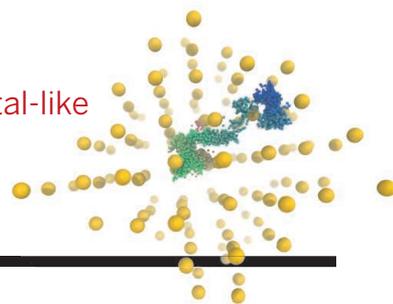


RESEARCH

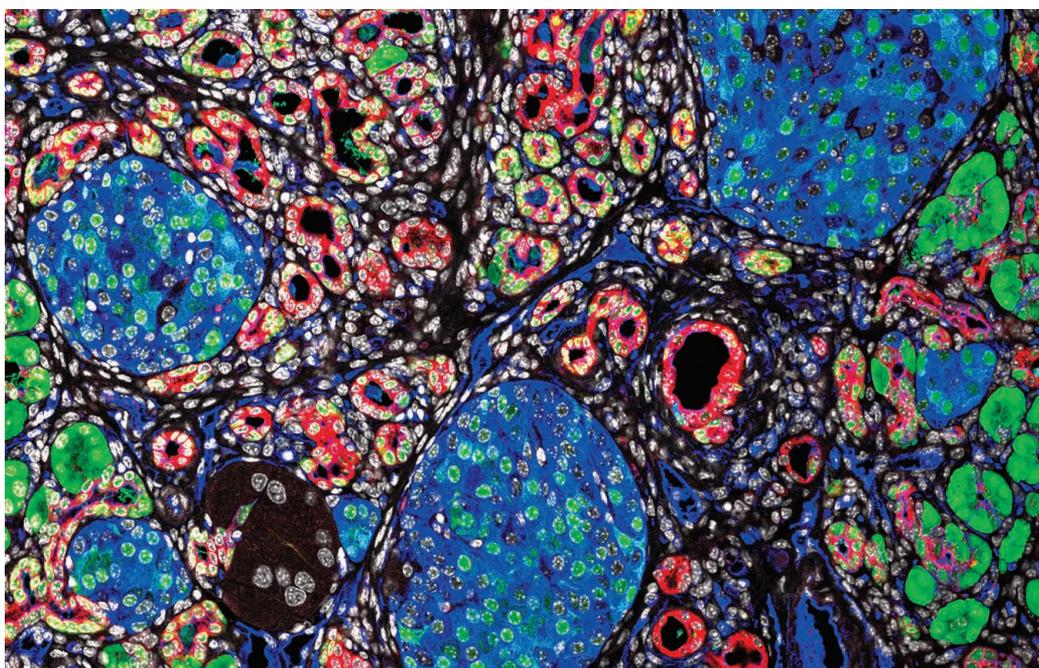
Colloids with metal-like
particle mobility

Girard *et al.*, p. 1174



IN SCIENCE JOURNALS

Edited by **Stella Hurtley**



CANCER

Sweet bystander becomes a villain

Patients with pancreatic cancer often have elevated blood levels of CA19-9, a carbohydrate antigen present on many proteins. CA19-9 is thus commonly used as a biomarker for diagnosing and monitoring disease progression. In a study of mice, Engle *et al.* found that CA19-9 may be more than an innocent bystander that marks the presence of pancreatic disease; it may play a causal role in disease (see the Perspective by Halbrook and Crawford). Transgenic mice expressing the human enzymes that add CA19-9 to proteins developed severe pancreatitis that could be reversed by treatment with CA19-9 antibodies. When the transgenic mice also harbored a *Kras* oncogene, they went on to develop pancreatic cancer. These unexpected observations suggest new avenues for the treatment of pancreatic disease. —PAK

Science, this issue p. 1156; see also p. 1132

An immunofluorescence image of a pancreas in a mouse model of pancreatic disease

PHYSICS

Improving precision with quantum amplification

Quantum mechanically, an object can be described by a pair of noncommuting observables, typically by its position

and momentum. The precision to which these observables can be measured is limited by unavoidable quantum fluctuations. However, the method of “squeezing” allows the fluctuations to be manipulated, while preserving the Heisenberg

uncertainty relation. This allows improved measurement precision for one observable at the expense of increased fluctuations in the other. Burd *et al.* now show that an additional displacement of a trapped atom results in amplification

of the squeezing and a further improvement in the precision with which the displacement can be determined (see the Perspective by Schleier-Smith). This technique should be useful for a number of applications in metrology. —ISO

