RESEARCH

Hox gene function in the sea anemone *Nematostella vectensis*

He et al., *p. 1377*

IN *SCIENCE* JOURNALS

Edited by **Stella Hurtley**

Killer whales are still being damaged by PCBs in the environment.

PERSISTENT CHEMICALS

PCB—still a problem

Until they were recognized as highly toxic and carcinogenic, polychlorinated biphenyls (PCBs) were once used widely. Their production was banned in the United States in 1978, though they are still produced globally and persist in the environment. Persistent organic compounds, like PCBs, magnify across trophic levels, and thus apex predators are particularly susceptible to their ill effects. Desforges *et al.* looked at the continuing impact of PCBs on one of the largest marine predators, the killer whale. Using globally available data, the authors found high concentrations of PCBs within killer whale tissues. These are likely to precipitate declines across killer whale populations, particularly those that feed at high trophic levels and are the closest to industrialized areas. —SNV

Science, this issue p. 1373

SINGLE-CELL GENOMICS

Single-cell chromatin and RNA analysis

Single-cell analyses have begun to provide insight into the differences among and within the individual cells that make up a tissue or organism. However, technological barriers owing to the small amount of material present in each single cell have prevented parallel analyses. Cao *et al*. present sci-CAR, a pooled barcode method that jointly analyzes both the RNA transcripts and chromatin profiles of single cells. By applying sci-CAR to lung adenocarcinoma cells and mouse kidney tissue, the authors demonstrate precision in assessing expression and genome accessibility at a genome-wide scale. The approach provides an improvement over bulk analysis, which can be confounded by differing cellular subgroups. —LMZ

Science, this issue p. 1380

MOLECULAR BIOLOGY

How cells ensure symmetric inheritance

Parental histones with modifications are recycled to newly replicated DNA strands during genome replication, but do the two sister chromatids inherit modified histones equally? Yu *et al*. and Petryk *et al*. found in mouse and yeast, respectively, that modified histones are segregated to both DNA daughter strands in a largely symmetric manner (see the Perspective by Ahmad and Henikoff). However, the mechanisms ensuring this symmetric inheritance in yeast and mouse were different. Yeasts use subunits of DNA polymerase to prevent the lagging-strand bias of parental histones, whereas in mouse cells, the replicative helicase MCM2 counters the leading-strand bias. —SYM

Science, this issue p. 1386, p. 1389; see also p. 1311

CREDITS: (TOP) HE *ET AL.*; (BOTTOM): PHOTO: AUDUN RIKARDSEN

BIOPHYSICS

Manta rays' unique filtration system

Manta rays feed by opening their mouths as they swim, catching tiny plankton while simultaneously expelling water through their gills. How their filtering apparatus allows food that is smaller than their filter pore size to be captured, especially without clogging, remains elusive. Divi *et al*. examined the fluid flow around the filter-feeding mouth of the manta ray using physical and computational modeling. Flow separation happened behind the leading edge of each filter lobe, causing a large vortex within each pore. This meant that tiny particles were repelled away from the filters instead of passing through. Contact forces caused the particles to "ricochet" away from the filter pore and backward to the faster-moving freestream flow; thus, the particles collected above the filter, rather than on top of it (which would cause it to clog). This unique filtration system may hold interesting industrial applications. —PJB

Sci. Adv. 10.1126/sciadv.aat9533 (2018).

FIBROSIS

PD-1$^+$ T cells prompt pulmonary fibrosis

Although immunological T cells expressing programmed cell death 1 (PD-1) are sometimes described as exhausted, they are not too exhausted to wreak havoc in a variety of settings. Celada *et al*. examined cells from patients with sarcoidosis or idiopathic pulmonary fibrosis and saw an increase in PD-1$^+$ CD4$^+$ T cells relative to healthy controls. These cells were mostly T helper 17 cells and were able to induce fibroblasts to produce collagen in vitro. Blocking PD-1 in the coculture system prevented this induction and associated cytokine production from the T cells. Furthermore, blocking PD-1 in a mouse model of pulmonary fibrosis reduced fibrosis symptoms. —LP

Sci. Transl. Med. **10**, eaar8356 (2018).

