DIRECTED EVOLUTION

Revolution in an RNA-packaging capsid

A rtificial nucleocapsid proteins, which could be analogous to those used by viruses to package their genomes, are a promising way to protect and deliver RNAs. Using an escalating challenge by nucleases, Tetter et al. evolved a protein that forms multimeric, spherical cages into a highly efficient capsid that selectively packages its own encoding RNA. Cryo-electron microscopy of the final design and intermediates revealed a stepwise expansion in size, enabled by destabilizing amino acid substitutions and a domain swap that results in a change of oligomerization interfaces for the base units of the cage. In addition to altering the protein, directed evolution resulted in changes to the encoding RNA structure that enabled efficient uptake versus other cellular RNAs. —MAF Science, abg2822, this issue p. 1220

Directed evolution has transformed a simple oligomeric protein into a massive, capsid-like structure capable of packaging its own encoding RNA.

ELECTROCHEMISTRY

Shuttling protons in ammonia synthesis

An electrochemical route to ammonia could substantially lower the greenhouse gas emissions associated with the current thermal Haber-Bosch process. One relatively promising option under study involves reductive formation of lithium nitride, which can be protonated to ammonia. However, the ethanol used to date as a local proton source in these studies may degrade under the reaction conditions. Suryanto et al. report the use of a tetraalkyl phosphonium salt in place of ethanol (see the Perspective by Westhead et al.). This cation can stably undergo deprotonation–reprotonation cycles and, as an added benefit, it enhances the ionic conductivity of the medium. —JSY Science, abg2371, this issue p. 1187; see also abi8329, p. 1149

NANOPHOTONICS

Imaging polariton dynamics

Two-dimensional (2D) materials can confine light to volumes much shorter than the wavelength, and, together, the long propagation lengths make them attractive materials for developing nanophotonic platforms. Characterizing the spatiotemporal control of 2D polariton wave packets has been hindered for the same reasons that make their potential applications exciting: They have extremely small wavelengths and are strongly confined inside the material. Kurman et al. developed a new pump-probe technique based on electron emission that provides access to the spatiotemporal dynamics of 2D polaritons. The nanometric spatial resolution and femtosecond temporal resolution will be useful for probing the excitation dynamics of these materials. —ISO Science, abg9015, this issue p. 1181

PLANT SCIENCE

Cell size set by cell cycle regulation

In the Arabidopsis meristem, cell sizes are regularized despite asymmetric cell divisions. D’Ario et al. describe a balanced regulatory system that controls the duration of the growth phase of the cell cycle preceding DNA synthesis. KIP-related protein 4 (KRP4) inhibits progression to DNA synthesis. Because the amount of KRP4, which binds to mitotic chromosomes, is titrated to the amount of chromosomal DNA, daughter cells begin with similar amounts of KRP4 despite possible asymmetric cell divisions. Deviations are adjusted as excess KRP4 is degraded and the cell size is normalized. —PJH Science, abb4348, this issue p. 1176

SURFACE CHEMISTRY

Bonding to a quantum coral

Chemical bonds generally form between electronic states of atoms; in principle, other...
electronic states could also form bonds. Stilp et al. found that the electronic states created within quantum corrals, large rings of iron atoms on a copper surface, can form chemical bonds with metal atoms on an atomic force microscope tip. The corral states form from many electrons but have a large spatial extent compared with an atomic orbital. The covalent bond to a 48-atom corral state had an energy of just 5 millielectron volts. —PDS

**CANCER**

**Depleting adenine to prime for apoptosis**

Triple-negative breast cancer (TNBC) is difficult to treat. Daniels et al. identified a metabolic vulnerability in TNBC patient cells and cell lines that may create a therapeutic opportunity for patients. The authors searched for metabolism-perturbing small-molecule compounds that sensitized TNBC lines to apoptosis induced by BH3 mimetics that block apoptotic proteins. They found that inhibition of the rate-limiting enzyme of the nicotinamide adenine dinucleotide salvage pathway, specifically the loss of adenine downstream of inhibition, primed TNBC cells for apoptotic death. —LKF


