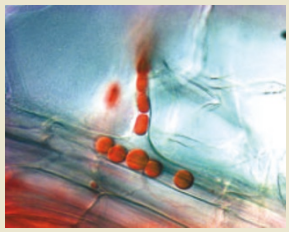
Plant probiotic



Considerable interest centers on nontransgenic approaches to improve crop productivity. One such approach may be to simply douse seeds with a beneficial endophytic fungus, *Piriformospora indica*. A new report suggests that application of the fungus to barley not only increases yield, but also enhances salinity tolerance and disease resistance of the crop. In contrast to mycorrhizal fungi, which cannot be cultured axenically, *P. indica* can be easily grown on various substrates. Kogel and colleagues now demonstrate that after entry of *P. indica* through root hairs into barley rhizodermal cells (see image), the fungus mediates beneficial systemic effects on the infected plant by eliciting elevated antioxidative capacity. Importantly, their findings challenge the widely held impression that disease resistance is inevitably associated with a yield penalty. Earlier this year, Oelmüller and coworkers reported that inoculation with *P. indica* promoted expression of genes responsible for nitrogen assimilation and starch metabolism in tobacco and thale cress. Together, these findings open the way for simple and effective approaches to improve yields of many crops, particularly for those monocotyledonous species with complex genetics that are recalcitrant to transformation. (*Proc. Natl. Acad. Sci. USA* **102**, 13386–13391, 2005; *J. Biol. Chem.* **280**, 26241–26247, 2005) *PH*

ClipPed to pieces

The increasing prevalence of antibiotic-resistant bacteria has lent urgency to the search for new antibiotics. In October's *Nature Medicine*, Brötz-Oesterhelt and colleagues describe a class of antibiotic that acts through an apparently novel mechanism: binding to the ClpP protease. The new agents, which comprise acyldepsipeptides (ADEPs) recovered from the fermentation medium of *Streptococcus hawaiiensis* NRRL 15010 and several improved derivatives, are active *in vitro* against a range of Gram-positive bacteria, including multidrug-resistant strains of *Staphylococcus aureus*, *Streptococcus pneumoniae* and *Enterococcus*. They also have strong activity in mice against lethal systemic infections caused by *Enterococcus faecalis*, *S. aureus*, and *S. pneumoniae*. Experiments with the Gram-positive bacterium *Bacillus subtilis* showed that ADEPs do not act on the usual antibiotic targets—synthesis of DNA, RNA, protein, fatty acids and cell wall. The new target, ClpP, was discovered by selecting for an ADEP-resistant *Escherichia coli* mutant of an ADEP-sensitive *E. coli* strain, transforming the sensitive strain with a genomic library of the resistant strain and sequencing the mutant gene that conferred resistance. Moreover, ADEPs were found to release the tight regulation of ClpP activity, leading to uncontrolled proteolysis that ends in cell death. (*Nat. Med.* **11**, 1082–1087, 2005) *KA*

Peptides come full circle

Dublin-based Elan's calcium-channel blocker ziconotide (Prialt), a ω-conotoxin MVIIA peptide from *Conus* snails, was approved by the US Food and Drug Administration in December 2004 for the treatment of neuropathic pain. One problem in turning such peptides into therapeutics is their susceptibility to protease degradation in the body. Now Clark and colleagues have shown that by cyclyzing the peptides, they can create perfectly active versions that are resistant to proteolysis. They used as their test peptide conotoxin MII, a 16-amino-acid snail peptide that binds the α2β-nicotinic acetylcholine receptor; importantly, MII has a structure in which its C- and N-termini are within 11 Å of each other. Creating cyclized peptides with protein linkers of various sizes, the researchers found that a six- or seven-amino-acid linker produced a peptide that has the same three-dimensional structure as the native peptide, is resistant to proteases, both isolated and in serum, and has the full activity of the native peptide against acetylcholine receptors. In contrast, a cyclic peptide with a five-amino-acid linker had no biological activity. The approach could be applied to stabilize not only conotoxins but also peptides and proteins from other sources that have closely apposed ends. (*Proc. Natl. Acad. Sci. USA* **102**, 13767–13772, 2005) *LD*

Low-cost genome quilting

Researchers have devised a DNA sequencing technology that combines a clever approach to generating paired genome-fragment tags, an emulsion PCR-based amplification step, an optimized polymerase colony (polony)-based sequencing-by-ligation protocol and a conventional epi-fluorescence microscope with a sophisticated algorithm that allows them to stitch together the fragmented sequence reads into one continuous thread—all in just a few hours. Shendure *et al.* propose an alternative to current Sanger sequencing-based technologies that avoids construction of bacterial colony–based fragment libraries and allows high-throughput processing of the entire set of fragments representing a genome in parallel and in one tube. The generation of paired genome 17–18 bp tags separated by about 1,000 bp of genome sequence sets the pattern for an assembly algorithm that, in addition to looking for overlapping sequence information, takes into account the separation between the tags to seam together the final sequence. As a proof of concept, the authors resequence the genome of an evolved *Escherichia coli* strain and show that they are able to identify all expected single nucleotide substitutions in the sequence thanks to an error rate estimated at less than one error per 10^6 base calls. (*Science* **309**, 1728–1732, 2005) *GTO*

Antigen-specific T-cell tracker

Analysis and isolation of antigen-specific T cells is important for tracking the immune response during disease or after vaccination. However, existing assays, such as the use of multimers of major histcompatibility complex (MHC) class II proteins or quantification of secreted cytokines by enzyme-linked immunosorbent assay or immunospot, are limited by their complexity and inability to account for activated T cells that do not express cytokines, respectively. Now, two independent research groups have developed simple antibody-based assays that target a soluble cytokine, CD40 ligand or CD154, expressed on the surface of activated $CD4^+$ T lymphocytes. Roederer and colleagues show that by using a fluorescently conjugated CD154-specific antibody during stimulation with *Staphylococcus* enterotoxin B, they detected *de novo* synthesis of CD154 and sorted antigen-specific $CD4^+$ T cells. Similarly, Thiel and colleagues applied CD154 monoclonal antibodies to *in vitro* stimulated T-helper cells to isolate those cells specifically responding to antigen. Both groups demonstrate that their assays are compatible with intracellular cytokine staining and, unlike other assays, can be used in conjunction with assays that require live cells. (*Nat. Med.* **11**, 1113–1117, 2005; *Nat. Med.* **11**, 1118–1124, 2005) *NC*

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