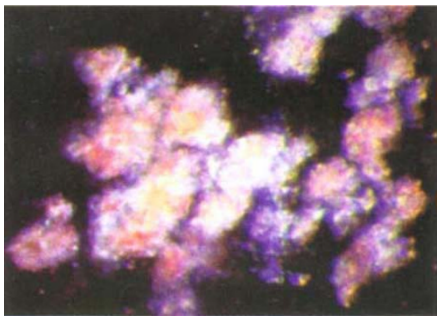
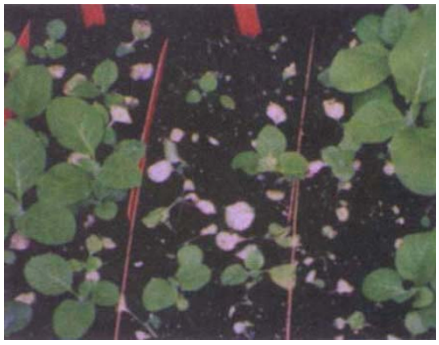


Using galactose-conjugated proteins as an affinity matrix, a subpopulation of purely hematopoietic stem cells, which contain progenitor cells of all lineages, can be isolated from a mixed CD34⁺ population (see p. 1007).



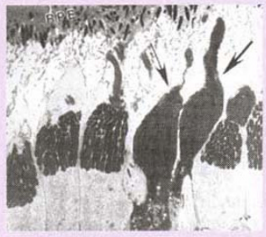
Many plants generate both a local and systemic response to fight pathogen infection, but these responses can have deleterious side effects for the plant itself: The local (hypersensitive) response includes cell death and induction of pathogenesis-related (PR) proteins, which have antimicrobial activity; the systemic acquired response (SAR) involves induction of salicylic acid (SA). Pokeweed antiviral protein (PAP) is known to be a potent activator of SAR and PR. Transgenic tobacco constitutively expressing mutant PAPs have been engineered that show little sign of detrimental effects, but retain resistance to fungal pathogens. The mutant PAPs activate PR protein expression and induce SAR without increasing SA levels or inducing cell death (see p. 992).

Regulating inflammation

Gene therapy approaches are being designed for either systemic or targeted delivery of protein therapeutics. Varley et al. have tested the possibility of creating a temporally regulated gene therapy system that would respond to local inflammation (see p. 1002). By injecting mice with an adenovirus vector containing a two-component system—where a complement factor promoter regulates production of the HIV transactivator protein, Tat, which in turn stimulates expression of a heterologous protein from an HIV promoter—large amounts of recombinant protein are made upon induction of an inflammatory reponse.

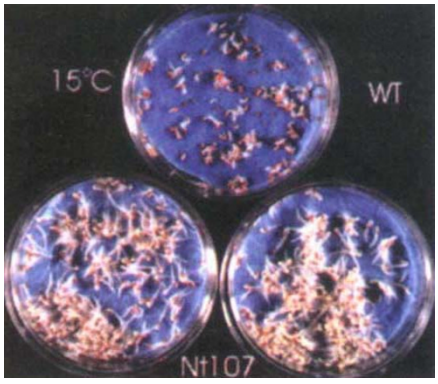
retinitis PIGmentosa

Retinitis pigmentosa (RP) is a degenerative retinal disease marked by early deterioration of rod photoreceptors followed by a slow loss of cones that eventually ends in blindness. The transgenic pig model (see pp. 947 and 965) developed by Petters et al. mimics this degenerative pattern. Both the size and photoreceptor distribution in the pig resemble those of the human eye and should make the pig better than existing rodent models for testing therapeutics.



Knocking out IL-6

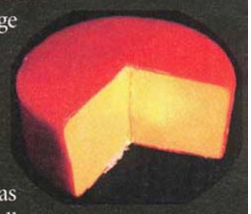
Cytokines are important regulators of the immune system; however, inappropriate expression can play a role in inflammation, degenerative disease, and cancer. Although model systems have been developed that can specifically block cytokine-receptor interactions, these are not sufficiently robust for therapeutic applications. By injecting an interleukin (IL)-6 superantagonist—which binds to, but does not activate, the receptor—into transgenic mice with high circulating levels of human IL-6, Ciapponi et al. are able to induce an immune response to IL-6 (see pp. 952 and 997) presumably because of the amino acid differences between the superantagonist and wild-type cytokine. The resultant circulating antibodies neutralized IL-6 activity in vitro and in vivo.



By overexpressing genes that are involved in scavenging reactive oxygen species—namely glutathione *S*-transferase and glutathione peroxidase—Roxas et al. have created transgenic seedlings that show enhanced growth under both chilling and salt stress conditions (see p. 988).

Cheese ripe for biotech

Lysis of *Lactococcus lactis* bacteria during cheese ripening—an inherently slow process—enhances the flavor as a result of the release of cytosolic enzymes. Two systems have been developed that can enhance the rate of bacterial lysis and thus accelerate cheese ripening (see pp. 950, 976 and 980). By comparing the well characterized sequence and structure of the bacteriophage λ repressor with that of a temperate lactococcal bacteriophage, a temperature-sensitive repressor was designed that allows gene expression to be induced at the normally elevated cheese-ripening temperatures. Another controlled gene expression system, regulated by the food preservative peptide nisin, has been used to express lysin and holin, which also lead to lysis of *Lactococcus* and subsequent accelerated cheese ripening.



Clotted breast milk

Transgenic livestock may find initial commercial success in pharmaceutical applications. Using a mammary gland specific promoter, and adding introns to the cDNA, Paleyanda et al. have generated transgenic pigs that secrete in their milk active human blood clotting factor VIII—a potential treatment for patients with hemophilia A (see pp. 945 and 971). While the mammary gland has previously been used to produce proteins of pharmaceutical interest, human factor VIII's complexity presented unique challenges to transgenic technology, and isolation of the natural molecule in sufficient quantities and purity from either plasma or cells in culture has proved difficult.

Inside-out bioremediation

Soil microbes are attractive targets in which to introduce genetic modifications that will allow them to detoxify pollutants such as pesticides. Although genes encoding enyzmes that hydrolyze synthetic organophosphorus compounds—such as organophophorus hydrolase (OPH)—can be introduced into bacteria, the expressed enzyme is present inside the cell, sequestering it from its substrate because of the barrier of the cell membrane. By linking OPH to the outer membrane protein A, the active fusion protein can be expressed on the cell surface. Richins et al. create a live biocatalyst that can degrade the pesticides parathion and paraoxon (see pp. 953 and 984).