THIS MONTH IN NATURE BIOTECHNOLOGY

Integrating assays

Unlike the viral polymerase and protease, the HIV integrase protein has yet to be exploited as a target for antiviral therapy, as a result of problems with safely and efficiently generating preintegration intermediates from infected cells. Bushman and colleagues (p. 578) take us a step closer by producing the viral proteins from noninfectious HIV-derived vectors. Using extracts from "infected" cells in an integration assay on DNA-coated microtiter plates, they identified a new compound with inhibitory activity from a chemical library.

Antiviral antisense

Antisense phosphorothioate oligonucleotides have been shown to inhibit the expression of the influenza A virus PB2 polymerase gene in cultured cells. Mizuta and colleagues (p. 583) have now examined the clinical potential of these oligonucleotides by complexing them with a recently described liposomal delivery agent, Tfx-10. Intravenous delivery of the liposomally complexed oligonucleotides enhanced the survival of mice that had been challenged with influenza A virus.

Potent peptidomimetics

Pharmacological limitations of peptides, such as poor bioavailability and pharmacokinetics, have prevented their wide use as therapeutic agents. To address this problem, Falcioni and co-workers (p. 562) have developed peptide analogs incorporating unnatural amino acids and dipeptide mimetics. These peptidomimetic compounds exhibited potent inhibition of antigen presentation by autoimmune-associated alleles of the class II major histocompatibility complex in a mouse model system of arthritis.

Hot spot phage display libraries

On page 568, Chowdhury and Pastan describe a trick for rapidly isolating high-affinity scFvs from small libraries. First they identified DNA sequences in the variable regions that are naturally prone to hypermutations, and then they selected some of these hot spots for random mutagenesis. Panning of these hot spot libraries yielded mutant scFvs with markedly higher affinities than those obtained the standard way.

Research Briefs written by Natalie DeWitt and Robert Frederickson.

Controlling DNA delivery

Expression of therapeutic proteins from DNA fragments delivered directly into tissues or organs has found application in both gene therapy and tissue engineering. However, the short duration of gene expression and the lack of fine control over where the transferred gene is expressed have limited the success of this approach. Shea and colleagues (pp. 534 and 551) provide a solution to this problem by delivering DNA embedded in a biodegradable polymer that allows sustained release of the plasmid in a controlled local environment.

Filamentous fungi produce as much as 40% of commercially available enzymes, so transgenic technologies for these organisms are of considerable importance for the fungal biotechnologist's toolkit. In this issue, Gouka et al. (p. 598) describe a new method for introducing genes into *Aspergillus* using *Agrobacterium*-based homologous recombination. The beauty of this method is that it avoids introduction of undesired foreign DNA into the fungi, which may improve market acceptance of products derived from these strains.

Transgenic canola with heart

Stearate is a key ingredient in shortening, margarine, and other foods, but conventional methods for producing this fatty acid from plant oils has the unfortunate side effect of creating *trans* fatty acids implicated in heart disease. In this issue, Facciotti et al. (p. 593) describe a way of coaxing transgenic plants to produce high levels of stearate directly. First they engineered a tropical plant enzyme to improve its stearate production, and then they transferred the mutant enzyme to *Brassica*. They ended up with a transgenic oilseed crop plant that produces 55–68% more stearate than plants expressing the wild-type enzyme.

Double-stranded DNA chips

Church and colleagues describe their new spin on DNA chips (pp. 536 and 573), which could drive the study of protein–DNA interactions into the fast lane of microarray technology. They created double-stranded DNA oligonucleotide arrays by first attaching single-stranded oligonucleotides to glass, and then adding primers, polymerase, and dNTPs to produce a complementary second strand. They went on to show that restriction enzymes and methylases could effectively modify the double-stranded DNAs, suggesting that such chips could be a valuable tool for high-throughput studies of protein binding to double-stranded DNA.

Hols and co-workers (p. 588) report the metabolic engineering of *Lactococcus lactis* for the stereospecific production of the amino acid L-alanine. Expression of the *Bacillus sphaericus* L-alanine dehydrogenase in an L-lactate-deficient strain of *L. lactis* resulted in production of alanine as the sole end product of sugar metabolism. Exclusive production of the L stereo-isomer was achieved by disruption of the endogenous alanine racemase gene.

In silico vaccine design?

To elicit a T-cell immune response, proteins from pathogens and tumors must contain peptides capable of binding to the human MHC (HLA-DR) on the surface of antigen-presenting cells. Generally the more promiscuous this binding, the stronger the immune response. In this issue, Hammer and colleagues (pp. 533 and 555) describe an in silico approach for finding such promiscuous T-cell epitopes. Using a database of structural and biochemical profiles of the HLA-DR binding groove, they generated matrices that describe the peptide-binding specificities for most HLA-DR alleles. They integrated this tool into prediction software that could pave the way for vaccine design based on little more than a database of pathogen and tumor antigen protein sequences—and a computer.