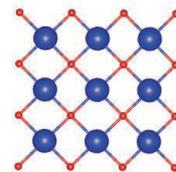


RESEARCH

Avoiding polar catastrophe on perovskite surfaces

Setvin et al., p. 572



IN SCIENCE JOURNALS

Edited by Stella Hurtley



GENETICS

Myoediting for Duchenne muscular dystrophy

Duchenne muscular dystrophy (DMD) is an X-linked recessive disorder that results in progressive weakening and muscle loss. Long *et al.* used CRISPR-Cas9 genome editing to correct the hotspot mutations that disrupt expression of the dystrophin gene in DMD. So-called myoediting abolished RNA splice sites and allowed the removal of the most common mutations. The approach successfully restored dystrophin expression in patient-derived induced pluripotent stem cells and restored mechanical force contraction in derived cardiomyocytes to near normal. —ASH

Sci. Adv. 10.1126/sciadv.aap9004 (2018).

A new technology brings hope in the fight against DMD.

NEAR-FIELD COSMOLOGY

Dwarf galaxies move in unexpected ways

Massive galaxies like our Milky Way are orbited by satellite dwarf galaxies. Standard cosmological simulations of galaxy formation predict that these satellites should move randomly around their host. Müller *et al.* examined the satellites of the nearby elliptical galaxy Centaurus A (see the Perspective by Boylan-Kolchin). They found that the satellites are distributed in a planar arrangement, and the members of the plane are orbiting in a coherent direction. This is inconsistent with more than 99% of comparable galaxies in simulations. Centaurus A, the Milky Way, and Andromeda all have highly

statistically unlikely satellite systems. This observational evidence suggests that something is wrong with standard cosmological simulations. —KTS

Science, this issue p. 534;
see also p. 520

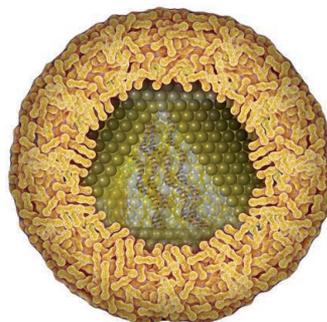
EMERGING INFECTIONS

Fearsome flaviviruses

Although Zika virus was identified more than half a century ago, its impact on the unborn children of infected pregnant women was only detected in the recent devastating epidemic. Unfortunately, Zika virus may not be unique in its ability to inflict fetal damage. To investigate this possibility, Platt *et al.* infected pregnant immunocompetent mice with related viruses. Two other flaviviruses, West Nile virus and Powassan

virus, caused fetal demise. These viruses could also replicate in human maternal and fetal explant tissue. If these or other neurotropic flaviviruses take off in the human population, we may again experience congenital infections with devastating effects. —LP

Sci. Transl. Med. 10, eaao7090 (2018).



West Nile virus, like its cousin Zika, may damage fetuses.

TOPOLOGICAL MATTER

A phonon merry-go-round

Chirality is associated with the breaking of symmetry, often described as left- or right-handed behavior. Such asymmetry can be seen, for example, in the electronic responses of particular materials or the reactions between particular chemical species. Zhu *et al.* observed a chiral phonon mode in a monolayer of the transition metal dichalcogenide WSe_2 , detected spectroscopically as the circular dichroism of the phonon-assisted transition of holes. Phonon chirality could be used to control the electron-phonon coupling and/or the phonon-driven topological states of solids. —ISO

Science, this issue p. 579

BIOCHEMISTRY

Remember the sugar when making proteins

Eukaryotes have an elaborate trafficking and quality-control system for secreted glycoproteins. The glycosylation pathway begins in the endoplasmic reticulum with the enzyme oligosaccharyl-transferase (OST), which attaches a long chain of sugars to asparagine residues of target proteins. Wild *et al.* report a cryo-electron microscopy structure of yeast OST, which includes eight separate membrane proteins. The central catalytic subunit contains binding sites for substrates and is flanked by accessory subunits that may facilitate delivery of newly translocated proteins for glycosylation. —MAF

