RESEARCH

IN *SCIENCE* JOURNALS

Edited by **Michael Funk**

CLOUD PHYSICS

Aerosols give clouds a lift

It has been observed that atmospheric aerosols can strengthen updrafts in deep convective clouds such as those that form in thunderstorms. Past work has linked such invigoration with the latent heat released by water condensation or freezing in chains of processes that depend on aerosol concentrations. Abbott and Cronin suggest a third possibility in which updrafts intensify because high aerosol concentrations increase environmental humidity by mixing more condensed water into the surrounding air, which in turn favors stronger updrafts. —HJS *Science*, this issue p. 83

Atmospheric aerosols invigorate thunderstorms by increasing humidity and thus stimulating convection.

PHOTO: ANDREAS THALLER/ALAMY STOCK PHOTO

CELL CYCLE

Checking fidelity in cell division

Everything has to go right during cell division, so a checkpoint mechanism known as the spindle-assembly checkpoint prevents mitosis from proceeding unless the kinetochores that attach chromosomes to the spindle microtubules are properly engaged. Two papers now reveal the detailed molecular choreography that allows a single, unattached kinetochore to arrest cell division: Lara-Gonzalez *et al.* used a visual probe that tracks a specific form of one of the checkpoint complex proteins, and Piano *et al.* used a biochemical reconstitution of the checkpoint. Together, these studies reveal how protein interaction, spatial constraints, phosphorylation, and catalytic conversion of the protein Mad2 to its active form allow this all-important sensor to function. —LBR

Science, this issue p. 64, p. 67

PROTEIN FOLDING

One sequence encoding two structures

Most proteins have stable, folded structures, but there are rare examples of metamorphic proteins that can switch between two different folds that may each have a different function. Dishman *et al.* investigated the evolution of XCL1, which is a member of the chemokine family that interconverts between the chemokine fold and a second, noncanonical fold that forms dimers. The authors used nuclear magnetic resonance spectroscopy to investigate the structures of inferred evolutionary ancestral sequences. Their results suggest that XCL1 evolved from an ancestor with the chemokine fold and then transitioned to prefer the noncanonical fold before reaching the modern-day metamorphic protein. —VV

Science, this issue p. 86

MATERIALS SCIENCE

Stretching diamond to the limit

Diamond is thought of as being unbendable, but thin samples can actually deform elastically. Applying relatively large amounts of strain to diamond may shift its electronic properties, which is of interest for a number of applications. Dang *et al.* elastically stretched micrometer-sized plates of diamond along different crystallographic directions. These relatively large samples show that deep-strain engineering can be accomplished in more uniform diamond specimens and may have a large impact on the electronic properties. —BG

Science, this issue p. 76

PROTEIN SYNTHESIS

Co-co assembly for oligomers

Most of the human proteome forms oligomeric protein complexes, but how they assemble is poorly understood. Bertolini *et al.* used a ribosome-profiling approach to explore the existence of a cotranslational assembly mode based on the interaction of two nascent polypeptides, which they

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call the "co-co" assembly. Proteome-wide data were used to show whether, when, and how efficiently nascent complex subunits interact. The findings also show that human cells use co-co assembly to produce hundreds of different homo-oligomers. Co-co assembly involving ribosomes translating one messenger RNA may resolve the long-standing question of how cells prevent unwanted interactions between different protein isoforms to efficiently produce functional homo-oligomers. —SMH

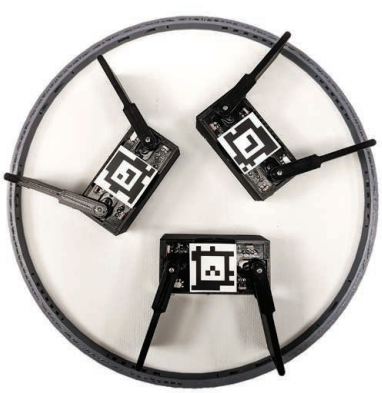
Science, this issue p. 57

ACTIVE MATTER

Shake, rattle, and help each other along

In classical statistical mechanics, the deterministic dynamics of a many-body system are replaced by a probabilistic description. Chvykov *et al.* work toward a similar description for the nonequilibrium self-organization of collectives of active particles. In these systems, continuously input energy drives localized fluctuations, but larger-scale ordering can emerge, such as in the flight of a flock of birds. A key concept in their theory is the importance of rattling, whereby ordered patterns emerge through local collisions between neighbors at specific frequencies. The authors demonstrate this behavior using a set of flapping robots and produce related simulations of the robot behavior. —MSL

