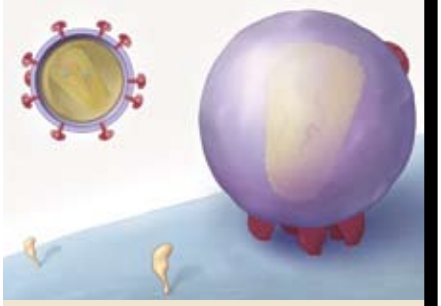
OCTOBER 2008

Notebook



TOP: COURTESY OF PUBLIC LIBRARY OF SCIENCE RIGHT: © KAZUHIKO KUROSAWA

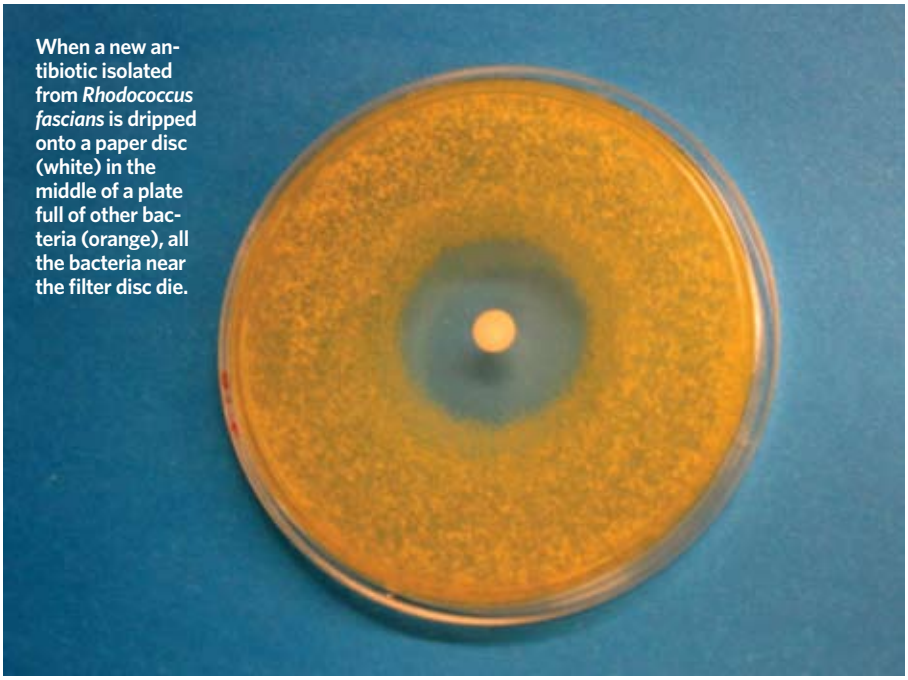
THE AGENDA

GOT VIRUS, NO VACCINE » If you've got viruses on the brain – thanks to Ari Hellenius's research using viruses (p. 46) and the Hot Paper on HIV (p. 57) – tune in to the AIDS Vaccine 2008 meeting in Cape Town, South Africa, Oct. 13–16. If you can't go there yourself, check out the conference Web site (http://tinyurl.com/55kf6b) for information about speakers, including Lawrence Corey and Robert Gallo.

GOT DEVICE, NO MONEY » Do you have a medical device, but not enough investors? Attend the first Medical Device Investor Day on Oct. 22 in Boston. After a keynote address from David Cassak of Windhover Information (in our feature on medical devices, p. 32), you'll hear from 15 investors about what they're looking for (http://tinyurl.com/5nhuns).

GOT SPOTLIGHT, NO US VISA » It's the 25th anniversary of the Orphan Drug Act (p. 67), and rare diseases are getting a lot of attention. Europe, too, is hosting several conferences this month about the diseases, including osteogenesis imperfecta and Rett Syndrome, in Rome, Paris, Warsaw, and Ghent. For more, visit: http://tinyurl.com/5lmgdh.

GOT WORK, NO ONE TO DO IT » After finding out if contract research organizations (CROs) are a good fit for you (p. 70), head on over to Frankfurt, Germany, for a global exhibition on pharmaceutical outsourcing: The 2008 International Contract Services Expo, Sept. 30 through Oct. 2. Now in its 8th year, the ICSE is a meeting place for pharmaceutical companies and the agencies to which they are looking to outsource (www.icsexpo.com/).



