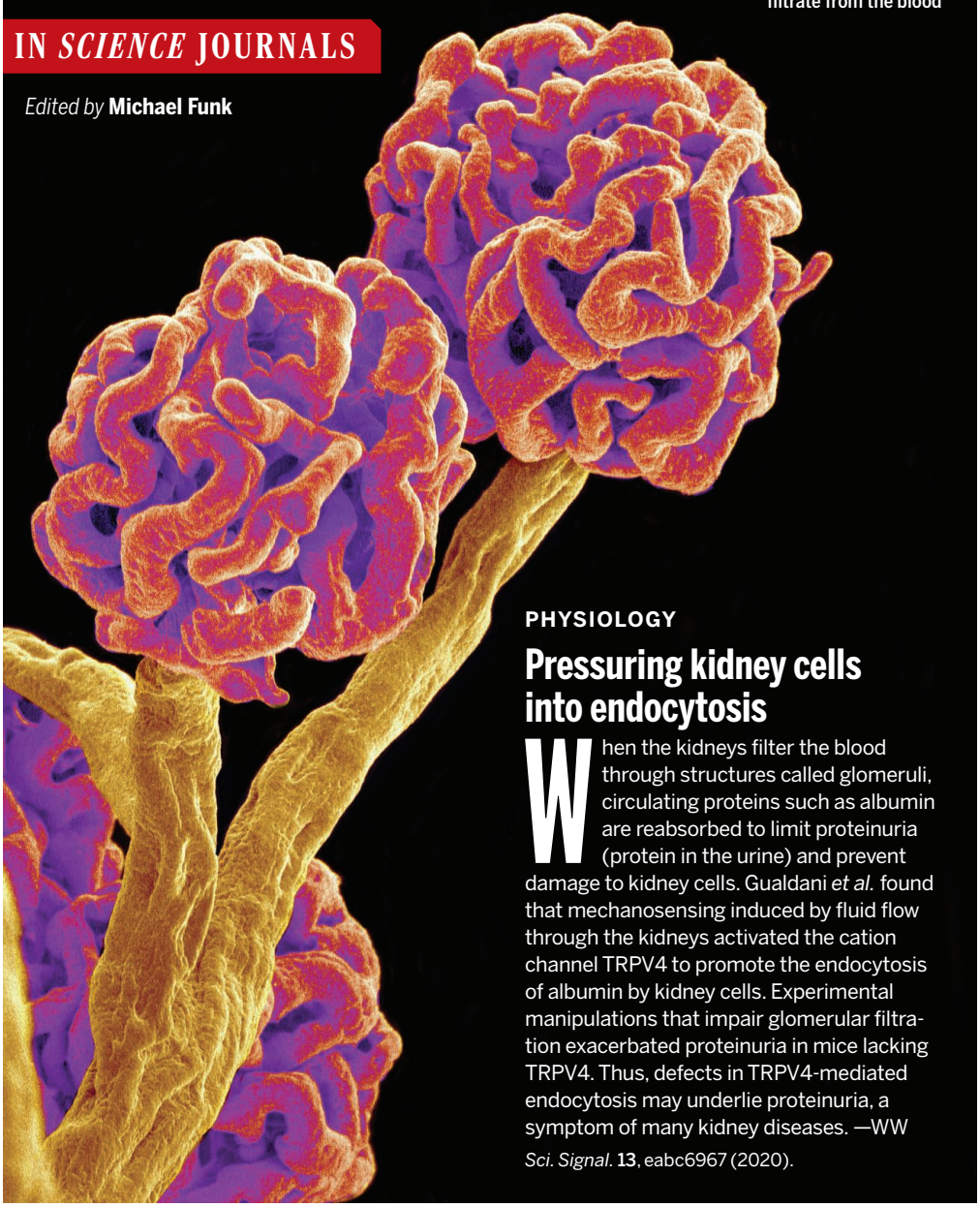
RESEARCH

IN *SCIENCE* JOURNALS

Edited by **Michael Funk**



Colored scanning electron microscope image of blood vessels in kidney glomeruli, which are structures that produce filtrate from the blood

IMAGE: SUSUMU NISHINAGA/CIENCE SOURCE

PHYSIOLOGY

Pressuring kidney cells into endocytosis

When the kidneys filter the blood through structures called glomeruli, circulating proteins such as albumin are reabsorbed to limit proteinuria (protein in the urine) and prevent damage to kidney cells. Gualdani *et al.* found that mechanosensing induced by fluid flow through the kidneys activated the cation channel TRPV4 to promote the endocytosis of albumin by kidney cells. Experimental manipulations that impair glomerular filtration exacerbated proteinuria in mice lacking TRPV4. Thus, defects in TRPV4-mediated endocytosis may underlie proteinuria, a symptom of many kidney diseases. —WW

Sci. Signal. **13**, eabc6967 (2020).

