THIS MONTH IN *NATURE BIOTECHNOLOGY*

Antisense scores a knockout

Traditional mammalian gene knockout experiments identify the first critical requirement for a gene product during development. Unfortunately, they often lead to primary lethality, providing very little information as to gene function. In this issue, Sam Driver and colleagues have developed a transient, antisense-based strategy to inhibit gene function in utero, permitting the stage-specific analysis of gene function and identification of secondary phenotypes (pp. 1184; Research News p. 1158).

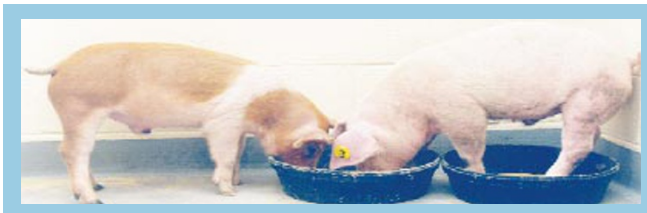
Mass analysis of receptor–DNA complexes

Electrospray ionization mass spectrometry (ESI-MS) precisely measures molecular masses without disrupting noncovalent protein interactions, and so provides a powerful tool for studying protein complexes. In this issue (p.1214), Naylor and colleagues take the method a step further, using it to analyze the effect of ligands on heterodimerization of full-length vitamin D and retinoid X receptors, and their binding to specific DNA sequences.

Fluorescent reporters have become indispensable tools to study both gene expression and the subcellular localization and interaction of proteins in the cell. In this issue, Wildt and Deuschle report the use of the red fluorescent product of the bacterial *cobA* gene as a transcriptional reporter in bacterial, yeast, and mammalian cells. This new reporter complements the existing set of green and blue fluorescent proteins, and should be less sensitive to the problem of cellular autofluorescence in response to UV light (see. p. 1175).

Antiviral protease inhibitors

Inhibitors of cysteine proteinases have been suggested to play a role in plant host defense against insect predators. Certain plant viruses, such as potyviruses, employ cysteine proteinases as part of their replication mechanism, suggesting that these inhibitors could be effective antiviral agents as well. In this issue, Gomez-Lim and colleagues demonstrate that tobacco plants engineered to express a rice cysteine proteinase gene are resistant to potyvirus infection (see p. 1223).



Although growth hormone–releasing hormone (GHRH) protein therapy avoids some of the negative effects of growth hormone therapy, such as insulin resistance and impaired glucose tolerance, the short half-life of the protein limits its therapeutic utility. In this issue, Schwartz and colleagues demonstrate that direct intramuscular injection of a plasmid encoding an engineered protease-resistant form of GHRH in pigs, coupled with a synthetic muscle promoter, results in significant long-term growth of the animals (see p. 1179).

A new vector for fetal gene transfer

Methods to transfer genes to fetuses in utero could be useful research tools, and could become important in strategies to correct human genetic deficiencies in utero. In this issue, Gaensler and colleagues report a new strategy for fetal gene transfer that uses cationic liposome–DNA complexes instead of viral vectors (p. 1188). With their method they achieved clinically significant levels of a therapeutic protein in fetal rats, without inflammatory response, toxicity, or gene transfer to maternal tissue.

Keeping tabs on estrogen

The health effects of estrogenic compounds in food constitute an issue of some controversy, with both harmful and protective effects attributed. The environmental effects of such compounds are more clearly worrisome, since estrogenic compounds, including some widely used pesticides, have been linked to feminization of wildlife and cancer in humans. In this issue, Lee and coworkers describe a rapid, nonradioactive, and high-throughput method to detect such compounds based on their ability to bind to the recombinant estrogen receptor (see p. 1219 and Research News p. 1162).

A synthetic FGF agonist

Fibroblast growth factors (FGFs) are in clinical trials as therapies for a variety of ischemic vascular disorders. However, their short in vivo half-lives could make it difficult to maintain therapeutic levels without frequent injections. This problem has prompted Ballinger et al. to search for more stable small-molecule mimetics to replace FGF (p. 1199). Using a combination of phage display and rational design, they engineered a peptide with no homology to FGF that binds to the FGF receptor and potently reproduces FGF's biological effects (see also pp. 1157–1158).

Mapping protein interactions by phage display

In this issue, Gishizky and coworkers describe yet another use for phage display—a method for mapping protein–protein interactions that is faster than two-hybrid systems and that allows the use of small synthetic baits such as phosphorylated peptides. The workers used phage libraries displaying protein fragments to pan the immobilized proteins or peptides of interest. Using this technique, they were able to identify known and novel protein interactions linking the epidermal growth factor receptor with the Ras/MAP kinase signaling pathway (see p. 1193).

Exploiting diversity

DNA shuffling is a powerful tool for protein engineering that allows the recombination of genes in vitro to generate libraries of hybrid proteins to screen for desired properties. However, the technique is limited by the requirement for high sequence homology between the parent genes. In this issue, Ostermeier et al. describe a method for generating hybrid proteins using more distantly related genes that may allow protein engineers to create a more diverse set of hybrid enzymes (see p. 1205 and Research News p.1159).

On page 1210, Tibbe et al. describe a cell analysis system for simultaneously extracting a population of cells from a complex mixture, and positioning the cells for optical examination. The cell mixture (in this case whole blood) is stained with fluorescent dyes and antibody-coated iron particles, and placed in a tiny chamber containing specially positioned magnets. Cells that bind the antibodies move to the top of the chamber, and then align along magnetic lines deposited using lithographic techniques. Once positioned, this specific population of cells can be examined for fluorescence, placed in new buffers, or otherwise manipulated.