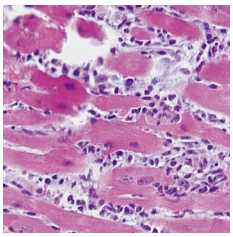
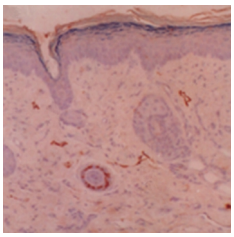
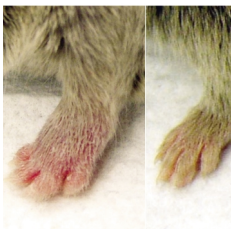


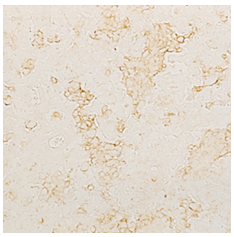
IL-12: Bad news for the heart? Myocarditis is associated with viral infections. In addition, several lines of evidence suggest that autoreactive $CD8^+$ T cells play a role in the disease. As IL-12 is part of the innate immune response to viral infections and has been implicated in autoimmune diseases, including myocarditis, Andrew Lichtman and colleagues investigated how IL-12 contributes to the differentiation of T cells that damage the heart. The researchers used a new mouse model of myocarditis that allowed the comparison of different populations of cytotoxic $CD8^+$ T cells specific for the same defined myocardial antigen. Their results (pages 671–680) showed that while IL-12 was not essential for the generation of cytolytic IFN-γ–producing effector T cells, only $CD8^+$ T cells primed in the presence of IL-12 were able to proliferate in vivo and infiltrate the heart in significant numbers. IL-12 thus seems to play an important role in the differentiation of the pathogenic $CD8^+$ T cells that underlie the autoimmune component of myocarditis.



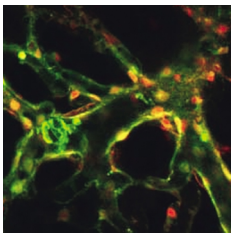
Therapeutic lymphangiogenesis. Mutations in VEGFR-3 cause hereditary lymphedema. While this is a rare disorder, secondary lymphedema, caused by surgical removal of lymph nodes, radiation therapy, or infectious diseases, is a common and disabling condition. Various lines of evidence suggest the potential of the VEGFR-3 ligand VEGF-C for the treatment of lymphedema. Working in two animal models of acute secondary lymphedema, Douglas Losordo and colleagues report (pages 717–725) that local transfer of naked plasmid DNA encoding human VEGF-C promoted lymphangiogenesis and improved physical, functional, and pathologic aspects of the disease in rabbits and mice. Their results also suggest that while plasmid transfer induces only transient expression of VEGF-C, once the lymphatic connection is re-established, drainage function can be maintained.



ICOS, IL-17, and arthritis. ICOS is a costimulator expressed on activated T cells and involved in Th2 function and class switching by B cells. Having previously shown that lack of ICOS enhances the susceptibility in mice to experimental autoimmune encephalomyelitis, Chen Dong and colleagues subsequently examined whether ICOS has a role in rheumatoid arthritis. Working with a well-established mouse model of arthritis, they report (pages 701–706) that in the absence of ICOS, mice normally susceptible to collagen-induced arthritis were completely protected against the disease. ICOS-knockout mice had reduced levels of anti-collagen IgM and IgG antibodies as well as lower levels of IL-17, a proinflammatory cytokine implicated in rheumatoid arthritis. These results warrant additional investigation into the potential of ICOS as a therapeutic target in rheumatoid arthritis.



CD44 and tuberculosis resistance. CD44 is an adhesion molecule involved in inflammatory processes. It is present on hematopoietic cells and linked to the cytoskeleton. As cell migration and phagocytosis are dependent on cytoskeletal rearrangements and important in the immune response against *Mycobacterium tuberculosis*, Jaklien Leemans and colleagues investigated the role of CD44 in pulmonary tuberculosis. Their results (pages 681–689) suggest that CD44 expressed on macrophages is involved in the binding and subsequent uptake of *M. tuberculosis*. Mice lacking CD44 exhibited a more severe pathological response to infection with *M. tuberculosis*: they had a profound defect in the early recruitment of macrophages to the lungs, enhanced mycobacterial outgrowth in lung and liver, and a reduced rate of survival compared with controls. CD44 is a unique molecule implicated in the clearance of mycobacteria.



Mitochondrial mechanotransmission. Endothelial cells in the lung generate a proinflammatory response to even modest elevations of vascular pressure. This involves expression of the leukocyte adhesion receptor P-selectin on endothelial cells, which increases leukocyte rolling on the vessel surface. Interested in the underlying mechanisms, Jahar Bhattacharya and colleagues applied real-time, in situ fluorescence microscopy in lung capillaries. As they report (page 691–699), pressure elevation increased the amplitude of cytosolic Ca^{2+} oscillations, which in turn increased the amplitude of mitochondrial Ca^{2+} oscillations and the production of reactive oxygen species. P-selectin expression could be inhibited by antioxidants and inhibitors of mitochondrial metabolism, demonstrating that mitochondria are the organelles that couple the mechanical effects of higher pressure to the capillary's proinflammatory response.