can bias signaling toward one pathway versus another. They identified a specific conserved residue in the ligand-binding site for multiple class A GPCRs that modulates signaling by one partner, β-arrestin, while minimally affecting that mediated by another, G proteins. Mutations in this residue resulted in conformational changes predicted to allosterically affect the interaction of the receptor with β-arrestin. —WW


**ELECTROCHEMISTRY**

**Graceful choreography for CO₂ and H₂O**

One challenge for efficient electrochemical reduction of carbon dioxide (CO₂) is that the gas is hydrophobic, but many of its desirable reactions require water (H₂O). García de Arquer et al. addressed this problem by combining a copper electrocatalyst with an ionomer assembly that intersperses sulfonate-lined paths for the H₂O with fluorocarbon channels for the CO₂. The electrode architecture enables production of two-carbon products such as ethylene and ethanol at current densities just over an ampere per square centimeter. —JSY

Science, this issue p. 661

**SIGNAL TRANSDUCTION**

**Liver disease defect identified**

The energy sensor adenosine monophosphate–activated protein kinase (AMPK) is implicated in liver damage in nonalcoholic steatohepatitis (NASH), a leading cause of liver-associated death in humans. Zhao et al. used mouse models of NASH and samples from human NASH patients to show that AMPK, the activity of which is lost in NASH, phosphorylates the enzyme procaspase-6. In normal liver cells, this modification limits the activation of caspase-6 and the consequent caspase activation cascade that leads to apoptosis. AMPK and caspase-6 may thus provide therapeutic targets for the treatment of NASH. —LBR

Science, this issue p. 652

**STRUCTURAL BIOLOGY**

**Architecture of an mRNA processor**

The 3′-end processing of the three major classes of RNA polymerase II transcripts in metazoan cells—polyadenylated messenger RNAs (mRNAs), histone mRNAs, and small nuclear RNAs (snRNAs)—requires three distinct machineries that share common features. Sun et al. reconstituted the active human histone pre-mRNA 3′-end processing machinery and solved its structure at near-atomic resolution by cryo–electron microscopy. This structure provides a basis for understanding the mechanism of the shared catalytic reactions between histone pre-mRNA and canonical pre-mRNA and snRNA 3′-end processing machineries. —SYM

Science, this issue p. 700

**MOSQUITO BIOLOGY**

**Heat seeking is cool**

Mosquitoes seek hosts using several cues, one of which is body heat. Greppi et al. hypothesized that cooling-activated receptors could be used for locating mammalian hosts if they were rewired downstream for repulsion responses (see the Perspective by Lazzari). A gene family conserved in insects and known to be responsible for sensing changes in temperature in fruit flies was the starting point. Genome-wide analyses and labeled CRISPR-Cas9 mutants allowed visualization of the receptor in neurons of *Anopheles gambiae* mosquitoes’ antennae and assessment of adult female mosquitoes with a disrupted copy of the receptor. This ancestral insect temperature regulatory system has been repurposed for host-finding by malaria mosquitoes. —CA

Science, this issue p. 681; see also p. 628

**BIOCHEMISTRY**

**Breaking the wall**

Lysostaphin is a bacteriolytic enzyme that is active against methicillin-resistant *Staphylococcus aureus*. It targets cell wall peptidoglycan, which comprises short glycan chains that cross-link to form the bacterial cell wall. In staphylococci, the cross-link is pentaglycine, which can be cleaved by lysostaphin. Lysostaphin weakly binds to pentaglycine through the enzyme’s SH3b domain. Gonzalez-Delgado et al. used nuclear magnetic resonance, x-ray crystallography, and mutational analysis to show that the SH3b domain has two binding sites on opposite sides of the enzyme. One site binds the pentaglycine cross-bridge, and the other site binds the peptide stem. Binding to the two sites induces clustering of lysostaphin. Weak binding, combined with high local concentration, likely allows the enzyme to rapidly and progressively degrade the peptidoglycan surface. —VV