Science, this issue p. 90



A trio of robots capable of emulating collective behaviors

TUMOR IMMUNOLOGY

Autophagy protects tumors from T cells

Tumors evade antitumor T cells by various mechanisms. Young *et al.* used a CRISPR screen to show that tumor necrosis factor–α (TNFα) and autophagy play a role in the T cell–mediated killing of tumor cells. Pharmacologic or genetic inhibition of autophagy in tumor cells increased TNFα-mediated T cell killing of tumor cells. Deletion of the gene *Rb1cc1* in tumor cells improved the efficacy of immune checkpoint blockade in a mouse tumor model. However, deleting the TNFα receptor in tumor cells partially abrogated the improved efficacy of immune checkpoint blockade in the absence of Rb1cc1. Thus, autophagy inhibition may improve T cell–mediated immunotherapies in patients who have cancer. —DAE

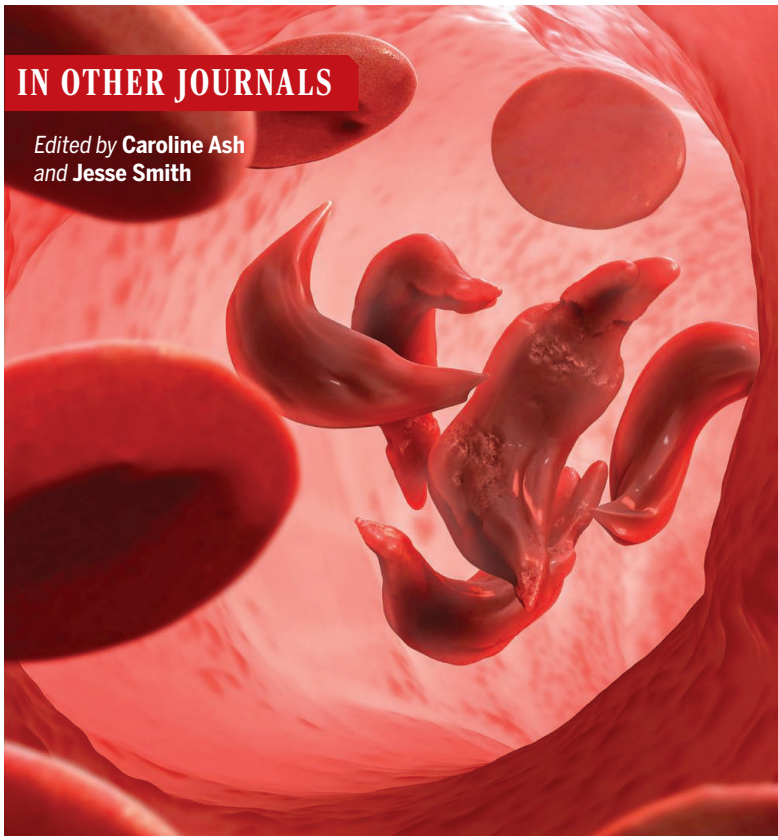
Sci. Immunol. **5**, eabb9561 (2020).

NEURODEGENERATION

Saving neurons in Parkinson's disease

Parkinson's disease is characterized by the progressive loss of dopaminergic neurons that leads to loss of motor control and cognitive decline. Kim *et al.* found that activating the kinase Akt1, such as with chlorogenic acid (a polyphenol found in coffee), prevented both neuronal death and motor and cognitive impairments in two mouse models of Parkinson's disease. Akt1 inhibited neuronal death by transcriptionally activating a gene involved in regulating programmed cell death. The clinical relevance of this mechanism was supported by correlative data collected from postmortem patient brain tissue. —LKF

Sci. Signal. **13**, eaax7119 (2020).



IN OTHER JOURNALS

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

NEUROSCIENCE

Oscillations around memory

Hippocampal oscillations in the theta range have been hypothesized to play a central role in organizing neuronal ensembles to link together item and contextual representations. Experimental evidence in rodents shows the importance of theta oscillations for associative memory. However, the role of hippocampal theta oscillations in human memory is not as well understood. Kota *et al.* administered an associative recognition memory task to epilepsy patients who happened to have electroencephalogram electrodes implanted for other medical reasons. Theta oscillatory power increase in the 2- to 5-Hz range and phase reset in the hippocampus reflected processes supporting recollection, rather than familiarity, during encoding and retrieval. These observations link theta-range activity to associative memory encoding and retrieval in humans. —PRS

