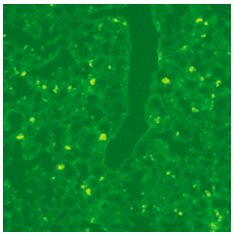
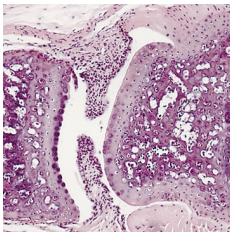
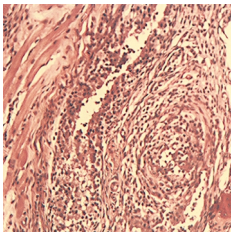


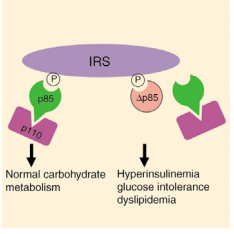
Skewing the immune response in the lung. Why do inhaled antigens frequently trigger allergic reactions? Or, in immunology-speak, why does antigen exposure via airway epithelia often result in a Th2-type response? On pages 1441–1448, Stephanie Constant and colleagues suggest some answers. They identify a resident population of antigen-presenting cells that take up the majority of intranasally-delivered antigens and present them to antigen-specific naive T cells, predominantly locally in the pulmonary tract. In response to antigen uptake, these resident antigen-presenting cells secrete Th2-promoting cytokines, including IL-10 and IL-6. Codelivery of LPS induced the expression of IL-12, but IL-10 and IL-6 levels stayed the same, as did the bias towards a Th2-type response.



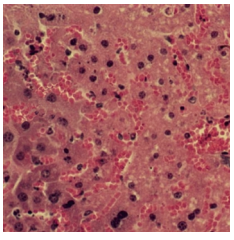
Osteoclasts and rheumatoid arthritis. Rheumatoid arthritis (RA) is associated with joint inflammation and progressive joint destruction. Both cartilage and bone tissues are destroyed. The latter, not seen in most other inflammatory joint diseases, is a major contributor to the debilitating symptoms of the disease. Indirect evidence suggested that bone destruction in RA — as in normal bone turnover — is mediated by osteoclasts. Georg Schett and colleagues now show (pages 1419–1427) that this is indeed the case. Wild-type mice that expressed human tumor necrosis factor from a transgene developed severe and destructive arthritis. Mice lacking c-fos (a factor essential for osteoclast differentiation) and carrying the transgene also developed arthritis, with comparable levels of synovial inflammation and cartilage destruction, but showed no sign of bone erosion. This suggests that RA patients may benefit from therapeutic inhibition of osteoclasts.



Map makes *Staphylococcus* mean. *Staphylococcus aureus* (SA) is an opportunistic pathogen with a diverse battery of virulence factors, each of which can act alone or in concert in the development of persistent infections. One such factor, the MHC class II analog protein (Map) was named for its homology with MHC class II molecules, and subsequent studies have shown that it can interfere with innate host defense systems. On pages 1461–1471, Eric Brown and colleagues demonstrate, using a chronic SA infection model in the mouse, that Map can also interfere with acquired immunity. The authors data, using MAP-positive and -negative SA strains in immuno-competent and -compromised hosts, suggest that Map promotes SA persistence and survival by altering T cell function in vivo. The mechanisms by which Map exerts its function, however, remain to be determined, as does the significance of the intriguing homology to MHC class II.



PI 3-kinase activity in the liver. PI 3-kinase is thought to act downstream of insulin signaling, but results from targeted disruption in mice of PI 3-kinase function — both globally and in specific tissues — have failed to yield a clear picture of when and where PI 3-kinase is required to mediate insulin's function. Taking advantage of the fact that systemic administration of adenovirus leads to accumulation of virus in the liver, Wataru Ogawa and colleagues have used an adenoviral vector carrying a dominant-negative mutant of P1 3-kinase to abolish the function of the enzyme specifically in the liver. Mice infused with the virus exhibited dyslipidemia and hyperinsulinemia, as well as a marked increase in blood glucose levels in response to glucose intake (pages 1483–1491). These results provide evidence that PI 3-kinase activity in the liver is required for normal carbohydrate and lipid metabolism in vivo.



Transducing hepatitis. T-cell mediated immune responses play a major role in hepatitis-induced liver injury. Studies investigating concanavalin A–induced (Con A-induced) hepatitis have revealed the involvement of multiple cells and cytokines; however, the mechanisms underlying these interactions are not completely understood. Bin Gao and colleagues (pages 1503–1513) investigated the roles of IFN-γ, IL-6, and members of the JAK-STAT and SOCS families of proteins in Con A-induced hepatitis by studying disease development and progression in various mutant mouse strains. Their results lead to a model in which disease is controlled, on one hand, by IFN-γ–activated STAT1 which stimulates immune cells and promotes liver cell death and, on the other hand, by IL-6-activated STAT3 which suppresses IFN-γ signaling and induces anti-apoptotic factors. The two pathways negatively regulate each other through the induction of SOCS. Elevated levels of IL-6 and IFN-γ are also observed in several human liver disorders, suggesting that modulation of the mutual antagonism between STAT 1 and STAT 3 may help to limit T cell–mediated liver damage in patients.