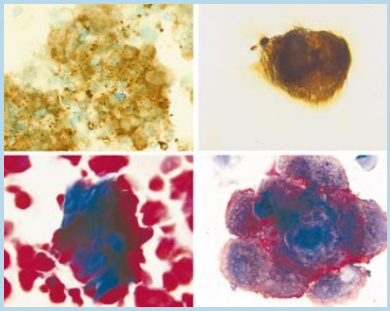
Cell source for spinal xenografts

Pigs are generally viewed as an ethically acceptable source of tissue for human organ transplantation and cell-based therapies; unfortunately, however, their cells are rapidly rejected by the human immune system. Here Imaizumi et al. demonstrate the feasibility of using transgenic pigs to obtain large quantities of cells engineered to be more immunologically compatible, as a source of cells to repair damaged spinal cords of rats. The researchers generated transgenic pigs expressing an inhibitor of human complement—a modification they expect will help mitigate graft rejection. From the pigs' olfactory bulbs, they collected olfactory ensheathing cells and Schwann cells, which have been previously shown to promote remyelination and axonal regeneration when cultured in vitro and grafted into rats. One month after injection into the spinal cord of immunosuppressed rats, the transplanted cells had migrated along the host spinal cord, promoted remyelination, and restored conduction of the regenerated axons across the transected spinal cord (see pp. 925 and 949). *ND*

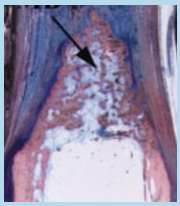
Gene transfer to airway epithelia

Gene therapy to replace the defective cystic fibrosis transmembrane conductance regulator (CFTR) is a potential strategy for treating cystic fibrosis. However, gene transfer to airway epithelial cells by current gene therapy vectors is inefficient, making the clinical benefit of such an approach unlikely. Now on page 970, Alton and colleagues decribe a Sendai virus (SeV) vector that boosts transfection efficiency by several log orders over cationic liposomes or adenovirus, to levels compatible with therapeutic application. They achieved high levels of reporter gene transfer to lungs of mice and ferrets. Gene transfer was mediated by the sialic acid receptor, which is present on most cell types, including the apical side of the conducting airways. Based on this study, the SeV vector appears to posess important advantages for gene transfer to airway epithelium: its uptake is not inhibited by mucus, and it mediates gene transfer to the cytoplasm where exogenous gene expression occurs, removing the barrier of nuclear import. *ND*

This Month in Nature Biotechnology written by Natalie DeWitt, Judy Jamison, and Meeghan Sinclair.



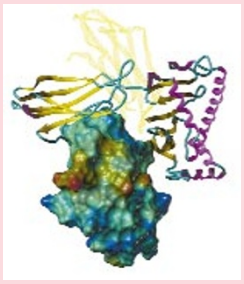
In this issue, two groups report progress in engineering bone for engraftment to treat bone defects. On page 954, Kale et al. report for the first time the ex vivo generation of crystalline human bone within a three-dimensional cellular matrix. In the presence of serum-free medium containing transforming growth factor β1 (TGF-β1), which is known to modulate early osteogenesis, the cells aggregated into "bone cell spheroids," which then began producing bone-specific proteins, culminating in the formation of microspicules containing organized human bone.



On page 959, Petite et al. exploited the similarity of coral exoskeleton to the porous architecture of natural bone, using coral as a scaffold for marrow stromal cells expanded in vitro. These were implanted into relatively large (25 mm) defects in sheep metatarsals. They observed substantial regeneration in bone implanted with the coral–MSC implants, which exceeded that of coral alone or coral plus fresh bone marrow that had not undergone in vitro expansion. Both studies support an emergent theme in tissue engineering—that mimicking natural cellular interactions and three-dimensional environment is essential for in vitro tissue regeneration (See also p. 927). ***JJ***

On page 989, De Wildt et al. demonstrate that arrays can be applied to the high-throughput screening of recombinant antibodies. The authors first selected from a phage display library antibodies that bound to tubes coated with antigen, and then used robotics to array the selected clones onto antigen-coated filters. Binders were detected using a labeled ligand. Using this approach, they were able to select antibodies to even rare components in a bacterial lysate, more effectively than conventional approaches. The arrays will be useful for parallel screening of many different antibodies against different antigens, and for elimination of background and false positives early on in a screening process (see pp. 932 and 989). ***MS***

Tempering cytotoxic T-cell responses



The challenge in treating certain immune disorders, such as autoimmune disease and host–graft disease, is to disarm the destructive potential of cytotoxic T lymphocytes (CTL) while avoiding generalized immunosuppression. Jameson and colleagues reasoned that by specifically interfering with protein–protein interactions involved in CTL activation, they could block its harmful effects while avoiding damage to resting cells. They rationally designed about 50 peptide mimetics corresponding to the protein-binding region of the murine CD8 protein, which serves as a scaffold for protein-protein interactions required for T-cell activation. One peptide exhibited dose-dependent inhibition of CD8-dependent CTL activity, without affecting mixed lymphocyte reactions. When administered to mice infected with a murine retrovirus, the peptide selectively inhibited the antiviral CTL response without impinging on the resting repertoire of cells (see p. 984). *ND*

Engineering polyketide production

Polyketides are natural products with anticancer, immunosuppressive, antimicrobial, and antiparasitic activities. The polyketide antifungal ansatrienin A is produced by *Streptomyces collinus* with coenzyme A–activated cyclohexanecarboxylic acid (CHC-CoA) as an intermediate in its synthesis. Now Cropp et al. have identified four CHC-CoA biosynthetic genes in *S. collinus*. By expressing the CHC-CoA biosynthetic gene cluster in a strain used to produce another polyketide, the antiparasitic doramectin, they were able to produce this valuable compound without the usual CHC supplementation to the fermentation. The CHC-CoA biosynthetic gene cluster has potential for directed biosynthesis in other important polyketide organisms (see p. 980). *MS*