as cash. Searching for ways around this tradeoff has proven to be challenging, but Basu *et al.* describe experimental findings in support of the retrospective view that the introduction of recordkeeping in Sumer several millennia ago (an example is shown above) enhanced returns in economic exchanges while simultaneously reducing risk. In a multi-trustee and multi-round trust game, each investor decided how much money to send to a trustee, where it would be tripled before the trustee decided how much of the proceeds would be sent back to the investor. Over many rounds, reputations were formed, and investors who were allowed to enter written tallies of trustee historical performance gained twice as much as those who had to keep all of the data in their heads. Furthermore, the variation in returns to the recordkeeping investors across trustees was less by one-third, presumably because the investors could adjust their allocations on the basis of the specific reputation of the trustee rather than a group average. — GJC

*Proc. Natl. Acad. Sci. U.S.A.* **106**, 1009 (2009).

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*Nat. Cell Biol.* **11**, 65 (2009).

CLIMATE SCIENCE

## Refreshing CLIMAP

A seminal quantitative global reconstruction of sea surface temperatures during the Last Glacial Maximum (LGM) was completed over 3 decades ago. This CLIMAP (Climate Long-Range Investigation, Mapping and Prediction) project revealed important features such as the regional inhomogeneity of temperature change between the LGM and the pre-industrial Holocene, colder LGM temperatures at high latitudes than at low

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latitudes, and a relatively modest difference of about 2°C in tropical sea surface temperatures. Nevertheless, CLIMAP was a first iteration and contained a number of weaknesses, such as sparse data coverage in most regions and a limited number of techniques from which to estimate temperatures. Now, an expanded and improved reconstruction of LGM temperatures has been assembled by Waelbroeck *et al.* in the MARGO (Multiproxy Approach for the Reconstruction of the Glacial Ocean Surface) project. Incorporating a wide variety of temperature proxies and a spatially better-resolved set of data, MARGO strengthens many of the conclusions stemming from CLIMAP and clarifies other ambiguities and inconsistencies. — HJS

*Nat. Geosci.* **2**, 10.1038/NGEO411 (2009).

## IMMUNOLOGY

## Putting the Pieces in Place

T cells require two signals, which are delivered via antigen-presenting cells, to be activated. The T cell receptor (TCR) engages major histocompatibility complexes that present peptides derived from pathogens, and the costimulatory receptor CD28 interacts with its ligand, B7. Engagement of CD28 is critical for T cells in distinguishing between foreign and self-antigens because antigen-presenting cells express high levels of B7 only during infection. Park *et al.* demonstrate that phosphoinositide-dependent kinase 1 (PDK1) integrates signals downstream of the TCR and CD28 to promote T cell activation through activation of the transcription factor NF- $\kappa$ B. PDK1-deficient T cells exhibited impaired TCR/CD28-induced activation and a selective impairment in NF- $\kappa$ B activation. In T cells, NF- $\kappa$ B is activated after the assembly of the CARMA1-Bcl10-MALT1 (CBM) complex that itself depends on protein kinase C- $\theta$  (PKC- $\theta$ ). TCR signaling recruited PKC- $\theta$  to the immunological synapse, whereas CD28 signaling drove recruitment of PDK1 and its subsequent autophosphorylation. The phosphorylation of PDK1 facilitated its interaction with PKC- $\theta$  and CARMA1, resulting in their activation and the assembly of the CBM complex that leads to NF- $\kappa$ B activation. — KM

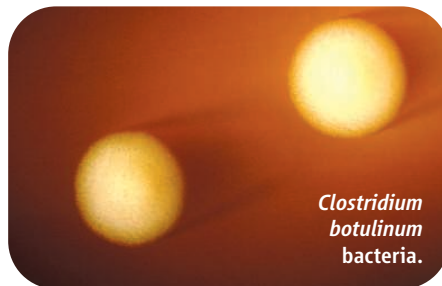
*Nat. Immunol.* **10**, 158 (2009).

## CHEMISTRY

## Blocking Botulism

The known antidotes for botulinum neurotoxin (BoNT) exposure are antitoxins, so there is considerable interest in identifying small-molecule inhibitors of its action. All BoNTs consist of a light-chain (LC) protease that is translocated by a heavy-chain (HC) channel. Fischer *et al.* have used chemical semisynthesis to develop analogs

of toosendanin, a traditional Chinese medicine extracted from *Melia toosendan* that has been reported to inhibit the action of BoNTs in mon-



*Clostridium botulinum* bacteria.

keys. Single-molecule assays showed that toosendanin and a more potent tetrahydrofuran derivative inhibited translocation of serotypes A and E of the LC, and two in vivo assays confirmed this activity. However, once the LC cargo was delivered, toosendanin could increase the propensity of the HC channel to remain in an open state that would disrupt endosomal processes. Thus, the binding site for toosendanin apparently depends on the state of the cargo within the chaperone. As this channel-opened state occurs at much higher concentrations (by a factor of about 2000) than does inhibition, further exploration of this class of channel blockers is warranted. — PDS

*Proc. Natl. Acad. Sci. U.S.A.*  
10.1073/pnas.0812839106 (2008).

## ASTROPHYSICS

## Diminished Competition

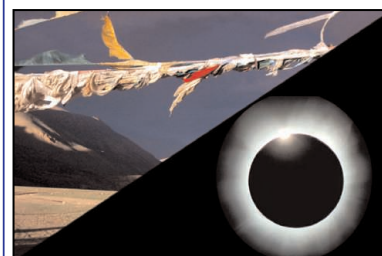
Most galaxies harbor giant black holes at their centers. For the most part, the black holes just sit quietly, but if their neighborhoods contain enough gas, they become active by accreting the gas, releasing large amounts of radiation in the process. Over time, the gas surrounding an active black hole gets heated and may even be expelled from the galaxy, a process that depletes the reserves of cold gas that feed star formation. In order to understand how black holes affect the galaxies that host them, Schawinski *et al.* studied a sample of local galaxies with active black holes and moderate luminosities, selected by virtue of their x-ray emission to avoid missing galaxies that would otherwise be obscured by dust. Color comparisons revealed that this sample falls in between galaxies that are actively forming stars and those that are quiescent, irrespective of the amount of dust. The colors suggest that star formation has stopped in these galaxies long before the effects of black hole growth can be detected—a challenge to scenarios where substantial levels of star formation coexist with black-hole growth. — MJC

*Astrophys. J.* **692**, L19 (2009).

## TIBET

## &amp; Total Solar Eclipse

July 8-24, 2009



Centerline of totality for this Eclipse arcs from India across Bhutan and China. See the eclipse south of Shanghai, near **Hangzhou**, reputedly Marco Polo's favorite city in China. This will be an excellent location for getting the best view of the Total Solar Eclipse.

Start in **Chengdu**, vibrant capital city of Sichuan, and then fly west to explore the cultural heart of Tibet. The Tibetan Plateau has long been a place of fascination for Western naturalists and explorers.

Our first destination in Tibet is **Tsedang** near some of the oldest villages and sacred sites in Tibet. They pre-date Buddhism in this area by more than 1,000 years.

From Tsedang, follow the Yarlung Tsangpo & Kyichu rivers upstream to **Lhasa**, historic center of the Tibetan world renowned for its sacred sites, each with distinctive esoteric rituals, colorful iconography, and profound spiritual



significance to the Tibetan people. These include the **Jorkang Temple**, the **Potala** and **Norbulinka Palace**, the winter and

summer residences of the Dalai Lama, and **Ganden Monastery**, poised dramatically on a ridge above the Lhasa Valley.

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