GLACIAL CYCLES
An underground record of past deglaciations
Understanding more exactly how the timing of deglaciations depends on changes in insolation, or the energy received by Earth from the Sun, requires precise and independent records of both environmental change and solar energy input. Bajo et al. strengthened the weak link of that two-member chain, the environmental record, by developing a precise, radiometrically dated chronology of the 11 deglaciations of the past million years derived from speleothems. This allowed them to show more clearly how the initiation and duration of glacial terminations over that period depended on solar obliquity and precession. —HJS
Science, this issue p. 1235

Speleothems, or cave formations, in the Corchia cave system in Italy have provided precise records of the timing of two deglaciations at around 960,000 and 875,000 years ago.

FRUSTRATED MAGNETISM
Looking for a crystalline 2D spin ice
Spin ices—materials in which local magnetic spins respect “ice rules” similar to those in water ice—are typically three-dimensional. Two-dimensional (2D) ice rules can also be formulated and have been found to be satisfied in engineered nanomagnetic systems, usually referred to as artificial spin ices. Zhao et al. used neutron scattering and thermodynamic measurements to study a crystalline candidate for a 2D spin ice, the intermetallic compound HoAgGe. They found that at low temperatures, the local spins on the distorted kagome planes of this quasi-2D material respect 2D ice rules. Increasing the temperature led to a series of transitions consistent with theoretical expectations. —JS
Science, this issue p. 1218

CORONAVIRUS
Structure of the nCoV trimeric spike
The World Health Organization has declared the outbreak of a novel coronavirus (2019-nCoV) to be a public health emergency of international concern. The virus binds to host cells through its trimeric spike glycoprotein, making this protein a key target for potential therapies and diagnostics. Wrapp et al. determined a 3.5-angstrom-resolution structure of the 2019-nCoV trimeric spike protein by cryo-electron microscopy. Using biophysical assays, the authors show that this protein binds at least 10 times more tightly than the corresponding spike protein of severe acute respiratory syndrome (SARS)-CoV to their common host cell receptor. They also tested three antibodies known to bind to the SARS-CoV spike protein but did not detect binding to the 2019-nCoV spike protein. These studies provide valuable information to guide the development of medical countermeasures for 2019-nCoV. —VV
Science, this issue p. 1260

ORGANIC CHEMISTRY
Asymmetry on the plus side
Numerous positively charged metal catalysts have been paired with chiral negative ions to select for just one of two mirror-image products. Genov et al. now report a potentially general strategy to invert the charges in this paradigm. Because intrinsically negative metal catalysts are comparatively rare, the authors appended a sulfonate group to the common bipyridyl ligand. Iridium complexes of this ligand paired with chiral positive ions could borylate just one of two aryl rings appended to carbon or phosphorus centers with high enantioselectivity. —JSY
Science, this issue p. 1246

FUNCTIONAL AMYLOIDS
How amyloid can be a substrate of memory
Formation of memories requires changes in the molecular composition of the synapse. How these changes occur and what maintains this altered synaptic composition so
that memory can persist are unknown. Hervas et al. report the structure of a synaptic translation regulator called Orb2 isolated from the brains of adult fruit flies that is important for the maintenance and recall of memory. Orb2 forms an amyloid and changes its activity from a translation repressor to an activator. The amyloid core is composed of polar hydrophilic residues, as opposed to the hydrophobic ones found in nonfunctional or pathological amyloids. The structure provides insights into how amyloids could be a stable yet malleable substrate of memory. —SMH
Science, this issue p. 1230

T CELLS
Revisiting memory
Certain T cell subsets express a receptor that makes them susceptible to nicotinamide adenine dinucleotide (NAD)—induced cell death (NICT), which can occur during isolation from tissues. This susceptibility has complicated our understanding of what cells are present and active both during and after the acute response. Künzi et al. used an NICT blocker to study the persistence of T follicular helper (TH) cells in mice after infection with a virus. They report that TH cells persisted for more than 400 days after infection and that long-lived TH cells are glycolytic and marked by high expression of folate receptor 4. Upon reinfection, these “memory” TH cells were capable of self-renewal and could also give rise to effector and central memory cells. —AB

TISSUE ENGINEERING
Strategic lumbar support
Diskectomy is a common treatment for herniated or slipped intervertebral disks that can help to alleviate symptoms but does not prevent reherniation or progression of disk degeneration. Sloan et al. developed a two-part, acellular tissue-engineered therapy to prevent degeneration after diskectomy. Injecting hyaluronic acid into the inner region of the disk and applying a photo-cross-linked collagen patch to the outer ring of fibrous tissue healed disk defects and maintained biomechanical support in the lumbar spines of sheep for 6 weeks after diskectomy. —CC

