

# RESEARCH

## IN SCIENCE JOURNALS

Edited by Michael Funk

A Hubble Space Telescope image of galaxy cluster Abell 370, which acts as a lens and bends light from distant stars

### COSMOLOGY

#### Gravitational lenses in galaxy clusters

**T**he large mass of a galaxy cluster deflects light from background objects, a phenomenon known as gravitational lensing. The large-scale gravitational lens caused by the whole cluster can be modified by smaller-scale mass concentrations within the cluster, such as individual galaxies. Meneghetti *et al.* examined these small-scale gravitational lenses in observations of 11 galaxy clusters. They found small lenses that were an order of magnitude smaller than would be expected from cosmological simulations. The authors conclude that there is an unidentified problem with either prevailing simulation methods or standard cosmology. —KTS  
*Science*, this issue p. 1347

### STRUCTURAL BIOLOGY

#### Coupling transcription and translation

In bacteria, the rate of transcription of messenger RNA (mRNA) by RNA polymerase (RNAP) is coordinated with the rate of translation by the first ribosome behind RNAP on the mRNA. Two groups now present cryo-electron microscopy structures that show how two transcription elongation factors, NusG and NusA, participate in this coupling. Webster *et al.* found that

NusG forms a bridge between RNAP and the ribosome when they are separated by mRNA. With shortened mRNA, NusG no longer links RNAP and the ribosome, but the two are oriented so that newly transcribed mRNA can enter the ribosome. Wang *et al.* provide further insight into the effect of mRNA length on the complex structures. They also include NusA and show that the NusG-bridged structure is stabilized by NusA. —VV

*Science*, this issue p. 1355, p. 1359

### GLOBAL CLIMATE

#### The states of past climate

Deep-sea benthic foraminifera preserve an essential record of Earth's past climate in their oxygen- and carbon-isotope compositions. However, this record lacks sufficient temporal resolution and/or age control in some places to determine which climate forcing and feedback mechanisms were most important. Westerhold *et al.* present a highly resolved and well-dated record of benthic carbon and

oxygen isotopes for the past 66 million years. Their reconstruction and analysis show that Earth's climate can be grouped into discrete states separated by transitions related to changing greenhouse gas levels and the growth of polar ice sheets. Each climate state is paced by orbital cycles but responds to variations in radiative forcing in a state-dependent manner. —HJS

*Science*, this issue p. 1383

### CIRCADIAN RHYTHMS

#### Keeping rhythm requires communication

In mammals, daily cycles in physiology require the synchronized activity of circadian clocks in peripheral organs such as the liver, a hub of metabolism. Guan *et al.* generated mice with hepatocytes that lack two transcriptional repressors known to be essential for clock function. This experimental manipulation unexpectedly disrupted rhythmic gene expression and metabolism not only in hepatocytes but also in other liver cell types. Feeding behavior also coregulated circadian rhythms in multiple liver cell types. Cell-cell communication thus appears to be important in maintaining the robustness of peripheral circadian clocks. —PAK

*Science*, this issue p. 1388

### TROPHIC CASCADES

#### A lethal combination

It is well established that predators are essential for the structuring and maintenance of biotic communities. One of the first demonstrations of this importance came from studies of the importance of sea otters to the maintenance of kelp forests. Rasher *et al.* now show that the effects caused by the absence of this predator can be further exacerbated by climate warming. In North Pacific kelp forests, otter absence led to a decline of slow-growing calcareous algae through sea urchin herbivory, and this pattern was amplified by warming

temperatures. Keystone predators are thus essential not only for trophic structure but also for mitigating the impacts of climate change. —SNV

*Science*, this issue p. 1351

## PARKINSON'S DISEASE *PARK7* preservation

Mutations in the gene *PARK7* lead to the development of early-onset Parkinson's disease (PD), a neurodegenerative condition for which there are currently no effective treatments. Boussaad *et al.* identified an exonic splicing mutation in *PARK7* linked to PD and studied the effect of this mutation in patient-derived cellular models. The mutation resulted in impaired splicing, reduced production of the protein DJ-1, and consequent mitochondrial dysfunction. Rescuing the aberrant splicing with a chemical rectifier of aberrant splicing rescued neuronal loss in patient-derived brain organoids. These results suggest that precision medicine targeting specific molecular signatures could be an effective strategy for PD and possibly other neurodegenerative diseases. —MM

*Sci. Transl. Med.* **12**, eaau3960 (2020).

