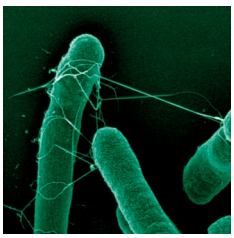
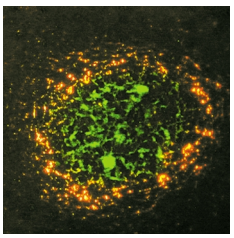
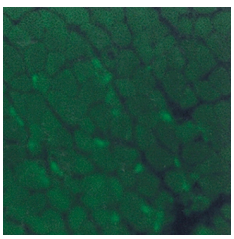


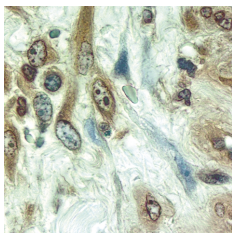
Spreading *E. coli* all over the gut. Enteroaggregative *Escherichia coli* (EAEC) is an emerging diarrheal pathogen defined by its aggregative adherence to human cells in culture. The bacteria are thought to adhere to intestinal mucosa in a thick biofilm that may mediate their persistence in the human intestine. Searching for genes associated with the pathogen's virulence and/or those that encode immunogenic molecules that could serve as vaccines, James Nataro and colleagues have identified a locus that is present in 80% of EAEC strains. As they report (pages 1329–1337), the *aap* gene encodes a secreted protein — which they name dispersin — that coats the bacterial surface and promotes dispersal of the bacteria on the intestinal mucosa. These results suggest that dispersin plays a role in EAEC pathogenesis and might be a suitable target for vaccine development.



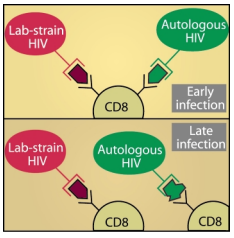
Manipulating primate lymphoid microenvironments. The lymphotoxin (LT) system plays a key role in the development and maintenance of lymphoid tissues. In mice, the interruption of lymphotoxin-β receptor (LTβR) signaling results in the collapse of several lymphoid microenvironments including follicular dendritic cells (FDCs) that trap immune complexes (ICs) on their dendritic surface and subsequently serve as long-term antigen reservoirs. This IC trapping may be exploited by pathogens such as HIV that can persist in FDC networks during treatment, and may also aid the progression of autoimmune diseases. Jeffrey Browning and colleagues (pages 1359–1369) examined the effects of perturbing FDC networks in nonhuman primates. In cynomolgus monkeys treated with the decoy receptor LTβR-Ig, splenic FDC networks collapsed and prohibited IC trapping in lymphoid tissues, whereas the Ab response to neo-antigen challenge was unaffected. Three months after cessation of treatment, FDC networks reappeared in the germinal centers, suggesting that FDC disruption may represent a candidate for the transient alteration of human immune function during disease.



The role of complement in myasthenia gravis. Myasthenia gravis (MG) is an autoimmune disorder characterized by muscle weakness and chronic fatigue due to the development of autoantibodies against the acetylcholine receptor (AChR) located in neuromuscular junctions. Several lines of evidence suggest that complement activation resulting from autoantibody binding to AChR is key to MG pathogenesis. Given that decay-accelerating factor (DAF) is a membrane regulator of C3 activation that protects self cells from autologous complement attack, M. Edward Medof and colleagues (pages 1269–1274) investigated the susceptibility of DAF knockout mice to experimental autoimmune MG. Following anti-AChR antibody injection, mutant mice showed greater muscle weakness, postsynaptic junction membrane damage, reduced AChR levels, and localized C3b deposition greater than that observed in controls. The authors suggest that complement inhibitors may therefore have therapeutic value in the treatment of MG flares.



Making myofibroblasts. Myofibroblasts are contractile cells whose phenotype lies between fibroblasts and smooth muscle cells. They participate in wound healing and chronic fibrosis and are thought to derive from local fibroblasts in response to TGF-β signaling. Screening for genes that were upregulated during smooth muscle myogenesis, Lucia Schuger and colleagues identified *p311*, encoding a protein without functional domains suggested by sequence homology. They now report (pages 1349–1358) that forced P311 expression transformed fibroblasts into myofibroblasts in vitro, and that its expression in vivo during human wound healing is consistent with a proposed causative role. Surprisingly, P311 inhibited TGF-β signaling and collagen expression, suggesting that it exerts anti-fibrotic effects. These results raise the possibility that manipulation of P311 and its downstream effectors might facilitate wound healing and reduce scarring.



Dynamics of the CD8⁺ response to HIV. High levels of HIV-specific CD8⁺ T cells are present in patients throughout the course of HIV disease. While able to reduce viremia in the acute phase of infection, the CTL response fails to control viral replication in chronic infection. Seeking to understand this difference, Premlata Shankar and colleagues compared the CD8⁺ T cell response to lab strains of HIV with that to autologous virus in human patients. Their results (pages 1339–1347) suggest that the functional CD8⁺ T cell response to the patients' own viral isolates declines around the time when disease symptoms develop. CD8⁺ cells that recognize consensus epitopes seem to persist from an earlier response, but no longer effectively recognize autologous virus. Responses that target newly presented or substituted epitopes resulting from viral mutation have to be generated in the setting of HIV-induced CD4⁺ deficiency and cytokine imbalance. Therefore the response to autologous virus at later stages of disease might be functionally impaired.