

RESEARCH

IN SCIENCE JOURNALS

Edited by Michael Funk

EVOLUTIONARY BIOLOGY

Thriving in the benthic zone

Lobsters are among the most successfully adapted organisms of marine benthic ecosystems. Despite lacking an adaptive immune response, lobsters display a long life-span of up to 100 years. To help uncover the secret of their longevity, Polinski *et al.* sequenced the American lobster genome and identified genome-wide innovations in genes

related to chemosensory machinery, innate immunity, and cellular defense. These include a new class of chimeric receptors with the potential to integrate neuronal and immune sensory systems. The results provide insights on the mechanisms mediating the ecological success of this benthic predator. —DGL
Sci. Adv. 10.1126/sciadv.abe8290 (2021).

The genome of the American lobster has uncovered distinctive adaptations in this benthic invertebrate.

SUPERCONDUCTIVITY

Imaging an exotic state

Among the most intriguing of the many phases of cuprate superconductors is the so-called pair density wave (PDW) state. PDW is characterized by a spatially modulated density of Cooper pairs and can be detected with a scanning tunneling microscope equipped with a superconducting tip. Liu *et al.* used Josephson tunneling microscopy, modified for the task, to detect PDW in niobium diselenide, a superconductor with a layered hexagonal structure. The PDW state is expected to appear in other transition metal dichalcogenides as well. —JS
Science, abd4607, this issue p. 1447

EPIGENETICS

Methyl readers that repress transcription

DNA methylation is a conserved epigenetic mark required for gene silencing in many different organisms. However, how the methyl mark is able to silence genes is still largely unknown. Ichino *et al.* discovered two *Arabidopsis* proteins named MBD5 and MBD6 that are recruited to DNA by direct recognition of methylation. These methyl readers recruit the class C J-domain protein SILENZIO to chromatin to silence methylated genes and transposons. SILENZIO likely acts through

its interaction with heat shock chaperone proteins. —DJ
Science, abg6130, this issue p. 1434

ORGANIC CHEMISTRY

Easing oxygen into arenes

Although oxygen is all around us, it is often surprisingly difficult to use it for selective chemical oxidations, necessitating more expensive, wasteful alternatives. Li *et al.* report that careful ligand optimization produces palladium catalysts that can efficiently activate oxygen to hydroxylate a variety of aryl and heteroaromatic rings adjacent to a carboxylic acid substituent. The ligand binds to palladium through pyridine and

pyridone components, and the authors posit that tautomerization between dative and anionic coordination modes plays a role in its effectiveness. —JSY
Science, abg2362, this issue p. 1452

T CELLS

Rewiring aged T cells

Age-associated decline in T cell function contributes to impaired immune responses to infection and vaccination. Effector versus memory T cell differentiation is controlled in part by signaling and metabolic reprogramming mediated by mechanistic target of rapamycin complex 1 (mTORC1), which is typically activated at amino acid-producing

lysosomes. Jin *et al.* demonstrate that in naïve CD4⁺ T cells from older individuals, mTORC1 activation instead occurs at late endosomes and depends on the amino acid transporter SLC7A5. Late endosomal mTORC1 impairs T cell lysosomal function, reducing the degradation of PD-1 and proliferative responses. Silencing VPS39, a gene that promotes late endosome formation, was able to increase the proliferation of aged human T cells and memory responses of lysosome-defective T cells in a mouse viral infection model, demonstrating that targeting late endosomal mTORC1 activity may improve T cell function. —CO

Sci. Immunol. **6**, eabg0791 (2021).

