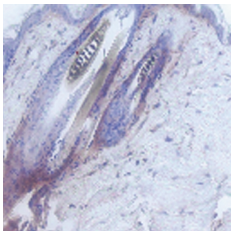
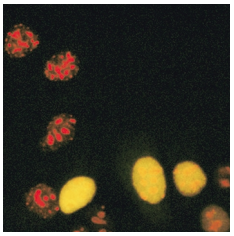
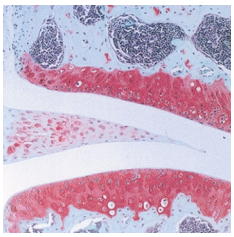


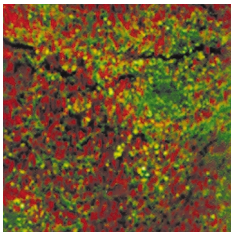
Testosterone and wound healing in mice and men. You might be more likely to get into a fight and get hurt if your testosterone levels are high, but that is only part of the bad news. As Gillian Ashcroft and Stuart Mills report, beginning on page 615, high testosterone levels also impair cutaneous wound healing. They found that testosterone levels correlated with the rate of wound healing in elderly human males. In male mice, castration accelerated wound healing and was associated with a dampened immune response as well as increased matrix deposition in the wound tissue. Consistent with these observations, systemic blockage of the androgen receptor accelerated wound healing in mice, suggesting that this might be a way to therapeutically improve wound healing in human patients.



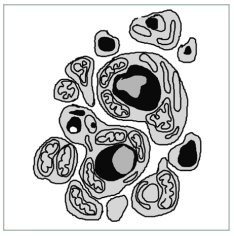
Skp2 and breast cancer. Skp2 is the substrate-targeting subunit of the SCF^{Skp2} ubiquitin ligase and is required for the ubiquitination and subsequent degradation of the cell-cycle regulator p27. As p27 is downregulated in aggressive human breast cancers, Michele Pagano and colleagues examined Skp2 expression in human breast cancer samples and studied Skp2 function in breast cancer cell lines. As they report, beginning on page 633, tumors expressing high levels of Skp2 are typically negative for expression of the estrogen receptor (ER), do not overexpress Her-2, and are associated with a poor prognosis. In these tumors, Skp2 might be a potential therapeutic target. Inhibition of Skp2 activity results in a decreased malignant potential of breast cancer cell lines assayed by their ability to grow in the absence of cell adhesion. The researchers also found that ectopic expression of Skp2 in ER-positive breast cancer cell lines abolished the antiproliferative effects of antiestrogens, raising the possibility that Skp2 overexpression plays a role in the development of resistance to these drugs.



The culprit prostaglandin receptor in experimental arthritis. Prostaglandins in general and prostaglandin E2 (PGE2) in particular have been implicated in rheumatoid arthritis. PGE2 can act through at least four different G protein–coupled receptors, EP-1 through 4. Seeking to identify the key player(s) involved, Laurent Audoly and colleagues (pages 651–658) induced arthritis in four different mouse strains, each lacking one of the four receptors. In wild-type mice and three of the four mutant strains, anti-collagen antibodies induced an arthritic condition that resembles human rheumatoid arthritis. Mice lacking the EP-4 receptor, in contrast, were resistant to collagen antibody–induced arthritis and exhibited lower levels of local and systemic inflammation. These results implicate EP-4 receptors in the arthritic response to PGE2 and suggest that they might constitute a novel and specific target for therapeutic intervention.



ATF2: An Achilles' heel of melanoma? The transcription factor ATF2 is involved in the cellular stress response and has been implicated in melanoma progression and resistance to treatment. Having previously identified a peptide that interferes with normal ATF2 function, Ze'ev Ronai and colleagues now show (pages 643–650) that expression of the peptide in tumor cells inhibited growth and metastasis of melanoma in a mouse transplant model. In addition, peptide expression sensitized melanomas to apoptosis-inducing drugs, which are not normally effective against these types of tumors. Results in cell culture suggest that these consequences are, at least in part, due to increased expression and activity of c-Jun, itself a transcription factor that is able to induce apoptosis in the absence of ATF2.



How vitamin E protects T cells. Vitamin E is essential for normal immune function and known to increase T cell numbers in man and mouse, but the underlying molecular mechanisms are not clear. Activated T cells express the cell death–promoting CD95 ligand, and many of them undergo CD95/CD95 ligand–mediated apoptosis. Peter Krammer and colleagues report now (pages 681–690) that vitamin E reduces the activities of the transcription factors AP-1 and NF-κB, which in turn leads to lower expression of CD95 ligand on activated T cells. As activation-induced cell death is a major cause of T cell depletion in AIDS, the researchers also examined the effects of vitamin E on peripheral T cells from HIV-positive individuals and found that vitamin E can protect these cells against apoptosis as well.