RESEARCH

IN SCIENCE JOURNALS

Edited by Michael Funk

ATMOSPHERIC CHEMISTRY

Cleaning in a flash

Hydroxyl radicals (OH) are the most important oxidizing species in the atmosphere and provide much of its ability to cleanse itself. It is known that nitric oxide production by lightning leads to the formation of OH and other atmospheric oxidants, such as ozone and hydroperoxyl radicals (HO₂), through a variety of chemical reactions. Brune et al. used airborne measurements of OH and HO₂ to show that lightning also produces them directly and in amounts much greater than expected. They found that this mechanism may be responsible for as much as one-sixth of the oxidizing capacity of Earth’s atmosphere. —HJS Science, this issue p. 711

CELL DIFFERENTIATION

Metabolic pathway regulates cell fate

Lineage-specific regulators direct cell fate decisions, but the precise mechanisms are not well known. Using an in vivo chemical suppressor screen of a bloodless zebrafish mutant, Rossmann et al. show that the lineage-specific chromatin factor trif1y directly regulates mitochondrial genes to drive red blood cell differentiation. Loss of trif1y reduces coenzyme Q synthesis and function, impeding mitochondrial respiration and leading to epigenetic alterations and repression of erythropoiesis. The loss of blood in the mutant fish can be rescued by the addition of coenzyme Q. This work establishes a mechanism by which a chromatin factor tunes a metabolic pathway in a tissue-specific manner. —BAP Science, this issue p. 716

NUCLEAR ASTROPHYSICS

Natural plutonium from supernovae

The rapid neutron capture process (r-process) produces many of the heavy chemical elements, but the astrophysical settings where it occurs remain unclear. Leading candidates are neutron star mergers and some types of supernovae. Wallner et al. analyzed the plutonium content of a deep-sea crust sample, identifying a few dozen atoms of the r-process isotope plutonium-244 that were delivered to Earth within the past few million years. There was a simultaneous signal of iron-60, which is known to be produced in supernovae. Comparing the ratios of these isotopes constrains the relative contributions of supernovae and neutron star mergers to r-process nucleosynthesis. —KTS Science, this issue p. 742

CORONAVIRUS

Kids armed with anti-coronavirus B cells

It remains unclear whether B cell repertoires against coronaviruses and other pathogens differ between adults and children and how important these distinctions are. Yang et al. analyzed blood samples from young children and adults, as well as tissues from deceased organ donors, characterizing the B cell receptor (BCR) repertoires specific to six common pathogens and two viruses that they had not seen before: Ebola virus and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Children had higher frequencies of B cells with convergent BCR heavy chains against previously encountered pathogens and higher frequencies of class-switched convergent B cell

Lightning generates an abundance of reactive species in the atmosphere.

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clones against SARS-CoV-2 and related coronaviruses. These findings suggest that encounters with coronaviruses in early life may produce cross-reactive memory B cell populations that contribute to divergent COVID-19 susceptibilities. —STS

**ALZHEIMER’S DISEASE**

**Developing an immunotherapy for AD**

Hyperphosphorylated tau aggregates contribute to neurodegeneration in patients with Alzheimer’s disease (AD), and reducing tau accumulation has had therapeutic effects in preclinical models. Ayalon et al. generated and characterized a humanized anti-tau monoclonal antibody called semorinemab, which they tested in mice and nonhuman primates and in a phase 1 clinical trial in humans. Semorinemab was able to bind all six human tau isoforms and had therapeutic effects in vivo in AD mice by reducing tau accumulation. In patients with AD, semorinemab crossed the blood–brain barrier and showed evidence of target engagement without evident side effects. These results support the idea that immunotherapies targeting tau might be effective in reducing tau pathology in AD. —MM


**PLANT SCIENCE**

**Computational analysis of cell walls**

Layers of intertwined fibers make up plant cell walls. The various types of fibers respond differently to deformation. Cellulose microfibrils, for example, can stretch or curve, changing their end-to-end length, and can also slide past each other, reorient relative directions, and bundle with neighboring microfibrils. Zhang et al. developed a computational model based on observations of onion skin epidermis that describes how these complex changes in space govern cell wall mechanics. The results inform ways to engineer multifunctional fibrous materials. —PJH

_Science, this issue p. 706_.

