RESEARCH

IN *SCIENCE* JOURNALS

Edited by **Michael Funk**

NEUROSCIENCE

Threat detection starts in the eyes

When a mouse sees something that quickly becomes larger in its visual field, perhaps indicating an attacking predator, it runs. Kim *et al*. identified a small group of neurons in the mouse retina that selectively respond to such looming visual stimuli and are required for innate defensive behaviors in response. These neurons perform this specific computation by integrating inputs from nearby neurons in a selective manner. Thus, neural circuits within the eyes, even before the information reaches the brain, perform specific computations to mediate innate, evolutionarily conserved behaviors. —TK

Sci. Adv. 10.1126/sciadv.abc9920 (2020).

Neural circuits in the retina help mice and other animals detect looming threats, such as a lunging predator.

ANTIBIOTIC RESISTANCE

PBT2 pumps up polymyxins

Bacterial resistance to antibiotics is a growing worldwide problem, and *Enterobacterales* with resistance to the polymyxin class of antibiotics are a critical threat. De Oliveira *et al*. repurposed a hydroxyquinoline compound called PBT2, currently in phase 2 clinical trials for neurodegenerative diseases, to break polymyxin antibiotic resistance in four different Gram-negative pathogens, including *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. In vitro, treatment with PBT2 disrupted the abundance of zinc and iron in the resistant bacteria, whereas in immunocompetent septic mice, PBT2 combined with polymyxins resulted in improved survival with reduced bacterial dissemination. These findings, although exciting, need to be confirmed in humans. —MN

Sci. Transl. Med. **12**, eabb3791 (2020).

DEVELOPMENTAL BIOLOGY

Functional screen for microcephaly genes

Genetic screens are widely used to identify regulators in biological processes. Human screens are currently limited to two-dimensional cell cultures, which lack the ability to score tissue-dependent gene function. Esk *et al*. combined CRISPR-Cas9 screening with barcoded cellular lineage tracing to enable loss-of-function screening in three-dimensional human cerebral organoid tissue. By testing microcephaly candidate genes, the endoplasmic reticulum was found to control extracellular matrix protein secretion regulating tissue integrity and brain size. This genetic screen in human brain tissue implicates multiple pathways in microcephaly and provides a tool for systematic testing of genes in organoids. —BAP

Science, this issue p. 935

WATER PHASES

Liquid-liquid transitions under pressure

Theoretical simulations suggest that deeply supercooled water undergoes a transition between high- and low-density forms, but this transition is difficult to study experimentally because it occurs under conditions in which ice crystallization is extremely rapid. Kim *et al*. combined x-ray lasers for rapid structure determination with infrared femtosecond pulses for rapid heating of amorphous ice layers formed at about 200 kelvin. The heating process created high-density liquid water at increased pressures. As the layer expanded and decompressed, low-density liquid domains appeared and grew on time scales between 20 nanoseconds and 3 microseconds, which was much faster than competing ice crystallization. —PDS

Science, this issue p. 978

PHOTO: IMAGE SOURCE/GETTY IMAGES

STELLAR ASTROPHYSICS

A relic star cluster under the floor

Globular clusters (GCs) are gravitationally bound assemblies of thousands to millions of stars that orbit in the outskirts of large galaxies. GCs consist of old stars with low metallicity containing low proportions of chemical elements heavier than hydrogen and helium. However, GCs appear to have a minimum metallicity, known as the floor, implying that at least some of those elements were required for their formation. Larsen *et al*. have found a GC in the nearby Andromeda Galaxy with a metallicity beneath the floor. This unexpected discovery will inform models of GC formation and incorporation into galaxies. —KTS

Science, this issue p. 970

ZIKA VIRUS

Domesticating Zika virus

Why hasn't Zika virus (ZIKV) disease caused as much devastation in Africa, its continent of origin, as it has in the Americas? Outside of Africa, this flavivirus is transmitted by a ubiquitous mosquito subspecies, *Aedes aegypti aegypti*, which emerged from the African forerunner subspecies *A. aegypti formosus* and acquired a preference for human blood and a peridomestic lifestyle. Now, this subspecies colonizes many intertropical cities, aided by climate change and human trash. Aubry *et al*. tested 14 laboratory mosquito colonies for their relative susceptibility to ZIKV. Quantitative trait locus mapping showed differences on chromosome 2 between mosquitoes from Gabon and Guadeloupe. Mouse infection experiments revealed that African mosquitoes transmitted a smaller virus inoculum than the South American insects. Increased susceptibility coupled with the ability of *A. aegypti aegypti* to breed in any discarded object containing water has amplified the problematic nature of this virus as it has circumnavigated the world. —CA

