

RESEARCH

IN SCIENCE JOURNALS

Edited by Michael Funk

TROPICAL FOREST

The carbon gain in restored logged forest

There is currently great interest in the capacity of global forest to store carbon and hence contribute to the mitigation of climate change in the coming decades. In a study of Southeast Asian tropical forest, Philipson *et al.* show that active restoration of logged forests generates higher rates of carbon accumulation than naturally regenerating forest. To estimate the economic feasibility of restoration treatments, they modeled the carbon price required to offset the cost of restoration, finding that the highest prices seen in recent years would be needed to approach those that could offset restoration costs. These results are important for tropical forest policy, establishing the importance of restoration for the carbon recovery potential of tropical forests.

—AMS *Science*, this issue p. 838

Efforts to restore tropical forests in Sabah, Malaysia, can accelerate carbon storage but require high prices on carbon.

ORGANIC CHEMISTRY

Trio of enzymes power divergent synthesis

Diterpene natural products are built from a 20-carbon building block, with a huge range of possible structures and modifications. Chemical synthesis of specific molecules, some of which have valuable biological activities, is tricky because of the need for selective oxidations and rearrangements when starting from widely available scaffolds. Zhang *et al.* characterized selectivities for three oxidative enzymes that each attack different positions on a common scaffold. They then seamlessly combined chemical transformations with the enzymatic oxidations to produce nine distinct compounds across three families of diterpenes. These results highlight the potential of hybrid organic-biocatalytic

synthetic schemes for divergent synthesis. —MAF

Science, this issue p. 799

IMMUNOLOGY

A loose BAF puts its foot on the cGAS

A signaling pathway in vertebrates called cGAS-STING detects the presence of intracellular DNA as a surrogate for both cellular damage and viral infection. At the same time, sensing of self-DNA must be suppressed to prevent the development of autoimmune responses. Guey *et al.* identify barrier-to-autointegration factor 1 (BAF) as a protein that intrinsically competes with the cGAS component of this pathway for binding to genomic self-DNA. When there is a breakdown in nuclear compartmentalization, cytosolic cGAS enzymatic activity is prevented because

of BAF. This work suggests that the regulation of DNA detection by the innate immune system relies on more complex mechanisms than simple physical separation alone. —STS

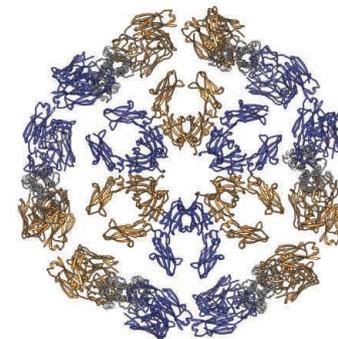
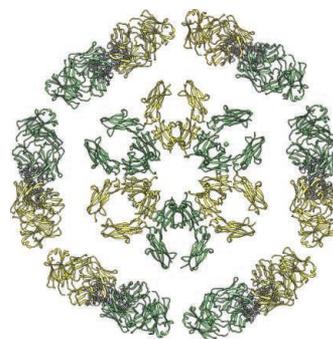
Science, this issue p. 823

STRUCTURAL BIOLOGY

Strength in numbers

Human cluster of differentiation 20 (CD20) is expressed

on malignant B cells and is the target of therapeutic antibodies used in cancer immunotherapy. Kumar *et al.* now present structures that explain why so-called type I antibodies efficiently activate the complement pathway to kill cells, whereas type II antibodies do not. Type I antibodies each bind to two CD20 dimers and form clusters that facilitate binding to a



Hexameric assembly models illustrate potential differences in compactness between therapeutic antibodies (rituximab, left; ofatumumab, right).

component of the complement pathway. The second-generation type I antibody ofatumumab has molecular features that make it more efficient at clustering than first-generation rituximab. By contrast, the type II antibody obinutuzumab interacts with just one CD20 dimer and cannot form higher-order assemblies. Understanding these mechanisms will inform the design of next-generation immunotherapies. —VV

Science, this issue p. 793

NEURODEVELOPMENT Mitochondrial dynamics and cell fate

Radial glia cells, the stem cells of early brain development, can generate more of themselves or generate differentiating neurons. Iwata *et al.* now show that these fate decisions involve the mitochondria. Cells that have fragmented mitochondria shortly after mitosis are more likely to become neurons, whereas cells that are undergoing mitochondrial fusion are likely to continue being stem cells. —PJH