THERMOGALVANICS

Recovering low-temperature heat

Low-temperature heat sources are both abundant and largely dissipated into the environment. Yu *et al*. discovered a way to boost the concentration gradient in a liquid thermogalvanic cell that allows low-temperature heat to be recovered. The authors added a component that boosts the concentration gradient by forcing crystallization of the electrolyte at the cold end, and these crystals then melt at the hot end. This process boosts efficiency and is a potential method for recovering low-grade heat. —BG

Science, this issue p. 342

STRUCTURAL BIOLOGY

Attacking HIV by stabilizing its capsid

Current HIV treatments require drugs that must be taken daily, and care would be improved with an effective drug that is long-acting. GS-6207 (Lenacapavir) is a drug developed by Gilead Sciences that shows potential for a 6-month dosing interval and is in phase 2/3 clinical trials. Bester *et al*. describe structural and biophysical studies that provide a basis for the potent antiviral activity of GS-6207. The HIV capsid is cone shaped, and GS-6207 binds two neighboring capsid subunits and stabilizes the curved capsid. GS-6207 also interferes with capsid binding of cofactors that play a role in viral infection. This insight into GS-6207 activity provides a platform for the rational development of improved long-acting therapies. —VV

Science, this issue p. 360

MUCOSAL IMMUNITY

A nose for inflammation

Nasal-associated lymphoid tissues (NALTs) are lymphoid organs in the nasal mucosa that are sites of inhaled antigen deposition. Bedford *et al.* studied the induction of immunity in NALTs and identified a role for conventional dendritic cells (cDCs) in suppressing T cell responses during the steady state. Similar cDCs are found in human NALTs in adenoids and tonsils and can also inhibit T cell responses and prevent immune activation. Inflammation in nasal mucosa caused by viral infection induces local recruitment of monocyte-derived DCs, which overrides the effects of cDCs and allows for T cell priming. These results provide mechanistic insight into steady-state and inflammatory responses in NALTs. —CNF

Sci. Immunol. **5**, eabb5439 (2020).

INORGANIC CHEMISTRY

Nitrogen lifts iron to hexavalence

The myriad ways that iron can interact with oxygen have been amply studied in biochemical and geochemical contexts. More recently, chemists have explored the extent to which nitrogen can likewise stabilize iron in high oxidation states. Martinez *et al*. now report that an iron center coordinated by carbene ligands can react

with an organic azide to form a pentavalent bis(imido) complex with two Fe=N bonds. One-electron oxidation then accessed the Fe(VI) oxidation state. Both compounds were sufficiently stable for crystallographic characterization. —JSY

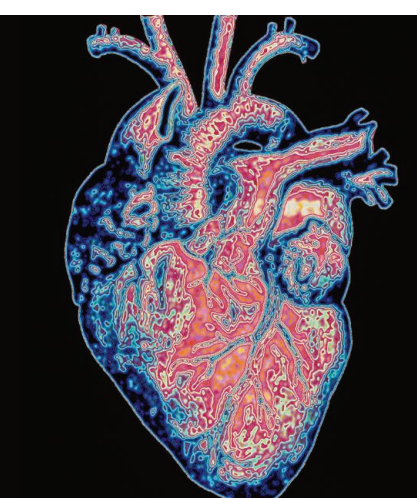
Science, this issue p. 356

PHYSIOLOGY

Metabolomics, at the heart

With heart failure a leading cause of death, a better understanding of metabolic function in the heart is a welcome advance. Murashige *et al*. measured more than 270 metabolites using liquid chromatography–mass spectrometry in human blood samples taken from an artery entering the heart and from a vein leaving it. Differences thus reflected the metabolic processes at work in the heart. Their results confirmed that hearts voraciously consume fatty acids. Hearts secreted, rather than consumed, amino acids, thus revealing active proteolysis. In patients with heart failure, ketone and lactate consumption increased, as did proteolysis. These findings could lead to strategies for fighting heart disease by altering metabolism. —LBR

Science, this issue p. 364



Artistic rendering of the human heart featuring exterior blood vessels, which deliver nutrients and oxygen to this energy-intensive organ

