HEMATOPOIESIS

Regulating HSC progenitors via cholesterol

Atherosclerosis is characterized by the buildup of cholesterol-containing lipoproteins in the vascular wall. This increased cholesterol augments hematopoietic stem and progenitor cell (HSPC) counts, and the resultant increase in leukocytes is associated with increased cardiovascular disease. Gu *et al*. describe a mechanism orchestrating HSPC specification from the hemogenic endothelium (HE) during embryogenesis (see the Perspective by Rajan and Berman). ApoA-I binding protein accelerated cholesterol efflux from the HE, activating the transcription factor Srebp2, which in turn transactivated Notch signaling. This mechanism also appears to be important for adult HSPC expansion in hypercholesterolemia. —BAP

Science, this issue p. 1085; see also p. 1041

STRUCTURAL BIOLOGY

Crystal structure of the KDEL receptor

Eukaryotic cells concentrate chaperones in the lumen of the endoplasmic reticulum (ER). These chaperones can be swept along the secretory pathway to the Golgi apparatus, from where they must be returned. For 20 years, cell biologists have known the identity of the KDEL (Lys-Asp-Glu-Leu) receptor responsible for this process, but the molecular basis for its function has remained elusive. Now, Bräuer *et al*. present crystal structures of the KDEL receptor, in both the apo ER state and KDEL retrieval signal–bound Golgi state. Comparisons of these two states identify the conformational switch that exposes the ER retrieval motif. The authors recapitulated the binding and release cycle of the receptor using purified components, confirming that the receptor is the minimal component required to bind KDEL ligands in the Golgi. —SMH

Science, this issue p. 1103

GLACIAL CYCLES

Resetting the glacial timer

The periodicity of glacial cycles changed from 100,000 to 41,000 years during the middle of the Pleistocene epoch. Why? Hasenfratz *et al*. measured the oxygen isotope composition and magnesium/calcium ratio in benthic and planktonic foraminifera from the Antarctic in order to reconstruct changes in the rate of transfer of ocean water from the depths to the surface over the past 1.5 million years (see the Perspective by Menviel). The emergence of the 100,000-year cycle coincided with a reduction in deep-water supply and a freshening of the surface ocean. This slowing may have caused more prolonged ice ages by making the Antarctic less responsive to orbitally paced drivers of carbon dioxide release. —HJS

Science, this issue p. 1080; see also p. 1040

PHASE SEPARATION

Organized for action

It is becoming increasingly clear that biomolecular condensates, which are concentrations of macromolecules not surrounded by a membrane, are a key organizational structure in eukaryotic cells (see the Perspective by Martin and Mittag). Now, two papers show how such condensates function in actin assembly or in a Ras signaling pathway. In both cases, the condensates form at the plasma membrane and increase the activity of signaling proteins by increasing their membrane dwell times. Case *et al*. show that the dwell time is dependent on cluster stoichiometry, so that stoichiometry of regulatory proteins can control actin assembly. Huang *et al*. demonstrate that the longer dwell time allows kinetic proofreading in receptor-mediated activation of Ras. —VV

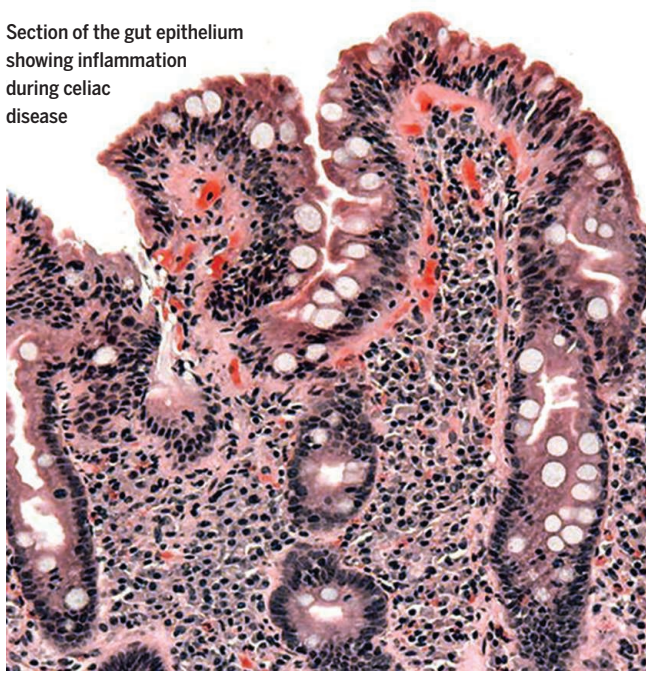
Science, this issue p. 1093, p. 1098; see also p. 1036

IMMUNOLOGY

Celiac immunity scarred for life

Celiac disease (CD) is an enteric inflammatory disorder initiated and perpetuated by exposure to dietary gluten and mediated by intraepithelial lymphocytes (IELs). Mayassi *et al*. compared IELs from CD patients, CD patients on a gluten-free diet, and healthy controls. In healthy humans, Vγ4/Vδ1$^+$ IELs dominated, which recognize immunoglobulin-like molecules called butyrophilins (BTNLs) that are involved in fatty acid and sterol metabolism. In CD and gluten-free CD patients, Vγ4/Vδ1$^+$ IELs were replaced by gluten-sensitive interferon-γ–producing Vδ1$^+$ IELs bearing T cell receptors. It seems that CD reaches a peak at which the loss of survival ligands, like the BTNLs, decimates Vγ4/Vδ1$^+$ IELs and allows Vδ1$^+$ IELs to predominate instead. This process, termed "immunological scarring," may contribute to other immunopathologies. —STS

Cell **176**, 967 (2019).



