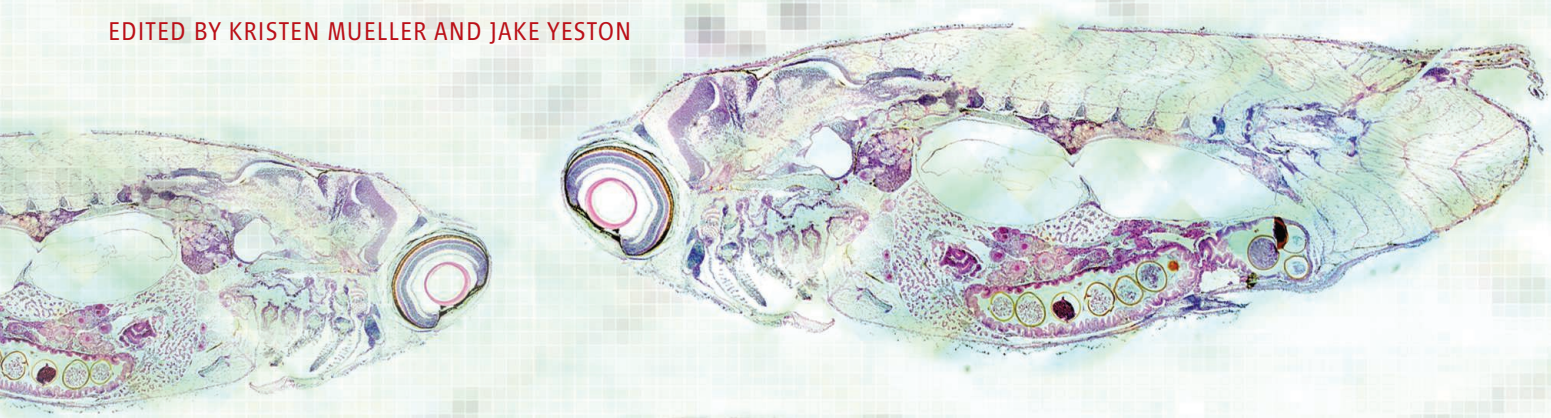
EDITED BY KRISTEN MUELLER AND JAKE YESTON



MICROBIOLOGY

TB Tolerance Exposed

One of the reasons tuberculosis (TB) continues to be a substantial public health problem is because the bacteria that cause TB, *Mycobacterium tuberculosis*, develop drug tolerance quickly. This requires patients to follow a 6-month-long drug regimen to ensure bacterial eradication, to which many patients fail to adhere. In order to identify new drug targets that may lead to shorter therapeutic regimens, Adams *et al*. dissected the development of drug tolerance in a zebrafish model of TB. Zebrafish infection with *Mycobacterium marinum* followed a similar disease course as human infection, which included the rapid development of drug tolerance. Multidrug-tolerant bacteria were present in macrophages just days after infection and were expanded and disseminated by granulomas. Bacteria acquired tolerance by replicating in macrophages, in both fish and mammalian cells. Upon infection, macrophages increased expression of bacterial efflux pumps, which can pump drugs out. Use of pump inhibitors demonstrated that these complexes mediated drug tolerance. Together, these studies suggest that adding efflux pump inhibitors to the standard TB therapies may be an effective way to reduce the course of treatment. — KLM

Cell **145**, 1 (2011).

BIOCHEMISTRY

How to Unwind

During DNA replication, ring-shaped helicases use energy from ATP hydrolysis to move along and separate DNA strands, creating space for new bases to be added to the emerging template. Initiation of replication in eukaryotes involves two key steps. First, the double hexamer Mcm2-7 helicase is loaded onto duplex DNA. Second, Cdc45 and GINS associate with each hexamer to form the active CMG helicase. To gain insight into these two steps, Costa *et al*. determined the structures of Mcm2-7 and the full CMG helicase by single-particle electron microscopy. Structural models of Mcm2-7 showed a ring that was open between Mcm2 and Mcm5 and could either be planar or form a slight spiral. The full helicase was constrained to the planar conformation, and GINS and Cdc45 bridged the gap to form a large channel. Imaging of CMG purified in the presence of an ATP analog revealed a conformational change induced by nucleotide binding; the gap between Mcm2 and Mcm5 closed and the channel was divided into two smaller pores. The tendency of Mcm2-7 to form open rings might facilitate loading onto duplex DNA. Upon binding of Cdc45 and GINS, the structural data are consistent with a model in which CMG promotes duplex opening and accommodates a single strand in each of its pores. The two helicases loaded onto DNA could then move apart, leaving the extruded DNA between them accessible for replication. — VV

Nat. Struct. Mol. Biol. **18**, 10.1038/nsmb.2004 (2011).