Science, this issue p. 1163;
see also p. 1137

RADIOTRACER CHEMISTRY

A metal-free route to PET probes

Positron emission tomography (PET) is a widely used imaging technique for medical diagnostics and pharmaceutical development. As the name implies, it requires tracers that emit positrons, typically through labeling with fluorine or carbon radioisotopes. W. Chen *et al.* devised a versatile technique to incorporate radioactive fluoride into aromatic rings. The metal-free photochemical method directly substitutes aryl carbon-hydrogen bonds with [¹⁸F]fluoride and so is particularly well suited to late-stage transformation of complex molecules into tracers. —JSY

Science, this issue p. 1170

CORAL REEFS

Little fish make a big contribution

Coral reefs represent one of the most biodiverse and rich ecosystems. Such richness conjures up images of coral heads and large colorful reef fishes. Brandl *et al.* show, however, that one of the most striking and important parts of the reef ecosystem is almost never seen

(see the Perspective by Riginos and Leis). Small cryptobenthic fish, like blennies, make up nearly 40% of reef fish biodiversity. Furthermore, the majority of cryptobenthic fish larvae settle locally, rather than being widely dispersed, and have rapid turnover rates. Such high diversity and densities could thus provide the biomass base for larger, better-known reef fish. —SNV

Science, this issue p. 1189;
see also p. 1128

BIOCATALYSIS

Light teaches (co)enzymes new tricks

Light is widely used in organic synthesis to excite electrons in a substrate or catalyst, opening up reactive pathways to a desired product. Biology uses light sparingly in this way, but coenzymes such as flavin can be driven to excited states by light. Biegasiewicz *et al.* investigated this reactivity and found a suite of flavoenzymes that catalyze asymmetric radical cyclization when exposed to light. “Ene”-reductases, when reduced and illuminated, converted starting materials containing an α -chloroamide and an alkene into five-, six-, seven-, or eight-membered lactams. Different enzymes furnished different stereochemistry in the products, likely because of changes in active-site pocket geometry. —MAF

Science, this issue p. 1166

STRUCTURAL BIOLOGY

Keeping the gate open

Cystic fibrosis is a progressive disease that affects lung function and is often fatal. It is caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR). One class of mutants impairs ion conductance, and the drug ivacaftor acts by increasing the ion flux. Liu *et al.* describe high-resolution structures of CFTR bound to ivacaftor and to an investigational drug GLPG1837 that also potentiates ion flow.

The two drugs bind at the same site in the transmembrane region. This site coincides with a hinge involved in channel gating, suggesting that the drugs may stabilize the open conformation of the channel. —VV

Science, this issue p. 1184

ISLET TRANSPLANTATION

Revascularizing eye-lets

Pancreatic islet transplantation is a potentially promising therapy for type 1 diabetes, but poor revascularization hinders islet long-term viability. Figueiredo *et al.* studied the role of protein tyrosine phosphatase 1B (PTP1B) in regulating islet vascularization. Islets from PTP1B^{-/-} mice retained more endothelial cells during in vitro culture and restored normoglycemia when transplanted into the anterior chamber of the eye in diabetic mice. Future work is needed to determine whether targeting PTP1B can improve islet transplantation in human patients. —CC

Sci. Transl. Med. **11**, eaar6294 (2019).