SPECTROSCOPY
Reading a molecule without destroying it
Achieving efficient quantum control of ultracold molecular systems may open opportunities in molecular precision spectroscopy, quantum information, and related fields. Sinhal et al. report a quantum-nondemolition protocol for the detection of the spin-rovibronic state of a single trapped cold molecular ion co-trapped with an atomic ion. They show that monitoring the motion of Ca+ under coherent motional excitation of the Ca+-N2+ string makes it possible to detect the N2+ state without destroying either the molecule or the state itself. The procedure can be repeated multiple times while preserving the high readout fidelity. —YS
Science, this issue p. 1213

GENETIC DISEASE
Contracting disease-causing repeat expansions
Ongoing CAG/CTG expansions in the gene encoding huntingtin in the brains of Huntington’s disease (HD) patients result in pathological accumulations of protein aggregates. It is possible that targeting these somatic expansions could be therapeutically valuable. Nakamori et al. investigated these genetic instabilities in a highly specific way by using a small molecule called naphthyridine-azaquinolone (NA). NA binds selectively to the unusual structures formed by the expanded DNA in the gene encoding huntingtin. NA injections into the striatum of a HD mouse model induced contractions of the expanded repeat and reduced levels of the mutant protein aggregates, with no effects genome-wide. Thus, targeting the root cause of expanded-repeat diseases is possible and could be a valuable strategy for tackling many similar diseases. —SMH
Nat. Genet. 52, 146 (2020).

AUTOIMMUNITY
Cells gone rogue
Autoantibodies are proteins produced by the immune system that attack a person’s own tissues and organs, leading to autoimmune disease. Autoantibodies can be present in the serum years before the clinical onset of autoimmunity, but it is not understood how they cause disease. Singh et al. used multi-omics single-cell technology to trace the evolution of “rogue” cell clones responsible for producing pathogenic autoantibodies in the blood of patients with the autoimmune disease cryoglobulinemic vasculitis. The researchers found that a benign antibody can transform into one that causes inflammation of blood vessels in the skin, kidney, nerves, and joints. The gene mutations that accumulate in the rogue cells during the early stages of autoimmune disease have also been identified in cancer cells from patients with lymphoma. —PNK
Cell 180, 878 (2020).
**MEDICINE**

**New therapies for sickle cell disease**

Sickle cell disease can be treated with matched bone marrow transplants from family members, but this treatment is not available to all patients. Sickle cell disease results from a hemoglobin subunit gene mutation and can be overcome by expression of different hemoglobin subunits. Recent developments have highlighted the possibility of gene therapy and engineered cell therapy to replace mutated bone marrow cells. In a Perspective, Tisdale et al. discuss the developments in anti-sickling drugs and gene and cell therapies and what is needed to treat patients effectively, including those in low- and middle-income countries. —GKA  
Science, this issue p. 1198

**CELL BIOLOGY**

**Phase separation can be skin deep**

The skin’s barrier arises from proliferative cells that generate a perpetual upward flux of terminally differentiating epidermal cells. Cells near the body surface suddenly lose their organelles, becoming dead cellular ghosts called squames. Working in mouse tissue, Garcia Quiroz et al. found that as differentiation-specific proteins accumulate in the keratinocytes, they undergo a vinegar-in-oil type of phase separation that crowds the cytoplasm with increasingly viscous protein droplets (see the Perspective by Rai and Pelkmans). Upon approaching the acidic skin surface, the environmentally sensitive liquid-like droplets respond and dissipate, driving squame formation. These dynamics come into play in human skin barrier diseases, where mutations cause maladapted liquid-phase transitions. —SMH  
Science, this issue p. 1211; see also p. 1195

**NEUROSCIENCE**

**Spreading edema after stroke**

The brain is enveloped in a cushion of cerebrospinal fluid (CSF), which normally provides protection and helps to remove metabolic waste. CSF transport has also recently been shown to play unexpected roles in neurodegeneration and sleep. Mestre et al. used multimodal in vivo imaging in rodents and found that, after a stroke, an abnormally large volume of CSF rushes into the brain, causing swelling (see the Perspective by Moss and Williams). This influx of CSF is caused by constrictions of arteries triggered by a well-known propagating chemical reaction-diffusion wave called spreading depolarization. CSF transport can thus play a role in brain swelling after stroke. —SMH  
Science, this issue p. 1212; see also p. 1193

