EDITED BY GILBERT CHIN AND JAKE YESTON

IMMUNOLOGY

AID-ing Up MicroRNA Functions

MicroRNAs are key regulators of gene function, yet the full scope of their influence is not known. In the immune system, miR-155 has multiple roles, although B cells show a particular dependence on its effects. Two studies now provide evidence that this is largely due to its targeting of the enzyme activation-induced cytidine deaminase (AID), which regulates somatic hypermutation and class-switch recombination of antibody genes.

After identifying miR-155 response elements in the 3′ region of AID mRNA, Teng *et al.* designed constructs containing a reporter linked either to a functional AID locus or to one in which the miR-155 elements had been mutated. In the latter case, loss of the ability to respond to miR-155 led to increases in AID expression and class-switch recombination in stimulated B cells. In contrast, somatic hypermutation was unaffected, although affinity maturation was unexpectedly impaired. Dorsett *et al.* noted similar effects of mutations in the AID mRNA miR-155 binding site, which again corresponded with increased AID levels. A higher rate of AID-associated chromosomal translocations was also detected, suggesting that beyond its influence on normal B cell functions, this microRNA helps minimize potential oncogenic events. — SJS

Immunity **28**, 621; 630 (2008).

BIOMEDICINE

A Brush with Infection

The human mouth harbors a surprisingly diverse complement of bacteria. Although most are harmless, a subset—if they enter the bloodstream—are believed to cause a potentially life-threatening heart condition called infective endocarditis, especially in individuals with preexisting heart valve damage. For this reason, at-risk patients are often prescribed prophylactic antibiotics before invasive dental procedures such as tooth extraction. This practice has become increasingly controversial, however, both because of general concerns about the overuse of antibiotics and because the extent of bacteremia caused by tooth extraction has never been compared to that caused by other seemingly less traumatic activities, such as tooth brushing or mastication. Using 16*S* ribosomal RNA sequencing and quantitative polymerase chain reaction assays, Lockhart *et al*. profiled the bacteria in sequential blood samples drawn from patients who had undergone a tooth extraction with or without antibiotic treatment and from untreated patients who simply brushed their teeth. Thirty-two bacterial species that can cause infective endocarditis were identified in blood samples from patients after a tooth extraction and, as expected, antibiotic treatment significantly reduced their numbers. Surprisingly, brushing alone also caused a substantial increase in infective endocarditis–causing bacteria. Given that tooth brushing is a daily activity, the authors conclude that it could pose a risk for bacteremia comparable to that of a tooth extraction, thus underscoring the need for controlled clinical trials to evaluate current practices. — PAK

Circulation **117**, 3118 (2008).

CLIMATE SCIENCE

Charting Global Runoff

One widely expected potential consequence of climate warming is an intensification of the hydrological cycle, including more precipitation and more extreme precipitation events. Evidence that such intensification already has begun is available for some regions, but the question of whether or not the phenomenon is global remains unanswered. Milliman *et al.* have analyzed the runoff records of 137 rivers located on six continents, covering the last 50 years of the 20th century, in order to provide that answer. They find that global discharge has not changed significantly over that time, although regional changes were clearly apparent: Discharge decreases occurred disproportionately in Africa, Asia, and Australia, while Europe, North America, and South America experienced increases more often. Thus, the evidence seems not to show an intensification of the global hydrological cycle over the last half of the 20th century. That time period is too short, however, to draw firm conclusions about longer-term trends. — HJS

Global Planet. Change **62**, 187 (2008).

CHEMISTRY

Sensors with Sparkle

For sensing applications, diamond nanowires offer advantages in terms of stability, as well as the capacity for facile tailoring of electronic properties, both of the bulk material itself (through doping) and of the surface (through termination either with hydrogen or oxygen). Yang *et al*. have

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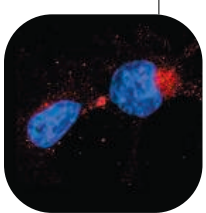
grown vertically aligned, boron-doped diamond nanowires at high density (3- to 10-nm-long wires spaced 11 nm apart) and anchored single-stranded DNA molecules to the ends via phenyl groups that were attached electrochemically. They found that the redox potentials and peak currents of the $[Fe(CN)_6]^{3-}/[Fe(CN)_6]^{4-}$ couple, as measured by cyclic voltammetry, are highly sensitive to DNA hybridization in this environment and can reveal single-base mismatches in the incoming strands being detected, with a 2-pM sensitivity limit. — PDS

Angew. Chem. Int. Ed. **47**, 10.1002/anie.200801706 (2008).