NEURODEVELOPMENT

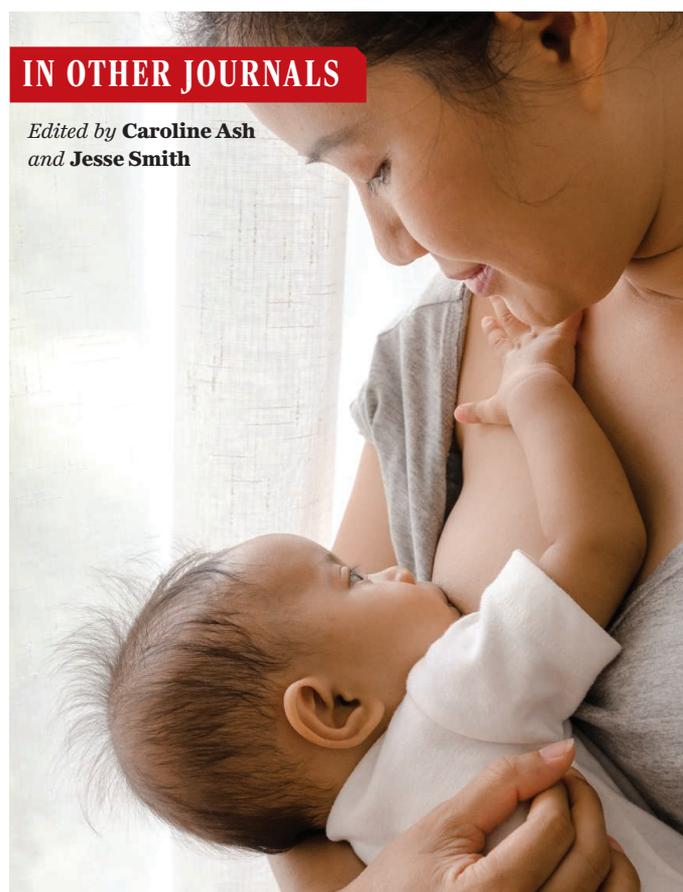
Rescued by a dietary supplement

Patients with Rett-like syndrome show impaired motor and cognitive development. Soto *et al.* studied this disorder in a 5-year-old patient with a mutation in an *N*-methyl-D-aspartate (NMDA) receptor subunit. The electrophysiological and morphological defects in neurons expressing this mutant were improved by the NMDA receptor agonist D-serine. D-Serine itself can be toxic, but it can be converted to its stereoisomer L-serine, a natural component of various foods. Supplementing the patient's diet with L-serine powder increased her D-serine levels and improved her motor and cognitive performance after about 1 year of treatment. —LKF

Sci. Signal. **12**, eaaw0936 (2019).

IN OTHER JOURNALS

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



IMMUNOLOGY

BeATing back obesity

Children who are breastfed appear to be at a lower risk for obesity later in life. One explanation is that breast milk may somehow prevent the premature transition from beige adipose tissue (BeAT) to white adipose tissue during childhood and adolescence. Yu *et al.* report that alkylglycerol ether lipids found in breast milk maintain the BeAT of infant mice. Adipose tissue macrophages metabolize these lipids into platelet-activating factor, which then induces macrophage release of interleukin-6, signal transducer and activator of transcription 3 (STAT3) signaling in adipocytes, and the development of BeAT. Although usually inactivated in adulthood, this pathway resurfaces in obese adipose tissue, indicating a degree of metabolic flexibility that could be exploited for therapeutic applications. —STS

J. Clin. Invest. **129**, 2485 (2019).

Lipids in breast milk delay the transition from beige to white adipose tissue and protect against obesity.

INFORMATION STORAGE

Storing information in molbytes

Present technologies for storing information have been developed over many decades, and

each has its own weaknesses and strengths. In this work, Cafferty *et al.* present a possible alternative storage approach that uses mixtures of small organic molecules (“molbytes,” oligopeptides in the present

ALSO IN SCIENCE JOURNALS

Edited by Stella Hurtley

ROBOTICS

Hand it to you

Our ability to grab, hold, and manipulate objects involves our dexterous hands, our sense of touch, and feedback from our eyes and muscles that allows us to maintain a controlled grip. Billard and Kragic review the progress made in robotics to emulate these functions. Systems have developed from simple, pinching grippers operating in a fully defined environment, to robots that can identify, select, and manipulate objects from a random collection. Further developments are emerging from advances in computer vision, computer processing capabilities, and tactile materials that give feedback to the robot. —MSL

Science, this issue p. 1149

RUMINANT GENOMICS

Phylogeny and characteristics of ruminants

Ruminants are a diverse group of mammals that includes families containing well-known taxa such as deer, cows, and goats. However, their evolutionary relationships have been contentious, as have the origins of their distinctive digestive systems and headgear, including antlers and horns (see the Perspective by Ker and Yang). To understand the relationships among ruminants, L. Chen *et al.* sequenced 44 species representing 6 families and performed a phylogenetic analysis. From this analysis, they were able to resolve the phylogeny of many genera and document incomplete lineage sorting among major clades. Interestingly, they found evidence for large population reductions among many taxa starting at approximately 100,000 years ago, coinciding with the migration of humans out of Africa. Examining the bony appendages on the head—the so-called headgear—Wang *et al.*

describe specific evolutionary changes in the ruminants and identify selection on cancer-related genes that may function in antler development in deer. Finally, Lin *et al.* take a close look at the reindeer genome and identify the genetic basis of adaptations that allow reindeer to survive in the harsh conditions of the Arctic. —LMZ

Science, this issue p. 1152, p. 1153, p. 1154; see also p. 1130

MOLECULAR MACHINES

Flexible domains in a well-oiled machine

Motors convert one form of energy into another. For biological motors, adenosine triphosphate (ATP) serves as chemical energy and its hydrolysis is coupled to conformational changes that exert mechanical force. ATP synthases reverse this process in a multistep process: first converting an electrochemical gradient to rotational kinetic energy, and then coupling rotation to formation of high-energy phosphodiester bonds. Murphy *et al.* investigated these energy changes in the dimeric mitochondrial F_1F_0 ATP synthase from *Polytomella* sp., a unicellular alga. They solved high-resolution cryo-electron microscopy structures of the ATP synthase complex, extracting 13 rotational substates. This collection of structures revealed that the rotation of the F_0 ring and central stalk is coupled with partial rotations of the F_1 head. This flexibility may enable the head to better couple continuous rotation with discrete ATP synthesis events. —MAF

