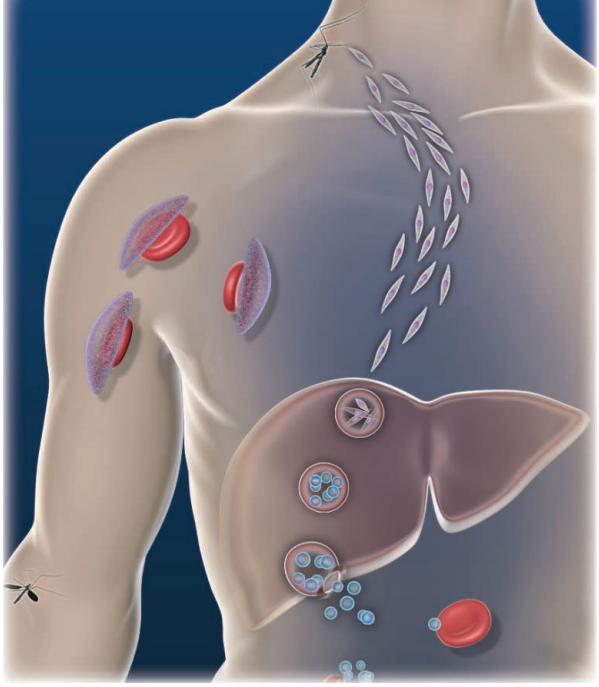


<< Malaria Sporozoite Vaccine

Each year, hundreds of millions of people are infected with *Plasmodium falciparum*, the mosquito-borne parasite that causes malaria. A preventative vaccine is greatly needed. **Seder *et al.*** (p. 1359, published online 8 August; see the Perspective by **Good**) now report the results from a phase I clinical trial where subjects were immunized intravenously with a whole, attenuated sporozoite vaccine. Three of 9 subjects who received four doses and zero of 6 subjects who received five doses of the vaccine went on to develop malaria after controlled malaria infection. Both antibody titers and cellular immune responses correlated positively with the dose of vaccine received, suggesting that both arms of the adaptive immune response may have participated in the observed protection.

Merging Coma

Galaxy clusters grow through mergers and accretion of matter to become the largest gravitationally bound structures in the universe. **Sanders *et al.*** (p. 1365) report long, high-resolution observations with NASA's Chandra X-ray Observatory that probe hot, ionized gas at the core of the Coma cluster—one of the nearest and best-studied galaxy clusters. The data reveal several large-scale, filament-shaped x-ray brightness enhancements, which provide insight into the cluster's merging history.

Polymer Dynamics

While free surfaces should allow polymer chains to move faster than in the bulk, the presence of a substrate might slow down the motion if there is an attraction between the two. **Tress *et al.*** (p. 1371; see the Perspective by **Russell**) used dielectric spectroscopy to study "polymer islands" deposited on a substrate from dilute solution, where some islands contained just a few or only one polymer chain. The confinement of the polymer chain to small-surface geometries had virtually no influence on the dynamics of the polymers, aside from the segments in direct contact with the substrate.

The Pull of Phosphorus

Lewis acidity is primarily associated with compounds like boranes that lack a full complement of electrons in their coordination sphere and therefore attract electron donors (Lewis bases) to fill the gap. **Caputo *et al.*** (p. 1374; see the Perspective by **Gabbaï**) now show that a class of 4-coordinate phosphonium salts can act as surprisingly potent Lewis acids, despite their electronic saturation. The phosphorus cations, bearing fluorine and fluorinated aromatic substituents, can sever an alkyl carbon-fluorine bond by pulling away its fluoride—a process rendered catalytic through the use of a silane acceptor.