**GALAXIES**

**Spiral features in the early Universe**

The early assembly of galaxies is thought to have produced disturbed and asymmetric objects. Morphological features seen in nearby galaxies, such as stellar disks, bulges, and spiral arms, require time to form and would be disturbed by the frequent galaxy mergers that occurred at early times. Tsukui and Iguchi identified a distant galaxy containing a disk of gas with a spiral morphology. The galaxy also has a compact central mass concentration due to a combination of a supermassive black hole and a possible stellar bulge. These features must have formed within 1.4 billion years after the Big Bang. —KTS

*Science*, abe9680, this issue p. 1201

**ATMOSPHERIC SCIENCE**

**Atmospheric ozone and pandemic lockdowns**

In response to the global spread of COVID-19, many countries implemented measures that limited mobility and resulted in a decrease in economic activity. Miyazaki et al. studied the global-scale impacts of these lockdowns on free tropospheric ozone, which is important for controlling the atmospheric oxidation capacity and as a climate-forcing agent. They found that reduced industrial and transportation activities associated with the pandemic, especially in Asia and the Americas, reduced the release rate of reactive nitrogen oxides to the atmosphere and led to the production of smaller amounts of ozone. This work illustrates the connections between pollutant emissions and the resultant impacts on atmospheric composition and climate. —JPDA


**PLANT SCIENCE**

**The hard way to produce red**

The common garden petunia delivers flowers in a variety of colors and color patterns, which are pollinated by bees, hawkmoths, or hummingbirds (which are particularly fond of the color red). Throughout evolution, petunia lineages have gained, lost, and shifted color. For example, *Petunia exserta* has evolved a red hue new to the genus. Barardi et al. investigated how *P. exserta* acquired color from a colorless ancestor. The authors found that disabling mutations in a transcription factor freed up substrate for anthocyanin biosynthesis, and another transcriptional activator promoted anthocyanin biosynthesis after it shifted expression domains. The red color depends on delphinidins, which tend to be blue or purple, but when dihydroxylated in *P. exserta*, these pigments contribute to the red hue. In addition, lack of acylation on the anthocyanidin backbone also helps to shift the pigment toward red. —PJH


**IN OTHER JOURNALS**

**Edited by Caroline Ash and Jesse Smith**

**CELL BIOLOGY**

**Waste management on the go**

When some cells migrate, cellular fibers are pulled out from the trailing edge of cells, and 0.5- to 2-µm-diameter vesicle-like enlargements called migrasomes appear. As cells continue to inch forward, the fibers stretch to their breaking point, fragmenting and leaving the enigmatic migrasomes behind. Jiao et al. found that migrasomes resemble a dumpster containing damaged mitochondria and neutrophils. Within the cell, damaged mitochondria tend not to engage with inward-moving motor proteins. Instead, they accumulate at the periphery of the cell and collect in the trailing fibers,

Radio telescope images reveal that galaxies with characteristic spiral features were present in the early Universe.
CANCER
Astronomy accelerates tumor imaging
Immunohistochemical stains for individual markers revolutionized diagnostic pathology decades ago but cannot capture enough information to accurately predict response to immunotherapy. Newer multiplex immunofluorescent technologies provide the potential to visualize the expression patterns of many functionally relevant molecules but present numerous challenges in accurate image analysis and data handling, particularly over large tumor areas. Drawing from the field of astronomy, in which petabytes of imaging data are routinely analyzed across a wide spectral range, Berry et al. developed a platform for multiplex spatial imaging of whole-tumor sections with high-fidelity single-cell resolution. The resultant AstroPath platform was used to develop a multiplex immunofluorescent assay highly predictive of responses and outcomes for melanoma patients receiving immunotherapy. —YN

Science, aba2609, this issue p. 1166

NANOMATERIALS
A family of thin materials
Two-dimensional (2D) materials have attracted interest because of the unusual properties that emerge in these confined structures. There is a growing family of 2D metal carbides and nitrides known as MXenes that contain an odd number of layers in which metals (M) sandwich carbon or nitrogen (X) layers. VahidMohammadi et al. reviewed the progress in synthesizing this growing library of materials. Mixed-metal combinations can be used, as well as a range of surface terminations, making it possible to tune the properties. However, there are still challenges in improving the synthesis methods and developing techniques that can be scaled up. —MSL

