New antibiotics show some backbone

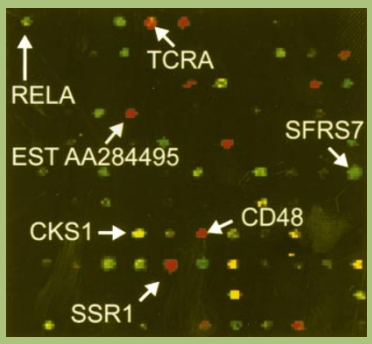
By synthesizing a short peptide similar to a family of naturally occurring defense proteins, researchers have created molecules that could lead to an entirely new class of antibiotics (*Nature* **404**, 565, 2000). The sequence of the new β-peptide, which by virtue of its a β-amino acid backbone is resistant to proteolysis in the bloodstream, is based on that of the magainins, short naturally occurring peptides that attack bacterial membranes. In initial tests, the new compound showed impressive antibacterial activity, even against antibiotic-resistant strains. Samuel Gellman, a senior author on the new work, adds that the applications could be even broader: "I am hoping that β-peptides. . .will prove useful for targeted disruption of specific protein–protein interactions," and for new treatments for viral diseases and cancer. The team is now working on improving the anitbacterial activity of the new β-peptide in vitro before beginning animal testing. *AD*

Drug smugglers come under umbrella

At the March 26–30 meeting of the American Chemical Society in San Francisco, a new type of peptide tag was described that can smuggle water-soluble drugs, such as Taxol (paclitaxel) and cyclosporine, through the cell membrane. This peptide tag comprises a repeating series of up to nine arginine residues that resembles the cationic subunits of HIV Tat protein, a natural viral protein that also boosts the uptake of drugs into target cells (*Nat. Biotechnol.* **17**, 942, 1999). Using different cationic amino acids and ornithine (a structural analog of arginine), Paul Wender and his team have shown that the remarkable properties of the arginine tag are attainable to it's hydrogen bonding capacity. In a related study in *J. Am. Chem. Soc.* (**122**, 2671–2672, 2000), Steven Regen and colleagues have designed molecular umbrellas, comprising an inner hydrophilic layer and an outer hydrophobic lipid layer, that can be used to envelop a drug, protect it within the membrane, and release it into the cytosol. The system is now being tested with genuine peptide and nucleic acid drugs. *AM*

Research News Briefs written by Alan Dove and Andrew Marshall.

Array for membrane proteins



Microarray technology and cell fractionation methods have been elegantly combined to enable the rapid identification of gene products that are likely to be secreted or associated with cell membranes (*Nat. Genet.* **25**, 58–62, 2000). Secreted and membrane-bound proteins are particularly important as targets for drug development. Patrick Brown and his colleague isolated mRNA from cell membranes using established techniques, then used DNA microarrays to determine what genes were represented in the membrane-associated pool. By comparing this result to the DNA microarray analysis of non-membrane-associated mRNA from the same cells, they were able to determine the probability that a particular gene transcript would be membrane-associated (see inset). Their approach identified more than 275 human genes and 285 yeast genes encoding previously unknown secreted or membrane-associated proteins. Since microarrays can also be used to profile the expression patterns of genes, it should also be possible to determine which putative membrane-associated genes are turned on or off under different conditions. *AD*

Transgenic pest control on the fly

A transgenic alternative to the sterile insect technique for pest control has been proposed by a collaboration of researchers in the UK. The conventional insect control method, developed in the 1950s, involves the breeding of a large population of sterile males, which are then released into the wild to compete with fertile males for mates, thus depleting populations. Unfortunately, the process of rearing huge numbers of insects and separating them by sex has restricted the utility of the approach. Using transgenic techniques to address these problems, Luke Alphey and his colleagues have created a tetracycline-inducible transgene system that reliably kills *Drosophila* females unless the insects are fed the antibiotic. In the absence of tetracycline, expression of a gene controlled by a female-specific enhancer leads to the induction of a toxin gene. The flies can be raised and bred normally on medium containing tetracycline, but are unable to produce viable offspring in the absence of the antibiotic. As the system does not require raising the flies to adulthood for sexing, it should significantly simplify the sterile insect technique. Having proved the concept in *Drosophila*, Alphey is working to adapt the system to "the medfly and the yellow fever mosquito." The findings are described in *Science* (**287**, 2476–2478, 2000). *AD*

Genetic testing of the other half

A significant problem in the development and reliability of genetic tests for disease predisposition is the detection of heterozygous mutations. In most cases, a mutation is found only on one chromosome, and the presence of the wild-type allele on the homologous chromosome produces misleading results. In a recent issue of *Nature* (**403**, 723–724, 2000), researchers describe a new system for converting a diploid chromosome complement to a haploid state, allowing highly reliable testing for mutations. Bert Vogelstein and his collaborators fused lymphocytes from human blood samples to mouse cells, allowing the human chromosomes to be transferred into the mouse cells. In over a quarter of the fused cells, human chromosomes had been transferred without their homologs, resulting in an artificial haploid for that chromosome. In 22 patients with hereditary non-polyposis colorectal cancer, conventional testing on diploid cells revealed disease-causing mutations in only 10 of the patients. Using the new technique, disease-causing mutations were identified in all of the patients. Vogelstein explains that the new method is "not a replacement for conventional methods of genetic testing. It simply provides improved templates for all of those kinds of tests." The new approach is being applied to their ongoing diagnostics research, and Vogelstein expects the technology to be marketed widely within a few months. *AD*