Science, this issue p. 858

METALLURGY Temperature-stable superelasticity

Shape memory alloys are superelastic, which means that they can recover their original shape after a large amount of strain. However, in most alloys, this behavior tends to only work well for a small range of temperatures. Xia *et al.* identified an iron-manganese-aluminum-chromium-nickel alloy for which superelasticity is virtually temperature independent (see the Perspective by La Roca and Sade). This distinctive property is attractive for a variety of applications in which large temperature variations are normal, such as in space exploration. —BG

Science, this issue p. 855;
see also p. 773

ECOLOGY Ozone pollution threatens biodiversity

Terrestrial ecosystem composition and biodiversity are tightly linked to environmental factors, and there are concerns that they may be at risk from anthropogenic ozone pollution. In a Review, Agathokleous *et al.* synthesize widespread evidence that ozone pollution can affect key ecological processes and functions of terrestrial ecosystems and alter the diversity of plants, insects, and soil microorganisms. They also identify areas of high endemic richness throughout the world that will also be at high ozone risk by the end of the century. These advances in our understanding of ozone pollution and its effects present new challenges for the preservation of terrestrial biodiversity. —YL

Sci. Adv. 10.1126/
sciadv.abc1176 (2020).

CELL TRANSPLANTATION A second transplant for intestinal disease

Allogeneic hematopoietic cell transplantation (HCT) is a beneficial treatment for blood and bone marrow cancers. However, HCT can lead to graft-versus-host disease (GvHD), which affects various organs, including the gut. Fecal microbial transplantation (FMT) from a healthy donor has successfully treated intestinal disorders such as *Clostridium difficile* infection and ulcerative colitis. Van Lier *et al.* conducted a single-arm clinical trial to investigate whether such FMTs could ameliorate symptoms of intestinal GvHD in 15 HCT recipients. Within a month of treatment, intestinal GvHD resolved and gut microbial diversity was restored in 10 of 15 study participants. Although confirmation is required in larger trials, FMT may be a promising treatment for intestinal GvHD. —MN

Sci. Transl. Med. 12,
eaaz8926 (2020).

IN OTHER JOURNALS

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



Mare's milk has a high lactose content and rapidly ferments into products that are digestible by lactose intolerant Central Asian herdspeople.

SIGNAL TRANSDUCTION Plants take the splice to the fight

Plants transiently activate immune responses using layers of diverse regulatory mechanisms. This strategy minimizes any potential damage from an overly active protective response. Dressano *et al.* discovered in the model plant *Arabidopsis* that when an immune response was activated, the plant's immunoregulatory RNA binding protein (IRR) became dephosphorylated. Dephosphorylation altered IRR's interaction with messenger RNA transcripts, including that of calcium-dependent protein kinase 28 (CPK28), a key negative regulator of pattern recognition receptor signaling complexes. CPK28 is acutely regulated by changes in calcium concentration and its own phosphorylation state. However, altered splicing results in the expression of a truncated CPK28 protein that

cannot bind calcium, and thus an enhanced immune response can be triggered. —LBR

Nat. Plants 6, 1008 (2020).

IMMUNOLOGY The thymus X factor

The thymus is an organ that facilitates the maturation of thymocytes into T cells and is notable for its variable size and composition. It is largest during early life, then it shrinks with age and in response to injury and infection. Thymic development also affects T cell output but remains poorly understood. Chan *et al.* report that liver X receptors (LXRs), nuclear receptors important for immunity and metabolism, play an important role in thymus dynamics. In mice, thymic epithelial cells use LXR $\alpha\beta$ for self-renewal and thymic regeneration. Meanwhile, LXR $\alpha\beta$ makes thymocytes more resistant to negative selection, thereby boosting the production

PHOTO: PAUL&39;S LADY/SHUTTERSTOCK

CATALYSIS

Making chemistry less precious

Much of modern chemistry relies on catalysis by precious metals such as platinum, palladium, and rhodium. By contrast, more abundant metals such as iron and copper suffice in biochemistry. Bullock *et al.* review the opportunities presented from the study of enzymes to shift the balance in synthetic catalysts further toward the use of these abundant metals. Whether by modifying the enzymes themselves or by designing ligand and support architectures that take advantage of the cheaper metals' characteristic electron transfer properties, recent work points toward substantial progress. —JSY

