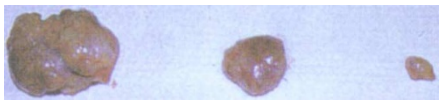
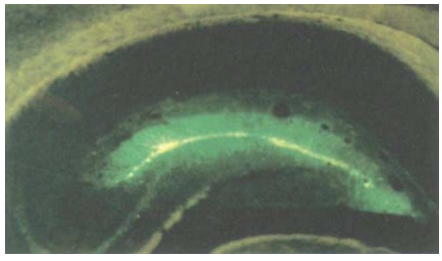


By introducing 2′-amino pyrimidine residues into a catalytically active protein kinase Cα ribozyme, Sioud and Sørensen have designed a catalyst that is over 14,000-fold more stable than its unsubstituted counterpart yet retains most of its biological activity. A single injection of the ribozyme into a tumor transplanted into a rat almost completely inhibits tumor growth (see p. 556).

Getting the lead (nickel, zinc, etc. ...) out

Sulfur-oxidizing bacteria can use a range of metals, resulting in the production of soluble metal sulfates along with sulfuric acid. As a result they have been useful for leaching and recovering metals. Sulfate-reducing bacteria employ a range of carbon sources and sulfate as an electron acceptor. The reduced sulfate is responsible for the formation of sediments and these bacteria have been used for the bioremediation of simple metal mixtures at relatively neutral pH. White et al. have been able to integrate these two opposing biological processes in a manner compatible with the bioremediation of contaminated soils (see p. 572). In a feedback reactor, the oxidizing and reducing activities of the two classes of bacteria remove most of the metals contained within artificially or environmentally contaminated soils.

On again off again



In order to regulate gene expression in the brain, in a manner that will allow the behavioral effects of gene expression in animal models to be elucidated, Harding et al. have developed a tetracycline-regulated adenoviral vector in which genes can be turned on, off, and on again (see pp. 518 and 553). By separating the elements needed for gene expression, the authors were able to get around the inherent leakiness of the system in a manner that allows long-term regulated gene expression.

Research Briefs written by Philip Bernstein.

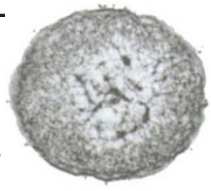
Colocalization comes alive

Interactions between different proteins often regulate the function of the individual components. Several approaches, including the yeast two-hybrid system, co-immunoprecipitation, and in situ immunodetection on fixed cells, have been used to identify binding partners to physiologically important proteins. These techniques, however, leave unanswered questions regarding the putative association of these proteins in living cells. In order to determine whether Bcl-2 and Bax (proteins implicated in apoptosis) are dependent upon each other for their activity, Mahajan et al. have created fusions of each of the proteins to spectral mutants of green fluorescent protein (see pp. 514 and 547). Using fluorescence resonance energy transfer, they show that Bcl-2 and Bax interact in the mitochondria of living cells, supporting the hypothesis that this interaction is required for biological activity.

Subtracting antibodies

Cell surface and secreted proteins, are potential therapeutic and diagnostic targets. Scherer et al. have developed a method in which polyclonal antiserum is used to identify these ligands in a cell specific manner (see p. 581). Rabbit antiserum generated by immunization with surface and secreted proteins from adipocytes are immunodepleted using proteins from a control cell line, which allows cell specific proteins—including a novel protein that associates with the adipocyte plasma membrane—to be cloned from a cDNA expression library.

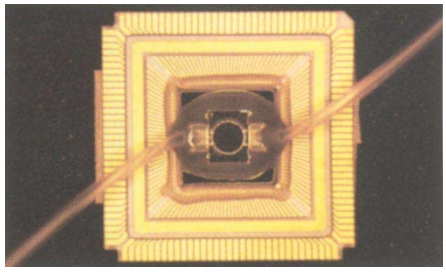
By displaying foreign proteins on their cell surface, microbes can be transformed into vaccine delivery systems, tools for screening ligands, or biocatalysts with novel enzymatic activities. Jung et al. (see p. 576) have used the ice nucleation protein of *Pseudomonas syringae* to anchor an overexpressed levansucrase on *E. coli*, which converts sucrose to the high molecular branched-chain levan.



Alphavirus vaccines

As an alternative to a plasmid-based DNA vaccine vector, Berglund et al. have developed a DNA vector that consists of a recombinant Semliki Forest virus cDNA under the control of a strong CMV promoter (see pp. 517 and 562). The synthesized RNA is able to undergo self replication. Subsequent translation results in further amplification and high-level production of the virally encoded proteins, including a recombinant antigen. Immunization of mice with a naked expression vector encoding an influenza antigen produces a humoral and cellular immune response affording protection from lethal influenza challenge.

Chip'd laboratory



A diagnostic laboratory that is designed to detect a bacterial pathogen in blood could reasonably be expected to occupy a few rooms (or at least a bench top). Cheng and colleagues have been thinking small, much smaller in fact; creating 1 cm^2 chips that function as labs (see pp. 513 and 541). The patterned silicon chips address different cell types to different regions of the microelectrode array where bacteria are lysed by an alternating current. Although not yet integrated onto the same chip, the isolated DNA or RNA is used to identify the putative pathogen by its ability to bind an addressable nucleic acid probe.

From protection to function

The characteristics of a cell, in response to varying environmental stresses, are determined by the genes that it expresses. To quantitatively identify genes whose expression patterns are altered in response to varying stimuli, Tavazoie and Church have developed a method to monitor DNA–protein interactions on a genome-wide scale (see p. 566). Using in vivo methylase protection, protein occupancy on the *E. coli* genome was determined. Binding sites were found upstream of several uncharacterized genes. Differential protection, in response to altered growth conditions, offers clues as to the genes' function.