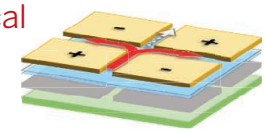
RESEARCH

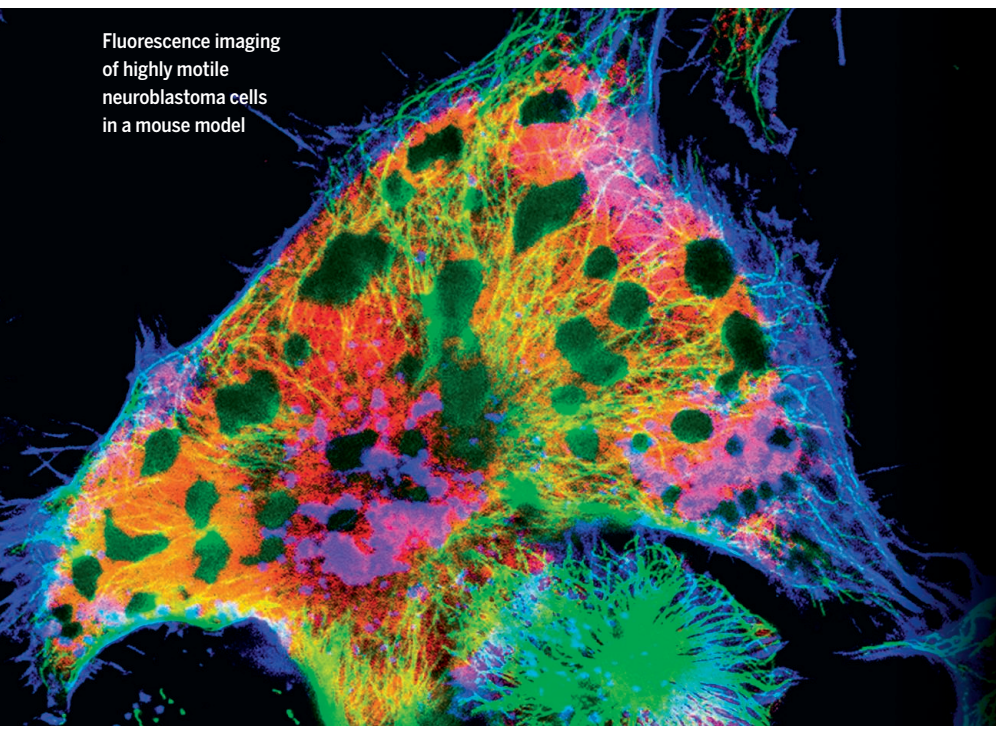
Progress toward practical valleytronic devices

Li et al., *p. 1149*



IN *SCIENCE* JOURNALS

Edited by **Stella Hurtley**



Fluorescence imaging of highly motile neuroblastoma cells in a mouse model

CANCER

A systematic look at a childhood tumor

Neuroblastomas—the most common tumor type in infants—develop from fetal nerve cells, and their clinical course is highly variable. Some neuroblastomas are fatal despite treatment, whereas others respond well to treatment and some undergo spontaneous regression without treatment. Ackermann *et al.* sequenced more than 400 pretreatment neuroblastomas and identified molecular features that characterize the three distinct clinical outcomes. Low-risk tumors lack telomere maintenance mechanisms, intermediate-risk tumors harbor telomere maintenance mechanisms, and high-risk tumors harbor telomere maintenance mechanisms in combination with RAS and/or p53 pathway mutations. —PAK

Science, this issue p. 1165

MICROBIOLOGY

Actively persistent *Salmonella*

A proportion of *Salmonella* cells can enter a reversible state of growth arrest, which allows them to tolerate environmental stress such as antibiotics. Stapels *et al*. found that these cells are not dormant but are actively modulating their environment. *Salmonella* within their host macrophage niche deployed a specialized type 3 secretory system called SPI-2 to deliver virulence factors, including SteE, into host cells. SteE changed the cytokine profile of the infected macrophages to reprogram them into a noninflammatory and infection-permissive state. Thus, when antibiotics were removed, the *Salmonella* could reemerge and cause disease. —CA

Science, this issue p. 1156

HUMAN GENETICS

Genetic architecture of developmental disorders

The genetics of developmental disorders (DDs) is complex. Martin *et al*. wanted to determine the degree of recessive inheritance of DDs in protein-coding genes. They examined the exomes of more than 6000 families in populations with high and low proportions of consanguineous marriages. They found that 3.6% of DDs in individuals of European ancestry involved recessive coding disorders, less than a tenth of the levels previously estimated. Furthermore, among South Asians with high parental relatedness, rather than most of the disorders arising from inherited variants, fewer than half had a recessive coding diagnosis. —LMZ

