**RESEARCH**

**IN SCIENCE JOURNALS** Edited by Stella Hurtley

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**Cassini enters Saturn’s ionosphere**

The upper reaches of most planetary atmospheres contain a layer that is ionized by incoming solar radiation—the ionosphere. As it went through its final orbits around Saturn, the Cassini spacecraft dipped close enough to the planet to pass directly through the ionosphere. Wahlund et al. examined the plasma data collected in situ and found that Saturn’s ionosphere is highly variable and interacts with the planet’s inner ring. They also observed decreases in ionization within regions shaded from the Sun by the rings. —KTS

Science, this issue p. 66

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**Research**

Vivax malaria uses transferrin receptor to gain entry

Gruszczyn et al., p. 48

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**Materials Science**

Liquids show their strength

Dielectric elastomer actuators are electrically powered muscle mimetics that offer high actuation strain and high efficiency but are limited by failure caused by high electric fields and aging. Acome et al. used a liquid dielectric, rather than an elastomeric polymer, to solve a problem of catastrophic failure in dielectric elastomer actuators. The dielectric’s liquid nature allowed it to self-heal—something that would not be possible with a solid dielectric. The approach allowed the authors to exploit electrostatic and hydraulic forces to achieve muscle-like contractions in a powerful but delicate gripper. —MSL

Science, this issue p. 61

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**Topological Matter**

Heating up the quantum spin Hall effect

Taking practical advantage of the topologically protected conducting edge states of topological insulators (TIs) has proven difficult. Semiconductor systems that have been identified as two-dimensional TIs must be cooled down to near liquid helium temperatures to bring out their topological character. Wu et al. fabricated a heterostructure consisting of a monolayer of WTe₂ placed between two layers of hexagonal boron nitride and found that its topological properties persisted up to a relatively high temperature of 100 K. Engineering this so-called quantum spin Hall effect in a van der Waals heterostructure makes it possible to apply many established experimental tools and functionalities. —JS

Science, this issue p. 76

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**Cancer Immunotherapy**

Good bacteria help fight cancer

Resident gut bacteria can affect patient responses to cancer immunotherapy (see the Perspective by Jobin). Routy et al. show that antibiotic consumption is associated with poor response to immunotherapeutic PD-1 blockade. They profiled samples from patients with lung and kidney cancers and found that nonresponding patients had low levels of the bacterium Akkermansia muciniphila. Oral supplementation of the bacteria to antibiotic-treated mice restored the response to immunotherapy. Matson et al. and Gopalakrishnan et al. studied melanoma patients receiving PD-1 blockade and found a greater abundance of “good” bacteria in the guts of responding patients. Nonresponders had an imbalance in gut flora composition, which correlated with impaired immune cell activity. Thus, maintaining healthy gut flora could help patients combat cancer. —PNK

Science, this issue p. 91, p. 104, p. 97; see also p. 32

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**Gas Giant Planets**

Cassini has collected data on the plasma in Saturn’s ionosphere.

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**Credits:** (Top to Bottom) Gruszczyn et al.; NASA/JPL-CALTECH
MOLECULAR BIOLOGY
Mitosis-specific role of ATR
The ATR (ataxia telangiectasia mutated and Rad3-related) kinase plays important roles in the S phase and during the DNA damage response to safeguard genome integrity. Kabeche et al. identified a distinct ATR activation pathway in mitosis that is also critical for suppressing genome instability (see the Perspective by Saldivar and Cimprich). ATR is recruited by Aurora A and activated by R loops at centromeres of mitotic chromosomes; this leads to Aurora B activation, which is necessary for accurate chromosome segregation. This mitotic, R loop–driven ATR signaling pathway could potentially be exploited in the search for cancer therapeutics.—SYM
Science, this issue p. 108; see also p. 30

