IMMUNOLOGY

Internal Indigestion

T cell–mediated responses to extracellular pathogens are initiated through a process called cross-presentation: Pathogens are internalized by dendritic cells via phagocytosis, partially degraded, and then presented on the cell surface by class I major histocompatibility molecules for recognition by cytotoxic T cells. Several immune cell types possess phagocytic capacity; in most cases, however, this leads to pathogen degradation. In contrast, dendritic cells that express CD8 are able to cross-present because of the low proteolytic activity and slightly alkaline pH of their phagosomes.

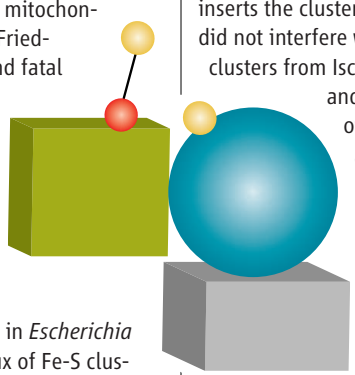
Savina *et al.* demonstrate that in contrast to non–cross-presenting dendritic cell subsets, $CD8^+$ dendritic cells assemble the NADPH oxidase complex (NOX_2) in their phagosomal membranes, which results in reactive oxygen species production and the maintenance of a high pH. Proper localization of a NOX_2 subunit to the phagosome was dependent on the small GTPase Rac2. In the absence of Rac2, NOX_2 did not assemble, high phagosomal pH was not maintained, and consequently, $CD8^+$ dendritic cells were not active in cross-presentation. These data provide a molecular rationale for why only particular subsets of phagocytes can trigger cytotoxic T cell responses to extracellular infections. — KLM

Immunity **30**, 10.1016/j.immuni.2009.01.013 (2009).

BIOCHEMISTRY

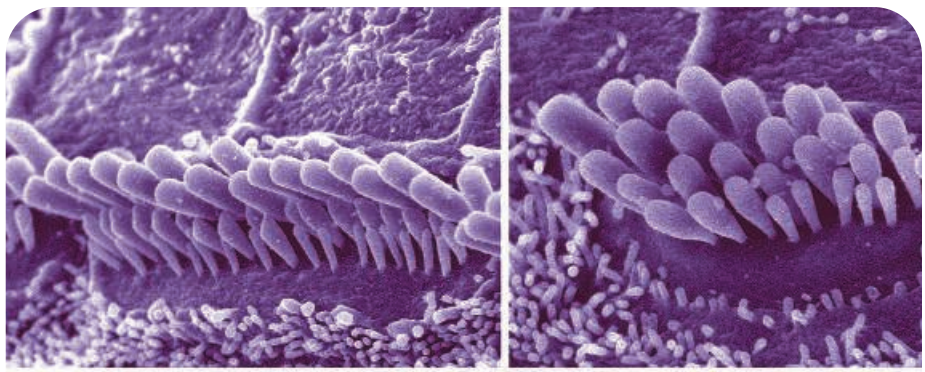
Matching Supply and Demand

In humans, a deficiency of the mitochondrial protein frataxin leads to Friedreich's ataxia, a progressive and fatal neurodegenerative disease. Frataxin has been implicated in heme metabolism and in the assembly of Fe-S clusters. In particular, it has been proposed to act as either an iron chaperone or an iron-storage protein.



Adinolfi *et al.* propose that in *Escherichia coli*, frataxin fine-tunes the flux of Fe-S cluster synthesis. Using absorbance and CD spectroscopy, they showed that the bacterial frataxin ortholog CyaY (green in the above schematic) inhibits the formation of Fe-S clusters on the scaffold protein IscU (gray). Clusters are synthesized on IscU when iron (red) combines with sulfur (yellow) that has been extracted from cysteine by the disulfurase IscS (blue); IscU then inserts the clusters into the final acceptors. CyaY did not interfere with the transfer of assembled clusters from IscU to the acceptor ferredoxin and also did not affect the ability of IscS to convert cysteine to alanine. Fluorescence and NMR data revealed that CyaY did not compete with IscU for binding to IscS and that the IscS-binding surface of CyaY mapped to its iron-binding region. Mutants designed to disrupt the iron-binding capacity of CyaY reduced its inhibitory effect. The authors suggest that frataxins are iron sensors that interact with the IscS-IscU system at high iron concentrations and restrict the supply of clusters in the absence of needy acceptors. — VV

Nat. Struct. Mol. Biol. **16**, 390 (2009).



MOLECULAR BIOLOGY

RNA Silencing

Progressive hearing loss is a common disorder that appears to arise from a diverse range of genetic mechanisms, probably reflecting the anatomical and functional complexity of the human ear. Two studies of mice and humans with hearing loss have converged on a pathogenic mutation that is distinct from the 50 previously characterized mutations in that it affects a small regulatory RNA rather than a protein-coding gene.

In a genetic screen for hearing-impaired mice, Lewis *et al.* identified a mutation that, when present in heterozygous form, caused abnormalities of inner and outer hair cells [sensory receptors in the ear that are critical for hearing; wild-type (left) and heterozygous (right) inner cells are shown above] and progressive hearing loss beginning when the mice were 4 to 6 weeks old. The mutation resides within the functional "seed" region of a microRNA called miR-96 that is expressed in hair cells and that, like other microRNAs, is presumed to bind to and alter the expression of protein-coding messenger RNAs. Supporting the causal role of miR-96 in hearing loss, Mencia *et al.* found that two Spanish families with inherited progressive hearing loss harbored mutations in the seed region of the same microRNA and that these mutations impaired the processing of the RNA to its mature form. — PAK

Nat. Genet. 10.1038/ng.369; 10.1038/ng.355 (2009).

