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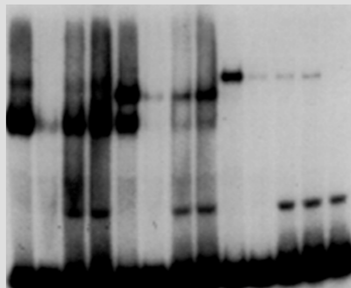
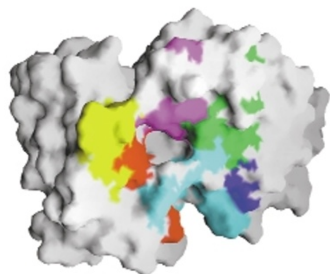


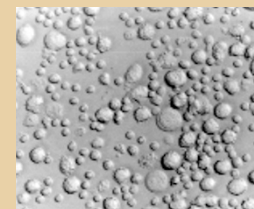
On page 877, Shimizu et al. describe a simplified technology for rapidly identifying drug receptors. The system employs beads coated with a novel latex polymer and chemically active epoxy group to which drugs can be easily attached by simple mixing. The authors used the beads to purify a protein known to bind to the immunosuppressive drug FK506, and go on to use the method to isolate the receptor of an anti-inflammatory drug that targets nuclear factor (NF)-κB—the first in a new class of receptors for this type of drug. The superior performance of the beads as compared with conventional agarose suggests that the approach could be useful in parallel small-scale purification of drug receptors. *ND*



Different combinatorial strategies have been employed to generate antibodies with novel specificities. On page 852, Söderlind et al. describe a new approach in which antibody framework regions are combined with sequences encoding in vivo-formed complementarity-determining regions (CDRs) of different germline origin (i.e., the hypervariable regions of the variable domains that interact with an antigen) and assembled by overlap extension using PCR. This approach yielded a human antibody single-chain fragment (scFv) library consisting of 2 × 10^9 members, which contained specific and strong binders to a variety of antigens. The approach, by varying up to as many as six in vivo-formed CDRs at a time, allows the creation of a high degree of functional variation in antibody molecules. *MS*

Protein interaction blockers

In this issue, Park and Raines (see p. 847) describe the development of a genetic selection method for searching peptide libraries for molecules that inhibit protein–protein interactions. They demonstrate their method using the dimerization of HIV-1 protease as a target. An inactive version of dimeric HIV protease is tethered to the bacteriophage lambda repressor DNA-binding domain. Because the DNA-binding domain functions as a dimer, dimerization of which is mediated by the HIV protease domain, this system can be used to study peptides that disrupt protein–protein interactions in HIV protease. The authors used the approach to screen a library of peptides for those able to interfere with the dimerization process by coupling the lambda operator to selectable markers. The method allowed them to find rare peptides that interfere with protein interactions. *MS*



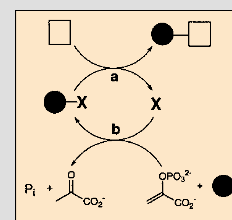
Cell therapies require that stem cells be "purged" of contaminating tumor cells or more immature progenitor cells. Although methods using viruses or antibody selections have been developed for this purpose, they tend to be expensive and labor intensive. On page 882, Eppich et al. show that hematopoietic stem cells can be selected by simply applying pulsed electric fields that create pores in cellular membranes, eventually resulting in cell death. The sensitivity of cells to lysis is proportional to their size; this permits the extremely small hematopoietic stem cells to be rapidly enriched. The authors found that in blood cell samples contaminated by tumor cells and mature blood cells, the method could enrich for stem cells by at least two orders of magnitude. *ND*

Technical Reports

On p. 893 Luo and Saltzman test the idea that DNA transfection efficiency is limited by a simple physical barrier, getting DNA to the cell surface. Using dense silica nanoparticles, they were able to increase the concentration of DNA–transfection reagent complexes on cell surfaces by associating them with the nanoparticles, which settle under gravity on cells. This resulted in up to an 8.5-fold enhancement in vitro over the best commercially available transfection reagents. Such a simple approach to overcoming the physical limitations of transfection will most likely be used by many laboratories. *MS*

For a number of organisms, including plants, worms, flies, and mice, injection of double-stranded (ds) RNA has been shown to silence the corresponding gene by specific degradation of the transcript. However, the method has been of limited value in the analysis of gene function because the transient nature of the dsRNA interference (RNAi) makes it unsuitable for the study of older individuals. On page 896, Kennerdell and Carthew describe a way of overcoming this problem in *Drosophila melanogaster* by expressing dsRNA from a transgene under control of a regulatable promoter, which they introduced by P-element transposons or injection. Expression of the hairpin form of RNAi effectively silenced expression of *lacZ* in late-stage fly larvae. *ND*

Review



The production of specific glycosidic linkages in complex carbohydrates and glycoconjugates is a significant challenge to synthetic chemists, requiring laborious protection strategies and lengthy sequences of reactions. Recently, several synthetic methods have been adopted that broaden the range of glycoconjugates available for production on a large scale. On p. 835, Koeller and Wong describe new approaches for producing complex carbohydrates and outline how they are being exploited to synthesize antivirals, antimicrobials, and immunomodulators. They also highlight the need for further studies to identify a greater range of enzymes involved in glycosidic linkage, improve glycoform heterogeneity, and automate production methods. *AM*

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