SPECTROSCOPY

The travel time of light in a molecule

There is currently considerable interest in experimental studies of various ultrafast processes. Of particular interest are the real-time dynamics of photoionization, one of the most fundamental processes caused by the light-matter interaction, in which the absorption of a photon leads to the ejection of an electron and the formation of anion. Using an electron interferometric technique, Grundmann *et al*. report a birth time delay on the order of a few hundred zeptoseconds between two electron emissions from the two sides of molecular hydrogen, which is interpreted as the travel time of the photon across the molecule. The proposed technique is generally applicable to more complex systems, and further studies are necessary to support this interpretation. —YS

Science, this issue p. 339

ECOLOGY

Species richness maintains mutualisms

Mutualistic communities of species that benefit each other are ubiquitous in ecosystems and are important for ecosystem functioning. However, the relationship between the persistence of mutualisms and species richness has remained unclear. Vidal *et al*. used a synthetic mutualism in brewer's yeast to experimentally test whether species richness buffers mutualistic communities against exploitation by species that do not provide benefits in return. They showed that richer mutualist communities survive exploitation more often than pairwise mutualisms and that higher species richness and functional redundancy allow mutualist communities to persist in the presence of exploiters. These results provide experimental support for the hypothesis that species richness is necessary for the function and maintenance of mutualistic communities. —AMS

Science, this issue p. 346

IN OTHER JOURNALS

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

PHYSIOLOGY

Enduring muscular courtship

Several species of male amphibians and reptiles hold tight to their partners, possibly to prevent them mating with their rivals. The southern alligator lizard (*Elgaria multicarinata*) clamps its mate's head in its jaws for hours. This extreme muscular performance runs counter to expectations of reptilian muscle resilience. Nguyen *et al.* tested the sustained bite force of the adductor muscles of the lizard's jaw for fatigue. Muscle fibers can specialize, in terms of performance, into fast-acting twitch fibers and into slow-acting tonic fibers that are capable of fatigue-resistant contraction. Tonic fibers also exhibit slow calcium fluxes and relax slowly. The lizards' jaw muscle appears to have evolved to comprise fast-twitch fibers for eating and slow-tonic fibers that can sustain an extended courtship grip. —CA

Proc. R. Soc. London Ser. B **287**, 20201578 (2020).

The southern alligator lizard *Elgaria multicarinata* will grip the head of its mate for hours, thanks to specialized jaw muscle fibers.

IMAGES: (LEFT TO RIGHT) ALFRED PASIEKA/SCIENCE SOURCE; NHMLA COMMUNITY SCIENCE PROGRAM/CC BY-NC

SINGLE-CELL METHODS

Watching information flow inside cells

Each human cell has an information network like a subway system underpinning the function of one of the world's major cities. Instead of human couriers, within our cells, messenger RNAs (mRNAs) carry information. Thousands of mRNAs emerge from the cell's nucleus with instructions

ALSO IN *SCIENCE* JOURNALS

Edited by **Michael Funk**

CORONAVIRUS

COVID-19 risks for children

There has been substantial discourse about how children are affected by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. A fraction of children develop a hyperinflammatory syndrome that is clearly a cause for concern. However, many children seem to develop mild or asymptomatic infections, yet they are harmed by the lockdown measures to prevent SARS-CoV-2 spread. In a Perspective, Snape and Viner discuss what is known about coronavirus disease 2019 (COVID-19) in children and young adults and whether they can spread the virus. They discuss the impacts of lockdowns on education, social care, and mental health, as well as deleterious effects on child health in terms of accidents at home and maintaining vaccination programs. Although more research is needed, such harms should be considered when evaluating control measures in the future. —GKA

Science, this issue p. 286

NEUROSCIENCE

Improving prosthetics

People who use upper- and lower-limb prosthetics face numerous challenges caused by limitations in the interface between person and machine. Ideally, prosthetics should have bidirectional communication between the user and the device so that people can easily and intuitively use their devices. Key to bidirectional interfacing is motor control and sensing. In a Perspective, Raspopovic discusses approaches to providing improved motor control and sensing through various sensors and implants. Recent studies suggest that motor control and sensing can be combined to improve the experience for users of prosthetics, but there are many challenges to overcome to ensure that such neurotechnologies improve quality of life and can be tolerated. —GKA

