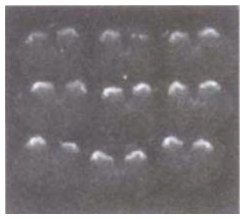
The fructan beet

Although identical in appearance to its non-transformed counterpart, the addition of a gene encoding 1-sucrose:sucrose fructosyl transferase has effectively created a fructan beet whose primary carbohydrates are low molecular weight fructans as opposed to sucrose (see pp. 822 and 843).

Painless PNA



Galanin is a neuropeptide that has a variety of biological effects that may depend in part on the receptor to which it binds. To elucidate the function of various receptors, antisense reagents can be used to alter their levels. For antisense (either as a therapeutic or as a research tool) to be effective, an oligonucleotide must be efficiently delivered to its target cell. Peptide nucleic acids (PNAs) though effective binders of RNA are particularly difficult to ferry across the plasma membrane. By linking a 21-mer PNA that interacts with galanin receptor type 1 mRNA to a naturally occurring cell penetrating peptide (isolated from *Drosophila*), Pooga et al. have been able to down regulate the receptor in rats, leading to decreased galanin binding and a resultant increased tolerance to pain (see pp. 819 and 857).

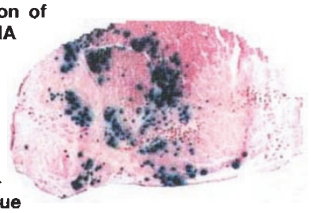
A sweet combination

Sugar nucleotides and oligosaccharides, which are expressed on cell surfaces and have roles in recognition processes, are potential pharmaceuticals. Production costs are currently high, however, as chemical synthesis is a multi-step process. By engineering *Escherichia coli* to overexpress the UDP-Gal biosynthetic genes and combining the activity of this engineered bacterial with *Corynebacterium ammoniagenes*, which produces UTP—a substrate for UDP-Gal biosynthesis—from an inexpensive precursor, Koizumi et al. have developed an efficient strategy for the production of the trisaccharide portion of a receptor present on some pathogenic bacteria (see p. 847).

Research Briefs written by Philip Bernstein.

Essential genes?

By knocking out genes in *Escherichia coli* that are conserved in *Mycoplasma genitalium* (which is considered to have a minimal genome) but did not have a predicted function, essential bacterial genes should be able to be defined. Of the 26 *E. coli* genes that met this criteria, only 6 fulfilled the definition of essential—that is being necessary for growth (see pp. 821 and 851). Thus Arigoni et al. have shown that conservation across a wide variety of species does not necessarily indicate that the gene is necessary for life, at least in the genetic background in which it is found. The authors propose that other metabolic pathways may be able to substitute for the function of highly conserved genes.



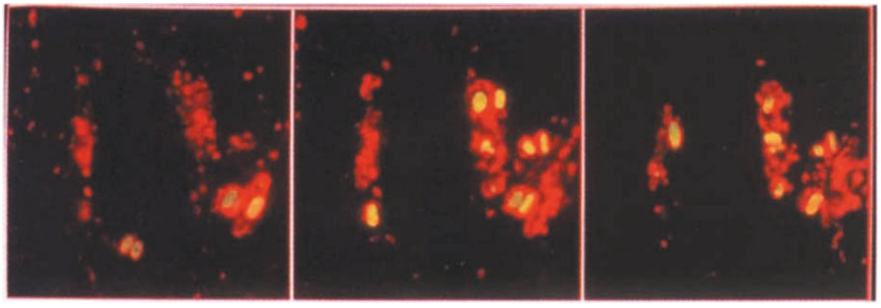
Direct injection of plasmid DNA into muscle is a simple method of delivery for DNA vaccine therapeutics, but it is limited mostly due to low efficiency of gene transfer. By applying a small electric pulse after plasmid DNA injection, Aihara and Miyazaki have increased both the number of muscle fibers taking up DNA and the copy number of plasmids introduced, resulting in a 100-fold increase in serum levels of protein over DNA injection alone (p. 867).

Transforming fungi

Filamentous fungi—important in food production, heterologous expression of genes, medical applications, and in the laboratory—have been difficult to transform and thus metabolically engineer. *Agrobacterium tumefaciens* can transfer part of its Ti plasmid to plants and has thus been used for the successful transformation of a variety of previously recalcitrant species. de Groot et al. have used *A. tumefaciens* to achieve the first trans kingdom transformation between a prokaryote and a variety filamentous fungi (see pp. 817 and 839). Not only will this allow the improvement of the biotechological applications of fungi, but improvements in this technique should allow the development of functional genomics analyses, which in turn can improve the medical, food, and production applications of this organism.

Rationally designed superagonist

Strategies for engineering proteins with enhanced activity are either based on structural models of ligand–receptor interactions or by selection from randomly mutagenized libraries. The higher order structures of glycoprotein hormones have not been solved. Rather than relying on a combinatorial approach to design an analog of human thyroid-stimulating hormone (hTSH) with enhanced bioactivity, Grossman et al. have drawn structural conclusions from other members of the cystine knot growth factor superfamily (see p. 871). Positively charged residues in their peripheral loops help determine receptor binding interactions. The introduction of seven lysine residues into the peripheral loop of hTSH, based upon evolutionary conservation of related family members, resulted in an analog with increased bioactivity both in vitro and in vivo.



By transforming a strain of *Escherichia coli* that has a deficiency in cell wall biosynthesis with a gene encoding the invasin protein form *Yersinia pseudotuberculosis*, Grillot-Courvalin et al. have created a bacterial DNA delivery system that releases plasmid DNA upon infection of mammalian cells (see pp. 818 and 862). These recombinant *E. coli* may provide a new vector for DNA vaccine delivery.