RESEARCH

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Edited by Stella Hurtley

NEUROSCIENCE
Resolving a ticklish problem

What is the neural correlate of ticklishness? When Ishiyama and Brecht tickled rats, the animals produced noises and other joyful responses. During the tickling, the authors observed nerve cell activity in deep layers of the somatosensory cortex corresponding to the animals’ trunks. Furthermore, microstimulation of this brain region evoked the same behavior. Just as in humans, mood could modulate this neuronal activity. Anxiety-inducing situations suppressed the cells’ firing, and the animal could no longer be tickled. —PRS

Science, this issue p. 757

WILDLIFE DISEASE
British squirrels infected with leprosy

With the exception of armadillos in the Americas, leprosy infections are considered almost exclusively restricted to humans. Avanzi et al. examined warty growths on the faces and extremities of red squirrels in the British Isles and found that two species of leprosy-causing organisms were to blame (see the Perspective by Stinear and Brosch). Mycobacterium leprae in the southern population of Brownsea Island squirrels originated from a medieval human strain. M. lepromatosis was found in red squirrels from elsewhere in the United Kingdom and Ireland. Human leprosy is proving hard to eradicate, despite available drugs. Perhaps other wildlife species are also reservoirs for this stubborn disease. —CA

Science, this issue p. 744; see also p. 702

INORGANIC CHEMISTRY
Coordinated scission of N–H or O–H bonds

Ammonia and water both have well-explored acid-base chemistry at room temperature, revolving around proton exchange. In contrast, radical chemistry involving H-atom exchange is comparatively rare in these molecules in the absence of a high-energy stimulus. Bezdek et al. now show that coordination of ammonia or water to a molybdenum complex substantially weakens the N–H or O–H bonds, so much so that heating to 60°C liberates hydrogen (see the Perspective by Hoover). Theoretical and electrochemical analyses reveal the underpinnings of the bond-weakening phenomenon. —JSY

Science, this issue p. 730; see also p. 707

NANOPHOTONICS
A cool route to nanospectroscopy

Confining light to a cavity is often used to enhance the interaction between the light and a particle stored within the cavity. Benz et al. worked with a self-assembled monolayer of biphenyl-4-thiol molecules sandwiched between a gold film and a gold nanoparticle. They used laser irradiation to move atoms in the nanoparticle and produced a “picocavity” that was stable at cryogenic temperatures. The authors were then able to obtain time-dependent Raman spectra from individual molecules. Such subwavelength cavities that can localize light to volumes well below 1 nm³ will enable optical experiments on the atomic scale. —ISO

Science, this issue p. 726

ARCTIC SEA ICE
Why we are losing sea ice

Arctic sea ice is disappearing rapidly, leading to predictions of an ice-free summer in the near future. Simulations of the timing...
of summer sea-ice loss differ substantially, making it difficult to evaluate the pace of the loss. Notz and Stroeve observed a linear relationship between the monthly-mean September sea-ice area and cumulative CO₂ emissions. This allowed them to predict Arctic summer sea ice directly from the observational record. Interestingly, most models underestimate this loss. —HJS

**EVOLUTIONARY GENOMICS**

**Identifying genes under recent selection**

Evolutionary analyses aim to identify recent genetic changes that are likely to have been subject to selection. Field et al. present a method to identify such changes, the singleton density score, which they applied to over 3000 human genomes. Over the past ~100 generations (2000 to 3000 years), Europeans are likely to have experienced selection for genetic variants, including those that affect skin and hair pigmentation, as well as height. —LMZ

*Science*, this issue p. 760

**IMAGING**

**A look at early multiple sclerosis**

In multiple sclerosis and similar diseases in animals, the brain becomes inflamed, which ultimately causes neurons to degenerate. Gerwien et al. found two protein-degrading enzymes that are absolutely required for this process: MMP-2 and MMP-9. MMP-9 resides in immune cells and is required for the entry of these cells into the brain as the disease begins. The authors developed tools to visualize MMP inhibitors at this initial stage of multiple sclerosis and its mouse equivalent, just as immune cells began their inflammatory infiltration of the brain. —KLK


**CELL BIOLOGY**

**A new paradigm for IP₃ signaling**

The second-messenger inositol trisphosphate (IP₃) stimulates calcium release from the endoplasmic reticulum (ER). Dickinson et al. triggered the focal release of IP₃ in animal cells and measured calcium “puffs”—intense, localized increases in calcium released from the ER (see the Focus by Leybaert). IP₃ diffused much more slowly within cells than had been originally measured in vitro. Thus, rather than functioning as a global cellular signal, IP₃ can produce local signals, increasing the complexity of information that can be encoded in responses to IP₃-generating stimuli. —NRG


**HOST DEFENSE**

**How macrophages build a wall**

Granulomas are a defining feature of infection with *Mycobacterium tuberculosis*, the causative agent of tuberculosis. Macrophages are the primary component of these cell structures, which are thought to protect the host by walling off the pathogen. Cronan et al. studied granulomas in optically transparent zebrafish infected with *M. marinum* to directly visualize how they form. They observed that macrophages in
ACCUMULATING IMPACTS

