In This Issue

Oil fallout and the *Deepwater Horizon* spill

Following the 2010 *Deepwater Horizon* oil spill, around 2 million barrels of oil, out of the 5 million barrels estimated to have been released, remained trapped within deep lateral plumes. To investigate the fate of the submerged oil, David Valentine et al. (pp. 15906–15911) examined data from Gulf of Mexico seafloor sediment cores for residual hopane, a hydrocarbon considered a conservative tracer for crude oil. The authors analyzed data from samples at more than 500 locations around the Macondo Well, origin of the leaked oil. A patchwork pattern of hopane contamination spanning an area of 3,200 km^2 likely originated from the Macondo Well and may represent up to 16% of the oil discharged to the environment. Sources of seafloor oil deposits may include lateral layers of oil-rich water that interacted with continental shelf sediment, as well as sinking oily particles, although the mechanism for oil sinking is unclear. The results suggest that the extent of oil fallout on the floor of the Gulf of Mexico is likely much larger than the study area but may be dispersed and heterogeneous, according to the authors. — P.G.

Controlled burning of surface oil slicks during the *Deepwater Horizon* event.

Modeling drug resistance in metastatic cancers

Molecularly targeted cancer drugs are often designed to inhibit the action of specific molecules implicated in tumor development. Generally considered less harmful to normal cells than chemotherapy and radiation, these promising drugs can produce rapid and dramatic reductions in the disease burden of certain metastatic cancers, but in most cases tumors rebound several months after treatment due to acquired drug resistance. Using a mathematical approach to examine the genetic heterogeneity of cancer cells, Ivana Bozic and Martin Nowak (pp. 15964–15968) present a theory that describes the full spectrum of resistance mutations present in a metastatic lesion prior to treatment. The authors demonstrate that most radiographically detectable lesions harbor at least 10 resistant subclones and bolster their findings by comparing model predictions with clinical data on the relative sizes of resistant subclones in colorectal cancer patients. Furthermore, the findings might help quantify the overall genetic heterogeneity of resistance prior to treatment and thus may be applied to designing treatment strategies aimed at controlling resistance, according to the authors. — T.J.

Bone remodeling in billfish

A basic tenet of bone biology states that most vertebrate animals maintain bone strength by remodeling, in which bone cells called osteocytes detect and orchestrate the repair of microdamage caused by repeated loading. Organisms without osteocytes, such as many members of the neoteleost group of fishes, were not thought to undergo bone remodeling. Ayelet Atkins et al. (pp. 16047–16052) examined bone from five species of billfish, including swordfish and marlins, which are anosteocytic members of the neoteleost group. The authors found that the rostral bones, which constitute the fishes' long, sword-like spears and endure repeated high stresses, contained high densities of structural footprints of remodeling, called secondary osteons, although billfish osteons were an order of magnitude smaller than mammal osteons and entirely without osteocytes. Further, the authors found that billfish rostral bone exhibited properties rare in skeletal tissue, displaying high stiffness, on the order of horse bone and far stiffer than other fish bone, and exceptionally high failure strains, deforming 100% more than mammalian bone before breaking. According to the authors, the results suggest that fish bones can repair damage despite lacking osteocytes, suggesting that osteocytes may not be the sole initiators of bone remodeling in fish or mammals. — P.G.

Inflammation and risk for depression

Depression and anxiety are associated with high levels of inflammatory molecules called cytokines, but it has not been clear whether inflammation causes these stress-related disorders. Georgia Hodes et al. (pp. 16136–16141) measured blood levels of cytokines such as IL-6 in nonaggressive mice before and after repeated social defeat stress invoked by exposure to an aggressive mouse for 10 minutes daily for 10 days. The authors classified the nonaggressive mice as susceptible based on a preference to spend more time near an empty cage rather than near a previously unencountered mouse on a subsequent social interaction test, whereas resilient mice showed the opposite pattern. Prior to exposure to an aggressive mouse, white blood cells called leukocytes released more IL-6 in susceptible mice, compared with resilient mice. Moreover, bone marrow transplantation of stem cells that give rise to leukocytes

lacking IL-6 reduced the development of subsequent social avoidance, compared with bone marrow transplantation resulting in high levels of IL-6. According to the authors, IL-6 may be a risk factor for the development of depression. — J.W.

