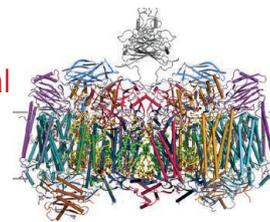


# RESEARCH

## Structure of a mycobacterial respiratory machine

Gong et al., p. 1020



## IN SCIENCE JOURNALS

Edited by Stella Hurtley

### ANIMAL CULTURE

#### Trendsetting flies

**T**hough once believed to be confined to humans, culture has now been demonstrated in many different animal species, from whales to parrots. Most such animals have high levels of cognition, but the basics of transmission and copying could easily occur in less cognitively advanced species. Danchin *et al.* show that mating culture can be passed on in *Drosophila* and model the process by which this occurs (see the Perspective by Whiten). Their results suggest that culture and copying may be much more widespread across the animal kingdom than previously believed. —SNV

*Science*, this issue p. 1025; see also p. 998



Fruitflies learn behaviors by copying one another.

### ARCHAEOLOGY

#### Paleolithic occupation of Tibet

Human colonization of the high-altitude Tibetan Plateau has generally been thought to have been confined to the past few thousand years of the Holocene. Zhang *et al.* report an investigation of the Nwya Devu archaeological site in central Tibet, 4600 meters above sea level, with Paleolithic occupation

dates of ~40 thousand to 30 thousand years ago (see the Perspective by Zhang and Dennell). The site has yielded a range of stone tools, indicating the adaptive ability of early modern humans to the harsh environment of the "roof of the world." The findings also suggest that people from Tibet and Siberia may have interacted at this time. —AMS

*Science*, this issue p. 1049; see also p. 992

### MICROBIOLOGY

#### A $\beta$ -barrel trigger for autophagy

Autophagy can help to clear pathogen infections. Chaudhary *et al.* showed that outer membrane proteins with a  $\beta$ -barrel tertiary structure from Gram-negative bacteria or mitochondria were recognized by specific receptors on macrophages and epithelial cells. Adding outer membrane

proteins to mouse macrophages induced autophagy and enabled the mice to successfully rid themselves of *Salmonella* Typhimurium infection. Thus, the immune responses activated by outer membrane proteins may contribute to pathogen clearance or autoimmune diseases. —WW

*Sci. Signal.* **11**, eaat7493 (2018).

### METALLURGY

#### Turning many into one

Single-crystal metal foils are valuable for their surface properties that allow for synthesis of materials like graphene. Jin *et al.* present a strategy for creating colossal single-crystal metal foils called "contact-free annealing" (see the Perspective by Rollett). The method relies on hanging and heating commercially available, inexpensive, cold-rolled metal foils. Almost as if by magic, the polycrystalline grains rotate and anneal into a large single-crystal sheet with a specific crystal orientation. The strategy allows for the creation of much larger and much cheaper single-crystal metal foils. —BG

*Science*, this issue p. 1021; see also p. 996

### SUPERCONDUCTIVITY

#### Squeezing into the third dimension

Cuprate superconductors are known to harbor charge order in part of their phase diagram. Curiously, the order has a two-dimensional (2D) character at zero magnetic field, whereas a 3D order appears at high fields. Kim *et al.* now show that in a yttrium-based cuprate, a 3D

charge order can be induced even at zero magnetic field. The authors compressed the material along one direction and measured a large inelastic x-ray scattering signal that was consistent with the formation of a 3D order. The measurements suggest that the induced order is associated with an optical lattice mode in the material. —JS

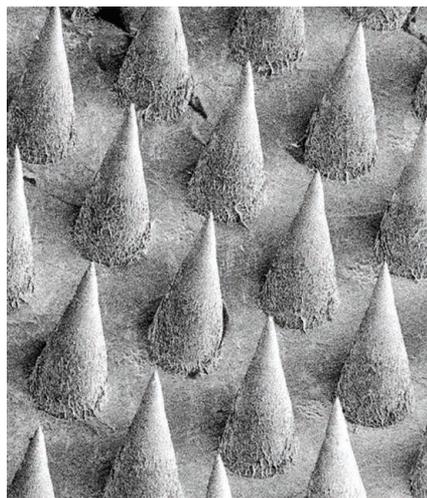
*Science*, this issue p.1040

## CELL BIOLOGY

### A stem cell-integrated microneedle patch

More than 600,000 people in the United States suffer a heart attack each year. Stem cell therapy has been used to improve treatment options for survivors, but so far, cardiac stem cell retention rates have been low. To better integrate the stem cells into viable heart tissue, Tang *et al.* created a microneedle patch. Its biocompatible needles penetrate the skin and serve as communication channels between the patch and the heart, getting nutrients to the heart while delivering stem cells to the injured area. When tested in rats and pigs after acute heart attack, the patch boosted the development of heart tissue, reduced scar size, and increased cardiac functions. —PJB