Science, this issue p. 545

STRUCTURAL BIOLOGY

Structure of the human spliceosome

Catalyzed by the spliceosome, precursor mRNA splicing proceeds in two steps: branching and exon ligation. Transition from the C (catalytic post-branching spliceosome) to the C* (catalytic pre-exon ligation spliceosome) complex is driven by the adenosine triphosphatase/helicase Prp16. Zhan *et al.* report the cryo-electron microscopy structure of the human C complex, showing that two step 1 splicing factors stabilize the active site and link it to Prp16. —SYM

Science, this issue p. 537

ECOPHYSIOLOGY

A demanding lifestyle

Polar bears appear to be well adapted to the extreme conditions of their Arctic habitat. Pagano *et al.*, however, show that the energy balance in this harsh environment is narrower than we might expect (see the Perspective by Whiteman). They monitored the behavior and metabolic rates of nine free-ranging polar bears over 2 years. They found that high energy demands required consumption of high-fat prey, such as seals, which are easy to come by

on sea ice but nearly unavailable in ice-free conditions. Thus, as sea ice becomes increasingly short-lived annually, polar bears are likely to experience increasingly stressful conditions and higher mortality rates. —SNV

Science, this issue p. 568;

see also p. 514

COLON CANCER

Biofilms provide refuge for cancerous bacteria

Familial adenomatous polyposis (FAP) causes benign polyps along the colon. If left untreated, FAP leads to a high incidence of colon cancer. To understand how polyps influence tumor formation, Dejea *et al.* examined the colonic mucosa of FAP patients. They discovered biofilms containing the carcinogenic versions of the bacterial species *Escherichia coli* and *Bacteroides fragilis*.

Colon tissue from FAP patients exhibited greater expression of two bacterial genes that produce secreted oncotoxins. Studies in mice showed that specific bacteria could work together to induce colon inflammation and tumor formation. —PNK

Science, this issue p. 592

MOLECULAR BIOLOGY

Self-defense by avoiding self-targeting

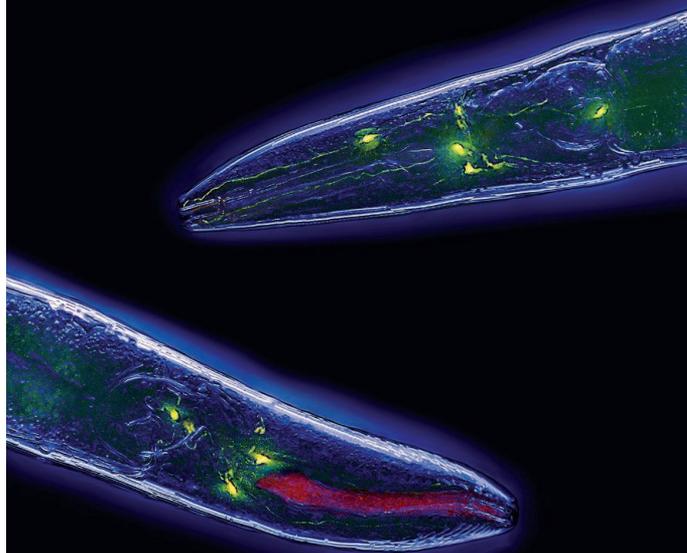
By silencing transposons, Piwi-interacting RNAs (piRNAs) protect the stability of animal genomes in germ lines. However, many piRNAs do not map to transposons, and their functions have remained undefined. Zhang *et al.* described the piRNA targeting logic in *Caenorhabditis elegans* and identified an intrinsic sequence signal in endogenous germline genes that confer resistance to piRNA silencing. Thus, diverse piRNAs silence foreign nucleic acids but spare self genes to defend the *C. elegans* genome. In addition, multiple foreign transgenes can be engineered to escape piRNA targeting, allowing successful expression in the germline. —SYM

