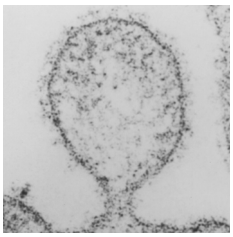
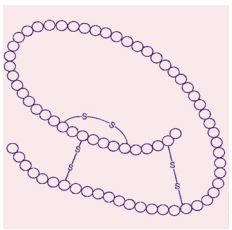
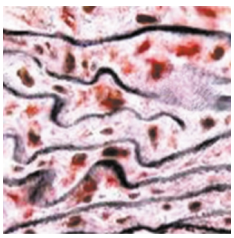


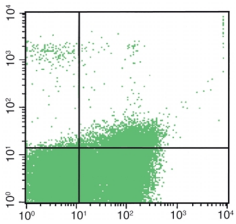
Immune suppression by measles virus. Measles virus infection is often associated with a generalized state of immunosuppression that facilitates health- and life-threatening secondary infections. To understand the mechanisms of immunosuppression, Michael Oldstone and colleagues studied mice that were genetically engineered to be susceptible to measles virus infection. These mice were infected with measles virus five days before challenge with *Listeria monocytogenes* and compared with age-matched naive and *L. monocytogenes*–infected mice that did not receive measles virus. The results (pages 805–810) demonstrated that concurrent measles virus infection suppresses innate as well as adaptive immune responses, which prevents effective clearance of the bacterial infection. Future studies are needed to determine how the virus exerts its effects, and it is hoped that these will aid in the development of improved treatment strategies. Figure reproduced with permission from *Viruses, Plagues and History* by Michael Oldstone, copyright 1998 by Oxford University Press Inc.



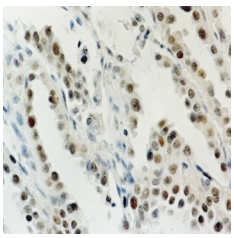
Proinsulin, diabetes, and the NOD mouse. Accumulating evidence supports a role for proinsulin as a key autoantigen in type I diabetes. In contrast to humans, who have one proinsulin gene, mice express two proinsulin isoforms, which are encoded by different genes. To study the role of proinsulin 2, the predominant isoform in the thymus, Christian Boitard and colleagues have introduced a null mutation for the gene into mice of the NOD genetic background, which spontaneously develop diabetes at a high frequency. As they report (pages 851–857), the absence of proinsulin 2 in these animals was associated with accelerated insulitis and diabetes, increased capacity to transfer diabetes, and elevated levels of anti-insulin autoantibodies. These results demonstrate the importance of proinsulin as an autoantigen in the NOD mouse and suggest that future studies in this system could shed light on the pathogenic or regulatory role of insulin-directed autoimmunity.



Cathepsin S promotes atherosclerosis. Remodeling of the ECM contributes to atherosclerosis at multiple stages, and several lines of evidence have implicated the elastolytic cathepsins S (Cat S) and K. Seeking direct evidence for a role of Cat S, Guo-Ping Shi and colleagues crossed mice lacking Cat S with atherosclerosis-prone LDL receptor–deficient mice. They found (pages 897–906) that the double mutants — when fed a high-cholesterol diet — had an attenuated response: atherosclerosis was reduced by more than 50% after 12 weeks on an atherogenic diet, and by 30% after 26 weeks. While this study does not reveal the mechanism by which Cat S contributes to atherogenesis, it does suggest several possible modes of action and underscores the possibility that Cat S may serve as a therapeutic target in arterial diseases.



Stem cells mobilized by crisis. Sickle cell disease affects 150 million people worldwide. The only curative therapy is hematopoietic stem cell transplantation. Because of the limited number of matched donors and the toxicity associated with allogeneic transplants, various gene therapy approaches in autologous stem cells are under development. Encouraged by the observation that sickle cell patients have increased numbers of cells expressing stem cell markers in the peripheral blood, Catherine Verfaillie and colleagues tested peripheral blood from patients during acute crisis and chronic stages of disease for the presence of primitive hematopoietic progenitors (pages 811–819). They found that during acute crisis, patients spontaneously mobilize significant numbers of progenitors with multiple-lineage and repopulation potential into the peripheral blood, suggesting that collection of these progenitors could yield a source of autologous cells suitable for genetic manipulation and subsequent transplantation.



Mismatch repair awry in lung cancer. Mutations in DNA mismatch repair genes cause inherited colon cancer syndromes, and somatic mutations and promoter methylation of these genes have been found in a variety of human cancers characterized by microsatellite instability (MSI). Having previously shown that MSI and loss of hMLH1 protein expression is common in lung cancer patients from Taiwan, Yi-Ching Wang and colleagues now report (pages 887–895) results from a comprehensive genetic and epigenetic analysis of 77 resected primary non-small cell lung tumors. Of these tumors, 70% had lost expression of either hMLH1 or hMSH2, and promoter methylation seemed to be the predominant cause. Moreover, promoter methylation of *hMLH1* (whose expression is lost in over 50% of the samples) appears to be an early event in tumorigenesis and can be detected in sputum samples. Thus it might serve as a potential diagnostic marker.