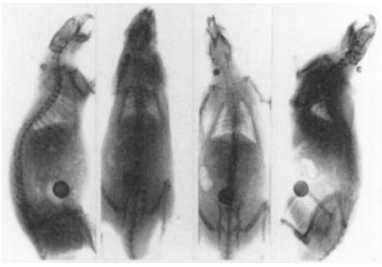


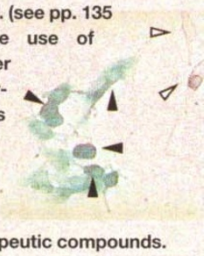
A therapeutic drug "store"

Implants that allow the slow release of therapeutics are often limited by the amount of drug that can be intercalated into the device. When all of the drug is released, another device must be implanted. In order to circumvent this limitation, Koole et al. (see p. 172) have developed hollow radiopaque porous spheres that are self healing and biocompatible. These reservoirs were implanted in rats (see opaque spheres at neck and abdomen), where their opacity allows refilling to be directed by needle injection and the ability to self-heal prevents leakage. The porous nature of the membrane allows first-order drug release into the animal.

Putting a shine on neuronal precursors

Neuronal precursor cells, which are distributed throughout the adult vertebrate forebrain, are scarce and difficult to isolate by enzymatic dissociation and purification. Large numbers of purified cells would be necessary to evaluate the therapeutic potential of this cell population. To these ends, Wang et al. (see p. 196) have transfected chick and rat forebrain cells with a gene encoding GFP driven by a promoter for a gene, *Tα1*, that is expressed early in neuronal ontogeny. The resultant fluorescence of these neuronal precursor cells allows them to be isolated by FACS.

Electroporation—the electrically induced increase in cell membrane permeability—has been used to deliver proteins or nucleic acids to cells in culture. Rols et al. (see pp. 135 and 168) describe the use of electroporation to deliver macromolecules to surface tumors, such as melanoma (arrows indicate delivery of β-galactosidase in situ), as a potential method for local delivery of therapeutic compounds.

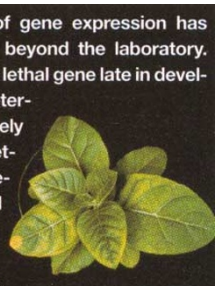


Research Briefs written by Philip Bernstein.

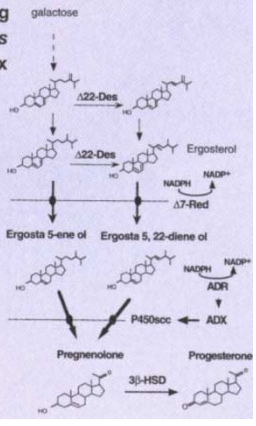
(Gram) positive vector for DNA vaccines

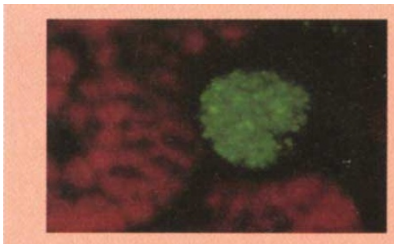
Viruses and lipid formulations are being developed to deliver antigen-encoding DNA as a vaccine. Intramuscular injection of "naked" DNA has shown promise in eliciting an immune response against the encoded antigen. The presentation of the encoded antigen by professional antigen presenting cells (APCs), such as dendritic cells and macrophages, enhances the development of immunity. *Listeria monocytogenes* is a Gram-positive bacteria that invades its host through the mucosa, replicates in the cytosol of its host's cells and thus may be used for oral (mucosal) vaccination. That these bacteria are found in the spleen (where APCs are abundant) makes them attractive as vaccine delivery vehicles. By engineering *L. monocytogenes*, gene encoding the lytic lysin protein, Dietrich et al. (see pp. 139 and 181) create bacteria that self-destruct in infected macrophages to deliver plasmid DNA for antigen presentation to specific $CD8^+$ T cells.

The regulated control of gene expression has applications within and beyond the laboratory. The role of an embryonic lethal gene late in development cannot be determined if it is constitutively expressed. High level heterologous protein synthesis is often best achieved when it is expressed at a defined point in its hosts development. Caddick et al. (see pp. 140 and 177) use the regulatory elements of the *Aspergillus nidulans alcA* promoter, which is inducible by ethanol, to create a controllable system for foreign gene expression in tobacco. They show that inducing the expression of invertase, which when constitutively expressed will not allow the plant to mature, results in blanching of the youngest leaves without effecting those that had matured prior to ethanol treatment.



By reconstituting *Saccharomyces cerevisiae* with six different mammalian and plant genes, researchers have created a self-sufficient microorganism that is able to synthesize progesterone using galactose as a carbon source.





Cupid's high-tech arrow

While systemic drug delivery can be useful for a wide variety of therapeutics, certain bioactive molecules—such as angiogenic factors—have to be targeted to have a therapeutic effect. Biodegradable microspheres are being used as drug delivery vehicles for systemic applications. Arras et al. (see pp. 134 and 159) absorbed fibroblast growth factor onto non-degradable microspheres (staining green) and injected these into a pig via its coronary artery. The porous microspheres, which are slightly larger than capillaries, localized to the heart where they slowly release growth factor, resulting in endothelial cell proliferation.

Artificial Protein A

Protein A from *Staphylococcus aureus* binds to IgG and can thus be used to purify these potential therapeutic compounds. To prepare a molecule with the similar binding characteristics that is not of bacterial origin, but is stable and less expensive to produce, Li et al. (see p. 190) use a rational strategy–based upon computer modeling of Protein A bound to the Fc domain of IgG–to synthesize an organic molecule mimic of this bacterial affinity ligand.

Implanting antibodies

Many pathogens use mucosal surfaces as ports of entry, thus delivering therapeutics at these sites would allow high levels of the drug to be maintained where they are most potent. Although systemic delivery of antibodies against some pathogens has been effective, their direct application to the mucosal surface holds greater promise. By implanting polymer disks loaded with antibodies into mouse vaginas (see pp. 137 and 163), antibodies can be maintained at high levels at the mucosal surface, but are also able to penetrate the epithelium where active antibodies can be detected in the blood.