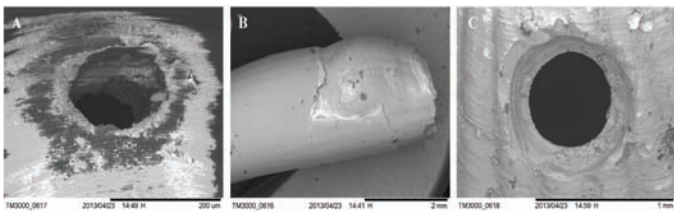
In This Issue

Oceanic deoxygenation effects at the seafloor

Oceanic deoxygenation is a likely consequence of global warming and may expand marine oxygen minimum zones, in turn potentially leading to reorganization of marine communities. Sarah Moffitt et al. (pp. 4684–4689) examined changes in fossilized fauna in sediment cores from the Santa Barbara Basin in the Pacific Ocean covering the period from 16,100 to 3,400 years ago that includes the changes in climate since the last glacial period. Episodes of warming were accompanied by abrupt transitions from oxygenated to hypoxic conditions over a period less than 100 years. The authors found major changes in seafloor diversity, trophic energy sources, and biomass documented in more than 5,400 fossils and trace fossils of diverse marine metazoans. Ecosystem reorganization coincided with abrupt climate warming and dissolved oxygen loss events. Although known time periods of marine biodiversity recovery from disturbances are around 100 years, the authors found that recovery of seafloor diversity following abrupt climate change and deoxygenation occurred over more than 1,000 years. The results suggest that future global climate change may result in ecosystem-level effects with millennial-scale recovery periods, according to the authors. — P.G.



SEM images of fossilized mollusk shells showing predation traces from annelid worms (*A*), crustaceans (*B*), and gastropods (*C*).

Land management and wetlands' carbon footprint

In the context of global climate, wetlands represent ecosystems that can sequester CO_2 and emit methane. The dichotomy has confounded attempts to quantitatively determine how wetlands may factor into future climate change scenarios, a contribution to the global greenhouse gas budget that depends on the relative land–atmosphere exchanges of two major greenhouse gases. To assess the potential future impact of natural versus managed wetlands, A. M. R. Petrescu et al. (pp. 4594–4599) combined a sustained pulse–response model with data from a network of wetland observational sites that monitors simultaneous CO_2 and methane fluxes. Analyzing areas across a wide range of climatic regions, ecosystem types, and management practices, the authors predict that the net greenhouse gas effect from natural ecosystems largely balances over the course of several centuries, with CO_2 uptake offsetting methane emissions. However, the authors found that net

Image courtesy of Alpo Hassinen (Mekrijärvi Research Station, University of Eastern Finland, Joensuu Campus).

Fen peatland near Joensuu, Finland, used for peat extraction until 2001, and now cultivated with a bioenergy crop.

climate impact of wetlands depends strongly on whether the areas are natural or managed, with significant increases in atmospheric forcing from greenhouse gases associated with land management, in particular for wetlands converted to croplands. The findings highlight how human activities influence the climate footprint of wetlands and suggest the need for mitigation strategies for managed wetlands. — T.J.

Ebola virus elicits a potent immune response

Despite the extensive Ebola outbreak in West Africa, remarkably little is known about the virus's pathogenesis. Anita McElroy et al. (pp. 4719–4724) explored the cellular immune responses to acute Ebola virus infection in four patients treated at Emory University Hospital in Atlanta, Georgia. Contrary to assumptions about the immunosuppressive nature of the virus, the study revealed strong activation of B and T cells in all four patients. Plasmablasts that were actively secreting antibodies accounted for up to 50% of all B cells in infected individuals, compared with less than 1% in healthy participants. The frequency of activated $CD4^+$ T cells in infected individuals ranged from 5–30%, compared with 1–2% in

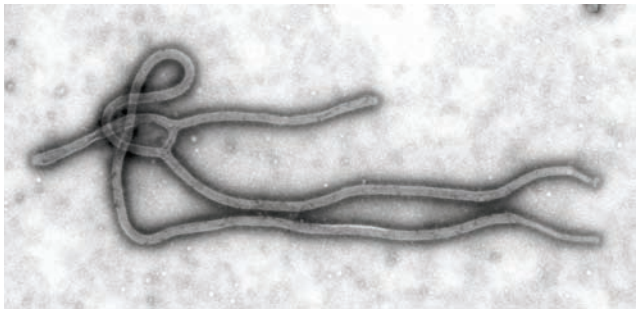


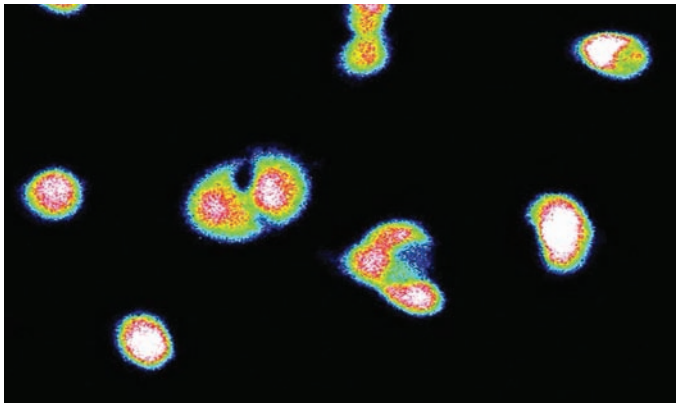
Image courtesy of Cynthia Goldsmith and Pierre Rollin (CDC, Atlanta).