Alarm Bells

The presence of DNA in the cytosol of mammalian cells is a danger signal, indicating, for example, that a DNA-containing virus has infected the cell. This signal triggers an innate immune response, which involves the expression of type I interferons, and is critical for antiviral immunity and responses to DNA vaccines. Cyclic GMP-AMP synthase (cGAS) was recently identified as a sensor of cytosolic DNA. **Li *et al.*** (p. 1390, published online 29 August) now use knockout mice to provide genetic evidence that, in multiple cell types, cGAS is the primary DNA sensor required for the type I interferon response in vivo.

Stealth Nod Factor Recognition

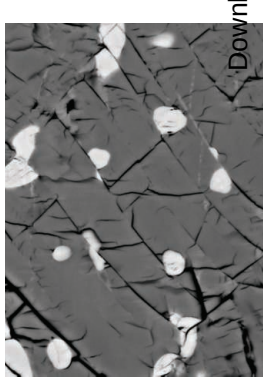
Legumes' symbiotic interaction with nitrogen fixing bacteria supplies the plant with nitrogen. Many important crop plants, however, cannot establish these symbioses and, thus, agriculture depends on externally applied fertilizers. Surprisingly, **Liang *et al.*** (p. 1384, published online 5 September) found that several nonleguminous plants, including *Arabidopsis*, tomato, and corn, were able to respond to the same Nod factors that initiate the microbial symbiosis in soybean.

Pain and Dependence

The properties and functions of μ-opioid receptors have been studied intensively with respect to the binding of endogenous or exogenous ligands. However, much less is known about the constitutive, ligand-independent, activation of opioid receptors. Working in mice, **Corder *et al.*** (p. 1394) observed the prolonged constitutive activation of μ-opioid receptors in the spinal dorsal horn after transient peripheral inflammation. The results suggest that constitutive activation of μ-opioid receptors depresses nociception—the perception of pain—for long periods of time and induces cellular and physical dependence on endogenous opioid signaling.

Delineating Deep Faults

Most large, damaging earthquakes initiate in Earth's crust where friction and brittle fracture control the release of energy. Strong earthquakes can occur in the mantle too, but their rupture dynamics are difficult to determine because higher temperatures and pressures play a more important role. **Ye *et al.*** (p. 1380) analyzed seismic *P* waves generated by the 2013 M_w 8.3 Sea of Okhotsk earthquake—the largest deep earthquake recorded to date—and its associated aftershocks. The earthquake ruptured along a fault over 180-kilometer-long and structural heterogeneity resulted in a massive release of stress from the subducting slab. In a set of complementary laboratory deformation experiments, **Schubnel *et al.*** (p. 1377) simulated the nucleation of acoustic emission events that resemble deep earthquakes. These events are caused by an instantaneous phase transition from olivine to spinel, which would occur at the same depth and result in large stress releases observed for other deep earthquakes.



CREDITS (TOP TO BOTTOM): C. BICKEL/*SCIENCE*; ALEXANDRE SCHUBNEL, LABORATOIRE DE GÉOLOGIE, ENS/CNRS

Additional summaries

Pushing Metathesis Forward

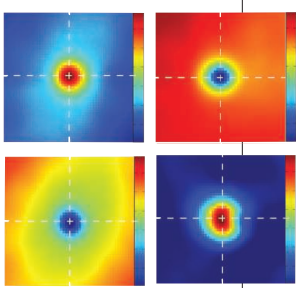
It has been 8 years since the Nobel Prize in chemistry recognized the pioneers of olefin metathesis catalysis. Essentially, a means of shuffling the four carbons in a pair of double bonds, the transformation has enabled efficient synthesis of numerous complex organic compounds—particularly those incorporating large rings—and also underlies the ROMP (ring-opening metathesis polymerization) process for the preparation of specialty polymers. Analogous metathesis of (triple-bonded) alkynes has been applied as well. **Fürstner** (p. 1357) reviews recent developments in the continuing optimization of this extraordinarily versatile reaction class. A long-standing deficiency has been the lack of stereoselectivity by the standard catalysts, precluding deliberate placement of substituents on the same (*Z*) or opposite (*E*) sides of the double-bond axis in the product, but recently introduced catalysts have shown promise in achieving high *Z* selectivity.