EDUCATION

Sizing Up Education Specialists

Attempts to include education training into already demanding science faculty schedules have been challenging. One solution is the introduction of Science Faculty with Education Specialties (SFES), scientists who take on education roles, into science departments. This may increase support for faculty development and innovation in teaching and increase departmental interest in research on teaching and learning. Minimal data are available on the purpose, structure, and outcomes of SFES, however. In order to learn more about these positions, Bush *et al*. surveyed SFES and non-SFES faculty members within the California State University System (CSU). Despite SFES existing across all science disciplines, faculty ranks, and CSU campuses, their role is still not well defined. SFES reported teaching the same amount as their non-SFES peers, and the same proportion of SFES reported being engaged in science education research as reported being engaged in basic science research. Although SFES had formal education training, the amount of actual training reported was minimal, which suggested that science departments still prefer to hire scientists trained in basic research. The majority of SFES thought that they are making a difference; however, almost 40% were considering leaving their positions because of concerns that their work in education was not supported, valued, or understood. — MM

CBE Life Sci. Educ. **10**, 25 (2011).

CELL BIOLOGY

A Less Toxic Treatment

Cells frequently tag proteins that are targeted for destruction by the proteasome with ubiquitin, a process that is important for maintaining cellular homeostasis and health. Besides defunct or aberrant cytosolic proteins, misfolded endoplasmic reticulum–derived proteins are "dislocated" back

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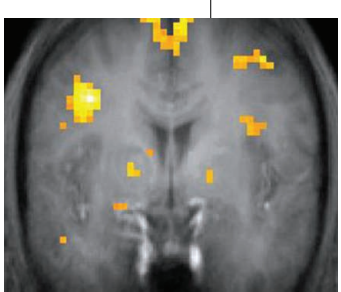
into the cytosol, ubiquitinated, and degraded by the proteasome. Proteasome inhibitors that block various stages of these processes exist and are useful for studying this biological process, but are often quite toxic. Ernst *et al.* describe an alternative approach to interfere with the ubiquitin proteasome (UPS) pathway. A highly active ubiquitin-specific protease domain was used to remove ubiquitin preemptively from substrates about to be destroyed, and so stabilize them. The technique allowed the uncoupling of dislocation and degradation of endoplasmic reticulum–derived misfolded proteins. This approach efficiently and globally blocked the UPS pathway, but was less cytotoxic than commonly used pharmacological inhibitors. — SMH

PLOS Biol. **8**, e1000605 (2011).

NEUROSCIENCE

Obesity's Chicken or Egg

Altered reward circuitry in the brain may play a role in obesity. One change that has been observed is that overweight people have fewer dopamine D2 receptors in the brain striatum; however, it is unclear whether this is a cause or consequence of overeating. Stice *et al.* used functional magnetic resonance imaging to look at vulnerability to obesity by examining neural responses to food and related cues in high-risk though still-lean adolescents. They found that a corticostriatal network responded to food receipt, but not to anticipation of food-related cues, more strongly in these high-risk people. A related network in high-risk individuals also responded more to the receipt of money. These people also showed greater activation of the oral regions of the somatosensory cortex in response to palatable food intake, a result specific for food rather than money. Thus, youths at risk for obesity initially had a generally elevated reward region responsivity. When coupled with an increased responsivity of oral somatosensory regions, this may result in overeating that subsequently produces dopamine receptor down-regulation and elevated incentive salience of food cues. — PRS



CREDIT: STICE *ET AL.*, *J. NEUROSCI.* **31**, 4360 (2011)

J. Neurosci. **31**, 4360 (2011).

GEOLOGY

Records in the River

The expansion of agriculture, mills, and deforestation after colonial settlement of eastern North America expanded erosion and greatly affected the hydrology of streams and rivers. However, Native Americans had been practicing agriculture and forest management for several centuries before that. Stinchcomb *et al.* show that river hydrology was modified by, and so records, this history as well. They focused on the Delaware River Valley, where artifacts show widespread settlement from about 1100 to 1600 CE, including expansion of maize agriculture and forest clearing. Carbon isotope, radiocarbon dating, and phytolith analyses document the increase in maize and other grasses. Analysis of sediments shows increased sedimentation during this interval in stream valleys and also an increase in flooding. Together, the data imply that perhaps half of the surrounding forests were cleared in the local floodplain. Flooding may have been further augmented by cooler and wetter conditions from 1450 to 1530 CE. Thus, pre-Columbian agriculture and deforestation also left a marked sedimentary record, at least locally in North America. — BH

Geology **39**, 363 (2011).

PHYSICS

Complex Quantum Simulation

Interactions between the charge, spin, and orbital degrees of freedom of electrons in condensed-matter systems can give rise to many complex electronic and magnetic phases. The narrow, or often fixed, range of variable materials parameters can be a limitation in probing and understanding the evolution of the order parameters of such complex correlated systems. An array of atoms trapped in an optical lattice has the potential to be extremely flexible in terms of tuning the parameters. Although the atoms tend to be isotropic, leading to somewhat trivial systems, much theoretical work has explored the possibilities of finding ways to imprint and detect more complicated order parameters on the lattice of trapped atoms. It is along such lines that Kitagawa *et al.* propose a spectroscopic technique based on two-particle interferometry that probes the phase-sensitive correlations between atom-atom interactions across the lattice. They show that the technique should allow the measurement of nontrivial order parameters in entangled ensembles of cold atoms, such as d- or p-wave pairing of electrons found in exotic superconductors and superfluids, and the realization of cold-atom systems that function as complex quantum simulators. — ISO

Phys. Rev. Lett. **106**, 115302 (2011).

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