*Sci. Adv.* 10.1126/sciadv.aat9365 (2018)



Cardiac stem cells growing on a microneedle array

## DISTANT GALAXIES

### Mergers drive a powerful dusty quasar

Massive galaxies in the early Universe host supermassive black holes at their centers. When material falls toward the black hole, it releases energy and is observed as a quasar. Astronomers found a population of powerful distant quasars that are obscured by dust, but it has been unclear how they are formed. Díaz-Santos *et al.* observed the dust-obscured quasar WISE J224607.56–052634.9 at submillimeter wavelengths, finding three small companion galaxies connected to the quasar by bridges of gas and dust. They inferred that galaxy mergers can provide both the raw material to power a quasar and large quantities of dust to obscure it. —KTS

*Science*, this issue p.1034

## CANCER

### Hunting and fishing for cancer genes

Mucosal melanoma is a rare, but deadly, form of melanoma that occurs in sun-protected tissues. Little is known about the genetic alterations that drive the growth of these tumors. Ablain *et al.* sequenced mucosal melanomas from 43 patients and found that a substantial fraction showed inactivation or loss of *SPRED1*, a gene that encodes a negative regulator of RAS–MAPK (mitogen-activated protein kinase) signaling. Using a platform called MAZERATI (Modeling Approach in Zebrafish for Rapid Tumor Initiation), they discovered that *SPRED1* loss may help explain the poor response of melanoma patients to drugs that inhibit the KIT tyrosine kinase. The results suggest that a combination of KIT inhibitors and drugs that inhibit MAPK signaling may be more effective. —PAK

*Science*, this issue p.1055

## IN OTHER JOURNALS

Edited by **Caroline Ash** and **Jesse Smith**



*Aquilegia coerulea* is found widely around the Northern Hemisphere.

## PLANT GENOMICS

### Columbine's puzzling chromosome

The columbine genus *Aquilegia* is found across the Northern Hemisphere and arose through two adaptive radiations, giving rise to 70 extant species. Filiault *et al.* deep sequenced *Aquilegia coerulea* to create a reference genome and compared it to 10 other sequenced *Aquilegia* spp. from Europe, Asia, and North America. Although the genomes generally exhibited low genetic diversity within species, consistent with previous studies, chromosome 4 showed an overall greater diversity, a higher number of older genetic variants, and different phylogenetic relationships among the species. The differences in chromosome 4 relative to the rest of the genome may be due to hybridization among species and a differential reduction in selection after *Aquilegia* diversified for this chromosome. —LMZ

*eLife* 7, e36426 (2018).

## BIOTECHNOLOGY

### Precision genome engineering

Genome editing through CRISPR-Cas systems has the potential to correct genetic mutations that occur in diseased cells, such as cancer cells.

However, the ability to selectively activate CRISPR-Cas systems in diseased cells is important to ensure that gene editing only occurs where it is wanted. Zhu *et al.* developed a system whereby gene editing could be activated by a magnetic field, thus allowing spatial control. The use of

**MICROBIOTA****Metabolic regulation of microbiota**

The gut microbiota affects human health, but we are only just beginning to develop a mechanistic understanding of some of the host-microbe interactions involved. Litvak *et al.* review how host colon epithelial cells mediate the symbiosis. Healthy colonocytes maintain anaerobic conditions in the gut lumen because their metabolism ensures rapid oxygen consumption. Such conditions select for obligate anaerobic organisms. These tend to be those that consume dietary fiber and produce short-chain fatty acids beneficial to the host. If there is a shift in colonocyte metabolism—because of disease, diet, or other damage—the epithelium becomes oxygenated. The presence of oxygen allows expansion of facultative aerobic organisms. Microbes in genera that include pathogens are often oxygen-tolerant, and dysbiosis can be the result. —CA

