MICROBIOLOGY

New Bacterial Defense Against Phage Invaders Identified

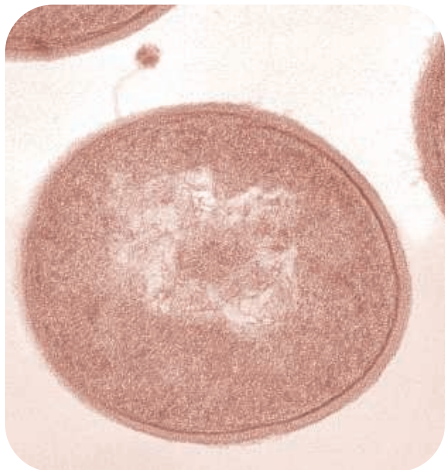
Humans are not alone in having to fend off pathogens; even the simplest organisms are under a constant threat of invasion. Bacteria, for example, are awash in a sea of viruses known as bacteriophages. "Every 2 days, half the bacteria on Earth are killed [by bacteriophages]," says phage expert Vincent Fischetti of Rockefeller University in New York City. "It's a constant battle." Researchers have now identified a new defense mechanism that helps bacteria hold their own in this battle.

On page 1709, a team led by Philippe Horvath and Rodolphe Barrangou of Danisco, a Danish company that produces bacterial cultures and other materials for the food-processing industry, reports that bacteria use a system, apparently akin to the RNA interference (RNAi) system of higher organisms, to block phage reproduction, thus making them resistant to infection.

The work could help the food and biotechnology industries, which use bacterial cultures to make products such as cheese and yogurt as well as proteins for human medicine. These industries, Fischetti says, "have a terrible problem with phage" ruining their cultures and could benefit from better phage-resistant bacterial strains.

The Danisco team's work also provides the first biological evidence for a function of so-called CRISPR sequences, which were identified in 2002 by Leo Schouls of the National Institute of Public Health in Bilthoven, the Netherlands, and his colleagues. These sequences, formally known by the descriptive name of "clustered regularly interspaced short palindromic repeats" because of the way they are arranged in the genome, are widely distributed in the genomes of both Bacteria and Archaea.

Accompanying the CRISPR sequences are a suite of perhaps four to 10 *cas* (*CRISPR-associated*) genes. Researchers have made a number of proposals about what these genes might do. For example, Eugene Koonin and Kira Makarova of the U.S. National Center for Biotechnology Information in Bethesda, Maryland, and their colleagues analyzed the *cas* sequences and, based on those structures, suggested in 2002 that they might encode a new DNA repair system. But more recently, Koonin says, another idea emerged as several groups found that the spacer sequences within CRISPR regions resemble those of sequences in phage and also in plasmids, small extrachromosomal pieces of DNA that can be transmitted between bacterial species.



Invasion. Bacteria such as this one may acquire key defensive sequences from infectious bacteriophage, attached at top.

In a second analysis, published by *Biology Direct* on 16 March of last year, Makarova, Koonin, and colleagues ▶

GEOLOGY

A Trace of the Earliest Plate Tectonics Turns Up in Greenland

Geologists have discovered the earliest known remnants—by billions of years—of plate tectonics, the large-scale movement of Earth's crust. The rocks are preserved in plain sight among the intensely studied ancient rocks of southwest Greenland, a group of geologists reports on page 1704. These days, hot new sea floor forms from magma at mid-ocean ridges, spreads away as it cools, and eventually dives back into the deep interior. In its early days, Earth was still so hot throughout that researchers have wondered whether the planet might have been ridding itself of heat by some entirely different means. But the new discovery "indicates there was a modern-day plate tectonics operating shortly after formation of Earth," says geologist Yildirim Dilek of Miami University in Oxford, Ohio.

Innumerable geologists have walked and flown over southwest Greenland's 12-kilometer-long stretch of baked, twisted, and tortured rock known as the Isua supracrustal belt. Dating from Earth's early adolescence 3.8 billion years ago, the Isua rocks hold clues to how the young planet worked, back when life might have gotten started. In fact, it was the search for microscopic signs of early life that brought geologist Harald Furnes of the University of Bergen, Norway, and colleagues to Isua in 2006. Furnes had long studied much younger scraps of ocean crust that had become stranded on land, called ophiolites, but that day he was looking for sea-floor lavas that might hold traces of ancient microbial borings.

Then Furnes and his colleagues came upon the sheeted dikes. These banded rocks are the hallmark of ophiolites and thus of sea-floor spreading. Built like a stack of cards, they are composed entirely of the thin sheets of once-molten rock injected into the crests of mid-ocean ridges as the newly formed plates spread away from the ridge. The Isua sheeted dikes are near previously identified components of ophiolites: distinctive "pillow" lavas extruded on the sea floor from underlying dikes, rock that solidified in magma chambers that fed the dikes, and never-melted mantle rock below that. "The major components [of an ophiolite] appear to be all there," says geologist Kent Condie of the New Mexico Institute of Mining and Technology in Socorro. "I'm convinced."

So Earth had sea-floor spreading almost 2 billion years earlier than previously known. What about the other end of the tectonic process? Today, old sea floor dives steeply into the deep interior on top of a relatively cold, rigid slab of tectonic plate, a process called subduction. But some geophysicists had suspected that old ocean plates might once have recycled themselves differently—say, by sinking straight into a hot magma mush as if it were quicksand.

