Lighting up pest control

"This makes Alien look like a cakewalk," says Richard ffrench-Constant, a professor of toxicology at the University of Wisconsin-Madison, referring to a potent natural pesticide that he and his collaborators have discovered. The active agent, *Photorhabdus luminescens*, colonizes a nematode that parasitizes insects. On infection, the nematode releases the bacteria into the insect's gut where they produce both powerful toxins that kill the host and luminescent proteins that cause it to glow in the dark (see picture). According to ffrench-Constant, the nematodes feast on the phosphorescent carcass, then move on to a new victim. Researchers in his laboratory and at DowElanco (Indianapolis, IN) have now cloned the genes responsible for producing toxins in dozens of naturally occurring strains of *Photorhabdus*. The results, reported at the annual meeting of the Entomological Society of America in December, show that each strain produces its own variant of the toxin. "The key point is that the *P. luminescens* toxin represents one of only a very few viable alternatives to Bt," says ffrench-Constant.

Aldolase abzymes

Scientists at The Scripps Research Institute, La Jolla, CA have succeeded in making broad scope antibody aldolases with enzymic rates comparable to the natural enzyme (*Science* 278:2085–2092, 1997). Using a process termed reactive immunization, the researchers immunized mice with 1,3-diketone hapten to generate antibodies that had the catalytic mechanism of an aldolase imprinted within their antibody binding site. Two monoclonal antibodies, 33F12 and 38C2, were identified by screening for molecules exhibiting spectrophotometric changes characteristic of aldolase activity. All but one of the antibody-catalyzed aldol reactions followed typical Michaelis-Menten kinetics. Compared with fructose 1,6-diphosphate aldolase, which has a limited range of substrates, the antibody aldolases are capable of catalyzing in excess of 100 different aldol additions or condensations. By adding a pyridoxal phosphate cofactor to the active site, antibodies were able to catalyze a new repertoire of pyridoxal-dependent reactions, ranging from transaminations, racemizations, and decarboxylations. According to Richard Lerner, one of the corresponding authors, "by changing the immune system selection pressure from simple binding to chemistry, [we can] evolve highly efficient enzymes." Lerner says the approach has recently been applied to make abzymes for the total synthesis of the chemotherapeutic agent, epithiolone.

Research News Briefs written by Harvey Bialy, Alexander Castellino, Alan Dove, Margret Einarson, and Orla Smith.

Turning on transgenics

A system developed at the University of Oxford and the Max-Planck Institute may allow stricter control over where and when an introduced transgene is expressed in plants (*PNAS* 95:376–381, 1998). By crossing two transgenic plant lines—one carrying a gene of interest driven by a minimal promoter in front of a bacterial *lac* operator, and a second "activator" line containing a tissue-specific plant promoter driving expression of a *lac*-binding chimeric protein—the European researchers produced F_1 progeny that express the transgene only in the desired tissues. "It should be possible to use the system. . .to modify the properties of seeds in such a way that they are commercially very useful, even if this makes them biologically inviable," states Ian Moore, a lead author on the study. Moore suggested that the approach could aid in selecting hybrid plant progeny after a cross, preventing transgenic plants from cross-pollinating wild strains, and permitting the coordinated expression of multiple transgenes. Further studies are proceeding in collaboration with Zeneca (Wilmington, DE) and Nickerson's Seeds.

Homing in on ovarian cancer

A novel twist to treating cancer by adoptively transferring T cells has been reported by researchers at the National Cancer Institute (*Nat. Med.* 4:168–172, 1998). The NCI team set out to target ovarian cancer cells by designing a chimeric receptor composed of the single-chain variable region of an antibody recognizing an ovarian cancer antigen (folate-binding protein) linked to the γ chain of the Fc receptor present on many immune cells. Mouse bone marrow cells were first transduced with the chimeric receptor construct and then transplanted into irradiated recipient mice. When challenged ten months after transplant with mouse sarcoma cells expressing folate-binding protein, these mice exhibited slower tumor growth than control mice. Intriguingly, $CD4^+/CD8^+$ T-cell depleted mice were no more susceptible to tumor growth than other mice, suggesting that NK cells, neutrophils, and monocytes may participate in the response. Patrick Hwu, the senior author of the study, says his group is currently involved in clinical studies using the chimeric receptor to transduce the T cells of ovarian cancer patients *ex vivo*. "The next step is to see if we can get an antitumor response with patient bone marrow cells that express our chimeric receptor," he says.

Tubulin structure resolved

The 3.7 Å resolution structure of tubulin reported recently in *Nature* (391:199–203, 1998) "should provide the basis for understanding how taxol works and aid the design of other microtubule-inhibiting drugs," according to Kenneth Downing of the Lawrence Berkeley National Laboratory in California, an author on the paper. It may also provide insights into the biological properties of tubulin that regulate microtubule growth and disassembly.

Julian Davies (TerraGen Diversity and Univ. of British Columbia, Vancouver, Canada) the keynote speaker at "The Second Monroe Wall Symposium on Natural Products Discovery, Biodiversity and Biotechnology" (organized by Rutgers University, *Nature Biotechnology*, and Simon Bolivar University, and held at the Institute for Advanced Studies of Simon Bolivar University, Caracas, Venezuela, January 7–9, 1998) contemplates the visible and invisible worlds from the conference site in the mountains above the city.

Correction: The report in last month's Research News Briefs describing an enzymatic approach to paclitaxel production incorrectly named Jonathan Dordick as head of the research team. The work was in fact a collaborative effort between Dordick and Douglas Clark of the University of California.