*Science*, this issue p. 1017

**STRUCTURAL BIOLOGY****Molecular-motor coordination**

The proteasome is a cytosolic molecular machine that recognizes and degrades unneeded or damaged proteins that have been tagged with ubiquitin. A heterohexameric adenosine triphosphatase motor pulls the substrate into the proteolytic chamber, while at the same time, a protein located at the entrance of this motor removes the ubiquitin. De la Peña *et al.* trapped the substrate inside the motor by inhibiting removal of ubiquitin. This allowed them to determine cryo-electron microscopy structures in the presence of substrate and adenosine triphosphate (ATP). The findings distinguish three sequential conformational

states that show how ATP binding, hydrolysis, and phosphate release are coordinated between the six subunits of the motor to cause the conformational changes that translocate the substrate through the proteasome. —VV

*Science*, this issue p. 1018

**BIOCHEMISTRY****Another N-end rule to add**

Proteins that emerge from a ribosome bear the N-terminal methionine (Met) residue. In bacteria, Met is formylated before translation starts, whereas in eukaryotes, most nascent proteins seemed to start with unmodified Met. Working in yeast, Kim *et al.* found that the N-terminal formylation of eukaryotic proteins is detectable even under normal conditions and is greatly increased upon specific stresses, which cause some Fmt1 formyltransferase to be retained in the cytoplasm. The retention of this normally mitochondrial protein was found to require the Gcn2 kinase. In addition, the Psh1 ubiquitin ligase was shown to target N-terminally formylated eukaryotic proteins for proteasome-dependent degradation by the so-called fMet/N-end rule pathway. —SMH

*Science*, this issue p. 1019

**STRUCTURAL BIOLOGY****An electron bridge in place of a ferry**

Respiratory complexes are massive, membrane-embedded scaffolds that position redox cofactors so as to permit electron transfer coupled to the movement of protons across a membrane. Gong *et al.* used cryo-electron microscopy to determine a structure of a stable assembly of mycobacterial complex III-IV, in which a complex III dimer is sandwiched between two complex IV monomers. A potential direct electron transfer

path stretches from the quinone oxidizing centers in complex III to the oxygen reduction centers in complex IV. A loosely associated superoxide dismutase may play a role in detoxifying superoxide produced from uncoupled oxygen reduction. —MAF

*Science*, this issue p. 1020

**SOLID-STATE PHYSICS****Separating structure and electrons in VO<sub>2</sub>**

Above 341 kelvin—not far from room temperature—bulk vanadium dioxide (VO<sub>2</sub>) is a metal. But as soon as the material is cooled below 341 kelvin, VO<sub>2</sub> turns into an insulator and, at the same time, changes its crystal structure from rutile to monoclinic. Lee *et al.* studied the peculiar behavior of a heterostructure consisting of a layer of VO<sub>2</sub> placed underneath a layer of the same material that has a bit less oxygen. In the VO<sub>2</sub> layer, the structural transition occurred at a higher temperature than the metal-insulator transition. In between those two temperatures, VO<sub>2</sub> was a metal with a monoclinic structure—a combination that does not occur in the absence of the adjoining oxygen-poor layer. —JS

*Science*, this issue p. 1037

**COSMOLOGY****Gamma rays reveal the Universe's history**

How many stars have formed in the Universe, and when did they do so? These fundamental questions are difficult to answer because there are systematic uncertainties in converting the light we observe into the total mass of stars in galaxies. The Fermi-LAT Collaboration addressed these questions by exploiting the way that gamma rays from distant blazars propagate through intergalactic space, which depends on the total amount of light emitted by all

galaxies. The collaboration found that star formation peaked about 3 billion years after the Big Bang (see the Perspective by Prandini). Although this is similar to previous estimates from optical and infrared observations, the results provide valuable confirmation because they should be affected by different systematic effects. —KTS

*Science*, this issue p. 1031;

see also p. 995

**NEUROSCIENCE****Memories reach the cortex rapidly**

How fast do learning-induced anatomical changes occur in the brain? The traditional view postulates that neocortical memory representations reflect reinforcement processes initiated by the hippocampus and that a genuine physical trace develops only through reactivation over extended periods. Brodt *et al.* combined functional magnetic resonance imaging (MRI) with diffusion-weighted MRI during an associative declarative learning task to examine experience-dependent structural brain plasticity in human subjects (see the Perspective by Assaf). This plasticity was rapidly induced after learning, persisted for more than 12 hours, drove behavior, and was localized in areas displaying memory-related functional brain activity. These plastic changes in the posterior parietal cortex, and their fast temporal dynamics, challenge traditional views of systems memory consolidation. —PRS