Science, this issue p. 1161

MOLECULAR BIOLOGY

DNA methylation promotes transcription

DNA methylation generally represses transcription, but in some instances, it has also been implicated in transcription activation. Harris *et al*. identified a protein complex in *Arabidopsis* that is recruited to chromatin by DNA methylation. This complex specifically activated the transcription of genes that are already mildly transcribed but had no effect on transcriptionally silent genes such as transposable elements. The complex thereby counteracts the repression effect caused by transposon insertion in neighboring genes while leaving transposons silent. Thus, by balancing both repressive and activating transcriptional effects, DNA methylation can act to fine-tune gene expression. —SYM

Science, this issue p. 1182

MATERIALS SCIENCE

Tunable materials respond to magnetic field

Although certain four-dimensional (4D) printed materials can respond to external stimuli, these are hard to control or

IMAGES (TOP TO BOTTOM): LI *ET AL.*; VSHYUKOVA/SCIENCE SOURCE

Published by AAAS

feature long response times. Jackson *et al.* created tunable materials that can respond to an applied magnetic field by incorporating liquids that contain ferromagnetic microparticles into 3D-printed polymer tubes. In tests, these structures responded to a magnetic field in under a second. The approach could see broad applications in fields that include soft robotics, transportation systems, and smart wearable technology. —PJB

Sci. Adv. 10.1126/sciadv.aau6419 (2018).

IMMUNOLOGY

Optimal affinity

Germinal center (GC) B cells are essential to generating protective antibody responses and are selected through a process of affinity maturation. Kwak *et al*. now define intrinsic properties of human GC B cells that are critical to antigen affinity discrimination. They identified B cell antigen receptor–containing actin-rich pod-like structures that facilitated formation of highly stable immunological synapses and antigen internalization when GC B cells engaged high-affinity antigens. These structures were important in setting thresholds for affinity selection and driving GC B cell responses. —CNF

Sci. Immunol. **3**, eaau6598 (2018).

COMPUTER SCIENCE

One program to rule them all

Computers can beat humans at increasingly complex games, including chess and Go. However, these programs are typically constructed for a particular game, exploiting its properties, such as the symmetries of the board on which it is played. Silver *et al*. developed a program called AlphaZero, which taught itself to play Go, chess, and shogi (a Japanese version of chess) (see the Editorial, and the Perspective by Campbell). AlphaZero managed to beat state-of-the-art programs specializing in these three games. The ability of AlphaZero to adapt to various game rules is a notable step toward achieving a general game-playing system. —JS

Science, this issue p. 1140; see also pp. 1087 and 1118

BATTERIES

Working toward fluoride batteries

Owing to the low atomic weight of fluorine, rechargeable fluoride-based batteries could offer very high energy density. However, current batteries need to operate at high temperatures that are required for the molten salt electrolytes. Davis *et al*. push toward batteries that can operate at room temperature, through two advances. One is the development of a room-temperature liquid electrolyte based on a stable tetraalkylammonium salt–fluorinated ether combination. The second is a copper–lanthanum trifluoride core-shell cathode material that demonstrates reversible partial fluorination and defluorination reactions. —MSL

Science, this issue p. 1144

QUANTUM MATERIALS

Twisting a route for surface plasmons

Graphene is an atomically thin material that supports highly confined plasmon polaritons, or nano-light, with very low loss. The properties of graphene can be made richer by introducing and then rotating a second layer so that there is a slight angle between the atomic registry. Sunku *et al*. show that the moiré patterns that result from such twisted bilayer graphene also provide confined conducting channels that can be used for the directed propagation of surface plasmons. Controlling the structure thereby provides a pathway to control and route surface plasmons for a nanophotonic platform. —ISO

Science, this issue p. 1153

IN OTHER JOURNALS

Edited by **Caroline Ash** *and* **Jesse Smith**

Fire feedback explains the Miocene expansion of the grassland biome.