Antiretroviral therapy and HIV incidence

Antiretroviral therapies (ART) can reduce HIV transmission by reducing the number of viral particles in the bloodstream of infected individuals. Jeffrey Eaton and Timothy Hallett (pp. 16202–16207) investigated whether the amount of HIV transmission that occurs during the first few months after becoming infected, when individuals are unlikely to have begun ART, is predictive of the impact of ART on incidence. The authors built a mathematical model of HIV prevalence and ART use based on surveys of households and pregnant women in South Africa since 1990. In the short term, the model predicted that a high proportion of early, pre-ART transmission resulted in smaller reductions in a population's HIV incidence, compared with a low proportion of pre-ART transmission. In the long term, high proportions of early transmission did not influence reductions in HIV incidence. The results suggest that the amount by which ART reduces HIV incidence is not predicted by the proportion of infections propagated in the first few months after infection. According to the authors, efforts to predict the impact of ART should focus on measuring biological factors and risk behaviors, rather than the proportion of early transmission. — J.P.J.

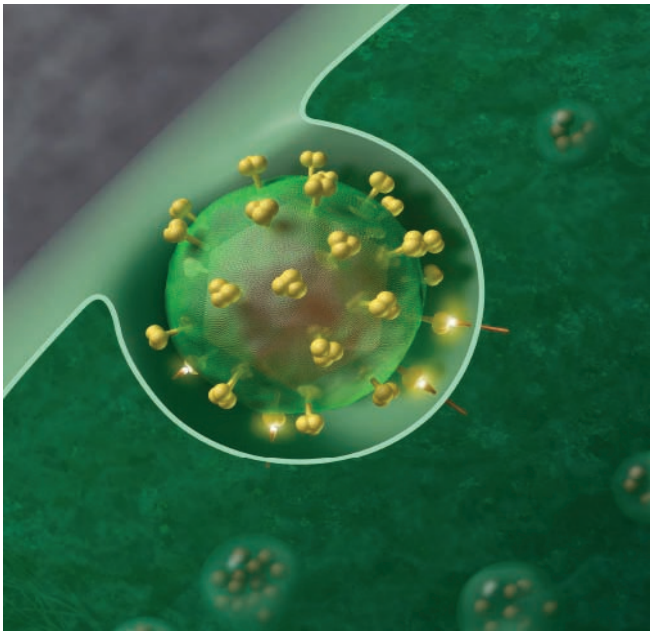
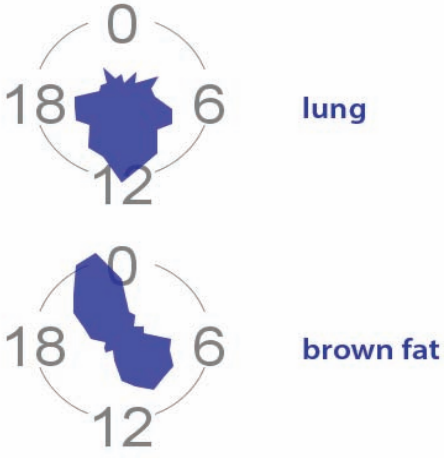


Image courtesy of Wikimedia Commons/J. Roberto Trujillo.

HIV-1.

Circadian gene expression

Circadian clocks drive biological processes including sleep, body temperature, and hormone levels, and research suggests that the processes may be regulated by circadian-controlled gene transcription. Ray Zhang et al. (pp. 16219–16224) used RNA sequencing and DNA microarrays to determine whether the circadian clock regulates rhythmic gene transcription in mouse organs. The authors monitored the expression of nearly 20,000 protein-coding and 1,000 noncoding genes, with sequences similar to noncoding genes found in humans, multiple times each day. The transcript levels of 43% of coding genes and 32% of the noncoding genes followed a circadian rhythm. Ten genes displayed rhythmic transcript levels in all 12 mouse organs studied, but most genes displayed rhythmic levels in only one or a few organs. Further, circadian transcript levels often peaked near dusk or dawn. The authors also examined which common drugs target the circadian genes identified in their study, finding that 56 of the 100 best-selling drugs in the United States and 119 drugs on the World Health Organization's list of essential medicines target circadian genes. Because many of the drugs targeting the circadian genes persist in the body for less than a full day, the authors suggest that timing drug dosage may improve the drugs' therapeutic benefits. — J.P.J.



Mouse organ genes display different circadian expression patterns.