CLIMATE CHANGE

Anthropogenic climate change is now in full swing. Our global average temperature is already having increased by 1°C from preindustrial levels. Many studies have documented individual impacts of the changing climate that are particular to species or regions, but individual impacts are accumulating and being amplified more broadly. Scheffers et al. review the set of impacts that have been observed across genes, species, and ecosystems to reveal a world already undergoing substantial change. Understanding the causes, consequences, and potential mitigation of these changes will be essential as we move forward into a warming world. —SNV

Science, this issue p. 719

AMYLOIDOGENESIS

Aggregation by design

Amyloid aggregation is driven by short sequences within proteins that self-assemble into characteristic amyloid structures. About 30 human proteins are implicated in amyloid-associated diseases, but many more contain short sequences that are potentially amyloidogenic. Gallardo et al. designed a peptide based on an amyloidogenic sequence in the vascular endothelial growth factor receptor VEGFR2. The peptide induced VEGFR2 to form aggregates with features characteristic of amyloids. Amyloids were toxic only in cells that required VEGFR2 activity, suggesting that the toxicity was due to loss of function of VEGFR2, rather than to inherent toxicity of the aggregates. The peptide inhibited VEGFR2-dependent tumor growth in a mouse tumor model. —VV

Science, this issue p. 720

CELL CYCLE

RNAi soothes the path to quiescence

Cells, such as those in stem cell niches and immunity memory cells, can exist in a nondividing, quiescent state, from which they can be aroused with the appropriate signal. RNA interference (RNAi) is an important epigenetic pathway in many organisms. Roche et al. found that in fission yeast, RNAi was an essential regulator of the quiescent state. RNAi promoted proper chromosome segregation during entry into quiescence. It also prevented inappropriate silencing of the ribosomal DNA during quiescence. —GR

Science, this issue p. 721

CHEMICAL PHYSICS

Watching as helium goes topsy-turvy

Theorists have long pondered the underpinnings of the Fano resonance, a spectral feature that resembles adjacent rightside-up and upside-down peaks. An especially well-studied instance of this feature appears in the electronic spectrum of helium as a transient state undergone delayed ionization. Two studies have now traced the dynamics of this state in real time. Gruson et al. used photoelectron spectroscopy to extract the amplitude and phase of the electron wave packet after inducing its interference with reference wave packets tuned into resonance at variable delays. Kaldun et al. used extreme ultraviolet absorption spectroscopy to probe the transient state while variably forcing ionization with a strong near-infrared field. —JSY

Science, this issue pp. 734 and 738

INFLUENZA EPIDEMIOLOGY

Lifelong protection against severe influenza

The first influenza attack that a child suffers can affect the way that their lifelong immunity to the virus builds up. A wide range of influenza A virus subtypes infect humans. Subtype H5 belongs to HA group 1 (which also includes H1 and H2 subtypes), and subtype H7 belongs to HA group 2 (which also includes the H3 subtype). Gostic et al. found that birth-year cohorts that experienced first infections with seasonal H3 subtype viruses were less susceptible to the potentially fatal avian influenza H7N9 virus (see the Perspective by Viboud and Epstein). Conversely, older individuals who were exposed to H1 or H2 subtype viruses as youngsters were less susceptible to avian H5N1-bearing viruses. A mathematical model of the protective effect of this imprinting could potentially prove useful to predict the age distribution and severity of future pandemics. —CA

Science, this issue p. 722; see also p. 706

EMERGING INFECTIONS

Global spread of aggressive mycobacteria

Many mycobacteria, in addition to those causing leprosy and tuberculosis, are capable of infecting humans. Some can be particularly dangerous in patients suffering from immunosuppression or chronic disease, such as cystic fibrosis (CF). Bryant et al. observed clusters of near-identical isolates of drug-resistant Mycobacterium abscessus in patients reporting to CF clinics. The similarity of the isolates suggests transmission between patients, rather than environmental acquisition. Although this bacterium is renowned for its environmental resilience, the mechanism for its long-distance transmission among the global CF patient community remains a puzzle. —CA

Science, this issue p. 751

CATALYSIS

Biological inspiration for reduction

Microorganisms have evolved sophisticated enzymatic machinery to reduce perchlorate and nitrate ions. Although the energetics of the pathways are different, the heme-containing active sites of the corresponding reductase enzymes are remarkably similar. Ford et al. constructed an inorganic catalyst to mediate these reactions based on these active sites, using a nonheme iron complex. A secondary coordination sphere near the iron center aligned the nitrate or perchlorate oxyanions and formed an iron-oxo complex. Regenerating the catalyst in the presence of protons and electrons released water—a potentially much more sustainable process than reduction strategies that require the use of harsh reagents. —NW

Science, this issue p. 741

ENHANCER FUNCTION

CRISPR screens illuminate enhancer function

The noncoding regions around a gene that control the transcription of the protein-coding region are difficult to identify. Leveraging a CRISPR interference system (CRISPRi), Fulco et al. identified enhancer-promoter connections to map specific noncoding regions affecting gene regulation for the GATA1 and MYC loci (see the Perspective by Einstein and Yeo). Going forward, such CRISPRi-mapping can be used to evaluate promoter-enhancer screens functionally in an unbiased way. —LMZ

Science, this issue p. 769; see also p. 705