**SUPERCONDUCTIVITY**

**Controlling interfacial superconductivity**

The interface between the oxides LaAlO_3_ and KTaO_3_(111) has been shown to superconduct at temperatures up to 2 Kelvin. Chen et al. show that this superconductivity can be controlled with electric fields. As they tuned the gating voltage, the researchers observed a dome-shaped variation of the superconducting critical temperature. This variation could not be ascribed to the change in carrier density, but rather seemed to reflect the change in the mobility of the carriers. —JS

_Science, this issue p. 721_.

**DNA REPAIR**

**Costs of moving stem cells**

Adult stem cells travel long distances to a wound to repair the damaged tissue. The potential cost of migration has been revealed in vitro studies of cancer cell lines, dendritic cells, and primary stem cells. If these cells have to squeeze into wounds, then this constriction may cause DNA damage. Sahu et al. show that adult stem cells in _Schmidtea mediterranea_, a highly regenerative planarian flatworm, accumulate DNA breaks as they move through tissue to repair injuries. —JS

_Science, this issue p. 773_.

**IN OTHER JOURNALS**

Edited by Caroline Ash and Jesse Smith

**Signal transduction**

**Imaging cancer cell by cell**

Experience in treating colorectal cancer shows that inhibition of the oncogene-activated mitogen-activated protein kinase (MAPK) signaling pathway is often more effective if the activity of the epidermal growth factor receptor, which acts upstream to activate the pathway, is also inhibited. To help clarify how such combined treatment might work, Ponsioen et al. used single-cell imaging of activity of the MAPK extracellular signal–regulated kinase (ERK) in patient-derived organoids. Oncogene-induced signaling showed that oscillations in ERK activity were amplified by epidermal growth factor signaling. The results help to explain how improved clinical practices in colorectal cancer treatment have been achieved. —LBR


*Colored scanning electron micrograph of a colon cancer cell.*

**Mucosal immunology**

**Building back colonic crypts**

Restoration of the colonic epithelium after mucosal injury depends on cell renewal initiated by intestinal stem cells (ISCs) and their progeny. Stromal cells near the base of colonic crypts secrete trophic factors for ISCs, but regulation of this process by proinflammatory mediators is not well understood. Cox et al. used mouse models of pathogen- or chemical-induced epithelial damage to investigate the contribution of interleukin-1 (IL-1) and its receptor (IL-1R1) to epithelial restitution. IL-1 release set off a signaling pathway supporting ISC renewal and proliferation and promoted innate lymphoid cell production of IL-22, a cytokine supporting colonocyte proliferation. These findings illustrate the need to consider the desirable regenerative properties of IL-1 when designing therapeutic approaches for chronic inflammatory diseases. —IRW

INFECTIONOUS DISEASE
Progress in RSV prevention
Respiratory syncytial virus (RSV) causes substantial morbidity and mortality in children, especially in low- and middle-income countries. Initial efforts to develop vaccines against RSV strains in the 1960s exacerbated lower respiratory tract illnesses caused by viral infection in certain children. However, renewed efforts to prevent RSV-induced illnesses has led to promising antibody treatments and vaccines that are being tested in pregnant women, infants, and young children. In a Perspective, Karron discusses changing strategies toward RSV disease prevention that could substantially reduce the burden of RSV infection. —GKA
Science, this issue p. 683

ORGANIC CHEMISTRY
Targeting distal C–H bonds in arenes
The Friedel-Crafts reaction is among the oldest in organic chemistry. For well over a century, chemists have relied on electronic effects intrinsic to aryl rings to append substituents at specific sites along the periphery. However, only in the past decade have they devised catalytic techniques that override these preferences so that new groups usually drawn to the neighboring sites of an existing substituent instead wind up two or three carbons away. Dutta et al. review progress in this field, highlighting elaborate directing groups and mediators as well as sophisticated ligand design. —JSY
Science, this issue p. 701

IMMUNOLOGY
A T cell sleeper agent against stress
Considerable changes in cellular metabolism occur when T cells transition from a resting to an activated state. One side effect of this process is an increase in reactive oxygen species (ROS). These molecules potentiate T cell receptor (TCR) signaling but can also result in detrimental oxidative stress (see the Perspective by Su and Dutta). Yue et al. describe one mechanism by which T cells can resolve this contradiction. Using mice with a T cell-specific deficiency in Schlafen 2 (SLFN2), they found that this protein binds to and protects transfer RNAs from oxidative stress–induced cleavage by the ribonuclease angiogenin. This process is downstream of ROS generation, which allows activated T cells to maintain protein synthesis despite the ROS that would otherwise inhibit translation. —STS
Science, this issue p. 703; see also p. 683