CORAL REEFS
Not enough time for recovery
Coral bleaching occurs when stressful conditions result in the expulsion of the algal partner from the coral. Before anthropogenic climate warming, such events were relatively rare, allowing for recovery of the reef between events. Hughes et al. looked at 100 reefs globally and found that the average interval between bleaching events is now less than half what it was before. Such narrow recovery windows do not allow for full recovery. Furthermore, warming events such as El Niño are warmer than previously, as are general ocean conditions. Such changes are likely to make it more and more difficult for reefs to recover between stressful events. —SNV
Science, this issue p. 80

SOCIAL SCIENCES
Global reciprocity drives cooperation
Cooperation among nations promotes international trade, law, peace, and environmental protection. But how does cooperation emerge and persist among independent, self-interested, and often competing nations? Frank et al. applied powerful causal inference techniques to a detailed global data set of country interactions from 1995 to 2015 to map international cooperation, influence, and reciprocity. In agreement with predictions from evolutionary game theory, reciprocity among nations, including powerful countries, is pervasive and leads to stable cooperation, even in the face of minor transgressions.—AC

TINNITUS
The sound of silence
Tinnitus reduces the quality of life for millions of sufferers worldwide. Using a guinea pig model of tinnitus induced by noise trauma, Marks et al. delivered precisely timed bimodal auditory-somatosensory stimulation to induce long-term depression (LTD) in the cochlear nucleus. Twenty minutes of treatment per day reduced physiological and behavioral evidence of tinnitus in the animals. The same bimodal protocol reduced tinnitus loudness in human subjects in a double-blind, sham-controlled, crossover clinical study. Unimodal stimulation did not reduce tinnitus in the animals or the humans. This approach thus holds promise for suppressing chronic tinnitus in patients.—OMS

IN OTHER JOURNALS
Edited by Caroline Ash and Jesse Smith

SIGNAL TRANSDUCTION
Unconventional thyroid hormone signals
Thyroid hormone canonically signals through thyroid hormone receptors to enhance transcription of target genes. There is also evidence that thyroid hormone can activate nontranscriptional signaling mechanisms. To sort out the relative importance of canonical and noncanonical signaling, Hones et al. generated mice in which thyroid hormone receptors were altered to prevent DNA binding and transcriptional effects (but noncanonical signaling remained) and compared thyroid hormone action in these animals with that in wild-type mice or mice lacking thyroid hormone receptors entirely. They found that in vivo, several physiological actions of thyroid hormone—including regulation of body temperature, glucose and triglyceride concentrations in the blood, and heart rate—all appear to be mediated by noncanonical or nontranscriptional mechanisms.—LBR

BIOCATALYSIS
Guiding an enzyme all around a ring
Most compounds of interest for pharmaceuticals, agrochemicals, and cosmetics have many C–H bonds, interspersed with a few carbon bonds to heavier elements that give them their distinct properties. Chemists therefore prize methods that let them selectively modify a variety of C–H bonds. Gilbert et al. report a versatile strategy that relies on a tethered amine to steer an engineered cytochrome P450 enzyme around 11- or 12-membered rings, transforming specific C–H bonds into C–O bonds. Subtle structural variation of the tether through click chemistry tunes the site selectivity.—JSY

MINOR PLANETS
An object from beyond the solar system
Gravitational interactions occasionally eject small bodies from the solar system, and this process is thought to have been
**OCEANS**

**Beneath the waves, oxygen disappears**

As plastic waste pollutes the oceans and fish stocks decline, unseen below the surface another problem grows: deoxygenation. Breitburg et al. review the evidence for the downward trajectory of oxygen levels in increasing areas of the open ocean and coastal waters. Rising nutrient loads coupled with climate change—each resulting from human activities—are changing ocean biogeochemistry and increasing oxygen consumption. This results in destabilization of sediments and fundamental shifts in the availability of key nutrients. In the short term, some compensatory effects may result in improvements in local fisheries, such as in places where stocks are squeezed between the surface and elevated oxygen minimum zones. In the longer term, these conditions are unsustainable and may result in ecosystem collapses, which ultimately will cause societal and economic harm. —CA