Science, this issue p. 587

IN OTHER JOURNALS

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

Confocal micrograph
of *Caenorhabditis*
elegans worms



CELL BIOLOGY

Targeting the demise of male mitochondria

In the nematode worm *Caenorhabditis elegans*, as in humans, offspring inherit mitochondria and mitochondrial DNA only from their mother. Sato *et al.* identified key molecular components of the machinery that recognizes male mitochondria and targets them for degradation. In a screen for kinases that might be required for the process, they identified IKKE-1, a protein kinase with similarity to the mammalian protein kinases TBK1 and IKKε. IKKE-1 interacted with a protein that they named ALLO-1, which had sequence similarity to autophagy receptors and was required for clearance of paternal organelles. The similarity of the role of IKKE-1 in removing male mitochondria to that of mammalian TBK1, which functions in the innate immune response, hints that the two processes might have a similar evolutionary origin. —LBR

Nat. Cell Biol. 10.1038/s41556-017-0008-9 (2018).

IMMUNOLOGY

High caloric intake induces inflammation

The consumption of high-calorie diets has become prevalent in industrialized nations and is associated with increased body mass, inflammation, and resulting pathologies. What are the underlying mechanisms

connecting diets of high-energy, processed food to inflammation? Christ *et al.* show that mice fed on a high-calorie Western diet developed systemic inflammation and functionally reprogrammed granulocyte monocyte precursor cells. After a standard chow diet was restored to the animals, inflammation persisted, indicating that

ALSO IN SCIENCE JOURNALS

Edited by Stella Hurtley

EARTH SYSTEMS

Integrating the biosphere into climate models

High-quality climate predictions are crucial for understanding the impacts of different greenhouse gas emission scenarios and for mitigating and adapting to the resulting climatic changes. Bonan and Doney review advances in Earth system models that include the terrestrial and marine biosphere. Such models capture interactions between physical and biological aspects of the Earth system. This provides insight into climate impacts of societal importance, such as altered crop yields, wildfire risk, and water availability. Further research is needed to better understand model uncertainties, some of which may be unavoidable, and to better translate observations into abstract model representations. —JFU

Science, this issue p. 533

NEURODEVELOPMENT

Brain mutations, young and old

Most neurons that make up the human brain are postmitotic, living and functioning for a very long time without renewal (see the Perspective by Lee). Bae *et al.* examined the genomes of single neurons from the prenatal developing human brain. Both the type of mutation and the rates of accumulation changed between gastrulation and neurogenesis. These early mutations could be generating useful neuronal diversity or could predispose individuals to later dysfunction. Lodato *et al.* also found that neurons take on somatic mutations as they age by sequencing single neurons from subjects aged 4 months to 82 years. Somatic mutations accumulated with increasing age and accumulated faster in individuals affected by inborn errors in DNA repair. Postmitotic

mutations might only affect one neuron, but the accumulated divergence of genomes across the brain could affect function. —PJH

Science, this issue p. 550, p. 555; see also p. 521

SURFACE SCIENCE

Compensating a polar surface

An ionic crystal surface can be electrostatically unstable, and the surface must reconstruct in some way to avoid this “polar catastrophe.” Setvin *et al.* used scanning probe microscopies and density functional theory to study the changes in the polar surface of the perovskite KTaO_3 . They observed several structural reconstructions as the surface cleaved in vacuum when heated to higher temperatures. These ranged from surface distortions to the formation of oxygen vacancies to the development of KO and TaO_2 stripes. Hydroxylation after exposure to water vapor also stabilized the surface. —PDS