## TROPICAL FOREST Degradation exceeds deforestation

Forest degradation is a ubiquitous form of human disturbance

of the forest landscape. Activities such as selective logging and extraction fall short of total deforestation but lead to loss of biomass and/or fragmentation. On the basis of remote sensing data at 30-meter spatial resolution, Matricardi *et al.* analyzed the extent of forest degradation across the entire Brazilian Amazon over a ~22-year period up to 2014. They found that the extent and rate of forest degradation was equal to or greater than deforestation, which has important implications for carbon, biodiversity, and energy balance. —AMS

*Science*, this issue p. 1378

## METABOLISM Finding calorie restriction mimetics

Calorie restriction extends the health span, and this may be partially mediated by a drop in core body temperature. Guijas *et al.* compared metabolomics data from calorie-restricted mice housed either at thermoneutrality or a cooler temperature. Calorie restriction induced the hypothalamus to produce the gasotransmitter nitric oxide and the opioid peptide leucine enkephalin only in mice housed at the cooler temperature. These and other metabolites differentially altered by ambient temperature may form the basis for treatments that can deliver the beneficial effects of calorie restriction. —WW

*Sci. Signal.* **13**, eabb2490 (2020).

## IN OTHER JOURNALS

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

### CLIMATE WARMING

#### Rapid response

**A**s the climate warms, Arctic temperatures are rising faster than temperatures at lower latitudes, a phenomenon called Arctic amplification. Loss of sea ice and snow cover at high northern latitudes have long been understood to contribute to this behavior, but other mechanisms have been suggested as well. Previdi *et al.* analyzed climate model simulations and conclude that this amplified warming response actually begins before sea ice loss becomes important and that fast atmospheric processes are instead responsible for its initiation. Therefore, the loss of sea ice is an amplifier of enhanced Arctic warming rather than a trigger. —HJS

*Geophys. Res. Lett.* **10.1029/2020GL089933** (2020).

### NEUROSCIENCE

#### Representation of what happened when

Episodic memory depends on the hippocampus and entorhinal cortex. Although the temporal coding properties of hippocampal neurons are well known, the temporal code in the entorhinal cortex, which provides important input to the hippocampus, is less understood. Bright *et al.* examined monkey entorhinal neuron responses in a 5-second period after presentation of an image. Entorhinal neurons were activated shortly after a visual stimulus and then decayed with a variety of rates, enabling reconstruction of when the image was presented. To determine whether the pattern of neuronal activation depended on the identity of the image presented, each image was shown twice during the experiment. These results suggest that entorhinal cortex context cells carry information about what happened in addition to when it happened. —PRS

*Proc. Natl. Acad. Sci. U.S.A.* **117**, 20274 (2020).

### HUMAN GENETICS

#### Extending genetic predictions

Polygenic risk scores (PRSs) aggregate genomic information to predict an individual's risk of developing diseases with a genetic basis. To determine links between PRSs and health, Wainberg *et al.* profiled the blood plasma of almost 5000 individuals and examined PRSs for 54 diseases. From this, they linked PRSs to 766 detectable traits, including those that affect proteins or metabolites or are clinically relevant. Because many of these relationships were known, this work confirms links between genotype and phenotype and provides a platform for future work. Unexpectedly, some healthy individuals with a PRS indicating high risk for disease had a blood profile similar to those from individuals with disease. This indicates that genetic information can help to separate disease risk factors from the consequences of a pathological condition and



Roadways in the Brazilian Amazon contribute to damaging forest degradation, even in the absence of outright deforestation.



ALSO IN *SCIENCE* JOURNALS

Edited by Michael Funk

## HUMAN GENOMICS

**A survey of transcription across tissues**

Some human genetic variants affect the amount of RNA produced and the splicing of gene transcripts, crucial steps in development and maintaining a healthy individual. However, some of these changes only occur in a small number of tissues within the body. The Genotype-Tissue Expression (GTEx) project has been expanded over time, and, looking at the final data in version 8, Aguet *et al.* present a deep characterization of genetic associations and gene expression and splicing in 838 individuals over 49 tissues (see the Perspective by Wilson). This large study was able to characterize the details underlying many aspects of gene expression and provides a resource with which to better understand the fundamental molecular mechanisms of how genetic variants affect gene regulation and complex traits in humans. —LMZ