NEUROSCIENCE
A brain circuit that drives and gates curiosity
Curiosity is what drives organisms to investigate each other and their environment. It is considered by many to be as intrinsic as hunger and thirst, but the neurobiological mechanisms behind curiosity have remained elusive. In mice, Ahmadlou et al. found that a specific population of genetically identified γ-aminobutyric acid (GABA)ergic neurons in a brain region called the zona incerta receive excitatory input in the form of novelty and/or arousal information from the prelimbic cortex, and these neurons send inhibitory projections to the periaqueductal gray region (see the Perspective by Farahbakhsh and Siciliano). This circuitry is necessary for the exploration of new objects and conspecifics. —PRS
Science, this issue p. 704; see also p. 684

RADIATION RISKS
Genomics of radiation-induced damage
The potential adverse effects of exposures to radioactivity from nuclear accidents can include acute consequences such as radiation sickness, as well as long-term sequelae such as increased risk of cancer. There have been a few studies examining transgenerational risks of radiation exposure but the results have been inconclusive. Morton et al. analyzed papillary thyroid tumors, normal thyroid tissue, and blood from hundreds of survivors of the Chernobyl nuclear accident and compared them against those of unexposed patients. The findings offer insight into the process of radiation-induced carcinogenesis and characteristic patterns of DNA damage associated with environmental radiation exposure. In a separate study, Yeager et al. analyzed the genomes of 130 children and parents from families in which one or both parents had experienced gonadal radiation exposure related to the Chernobyl accident and the children were conceived between 1987 and 2002. Reassuringly, the authors did not find an increase in new germline mutations in this population. —YN
Science, this issue p. 705, p. 725

CHIRAL NANOMATERIALS
What makes things twist?
Crystallization and chirality have been entangled since Pasteur’s observations on chiral tartaric acid crystals, yet there is still limited understanding of how chiral compounds form chiral crystal morphologies. For example, although a chiral seed crystal can promote a particular handedness, it is not clear why such seeds do not do so with 100% efficiency. Ben-Moshe et al. examined chiral nanocrystals of tellurium grown from solution using various electron microscopy and diffraction techniques (see the Perspective by Popov). They found that screw dislocation–mediated growth is responsible for chiral polyhedral shape formation, and chiral crystals can thus form even in the presence of achiral ligands. —ML
Science, this issue p. 729; see also p. 688

EVOLUTIONARY ECOLOGY
The evolution of ecological networks
Plants and the animals that eat their fruits and disperse their seeds form complex networks of mutualistic interactions. The structures of many such networks and the ecological forces that shape them are well known,
but their deeper evolutionary history has received little attention. Burin et al. address this knowledge gap in a study of frugivorous bird species in documented seed-dispersal networks around the world (see the Perspective by Bello and Barreto). Species occupying central positions in frugivory networks, which thus interact with many plant species, tend to belong to lineages that are more stable over macroevolutionary time scales. These patterns are more evident in regions with warmer and wetter climates and provide evidence that evolutionary processes can leave a signal on the structure of current ecological networks. —AMS

Science, this issue p. 733
see also p. 682

DROUGHT

Staying dry
Is precipitation all that a watershed needs to recover from drought? Conventional wisdom says yes, but this is not necessarily true. Peterson et al. studied streamflow and precipitation in 161 watersheds in southeastern Australia across the Millennium Drought, which stuck the region during the first decade of the 21st century (see the Perspective by Tauro). They found that runoff in approximately one-third of the watersheds had not returned to predrought levels even after 7 years despite the resumption of more normal precipitation. The authors suggest that these long-term changes are due to water loss from increased transpiration. Watersheds may thus have multiple states and a finite resilience to transient disturbances, and hydrological droughts can persist long after meteorological droughts. —HJS

Science, this issue p. 745;
see also p. 680

IMMUNOLOGY

RAFs not always required
The kinase extracellular signal–regulated kinase (ERK) is critical during differentiation and its activation usually requires RAF family kinases. Scheffler et al. found exceptions to this paradigm during some stages of B cell differentiation. Mice lacking two Raf isoforms had reduced numbers of pre-B and immature B cells in the bone marrow, fewer mature B cells in the periphery, and generated fewer plasma cells upon immunization. However, these isoforms were not necessary for ERK phosphorylation in mature and activated B cells. RAfs are thus mainly required for the transition of pro-B cells to pre-B cells and for the differentiation of activated B cells into antibody-secreting plasma cells. —AMV