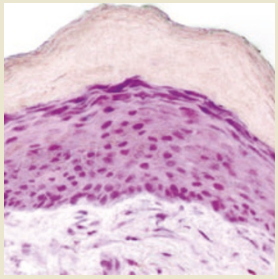
Retroviral gene therapy heals skin disorder



Junctional epidermolysis bullosa (JEB), a genetic disease of basement membrane components, causes blistering and sometimes fatal skin infections, often after minimal injury. Now De Luca and coworkers have shown that transplanting genetically modified skin cells onto the lesions of a JEB patient has long-lasting beneficial effects. The researchers transplanted the patient's own primary keratinocytes, which had been transduced with a retrovirus vector expressing *LAMB3*, a normal allele of which was missing in the patient. Normal-looking epidermis appeared within eight days and lasted for one year (the term of the follow-up). In biopsies done at one and four months, the researchers could detect vector-specific sequences and normal levels of the transcript throughout transplanted areas. They also found normal levels of associated proteins LAM5-γ2 and α6β6 integrin, indicating that the laminin was properly assembled. No inflammatory response was detected in the patient and a detailed analysis of the insertions in transplanted areas showed no evidence of clonal selection of cells with particular insertion sites. This last result allayed fears that random retrovirus insertion could lead to genotoxicity, as was previously observed in some severe-combined immunodeficient patients receiving retroviral gene therapy. (*Nat. Med.* **12**, 1397–1402, 2006) *LD*

Bacterial adjuvant boosts malaria vaccine

Low-titer, short-term antibody responses induced by otherwise good antigen candidates for malaria vaccines have long frustrated investigators. Researchers at the National Institutes of Health and Merck Research Laboratories have now succeeded in enhancing antibody responses in mice 1,000 times by conjugating one such weak antigen to an outer-membrane protein complex (OMPC) of the bacterium *Neisseria meningitidis*. Miller and colleagues conjugated Pfs25H, a recombinant form of the antigen Pfs25, which is expressed on the surface of mosquito zygotes and ookinetes during development of the mosquito parasite, *Plasmodium falciparum*, to the *N. meningitidis* OMPC. The transmission-blocking activity of sera from mice immunized with either Pfs25-OMPC or Pfs25 were comparable, showing that OMPC does not interfere with the antibody-inducing epitopes. In addition, antibody levels were significantly higher after 16 months in rhesus monkeys given conjugated vaccine than in those given nonconjugated Pfs25H, an important consideration as the antigens are expressed only in the mosquito and not the human host. Given these results, the authors hope the vaccine can soon proceed into human trials. (*Proc. Natl. Acad. Sci. USA* **103**, 18243–18248, 2006) *TM*

Smut genome

Infection of maize by the fungus *Ustilago maydis* results in dwarfism and reduced crop yield. Whereas haploid *U. maydis* obtains its nutrients from dead or decaying organic matter, the diploid form is a biotrophic parasite (or smut) that requires living plant tissue for growth. The diploid fungus invades plant cells and induces alterations in plant growth that result in plant tumor formation. To elucidate the mechanisms that it uses to invade its host, Kämper *et al.* sequenced the 20.5-Mb genomes of two different *U. maydis* strains and identified 6,902 predicted protein-encoding genes. The genomes contain a relatively small number of introns, are largely devoid of repetitive elements and exhibit highly conserved origins of DNA replication. Whereas the number of secreted cell wall–degrading enzymes is small compared with other fungal pathogens, 298 out of the 426 secreted proteins have unknown functions. Around 19% of all secreted proteins are organized in 12 clusters of 3 to 26 genes and expression of most clustered genes is specifically induced in plant tumors. Deletion mutagenesis of each gene cluster indicated that five clusters are important for pathogen virulence. Further characterization of these virulence-associated gene clusters and the other secreted proteins with unknown functions might ultimately result in enhanced fungal disease control. (*Nature* **444**, 97–101, 2006) *JWT*

From mesoangioblasts to muscles

A stem cell therapy for Duchenne muscular dystrophy has moved a step closer to clinical trials with a report of promising results in a canine model of the disease. Stem cell approaches have already shown efficacy in mouse models of muscular dystrophy, but only dystrophic dogs, which have a spontaneous mutation in the dystrophin gene, provide a close approximation of human symptoms, such as widespread muscle degeneration and early death. Cossu and colleagues used stem cells known as mesoangioblasts, a blood vessel–associated cell type recently identified by this group. After intravenous injection into dystrophic golden retrievers, mesoangioblasts circulated to distant parts of the body, crossed vessel walls and contributed to the repair of adjacent muscles, confirming the authors' previous findings in mice. The study compared treatment with allogeneic mesoangioblasts from healthy dogs (in combination with immunosuppressive drugs) and autologous mesoangioblasts that had been genetically corrected by introduction of a truncated, functional variant of the dystrophin gene. The wild-type cells proved much more effective, producing significant improvements in muscle function. (*Nature*, advance online publication 15 November 2006, doi:10.1038/nature05282) *KA*

Molecular MRI?

Although conventional magnetic resonance imaging (MRI) is not as sensitive as positron emission tomography or single-photon emission tomography for molecular imaging, the latter two techniques require ionizing radiation and lack the spatial and temporal resolution of MRI. Schröder *et al.* introduce HYPER-CEST (hyperpolarized xenon chemical exchange saturation transfer), which incorporates the spatial attributes of MRI with biochemical specificity by encapsulating hyperpolarized xenon in a molecular cage conjugated to a targeting moiety (in this case biotin). The depolarization associated with chemical exchange between the biotin/encapsulated xenon and free xenon outside the cage generates highly selective contrast at sites where the biotin binds. As the signal derives from the free xenon, the approach is ~10,000 times more sensitive than alternatives. Unlike most contrast agents, xenon is normally absent from living tissues, but can be inhaled for uptake into tissues. The authors validate the approach using biotin-tagged cages to detect avidin-coated beads *in vitro*. If the xenon biosensors can be applied *in vivo*, the work could offer exciting possibilities for biomedical imaging. (*Science* **314**, 446–449, 2006) *PH*

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