J. Neurosci. **40**, 9507 (2020).

TYPE 1 DIABETES

Interfering with diabetes

Insulin, discovered a century ago, remains the mainstay of treatment for type 1 diabetes, as autoimmunity destroys the patients' insulin-producing pancreatic β cells. A study by Quattrin *et al.* indicates that it may be possible to slow down the progression of this disease. In this phase 2 clinical trial, young patients with newly diagnosed type 1 diabetes were treated with golimumab, an antibody against the cytokine tumor necrosis factor–α, and compared with a placebo group. Although golimumab did not fully prevent disease progression, it produced partial remissions and decreased the amount of insulin required, offering a potentially promising addition to the therapeutic options for this patient group. —YN

N. Engl. J. Med. **383**, 2007 (2020).

CREDITS (LEFT TO RIGHT): CHVYKOV *ET AL.*; TIM VERNON/SCIENCE SOURCE

ALSO IN *SCIENCE* JOURNALS

Edited by **Michael Funk**

CORONAVIRUS

Effects on cancer in Africa

The COVID-19 pandemic struck many countries in Africa as they were already facing multiple public health challenges, in particular high incidence and mortality rates from cancer. In a Perspective, Addai and Ngwa discuss the effects of the COVID-19 response on cancer care, treatment, and outreach aimed at diagnosing patients early. The allocation of limited resources to COVID-19 patients, rather than to cancer patients, could increase the number of late-stage cancer diagnoses and resulting mortality. There have also been effects on fundraising and patient mental health, as well as on cancer research and training. However, opportunities have also been created, such as the development of localized diagnostic capability, more efficient radiotherapy administration, increased focus on understanding phytomedicine use, and use of telemedicine and online learning. —GKA

Science, this issue p. 25

MEDICINE

RNA targets in neuromuscular diseases

Neuromuscular diseases, such as Duchenne muscular dystrophy, are caused by dysfunction of skeletal muscle or the nervous system that controls muscle, with debilitating effects. However, several recent approvals of RNA therapies for some neuromuscular diseases highlight encouraging progress for treatment. In a Perspective, Ferlini *et al.* discuss antisense oligonucleotides that have been developed, and in some cases approved, for the treatment of neuromuscular diseases. They also discuss challenges in widening the applications of next-generation antisense oligonucleotides and possibly preventing the development of some neuromuscular diseases. —GKA

Science, this issue p. 29

CIRCADIAN RHYTHMS

Doubts in cancer-rhythms connections

Circadian clocks help to coordinate physiological processes with the daily cycles of light and dark and periods of feeding, activity, and rest. Being out of sync with such 24-hour cycles can have unhealthy effects. Sancar and Van Gelder review the available evidence regarding circadian disruption and predisposition to cancer and circadian variations in response to cancer chemotherapy. The literature can be difficult to interpret. For example, complete knockouts of clock genes are not the same as shift work. Overall, they find that the jury is still out on whether circadian disruption can promote cancer in general and if the timing of cancer treatment can be optimized. However, enough indications are present that further research is recommended. —LBR

Science, this issue p. 42

STRUCTURAL BIOLOGY

Anticoagulants take over

In its fully reduced form, vitamin K helps to catalyze an oxidation reaction essential for blood coagulations, but it must be regenerated in each reaction through reduction. Liu *et al.* determined the structures of the enzyme responsible, vitamin K epoxide reductase, bound to an oxidized vitamin K substrate or with anticoagulants, including the widely prescribed drug warfarin. Understanding how these molecules bind and inhibit explains some variations in the therapeutic response as well as resistance for anticoagulants used in pest control. —MAF

Science, this issue p. 43

TRANSCRIPTION

How to stop RNA polymerase

Timely and tunable cessation of RNA synthesis is vital for cellular homeostasis. RNA helicases such as the archetypal termination factor ρ actively dismantle transcription complexes, but the transitory nature of termination makes the process hard to study structurally. Said *et al.* assembled ρ-bound transcription complexes and studied them using cryo–electron microscopy with an approach that captured a series of functional states en route to termination. They found an extensive and dynamic network of ρ interactions with RNA polymerase, nucleic acids, and accessory Nus factors. ρ mediates stepwise rearrangements of these contacts, transforming an actively transcribing complex into a moribund pretermination intermediate. —DJ

Science, this issue p. 44

STRESS RESPONSES

Transcriptional control of proteostasis

Tissue homeostasis requires the coordinated activity of multiple cell types to initiate and then resolve inflammation. Intrinsic cellular stress-response pathways facilitate adaptation to stress and tissue restitution. Among these stress pathways, the unfolded protein response can elicit two divergent outcomes: adaptation to endoplasmic reticulum (ER) stress or termination by programmed cell death. You *et al.* identified QRICH1 as a transcriptional regulator controlling adaptation to ER stress at the level of protein translation and secretion. The authors further demonstrate the role of the QRICH1 program in inflammatory diseases of the colon and liver. —SMH