Section of the gut epithelium showing inflammation during celiac disease

QUANTUM OPTICS

Quantum walkers caught in a loop

A quantum walk is the quantum mechanical analog of a classical random walk, describing the propagation of quantum walkers (photons) through an optical circuit. Because quantum walks generate large-scale quantum superposed states, they can be used for simulating many-body quantum systems and the development of algorithms for quantum computation. Nejadsattari *et al*. describe the photonic simulation with cyclic quantum systems. Using a multiple-site optical system, they explored the wave function dynamics and the probability distribution of quantum walkers as they loop through the system from site to site. With the ability to simulate a variety of different quantum operations and gates, they claim that the versatility of the approach should allow the study of more complex many-body systems. —ISO

Optica **6**, 174 (2019).

PHOTO: SAMIR/WIKIMEDIA COMMONS

T CELLS

How sleep aids recovery

Sleep does wonders for our overall health. The benefits include a lower risk for heart disease, reduced stress, weight management, and improved mood. Dimitrov *et al*. uncover how a good night's sleep helps us heal faster from infection. T cells are immune cells that attach to invading viruses and mark them for destruction. The researchers found that integrins—the glue-like proteins used by T cells to stick to pathogens—are more activated when we sleep. In awake individuals, signaling molecules belonging to the $G\alpha_s$-coupled receptor agonist family (for example, adrenaline) were produced at greater levels. These molecules have an antistick effect, inhibit integrin production, and reduce the ability of T cells to attach to invading microbes. —PNK

J. Exp. Med. **216**, 517 (2019).

Sleep promotes T cell adhesion, which helps the clearance of pathogens.

SIGNAL TRANSDUCTION

Can we understand RB?

The tumor suppressor retinoblastoma (RB) protein is essential for normal development and suppression of aberrant cell proliferation. Its mode of action remains elusive though, in part because hundreds of proteins have been reported to interact with RB. Phosphorylation is known to alter RB structure in profound but specific ways. Sanidas *et al*. explored the consequences of cyclin-dependent kinase activity on 14 phosphorylation sites across RB. For example, monophosphorylation of RB at Ser^{811} triggers chromatin remodeling, alters the spectrum of genes repressed by RB, and promotes mitochondrial function. Monophosphorylated RBs interact with many different proteins in distinct ways to regulate multiple targets. This is just the start of understanding how the RB phosphorylation code affects cell function. —LBR

Mol. Cell. 10.1016/j.molcel.2019.01.004 (2019).

PHYSICS

A (theoretical) quantum refrigerator

How thermodynamics works at a scale where quantum rules apply has fascinated many physicists. Buffoni *et al*. propose an intriguing scheme for making a tiny refrigerator that exploits the laws of quantum mechanics. Their refrigerator consists of two qubits that were initially in contact with reservoirs at different temperatures. In a refrigeration cycle, the qubits first underwent a quantum measurement, which changed their state and caused them to exchange energy with the measurement apparatus; the cycle was closed by putting the qubits back in contact with their respective reservoirs, giving away more heat than they received. The researchers predict that the procedure is robust with respect to experimental noise and may be realizable with superconducting qubits. —JS

Phys. Rev. Lett. **122**, 070603 (2019).

MOLECULAR BIOLOGY

A small RNA regulator of autophagy

Autophagy serves an essential cellular-garbage disposal function. For example, the autophagy receptor p62 (or sequestosome-1) is needed for selective removal of intracellular pathogen material to the autophagosome for degradation. Notably, p62 must oligomerize to be able to bind to the autophagosome membrane. Horos *et al*. discovered that p62 also binds to small noncoding vault RNA 1-1, which inhibits autophagy by preventing p62 oligomerization. During starvation, vault RNA 1-1 expression decreases, and autophagy is reactivated. Demonstration of the direct regulation of protein function by an RNA raises the intriguing possibility of the existence of other physiological riboregulators, including Toll-like receptors or protein kinases important in viral infections. —SYM

Cell **176**, 1054 (2019).

ATMOSPHERIC CHEMISTRY

Cleansers in clean air

Hydroxyl radicals (OH) have been called the detergent of the atmosphere owing to their role as its primary oxidant. Models accurately simulate OH concentrations in polluted air but fail to predict them in more pristine conditions, underestimating their abundance by as much as an order of magnitude and thereby casting doubt on our understanding of their chemistry. Fittschen *et al*. propose that this is due not to a problem with the models, as is commonly believed, but rather to an artifact of the technique normally used to measure OH. They suggest that ROOOH, produced by the reaction of organic peroxy radicals (RO_2) and OH, produces an interference that can cause this underestimation. —HJS

Atmos. Chem. Phys. **19**, 379 (2019).

A small RNA regulator of autophagy

Steve Mao

Science **363** (6431), 1053-1054.
DOI: 10.1126/science.363.6431.1053-f