**COMETARY SCIENCE**

**Ammonium salts on comet 67P**

The distribution of carbon and nitrogen in the Solar System is thought to reflect the stability of carbon- and nitrogen-bearing molecules when exposed to the heat of the forming Sun. Comets have a low nitrogen-to-carbon ratio, which is contrary to expectations because they originate in the outer Solar System where nitrogen species should be common. Poch et al. used laboratory experiments to simulate cometary surfaces and compared the resulting spectra with comet 67P/Churyumov-Gerasimenko. They assigned a previously unidentified infrared absorption band to nitrogen-containing ammonium salts. The salts could contain enough nitrogen to bring the comet’s nitrogen-to-carbon ratio in line with the Sun’s. —KTS  
Science, this issue p. 1212

**WATER RESOURCES**

**Evaporating futures**

Drought and warming have been shrinking Colorado River flow for many years. Milly and Dunne used a hydrologic model and historical observations to show that this decrease is due mainly to increased evapotranspiration caused by a reduction of albedo from snow loss and the associated rise in the absorption of solar radiation (see the Perspective by Hobbs and Barsugli). This drying will be greater than the projected precipitation increases expected from climate warming, increasing the risk of severe water shortages in an already vulnerable region. —HJS  
Science, this issue p. 1252; see also p. 1192

**STRUCTURAL BIOLOGY**

**Snapshots of a rotary pump**

Vesicular- or vacuolar-type adenosine triphosphatases (V-ATPases) are ATP-hydrolysis-driven proton pumps. In neurons, V-ATPase activity generates a proton gradient across the membrane of synaptic vesicles so that neurotransmitters can be loaded into the vesicles. Abbas et al. developed a method to purify V-ATPase from rat brain and determined the structure of the entire complex by cryo-electron microscopy. Native mass spectrometry showed that the preparation was homogeneous and complemented structural studies by confirming the subunit composition. Three rotational states were resolved at better than 4-angstrom resolution, providing insight into the conformational changes that couple ATP hydrolysis to proton pumping. —VV  
Science, this issue p. 1240

**IMMUNOLOGY**

**Deadenylate or activate?**

When cells are quiescent, they undergo reversible cell cycle arrest and evince low basal metabolism. Naïve T cells are normally quiescent until they recognize cognate antigens through T cell receptor–costimulatory molecule signaling. T cell quiescence appears to be an active process, but the mechanistic details are poorly understood. Hwang et al. report that the transcription factors BTG1 and BTG2 are selectively expressed in quiescent T cells. In mice, T cells conditionally knocked out for both factors showed enhanced proliferation and a lowered threshold of activation both in vitro and in response to Listeria monocytogenes infection. Deficiency of BTG1 and BTG2 resulted in increases in global messenger RNA half-life, suggesting that...
messenger RNA deadenylation and degradation are important processes for maintaining T cell quiescence. —STS
Science, this issue p. 1255

CANCER
Inducing mortality by targeting mortalin
Oncogenic mutations in the kinase BRAF can enhance cell survival, even in cells exposed to targeted inhibitors. Wu et al. found that a heat shock protein family A (HSP70)–related chaperone protein called mortalin disrupted a protein-protein interaction that would ordinarily trigger cell death in BRAF mutant cells. Depleting mortalin or treating cells with either HSP70 derivatives or synthetic decoy peptides that mimic mortalin target sites increased the efficacy of the BRAF inhibitor vemurafenib in cells and in tumor-bearing mice. —LKF

STRUCTURAL BIOLOGY
Clustering for the kill
Cluster of differentiation 20 (CD20) is a membrane protein that defines most B cell populations and is the target of therapeutic antibodies to treat malignancies and autoimmune disorders. Rougé et al. present the structure of CD20 bound to the antibody rituximab that activates the complement system to kill B cells. CD20 forms a dimer and each monomer binds one rituximab antigen-binding fragment (Fab) to give 2:2 stoichiometry. The compact packing between Fab arms and CD20 gives rise to circular assemblies with a diameter similar to that of antibody hexamers known to recruit the first component of the complement cascade. —VV
Science, this issue p. 1224

ECOLOGY
What becomes of fragmented forests?
Understanding how tropical forests are changing in structure and extent over time is essential to protecting these habitats. Hansen et al. incorporated fragmentation metrics with spatially explicit forest loss data to paint a complete picture for local communities to use in forest fragmentation monitoring. This analysis reveals higher rates of loss in highly fragmented forests. The authors suggest prioritizing conservation efforts on preventing further fragmentation of large forested areas and restoring connectivity in regions with highly fragmented forests. —SN