CATALYSIS

Rhodium atoms for alkane dehydrogenation

Nanoparticles of rhodium dispersed on metal oxides are generally poor catalysts for alkane dehydrogenation because the reactants bind too strongly to the metal. Hannagan *et al.* performed first-principle calculations indicating that single rhodium atoms in a copper surface should be stable and selective for conversion of propane to propene and hydrogen. Model studies of single rhodium atoms embedded in a copper (111) surface revealed a very high selectivity to propene



An artist's rendition of the electron density redistribution occurring as a single methane molecule is activated by a rhodium atom within a copper surface lattice

and high resistance to the formation of surface carbon that would deactivate the catalyst. —PDS

Science, abg8389, this issue p.1444

MATERIALS SCIENCE

The making of a monolith

Amorphous calcium carbonate is a hard material that is difficult to make into large, clear blocks. It is also sensitive to heating, and compacting the starting nanoparticles too much tends to lead to crystallization. Mu *et al.* determined the optimal amount of water in amorphous calcium carbonate to create clear, solid monoliths through compression. The key is to regulate the amount of diffusion in the system so that particle boundaries fuse without triggering sample-wide crystallization. This fusion strategy may also work for similar amorphous inorganic ionic compounds. —BG

Science, abg1915, this issue p.1466

CORONAVIRUS

Masking out air sharing

The effectiveness of masks in preventing the transmission of severe acute respiratory syndrome coronavirus 2 has been debated since the beginning of the COVID-19 pandemic. One important question is whether masks are effective despite the forceful expulsion of respiratory matter during coughing and sneezing. Cheng *et al.* convincingly show that most people live in conditions in which the airborne virus load is low. The probability of infection changes nonlinearly with the amount of respiratory matter to which a person is exposed. If most people in the wider community wear even simple surgical masks, then the probability of an encounter with a virus particle is even further limited. In indoor settings, it is impossible to avoid breathing in air that someone else has exhaled, and in hospital situations where the virus concentration is the highest, even the best-performing masks used without other protective gear such as hazmat suits will not provide adequate protection. —CA

Science, abg6296, this issue p.1439

IN OTHER JOURNALS

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



MEDICINE

Acceptable algorithms for radiotherapy

Machine-learning applications in medicine have so far promised more than they have delivered. McIntosh *et al.* evaluated an algorithm that was integrated into the clinical workflow to plan curative-intent radiation therapy for prostate cancer. Human- and algorithm-generated treatment plans were compared in a blinded manner by physicians and one plan was selected. The machine-learning plans were generated faster than the human-generated plans and were selected by physicians for 72% of patients. However, when it came to treating patients, implementation of the machine-learning-generated plans decreased, likely because of the perception and preferences of the treating physicians and their experience

to ensure patient care. Thus, such real-world variables need to be accounted for in studies of medical applications for machine learning to increase its utility and acceptance in the clinical setting. —GKA

Nat. Med. **27**, 999 (2021).

STEM WORKFORCE

Grassroots effort for change

Efforts to increase diversity in STEM (science, technology, engineering, and math) will not be truly successful until the systemic issues within academia that have historically prevented marginalized populations from persisting and succeeding there are transformed. Stachl *et al.* present the details of a collaborative effort to improve the academic climate of an R1 (very high research activity) STEM department: that

ALSO IN SCIENCE JOURNALS

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CORONAVIRUS

Boosterism could save lives

Postinfection immune protection against severe acute respiratory syndrome coronavirus 2 reinfection is not fully understood. It will be devastating if waves of new variants emerge that undermine natural immune protection. Stamatatos *et al.* investigated immune responsiveness 4 to 8 months after previously infected individuals were given a messenger RNA–based vaccine developed for the original Wuhan variant (see the Perspective by Crotty). Before vaccination, postinfection serum antibody neutralization responses to virus variants were variable and weak. Vaccination elevated postinfection serum-neutralizing capacity approximately 1000-fold against Wuhan-Hu-1 and other strains, and serum neutralization against the variant B.1.351 was enhanced. Although responses were relatively muted against the variant, they still showed characteristic memory responses. Vaccination with the Wuhan-Hu-1 variant may thus offer a valuable boost to protective responses against subsequent infection with variant viruses. —CA

Science, abg9175, this issue p. 1413; see also abj2258, p. 1392

URBAN MANAGEMENT

Adapting to the new normal

Successfully responding to the impacts of climate change will be a challenge for many communities, especially cities. Considering the situation in the United States, Shi and Moser examine how stakeholders can help to build urban resilience even in the absence of federal leadership. They discuss how local and state governments, private industry, and civil society can engage to adapt to the extreme weather events and other consequences of changing

climate that are expected in the future. Preparing for these looming issues requires coherent, cohesive, and collective responses across all scales and sectors of society. —HJS

