Recruiting biocontrol bodyguards

PHOTO RESEARCHERS, INC.

Many plants emit volatile compounds when attacked by herbivorous insects. Certain predators of the latter exploit these airborne signals as lures to their next meal. Although manipulation of such interactions has long been suggested as an attractive alternative to pesticide use, most attempts to engineer increased terpenoid synthesis in plants have been frustrated by a dearth of cytosolic and plastidic precursors for these isoprenoids. Now, Bouwmeester and colleagues demonstrate that targeting of a strawberry sesquiterpene synthase to mitochondria significantly boosts emissions of two isoprenoids not normally produced by *Arabidopsis thaliana* without substantial effects on plant vigor. The transgenic plants attracted roughly twice as many predatory mites (*Phytoseiulus persimilis*; see image) as their wild-type counterparts. Fine-tuning of this approach by placing the engineered terpenoid synthesis under the regulation of a herbivore-inducible promoter could enable crops to be engineered to recruit novel carnivorous allies only when prey is to be had. (*Science* 309, 2070–2072, 2005) ***PH***

Connecting the dots

Large-scale protein interaction maps have been generated for model organisms, yet until now only limited sections of the human proteome had been probed. But now two groups have scaled up their yeast two-hybrid (Y2H) platforms to tackle humans. Using a matrix interacting protein screen, Stetzl *et al.* probed over 5,500 human proteins, searching through 25-million protein pairs. Computational analysis of over 3,000 interactions showed that they comprise a massive network of closely linked interactions in what has been dubbed 'the small world properties' of networks. In addition, the researchers found hundreds of previously uncharacterized proteins linked to disease-associated proteins and a high proportion of interactions with proteins involved in regulatory pathways. Vidal and coworkers similarly constructed a massive protein interaction map through their high-throughput Y2H system, jazzed up with three reporter systems and a mechanism for eliminating false positives, which plague Y2H systems. Searching a matrix of 7,200 × 7,200 of available open reading frames from the human 'ORFeome,' which they estimate represents 10% of the total human search space, they identified 2,754, mostly novel, interacting protein pairs. These protein pairs were found to be largely nonoverlapping with protein pairs discovered by other techniques, suggesting that each technique introduces some selection bias. Although these analyses provide important spatial information, temporal and dynamic features of the human proteome have yet to be considered. (*Nature* **437**, 1173–1178, 2005; *Cell* **122**, 957–968, 2005) *LD*

Targeting virulence

The severity of many bacterial infections is due in large part to the production of bacterial toxins encoded by specific virulence factor genes, which are not the target of most antibiotics. With the aim of discovering compounds that target a *Vibrio cholerae* virulence factor, Hung *et al.* have used an assay designed to identify compounds that specifically inhibit the expression of the virulence gene encoding cholera toxin. By screening a large, 50,000-member library of small molecules, the authors identify one compound, virstatin (4-[*N*-(1,8-naphtalimide)]-*n*-butyric acid), that actively inhibits the cholera toxin promoter. In addition, this compound also inhibits the expression of the toxin coregulated pilus, a structure involved in intestinal colonization. Administration of virstatin before infection provides substantial protection against cholera in mice, whereas therapeutic, post-infection treatment results in substantial attenuation of the deleterious effects of *V. cholerae*. Besides the obvious advance this study represents in the quest for finding new therapies against cholera, compared with other antimicrobial approaches, the strategy may exert less selective pressure for resistant strains as nonvirulent bacteria would be spared. (*Science*, published online 13 October 2005; 10.1126/science.1116739) *GTO*

Dainty immunosensors

Using spatially orientated, single-chain Fv (scFv) antibody fragments, rather than whole antibodies, as binding molecules, researchers in Switzerland have built a microcantilever array–based sensor that can detect antigen concentrations as low as ~1 nM. Gerber and colleagues achieved this substantial boost in sensitivity over previous label-free immunosensors by covalently linking the scFvs to cysteine and then exposing a gold-coated microcantilever surface to a solution of such scFvs—as a result of the cysteine/gold reaction, the receptors were immobilized in a highly directed orientation. Simple mechanical devices, microcantilevers detect tiny amounts of molecules in both air and solution. When the cantilever is in the static mode, a molecular interaction, such as the binding of antigen to scFv, is transduced into mechanical motion and detected by the deflection of a laser due to the bending of the cantilever. The improvement in sensitivity achieved here results not only from the high affinity of the scFvs but also from their small size and better orientation on the cantilever surface, providing a higher density of receptors. Although these devices are not yet completely reusable, their greater sensitivity should enable applications in both basic research and medical diagnostics. (*Proc. Natl. Acad. Sci. USA* **102**, 14587–14592, 2005) *TM*

ES cells without ethical objections?

"Altered nuclear transfer" has been proposed as a way of assuaging ethical objections to the destruction of embryos that accompanies the derivation of human embryonic stem (ES) cell lines. As described by William Hurlbut, the nuclear donor cells would be genetically modified in such a way that the resulting embryos are a source of ES cells but are incapable of normal development. For example, he suggests, by disrupting genes essential for trophectoderm development, such as *Cdx2*, one could produce "a limited cellular system, from which the ES cells would be obtained, [that] would fail to establish even the most basic features of human organismal infrastructure and would be incapable of implantation." Meissner and Jaenisch have now put this idea to the test. Using RNA interference to suppress *Cdx2* in mouse fibroblasts, they generated cloned mouse embryos deficient in this gene product. As intended, the embryos did not produce trophoblast or implant in the uterus but did yield pluripotent embryonic stem cells. (*Perspect. Biol. Med.* **48**, 211–228, 2005; *Nature*, published online 16 October 2005; 10.1038/nature04257) *KA*

Research Highlights written by Kathy Aschheim, Laura DeFrancesco, Peter Hare, Teresa Moogan & Gaspar Taroncher-Oldenburg.