**CANCER**

**Active tumor penetration**

Anticancer nanoparticle development has relied on the assumption that nanoparticles passively cross leaky blood vessels to enter solid tumors. Using transmission electron microscopy to analyze a glioblastoma xenograft model, Sindhwani et al. found that gaps between endothelial cells lining blood vessels are infrequent and do not account for observed nanoparticle accumulation in tumors. Instead, nanoparticles actively enter tumors by transendothelial extravasation. They also show...
CONSERVATION

Marine mapping for saving seabirds

Seabirds are widely threatened by human activity, both at their breeding grounds and at sea. For conservation to be effective, reliable information on the birds’ ranges is essential. In waters around the United Kingdom, Cleasby et al. used a combination of GPS electronic tracking data, species distribution modeling, and mapping techniques to identify high-density aggregations of guillemots, razorbills, kitiwakes, and shags. Their methods identified hotspots of breeding-season distributions for these birds, an improvement on previous techniques, which were solely based on foraging ranges. A combination of species distribution modeling and hotspot mapping can thus offer accurate guidance for identifying important areas for seabird protection. —AMS


Hotspots for breeding seabirds—such as these shags, kitiwakes, razorbills, and guillemots on the Farne Islands, UK—can now be identified by a combination of location techniques.

MATERIALS SCIENCE

When changing is in phase

Shape memory materials can respond to stimuli like heat, light, or moisture to switch between two or more preprogrammed shapes. Spatial variation in the material can allow for complex patterns of bending, folding, buckling, or twisting to make three-dimensional shapes, but these are often one-way processes. Deng et al. show that a simple composite made of wax droplets in a silicone matrix can form a programmable, reversible three-dimensional shape-changing material. When the material is stretched, specific wax particles can be melted and cooled, changing their shape and leaving a residual stress. On relaxation of the matrix, it will buckle and fold into complex shapes such as a pneumatic actuator or it can be used for rewritable “paper.” Similar effects can be seen with polycaprolactone particles in a polycrylamide hydrogel. —MSL


NEURODEVELOPMENT

The eyes have the signals

Anterior segment dysgenesis is a genetic disorder that causes errors in the development of the iris, cornea, or lens of the eye. This anterior portion of the eye develops from migrating neural crest cells. Developmental errors here can lead to complications that include glaucoma and blindness in a growing child. Portal et al. ablated the primary cilia of key neural crest cells in mice. Disrupting the cilia altered the hedgehog signaling pathway and impaired corneal innervation. This outcome in mice replicates defective eye development seen clinically. —PJD


That the vascular architecture in human tumor samples is mostly intact, which supports the observations that nanoparticles enter tumors by means of an active process rather than by a generalized leakiness. —SYM


COSMIC DUST

Ages of interstellar dust in a meteorite

Some primitive meteorites contain presolar grains, which are solid particles that formed in the interstellar medium before being incorporated into the Solar System. Presolar grains were known to be older than the Sun but had not been precisely dated. Heck et al. examined neon isotopes in presolar silicon carbide grains extracted from the Murchison CM2 meteorite. This allowed them to calculate how long each grain had remained in the interstellar medium, a period of time ranging from 3.9 ± 1.6 million years up to 3 ± 2 billion years before the formation of the Solar System, making the grains the oldest known solid material. Most grains had presolar ages of less than 300 million years, constraining astronomers’ models of how long dust survives in the interstellar medium. —KTS


Organic chemistry

Machine learning for asymmetric catalysis

Catalysts can introduce asymmetry in the outcome of chemical reactions, favoring one mirror-image product over another. Many of the most effective catalysts for this application were optimized through trial and error, but more recently, parameterization and systematic analysis have played an increasing role. Singh et al. now showcase the predictive power of machine learning applied to the ligands used for asymmetric hydrogenation. A random forest algorithm trained on several different families of chiral binaphthyl phosphorus compounds predicted selectivity in hydrogenation of alkenes and imines with a root-mean-square error of just over 8%. —JSY


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Steve Mao

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