example of science relevant to society and human health at its best.” He also praises the editors of *Eukaryotic Cell* for rushing this “groundbreaking” paper into print, “greatly accelerating the dissemination of this key information such that it could be applied in clinical microbiology laboratories around the country.”

David C. Holzman is the Journal Highlights Editor for Microbe.

**RESEARCH ADVANCES**

**Newly Recognized Components in the Innate Immune Response**

Carol Potera

A newly recognized multiprotein complex plays a crucial role in recognizing one class of bacterial pathogens and then signaling other components of the innate immune system, according to Andreas Bäumler of the University of California, Davis (UCD), and his collaborators. These findings “considerably change our understanding of the mechanisms that trigger this pathway,” he says. Details appear in the April 11, 2013 *Nature* (doi:10.1038/nature12025).

The innate immune system depends on conserved pathogen-associated molecular patterns to distinguish between pathogens and harmless bacteria that colonize humans or other mammals. One such pattern, for example, is the presence of bacterial products in the cytoplasm of host cells, where they do not belong, according to Bäumler. How the innate immune system detects those patterns is “not fully resolved.”

“NOD1 senses cytosolic microbial products by monitoring the activation state of small Rho GTPases,” Bäumler and his collaborators now report. NOD1 is part of a host signaling pathway that activates necrosis factor (NF)-κB that, in turn, triggers inflammatory responses that are directed against pathogens. No one suspected that NOD1 “played such a significant role in activating the innate immune system independent of peptidoglycan,” he says, referring to the key component of bacterial cell walls.

To tease out the components of the innate immune system involved in responding to the pathogen *Salmonella typhimurium*, the UCD researchers tested a series of mutants in HeLa cells and in mice. The experiments with mutants of *S. typhimurium*, which lacked various specific proinflammatory effector proteins, helped to establish precisely which factors trigger NOD1 and then NF-κB. The experiments with *S. typhimurium*-infected mice showed that NOD1 is needed to produce intestinal inflammation in vivo.

Other enteric infections, such as those caused by *Yersinia pseudotuberculosis*, *Shigella*, *Acetobacter*, and *Escherichia coli*, produce toxins that likely target the same pathway, according to Bäumler. For example, when fruit flies encounter cytotoxic necrotizing factor 1, a toxin produced by uropathogenic *E. coli*, the innate immune system of the flies induces a protective response via a series of signaling proteins that resemble those that activate NF-κB in mammalian cells, he says, citing research by Lynda Stuart at Harvard Medical School in Boston, Mass., and her collaborators. “They basically made the same observation, but didn’t look for NOD1.” Plants also defend themselves against pathogens with similar mechanisms, described as the “guard hypothesis.”

“Mainstream mammalian immunologists are accepting the revolutionary idea of effector-triggered immunity,” Stuart says. “Convergent evolution has generated common strategies to sense pathogens that are universal across different taxa.”

NF-κB not only is part of the response to bacterial pathogens but also comes into play in chronic conditions such as colitis and arthritis. Inflammatory pathways “might be triggered erroneously because the host thinks there’s an infection,” Bäumler says. A better understanding of innate immune responses might lead to ways of tempering those inflammatory responses in those or other diseases.

Carol Potera is a freelance writer in Great Falls, Mont.

**RESEARCH ADVANCES**

**Membrane Proteins of *S. oneidensis* Transfer Electrons to Minerals**

Barry E. DiGregorio

Cytochrome proteins on the outer surface of *Shewanella oneidensis* bacteria interact directly with iron oxides in minerals to produce electrical currents, according to Thomas A. Clarke and David J. Richardson of the University of East Anglia in Norwich, United Kingdom, and their collaborators there.