*Science, this issue p. 46*

**CELL BIOLOGY**

**Biophysical responses of proteins to stress**

Much recent work has focused on liquid-liquid phase separation as a cellular response to changing physicochemical conditions. Because phase separation responds critically to small changes in conditions such as pH, temperature, or salt, it is in principle an ideal way for a cell to measure and respond to changes in the environment. Small pH changes could, for instance, induce phase separation of compartments that store, protect, or inactivate proteins. Franzmann et al. used the yeast translation termination factor Sup35 as a model for a phase separation–induced stress response. Lowering the pH induced liquid-liquid phase separation of Sup35. The resulting liquid compartments subsequently hardened into gels, which sequestered the termination factor. Raising the pH triggered dissolution of the gels, concomitant with translation restart. Protecting Sup35 in gels could provide a fitness advantage to recovering yeast cells that must restart the translation machinery after stress. —SMH

*Science, this issue p. 47*

**MALARIA**

**Vivax malaria host receptor**

Human malaria is caused by half a dozen species of *Plasmodium* protozoan parasites, each with distinctive biology. *P. vivax*, which causes relapsing malaria, specifically parasitizes immature red blood cells called reticulocytes. Gruszczyk et al. identified TR1 (host transferrin receptor 1) as an alternative receptor for *P. vivax*. TR1 binds to a specific *P. vivax* surface protein. However, the parasite that causes cerebral malaria, *P. falciparum*, does not share TR1 as a receptor: *P. falciparum* could still infect cells in which TR1 expression was knocked down, but *P. vivax* could not. Monoclonal antibodies to the *P. vivax* protein successfully hindered *P. vivax* infection of red blood cells. —CA

*Science, this issue p. 48*

**COMPARATIVE GENOMICS**

**Examining the consequences of selfing**

The *Caenorhabditis* genus of nematodes includes a mix of closely related outcrossing and self-fertilizing (selfing) species. Genome size differs widely among these different species. Yin et al. generated a genome assembly for the outcrossing nemate *C. nigonii* and compared it with that of its close relative, the selfing *C. briggae*. *C. briggae* has experienced a substantial decrease in genome size since the two species’ recent divergence. The underlying causes of this size difference appear to involve a decrease in protein-coding genes and changes in other types of sequences that have homology with RNAs expressed primarily in *C. nigonii* males. One of the implicated gene families, the mss family, compromises sperm competitiveness. Thus, in nematodes, selfing appears to result in a decrease in genome size owing to selection to reduce male reproductive function. —LMZ

*Science, this issue p. 55*

**STELLAR ASTROPHYSICS**

**Observing more massive stars**

The number of stars that form at each mass is known as the initial mass function (IMF). For most masses, the IMF follows a power-law distribution, first determined by Edwin Salpeter in 1955. Schneider et al. used observations of the nearby star-forming region 30 Doradus (also known as the Tarantula Nebula) and combined these with stellar modeling to determine its IMF. They found more stars above 30 solar masses than predicted by the Salpeter distribution. Because the most massive stars also have the biggest influence on their surroundings—for instance, through ultraviolet radiation, stellar winds, supernova explosions, and production of heavy elements—this excess will have wide-ranging implications. —KTS

*Science, this issue p. 69*

**POLYMERS**

**A healing squeeze**

The very long molecules found in synthetic polymers, and their tendency to entangle and partially crystallize, impart many of the polymers’ useful properties. However, these same characteristics also mean that chain dynamics are slow, which impedes potential self-healing. Yanagisawa et al. developed a family of ether-thiourea linear polymers that form hydrogen-bonded networks and still manage to stay amorphous. The polymers are stiff, showing the strength of the hydrogen bonding; however, because these bonds can easily reform, the polymer is also able to self-heal when compressed. —MSL