When a new antibiotic isolated from *Rhodococcus fascians* is dripped onto a paper disc (white) in the middle of a plate full of other bacteria (orange), all the bacteria near the filter disc die.

Bacteria Gladiators

Kazuhiko Kurosawa was running out of variables. For eight months he had made hundreds of cultures of *Rhodococcus fascians* – manipulating pH, temperature, salt concentration, media type, oxygen levels, even degree of agitation – each time attempting to provoke the bacteria into transcribing a set of genes he knew lay dormant in its genome. But the soil-dwelling bacteria remained recalcitrant.

Anthony Sinskey's lab at Massachusetts Institute of Technology, which Kurosawa joined in 2003, first became interested in *Rhodococcus* while in collaboration with Merck. The company hoped to use the bacteria to more efficiently make a precursor for one of its HIV protease inhibitors, Crixivan. While analyzing the *Rhodococcus* genome, the MIT researchers were surprised to find close to 100 genes for nonribosomal peptides, and 30 clusters of genes for polyketides, two major classes of antibiotics. But unlike most other soil-dwelling bacteria, *Rhodococcus* was not known to produce an antibiotic. Finding the genes "was like Christmas morning," says Philip Lessard, one of the investigators. Unfortunately, he adds, there appeared to be "some assembly required."

However, Sinskey's funding was wrapped up in the lab's main projects. So in 2004 Kurosawa embarked on an "under-the-table study" to provoke one species of the bacteria, *Rhodococcus fascians*, into using those genes, he recounts in an E-mail. (Despite the need for new antibiotics, Lessard says funding for new antibiotics is often hard to come by because of the availability of cheap and still-effective front line antibiotics like penicillin and ampicillin.) Lessard recalls every roller in the lab constantly drumming with Kurosawa's cultures. After the two researchers ran out of variables to test, they took a hint from nature and decided to introduce *R. fascians* to an environmental hazard it had yet to confront in the lab—other bacteria. ▶

In the wild, *R. fascians* lives in soil populated by thousands of microbes. The researchers planned a "kindergarten" version of the scenario, Lessard says, pitting *R. fascians* against just one other bacterium – a strain of *Streptomyces padanus*, an aggressive antibiotic producer that Kurosawa isolated from the soil in a flowerpot by his lab bench.

Initially, however, they overshot the mark. "*Streptomyces* really did kill everything," says Lessard. But one day Kurosawa approached Lessard holding a plate on which the *Streptomyces* had been wiped out. Lessard, who now works for Agrivida, an agricultural biotech (and retains no patents on the antibiotic), was skeptical—the plate was probably contaminated, he reasoned. But Kurosawa didn't think so. By sequencing the genes encoding ribosomal RNA of the bacteria left on the plate, he proved it was the original strain of *R. fascians*. Then, Kurosawa used high performance liquid chromatography (HPLC) to analyze the secreted substance, and became "full of confidence" that the bacteria were producing an antibiotic, he recalls. The eager biologist reported his results at a lab meeting in April of 2005. "Prof. Sinskey said, 'No one believes that. Kazu, you should isolate the antibiotic and elucidate the molecule.'"

It took a year of "painfully tedious" work to purify the secreted antibiotic, recalls Kurosawa, still based at MIT (where this author studied journalism). He relied on the other labs to do NMR structural studies of the molecule in their spare time. The molecule turned out to be an aminoglycoside (*J Am Chem Soc*, 130:1126–7, 2008). When tested for antimicrobial activity, it proved particularly effective against *Heliobacter pylori*, a bacteria that causes stomach ulcers in humans.

But there was a mystery. Pulse field gel electrophoresis revealed a strange chunk of DNA in the *R. fascians* genome, about 150 genes that did not exist in the parent strain. Analysis of a tiny extract showed it belonged to *Streptomyces*. And "in every case we've looked," adds Lessard, "the loss of the ability to make the antibiotic correlates with the loss of this DNA element." In the end, *R. fascians* may never have actually used the antibiotic-coding genes that prompted the research in the first place. But do the *Streptomyces* genes encode the antibiotic, or simply provoke *R. fascians* into making it? The project "was a success followed by ten unknowns," says Lessard.