CELL BIOLOGY

Not So Identical Twins

During mitosis, somatic cells divide into two apparently identical daughter cells—but are they really the same? The production of nonidentical daughters occurs during differentiation when one daughter enters one developmental lineage while its sister remains a stem cell.



Catenin (red) in the nuclear bay of one daughter cell.

Fuentealba *et al*. see unequal inheritance even in divisions that had been thought to generate identical daughters; proteins destined for degradation, such as ubiquitinylated Smad1 transcription factor and phospho-β-catenin, were asymmetrically partitioned into one daughter. The process by which these proteins are preferentially inherited involves their microtubule-dependent association with peripheral centrosomal proteins, which is maintained through several rounds of division and in a variety of cell types. The unequal partitioning of misfolded and aggregated proteins in so-called aggresomes has already been observed, and this capacity for keeping one daughter free of defunct proteins may help to avoid a wholesale loss of cell populations if the load of such potentially damaging proteins becomes too great. — SMH

Proc. Natl. Acad. Sci. U.S.A. **105**, 7732 (2008).

GEOLOGY

Crust on the Move

Earth's plates move at speeds on the order of about 10 cm/year, so that over 100 million years, about 1000 km of ocean crust are consumed back into the mantle along every subduction zone. The mantle is about 2500 km thick, so some swirling, mixing, bending, and storage of these relic slabs are required over several billion years of plate tectonics. Some mantle volcanic rocks carry signatures of melting of old consumed ocean crust. Two seismic studies help clarify the fate of recently subducted crust through the upper half of the mantle. Li *et al.* provide an updated *P*-wave tomographic model of Earth's mantle, which reveals large-scale (>100 km) density variations. The geometry of subducted crust, which tends to be colder and denser than ambient mantle, varies: Slabs subducted eastward beneath North and South America appear to be visible to a depth of about 1200 km. The results confirm that some crust that subducted south of Japan is ponded at about 650 km in the mantle, a region of a major phase transition, but that subducted crust to the north and south has proceeded deeper. Separately, Courtier and Revenaugh show *S*-wave reflections from depths of >1000 km beneath North America and the South Pacific that probably map relic slabs there. — BH

Geochem. Geophys. Geosyst. **9**, 10.1029/2007GC001806 (2008); *J. Geophys. Res.* **113**, 10.1029/2007JB005261 (2008).

Science Signaling
AAAS

<< Receptor Rendezvous

B cell systems that protect organisms from viral infection walk a fine line because the molecules they detect—such as unmethylated DNA—can be derived from the host, and an overzealous defense results in autoimmune disease. Chaturvedi *et al*. describe how components of the adaptive and innate immune systems—B cell receptors (BCRs) and Toll-like receptor 9 (TLR9), respectively—act together to sense DNA-containing antigens. The answer was not obvious because BCRs are thought to act primarily on the cell surface, whereas TLR9 is normally present on endocytic vesicles. In mouse B cells in which the BCR was activated, TLR9 was relocated into autophagosomes. When cells were stimulated only through TLR9 with unmethylated DNA, p38 mitogen-activated protein kinase was detected only in endosomes. However, if the BCR was activated with an antibody to immunoglobulin M (alone or with DNA to activate TLR9), p38 was detected in large autophagosome-like structures. The recruitment of TLR9 to this compartment depended on physical internalization of the BCR, and activation of phospholipase D was also necessary. — LBR

Immunity **28**, 799 (2008).

CREDIT: FUENTEALBA *ET AL., PROC. NATL. ACAD. SCI. U.S.A.* **105**, 7732 (2008)

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