Science, abc8054, this issue p. 1408

CELL BIOLOGY

Tailoring stress responses

When faced with environmental stress, cells respond by shutting down cellular processes such as translation and nucleocytoplasmic transport. At the same time, cells preserve cytoplasmic messenger RNAs in structures known as stress granules, and many cellular proteins are modified by the covalent addition of ubiquitin, which has long been presumed to reflect degradation of stress-damaged proteins (see the Perspective by Dormann). Maxwell *et al.* show that cells generate distinct patterns of ubiquitination in response to different stressors. Rather than reflecting the degradation of stress-damaged proteins, this ubiquitination primes cells to dismantle stress granules and reinitiate normal cellular activities once the stress is removed. Gwon *et al.* show that persistent stress granules are degraded by autophagy, whereas short-lived granules undergo a process of disassembly that is autophagy independent. The mechanism of this disassembly depends on the initiating stress. —SMH

Science, abc3593 and abf6548, this issue p. 1409 and p. 1410; see also abj2400, p. 1393

EPIGENOME

MeCP2 binds hydroxymethylated CA repeats

Despite decades of research on the Rett syndrome protein MeCP2, its function remains unclear. Ibrahim *et al.* show that MeCP2 is a hydroxymethylated cytosine-adenosine (CA) repeat-binding protein that modulates chromatin architecture at a

distance from the transcription start site (see the Perspective by Zhou and Zoghbi). MeCP2 accumulates and spreads around modified CA repeats and competes for nucleosome occupancy. Loss of MeCP2 results in a widespread increase in nucleosome density inside lamina-associated domains and transcriptional dysregulation of genes enriched in CA repeats. These results shed light on the underlying molecular mechanism of Rett syndrome, a severe disease associated with mutations in MeCP2. —DJ

Science, abd5581, this issue p. 1411; see also abj5027, p. 1390

MICROBIOLOGY

Cell death limits pathogens

During infection, *Yersinia* inhibition of the protein kinase TAK1 triggers cleavage of the pore-forming protein gasdermin D (GSDMD), which leads to a kind of inflammatory cell death called pyroptosis. In a genome-wide screen, Zheng *et al.* identified a lysosome-tethered regulatory supercomplex as being a critical driver of *Yersinia*-induced pyroptosis. The activity of the GTPase Rag and lysosomal tethering of Rag-Ragulator were required to recruit and activate the kinase RIPK1 and protease caspase-8 to cleave GSDMD, which causes cell death and limits infection. By contrast, Rag-Ragulator was not required for inflammasome-mediated pyroptosis. Thus, metabolic signaling on lysosomes can regulate cell death during pathogenic bacterial infection. —SMH

Science, abg0269, this issue p. 1412

FERROELECTRICS

Stacking a ferroelectric

Properties of layered van der Waals structures can depend sensitively on the stacking arrangement of constituent layers. This phenomenon has been

exploited to engineer superconducting, correlated insulator, and magnetic states. Two groups now show that ferroelectricity can also be engineered through stacking: Parallel-stacked bilayers of hexagonal boron nitride exhibit ferroelectric switching even though the bulk material is not ferroelectric (see the Perspective by Tsymal). To explore these phenomena, Yasuda *et al.* used transport measurements, whereas Vizner Stern *et al.* focused on atomic force microscopy. —JS

Science, abd3230 and abe8177, this issue p. 1458 and p. 1462; see also abi7296, p. 1389