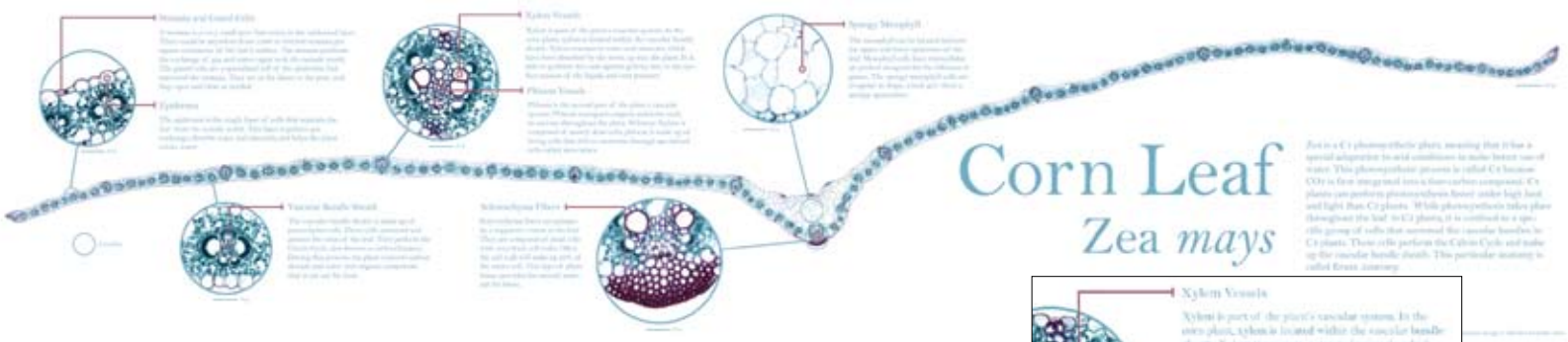
—Megan Scudellari

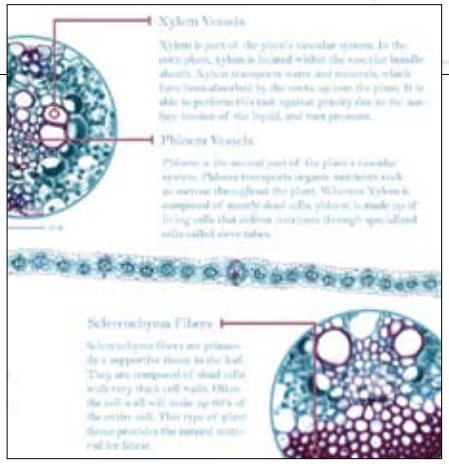
Pimp my poster

Colin Purrington hates most poster presentations, although he doesn't want to. About 10 years ago, Purrington, an evolutionary biologist at Swarthmore College in Pennsylvania, created a Web site offering tips for how to make more successful posters. The tips run from the practical (using a Photoshop plug-in to test how a poster will look to colleagues with color-vision deficiencies) to the innovative (recording a message or audio sample onto one of the recordable cards available at drug stores and then affixing the card onto a poster). He also started a group on the photo-sharing site Flickr called "Pimp My Poster," where scientists can submit their posters and get instant feedback.

On a rainy evening last May, a group of about 25 researchers gathered in a small meeting room at Columbia University to hear Purrington talk about how to make their posters better. One of the first questions that came up was: How did posters become so uninspired? Purrington blames two culprits: PowerPoint and the poster printer. "PowerPoint was never designed for making posters," he explains. He prefers the text and image capabilities of Adobe's InDesign program.

One of Purrington's biggest problems with PowerPoint is that, as presentation software, it's not conducive to printing. Printing can be expensive – usually around $50 per poster – which Purrington says makes researchers fearful of trying out new ideas that may lead to mistakes. He suggests incorporating high-tech elements, such as audio and video clips (e.g., bird calls), or software-generated 3-D images for people working with structural chemistry, complete with 3-D glasses for each viewer. Attach an iPod with Velcro, and you have another source of audio and video. ▶





A poster illustrating anatomy and photosynthesis in corn, by Michael Franklin, Rochester Institute of Technology, on Purrington's Flickr page.

COURTESY OF MICHAEL FRANKLIN / ROCHESTER INSTITUTE OF TECHNOLOGY