CRISPR sequences also might be used to protect valuable cultures of bacteria, including those used for making cheese and yogurt, from predatory viruses or undesirable genetic material, according to Barrangou. “There is a great risk of phage attack in large industrial fermentation processes,” he says. To protect against such damage, CRISPR sequences could be engineered into starter cultures, or bacterial strains could be selected on the basis of their CRISPR robustness. “CRISPR is a hot topic with lots of interest across many countries,” he says.

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Cecropin-Producing Tomatoes Resist Bacterial Wilt, Spot

As part of an effort to fight several bacterial diseases that can lead to 10% losses of tomato crops, researchers from the Republic of China on Taiwan moved genes encoding the antibacterial cecropin B peptides from lepidoptera into tomatoes. The resulting transgenic tomatoes now show resistance to two key diseases, namely bacterial wilt and spot, according to Hueih-Min Chen of National Nano Device Laboratories in Hsinchu, Taiwan, and his collaborators. Details of the research appear in the February Applied and Environmental Microbiology (76:769–775).

“Twenty-five percent of all crops are destroyed by disease,” says Robert Hancock of the University of British Columbia in Vancouver, Canada. Wilt and spot, caused by the gram-negative pathogens \textit{Ralstonia solanacearum} and \textit{Xanthomonas campestris} pv. vesicatoria, respectively, are particularly costly for tomato growers. Moreover, pesticides are largely ineffective against these diseases, particularly \textit{X. campestris}-caused spot.

Chen and his collaborators found that, at low concentrations, the positively charged, 31-to-39-amino-acid cecropins, which derive from the giant cecropia moth, exhibit lytic antibacterial activity against a number of gram-negative and some gram-positive bacteria, whose membranes are negatively charged, but not against eukaryotic cells, which have neutral membranes.

Thus, for example, extracts of cecropin B expressed in the transgenic tomatoes showed broad-spectrum antimicrobial activity, according to Chen and collaborators. Moreover, the transgenic tomatoes are resistant to the two bacterial diseases, he says. Their work arises from general Taiwanese efforts to promote the transformation of antibacterial peptide genes into crops of global importance, through the Taiwan National Science and Technology Program for Agricultural Biotechnology, and a foundation, the Development Program of Industrialization for Agricultural Biotechnology.

Ironically, however, that apparent resistance to \textit{Ralstonia} probably results from the transgenic peptides acting as immunomodulators, rather than from their antibacterial activity, according to Hancock. “\textit{Ralstonia} is almost completely resistant to cationic peptides,” he says. “We’ve done a bunch of studies showing that different [antimicrobial] peptides work in plants—primarily potato, but also cotton and tobacco.” The study by Chen confirms similar work by researchers at St. Louis-based Monsanto, Hancock further notes.

In vitro, chemically synthesized cecropin B is far more effective against \textit{X. campestris}, with an \( S_{50} \) of 0.29 µg/ml, than against \textit{R. solanacearum}, for which \( S_{50} \) is 529.6 µg/ml. Nonetheless, the levels expressed in the transgenic plants, roughly 0.05 µg in 50 mg of leaf material, are smaller even than the \( S_{50} \) for \textit{X. campestris}, leading the researchers in Taiwan to suggest that the compound may be acting by boosting innate immune defenses in the plants.

Genes encoding cecropins are also used to transform tobacco and potato plants. In the case of the potatoes, inserting the cecropin gene induced a
range of changes in the host plant, including its shape, size, and color, Chen says. However, transformed tomato plants maintain their usual physical attributes.

Transgenic plants have such a bad name—especially in Europe, despite a lack of data showing risks to consumers—that these cecropin-producing tomatoes are unlikely to gain a market, according to Hancock. “We were unable to raise enough money or find a large partner for our own company [which aimed to commercialize these transgenic crops], because of the bad reputation attached to genetically modified plants,” he says. “We have also had huge resistance to this idea from food producers.”

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Progress and Shortcomings in Federal Biodefense, Synthetic DNA Arenas

In January during his State of the Union speech before Congress, President Barack Obama alluded briefly to an “initiative that will give us the capacity to respond faster and more effectively to bioterrorism or an infectious disease—a plan that will counter threats at home and strengthen public health abroad.” Although details about that initiative are not yet available, the fiscal year 2011 budget request from the administration calls for investing $476 million in advanced research and development, $171 million more than the 2010 enacted level to “accelerate development of new medicines, vaccines, and diagnostics for biodefense” within the within the Department of Health and Human Services (HHS), going beyond research programs funded by the National Institutes of Health (NIH) in Bethesda, Md.

Just before that initiative was announced, the bipartisan Commission on the Prevention of Weapons of Mass Destruction Proliferation and Terrorism released a strongly worded report criticizing federal officials and Congress for “not taking the necessary steps to protect the country from the threats posed by weapons of mass destruction and terrorism.” While it gave “failing grades” to federal efforts to develop a “rapid and effective response to bioterrorism,” it praised a federal “review of domestic programs to secure dangerous pathogens” and also the development of an “Interagency Bioforensics Strategy.”

Even as the Obama administration seeks to accelerate research in this area, however, it and the Congress also continue to seek safeguards and possible new restrictions that could hamper research on many types of microbial pathogens. Last year, for example, Senator Joseph Lieberman of Connecticut, who chairs the Senate Homeland Security and Governmental Affairs committee, proposed the Weapons of Mass Destruction Prevention and Preparedness Act. Among other things, it seeks to restructure the Select Agent Program by creating a tiered system to enhance security requirements for more dangerous pathogens and lessen controls on others. However, there seems little likelihood that this bill will move forward anytime soon. Meanwhile, the biennial review of those select agents that is under way appears unlikely to adopt the proposals for reclassifying those agents that are outlined in the Lieberman bill.

The initiative to which Obama alluded in January appears to arise in part from the “National Strategy for Countering Biological Threats,” which the administration announced last December. Key elements of that strategy include promoting “global health security” and reinforcing “norms of safe and responsible conduct.” That new “strategy” outlines solid principles, according to Gerald Epstein, director of the Center for Science, Technology and Security Policy (CSTSP) at the American Association for the

Recent Insights about Avenues for Generating Antibiotic Resistance

RNA polymerase in slowly growing Escherichia coli cells can bypass some kinds of damaged sites along DNA, leading to transcriptional mutagenesis, according to Paul Doetsch at Emory University School of Medicine in Atlanta, Ga., and his collaborators. This type of mutagenesis has “important implications,” perhaps explaining how “pathogenic microorganisms may acquire resistance to antibiotics,” he says. Details appear in the February 12 Proceedings of the National Academy of Sciences (doi: 10.1073/pnas.0913191107).

In a separate development, subjecting either E. coli or Staphylococcus aureus cells to low doses of antibiotics can lead to mutant strains that are sensitive to the applied antibiotic but have cross-resistance to other antibiotics, according to James Collins of Boston University and the Howard Hughes Medical Institute in Boston, Massachusetts, and his collaborators. The low doses of antibiotics produce reactive oxygen species, which appear to be responsible for mutagenesis. Of several antibiotics tested, ampicillin appears to give rise to the widest range of drug resistances. Details appear in the February 12 Molecular Cell (37:311–320).