SKIN INFLAMMATION

Hitting the brakes on fibrosis

Issue fibrosis is the culminating event of many human inflammatory diseases. Few antifibrotic therapies are available, and the cellular and molecular mechanisms driving fibrosis remain unclear. Using single-cell transcriptomics, Odell et al. found that skin from patients with diffuse cutaneous systemic sclerosis was enriched for dendritic cells (DCs) producing the epidermal growth factor receptor (EGFR) ligand epiregulin. DC production of epiregulin could be induced by type I interferon and promoted NOTCH-mediated extracellular matrix gene expression in fibroblasts. In mouse models of bleomycin-induced skin and lung fibrosis, an epiregulin-neutralizing antibody alleviated fibrosis. These results identify a role for epiregulin-producing DCs in maintaining fibrosis and suggest that blocking epiregulin’s EGFR activity could be a promising therapeutic strategy for treating fibrotic diseases. —CO
Sci. Immunol. 7, eabq6691 (2022).

SYNTHEtic BIOLOGY

Exploring receptor design principles

Chimeric antigen receptor T cell technology, in which cells of the immune system are modified with customized receptors, has proved effective in cancer therapy. To explore the range of cell responses that can be encoded in such receptors and to make their design more quantitative and predictive, Daniels et al. tested about 200 of 2400 possible combinations of 13 signaling motifs found in such receptors and used machine learning to predict other effective combinations. Using these design rules, the authors constructed receptors in human T cells with improved signaling characteristics that contributed to better tumor control in a mouse model. —LBR
Science, abq0225, this issue p. 1194

ORGANIC CHEMISTRY

Illuminating C–N bond formation

Forming carbon–nitrogen (C–N) bonds is integral to pharmaceutical synthesis. Palladium (Pd) catalysis is an especially efficient means to this end, but alkyl amines can deactivate the catalyst by tight binding. Several recent approaches to circumventing this problem in allylic amination have focused on modifying either the amines or the Pd coordination environment. Cheung et al. report a distinct protocol that operates through photoinduced electron transfer to form versatile Pd(I) intermediates. This method is also compatible with more densely substituted carbon frameworks and can selectively produce just one of two mirror image products. —JSY
Science, abq1274, this issue p. 1207

QUANTUM MATERIALS

Probing the Moiré lattice

The optoelectronic properties of bilayers of two-dimensional materials exhibit a wealth of properties dependent on the twist angle. A direct probe of the transport properties and their correlation with the atomic registry has been lacking. Susarla et al. used cryogenic transmission electron microscopy and spectroscopy to simultaneously image the structural reconstruction and the associated spatial localization of the lowest-energy intralayer exciton in a rotationally aligned bilayer heterostructure of tungsten disulfide and tungsten.

MEMBRANES

Material design maximizes performance

Zeolites are able to separate molecules with similar size and shape because of their well-defined, uniform pore size and specific adsorption properties. However, it has been a challenge to retain these features when blending a zeolite with a polymeric matrix support. Tan et al. developed a method to put high loadings of the aluminosilicate SSZ-39, which is known for its attraction of carbon dioxide, into a commercial polyimide selected for its compatibility with the zeolite. The resulting mixed matrix membranes were flexible and defect free, showing excellent separation of carbon dioxide that even exceeded the performance of pure zeolite membranes. —MSL
Science, ade1411, this issue p. 1189
Sister species may occupy different niches, but whether ecological divergence occurs during or after allopatric speciation is poorly understood. Anderson and Weir used trait data on more than 1000 pairs of sister taxa, including birds, mammals, and amphibians, to model trait divergence over time. They found few examples of clear divergent adaptation, with greater support for a model of sister taxa evolving under similar selective pressures toward similar trait optima. —BEL

Science, abo7719, this issue p. 1214

EVOLUTIONARY ECOLOGY
Similar but separate species
Speciation often requires a period of allopatry, when populations are separated long enough to diverge into distinct species.

The closely related Amazonian songbirds Lepidothrix iris (left) and L. natererei (right) evolved with similar traits despite living in different places.