*Science*, this issue p. 1318;  
see also p. 1298

## HUMAN GENOMICS

**The role of sex in the human transcriptome**

In humans, the inheritance of the XX or XY set of sex chromosomes is responsible for most individuals developing into adults expressing male or female sex-specific traits. However, the degree to which sex-biased gene expression occurs in tissues, especially those that do not contribute to characteristic sexually dimorphic traits, is unknown. Oliva *et al.* examined Genotype-Tissue Expression (GTEx) project data and found that 37% of genes in at least one of the 44 tissues studied exhibit a tissue-specific, sex-biased gene expression. They also identified a sex-specific variation

in cellular composition across tissues. Overall, the effects of sex on gene expression were small, but they were genome-wide and mostly mediated through transcription factor binding. With sex-biased gene expression associated with loci identified in genome-wide association studies, this study lays the groundwork for identifying the molecular basis of male- and female-based diseases. —LMZ

*Science*, this issue p. 1331

## HUMAN GENOMICS

**Cell type–specific quantitative trait loci**

Understanding how human genetic variation affects phenotype requires tissue- or even cell type–specific measurements. Kim-Hellmuth *et al.* used computational methods to identify cell-type proportions within bulk tissues in the Genotype-Tissue Expression (GTEx) project dataset to identify cell-type interaction quantitative trait loci and map these to genetic variants correlated with expression or splicing differences between individuals. By characterizing the cellular context, this study illustrates how genetic variants that operate in a cell type–specific manner affect gene regulation and can be linked to complex traits. This deconvolution and analysis of cell types from bulk tissues allows greater precision in understanding how phenotypes are linked to genetic variation. —LMZ

*Science*, this issue p. 1332

## HUMAN GENOMICS

**Telomere length within individuals**

Telomeres are DNA-protein complexes that protect chromosome ends. Their length is of great interest because short telomeres are associated with specific diseases and with aging. Demanelis *et al.* measured

telomere length from 952 Genotype-Tissue Expression (GTEx) project donors across tissues, of which 24 tissue types have measurements for more than 25 samples. This dataset shows that telomere length is not constant but is correlated across tissues. Most tissue telomeres shorten with age, but some, such as those in the testis and cerebellum, do not. In African Americans, telomeres are longer on average than those from individuals of primarily European descent across many tissue types. This observation is consistent with variability being passed from germ cells to zygote to differentiated cells during development. —LMZ

*Science*, this issue p. 1333

## HUMAN GENOMICS

**Functional rare variation in transcriptomes**

Every human genome contains tens of thousands of rare genetic variants—which include single nucleotide changes, insertions or deletions, and larger structural variants—and some may have a functional effect. Ferraro *et al.* examined data from individuals in the Genotype-Tissue Expression (GTEx) project for outliers across tissues caused by gene expression, splicing, and allele-specific expression. Single rare variants were observed that affected the expression and allele-specific expression of multiple genes and, in the case of a gene fusion event, splicing. Experimental and computational validation suggest that many individuals carry more than 50 rare variants that affect transcription in some way. Although most variants were predicted to not affect an individual's phenotype, a small percentage showed likely disease-related associations, emphasizing the importance of studying the impact of rare genetic variation on the transcriptome. —LMZ

*Science*, this issue p. 1334

## SEISMOLOGY

**The great seismic quiet period**

Noise from trains, airplanes, industrial processes, and other sources is recorded on seismometers worldwide. Disentangling this noise is important for extracting out natural signals, but the noise can also roughly track population movements. Lecocq *et al.* compiled seismic observations around the world and found a substantial decrease in noise resulting from lockdown measures imposed in response to the coronavirus disease 2019 pandemic (see the Perspective by Denolle and Nissen-Meyer). These observations tightly correspond to when the measures went into effect and offer a way to track aggregate behavior. This quiet period also offers the chance to extract anthropogenic sources of noise from those of natural processes. —BG

*Science*, this issue p. 1338;  
see also p. 1299

## MICROBIOLOGY

**Microbial therapies**

The gut microbiota, diverse microorganisms that inhabit our intestines, have an increasingly recognized number of roles in maintaining human health. These roles include maintaining digestive health and also more systemic roles such as brain health. In a Perspective, Wargo discusses the developments in modulating gut microbiota to treat patients with various diseases, including irritable bowel disease, metabolic syndrome, autism, and cancer. Treatment can be achieved by fecal microbiota transplantation from healthy donors or by using distinct bacterial communities that are associated with overall health. The advances and challenges of this exciting approach to health are discussed. —GKA

*Science*, this issue p. 1302

## FERROELECTRICS

## Switching to the atomic scale

Ferroelectric materials are attractive because they provide a way to change electrical resistance by using an electric field. Lee *et al.* used simulations to explain the persistence of ferroelectric behavior in very thin films of hafnium oxide (see the Perspective by Noheda and Íñiguez). The authors' calculations show that ferroelectric properties should be found in films below 1 nanometer thick. This makes the material very attractive for the next generation of random access memory. —BG

