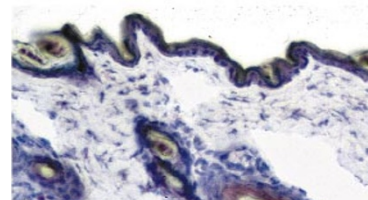


IN BRIEF

THIS MONTH IN NATURE BIOTECHNOLOGY



The nuclear arms race generated thousands of disposal sites containing radioactive toxic wastes dumped into the ground. Bioremediation is regarded as a relatively cheap and effective way of cleaning up these sites; however, this will require microorganisms that can detoxify heavy-metal and organic pollutants while withstanding high doses of radiation. In this issue Brim et al. have demonstrated the feasibility of this strategy by genetically engineering microbes that can detoxify radioactive wastes with mixed compositions. They started with *Deinococcus radiodurans*—the most radiation-resistant organism yet known, and engineered it to express an *Escherichia coli* enzyme that converts ionic mercury to a less toxic form, and a *Pseudomonas* enzyme that breaks down toluene (see page 85).



Macrophage therapies become more selective

Macrophages are multifunctional immune cells that play important regulatory roles in the skin's response to inflammatory agents. This has led to the suggestion that elimination of these cells could be beneficial in the treatment of chronic inflammatory dermatoses of the skin. Although systemic elimination of macrophage function has been shown to have therapeutic potential, it is often associated with general immunosuppression. To avoid this problem, Thepen et al. have targeted a specific local subset of macrophages, based on their enhanced expression of an immunoglobulin receptor during the inflammatory response. By injecting a toxin linked to an antibody that binds the macrophage receptors, they were able to demonstrate local elimination of the macrophages and resolution of the inflammatory response in a mouse model system (see p. 25 and 48).

Screening for site-specific proteases

Site-specific proteases are key players in the etiology of certain diseases—Alzheimer's being a prime example. In this issue, Döbeli and colleagues describe a generally applicable and high-throughput assay system for detecting site-specific proteases from crude cell homogenates (see p. 66). The protein substrate is coupled to ceramic beads and incubated with cell homogenates; then the peptides are washed, released, and analyzed by mass spectrometry, allowing for purification of proteases that clip a protein at the site of interest.



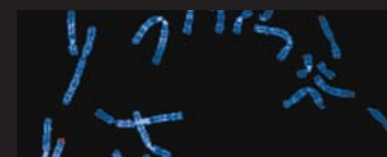
On page 43, Yoon and colleagues use a chimeric oligonucleotide to restore pigmentation in hairs of albino mice. A point mutation in the gene for tyrosinase, a key enzyme in melanin biosynthesis, leads to loss of pigmentation in mice. The workers designed a chimeric oligonucleotide that would correct the point mutation, and applied it to mice topically or by intradermal injection. After treatment they observed that black pigmentation was restored in a small number of hairs. They confirmed that the point mutation was corrected by DNA sequence analysis, and that tyrosinase activity was restored by enzymatic assays (see also p. 20).

Glow worm



Although the silkworm *Bombyx mori* is an insect of great economic importance, it has until now resisted efforts for efficient germline transgenesis, most likely because the usual insect transgenesis strategies rely on transposons that do not function in lepidopteran insects like silkworms. Toshiki et al. now have succeeded in silkworm transgenesis using *piggyBac*, a transposon discovered in another lepidopteran species. In this study, they transformed the silkworms with GFP and got glowing green worms. One can easily imagine more pragmatic applications, however, like engineering silk glands for production of novel fibers or proteins of pharmaceutical interest (see p. 81).

Longer life in vitro with telomerase



Germ cells and most stem cells do not suffer the progressive shortening of telomere length that can limit the proliferative capacity of many somatic cells in vitro. Ectopic expression of telomerase reverse transcriptase (TERT), a ribonucleoprotein complex that adds telomeric DNA to the ends of chromosomes, has been shown to extend the proliferative potential of certain somatic cells. The use of TERT overexpression to enhance the culture lifespan of somatic cells for tissue engineering purposes requires that the process not lead to tumorigenic potential or disturb the differentiated cell phenotype. On page 39, Thomas et al. demonstrate that TERT expression in bovine adrenocortical cells extends their lifespan without affecting their capacity to form functional adrenal tissue after transplantation into adrenalectomized immunodeficient mice (see also p. 22).

A new array of possibilities

The development of rapid, cost-effective strategies to screen for disease-associated genetic mutations is an important goal of molecular diagnostics. Although DNA chips are powerful tools for high-throughput, parallel sequence analysis, efforts are being undertaken to develop alternative technologies. On page 91, Walt and colleagues demonstrate the application of their fiber-optic gene array technology into a platform for the analysis of cystic fibrosis related mutations. Their array comprises a collection of chemically encoded microspheres linked to individual molecular beacon probes, which have been distributed in tiny wells at the tip of individual optical fibers. Specific advantages of their system include the elimination of the need for target labeling, and the capacity for parallel analysis of subnanomolar concentrations of target DNA.

Research briefs written by Natalie DeWitt and Robert Frederickson