Science, this issue p. 45

STEM CELLS

Protecting the lung from hypoxic stress

The lung experiences constantly changing oxygen concentrations and must recognize and respond to a low-oxygen environment. Shivaraju *et al.* reveal that airway stem cells directly sense hypoxia and respond by differentiating into protective neuroendocrine (NE) cells that secrete a peptide that mitigates tissue damage (see the Perspective by Zacharias). This work suggests that the observed NE cell hyperplasia that accompanies lung diseases such as asthma, cystic fibrosis, and chronic obstructive pulmonary disease represents a compensatory physiologic response. More broadly, it raises the possibility that stem cells throughout the body sense hypoxia and differentiate into organ-specific NE cells. —BAP

Science, this issue p. 52; see also p. 32

BATTERIES

When two is better than four

Batteries based on the reaction of zinc and oxygen have been used for more than a century, but these have been primary (that is, nonrechargeable) cells. These batteries use an alkaline electrolyte and require a four-electron reduction of oxygen to water, which is a slow process. Sun *et al.* show that with the right choice of nonalkaline electrolyte, the battery can operate using a two-electron zinc-oxygen/zinc peroxide chemistry that is far more reversible. By making the electrolyte hydrophobic, water is excluded from the near surface of the cathode, thus preventing the four-electron reduction. These batteries also show higher energy density and better cycling stability. —MSL

Science, this issue p. 46

MEMBRANES

Finding the path to better desalination

Polyamide membranes have been used in large-scale desalination for decades. However, because of the thinness of the membranes and their internal variability, it has been hard to determine which aspects of the membranes most affect their performance. Culp *et al.* combined electron tomography, nanoscale three-dimensional (3D) polyamide density mapping, and modeling of bulk water permeability with zero adjustable parameters to quantify the effect of 3D nanoscale variations in polymer mass on water transport within the polyamide membrane (see the Perspective by Geise). They found that variability in local density most affects the performance of the membranes. Better synthesis methods could thus improve performance without affecting selectivity. —MSL

Science, this issue p. 72; see also p. 31

CORONAVIRUS

Pandemic progress in Kenya

By the end of July 2020, Kenya had reported only 341 deaths and ~20,000 cases of COVID-19. This is in marked contrast to the tens of thousands of deaths reported in many higher-income countries. The true extent of COVID-19 in the community was unknown and likely to be higher than reports indicated. Uyoga *et al.* found an overall seroprevalence among blood donors of 4.3%, peaking in 35- to 44-year-old individuals (see the Perspective by Maeda and Nkengasong). The low mortality can be partly explained by the steep demographics in Kenya, where less than 4% of the population is 65 or older. These circumstances combine to result in Kenyan hospitals not currently being overwhelmed by patients with respiratory distress. However, the imposition of a strict lockdown in this country has shifted the disease burden to maternal and child deaths as a result of disruption to essential medical services. —CA

Science, this issue p. 79; see also p. 27

CORONAVIRUS

Avoiding spread of SARS-CoV-2 in cars

The evidence has become clear that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is transmitted by aerosols, so enclosed spaces such as automobiles are thus high risk. Mathai *et al.* numerically calculated the flow patterns of aerosol droplets inside the cabin of a four-windowed car. Having the windows closed and the air-conditioner on results in considerable transfer of air and aerosols between occupants. However, having all the windows fully open separates the airflows on the right and left sides of the cabin and thus best reduces disease transmission if the passenger is seated in the back, on the opposite side from the driver. —KKG

Sci. Adv. 10.1126/sciadv.abe0166 (2020).

AGING

Slowing cellular senescence

Whereas cellular senescence is known to promote aging, many of the mechanisms controlling this process remain poorly understood. Using human mesenchymal precursor cells (hMPCs) carrying pathogenic mutations of the premature aging diseases Werner syndrome and Hutchinson-Gilford progeria syndrome, Wang *et al.* conducted a genome-wide CRISPR-Cas9–based screen to identify genes that could affect cellular senescence. They identified *KAT7*, a histone acetyltransferase gene, as a driver of senescence in hMPCs. Inactivation of *Kat7* in mice aging normally and in prematurely aging progeroid mice extended their life span. Although *KAT7* requires further study in other cell types, these experiments highlight the value of genome-wide CRISPR-Cas9 screens and further illuminate the mechanisms controlling senescence. —MN

Sci. Transl. Med. **13**, eabd2655 (2020).