NEURODEVELOPMENT

Versatile embryonic neural crest cells

Embryonic neural crest cells carry subspecialties that are defined but malleable. — PJH

Science, this issue p. 1570

BIOCHEMISTRY

Making error-free DNA from RNA

DNA polymerase enzymes copy DNA into new strands of identical DNA. Reverse transcriptase (RT) enzymes copy RNA into DNA. Unlike many DNA polymerases, RT enzymes do not have a proofreading function that checks for errors in the newly synthesized DNA. Ellefson et al. use in vitro directed evolution and protein engineering to build an error-correcting RT from a prokaryotic DNA polymerase.

The RT “xenopolymerase” shows increased fidelity as compared to natural RTs and should streamline and increase the precision of transcriptomics methods. — GR

Science, this issue p. 1590

QUANTUM INFORMATION

How to single out the right atoms

For a quantum computer to be useful, its qubits have to be able to change their state in response to external stimuli. But when a large number of qubits are packed in a three-dimensional (3D) structure to optimize the use of space, altering one qubit can unintentionally change the state of others. Wang et al. devised a clever way to perform high-fidelity quantum gates only on intended qubits in a 3D array of Cs atoms. Although the operation initially changed the state of some of the other atoms, additional manipulation recovered their original state. The technique may be applicable to other quantum computing implementations. — JS

Science, this issue p. 1562

INNER IMMUNITY

Mounting the intestinal barricades

Gut microbiota are important for health and well-being, but they need to be kept under control and prevented from doing any harm. Birchennough et al. investigated the microbial molecules that trigger protective mucus secretion from a class of goblet cells in the colon. Once the molecules are detected, an alarm signal is transmitted from these cells via innate immune signal mediators and inflammasome components to adjacent cells, generating more mucus and repelling the invaders. Subsequently, the sentinel goblet cells are expelled from the epithelium and their remains may also add to the protective barricade. — CA

Science, this issue p. 1535

STRUCTURAL BIOLOGY

Holding kinases at the ready

About 60% of kinases only reach their active state in the presence of the molecular chaperone Hsp90 and its co-chaperone Cdc37. It is unclear how the chaperones facilitate kinase function or why only some kinases are chaperone-dependent. Verba et al. determined a 3.9 Å cryo–electron microscopy structure of Hsp90:Cdc37 in complex with the kinase Cdk4. Together, Hsp90 and Cdc37 trap the kinase in an open, partially unfolded state. Taking on this state probably has direct functional benefits. — VV

Science, this issue p. 1542
ORGANIC CHEMISTRY

Catalysis gets all tied up in knots

Over the past decade, chemists have used metal ion templating to prepare a wide variety of knotted molecular strands. Marcos et al. now show that one such pentafoil knot can be applied to catalysis. When held taut by zinc ions, the knot can capture a chloride or bromide ion from a halocarbon, thereby unleashing the reactivity of the residual cation for applications such as Lewis acid catalysis. Removing the zinc ions lowers the knot’s affinity for the halides, offering a reversible modulation mechanism for the catalysis. — JSY

Science, this issue p. 1555

NANOMATERIALS

Multimetal nanoparticle synthesis

Multicomponent nanoparticles can be difficult to synthesize. Rather than mixing in one type of particle, the compounds often separate and form distinct particles. Using dip-pen lithography, Chen et al. show how adding reactants to very small volumes forces the reactants to form single particles containing various combinations of five different transition metal ions. Scanning transmission electron microscopy and energy-dispersive x-ray spectroscopy revealed the shapes of the nanoparticles and how metallic composition varied within them. For example, the quinary particle containing gold, silver, cobalt, copper, and nickel consisted of three domains of binary alloys. — PDS

Science, this issue p. 1565

PHYSICS

A partially protected surface state

A signature feature of topological insulators is conductive surface states that are immune to certain types of disorder. This “topological protection” appears to be at work in compounds such as Bi$_2$Se$_3$ in which electrons interact with one another only weakly. Whether these protected surface states exist in SmB$_6$, a material whose insulating bulk is caused by strong electronic correlations, is still a subject of debate. Park et al. used a tunneling technique to find states on the surface of SmB$_6$ that appeared to have the same linear dispersion as those in Bi$_2$Se$_3$ but were only partially protected. The loss of protection was caused by