BIOSYNTHESIS

How algae turn tides toxic

Algal blooms can devastate marine mammal communities through the production of neurotoxins that accumulate within the food web. Brunson *et al*. identified a cluster of genes associated with biosynthesis of the neurotoxin domoic acid in a marine diatom (see the Perspective by Pohnert *et al*.). In vitro experiments established a series of enzymes that create the core structure of the toxin. Knowledge of the genes involved in domoic acid production will allow for genetic monitoring of algal blooms and aid in identifying conditions that trigger toxin production. —MAF

Science, this issue p. 1356; see also p. 1308

ULTRAFAST OPTICS

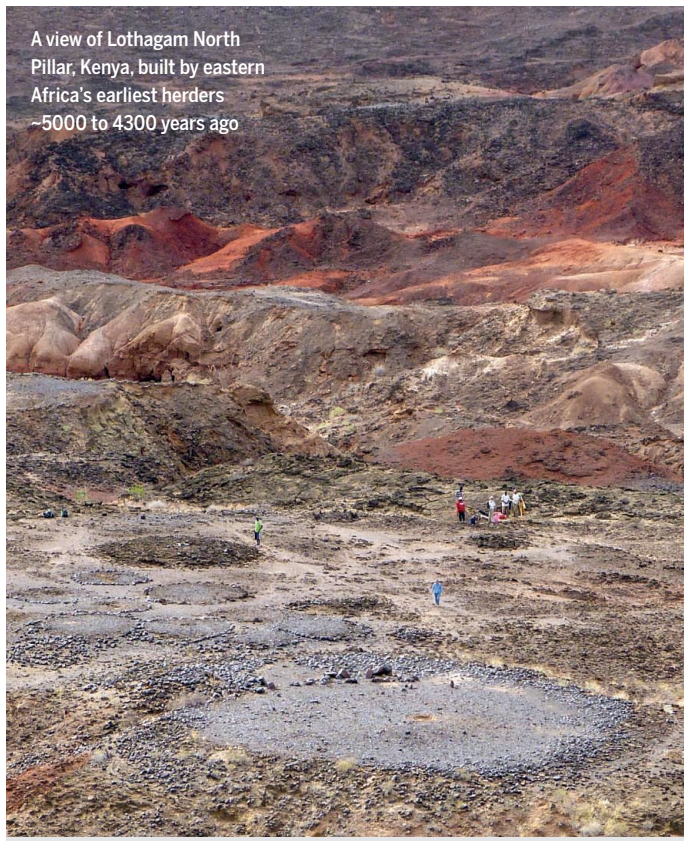
Making ultrafast cycles of light

The ability to generate coherent optical frequency combs has had a huge impact on precision metrology, imaging, and sensing applications. On closer inspection, the broadband "white light" generated through the interaction of femtosecond mode-locked laser pulses is composed of billions or trillions of precisely spaced wavelengths of light. Carlson *et al*. demonstrate an alternative to the mode-locked laser approach—the electro-optic modulation of a continuous-wave laser light source can also generate optical frequency combs (see the Perspective by Torres-Company). The electro-optic modulation techniques can operate at much higher repetition rates than mode-locked lasers, which means they could potentially yield even more precise measurements. —ISO

Science, this issue p. 1358; see also p. 1316

IN OTHER JOURNALS

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



A view of Lothagam North Pillar, Kenya, built by eastern Africa's earliest herders ~5000 to 4300 years ago

ARCHAEOLOGY

A massive cemetery at Lake Turkana

The oldest monumental architecture in eastern Africa was built about 5000 years ago. Apparently, these are commemorative structures built by pastoralists. Hildebrand *et al*. report a detailed excavation and ground-penetrating radar survey at the Lothagam North Pillar Site in Kenya. A massive mortuary was revealed, containing the skeletal remains of nearly 600 individuals buried over several centuries. Associated personal ornamentation included beads, colored stone, tusks, and a headpiece with over 400 teeth from more than 100 gerbils. There appeared to be no differentiation by hierarchy, gender, or age. The authors suggest that this site and others like it would have been stable landmarks at which mobile communities could gather and interact. —AMS

Proc. Natl. Acad. Sci. U.S.A. **115**, 8942 (2018).

STEM CELLS

The blood, by night and day

Many developmental events have now been associated with the daily cycle. But what is happening physiologically during the hours of light and dark? Bone turnover, immunity, and stem cell migration from the bone marrow are certainly affected. Golan *et al*. observed two peaks in bone marrow hematopoietic stem and progenitor cells (HSPCs) after

PHOTO: KATHERINE GRILLO

ALSO IN *SCIENCE* JOURNALS

Edited by **Stella Hurtley**

EPIGENOMICS

Dissecting the epigenomic footprint

Genome-wide epigenetic marks regulate gene expression, but the amount and function of variability in these marks are poorly understood. Working with human-derived samples, Onuchic *et al*. examined disease-associated genetic variation and sequence-dependent allele-specific methylation at gene regulatory loci. Regulatory sequences within individual chromosomal DNA molecules showed full or no methylation at specific sites corresponding to "on" and "off" switches. Interestingly, methylation did not occur on each DNA molecule, resulting in a variable fraction of methylated chromosomes. This stochastic type of gene regulation was more common for rare genetic variants, which may suggest a role in human disease. —LMZ