Science, this issue p. 1155

FISHERIES

A small, interconnected world

Countries manage their fisheries as if they were a local resource. To some degree, this may reflect

reality, but marine fish, perhaps more than any other vertebrate group, are connected across large distances through ocean currents. Ramesh *et al.* model how these currents distribute the fish larvae of more than 700 species. They used network analysis to assess the degree to which populations found in one part of the world may have come from another. It seems that global fish populations represent a small-world network where connections across populations are tight and particular hubs of productivity are widely important. Such connectivity has wide-ranging implications for conservation, management, and food supplies globally. —SNV

Science, this issue p. 1192

MUCOSAL IMMUNITY

Context shapes antimicrobial immunity

The gut bacterium *Akkermansia muciniphila* is associated with protection from obesity, enhanced wound healing, and augmented antitumor responses. Ansaldo *et al.* found that this microbe induces antigen-specific immunoglobulin G1 (IgG1) antibodies generated by B cells with CD4⁺ T cell help. This is in contrast to most antimicrobial responses, which involve the T cell-independent production of IgA antibodies. In a gnotobiotic setting in which all components of the microbiome are defined, *A. muciniphila*-specific T cells expanded only when *A. muciniphila* was present. The T cells primarily displayed a phenotype associated with B cell help. However, in mice with a conventional gut microbiota, other proinflammatory *A. muciniphila*-specific T cell populations also expanded. Thus, anti-*A. muciniphila* immunity is context dependent, which may explain the variable immune responses to this microbe reported in patients. —STS

Science, this issue p. 1179

CONSERVATION

Integrating knowledge systems for wildlife health

Knowledge held by local or indigenous populations is often crucial for supporting wildlife health and conservation efforts. In a Perspective, Kutz and Tomaselli highlight efforts to integrate these different forms of knowledge in a mutually respectful manner. For example, use of a participatory epidemiology approach that integrates scientific and indigenous knowledge was key to eradicating rinderpest in its last foci in East Africa. A similar approach led to a greater understanding of the mechanisms driving muskox population declines in the Canadian Arctic. Thus, going forward, rigorous research design that is based on ongoing iteration and feedback could enable inclusion of qualitative local indigenous knowledge in models and decision-making. —JFU

Science, this issue p. 1135

COLLOIDAL MATERIALS

Mobile particles in colloidal crystals

The crystallization of nanoparticles can be controlled by functionalizing them with DNA strands that direct assembly through hybridization. The design rules for interactions between pairs of particles resemble those for ionic compounds. Inspired by molecular dynamics simulations, Girard *et al.* show that larger particles (~10 nanometers in diameter) that have mutual repulsive interactions can form a stable lattice only if much smaller conjugate particles (~1.5 nanometers in diameter) are present. These smaller particles are mobile and diffuse through the lattice, so the bonding interaction resembles the classical picture of electrons in metals. —PDS

Science, this issue p. 1174

CANCER

The microbiota in colorectal cancer

Several types of bacteria have been associated with colorectal cancer, but do these bacteria have a role in tumorigenesis? Data remain unclear, but evidence suggests that some types of bacteria can influence tumor progression and responses to therapy. In a Perspective, Garrett discusses how to advance microbiota research to potentially improve prevention, diagnostics, and therapy of colorectal cancer. —GKA

Science, this issue p. 1133

INFLAMMATION

A colitis circuit

Cytokines are known to play a critical role in maintaining gut homeostasis, but their specific cellular sources are less well understood. Bernshtein *et al.* used a murine model of inflammatory bowel disease in which macrophages specifically lacked expression of the interleukin-10 receptor (IL-10R). The mice developed symptoms of spontaneous colitis similar to those observed in children with IL-10R mutations. The macrophage-derived cytokine IL-23 was critical for inducing the pathology. IL-23 triggered accumulation of IL-22-producing T helper 17 cells that, in turn, promoted production of chemokines by colonic epithelial cells and destructive neutrophil recruitment. —CNF

Sci. Immunol. **4**, eaau6571 (2019).

HYDROLOGY

Modeling groundwater depletion

Understanding the full effects of human activities on groundwater resources has been a persistent challenge to hydrologic models. Such models often seek to inform best practices for resource management. One important gap in our understanding is how groundwater depletion affects surface water behavior. Condon and Maxwell

simulated the impact of 100 years of groundwater declines across the continental United States. Their integrated model illuminates the nature of connections between groundwater pumping and changes in natural watersheds, including the widespread impacts of pumping on evapotranspiration rates and streamflow. —KVH

Sci. Adv. 10.1126/sciadv.aav4574 (2019).