IN OTHER JOURNALS

Edited by Kristen Mueller and Jesse Smith

CYSTIC FIBROSIS

Mini-guts for testing drug therapy

Cystic fibrosis is caused by mutations in the CFTR gene, which reduce the function of the CFTR protein. New drugs for treating cystic fibrosis modulate CFTR protein function, but drug efficacy is dependent on which CFTR mutation a patient carries. Dekkers et al. show that the efficacy of these drugs can be individually assessed using epithelial cells cultured as mini-guts from rectal biopsies from cystic fibrosis patients. The drug response observed in these rectal organoids can help predict which patients may be potential responders to the drug. This preclinical test may help to quickly identify responders to CFTR-modulating drug therapy, even when patients carry very rare CFTR mutations. — OMS


IMMUNOLOGY

Nanoparticles restore tolerance

Autoimmune diseases, such as type 1 diabetes, are caused by immune cells attacking healthy cells. One way to treat type 1 diabetes is to activate T regulatory (T$_{reg}$) cells to suppress inflammatory T cell activity and restore tolerance, so that the inflammatory T cells stop destroying pancreatic β cells. Yeste et al. used gold nanoparticles to induce tolerance in a mouse model of type 1 diabetes. The mice had more T$_{reg}$ cells and less severe disease symptoms when given nanoparticles coated with proteins that induced tolerance. Nanoparticle-based therapies may be useful in restoring tolerance in other autoimmune diseases as well. — JFF


INFECTIONOUS DISEASE

Disease information-seeking behavior

Chickenpox is usually a mild disease of children and, consequently, national vaccination and reporting policies vary widely. In countries that do not immunize against chickenpox, Google Trends recorded a strong seasonal signal in search behavior for information about chickenpox. Tellingly, Bakker et al. found that the seasonal search signal reverses between the Southern and Northern Hemispheres and declines when a country mandates vaccination. Thus, Google data allow for monitoring of an underreported viral infection, forecasting outbreaks and measuring the impact of immunization for chickenpox, and perhaps also for other seasonal childhood infections. — CA


Google Trends data allow for monitoring of disease outbreaks.
DISTANT GALAXIES
Shining brightly in the early universe
Galaxies that formed early in the history of the universe were powerful sources of ultraviolet radiation. This radiation ionized the surrounding intergalactic medium during the “epoch of reionization,” Inoue et al. detected atomic emission lines from a galaxy at high redshift—seen as it was when the universe was only ~5% of its current age (see the Perspective by De Breuck). Data from optical, infrared, and submillimeter observatories determined its gas and dust content and the amount of ultraviolet radiation it emitted. Studying similar galaxies in such a manner will allow astronomers to determine how the first galaxies formed, evolved, and influenced their surroundings. — KTS

DNA NANOTECHNOLOGY
Simplifying DNA origami design
Many intricate nanostructures have been made with DNA origami. This process occurs when a long DNA scaffold develops a particular shape after hybridization with short staple strands. Most designs, however, require a difficult iterative procedure of refining the base pairing. Veneziano et al. now report algorithms that automate the design of arbitrary DNA wireframe structures. Synthesizing and structurally characterizing a variety of nanostructures allowed for verification of the algorithms’ accuracy. — PDS

MICROBIOTA
Gut microbiota and undernutrition
Poor nutrition during the early years of life can have severe consequences for subsequent skeletal, immunological, and intellectual development. Blanton et al. review the evidence showing that undernutrition is not caused by food insecurity alone. Other factors range from the length of the breastfeeding period and the availability of milk oligosaccharides, enteropathogen exposure, and enteric dysfunction marked by villus atrophy and loss of gut barrier function. Unfortunately, nutritional restoration with or without antibiotic treatment may not be effective in the longer term. Differences in the succession of microbial establishment and maturity can explain much of family discordances in nutritional status. The evidence indicates that microbiota-directed therapeutics could be a promising route to nutritional restoration in these children. — CA

QUANTUM PHYSICS
Quantum enhanced metrology
Exploiting the quantum-mechanical properties of quantum systems offer the possibility of developing devices for enhanced precision measurement and sensing applications. These devices have, however, required low-noise detection capabilities that have hampered their development. Hosten et al. describe a method that manipulates a coherent cloud of cold rubidium atoms in a way that relaxes the ultrasensitive detection requirements. The general method may be applied to other coherent quantum systems. — ISO

CLIMATE CHANGE
Coming to a drought near you
Extreme weather events such as droughts and storms are rarely out of the headlines. Is climate change influencing their occurrence and severity? As Stott explains in a Perspective, researchers are now able to determine the contribution of climate change to individual extreme temperature events; for example, the extremely hot conditions in east China in 2013 have become 60 times more likely as a result of climate change. However, determining the contribution of climate change to extreme precipitation events remains difficult, in part because models capture rainfall extremes less accurately than they do temperature extremes. — JFU

