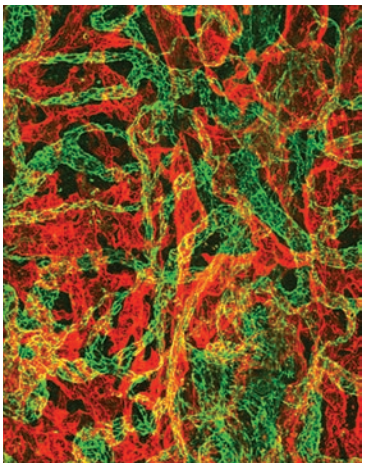
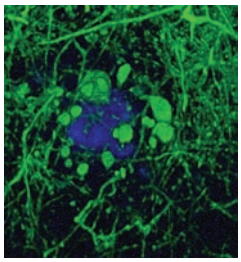
Lymphangiogenesis in the airways



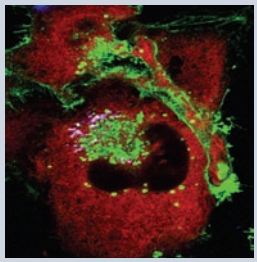
Edema, a cardinal sign of inflammation and clinically significant feature of inflammatory disease, results when the amount of leakage from inflamed blood vessels exceeds the capacity of lymphatic vessels for drainage. Despite the recognition that angiogenesis and mucosal swelling can increase airflow resistance in obstructive lung disease, little is known about the status of lymphatic vessels and factors that influence fluid drainage from the respiratory tract. Donald McDonald and colleagues now show persistent lymphangiogenesis in 2 mouse models of airway disease: chronic respiratory tract infection with *Mycoplasma pulmonis* and adenoviral transduction of airway epithelium with VEGF family growth factors (pages 247–257). The authors identified the growth factors and receptors responsible for the lymphangiogenesis and made the surprising discovery that — unlike the accompanying angiogenesis — the lymphatic growth is not readily reversible. After antibiotic treatment of the infection, inflammation and remodeling of blood vessels quickly subsided, but lymphatic vessels persisted. The authors also show that impaired growth of new lymphatics in airway inflammation may lead to "bronchial lymphedema," which exacerbates the swelling and airflow obstruction and wheezing naturally accompanying asthma and airway inflammation. Correction of defective lymphangiogenesis may benefit the treatment of asthma and other inflammatory airway diseases.

A window into the brain



The aggregation and buildup of amyloid-β peptide (Aβ) in the extracellular space of the brain plays a key role in the pathogenesis of Alzheimer disease (AD). Several approaches to decreasing Aβ production or increasing its clearance from the brain are being studied as potential treatments for AD; however, it is not known whether, upon clearance of Aβ, significant structural damage to nerve processes remain. David Holtzman and colleagues use an *APP* transgenic mouse model of AD that expresses yellow fluorescent protein in a subset of neurons to investigate the structural changes in AD brains after treatment (pages 428–433). Using multiphoton microscopy, the authors monitored amyloid deposition and clearance through cranial windows. In vivo studies suggested that amyloid-associated dystrophic neurites are relatively stable structures in the AD mice over several days. However, a significant reduction in the number and size of dystrophic neurites was seen 3 days after Aβ deposits were cleared by anti-Aβ antibody treatment. This analysis suggests that ongoing axonal and dendritic damage is secondary to the buildup of Aβ and is in part rapidly reversible.

Immune complexes pay a Toll



Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by pathogenic autoantibodies to nucleoproteins and DNA. Andrew Luster and colleagues now show that serum from patients with active SLE, as well as DNA-containing immune complexes isolated from lupus serum (SLE-IC), stimulate cells in a Toll-like receptor 9–dependent (TLR9-dependent) manner, whereas serum or complexes isolated from patients with other autoimmune rheumatic diseases do not (pages 407–417). This stimulation required the presence of DNA in the complex as well as the Fc portion of IgG. Further, the authors demonstrated that CD32 (FcγRIIa) is required to facilitate the internalization of SLE-IC into a subcellular compartment containing TLR9. Stimulation of plasmacytoid dendritic cells by SLE-IC through the CD32-TLR9 pathway induced the production of more than 20 proinflammatory cytokines and chemokines, which likely contribute to the pathogenesis of SLE. These findings suggest a novel mechanism whereby endogenous DNA-containing immune complexes contribute to the pathogenesis of lupus. In addition, these findings demonstrate a functional interaction between Fc receptors and TLRs, which may be relevant to other TLR ligand–containing immune complexes.

HIV-specific T cells don't give up the fight

HIV-specific $CD4^+$ T helper lymphocytes are preferred targets for infection. Although complete interruption of combination antiretroviral therapy (ART) often constitutes part of therapy, there is grave concern that the ensuing resumption of viral replication might destroy these T helper populations. As it remained unclear whether the return of HIV-1 replication physically destroys HIV-1–specific T helper cells in the peripheral blood, Rodney Phillips and colleagues use HLA class II tetrameric reagents specific for a Gag p24 antigen to directly visualize and track the HIV T helper population associated with that peptide (pages 443–450). The authors studied patients with early-stage HIV infection who were given a short, fixed course of ART as part of a clinical study and found that the return of viral replication that follows the cessation of ART does not destroy T helper cells. However, the return of the antigen does drive the cells to an effector form and increases their turnover. These findings show that HIV-specific CD4 cells can be visualized, quantified, and tracked through a crucial phase of treatment cessation.