*Science*, this issue p. 1343;  
see also p. 1300

## ULTRACOLD PHYSICS

## Laser cooling of symmetric top molecule

Experimental progress over the past few decades has led to the mastery of ultracold atomic gases. A major thrust of current research is to extend this success to ultracold molecules, which would open qualitatively new perspectives for quantum information science, precision measurement, quantum chemistry, and other fields. The internal degrees of freedom in molecules preclude immediate implementation of conventional methods. Using a specific combination of rovibronic optical transitions, Mitra *et al.* report direct Sisyphus laser cooling of the symmetric top molecule  $\text{CaOCH}_3$  to temperatures below 1 millikelvin (see the Perspective by Hudson). The proposed scheme for cooling is potentially applicable to a wide range of nonlinear polyatomic molecules. —YS

*Science*, this issue p. 1366;  
see also p. 1304

## COLLOIDS

## Self-limiting bonding

Although many routes have been developed to link together colloidal particles into controlled superstructures from dimers all

the way up to three-dimensional lattices, they generally depend on coating the nanoparticle surfaces in specific ways to control the way they link up. By contrast, Yi *et al.* developed a ligand chemistry such that, when two particles link together, it changes the electrostatic properties to limit subsequent bonding (see the Perspective by Gang). Particles are coated with complementary polymer strands that undergo an acid-base neutralization reaction. This bonding is controlled by the length of the flexible ligands, whereas the arrangement of the bonded particles is controlled by electrostatic repulsions, thus giving two parameters to tune the shape of the assemblies that form. —MSL

*Science*, this issue p. 1369;  
see also p. 1305

## ATMOSPHERIC AEROSOLS

## A multiphase effect

Aerosols exert a primary influence on atmospheric chemistry. One of the main controls on their internal chemistry is their acidity, so understanding what determines aerosol pH is fundamental for determining their environmental effects. Zheng *et al.* considered how buffering capacity in a multiphase aerosol system differs from bulk solution and found an important role for water content in determining pH in ammonia-buffered regions. Their conclusions underscore the important influence of ammonia emissions in the Anthropocene. —HJS

*Science*, this issue p. 1374

## CORONAVIRUS

## A gateway to the cytosol

Coronaviruses transform host cell membranes into peculiar double-membrane vesicles that have long been thought to accommodate viral genome replication. However, because these compartments appeared to be completely sealed, it has remained unknown how the newly made viral RNA could be exported to the cytosol for

translation and packaging into new virions. Wolff *et al.* used cryo-electron microscopy to identify a molecular pore that spans the double membrane (see the Perspective by Unchwaniwala and Ahlquist). Six copies of a large coronavirus transmembrane protein formed the core of this structure, which may constitute a viral RNA export channel and provide a target for future antiviral interventions. —SMH

*Science*, this issue p. 1395;  
see also p. 1306

## IMMUNE DEVELOPMENT

## To each their own

The recombination activating genes *Rag1* and *Rag2* play central roles in assembling functional T and B cell receptors in developing lymphocytes. Expression of *Rag1* and *Rag2* in hematopoiesis is restricted to these two lymphoid lineages, but precisely how this is accomplished has remained a mystery. Miyazaki *et al.* identified three key enhancer elements that recruit the transcription factor E2A to promote the expression of *Rag1* and *Rag2* during lymphocyte development. By generating mouse strains lacking one or more of these enhancer elements, they report that T and B cells use distinct enhancer modules to activate and maintain expression of *Rag1* and *Rag2*. —CNF

*Sci. Immunol.* **5**, eabb1455 (2020).

## HEALTH AND MEDICINE

## 3D printed composites for cartilage repair

Damage to cartilage of the joints is a common debilitating injury. However, because of its limited capacity for self-repair, regeneration of damaged cartilage has thus far remained beyond reach. Sun *et al.* created a composite that recreates key elements of the native structure of articular cartilage by three-dimensionally printing structural elements and cells together in a gradient manner. When tested in rabbits, the

composite showed high levels of cartilage maturation as well as evidence of lubrication at the joint surface, which is essential to maintaining functionality of the joint. Further assessment of these materials in larger animal models is needed, but such gradient composites may provide a basis for future tissue-engineered cartilage replacements. —JST

*Sci. Adv.* **10**, 1126/sciadv.aay1422 (2020).