Science, this issue p. 1354

CANCER

Waking up in a trap

Cancer patients who have undergone successful treatment can experience relapse of their disease years or even decades later. This is because cancer cells that have disseminated beyond the primary tumor site enter a state of dormancy, where they remain viable but not proliferating. Eventually, by mechanisms that are poorly understood, these clinically undetectable cells "wake up" and form actively growing metastases. Studying mouse models, Albrengues *et al*. found that sustained lung inflammation and the accompanying formation of neutrophil extracellular traps (NETs) could convert dormant cancer cells to aggressive lung metastases (see the Perspective by Aguirre-Ghiso). Awakening of these cells was associated with NET-mediated remodeling of the extracellular matrix and could be prevented by an antibody against the remodeled version of a matrix protein called laminin-111. —PAK

Science, this issue p. 1353; see also p. 1314

ARCHAEOLOGY

Classic Maya civilization in detail

Lidar (a type of airborne laser scanning) provides a powerful technique for three-dimensional mapping of topographic features. It is proving to be a valuable tool in archaeology, particularly where the remains of structures may be hidden beneath forest canopies. Canuto *et al*. present lidar data covering more than 2000 square kilometers of lowland Guatemala, which encompasses ancient settlements of the Classic Maya civilization (see the Perspective by Ford and Horn). The data yielded population estimates, measures of agricultural intensification, and evidence of investment in landscape-transforming infrastructure. The findings indicate that this Lowland Maya society was a regionally interconnected network of densely populated and defended cities, which were sustained by an array of agricultural practices that optimized land productivity and the interactions between rural and urban communities. —AMS

Science, this issue p. 1355; see also p. 1313

ORGANIC CHEMISTRY

Two ways out of an oxetane

Oxetanes are highly reactive four-membered rings that contain three carbon atoms and an oxygen atom. Recently, they were implicated as transient intermediates in Lewis acid–catalyzed intramolecular metathesis reactions of ketones with olefins. Ludwig *et al*. now report that by replacing the Lewis acid with a strong Brønsted acid, they can change the course of the oxetane ring-opening. In a so-called interrupted metathesis, the oxygen atom migrates and then departs through dehydration, while the remaining carbon framework cyclizes to form tetrahydrofluorene compounds. —JSY

Science, this issue p. 1363

ORGANIC CHEMISTRY

Arenes and amides from a single source

Pharmaceutical synthesis often requires the formation of adjacent carbon-carbon and carbon-nitrogen bonds. Monos *et al*. present a method that delivers the carbon and nitrogen components in a single reagent, specifically, an aryl ring tethered through sulfur dioxide to an amide. A light-activated catalyst primes an olefin to react with the nitrogen, which in turn leads to migration of the aryl ring and loss of the sulfur bridge. The efficient room-temperature process is applicable to a variety of different arenes, including heterocycles. —JSY

Science, this issue p. 1369

EVO-DEVO

Hox code in segmentation and patterning

Hox genes encode conserved transcription factors that are best known for their role in governing anterior-posterior body patterning in diverse bilaterian animals. He *et al*. used a combination of CRISPR mutagenesis and short hairpin RNA–based gene knockdowns to interrogate *Hox* gene function in a cnidarian, the sea anemone *Nematostella vectensis* (see the Perspective by Arendt). Four homeobox-containing genes constitute a molecular network that coordinately controls the morphogenesis of radial endodermal segments and the patterning of tentacles. Thus, an ancient Hox code may have evolved to regulate both tissue segmentation and body patterning in the bilaterian-cnidarian common ancestor. —BAP

Science, this issue p. 1377; see also p. 1310

ANTIBODIES

Giving antibodies a boost

Persistent immune activation during chronic infections is often associated with increased generation and deposition of immune complexes. The actions of antibody-based drugs can thus be severely impaired in individuals with chronic infections. Using lymphocytic choriomeningitis virus (LCMV) as a model of chronic infection, Wieland *et al*. examined how to enhance antibody functions in this setting. The ability of antibodies to deplete target cells was dependent on antigen expression levels. Furthermore, afucosylation of antibodies directed against CD4 and CD8α enhanced their ability to deplete $CD4^+$ and $CD8^+$ T cells in mice persistently infected with LCMV. Whether afucosylation can be universally used to enhance antibody functions during chronic infections remains to be seen. —AB

Sci. Immunol. **3**, eaao3125 (2018).

BIOCHEMISTRY

Using kinase inhibitors on pseudokinases

Pseudokinases are structurally similar to kinases but lack catalytic activity. Instead, pseudokinases often promote protein degradation by acting as scaffolds for ubiquitin ligases and their substrates. The pseudokinases TRIB1 and TRIB2 are implicated in leukemia and other cancers. Jamieson *et al*. and Foulkes *et al*. found that these proteins bound to clinically approved kinase inhibitors,

which induced structural changes that led to their degradation upon interacting with ubiquitin ligases. Thus, these drugs might be repurposed to block the function of TRIBs in cancer patients. —LKF

Sci. Signal. **11**, eaau0597, eaat7951 (2018).