Science, abf1581, this issue p. 1165

ECOLOGY
Estimating resilience in complex systems
Resilience is an important concept in the study of critical transitions and tipping points in complex systems and is defined by the size of the disturbance that a system can endure before tipping into an alternative stable state. Nevertheless, resilience has proved robust to measurement. Arani et al. show how the mathematical concept of mean exit time, the time it takes for a system to cross a threshold, can help to solve this problem and characterize the resilience of complex systems. They derived a model approach to estimate exit time from time series data and applied it to examples from a grazed plant population model, lake cyanobacterial data, and Pleistocene-Holocene climate data. This approach may improve our understanding of the dynamical properties of complex systems under threat. —AMS

Science, aay4895, this issue p. 1168

X-INACTIVATION
Visualizing Xist RNA dynamics
The noncoding RNA Xist, which controls the process of X chromosome inactivation in mammals, accumulates and spreads over the chromosome from which it is transcribed. The underlying basis for this unusual behavior is poorly understood. Using a new imaging approach called RNA-SPLIT for time-resolved analysis of Xist RNA molecules at super-resolution, Rodermund et al. analyzed fundamental parameters of Xist RNA behavior in normal cells and after the perturbation of factors implicated in Xist RNA function. The authors provide new insights into the basis of Xist RNA localization and confinement within the territory of a single X chromosome. —DJ

Science, abe7500, this issue p. 1167

QUANTUM SIMULATION
Prethermal time crystal
Characterizing and understanding different phases of matter in equilibrium is usually associated with the process of thermalization, where the system equilibrates. Recent efforts probing nonequilibrium systems have revealed that periodic driving of the system can suppress the natural tendency for equilibration yet still form new, nonequilibrium phases. Kyprianidis et al. used a quantum simulator composed of 25 trapped ion qubits and spins to observe such a nonequilibrium phase of matter: the disorder-free prethermal discrete time crystal. The flexibility and tunability of their quantum simulator provide a powerful platform with which to study the exotic phases of matter. —ISO

Science, abg8102, this issue p. 1192

ANTIMICROBIAL DRUGS
Turning down tolerance
Persisters, which are found in abundance in biofilms, adopt a quiescent state and survive antimicrobial treatments, seeding disease recurrence and incubating new resistance mutations. Building on work implicating the reactive small-molecule hydrogen sulfide in bacterial defense against antibiotics, Shatalin et al. conducted a structure-based screen for inhibitors of a bacterial hydrogen sulfide–producing enzyme and found a group of inhibitors that act through an allosteric mechanism (see the Perspective by Mah). These inhibitors potentiated bactericidal antibiotics in vitro and in mouse infection models. They also suppressed persister bacteria and disrupted biofilm formation. This strategy of taking out persisters may be promising for treating recalcitrant infections and holding the line against drug-resistant bacteria. —MAF

Science, abd3377, this issue p. 1169; see also abj3062, p. 1153

NEURODEVELOPMENT
Gliogenesis in the adult mouse brain
Neural stem cells in the adult mouse brain can generate both neurons and glia. Exactly where each stem cell is positioned can determine what type of neurons it generates. Delgado et al. show that neural stem cells are also choosy about what sorts of glia they make and when (see the Perspective by Baldwin and Silver). Injury or selective deletion of platelet-derived growth factor receptor β (PDGFRβ) from the stem cells kicked them into overdrive and revealed their selectivity with respect to gliogenesis. An unusual type of glial progenitor cell, intraventricular oligodendrocyte progenitors, are found nestled between the cilia of ependymal cells derived from tight clusters of PDGFRβ-expressing stem cells. —PJH