Science, this issue p. 572

CARBON FIXATION

About-face for citrate synthase

Classically, it is thought that citrate synthase only works in one direction: to catalyze the production of citrate from acetyl coenzyme A and oxaloacetate in the tricarboxylic acid (TCA) cycle. The TCA cycle can run in reverse to cleave citrate and fix carbon dioxide autotrophically, but this was thought to occur only with alternative enzymes, such as citrate lyase. Now Nunoura *et al.* and Mall *et al.* have discovered thermophilic bacteria with highly efficient and reversible citrate synthase that requires reduced ferredoxin (see the Perspective by Ragsdale). This function is undetectable by metagenomics, but classical

biochemistry filled in the gaps seen between the genome sequences and the phenotypes of the organisms. The direction of catalysis depends on the availability of organic versus inorganic carbon and reflects a flexible bet-hedging strategy for survival in fluctuating environments. In evolutionary terms, this capacity might predate the classical TCA cycle and is likely to occur in a wide range of anaerobic microorganisms. —CA

Science, this issue p. 559, p. 563; see also p. 517

CANCER IMMUNOTHERAPY

HLA genotype affects response

Immunotherapy works by activating the patient's own immune system to fight cancer. For effective tumor killing, CD8^+ T cells recognize tumor peptides presented by human leukocyte antigen class I (HLA-I) molecules. In humans, there are three major HLA-I genes (*HLA-A*, *HLA-B*, and *HLA-C*). Chowell *et al.* asked whether germline HLA-I genotype influences how T cells recognize tumor peptides and respond to checkpoint inhibitor immunotherapies (see the Perspective by Kvistborg and Yewdell). They examined more than 1500 patients and found that heterozygosity at HLA-I loci was associated with better survival than homozygosity for one or more HLA-I genes. Thus, specific HLA-I mutations could have implications for immune recognition and for the design of epitopes for cancer vaccines and immunotherapies. —PNK

Science, this issue p. 582; see also p. 516

AUTOIMMUNE DISEASE

The X chromosome link to lupus

Nine out of 10 people who develop systemic lupus erythematosus (SLE) are women.

Furthermore, individuals with Klinefelter syndrome (47,XXY) also have increased incidence of SLE. This suggests that X chromosome dosage could be an important risk factor in SLE. Using sensitive quantification methods, Souyris *et al.* demonstrate that Toll-like receptor 7 (TLR7), which is encoded on the X chromosome, escapes X inactivation in B cells and myeloid cells in females and Klinefelter individuals. TLR7 binds single-stranded RNA and activates type I interferon signaling, a pathway that is also activated in SLE patients. Thus, biallelic expression of TLR7 appears to contribute to greater SLE risk. —AB

Sci. Immunol. **3**, eaap8855 (2018).

CANCER

The cytoskeleton-EGFR connection

Some cancers are caused by aberrant epidermal growth factor receptor (EGFR) signaling. Two papers now reveal connections between this receptor and cytoskeletal remodeling (see the Focus by Chiasson-MacKenzie and McClatchey). Pike *et al.* delineated a cytoskeletal pathway that delayed receptor internalization, thereby increasing EGFR signal duration from the membrane. Roth *et al.* identified a cytoskeleton-associated effector of EGFR signaling that promoted migration and proliferation of mammary epithelial cells and was associated with poor prognosis in breast cancer patients. —LKF

Sci. Signal. **10**, eaan0949, eaaq1060; see also eaas9473 (2018).

SUPERCONDUCTIVITY

A nonlinear peek into stripes

In many theoretical models of high-temperature superconductors, remnants of superconductivity persist to

temperatures higher than the transition temperature, T_c . Rajasekaran *et al.* used nonlinear terahertz spectroscopy to probe this region of the phase diagram of a cuprate superconductor that is well known for a stripe phase that appears for certain doping levels (see the Perspective by Ergeçen and Gedik). For a sample deep in the stripe phase, a large nonlinear signal persisted from the superconducting region up to temperatures much higher than T_c . The findings suggest the formation of a peculiar spatially modulated superconducting state called the pair-density wave. —JS

Science, this issue p. 575;
see also p. 519