Science, this issue p. 786

NEURODEVELOPMENT

Neural progenitors disrupted

Symptoms of Huntington's disease (HD) manifest in adulthood despite the aberrant protein being present much earlier in persons carrying the disease-causing mutation. Barnat *et al.* studied the cellular effects of the HD mutation on human and mouse fetal brain development (see the Perspective by DiFiglia). The authors found that neural progenitor cells at the brain's ventricular zone reach out to both the apical and basal surfaces of the neuroepithelial wall, and their cellular nuclei shuttle back and forth as the cell cycle progresses. With the aberrant protein, these epithelial junctions are disrupted, epithelial polarity is disturbed, and the cell cycle favors premature neuronal differentiation. —PJH

Science, this issue p. 787;
see also p. 771

CORONAVIRUS

Prototype DNA vaccines for SARS-CoV-2

The development of a vaccine to protect against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an urgent biomedical need. Yu *et al.* designed a series of prototype DNA vaccines against the SARS-CoV-2 spike protein, which is used by the virus to bind and invade human cells. Analysis of the vaccine candidates in rhesus macaques showed that animals developed protective humoral and cellular immune responses when challenged with the virus. Neutralizing antibody titers were also observed at levels similar to those seen in humans who have recovered from SARS-CoV-2 infection. —PNK

Science, this issue p. 806

CORONAVIRUS

Immunity from reinfection

One of the many open questions about severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is whether an individual who has cleared the virus can be infected a second time and get sick. Chandrashekar *et al.* and Deng *et al.* generated rhesus macaque models of SARS-CoV-2 infection and tested whether natural SARS-CoV-2 infection could result in immunity to viral challenge. They found that animals indeed developed immune responses that protected against a second infection. Although there are differences between SARS-CoV-2 infection in macaques and in humans, these findings have key implications for public health and economic initiatives if validated in human studies. —PNK

Science, this issue p. 812, p. 818

NEUROSCIENCE

Nuclear transport controls chronic pain

Chronic neuropathic pain is debilitating and difficult to treat. Marvaldi *et al.* now show that chronic pain is regulated by a specific nuclear import factor in peripheral sensory neurons (see the Perspective by Yousuf and Price). Importin $\alpha 3$ is required for nuclear import of the transcription factor c-Fos in sensory neurons, and perturbation of this pathway ameliorates sustained neuropathic pain in mice. Candidate drugs were identified that mimic this pathway and alleviate neuropathic pain in mouse models. Identification of a nuclear transport factor that regulates pain mechanisms offers opportunities for future analgesic development. —SMH

Science, this issue p. 842;
see also p. 774

ELECTROCHEMISTRY

Delivering protons with electrons

Many chemical reactions involve concurrent transfer of a proton and an electron. In electrochemical synthesis, this mechanism could prove useful in lowering the energy necessary for cathodic electron transfer alone, but it is hindered by competing direct coupling of the protons and electrons to make hydrogen instead. Chalkley *et al.* now report a molecular mediator consisting of a dimethylaniline base tethered to a cobaltoxide electron acceptor. This construct can deliver both a proton and an electron to a substrate from an acid and a cathode while skirting the hydrogen pathway. —JSY

Science, this issue p. 850

CORONAVIRUS

Heterogeneity and herd immunity

In response to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), some politicians have been keen to exploit the idea of achieving herd immunity. Countering this possibility are estimates derived from work on historical vaccination studies, which suggest that herd immunity may only be achieved at an unacceptable cost of lives. Because human populations are far from homogeneous, Britton *et al.* show that by introducing age and activity heterogeneities into population models for SARS-CoV-2, herd immunity can be achieved at a population-wide infection rate of ~40%, considerably lower than previous estimates. This shift is because transmission and immunity are concentrated among the most active members of a population, who are often younger and less vulnerable. If nonpharmaceutical interventions are very strict, no herd immunity is achieved, and infections will then resurge if they are eased too quickly. —CA