OCEAN BIOLOGY
The microbial key to coral reef health
Coral reefs around the world are under threat from global warming, overfishing, and pollution. Ocean warming is particularly dangerous, causing bleaching that can lead to the death of the coral. In a Perspective, Ainsworth and Gates explains that the microbes associated with coral reefs are critical to reef survival. Corals that have more pathogenic bacteria are more likely to die after bleaching. The loss of beneficial bacteria has also been linked to the development of lesions and tissue necrosis in corals. If climate change leads to reefs with lower coral diversity, reduced microbial diversity is likely to result, making the reefs less resilient to further stress. — JFU

ORGANIC DEVICES
Mind the mobilities
The operational speed of devices such as transistors depends on how fast charge carriers move through their active semiconductor material. In a Perspective, McCulloch et al. discuss how several recent claims of very high carrier mobilities in organic semiconductors overstate the values by at least an order of magnitude. These indirect measurements based on the transistor devices themselves can be flawed because the modeling of the current flow is inadequate. — PDS

PROSTATE DEVELOPMENT
Clues to cancer from an identity change
The prostate and seminal vesicle have closely related developmental histories and both are regulated by the same androgenic hormones. A better understanding of the molecular mechanisms controlling the development of the two tissues could help solve why cancer arises frequently in the prostate but only rarely in seminal vesicles. Working with cell and mouse models, Dutta et al. show that forced expression of a single gene, the homeobox gene NKX3.1, causes seminal vesicle epithelium to differentiate into prostate. NKX3.1 regulates the expression of a gene program associated with prostate differentiation by interacting with the G9a histone methyltransferase. Disruption of this regulatory network probably contributes to prostate cancer development. — PAK

DRIVING ETHICS
Codes of conduct in autonomous vehicles
When it becomes possible to program decision-making based on moral principles into machines, will self-interest or the public good predominate? In a series of surveys, Bonnefon et al. found that even though participants approve of
autonomous vehicles that might sacrifice passengers to save others, respondents would prefer not to ride in such vehicles (see the Perspective by Greene). Respondents would also not approve regulations mandating self-sacrifice, and such regulations would make them less willing to buy an autonomous vehicle. — BJ

**MUCOSAL IMMUNOLOGY**

*Location matters for immunosuppression*

In the gut, food antigens and resident microbes can trigger unwanted immune responses. Immunosuppressive cell types in the gut, such as regulatory T cells (T_{regs}) and intraepithelial T lymphocytes (IELs), help to keep these responses at bay. Sujino et al. report that the specific anatomical location within the gut shapes the properties of the suppressive T cell populations that reside there (see the Perspective by Colonna and Cervantes-Barragan). Using mice, they find that T_{regs} primarily reside in the lamina propria. T_{regs} migrate to the intestinal epithelium, where they convert to IELs in a process that depends on the microbiota and the loss of a specific transcription factor. T_{regs} and IELs also play distinct but complementary roles in suppressing intestinal inflammation. — KLM

*Science, this issue p. 1581; see also p. 1515*

**POLYMERS**

*Highly branched polymers deliver*

Tantalizing promise, largely unfulfilled, haunts gene therapy for human disease. Among several barriers to success, efficient gene delivery to targeted cells remains daunting. Zhou et al. broke one barrier through the synthesis of a new class of delivery vector. The pathway results in the synthesis of highly branched poly(β-amino ester) (HPAE), using a one-pot Michael addition. The transfection efficiency of HPAE over existing vectors improved by as much as three orders of magnitude. Gene delivery by HPAE was able to correct a genetic defect in a recessive dystrophic epidermolysis bullosa graft mouse model. — PLY

*Sci. Adv. 10.1126.sciadv.1600102 (2016).*

**NEUROGENOMICS**

*Single-nucleus gene expression*

Identifying the genes expressed at the level of a single cell nucleus can better help us understand the human brain. Blue et al. developed a single-nuclei sequencing technique, which they applied to cells in classically defined Brodmann areas from a postmortem brain. Clustering of gene expression showed concordance with the area of origin and defining 16 neuronal subtypes. Both excitatory and inhibitory neuronal subtypes show regional variations that define distinct cortical areas and exhibit how gene expression clusters may distinguish between distinct cortical areas. This method opens the door to widespread sampling of the genes expressed in a diseased brain and other tissues of interest. — LMZ

*Science, this issue p. 1586*