PALEOECOLOGY

Fire and grassland evolution

Global grassland underwent a massive expansion in the late Miocene epoch, 5 million to 8 million years ago. Karp *et al.* examined the role of fire in this expansion, through measurements of fire-derived hydrocarbons and grass-diagnostic carbon isotopes in sediments in Pakistan. They found evidence of a simultaneous increase in seasonality of precipitation and the occurrence of regular fire along with the opening of the landscape and the expansion of grasslands. Their results indicate that a grassland-fire feedback system was a key driver in the expansion of grasslands, a relationship that has remained an integral feature of this ecosystem ever since. —AMS

Proc. Natl. Acad. Sci. U.S.A. **115**, 12130 (2018).

NEUROSCIENCE

Inhibition in the fear-learning circuitry

Many mental health disorders can be traced to abnormal associative learning. The basolateral amygdala of the brain plays a central role in associative learning and the formation of emotional memories and motivated behaviors. The relevance of the amygdala's anatomical substructure for the acquisition of memories is less clear. Tipps *et al*. used neuron-specific chemogenetics to systematically probe the circuitry and signaling mechanisms involved in auditory fear learning in mice. Stimulating inhibitory interneurons or inhibiting pyramidal cells was enough to induce an association between a behavior and an auditory cue. This understanding is key to developing

PHOTO: RICHARD DU TOIT/MINDEN PICTURES/GETTY IMAGES

ALSO IN *SCIENCE* JOURNALS

Edited by **Stella Hurtley**

CARBON CYCLE

Animals count

Flux across the carbon cycle is generally characterized by contributions from plants, microbes, and abiotic systems. Animals, however, move vast amounts of carbon, both through ecosystem webs and across the landscape. Schmitz *et al*. review the different contributions that animal populations make to carbon cycling and discuss approaches that allow for better monitoring of these contributions. —SNV

Science, this issue p. 1127

HUMAN GENOMICS

Complex processes in the settling of the Americas

The expansion into the Americas by the ancestors of present day Native Americans has been difficult to tease apart from analyses of present day populations. To understand how humans diverged and spread across North and South America, Moreno-Mayar *et al*. sequenced 15 ancient human genomes from Alaska to Patagonia. Analysis of the oldest genomes suggests that there was an early split within Beringian populations, giving rise to the Northern and Southern lineages. Because population history cannot be explained by simple models or patterns of dispersal, it seems that people moved out of Beringia and across the continents in a complex manner. —LMZ

Science, this issue p. 1128

ANTIMALARIALS

A path to tackle liver-stage parasites

Malaria parasites are evolutionarily prepared to resist drug attack. Resistance is emerging to even the latest frontline combination therapies, which target the blood stages of the *Plasmodium* parasite. As an alternative strategy, Antonova-Koch *et al*. investigated the possibilities of drugs against liver-stage parasites (see the Perspective by Phillips and Goldberg). To do so, they devised a luciferase-reporter drug screen for the rodent parasite *Plasmodium berghei*. Three rounds of increasingly stringent screening were used. From this regime, several chemotypes that inhibit *Plasmodium* mitochondrial electron transport were identified. Excitingly, several new scaffolds, with as-yet-unknown modes of action but solely targeting the parasites' liver stages, emerged as promising drug leads for further development. —CA

Science, this issue p. 1129; see also p. 1112

NANOMATERIALS

No barriers to growing a row

Classical nucleation theory predicts that two-dimensional islands on a surface must reach a critical size before they continue to grow; below that size, they dissolve. Chen *et al*. used phage display to select for short peptides that would bind to molybdenum disulfide (MoS_2) (see the Perspective by Kahr and Ward). Hexagonal arrays of these peptides grew epitaxially as dimers but without a size barrier—the critical nuclei size was zero. Although two-dimensional arrays formed, growth occurred one row at time. Classical nucleation theory indeed predicts the absence of a barrier for such one-dimensional growth. —PDS

Science, this issue p. 1135; see also p. 1111

CLIMATE IMPACTS

Drivers of the "Great Dying"

Though our current extinction crisis is substantial, it pales in comparison to the largest extinction in Earth's history, which occurred at the end of the Permian Period. Referred to as the "Great Dying," this event saw the loss of up to 96% of all marine species and 70% of terrestrial species. Penn *et al*. explored the extinction dynamics of the time using Earth system models in conjunction with physiological data across animal taxa (see the Perspective by Kump). They conclude that increased marine temperatures and reduced oxygen availability were responsible for a majority of the recorded extinctions. Because similar environmental alterations are predicted outcomes of current climate change, we would be wise to take note. —SNV