*Science*, this issue p. 1045;

see also p. 994

**CANCER GENOMICS****scTrio-seq identifies colon cancer lineages**

To better design treatments for cancer, it is important to understand the heterogeneity

in tumors and how this contributes to metastasis. To examine this process, Bian *et al.* used a single-cell triple omics sequencing (scTrio-seq) technique to examine the mutations, transcriptome, and methylome within colorectal cancer tumors and metastases from 10 individual patients. The analysis provided insights into tumor evolution, linked DNA methylation to genetic lineages, and showed that DNA methylation levels are consistent within lineages but can differ substantially among clones. —LMZ

*Science*, this issue p. 1060

## IMMUNOLOGY

### Caspase-8 is a player in pyroptosis

The activation of certain pattern-recognition receptors by pathogen-associated molecular patterns results in the formation of inflammasome complexes. Inflammasome complexes can initiate both the maturation of inflammatory cytokines and pyroptotic cell death via the caspase-mediated cleavage of gasdermin D (GSDMD). As of now, the only known regulators of GSDMD in macrophages are caspase-1 and caspase-11. Orning *et al.* report an additional pathway controlling GSDMD processing. YopJ, an effector molecule produced by *Yersinia* (the causative agent of plague), inhibits TAK1- $\text{I}\kappa\text{B}$  kinase signaling. This, in turn, results in caspase-8-directed cleavage of GSDMD, pyroptosis, and the release of interleukin 1 $\beta$  (IL-1 $\beta$ ) and IL-18. Thus, in the arms race between host and pathogen, the host recognizes signaling disturbances as pathogenic and counters with inflammation and cell death. —STS

*Science*, this issue p. 1064

## CANCER BIOLOGY

### Fluid mechanics influence metastasis

To reach distant organs, circulating tumor cells that are shed from primary tumors must

withstand considerable shear forces in the lymph and blood. In a Perspective, Goetz discusses the influence of flow mechanics on tumor cell distribution to distant sites and the formation of metastases. Understanding this process more clearly may help identify targets to prevent metastatic outgrowth, the main cause of death in cancer patients. —GKA

*Science*, this issue p. 999

## SURGICAL ADHESIONS

### Getting adhesions unstuck

Peritoneal adhesions are ectopic fibrotic tissues induced by surgical perturbations that result in postoperative morbidities such as small bowel obstruction.

The cellular origin of adhesions remains unclear. Now, Tsai *et al.* show that mesothelial cells overlying organs and the abdominal wall give rise to adhesions after surgery in mice. The injured mesothelium up-regulated mesothelial-specific genes known to be highly expressed during fetal development. Targeting adhesions with antibodies against the mesothelial marker mesothelin eliminated adhesions that had formed after surgery. Injured mesothelium responded to hypoxia, and this was mediated by the hypoxia-inducible factor 1 alpha (HIF1 $\alpha$ ) pathway. Blocking HIF1 $\alpha$  with small-molecule inhibitors prevented adhesion formation in mice after surgery. —OMS

*Sci. Transl. Med.* **10**, eaan6735 (2018).

## CANCER IMMUNOLOGY

### Immunoediting of polychromatic tumors

As tumors grow, they evolve genetically. The resulting genetic heterogeneity contributes to the emergence of variants that may ultimately display increased resistance to immune effector mechanisms and enhanced metastatic potential. Milo *et al.* used multicolor barcoding of a mouse lymphoma line to determine whether increased

immune selection pressure by the host accelerates the emergence of dominant clones. When barcoded male lymphoma cells were given to male and female recipients, clonal dominance emerged more rapidly in female recipients because more neoantigens were available to elicit a host T cell response. Checkpoint blockade with anti-PD-1 (programmed cell death protein 1) promoted a similar contraction of intratumor diversity. These findings provide fresh insights into the immunoediting mechanisms by which active antitumor immunity directs the in vivo selection of less immunogenic tumor variants. —IRW

*Sci. Immunol.* **3**, eaat1435 (2018).

## MATERNAL CARE

### Spider nursery

Mammals produce milk to feed their offspring, and maternal care often continues well after the young can forage for themselves. Though other cases of milk-like secretions have been found, this combination of ongoing maternal care has largely been considered a uniquely mammalian trait. Chen *et al.* describe an ant-mimicking jumping spider that secretes a nutritious milk-like substance on which its young offspring are entirely dependent. The spider also continues to care for the spiderlings as they mature and become independent. Thus, this type of maternal care may be more widespread than has been assumed. —SNV

*Science*, this issue p. 1052