Science, this issue p. 290

NEURODEVELOPMENT

A moment in time

As the brain develops, it does not simply get bigger. Like a building that depends on temporary scaffolds as its structures are assembled, the developing brain sets up the circuits that characterize the adult brain. Molnár *et al*. review the current state of knowledge about how brain connections are built and how autonomously established patterns are reshaped by activity from the sensory periphery. With the help of a transient population of neurons, the spontaneous activity of early circuits is molded by increasing inputs from the external world. When these normal developmental interactions are disrupted, consequent miswiring drives dysfunction in the adult brain. —PJH

Science, this issue p. 308

INNATE IMMUNITY

Cells drop a bomb on pathogens

Lipid droplets (LDs) accumulate in cells to serve as lipid storage organelles. They are also an attractive source of nutrients for many pathogens. Bosch *et al*. show that various proteins involved in innate immunity form complexes on LDs in response to bacterial lipopolysaccharide (see the Perspective by Green). Upon activation, LDs became physically uncoupled from mitochondria, driving a shift in cells from oxidative phosphorylation to aerobic glycolysis. This work highlights the ability of LDs both to kill pathogens directly and to establish a metabolic environment conducive to host defense. This may inform future antimicrobial strategies in the age of antibiotic resistance. —STS

Science, this issue p. 309; see also p. 294

CELL BIOLOGY

The nucleus makes the rules

Single cells continuously experience and react to mechanical challenges in three-dimensional tissues. Spatial constraints in dense tissues, physical activity, and injury all impose changes in cell shape. How cells can measure shape deformations to ensure correct tissue development and homeostasis remains largely unknown (see the Perspective by Shen and Niethammer). Working independently, Venturini *et al.* and Lomakin *et al.* now show that the nucleus can act as an intracellular ruler to measure cellular shape variations. The nuclear envelope provides a gauge of cell deformation and activates a mechanotransduction pathway that controls actomyosin contractility and migration plasticity. The cell nucleus thereby allows cells to adapt their behavior to the local tissue microenvironment. —SMH

Science, this issue p. 311, p. 310; see also p. 295

DEVELOPMENTAL BIOLOGY

Fiber tension enables tissue scaling

Tissue development, homeostasis, and repair require cells to sense mechanical forces. Although many molecular actors implicated in cell mechanosensitivity have been extensively studied, the basis by which cells adapt their mechanical responses to their geometry remains poorly defined. López-Gay *et al*. now identify how two fundamental epithelial structures—stress fibers and tricellular junctions—endow *Drosophila* cells with an internal ruler to scale their mechanical response with their area. This work explains how cells of different sizes within an epithelial tissue collectively adapt their mechanical response to control tissue shape and proliferation. Scaling of biological properties with size is a core property of other biological systems. —BAP

Science, this issue p. 312

NEUROSCIENCE

How neuron types encode behavioral states

What is the contribution of molecularly defined cell types to neural coding of stimuli and states? Xu *et al*. aimed to evaluate neural representation of multiple behavioral states in the mouse paraventricular hypothalamus. To achieve this goal, they combined deep-brain two-photon imaging with post hoc validation of gene expression in the imaged cells. The behavioral states could be well predicted by the neural response of multiple neuronal clusters. Some clusters were broadly tuned and contributed strongly to the decoding of multiple behavioral states, whereas others were more specifically tuned to certain behaviors or specific time windows of a behavioral state. —PRS

Science, this issue p. 313

MICROBIOTA

Metabolic signals from gut microbes

The gut is a stretchy, glandular, and highly innervated tube packed at its distal end with microorganisms. Disruption of the microbial community can lead to metabolic disorders such as obesity and diabetes. Muller *et al*. investigated how the microbiota interacts with the enteric nervous system to induce a metabolic outcome. A population of autonomous enteric neurons called CART$^+$ neurons are enriched in the ileum and colon,

where most of the microbiota resides. Stimulation or ablation of the CART$^+$ neurons alters blood glucose levels, insulin, and feeding behavior. Furthermore, by manipulating the microbiota, the density of enteric neurons responds plastically in an inducible and reversible manner. —CA

