ANIMAL CULTURE

Birds in the bin

It is now well accepted that humans are not the only animal to have complex culture, and we have also found that ecological novelty can lead to cultural innovation. Klump et al. documented the emergence of an evolving set of behaviors in response to human-generated resources, specifically garbage bins, in sulphur-crested cockatoos. This finding both documents the existence and spread of complex foraging culture among parrots, a lineage known to have high-level cognitive function, and illuminates how the spread of a cultural innovation can lead to regional distinct variations. —SNV

Cockatoos have devised methods of opening trash bins, and individuals can learn these methods from each other.

STRUCTURAL BIOLOGY

How to catch a dynamic state

AMP-activated protein kinase (AMPK) is a key sensor of energy status in eukaryotes. Its dynamic structure is regulated by allosteric factors including phosphorylation and binding of nucleotides and metabolites. Yan et al. developed conformation-specific antibodies that trap AMPK in a fully inactive state that has experienced a large, domain-level rotation. Biophysical experiments in cells and in vitro are consistent with the structural work and support a model in which the activation loop is fully exposed in the completely inactive, dephosphorylated state. These structures inform our understanding of the complex allosteric behavior in this crucial metabolic regulator. —MAF

PHOTOPHYSICS

Straining for high photoluminescence

The photoluminescence quantum yield in monolayer transition metal dichalcogenides generally drops at high emission intensities because the excitons undergo nonradiative annihilation. Kim et al. show that this process is resonantly amplified in these materials by van Hove singularities in their joint density of states. However, application of small mechanical strains (~0.5%) shifted the van Hove singularities and suppressed the nonradiative processes. Near-unity photoluminescence quantum yield at high exciton densities was seen in exfoliated monolayers of molybdenum sulfide, tungsten sulfide, and tungsten selenide, as well as centimeter-scale tungsten sulfide monolayers grown by chemical vapor deposition. —PDS

PLANT SCIENCE

Calcium signaling for host cell death

In response to microbial pathogens, some plants kill off their own cells to limit further spread of infection. The Toll/Interleukin-1 receptor/Resistance class of nucleotide-binding leucine-rich repeat receptors (known as TNLs) function in plants as immune receptors. These TNLs work together with a dedicated set of helper proteins. Jacob et al. reveal the structure of one of these helpers known as NRG1 (N REQUIREMENT GENE 1). The structure resembles a known animal cation channel. The authors demonstrate that helper NLRs directly control calcium ion influx to initiate host cell death, providing a mechanism for TNL outputs. —PJH

SPECTROSCOPY

Triplet-state lifetime quenched by oxygen

Little is known about the atomistic mechanism that nature uses to mitigate the destructive interaction of triplet-excited pigment chromophores with omnipresent oxygen. Peng et al. tackled this challenge by developing a technique based on conducting atomic force microscopy to populate and track triplets in a single pentacene molecule, a model π-conjugated system, placed on a sodium chloride surface (see the Perspective by Li and Jiang). The authors show how the triplet-state lifetime can be quenched in a controllable manner by atomic-scale manipulations with oxygen co-adsorbed in close vicinity. The presented single-molecule spectroscopy paves the way for further atomically resolved studies of triplet excited states that
BIOCHEMISTRY
Stimulating and suppressing HIFs

Collaboration report observations of this source at energies of tera— to peta–electron volts, extending the spectrum of this prototypical object. They combine these data with observations at lower energies to model the physics of the emission process. The multilambda data can be explained by a combination of synchrotron radiation and inverse Compton scattering. —KTS

Science, abh1155, this issue p. 452; see also abj5860, p. 392

MALARIA
An antimalarial advance

There is great need for antimalarial drugs in the face of growing resistance to existing therapies. Murithi et al. characterized MMV688533, an acylguanidine identified from compounds inhibiting known human drug targets that were screened for activity against Plasmodium falciparum. MMV688533 showed rapid in vitro killing of multiple P. falciparum strains as well as P. vivax. A single dose rapidly reduced parasitemia in a P. falciparum severe combined immunodeficient mouse model of infection, and this agent displayed favorable pharmacokinetic and toxicity profiles. MMV688533 selected for only low-grade resistance, with resistant parasites remaining sensitive to existing antimalarials. These findings suggest that MMV688533 is a promising antimalarial candidate with a low resistance risk and the promise of single-dose cure, which merits further study. —CNF