DEVELOPMENT

Endoderm Induction

There is great interest in generating pluripotent stem cells that might be used in regenerative therapies. However, before such cells can be applied effectively, methods that enable the directed differentiation of stem cells into a desired cell type, such as endoderm cells for the treatment of type I diabetes, are needed. The biological signaling factors activin A and Nodal are known inducers of endoderm, but Borowiak *et al.* have set out to find small, cell-permeant molecules that could channel embryonic stem cells into an endodermal lineage. Starting with a collection of 4000 compounds,

CREDITS (TOP TO BOTTOM): AGNIESZKA RZADZINSKA, *NAT. GENET.* 10.1038/NG.369; 10.1038/NG.355 (2009); ADAPTED FROM *NAT. STRUCT. MOL. BIOL.* **16**, 390 (2009)

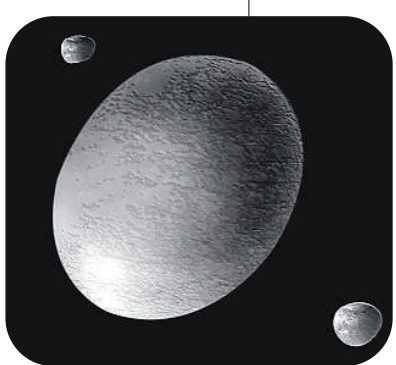
they identified 27 primary hits—chemicals that promoted the expression of an endodermal marker—and further narrowed this list by negative selection and the examination of cell morphology to 2. These heptanoic acid derivatives (IDE1 and IDE2) directed the differentiation of roughly 70 to 80% of mouse and human embryonic stem cells into definitive endoderm. IDE1 and IDE2 come from a library of histone deacetylase inhibitors and appear to act through activation of the TGF-β signaling pathway. — BAP

Cell Stem Cell **4**, 348 (2009).

ASTRONOMY

Icy Remnants

Like Pluto, the dwarf planet Haumea is one of the largest known Kuiper Belt objects that lie beyond the orbit of Neptune. It is thought to be the remnant of an even larger body, which fragmented as a result of a collision, leaving behind Haumea itself, its two moons, Hi'iaka and Namaka, and a cluster of smaller icy debris whose surface properties and orbits have been shown to match those of Haumea. Now Fraser and Brown have taken near-infrared images of Haumea and its two satellites (illustrated at right) with the Hubble Space Telescope. The data showed that, like Haumea, Hi'iaka and Namaka are peculiar Kuiper Belt objects in that they are covered in pure water ice, reinforcing the idea that they are fragments of the collision that formed the triple system. Had Haumea gravitationally captured its two satellites, their surfaces would not be expected to match that of the dwarf planet, because Kuiper Belt objects have a wide range of surface compositions. — MJC



CREDIT: NASA

Astrophys. J. **695**, L1 (2009).

CLIMATE SCIENCE

Dust in the Wind

The ice core record of the past 800,000 years shows that glacial periods tend to be cold and dry, with above-average amounts of wind-blown dust in the air. In Antarctica, for example, where most of the dust trapped in the ice comes from southern South America, the closest terrestrial neighbor to the cold continent, dust was deposited during the last glacial period at a rate between 20 and 50 times higher than today. That general pattern makes intuitive sense, but what was the cause of the elevated dustiness? Sugden *et al.* show that dust peaks in Antarctic ice cores from the last glacial period occurred when rivers of glacial meltwater deposited sediment directly onto outwash plains in Patagonia, where the dust was easily mobilized by the stronger glacial winds, and that they were absent when the glaciers terminated directly into pro-glacial lakes. These observations may help explain why dust concentrations in Antarctic ice decreased before the main phase of warming occurred in Antarctica, when sea level began to rise and Southern Hemisphere sea-ice extent started to shrink. — HJS

Nat. Geosci. **2**, 281 (2009).

CHEMISTRY

When Ceria Met Titania

Mixed metal oxides, especially of redox-active metals, can play an important role in catalysis. Both titanium oxide, or titania (TiO_2), and cerium oxide (ceria, CeO_2) are widely applied individually, often in tandem with lower–oxidation-state transition metals such as platinum, palladium, and gold. It has been largely unclear, however, how these two high-valent metal oxides might behave chemically in tandem with one another. Park *et al*. sought to answer this question. Specifically, they used a combination of scanning tunneling microscopy (STM), photoemission spectroscopy, and density functional theory (DFT) calculations to examine the structures that form when ceria nanoparticles are grown on the TiO_2 (110) surface; growth was induced by deposition of cerium atoms onto the surface, followed by annealing in oxygen. The STM images revealed a structure for the adsorbed ceria nanoparticles that was rather distinct from that seen for adsorption on metal surfaces—dimers run diagonally to the rows and troughs of the titania surface—and photoemission revealed a reduced Ce^{3+} oxidation state. DFT calculations were consistent with the formation of Ce_2O_3 dimers. When gold was co-deposited along with the cerium, a highly active catalyst for the water-gas–shift and CO oxidation reactions resulted; much more effective than gold deposited on either metal oxide surface alone. — PDS

Proc. Natl. Acad. Sci. U.S.A. **106**, 4975 (2009).

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