Science, this issue p. 1130; see also p. 1113

POLYMERS

Beating the heat by blending

Charge carriers move through semiconductor polymers by hopping transport. In principle, these polymers should be more conductive at higher temperatures. In practice, conductivity drops at high temperatures because interchain contacts are disrupted, which limits potential applications. Gumyusenge *et al*. now show that appropriate blending of a semicrystalline conjugated polymer with an insulating polymer that has a high glass-transition temperature creates a morphology that stabilizes a network of semiconductor channels. High charge conductivity was maintained in these materials up to 220°C. —PDS

Science, this issue p. 1131

VALLEYTRONICS

Making a practical valleytronics device

Two-dimensional materials with a hexagonal lattice, such as graphene, have two distinct "valleys" in their band structure. Researchers in the emerging field of valleytronics hope that these valley degrees of freedom can be exploited as information carriers, but making valleytronic devices is tricky. Li *et al*. created chiral valley Hall states on the boundary between oppositely gated regions of bilayer graphene. They then guided these so-called kink states through their sample using spatially modulated gating, demonstrating right and left turns, as well as a valley valve function. —JS

Science, this issue p. 1149

BIOPHYSICS

How membrane viscosity affects respiration

In bacteria, energy production by the electron transport chain occurs at cell membranes and can be influenced by the lipid composition of the membrane. Budin *et al*. used genetic engineering to influence the concentration of unsaturated branched-chain fatty acids and thus control membrane viscosity (see the Perspective by Schon). Experimental measurements and mathematical modeling indicated that rates of respiratory metabolism and rates of cell growth were dependent on membrane viscosity and its effects on diffusion. Experiments on yeast mitochondria also showed similar effects. Maintaining efficient respiration may thus place evolutionary constraints on cellular lipid composition. —LBR

Science, this issue p. 1186; see also p. 1114

REGENERATION

Do endothelial cells hold the key to success?

Endothelial cells line the inner vascular wall, and their phenotype and behavior can vary according to the organ in which they are situated and

the environment. Not only do endothelial cells form the barrier of vessel walls, they also can participate in signaling with the surrounding tissue to promote regeneration and growth. In a Perspective, Gomez-Salinero and Rafii discuss how endothelial cells contribute to wound healing, regeneration, and disease states, such as cancer, and how our growing understanding of endothelial cell plasticity might advance regenerative medicine and the development of artificial organs for transplant. —GKA

Science, this issue p. 1116

SIGNAL TRANSDUCTION

Regulation of RAS by ubiquitination

The protein LZTR1 is mutated in human cancers and developmental diseases. Work from two groups now converge to implicate the protein in regulating signaling by the small guanosine triphosphatase RAS. Steklov *et al*. showed that mice haploinsufficient for LZTR1 recapitulated aspects of the human disease Noonan syndrome. Their biochemical studies showed that LZTR1 associated with RAS. LZTR1 appears to function as an adaptor that promotes ubiquitination of RAS, thus inhibiting its signaling functions. Bigenzahn *et al*. found LZTR1 in a screen for proteins whose absence led to resistance to the tyrosine kinase inhibitors used to treat cancers caused by the BCR-ABL oncogene product. Their biochemical studies and genetic studies in fruitflies also showed that loss of LZTR1 led to increased activity of RAS and signaling through the mitogen-activated protein kinase pathway. —LBR

Science, this issue p. 1177, p. 1171

CANCER

Expanding the landscape of immunotherapy targets

Most searches for druggable tumor-specific antigens (TSAs) start with an examination of peptides derived from protein-coding exons. Laumont *et al*. took a different approach and found numerous TSAs that derived from aberrant expression of noncoding sequences in murine cell lines and in B-lineage acute lymphoblastic leukemia and lung cancer patient samples. They validated the immunogenicity and efficacy of TSA vaccination for select antigens in mouse models of cancer. Noncoding regions are a potentially rich source of TSAs that could greatly expand the number of targetable antigens across different cancers, including those with low mutational burdens. —CAC

Sci. Transl. Med. **10**, eaau5516 (2018).

CELL BIOLOGY

Cleaving a different function for p62

The scaffold protein p62 has a critical role in autophagy, the regulated intracellular degradation of proteins and organelles. Sanchez-Garrido *et al*. identified a proteolytic fragment of human p62, called p62^{TRM}, that had a distinct function from full-length p62 (see the Focus by Martens). Instead of promoting autophagy, p62^{TRM} regulated responses to nutrient availability. This function was lost in p62 variants with disease-associated mutations in the cleavage site, suggesting that defective nutrient sensing may account for some of the symptoms of patients with p62 mutations. —WW

Sci. Signal. **11**, eaat6903, eaav3530 (2018).