Science, this issue p. 991

A feeding female *Aedes aegypti* mosquito, the primary species that transmits Zika virus

PHOTOS: B. G. THOMSON/SCIENCE SOURCE; NOKURO/ALAMY STOCK PHOTO

CORONAVIRUS

A strong cocktail against SARS-CoV-2

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is initiated by the trimeric spike protein that decorates the virus and binds the ACE2 receptor. Antibodies against the spike that neutralize viral infection have potential as therapeutics. Tortorici *et al*. describe two very potent antibodies, S2E12 and S2M11. Electron microscopy structures characterized the binding and showed that S2E12 traps the spike in a conformation that cannot bind ACE2. Both antibodies protected hamsters against SARS-CoV-2 challenge and may be useful in antibody cocktails to combat the virus and prevent the development of resistance. —VV

Science, this issue p. 950

GEOPHYSICS

Finding the Emperor's head

Volcanic island and seamount chains form from deep-seated plumes of hot material upwelling through the mantle. The most famous of these is the Hawaiian-Emperor seamount chain. However, a large volcanic structure associated with a plume head that should precede the chain has long been missing. Wei *et al*. finally identified the likely location of this structure in the mantle under eastern Russia. The structure was likely subducted 20 million to 30 million years ago, and the location helps constrain several geodynamic processes. —BG

Science, this issue p. 983

IN OTHER JOURNALS

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

LIGHT POLLUTION

Too bright to breed

Most coral species reproduce through broadcast spawning. For such a strategy to be successful, coordination has had to evolve such that gametes across clones are released simultaneously. Over millennia, lunar cycles have facilitated this coordination, but the recent development of bright artificial light has led to an overpowering of these natural signals. Ayalon *et al*. tested for the direct impact of different kinds of artificial light on different species of corals. The authors found that multiple lighting types, including cold and warm light-emitting diode (LED) lamps, led to loss of synchrony and spawning failure. Further, coastal maps of artificial lighting globally suggest that it threatens to interfere with coral reproduction worldwide and that the deployment of LED lights, the blue light of which penetrates deeper into the water column, is likely to make the situation even worse. —SNV

Curr. Biol. 10.1016/j.cub.2020.10.039 (2020).

Night light from coastal cities overpowers natural signals for coral spawning from neighboring reefs.

SIGNAL TRANSDUCTION

How RAS mutations really work

Mutations in the small guanosine triphosphatase RAS occur in many human tumors and are thought to act by activating the mitogen-activated protein kinase (MAPK, also called ERK) signaling pathway. Gillies *et al*. used imaging of live single cells to measure MAPK activity in cells expressing a single wild-type or mutant isoform of human RAS. The dynamic range of the signaling pathway and its growth factor responsiveness were surprisingly

ALSO IN *SCIENCE* JOURNALS

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CORONAVIRUS

Tackling other infectious diseases

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has pushed drug discovery and clinical testing to a pace previously considered impossible. In a Perspective, Gupta discusses how the structure of drug development for coronavirus disease 2019 (COVID-19) can be implemented to treat other infectious diseases that kill millions globally each year. By focusing research, implementing operational efficiencies, and ensuring large-scale financing, the author suggests that extensive drug development pipelines can be built to tackle other severe infections. —GKA

Science, this issue p. 913

FIRE ECOLOGY

Fire's growing impacts on ecosystems

Fire has played a prominent role in the evolution of biodiversity and is a natural factor shaping many ecological communities. However, the incidence of fire has been exacerbated by human activity, and this is now affecting ecosystems and habitats that have never been fire prone or fire adapted. Kelly *et al*. review how such changes are already threatening species with extinction and transforming terrestrial ecosystems and discuss the trends causing changes in fire regimes. They also consider actions that could be taken by conservationists and policy-makers to help sustain biodiversity in a time of changing fire activity. —AMS

Science, this issue p. 929

VIROLOGY

Riding the calcium waves

Rotavirus causes severe diarrhea and vomiting in children worldwide, yet how infection causes these diseases remains poorly understood. A leading theory is that virus-infected cells secrete paracrine signaling molecules that dysregulate epithelial cells. Chang-Graham *et al*. found that rotavirus-infected cells trigger cell-to-cell signaling that manifests as intercellular calcium waves (see the Perspective by Stanifer and Boulant). This signal results from the repeated release of adenosine 5′-diphosphate by rotavirus-infected cells. This release activates receptors on nearby uninfected cells, resulting in a calcium signal. The intercellular calcium waves activate chloride and serotonin secretion, which contributes to diarrhea and vomiting. Blocking this paracrine signal could represent a target for antidiarrheal pharmacotherapy. —SMH