GENOMICS
Australian disappearances

One of the highest levels of extinction occurred in Australia, where 34 mammals have disappeared since European colonization. One suggestion for this vulnerability is the small population sizes and thus lack of genetic diversity, an explanation that could be predictive of future losses. To investigate this possible mechanism, Roynod et al. obtained genomic data from eight extinct rodent species from museum samples in Australia collected ~150 years ago and compared them with 42 closely related extant species. Unexpectedly, the authors found relatively high genetic diversity among the specimens, indicating that the populations were in fact quite large. From these data, the authors estimate that ~10 million years of unique evolutionary history has been lost in Australia since European colonization. Large population sizes and diversity of species seem to have offered little protection against the depredations of humans. —LMZ


CANCER
Cancer-killing viruses to the brain

Oncolytic viruses can selectively infect cancer cells to stimulate cell death and antiviral and antitumor immune responses. Fares et al. report a phase 1 trial in patients with high-grade glioma treated with an engineered oncolytic adenovirus delivered by neural stem cells (NSCs). Delivery of oncolytic viruses in NSCs has been previously shown in mouse models to improve the delivery and distribution of virus particles within gliomas. The 12 patients underwent surgical resection, and the NSCs containing oncolytic virus
NEUROIMMUNOLOGY
Getting around the blood–brain barrier
The meninges comprise three membranes that surround and protect the central nervous system (CNS). Recent studies have noted the existence of myeloid cells resident there, but little is known about their ontogeny and function, and whether other meningeal immune cell populations have important roles remains unclear (see the Perspective by Nguyen and Kubes). Cugurra et al. found in mice that a large proportion of continuously replenished myeloid cells in the dura mater are not blood derived, but rather transit from cranial bone marrow through specialized channels. In models of CNS injury and neuroinflammation, the authors demonstrated that these meningeal myeloid cells have an immunoregulatory phenotype compared with their more inflammatory blood-derived counterparts. Similarly, Brioneschi et al. show that the meninges host B cells that are also derived from skull bone marrow, mature locally, and likely acquire a tolerogenic phenotype. They further found that the brains of aging mice are infiltrated by a second population of age-associated B cells, which come from the periphery and may differentiate into autoantibody-secreting plasma cells after encountering CNS antigens. Together, these two studies may inform future treatment of neurological diseases. —STS
Science, abf7844, this issue p. 409; abf9277, this issue p. 408; see also abf8857, this issue p. 397

PHYSIOLOGY
Intestinal HDL is hepatoprotective
High-density lipoprotein (HDL) is important for cholesterol metabolism and may have anti-inflammatory and antimicrobial properties. Although HDL is mainly produced by the liver, the intestine is also a source. Han et al. show in mice that intestinal HDL is not routed to the systemic circulation. Rather, in the form of HDL3, it is directly transported to the liver through the hepatic portal vein. There, it sequesters bacterial lipopolysaccharide from the gut that can trigger inflammation and liver damage. In various models of liver injury, loss of enteric HDL exacerbated pathology. By contrast, drugs elevating intestinal HDL improved disease outcomes. HDL3 is enriched in human portal venous blood, suggesting that enteric HDL may be targetable for the treatment of liver disease. —STS
Science, abf8761, this issue p. 411; see also abf8834, this issue p. 391

CORONAVIRUS
Intranasal vaccines
Among the many vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), intranasal forms fill an important gap. Most vaccines are administered intramuscularly, where they elicit systemic immune responses and central immune memory. But respiratory viruses predominantly enter the nasal passage first, suggesting that a strong mucosal immune response in the nasal cavity, as is induced by intranasal vaccines, may be beneficial. In a Perspective, Lund and Randall discuss the SARS-CoV-2 intranasal vaccines that are in clinical trials, the rationale for their use, and whether they may be viable for immunization or as a booster to improve protection from SARS-CoV-2. —GKA
Science, abg9857, this issue p. 397

