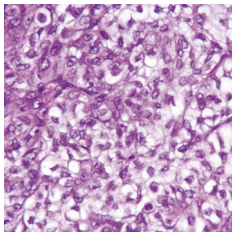
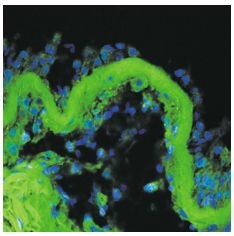
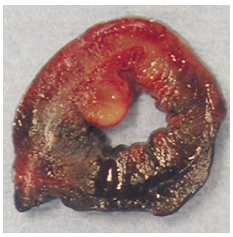


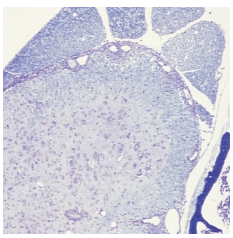
The two faces of TGF-β in cancer progression. TGF-β plays a complex role in epithelial carcinogenesis. The prevailing hypothesis is that it functions as a tumor suppressor in the early stages of the process, but as a pro-oncogenic factor later on. Lalage Wakefield and colleagues have used a model of breast cancer progression to analyze the consequences of decreased epithelial responsiveness to TGF-β at different stages of progression (pages 1116–1124). The authors found that the decrease in TGF-β receptor expression seen clinically in approximately 30–50% of human breast cancers plays a causal role in breast cancer progression up to the stage of histologically aggressive but nonmetastatic disease. At that point, however, TGF-β switches from tumor suppressor to prometastatic factor. These data have important implications for understanding epithelial carcinogenesis and for the design of new approaches to the prevention and treatment of breast cancer.



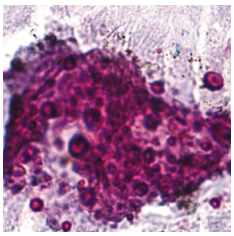
Less ECM is more in asthma. Allergic asthma is characterized by eosinophilic airway inflammation and structural changes in the airway wall. The remodeled phenotype, which may be the consequence of excessive repair processes following repeated airway injury, includes increased deposition of ECM proteins. Barry Kay and colleagues have now shown that specific reduction of bronchial mucosal eosinophils with anti–IL-5 treatment could reduce markers of airway remodeling in asthma (pages 1029–1036). At baseline, airway eosinophil infiltration and ECM protein deposition were increased in the basement membrane of asthmatics compared to nonasthmatic controls. Treatment of asthmatics with anti–IL-5 antibody, which specifically decreased airway eosinophil numbers, significantly reduced the deposition of the ECM proteins tenascin, lumican, and procollagen III. These data suggest that eosinophils may contribute to the tissue remodeling processes in asthma by regulating the deposition of ECM proteins.



The beat goes on with erythropoietin. Ischemic heart disease remains the primary cause of morbidity and mortality in the Western world. Current therapeutic strategies are aimed at relieving the ischemia by opening blocked arteries; however, none can directly protect the heart and thereby preserve ventricular function. Thus, Walter Koch and colleagues investigated a new therapeutic strategy whereby infarcted myocardium can be saved by erythropoietin (EPO) (pages 999–1007). EPO treatment shortly after myocardial infarction (MI) protected the heart against apoptosis in vivo, resulting in smaller infarcts, increased viable myocardium, and enhanced post-MI contractile function. EPO-mediated cell survival involved Akt activation, and the cardioprotective effects were seen without an increase in hematocrit, eliminating oxygen delivery as a factor in myocyte survival and function. These results demonstrate that EPO can directly protect the ischemic and infarcted heart.



Revealing the mysteries of $CD8^+CD28^-$ T cells. Previous in vitro assays with human cells have demonstrated that $CD8^+CD28^-$ T cells can have a regulatory role. Samia Khoury and colleagues have now addressed the important questions of whether these cells also exist in vivo and whether they can regulate experimental autoimmunity (pages 1037–1048). Adoptive transfer of $CD8^+CD28^-$ T cells, but not $CD8^+CD28^+$ T cells, into $CD8^{-/-}$ mice resulted in significant suppression of disease. Depletion of $CD8^+$ T cells from $CD28^{-/-}$ mice rendered these resistant mice susceptible to EAE. These data indicate that regulatory $CD8^+$ T cells play a critical role in suppressing EAE in $CD28^{-/-}$ mice, in part by controlling the outgrowth of reactive $CD4^+$ T cells. $CD8^+CD28^-$ T cells may represent a unique regulatory $CD8^+$ T cell population that functions in innate immunity.



***Cryptococcus neoformans*: the fungus among us.** Infection by *C. neoformans* occurs following inhalation of fungal cells that travel from the lung to the brain. The first line of defense includes recruited alveolar macrophages (AMs), which inhibit and kill microorganisms. Maurizio Del Poeta and colleagues identified a novel cryptococcal factor, antiphagocytic protein 1 (App1), whose expression is regulated by *inositol phosphoryl ceramide synthase 1* (*Ipc1*) (pages 1080–1094). Treatment with recombinant App1 significantly inhibited the phagocytosis of cryptococcal cells by AMs through a complement-mediated mechanism. The impact of the *Ipc1*-App1 pathway on pathogenicity had different outcomes depending on whether the host was immunocompetent or immunocompromised. This study identifies App1 as a novel regulator of phagocytosis and virulence through a complement-mediated mechanism and may set novel criteria for antifungal drug development.