Science, this issue p. 930; see also p. 909

PHOTOSYNTHESIS

Green to the core

Light from the Sun powers most life on today's Earth in some way. The core of the photosynthetic apparatus where charge separation occurs, the reaction center (RC), is thought to have originated a single time and diverged, yielding new kinds of complexes adapted to different tasks and environments. Chen *et al*. now present an important missing puzzle piece in our understanding of the evolution of RCs: a cryo–electron microscopy structure of the homodimeric type I RC from a green sulfur bacterium bound to a light-harvesting protein. The observed cofactor and pigment arrangement explain biochemical features of this RC and will aid in our understanding of how a single ancestral RC gave rise to the range of structures and functions seen in RCs today. —MAF

Science, this issue p. 931

NEURODEGENERATION

Two ways to get tangled?

Neurodegeneration in Alzheimer's disease dementia is associated with neurofibrillary tangles composed of aggregated tau protein. Darwich *et al*. describe an additional form of autosomal-dominant dementia with neurofibrillary tangles linked to a hypomorph mutation in valosin-containing protein (VCP). VCP was found to disaggregate pathologic tau, and the hypomorph mutation increased tau accumulation in cells and mice. These findings highlight the role of protein turnover in maintaining neuronal health and suggest that VCP may provide a therapeutic target for Alzheimer's disease. —SMH

Science, this issue p. 932

WILDLIFE DISEASE

Climate change alters disease risks

Climate change appears to be provoking changes in the patterns and intensity of infectious diseases. For example, when conditions are cool, amphibians from warm climates experience greater burdens of infection by chytrid fungus than hosts from cool regions. Cohen *et al*. undertook a global metanalysis of 383 studies to test whether this "thermal mismatch" hypothesis holds true over the gamut of host-pathogen relationships. The authors combined date and location data with a selection of host and parasite traits and weather data. In the resulting model, fungal disease risk increased sharply under cold abnormalities in warm climates, whereas bacterial disease prevalence increased sharply under warm abnormalities in cool climates. Warming is projected to benefit helminths more than other parasites, and viral infections showed less obvious relationships with climate change. —CA

Science, this issue p. 933

NEURODEVELOPMENT

Unlocking retinal regeneration in mice

Zebrafish can regenerate damaged retinal tissue, but mice cannot. Hoang *et al*. found that tracking changes in gene expression and chromatin accessibility upon injury revealed clues as to why retinal glial cells in zebrafish could generate new neurons but the same cell type in mice could not. In zebrafish, activated Müller glial cells shift into a proliferative phase, whereas in mice, a genetic network returns the glial cells to quiescence. A few transcription factors enforce quiescence in the mouse, and disruption of these allowed Müller glia to proliferate and generate new neurons after retinal injury. —PJH

Science, this issue p. 934

DEVELOPMENTAL BIOLOGY

Cells and the path of least resistance

For processes encompassing proper embryonic development, adult homeostasis, tumor cell dissemination, and immunity, certain cells must translocate from their site of origin. Migrating cells navigate physical features of their microenvironment; however, the in vivo importance of tissue topography for pathfinding is mostly unknown. Studying fruit flies, Dai *et al*. used border cells within the ovarian egg chamber to study path selection. Live imaging, genetics, mathematical modeling, and simulations showed that tissue microtopography provides an energetically favorable path of least resistance, whereas chemoattractants supply orthogonal guidance information and cell-cell adhesion contributes traction. The results provide insight into how cells integrate and prioritize topographical, adhesive, and chemoattractant cues to choose one path among many. —BAP

Science, this issue p. 987

IMMUNOLOGY

Maternal IgE activates fetal mast cells

Mast cells (MCs) are immune cells that participate in allergic reactions through their activation by immunoglobulin E (IgE) antibodies. MCs arise early during mammalian development, but it is unclear whether IgE-mediated activation occurs in fetal tissues and what the source of IgE stimulation is. Msallam *et al*. show that human and mouse fetal MCs can be sensitized by IgE of maternal origin, which crosses the placental barrier through the fetal neonatal Fc receptor (see the Perspective by Rothenberg). Prenatal maternal sensitization conferred transient allergen sensitivity after birth and resulted in the development of postnatal skin and airway inflammation in the offspring after their first exposure to allergen. Thus, both maternal IgE and fetal MCs may influence mother-to-child transmission of allergic disease during gestation. —PNK