ENZYMOLOGY
Go big or you’ll get lost
Rational mutagenesis is a common approach to investigating or engineering enzyme function in vitro, but the ease with which one can manipulate protein sequences belies many pitfalls in connecting sparse activity data to an enzyme’s true functional landscape. Using a high-throughput platform, Markin et al. expressed, purified, and performed an array of kinetic measurements on a target esterase, collecting data from >1000 mutations spanning the entire protein (see the Perspective by Baumer and Whitehead). Protein misfolding into an inactive state, rather than decreased equilibrium stability, was a crucial factor in negatively affected variants spread throughout the protein. When combined with prior mechanistic understanding and structures, four “functional components” help to rationalize the otherwise complex spatial pattern of effects of mutations on different aspects of enzyme function, all of which would be invisible from mutagenesis of just a few residues. —MAF
Science, abf8761, this issue p. 411; see also abf8834, this issue p. 391

NEURODEVELOPMENT
Developing neurons practice for real life
As a mouse runs forward across the forest floor, the scenery that it passes flows backwards. Ge et al. show that the developing mouse retina practices in advance for what the eyes must later process as the mouse moves. Spontaneous waves of retinal activity flow in the same pattern as would be produced days later by actual movement through the environment. This patterned, spontaneous activity refines the responsiveness of cells in the brain’s superior colliculus, which receives neural signals from the retina to process directional information. —PJH
Science, abd0830, this issue p. 412

QUANTUM DEVICES
Superconducting spin qubit
To date, the most promising solid-state approaches for developing quantum information-processing systems have been based on the circulating supercurrents of superconducting circuits and manipulating the spin properties of electrons in semiconductor quantum dots. Hays et al. combined the desirable aspects of both approaches, the scalability of the superconducting circuits and the compact footprint of the quantum dots, to design and fabricate a superconducting spin qubit (see the Perspective by Wendin and Shumeiko). This so-called Andreev spin qubit provides the opportunity to develop a new quantum information processing platform. —ISO
Science, abf0345, this issue p. 430; see also abk0929, this issue p. 390

PLANETARY SCIENCE
Single seismometer structure
Because of the lack of direct seismic observations, the interior structure of Mars has been a mystery. Khan et al., Knapmeyer-Endrum et al., and Stähler et al. used recently detected marsquakes from the seismometer deployed during the InSight mission to map the interior of Mars (see the Perspective by Cottaar and Koelemeijer). Mars likely has a 24- to 72-kilometer-thick crust with a very deep lithosphere close to 500 kilometers. Similar to the Earth, a low-velocity layer probably exists beneath the lithosphere. The crust of Mars is likely highly enriched in radioactive elements that help to heat this layer at the expense of the interior. The core of Mars is liquid and large, ~1830 kilometers, which means that the mantle has only one rocky layer rather than two like the Earth has. These results provide

also in science journals
Edited by Michael Funk
a preliminary structure of Mars that helps to constrain the different theories explaining the chemistry and internal dynamics of the planet. —BG

*Science*, abl2966, abf8966, abi7730, this issue p. 434, p. 438, p. 443
see also abj8914, p. 388

## MATERNAL IMMUNOLOGY

### Aire-expressing cells defend the fetus

The normal maternal immune system adapts to pregnancy by learning to tolerate both allogeneic paternal and pregnancy-associated antigens expressed by the fetus and placenta. Gillis-Buck *et al.* investigated the contribution of cells expressing the autoimmune regulator (*Aire*) gene to maintaining fetal health using a mouse model in which *Aire*-expressing cells were deleted during early pregnancy. Ablation of *Aire*-expressing cells did not impair fetal implantation, but resulted in intrauterine fetal growth restriction during both allogeneic and syngeneic pregnancies and was associated with increased activation of effector T cells. Selective deletion of extra-thymic *Aire*-expressing cells (eTACs) while preserving *Aire*-expressing thymic epithelial cells revealed that eTACs are required for maintaining tolerance and fetal health. These findings demonstrate an unanticipated role for eTACs as guardians of fetal health during pregnancy. —IRW


## ASTROPHYSICS

### Understanding the origin of Earth’s water

The deuterium to hydrogen (*D/H*) ratio in Earth’s oceans differs from the bulk composition of the protosolar nebula, which suggests that either some of Earth’s water was deposited by comets and asteroids or that large spatial fluctuations in *D/H* existed in the initial nebula. Luo *et al.* performed detailed laboratory measurements of the interaction of a tunable ultraviolet laser with molecules of deuterated water (HOD). The theoretical expectation was that dissociation to H+OH would be more common, but they found instead that dissociation to D+OH was more common and that the ratio of H+OH to D+OH reactions was highly wavelength dependent. This phenomenon may have played a key role in determining the chemical structure of the material from which Earth was formed. —ES