Science, this issue p. 314

MORPHOGENS

Engineering synthetic morphogens

Morphogens provide positional information during tissue development. For this behavior to occur, morphogens must spread out and form a concentration gradient; however, their mechanism of transport remains a matter of debate. Stapornwongkul *et al*. now show that in the presence of extracellular binding elements (binders), the inert green fluorescent protein (GFP) can form a detectable concentration gradient by diffusion in the developing fly wing (see the Perspective by Barkai and Shilo). When combining the expression of nonsignaling binders and receptors engineered to respond to GFP, a synthetic GFP gradient can substitute for a natural morphogen to organize growth and patterning. In related work, Toda *et al*. also show that GFP can be converted into a morphogen by providing anchoring interactions that tether the molecule, forming a gradient that can be recognized by synthetic receptors that activate gene expression. These synthetic morphogens can be used to program de novo multidomain tissue patterns. These results highlight core mechanisms of morphogen signaling and patterning and provide ways to program spatial tissue organization independently from endogenous morphogen pathways. —BAP

Science, this issue p. 321, p. 327; see also p. 292

ULTRACOLD CHEMISTRY

Non-Feshbach ultracold molecules

The formation of ultracold molecules has already had a profound impact on many research areas of physics. However, conventional methods of producing such molecules are attainable only for a limited number of systems or they suffer for strong dephasing. He *et al*. sought to pair atoms, through coupling of their spins, to the two-body relative motion mediated by the inherent polarization gradients in a strongly focused trapping laser. They report a successful assembly of an ultracold ^{87}Rb-^{85}Rb molecule in an optical tweezer and observed coherent, long-lived atom-molecule Rabi oscillations. They further demonstrate the full control of the internal and external degrees of freedom in the atom-molecule system. —YS

Science, this issue p. 331

HYDROGELS

Slippery surfaces using lipids

In engineered systems, a reduction in friction can come from the use of lubricants or through surface coatings that are inherently slippery. For most hydrogels, which are cross-linked polymers heavily swelled with water, surface lubrication typically comes from trapped liquids that help to form a slippery surface. Drawing inspiration from articular cartilage that in part uses a lipid boundary layer, Lin *et al*. designed hydrogels with small concentrations of lipids that are continuously exuded toward the surface to make a slippery layer (see the Perspective by Schmidt). Friction and wear of the hydrogels was reduced by up to a factor of 100, and the effect was observed even after the hydrogels were dried and rehydrated. —MSL

Science, this issue p. 335; see also p. 288

SIGNAL TRANSDUCTION

Intricacies of amino acid sensing

The way in which cells sense amino acids derived from external proteins taken up by micropinocytosis and then degraded in the lysosome turns out to be different from the way in which they sense external amino acids taken up through transporters in the plasma membrane. Both sources of amino acids end up activating the mechanistic target of rapamycin complex 1 (mTORC1) protein kinase complex. However, Hesketh *et al*. found that cultured human cells sense amino acids derived from exogenous proteins in late endosomes by a mechanism independent of the Rag guanosine triphosphatases (GTPases) that control mTORC1 activation in response to external amino acids. Furthermore, the GATOR GTPase had an inhibitory effect on mTORC1 activation in response to proteins processed through the lysosome, opposite to its role in sensing amino acids taken up across the plasma membrane. —LBR

Science, this issue p. 351

MICROBIOTA

A parasite's bilious defense

The enteropathogenic parasite *Giardia lamblia* is a frequent cause of self-limited diarrhea in infected adult travelers. By contrast, parasitic infection of children in endemic areas is not associated with diarrheal disease but rather with reduced body weight gain and growth. Riba *et al*. established a *G. lamblia* infection model in neonatal mice. Infected neonatal animals displayed reduced weight gain and growth. Analysis of these animals showed that *G. lamblia* induced bile secretion and that an altered gut microbiota composition, bile acid modification by commensal bacteria, and subsequent alterations of lipid metabolism contributed to this phenotype. —OMS

Sci. Transl. Med. **12**, eaay7019 (2020).

PLANETARY SCIENCE

Protecting Earth's early atmosphere

When planetary bodies form with nascent atmospheres, those atmospheres are at risk of being stripped away by solar winds. However, a planet's magnetic field, if sufficiently strong, can provide a shield against solar winds and preserve the atmosphere. Previous studies have shown that the early Earth had a geomagnetic field, but its strength remains poorly understood and questions remain as to how Earth's early atmosphere survived. Green *et al*. hypothesized that one part of the answer may be the magnetic field of the nearby early Moon, for which there is evidence from paleomagnetic studies of returned lunar samples. Models of the coupled Earth and Moon magnetospheres suggest that they may have provided an effective barrier to strong solar winds, protecting Earth's atmosphere until at least 2.5 billion years ago. —KVH

Sci. Adv. 10.1126/sciadv.abc0865 (2020).