Toward Synthetic Biology

The detection of an appropriate point to intervene in a cellular pathway and minimize off-target effects on other cellular processes present problems for the design of circuits that control cellular signaling pathways and thus direct cell function. **Galloway *et al.*** (p. 1358, published online 15 August; see the Perspective by **Sarkar**) report progress on these challenges in the yeast *Saccharomyces cerevisiae*. A molecular control system was developed to direct the yeast cells to one of three cell fates. To avoid disruption of other cellular controls, exogenous ribozyme-based controllers that interfaced with the endogenous control circuits were used, which avoided genetic alteration to the cells. After enhancing the control circuits with feedback loops to make their behavior more reliable, the circuits were used to modulate the abundance of particular components that acted as critical regulators of yeast cell-fate decisions. This allowed direction of cell fate in response to a chosen chemical stimulus. These strategies may be adaptable to allow similar direction of the physiological state of mammalian cells, for example, to allow therapeutic applications of synthetic biology.

Dissipating Static

The accumulation of a static charge on polymers and other insulators often causes little more than a slight annoyance but it can lead to the destruction of sensitive electrical equipment. Thus, approaches are required that prevent and dissipate static electricity through improved electrical conductivity, or that ensure complete discharge before a contact with a key piece of equipment. **Baytekin *et al.*** (p. 1368) show that surface charges will colocalize with radicals on the surface of a polymer, and that the addition of free radical scavengers causes a discharge of the surface as the charges are removed. The approach was used successfully to produce coatings that protected electronic circuits from damage caused by electrostatic discharge.



CCR5-Maraviroc Structure

The chemokine receptor CCR5, a G protein–coupled receptor best known as a co-receptor during HIV-1 infection, is important in a variety of physiological processes. **Tan *et al.*** (p. 1387, published online 12 September; see the Perspective by **Klasse**) now report the high-resolution crystal structure of CCR5 bound to the HIV-1 entry inhibitor, Maraviroc. The structure suggests that Maraviroc acts as a noncompetitive inhibitor by binding to a region of CCR5 that is distinct from the binding site of HIV-1 and chemokines. Comparison of the structure of CCR5 with the other HIV-1 co-receptor, the chemokine receptor CXCR4, provides insight into the co-receptor selectivity of the virus.

Amyloid Binding Partners

Amyloid-β (Aβ) is critical to the pathology of Alzheimer's disease (AD), but its role in normal physiology remains unclear. **Kim *et al.*** (p. 1399; see the Perspective by **Benilova and De Strooper**) found that murine-paired immunoglobulin-like receptor B (PirB) and its human ortholog, leukocyte immunoglobulin-like receptor B2 (LilrB2) both bound to oligomerized Aβ. Early in mouse development, ocular dominance plasticity was affected by interactions between oligomeric Aβ and PirB. In hippocampal brain slices from a mouse model of AD, reductions in long-term potentiation induced by Aβ required PirB. Furthermore, the memory defects characteristic of a mouse model of AD were dependent on function of PirB. Many binding partners for Aβ have been identified, and so the extent to which these findings can be exploited therapeutically remains unclear.

Extracellular Regulation

During *Caenorhabditis elegans* development, the hermaphrodite-specific neurons (HSNs) migrate and then extend axons toward their functional targets. Posttranslational modification of heparan sulfate proteoglycans are important for HSN development, and so **Pedersen *et al.*** (p. 1404) tested the effect of disrupting or reducing chondroitin and heparan sulfate synthesis during *C. elegans* development. The results suggest that proteoglycan biosynthesis is tightly regulated by a microRNA pathway to shape the cell surface glycosylation architecture required to direct neuronal migration.

CREDIT (TOP TO BOTTOM): BAYTEKIN *ET AL.*