Three bald mice

No need to fret about that spreading bald patch: a collaboration of scientists from the Johns Hopkins School of Medicine (Baltimore, MD) and the Centre National de la Recherche Scientifique–Institut Pasteur (Paris) have developed a mouse model that might enable greater insight into the molecular mechanisms of inherited hair loss (*Genes Dev.*, **16**, 1412–1422, June 2002). Pierre Coulombe and colleagues created mice lacking the *keratin 17* (*K17*) gene, which encodes one of 30 keratins found in epithelial tissues. Wild-type mice grow fur within one week of birth, but the *K17* knockouts failed to develop hair for several weeks. Regardless of the severity of the baldness, however, normal hair growth resumed three weeks after birth, coinciding with the start of a new cycle of hair growth. The researchers guessed that *K17* is less critical in the growth of adult hair, and that some other gene(s) could compensate for its loss of function. Indeed, *keratin 16* expression is induced when *K17* is missing, and might therefore play a role in adult hair growth (and loss). Further research is needed to determine how keratin proteins affect epithelial tissues in such a dramatic way. *CM*

Nanocrystals at arms length

Neurotransmitter uptake can now be watched *in situ* by probing cells with ligand-conjugated nanocrystals ("quantum dots"), say US researchers. Nanocrystals are brighter than ordinary fluorescent dyes, and can be conjugated to various ligands for cellular imaging. However, their fluorescence is quenched when they are directly attached to some molecules—including serotonin. Randy Blakely and colleagues at Vanderbilt University (Nashville, TN) therefore synthesized special probes in which serotonin molecules were joined to nanocrystals by a polyether linker arm. This "arms-length" linking helps to prevent quenching and allows the ligand more freedom to interact with its target, the serotonin transporter protein (SERT). The researchers then showed that the serotonin-labeled nanocrystals could block the action of SERT in transfected HeLa cells. The probes could also bind to SERT proteins in the membrane of human epithelial kidney cells, rendering the SERT locations visible by fluorescence microscopy (*J. Am. Chem. Soc.*, **124**, 4586–4594, 2002). The researchers now intend to improve the binding affinity of the probes, which is not as strong as that of existing antagonists and antibodies, and to design probes able to discriminate between serotonin transporters and serotonin receptors where these proteins coexist. *PM*

Research briefs written by Liz Fletcher, Ingrid Holmes, Judy Jamison, Christopher Martino, and Peter Mitchell.

Muzzling malaria

Malaria, caused by the *Plasmodium falciparum* parasite, kills around 1–3 million people each year, despite the widespread use of insecticides to eliminate its carrier, the mosquito. Now, a team of US and German researchers has succeeded in blocking the cycle of infection by genetically modifying these insects (*Nature* **417**, 452–455, 2002). The *Plasmodium* parasites, which are ingested when the mosquito feeds on the blood of infected hosts, wriggle through the insect's midgut wall, maturing into oocysts that subsequently generate thousands of wormlike sporozoites, which are spat into the bloodstream of the next human "meal". Marcelo Jacobs-Lorena and colleagues suspected that *Plasmodium* bridges the midgut and salivary gland epithelia by latching onto a host molecule, and so they screened a large number of artificial peptides, identifying one tissue-specific candidate—SM1. The researchers then engineered a strain of the *Anopheles stephensi* mosquito that could manufacture SM1 peptides in response to blood feeding. Infection by *Plasmodium berghei* was sharply reduced in these modified mosquitoes, as was the mosquitoes' ability to transmit the parasite to mice. Moreover, the mosquitoes' progeny also inherited the SM1-producing transgene. Anticipating that "resistant" *Plasmodium* variants will evolve, the authors hope to engineer mosquitoes carrying multiple genes, each of which would encode different parasite-inhibitory mechanisms. *JJ*

Sperm-boosting gene therapy

Worldwide, about one in five couples is infertile, and in 4–9% of instances this infertility is attributed to genetic defects in sperm. Now, Inder Verma and colleagues at The Salk Institute (La Jolla, CA) and Riken Institute (Tsukuba, Japan) have used gene therapy to repair one genetic fault in a strain (Sl/Sl^d) of infertile mice, successfully restoring sperm production (*Proc. Natl. Acad. Sci. USA* **99**, 7524–7529, 2002). Of the four viral vectors tested to transduce Sertoli cells, lentiviral vectors were the most promising. Lentiviral vectors were then used to express the *c-kit* ligand gene, missing in Sl/Sl^d mice, in Sertoli cells. All of the treated mice produced sperm. However, just small quantities of sperm were produced, and eggs had to be fertilized using intracytoplasmic injection of sperm. Analysis of the offspring showed that none carried the *c-kit* ligand transgene, suggesting that it had not integrated into germ cells. Verma says that although the results are encouraging, more research is needed: "We need to learn more about possible germline transmission, they need FDA approval, and we need to work with much larger quantities." *IH*

Smart fat

As ethical and social concerns continue to impede research on stem cells derived from embryos, researchers have turned to the less controversial riches within flab. Investigators at the stem cell company Artecel Sciences (Durham, NC) and Duke University Medical Center (Durham, NC) have preliminary evidence that stem cells derived from mouse and human fat can be differentiated into neurons (*Biochem. Biophys. Res. Commun.*, **290**, 763–769, 2002). Previously, researchers transformed stem cells from adult adipose tissue into fat, cartilage, muscle, and bone cells. Now, by tweaking the growth conditions, they have generated neuron-like cells. The differentiated cells developed a neuron-like structure and secreted proteins normally found only in brain cells. Further work needs to be done to determine whether or not the "neurons" will be viable in the long term, because they currently begin to die after the third day in culture. Artecel's Jeffrey Gimble, a co-author of the research, says that further optimization of the growth conditions will address this problem. There is as yet no evidence as to whether the "neurons" function like the real thing. Adult stem cells derived from bone marrow have already been differentiated into neurons, but adipose tissue is in greater abundance and is less painfully harvested from patients. *LF*