PALEOANTHROPOLOGY

Middle Pleistocene *Homo* in the Levant

Our understanding of the origin, distribution, and evolution of early humans and their close relatives has been greatly refined by recent new information. Adding to this trend, Hershkovitz *et al.* have uncovered evidence of a previously unknown archaic *Homo* population, the “Nesher Ramla *Homo*” (see the Perspective by Mirazon Lahr). The authors present comprehensive qualitative and quantitative analyses of fossilized remains from a site in Israel dated to 140,000 to 120,000 years ago indicating the presence of a previously unrecognized group of hominins representing the last surviving populations of Middle Pleistocene *Homo* in Europe, southwest Asia, and Africa. In a companion paper, Zaidner *et al.* present the radiometric ages, stone tool assemblages, faunal assemblages, and other behavioral and environmental data associated with these fossils. This evidence shows that these hominins had fully mastered technology that until only recently was linked to either *Homo sapiens* or Neanderthals. Nesher Ramla *Homo* was an efficient hunter of large and

small game, used wood for fuel, cooked or roasted meat, and maintained fires. These findings provide archaeological support for cultural interactions between different human lineages during the Middle Paleolithic, suggesting that admixture between Middle Pleistocene *Homo* and *H. sapiens* had already occurred by this time. —AMS

Science, abh3169 and abh3020, this issue p. 1424 and p. 1429; see also abj3077, p. 1395

MALARIA

A role for IgA in malaria

Immunoglobulin A (IgA) is known to play a protective role against pathogens at mucosal surfaces. However, the protective effects of IgA in the serum are less well understood, particularly in the context of pathogens such as *Plasmodium falciparum*. Tan *et al.* isolated and characterized serum IgA from three independent cohorts of humans exposed to *P. falciparum*. The authors also studied IgA antibodies isolated from individuals who were consistently resistant to malaria and found that these antibodies bound to a conserved site on sporozoites and were protective in mouse models *in vivo*. These results establish a role for serum IgA in the context of malaria and suggest a region of the circumsporozoite protein as a target for protective antibodies. —CSM

Sci. Transl. Med. **13**, eabg2344 (2021).

CELL BIOLOGY

Delayed repression of a tumor suppressor

The rapid induction or repression of gene expression in response to growth factors such as epidermal growth factor (EGF) has been intensively investigated. Uribe *et al.* examined genes they called delayed down-regulated genes (DDGs) that are repressed hours after EGF stimulation in mammary cells. One DDG encoded the transcription factor TSHZ2, which interacted with and inhibited mitotic proteins through multiple mechanisms. Overexpression

of TSHZ2 inhibited mammary tumor growth and progression in mice. In human breast tumors, decreased *TSHZ2* expression often correlated with increased methylation of its promoter.

—LKF

Sci. Signal. **14**, eabe6156 (2021).

MEDICINE

HIV antibody treatments

A recent clinical trial reported that treatment with a broadly neutralizing antibody failed to show efficacy in preventing HIV infection. However, further analysis of the data provides a glimmer of hope that could better inform both future trials aimed at achieving such passive immunity and vaccine development. In a Perspective, Burton discusses the data in the trial indicating that protection from HIV may be achievable with higher doses of infused therapeutic antibody. This trial highlights how inferences from animal studies could be improved for future human trials and helps to explain why higher serum antibody titers are needed for immune protection from HIV. —GKA

Science, abf5376, this issue p. 1397

CORONAVIRUS

A boost from infection

During clinical trials of severe acute respiratory syndrome coronavirus 2 vaccines, no one who had survived infection with the virus was tested. A year after the pandemic was declared, vaccination of previously infected persons is a reality. Reynolds *et al.* address the knowledge gap in a cohort of UK health care workers given the Pfizer/BioNTech vaccine in which half of the participants had experienced natural virus infections early in the pandemic (see the Perspective by Crotty). Genotyping indicated that a genetic component underlies heterogeneity in immune responses to vaccine and to natural infection. After vaccination, naïve individuals developed antibody responses similar to those seen in naturally infected

persons, but T cell responses were more limited and sometimes absent. However, antibody and memory responses in individuals vaccinated after infection were substantially boosted to the extent that a single vaccine dose is likely to protect against the more aggressive B.1.1.7 variant. It is possible that the messenger RNA vaccine has an adjuvant effect, biasing responses toward antibody generation. —CA

Science, abh1282, this issue p. 1418; see also abj2258, p. 1392