Science, this issue p. 846

SUPERCONDUCTIVITY

An elusive pocket

Superconductivity in copper oxide materials emerges by doping a special kind of correlated state called the Mott insulator. However, studying what happens when a small concentration of charge carriers—holes or electrons—is added to a Mott insulator is experimentally challenging. It has been predicted that the so-called “Fermi pockets” should become visible during experimentation, but such pockets have not been unambiguously observed. Kunisada *et al.* studied the unusual cuprate $\text{Ba}_2\text{Ca}_4\text{Cu}_5\text{O}_{10}(\text{F},\text{O})_2$, which has five copper oxide planes in a unit cell, whereas most cuprates have one or two (see

the Perspective by Vishik). They observed two Fermi pockets in both photoemission and quantum oscillations data, with the innermost copper oxide planes playing a crucial role. —JS

Science, this issue p. 833;
see also p. 775

INTERGROUP RELATIONS

Social contact and reconciliation

It has been theorized that positive intergroup relations can reduce prejudice and facilitate peace. However, supporting empirical evidence is weak, particularly in the context of real-world conflict. Mousa randomized Christian Iraqi refugees to soccer teams that were composed of either all Christian players or a mixture of Christian and Muslim players (see the Perspective by Paluck and Clark). Playing on the same team as Muslims had positive effects on Christian players' attitudes and behaviors toward Muslims within the context of soccer, but these effects did not generalize to non-soccer contexts. These findings have implications for the potential benefits and limits of positive intergroup contact for achieving peace between groups. —TSR

Science, this issue p. 866;
see also p. 769

TROPHIC RESILIENCE

Inflexible webs

It is clear that human activities are negatively affecting current ecosystems. Predicting how our activities will affect future systems is more challenging because it involves estimating the unknown. Nagelkerken *et al.* overcame some of these unknowns by constructing small versions, or mesocosms, of a marine ecosystem that included species representing all trophic levels (see the Perspective by Chown). They then exposed these systems to predicted future levels of carbon dioxide and acidification. The trophic structure was relatively resistant to acidification but not

to warming. Warmed systems experienced a reorganization of trophic structure that was not rescued by functional redundancy or other stabilizing responses. Such inflexibility may be a precursor of ecosystem collapse. —SNV

Science, this issue p. 829;
see also p. 770

PALEOANTHROPOLOGY

Bedding of grass and ashes

The Border Cave site in the KwaZulu-Natal region of South Africa has been a rich source of archaeological knowledge about Stone Age humans because of its well-preserved stratigraphic record. Wadley *et al.* now report the discovery of grass bedding in Border Cave, dated to approximately 200,000 years ago. The bedding, identified with a range of microscopic and spectroscopic techniques, was mingled with layers of ash. It also incorporated debris from lithics, burned bone, and rounded ochre grains, all of which were of clear anthropogenic origin. The authors speculate that the ash may have been deliberately used in bedding to inhibit the movement of ticks and other arthropod irritants. These discoveries extend the record of deliberate construction of plant bedding by at least 100,000 years. —AMS

Science, this issue p. 863

NEUROSCIENCE

PERKing up neurons without toxicity

Chronic activity of the unfolded protein response in some neurodegenerative diseases suppresses the protein synthesis that is necessary for neuronal function and survival and for cognition. Hughes *et al.* found that the phosphorylation of a threonine residue in the stress response kinase PERK reduced its interaction with the translation initiation factor eIF2 α but left the kinase activity of PERK intact. This partial inhibition

approach reduced neuronal loss and increased survival in a mouse model of prion disease without the pancreatic damage seen with catalytic inhibitors of PERK. —LKF

Sci. Signal. **13**, eabb4749 (2020).

AUTOIMMUNITY

Autoimmunity promotor

Tissue-resident memory T (Trm) cells are involved in peripheral immunity against reinfection, but their role in autoimmunity is unclear. Krebs *et al.* examined the contribution of Trm cells in patients with antineutrophil cytoplasmic antibody–dependent glomerulonephritis (ANCA-GN). They identified multiple T cell subsets in healthy kidney tissue biopsies, but a marked increase in CD4⁺ Trm cells was seen in kidney biopsies from patients with ANCA-GN. They infected mice with *Staphylococcus aureus*, which induced renal T helper 17 cells with a Trm cell phenotype and persisted in kidney tissue. In a mouse model of this disease, *S. aureus* infection aggravated kidney pathology and appeared to drive localized renal autoimmune responses. These findings provide critical insight into the role of CD4⁺ Trm cells in contributing to autoimmune disease. —CNF

Sci. Immunol. **5**, eaba4163 (2020=0).