Furnes thinks, but can't prove, that something like modern-day subduction was going on 3.8 billion years ago. Rocks adjacent to the Isua ophiolite geochemically resemble ▶

CREDIT: SYLVAIN MOINEAU

Published by AAAS

proposed that the Cas proteins and CRISPR spacer sequences, which were presumably picked up by the bacteria during prior phage infections, together constitute a bacterial immune system that works by a mechanism similar to that of RNAi in higher organisms. The idea is that the spacers make short RNA sequences that can bind to complementary sequences in messenger RNAs made by invading phages. This would block their translation into proteins and mark them for degradation by Cas proteins, some of which resemble those known to be involved in RNAi.

The Danisco group has now provided direct evidence for that hypothesis. Working with the bacterium *Streptococcus thermophilus*, which is widely used to make yogurt and cheese, the researchers found that infection of the bacteria with phage leads to incorporation of phage-related spacer sequences within a CRISPR region. Such bacteria became resistant to further infection by the phage strains that contributed those sequences. But "if you take the spacers out, the resistance is lost," says Horvath, who works at Danisco's lab in Dangé-Saint-Romain, France. The team also showed that at least one *cas* gene, which encodes a possible RNA-dicing nuclease, is necessary for the phage resistance. This shows, Fischetti says, that bacteria have "a very neat mechanism by which they are able to keep bacteriophage under control."

Dennis Romero, a member of the Danisco team at the company's lab in Madison, Wisconsin, says that the CRISPR system may have a wider function as well. "In addition to matching phage, the spacers also match chromosomal and plasmid sequences," he notes, and thus they might help control normal bacterial gene activity.

Whether or not that is the case, the findings open the door to using the CRISPR system to block specific gene activity in bacteria, just as RNAi is used in higher organisms. And then there is the possibility of producing more phage-resistant bacterial strains for industrial use. This could be accomplished by genetically engineering bacteria with appropriate CRISPR spacer sequences; Horvath says, however, that "Danisco has no plans to do that in light of consumer concerns about the use of GMO [genetically modified organisms], particularly in Europe."

The researchers plan instead to simply expose bacteria to various phage strains and then select for those that are resistant. They can, however, use their knowledge of the CRISPR spacers to help screen for bacteria that carry the right spacers to confer the resistance they want. "Although we can genetically engineer," Romero says, "we found that nature can do the work for us."

–JEAN MARX

Signature rock. Vertically layered rock discovered in Greenland confirms plate tectonics on early Earth.

CREDIT: H. FURNES *ET AL.*, *SCIENCE*

rocks called boninites. These rocks are cooked up only beneath island chains perched over subduction zones like those in today's western Pacific. If Isua has bona fide boninites, a magma mush would not work.

All the Isua rocks come from "a pretty well established subduction zone similar to what we have today," concludes Dilek. "They're hard to explain in any other way." Condie can't quite agree. "I don't think it's 100% definitive," he says. "There's just enough ambiguity that it may or may not" have been entirely modern subduction. Enough ambiguity that Isua geologists will be heading back to the field with new eyes this summer.

–RICHARD A. KERR

New Strategy to Fight AIDS

PRETORIA, SOUTH AFRICA—A new government plan aims to cut South Africa's HIV infection rate in half and to quadruple the number of infected persons receiving antiretroviral (ARV) therapy by 2011. The 5-year strategy, presented at a conference last week, sets targets to meet the commitments made by South Africa's vice president in December (*Science*, 1 December 2006, p. 1378). The government will ask Parliament for nearly $2 billion, about 40% of which would pay for ARV medications, and wants business donors to match that sum. Francois Venter, head of the Southern African HIV Clinicians Society, estimates that "more than a million" South Africans would be on ARVs in 5 years if the plan is fully implemented.

About 5.5 million South Africans are infected by HIV, and roughly 230,000 now receive ARV therapy. Robin Wood, co-director of the Desmond Tutu HIV Centre in Cape Town, calls the plan "a great advance." Although the goal may be difficult to reach, he says, "it's better to set targets too high than to have no targets."

–ROBERT KOENIG

Purdue Welcomes Mann Institute

Purdue University in West Lafayette, Indiana, has clinched a deal to join what the Alfred Mann Foundation hopes will be a billion-dollar-plus network to shepherd university biomedical inventions to the market.

Alfred Mann institutes are designed to be governed by a board equally split between the university and the California-based Mann Foundation. Some universities have balked at the proposed arrangement, fearing a loss of control over their intellectual property. Last year, two North Carolina universities turned thumbs down on a Mann endowment (*Science*, 26 May 2006, p. 1127), although Mark Crowell, technology transfer official at the University of North Carolina, Chapel Hill, says the door is still open to negotiations.

One provision gives priority to Indiana companies in licensing or purchasing technologies developed at the institute. Purdue President Martin Jischke won't discuss other details of the agreement, announced 16 March, but says everyone's very happy with it. Mann intends to finance at least 10 more institutes. A prototype was set up in 1998 at the University of Southern California in Los Angeles, and a second was created last October at Technion University in Israel.

–CONSTANCE HOLDEN

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