Science, this issue p. 941; see also p. 907

MATERIALS SCIENCE

Feeling temperature and touch

The range of receptors in our skin make it possible to sense when we are touching an object and also gives us a general sense of the temperature of that object. Achieving this in an artificial skin-like material has been a challenge because most of the approaches for sensing touch are themselves temperature sensitive. You *et al*. studied the ion relaxation dynamics in a conductive elastomeric film (see the Perspective by Liu). They show that the ion relaxation time can be used as a strain-insensitive intrinsic variable for detecting temperature and the capacitance can be used as a temperature-insensitive extrinsic variable for sensing the strain, thus decoupling the two so that their signals do not interfere with each other. —MSL

Science, this issue p. 961; see also p. 910

MATERIALS SCIENCE

A soft touch

Measuring the force it takes for a hand to grasp an object requires sensors to be placed on the fingertips, but these sensors will interfere with or affect how much force ends up being applied. Lee *et al*. developed a nanomesh sensor built from a series of electrospun materials (see the Perspective by Liu). Using a robotic tester, they show that this device can repeatably detect the pressure involved in gripping an object. They also show that the sensors can be attached to human fingers and that this does not affect the force used to grasp an object. —MSL

Science, this issue p. 966; see also p. 910

SURFACE SCIENCE

Telegraphing molecules

Scanning tunneling microscope (STM) tips have long been used to manipulate atoms and molecules through direct interactions. Civita *et al*. now show that at cryogenic temperatures, the bias voltage from an STM tip can propel a large organic molecule, dibromoterfluorene, long distances—tens of nanometers along straight tracks on the flat silver (111) surface (see the Perspective by Esch and Lechner). This electrostatic effect requires the molecule to be oriented along the track, and derivatives lacking bromide groups would change direction. In a dual-tip setup, changing the bias voltage sent and received molecules between two specific points about 60 nanometers apart. —PDS

Science, this issue p. 957; see also p. 912

ANTIFUNGAL DISCOVERY

Prospecting for antifungal molecules

Marine bacteria produce a plethora of natural products that often have unusual chemical structures and corresponding reactivity, which sometimes translate into a valuable biological function. Zhang *et al*. used a metabolomic screen to zero in on microbial strains from the microbiome of a sea squirt that produces a high diversity of chemical structures. They then screened these molecules for inhibition of fungi (see the Perspective by Cowen). A polycyclic molecule dubbed turbinmicin possessed potent antifungal activity against the multidrug-resistant fungal pathogens *Candida auris* and *Aspergillus fumigatus*. Preliminary mechanism-of-action and mouse toxicity studies suggest that this molecule works though a fungus-specific pathway and is well tolerated at therapeutic doses. —MAF

Science, this issue p. 974; see also p. 906

CANCER THERAPY

Unmasking sensitivity to chemotherapy

Although the activity of the epidermal growth factor receptor (EGFR) pathway is increased in triple-negative breast cancers (TNBCs), these tumors are generally insensitive to EGFR inhibitors. Cruz-Gordillo *et al*. found that insensitivity to the EGFR inhibitor erlotinib was due to the prosurvival protein Mcl-1. *MCL1* expression in TNBC cells was promoted by the ELP family of transcription-elongation regulators, particularly ELP4. These findings suggest that combining erlotinib with an Mcl-1 inhibitor might be effective in TNBC patients. —LKF

Sci. Signal. **13**, eabb9820 (2020).

DENDRITIC CELLS

Distinct dendritic cell responses

Dendritic cells (DCs) are critical for activating naïve T cells by presenting antigens and providing costimulation, processes that are enhanced by cytokine signals from the surrounding environment. Girard *et al*. used single-cell proteogenomics and flow cytometry to examine cell type–specific responses of human peripheral blood monocyte and DC subsets to type I interferon. Interferon-β induced maturation of the recently identified $CD1c^{+}$ $CD5^{-}$ DC3 subset, which was characterized by distinct expression of the costimulatory molecule GITRL, a tumor necrosis factor family ligand, and driven by nuclear factor κB signaling. These results identify conserved and cell type–specific features of the type I interferon response of human mononuclear phagocyte subsets, including the molecular signals that monocytes and DCs may leverage to instruct T cells. —CO

Sci. Immunol. **5**, eabe0347 (2020).