**MINITOPIC**

**Two New Views of Critical Early Steps in Biofilm Development**

The DNA-binding protein, called SinR, of *Bacillus subtilis* acts as a central molecular switch, inhibiting expression of other proteins required for holding biofilms together, according to Richard Lewis of Newcastle University in Newcastle upon Tyne, United Kingdom. Details appear in the April 12, 2013 *Journal of Biological Chemistry* (288: 10766–10778). Meanwhile, according to Gerard Wong at the University of California, Los Angeles and his collaborators at Washington University in St. Louis, Mo., and Northwestern University in Evanston, Ill., *Pseudomonas aeruginosa* cells extrude specific polysaccharides that guide other nearby *P. aeruginosa* cells into forming microcolonies, which subsequently coalesce into biofilms. Details appear in the May 8, 2013 *Nature* (doi: 10.1038/nature12155).
GAO at Odds with Other Agencies over High-Containment Labs

National oversight is needed for high-containment laboratories to determine how many such labs are needed, to develop uniform standards for their design, and to decrease the likelihood of accidents, according to the March 2013 report “High-Containment Laboratories: Assessment of the Nation’s Need Is Missing,” from the Government Accountability Office (GAO). However, the National Security Advisor outright rejects some recommendations in this GAO report, particularly one calling for a “single entity” to oversee such labs, arguing that establishing such an entity “is not in the best interests of U.S. national security.” Additionally, the President’s Office of Science and Technology Policy said that the strategic evaluation of such labs that is recommended in the report would be “unnecessarily broad and cumbersome.” However, the GAO report concludes, not having such an assessment “hampers planning for existing and future research priorities and capacity of high-containment laboratories.”

MINITOPIC

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How metal-reducing microorganisms such as S. oneidensis and Geobacter transfer electrons to minerals was unsolved until now. Part of the riddle is very small, and a microbial fuel cell can very easily reduce minerals without the involvement of pili or shuttles.

To better understand how proteins within that complex behave, Clarke, Richardson, and their collaborators embedded its three proteins within a synthetic version of the outer membrane, called a proteoliposome. “Our model system uses the MtrCAB cytochrome complex as an electron transport system, replicating its role in the cell,” Clarke says. “This allowed us to show that the cytochromes on the cell surface could very easily reduce minerals without the involvement of pili or shuttles.”

Before this set of experiments, Clarke continues, “There was evidence that shuttles were secreted and could reduce minerals, and that the pili secreted by Geobacter and Shewanella are conductive.” However, no one realized that “the cytochromes that stud the surface of S. oneidensis interact directly with minerals.”

“The authors of the PNAS study prepared MtrCAB proteoliposomes containing several electron donors in their interior so they could study the kinetics of electron transfer across the MtrCAB complex from the inside to external iron oxide minerals,” says Gemma Reguera at Michigan State University in East Lansing, who also studies these microorganisms but was not involved in this research. “The beauty of their approach is that it is direct and it is performed in a controlled environment free of biological noise, thus minimizing bias.”

“The current produced by bacteria is very small, and a microbial fuel cell will not compete with a lithium oxide battery of the same size,” Clarke says, alluding to a key shortcoming for anyone hoping to harness these bacteria as a source for electricity. On the plus side, the bacteria “produce current over a very long period if there is a constant supply of nutrients.” Another plus, the bacteria are not “fussy” about what and where they send electrons, and alternative minerals might improve the overall output of electricity, he suggests. “We have looked at iron oxides in the first instance but plan to look at manganese minerals later on.”

Barry E. DiGregorio is a freelance writer in Middleport, N.Y.

RESEARCH ADVANCES
“Transcriptors,” Reliable Parts—Gateway to Programmable Cells?

Marcia Stone

Transcriptors, DNA-based versions of transistors, could make cellular computers commercially competitive, thanks in this case to Drew Endy and his fellow bioengineers at Stanford University in California. They and others in this field will benefit from having standardized DNA sequences or “parts” that can be reliably used and swapped from one experiment to the next, and one research group to another.

Both digital transistors and transcriptors amplify “on-off” switches—gates for information input, output, and storage. Like transistors, transcriptors respond to commands in the computer-based Boolean language. As proof of concept, when inserted into Escherichia coli, transcriptors instructed such cells to light up in different colors with encoded fluorescent proteins. Eventually bacteria will be programmed to perform more complex tasks using engineered circuits involving dozens or hundreds of genes, Endy says. Details appear in the May 3, 2013 Science (340:599–603). Transcriptors are available in the public domain at www.biobricks.org/bpa/.

Transcriptors introduce a system of logic and rules into cells already able to store and transmit information, according to Endy. If, for example, both enzyme A and B are inside a cell, a