Science, abg8467, this issue p. 1205; see also abj1139, p. 1151

MEMBRANE PROTEINS
How Hedgehog gets its lipid tail
Phospholipid membranes serve as barriers between different cellular environments but are also crucial platforms for biosynthesis, signaling, and transport. In animals, the developmental signaling protein Hedgehog must be modified with an acyl group by the membrane-embedded enzyme Hedgehog acyltransferase (HHAT) to be recognized by its receptor. Using cryo–electron microscopy, Jiang et al. determined structures of HHAT bound to palmitoyl–coenzyme A or a palmitoylated peptide product. Two cavities connect at the active site, enabling acylation of Hedgehog in the lumen of the endoplasmic reticulum by lipid substrates from the cytosolic face of the membrane. —MAF

Science, abg4998, this issue p. 1215

How does Xist RNA spread and accumulate over the X chromosome? Kyprianidis et al. used a quantum simulator to observe a nonequilibrium, disorder-free state known as a prethermal time crystal. This state is characterized by the system remaining in a quiescent state despite being perturbed by periodic driving. The authors showed that this state can suppress the natural tendency for equilibration and observe unique collective behaviors that are not possible in equilibrium systems. These findings provide new insights into the mechanisms of X chromosome inactivation and have implications for understanding other complex systems. —ISO

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**METABOLISM**

**Anti-aging supplement effects in humans**

Synthesis of nicotinamide adenine dinucleotide (NAD⁺) decreases during aging, which is thought to limit the activity of enzymes that require it for their catalytic activity. Studies in animals indicate that replenishment of cellular NAD⁺ can have beneficial effects on aging and age-related diseases, but the situation in humans is less clear. Yoshino et al. report the effects of supplementation with the NAD⁺ precursor nicotinamide mononucleotide in overweight or obese postmenopausal women with prediabetes (see the Perspective by Hepler and Bass). The treatment improved insulin sensitivity in muscle, although a change in NAD⁺ content was not detected. The treatment also increased the expression of platelet-derived growth factor β. The results support potential therapeutic action of NAD⁺ supplementation in humans, but how various NAD⁺ precursors are processed in specific tissues remains to be fully explored. —LBR

Science, abe9985, this issue p. 1224; see also abj0764, p. 1147

**COGNITIVE SCIENCE**

**Discovering better theories**

Theories of human decision-making have proliferated in recent years. However, these theories are often difficult to distinguish from each other and offer limited improvement in accounting for patterns in decision-making over earlier theories. Peterson et al. leverage machine learning to evaluate classical decision theories, increase their predictive power, and generate new theories of decision-making (see the Perspective by Bhatia and He). This method has implications for theory generation in other domains. —TSR

Science, abe2629, this issue p. 1209; see also abi7668, p. 1150

**LYMPHOCYTE MIGRATION**

**A bouncer for bone marrow**

P2RY8 is a G protein–coupled receptor (GPCR) that is involved in restraining germinal center (GC) B cell migration and growth. It is unclear how the ligand of P2RY8, S-geranylgeranyl-l-glutathione (GGG), is involved in these processes. Using gain-of-function mouse models and genetically modified human T cells, Gallman et al. show that the expression of gamma-glutamyltransferase-5 on stromal cells and a transporter on hematopoietic cells are involved in catabolizing and transporting GGG, respectively, restraining P2RY8⁺ cells within GCs. GGG and P2RY8 interactions also restrain lymphocyte trafficking to the bone marrow. Thus, GGG and P2RY8 processing and interactions are crucial for the confinement of B cells within GCs and for inhibiting the migration of lymphocytes into bone marrow. —DAE


**EMERGING INFECTIONS**

**One shot for Lassa virus**

Up to 180 million people are at risk for infection with Lassa virus (LASV), and the endemic region for LASV is expanding. There is a critical need to develop a vaccine, preferably one that protects against multiple lineages of LASV, generates durable immune responses, and can be administered in a single dose. Mateo et al. investigated the ability of a recombinant measles virus vaccine expressing LASV proteins (MeV-NP) to protect nonhuman primates against multiple strains of LASV and to provide protection for a year after vaccination and found this vaccine to be very effective. MeV-NP is now in clinical trials. —CSM