IN OTHER JOURNALS
Edited by Caroline Ash and Jesse Smith

PLANT SCIENCE
Alternative crop plant dwarfing
Tall, thin stems carrying heavy grains late in the growing season are vulnerable to lodging, which is when strong winds or heavy rain flatten a field of plants. The Green Revolution of the 1960s reduced this risk with the introduction of genetic traits that shortened the average height of rice or wheat plants and increased grain yields worldwide. However, seedling growth was negatively affected and resistance to certain diseases reduced. Borrill et al. analyzed a plant dwarfism gene, Reduced Height 13 (Rht13), that delivers its height-reducing effects later in the plant’s life cycle. Rht13 encodes a nucleotide-binding site–leucine-rich repeat (NB-LRR) protein, a member of a group of proteins often implicated in plant disease resistance. A mutation in the Rht13 gene leaves the protein in a permanently activated state, which drives increased expression of certain disease-defense genes and results in dwarfed plants. In particular, overexpression of peroxidases might limit flexibility of cell walls, thus limiting cell elongation and overall plant height. —PJH

Proc. Natl. Acad. Sci. U.S.A. 119, e2209875119 (2022).

AQUATIC ECOLOGY
Zooplankton’s nutrient limits
Energy flow through food webs is limited by consumers’ ability to capture matter and energy from primary producers, which in turn depends on producer quantity and nutritional quality. In aquatic systems, studies have identified nitrogen, phosphorus, essential fatty acids, and sterols as key limiting nutrients. Anderson et al. used trait data on more than 1000 pairs of sister taxa, including birds, mammals, and amphibians, to model trait divergence over time. They found few examples of clear divergent adaptation, with greater support for a model of sister taxa evolving under similar selective pressures toward similar trait optima. —BEL

Science, abo7719, this issue p. 1214

SPIN ICE
Fractal-hopping monopoles
Spin ices have crystal lattices that consist of tetrahedra of magnetic ions. In a ground state, two of the four spins on each tetrahedron point in and two point out. When an excitation called the magnetic monopole is created, this rule is violated as the monopole moves through the crystal. Monopole dynamics are reflected in quantities such as magnetic noise, the measurements of which have shown a different frequency dependence from the one that the simplest model predicts. Hallén et al. solved this puzzle by realizing that the monopole motion is more restricted than previously thought and is limited to a cluster with a fractal structure (see the Perspective by Fliecker). —JS

Science, add1644, this issue p. 1218; see also ade2301, p. 1177

CELL BIOLOGY
A path to prevent TNF cytotoxicity
Tumor necrosis factor (TNF) is a central cytokine in inflammatory reactions and is a pharmacological target in several inflammatory disorders. Recent studies demonstrated that the pathological role of TNF in these diseases can originate from its ability to trigger cell death, an outcome that is normally actively repressed in cells. Huyghe et al. identified an unconventional lysosomal targeting process that prevents TNF cytotoxicity by degrading the caspase-8–activating complex that forms in response to TNF binding to TNF receptor 1 (TNFR1). Abrogating this detoxification mechanism caused TNFR1-mediated embryonic lethality or an inflammatory skin disease when locally inactivated in mice. —SMH

Science, add6967, this issue p. 1201

RESOURCES | IN SCIENCE JOURNALS

The Hebei University of Technology and the University of Toronto at Scarborough have joined forces to launch a new journal, RESOURCES, which will focus on the latest developments in the field of resources management and sustainable development. The journal aims to provide a platform for scientists, policymakers, and practitioners to share their research and insights, and to foster collaboration across disciplines. RESOURCES is open access, meaning that all articles will be freely available to readers worldwide. The first issue of the journal was published in December 2022, and it features a selection of papers on topics ranging from renewable energy to water management. For more information, visit the journal’s website at resourcesjournal.com.
**IMMUNOLOGY**

**Stress amps up IFN signaling**

Interferon (IFN) signaling stimulates the innate immune response to infection. Boccuni et al. investigated the interaction between IFN signaling and stress signaling mediated by the kinase p38. In IFN-treated macrophages, coincident stress signaling synergistically increased the expression of IFN-stimulated genes. In *Listeria*-infected cultured macrophages, this boost elicited greater production of pathogen-fighting factors, but it also increased cell death. Blocking p38 signaling preserved macrophage viability without sacrificing function. —LKF

*Sci. Signal.* **15**, eaq6389 (2022).