Electron microscope image of Ebola virus.

healthy participants. More than half of the CD8+ T-cell population in infected individuals expressed markers of activation and proliferation, the authors report. The markers persisted even after the virus was cleared from the plasma, up to 1 month after patients were discharged from the hospital. The study further reveals viral protein targets of the T-cell response in humans, identifying CD4+ and CD8+ T-cell responses to Ebola virus nucleoprotein and several other proteins. According to the authors, knowledge of the immune cell kinetics and viral proteins targeted by T cells during natural infection may aid the design of vaccines against Ebola virus. — A.G.

Drug candidate targets therapy-resistant cancer cells

Recurrent breast and ovarian tumors with high levels of estrogen receptor α (ERα) often resist treatment, and effective therapies are needed to improve patient outcomes. To identify a drug candidate with an unconventional mode of action, Neal Andruska et al. (pp. 4737–4742) carried out an unbiased screen of around 150,000



BHPI increases intracellular calcium, hyperactivating the unfolded protein response, and leading to cancer cell death.

small molecules and identified around 2,000 molecules that modulated ERα-induced gene expression in human breast cancer cells. The authors report that one of these molecules, called BHPI, selectively blocked the proliferation of drug-resistant, ERα-positive breast and ovarian cancer cells but did not affect the proliferation of counterpart ERα-negative cancer cells. BHPI distorted the normally mild, transient, and protective ERα-mediated activation of a cell stress response called the unfolded protein response (UPR), eliciting a massive, sustained, and toxic UPR that killed ERα-positive but not ERα-negative breast cancer cells. In a mouse model of breast cancer, BHPI-treated tumors displayed arrested growth and weighed 60% less than control tumors. According to the authors, the high potency of BHPI, its effectiveness in a broad range of therapy-resistant cancer cells, and its ability to induce rapid and substantial tumor regression make it a suitable candidate for further mechanistic and therapeutic exploration. — J.W.

Recoding dengue virus genome to disfavor mammalian host

The dengue virus (DENV) infects both insects and mammals. Because insects and mammals have evolved differences in how they encode proteins, arthropod-borne viruses, or arboviruses, have evolved carefully balanced genomes that can efficiently use the protein-encoding machineries of both their insect and mammalian hosts. Sam Shen et al. (pp. 4749–4754) recoded the genome of DENV to undo this balance and selectively shift the virus's protein-encoding preferences away from mammals. The authors found that recoded DENVs grew to high levels in insect cells, but were highly attenuated in newborn mice. Despite the recoded DENV having reduced virulence in newborn mice, the virus induced high levels of neutralizing antibodies. The authors also found that female mice inoculated with recoded DENV as newborns passed these antibodies onto their offspring, in which the antibodies revealed protective effects against wild-type DENV. This strategy of recoding genomes to disfavor a particular host could be used to develop new vaccine candidates against DENV, and potentially against other human arboviruses, the authors suggest. — S.R.

Neuronal activity during sleep

Fruit flies (*Drosophila melanogaster*) share several fundamental features of sleep with mammals, including a reduced ability to respond to external stimuli. Daniel Bushey et al. (pp. 4785–4790) monitored calcium levels in Kenyon cell neurons during sleep and wake periods in fruit flies. Some of the flies had been sleep-deprived for up to 34 hours before testing. The authors found that calcium levels in Kenyon cells declined during sleep and increased on waking, suggesting a decline in neuronal activity during sleep. Further, the authors found that awake flies displayed greater responsiveness to stimuli than did sleeping flies, and that flies that had been awake for between 5 and 8 hours before testing showed a greater number of spontaneously active cells, compared with flies that had recently woken. Cells in flies sleep-deprived for more than 29 hours exhibited decreased ability to respond consistently to repeated stimuli. The results were consistent with previous effects of sleep deprivation on rats, in which individual cortical neurons unpredictably entered a sleep-like state while the rats were awake, a phenomenon known as "local sleep during wake." According to the authors, calcium imaging of fruit flies suggests further similarities between sleep in mammals and fruit flies, and may explain impaired cognitive performance following sleep deprivation. — P.G.

Fruit flies share many features of sleep with mammals.