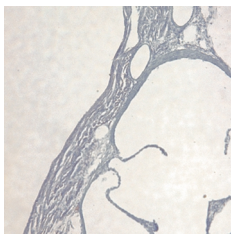
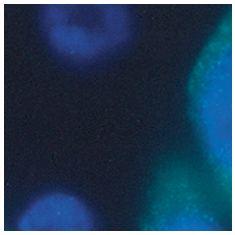
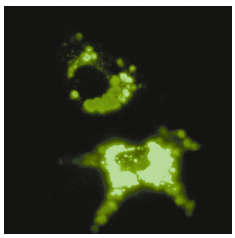


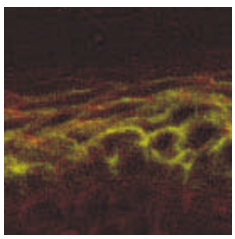
ABCA1—more is better! Efficient cholesterol efflux from macrophages is critical for preventing the early stages of atherosclerosis. The ABC transporter ABCA1, encoded by the gene mutated in Tangier disease, plays a key role in this process. Tangier disease patients have very low plasma HDL cholesterol levels, and heterozygous individuals have reduced levels. Upregulation of ABCA1 function might therefore be a potential strategy to prevent or treat atherosclerosis. Beginning on page 35, Michael Hayden and colleagues lend experimental support to this hypothesis. Mice lacking ApoE spontaneously develop atherosclerotic lesions. The presence of a human *ABCA1* transgene in these animals leads to reduced lesion size and increased cholesterol efflux from macrophages. These results disagree with a similar study published earlier this year (Joyce et al. *Proc. Natl. Acad. Sci.* USA. **99**:407–412; 2002), where an increase in lesions was seen in ApoE mutants expressing an *ABCA1* transgene. The discrepancy is likely due to differences in the transgenes used. In the transgene from Joyce et al. the human *ABCA1* gene was driven by control elements from the *ApoE* promoter, whereas the Hayden group used a construct containing endogenous *ABCA1* regulatory elements.



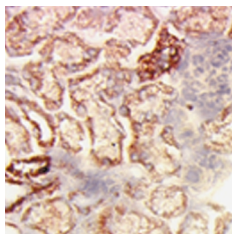
Arresting cells before mitosis. Nocodazole, vincristine, and colchizine disrupt microtubule function, which is thought to trigger the mitotic checkpoint and result in mitotic arrest. In their article beginning on page 91, Scott Kauffman and colleagues describe results from studying the cell cycle response of breast cell lines to these drugs. Rather than with mitotic arrest, a subset of the cell lines responded to high drug concentrations with pre-mitotic G1 and G2 arrest that prevented the cells from ever reaching mitosis. This suggests that the cell cycle effects of a commonly used class of chemotherapeutic agents are more complicated than previously thought. In addition, these results raise the possibility of a previously unrecognized checkpoint that couples cell cycle progression to microtubule integrity.



Mechanisms of action of anti-tumor antibodies. Efficacy of anti-tumor antibodies has been attributed to growth inhibition of tumor cells or antibody-dependent cytotoxicity through complement activation, macrophages, or NK cells. A report by Raphael Clynes and colleagues on pages 71–79, as well as a recent article published elsewhere (Kalergis and Ravetch. *J. Exp. Med.* **195**:1653; 2002) reveal another mechanism by which antibodies elicit specific anti-tumor effects. Dendritic cells are professional antigen-presenting cells that express Fc receptors on their surface. When these receptors bind the constant region of an antibody, the antibody itself and the (tumor) antigen bound to it are internalized. Dendritic cells then have the unique ability to present the antigen on both class I and class II MHC molecules, resulting in the activation of antigen-specific CD4 and CD8 cells. The two papers show that antigen/antibody complexes endocytosed by dendritic cells can trigger antigen-specific CD4 and CD8 responses. This suggests that Fc receptor-mediated enhancement of antigen presentation is likely to contribute to the anti-tumor immune response elicited by anti-tumor antibodies, and that Fc receptor targeting is a promising strategy in vaccine development.



The workings of a skin-smart bacterium. Over 30 years ago it was established that exfoliaive toxins present in some strains of *Staphylococcus aureus* are responsible for bullous impetigo and staphylococcal scalded skin syndrome, some of the most common bacterial infections. Patients have blisters in the living epidermis that, presumably, allow the bacteria to spread under and circumvent the stratum corneum, the major barrier against skin infections. Recently, the amino acid sequence and crystal structure of the exfoliative toxins suggested that they function as serine proteases. Having previously identified desmoglein 1, a desmosomal glycoprotein, as a target, John Stanley and collaborators show on pages 53–60 that the three known *S. aureus* exfoliative toxins act as serine proteases with exquisite specificity for desmoglein 1. They conclude that bullous impetigo and staphylococcal scalded skin syndrome can be attributed to hydrolysis of a single peptide bond in desmoglein 1.



The C5a receptor in sepsis. The complement activation product C5a is known to play an important role during sepsis in rodents and has been suggested as a potential target for therapeutic intervention. Recently, blocking agents against the C5a receptor (C5aR) have become available, focusing attention on its role in sepsis as well. As Peter Ward and co-workers report beginning on page 101, the C5aR is upregulated in several organs during sepsis in mice. Treating the animals with blocking antibodies reduces cytokine serum levels, bacterial content in the organs, and dramatically improves survival rates. As previously shown with anti-C5a antibodies, improved survival is only seen when treatment is concurrent with the induction of sepsis; a delay of six hours all but abolished the beneficial effects.