**MARBURG VIRUS**

**Fighting filoviruses**

Marburg virus (MARV) outbreaks remain a major global health concern, and an effective vaccine is urgently needed. Hunegnaw et al. report that ChAd3-MARV, a single-shot chimpanzee adenovirus-vectorized vaccine expressing the MARV glycoprotein, confers protection in nonhuman primates. Animals were protected as soon as 1 week after vaccination, and protection lasted up to 1 year, with antigen-specific antibodies serving as a predictor of protection. These results support the clinical use of ChAd3-MARV in humans. —CSM

*Sci. Transl. Med.* **14**, eaq6364 (2022).

**SYNTHETIC BIOLOGY**

**Building blocks for synthetic circuits**

The promise of chimeric antigen receptor T cell therapy, in which human T cells are engineered to attack tumors, has heightened interest in cell-based therapies. Li et al. developed a toolkit of programmable synthetic transcription regulators that feature a compact, human protein–based design and allow transcription to be regulated by US Food & Drug Administration–approved small molecules (see the Perspective by Salazar-Cavazos and Altan-Bonnet). The authors engineered human immune cells that kill tumors when activated by the appropriate small molecule, and they also demonstrated a dual-switch system that allows sequential control of immune cell function. This platform could be adapted to design cell therapies in a variety of contexts. —VV

*Science*, ade0156, this issue p. 1227; see also adf5318, p. 1175

**CELL BIOLOGY**

**Alike pathways for import**

Eukaryotic cells contain membrane-bounded organelles that import specific proteins from the cytosol. Organelles called peroxisomes are vital for human health because they house important metabolic enzymes. However, how enzymes are imported into peroxisomes has been mysterious, particularly because folded proteins and even protein oligomers can cross the peroxisomal membrane. Gao et al. found that multiple copies of a cohesive domain from the peroxisomal protein PEX13 form a dense meshwork within the membrane. Mobile import receptors can diffuse through this barrier to enter the organelle and bring bound cargo along. This mechanism resembles transport through the nuclear pore and explains how folded proteins are imported into peroxisomes. —SMH

*Science*, adf3971, this issue p. 1187

**SYNTHETIC BIOLOGY**

**Designing T cells to attack solid tumors**

T cells with modified receptors that recognize tumor antigens (chimeric antigen receptor or CAR T cells) have proved effective in treating B cell malignancies, but solid tumors create an immunosuppressive microenvironment that limits their function. To overcome this limitation, Allen et al. enhanced engineered T cells with a second synthetic receptor that could recognize a tumor antigen and cause the T cell to secrete the cytokine interleukin-2 (see the Perspective by Salazar-Cavazos and Altan-Bonnet). Interleukin-2 promoted local proliferation of the T cells despite the tumor’s immunosuppressive effects. Such engineered cells allowed effective treatment of solid tumors in mouse models. —LBR

*Science*, abal624, this issue p. 1186; see also adf5318, p. 1175

**CELL BIOLOGY**

**A lipid-triggered signal in starvation**

Nutrient starvation triggers changes in metabolism that are coordinated across the cell and its organelles. Jang et al. studied how endosomal signaling lipid turnover through MTM1, a phosphoinositide 3-phosphatase mutated in X-linked centro-nuclear myopathy in humans, reshapes the endoplasmic reticulum to control mitochondrial morphology and oxidative metabolism (see the Perspective by Zanelliati and Cohen). A lipid-controlled organelar relay transmits nutrient-triggered changes in endosomal signaling lipid levels to mitochondria to enable metabolic rewiring. —SMH

*Science*, abq5209, this issue p. 1188; see also adf5112, p. 1173

**SYNTHETIC BIOLOGY**

**Staying soft and conductive under strain**

Most electrically conductive materials tend to be stiff and brittle, whereas human tissue is soft and compliant. It is thus a challenge to make conductive biomaterials that are sufficiently compliant but do not show a loss or distortion in performance. Zhao et al. used a three-layer design to couple strain-induced cracked films with a strain-isolated conductive pathway (see the Perspective by Rafieedi and Lipomi). Upon an initial prestrain to 100%, the brittle solid film on top cracks to dissipate the strain energy. However, this cracking permits a type of parallel, interconnected charge transport in which the charge carriers move between the layers to circumvent the cracks. —MSL

*Science*, abn5142, this issue p. 1222; see also adf2322, p. 1174

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