*Science, this issue p. 72*

**HIV SUSCEPTIBILITY**

**Inhibiting natural killer cells in AIDS**

The human leukocyte antigen (HLA) gene complex varies enormously among individuals and helps explain individual variation in immunity to infectious diseases. Ransur et al. examined data from almost 10,000 HIV infections. Expression of the HLA-A and -B alleles was associated with higher viral load, reduced CD4+ T cell counts, and accelerated progression to AIDS. Higher levels of HLA-A expression increased expression of HLA-E, which blocks a specific receptor (NKG2A) on the immune cells that normally eliminate virus-infected cells. Thus, targeting NKG2A might provide a therapeutic avenue for HIV treatment. —CA

*Science, this issue p. 86*

**ECOLOGICAL GENOMICS**

**Yellow warblers already in decline**

As the climate changes, species’ ability to adapt to changing conditions may relate directly to their future persistence. Determining whether and when this will happen is challenging, however, because it is difficult to tease apart the causes of decline or maintenance. Bay et al. looked at the relationship...
between genomic variation and the environment in North American populations of the yellow warbler (see the Perspective by Fitzpatrick and Edelsparre). Genes linked to exploratory and migratory behavior were important for successful climate adaptation. Furthermore, populations identified as “genetically vulnerable” because of limited climate-associated genomic variation were already declining. —SNV

Science, this issue p. 83; see also p. 29

IMMUNOLOGY

Inflammatory ILC2s are itinerant sentinels

Group 2 innate lymphoid cells (ILC2s) are a population of immune cells that play important roles in tissue homeostasis and barrier immunity to helminths. Recent work has suggested that ILC2s are primarily long-term residents of tissues that do not readily recirculate. Huang et al. now demonstrate, however, that these findings do not necessarily hold true for the interleukin-25 (IL-25)–responsive KLRG1− “inflammatory” ILC2 (iILC2) subset (see the Perspective by Mjosberg and Rao). In response to exogenous IL-25 or helminth infection, iILC2 precursors in the small intestinal lamina propria proliferate and alter their expression of sphingosine 1-phosphate (S1P) receptors. They then traffic to both lymphatic and nonlymphatic organs in a partly S1P-dependent manner, participating in vital anti-helminth and tissue repair responses. —STS

Science, this issue p. 114; see also p. 36

HUMAN IMMUNOLOGY

Taking a look at lipid surveillance

Human group 2 innate lymphoid cells (ILC2s) play roles in maintaining homeostasis and defending against pathogens, but dysregulated ILC2 responses have been linked to asthma and allergic responses. Hardman et al. used an in vivo human skin challenge model to show that ILC2s express CD1a, which is regulated by the cytokine TSLP. CD1a+ ILC2s can present endogenous lipid antigens to CD1a-reactive T cells and induce inflammatory responses. CD1a+ ILC2s expressed the phospholipase PLA2G4A, contributing to CD1a-mediated T cell activation.

This pathway was involved in sensing Staphylococcus aureus–associated skin inflammation. Thus, lipid sensing by skin-resident ILC2s may contribute to atopic skin inflammation and pathogen surveillance. —CNF


CANCER IMMUNOTHERAPY

Taking aim at regulatory T cells

Cancer immunotherapy attempts to stimulate the patient’s immune system against a tumor, but it can be limited by the suppressive effects of the patient’s own regulatory T (Treg) cells. Nie et al. showed that coinhibiting a TNF (tumor necrosis factor) receptor reduced Treg cell activity and proliferation, stimulated antitumor immune memory, and even shrunk colon and breast tumors in mice that were unresponsive to common single-agent immunotherapies. Thus, adding anti-TNF therapeutics may help to increase and broaden the efficacy of immunotherapy for cancer patients. —LKF


OCEANS

To mine or not to mine

The seafloor contains large amounts of valuable minerals that are increasingly seen as viable mining targets. In a Perspective, Boetius and Haeckel argue that such mining would carry large environmental risks—for example, to little-known ecological communities in the deep sea. Mining impacts in such environments would be difficult and expensive to remediate, and research knowledge from small-scale experiments is difficult to extrapolate to the commercial scale. The authors call for an integrated research and regulatory framework that protects the seafloor. —JFU

Science, this issue p. 34

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