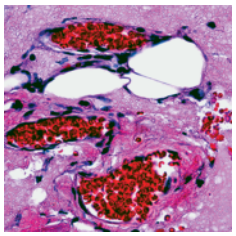
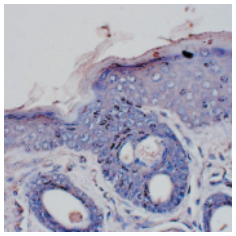
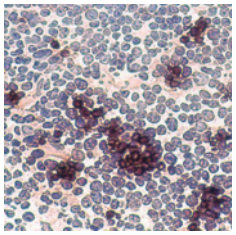


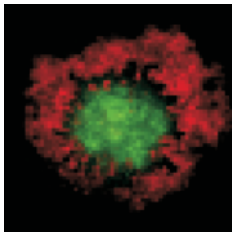
Annexin II critical for angiogenesis. Endothelial cells are critical to the maintenance of hemostatic balance because they provide the site of assembly for a variety of regulatory factors involved in the vascular injury response. Having generated annexin II–null mice in order to observe the physiologic roles of annexin II in hemostasis, Katherine Hajjar and colleagues now show that annexin II does indeed participate in the regulation of fibrin homeostasis (pages 38–48). The mice showed defective fibrinolytic function and impaired clearance of injury-induced arterial thrombi. Moreover, neoangiogenesis was abnormal in these mice, suggesting a key role for annexin II in plasmin-mediated activation of the vascularization process. This dual role in fibrinolytic surveillance and neoangiogenesis suggests that annexin II is an indispensable factor in hemostasis and a potential target for control of angiogenesis.



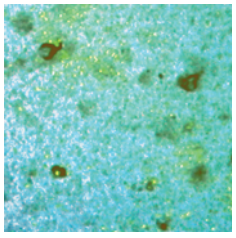
Avicins boost the stress response. Chronic disease states develop during the aging process as cellular stress responses and repair systems are worn down. In an effort to address the broad concept of disease mechanisms during stress and aging, Jordan Gutterman and colleagues examined avicins, triterpenoid electrophiles isolated from the Australian desert tree *Acacia victoriae*, and their ability to control transcription (pages 65–73). They found that avicin-treated cells had increased nuclear localization of the redox-regulated transcription factor Nrf-2. This, in turn, activated the transcription of genes containing the antioxidant response element (ARE) and a battery of stress response genes. In vivo experiments with mouse models stressed by UV exposure resulted in significantly less severe skin damage after avicin treatment. These studies show the potential of a new class of metabolites for the treatment of stress-associated diseases phenotypes.



A viral cure for type 1 diabetes. Viruses can both cause and prevent autoimmune disease. In order to understand this dualism, Matthias von Herrath and colleagues exposed prediabetic mice to viral infections (pages 74–84). Infection with lymphocytic choriomeningitis virus (LCMV) during the prediabetic period completely abrogated the diabetic process in two distinct mouse models. Induction of protection correlated with a reduced number of autoaggressive CD8 T cells in islets. Increased production of the chemokine CXCL-10 in pancreatic lymph nodes following the abrogative infection resulted in a redirection of the autoimmune process by recruitment of autoaggressors away from the β cells. Once in the pancreatic lymph node, CD8 lymphocytes underwent increased apoptosis, which was directly dependent on TNF-α and indirectly on IFN-γ production. Thus, virally induced proinflammatory cytokines and chemokines can influence ongoing autoaggressive processes beneficially at the preclinical stage if produced at the correct time, location, and level.



Ring around the rosy CTL. CTLs and target cells form a mature immunological synapse with a central cluster of T cell receptor/MHC-peptide interactions surrounded by a ring of the integrin LFA-1 and its counter receptor ICAM-1, as do $CD4^+$ helper T cells with antigen-presenting cells. Michael Dustin and colleagues describe a novel adhesive structure that is formed by $CD8^+$ human CTLs, but not by $CD4^+$ helper T cells, before MHC-peptides are detected (pages 49–57). The CTL ring junction acts as a presynapse, setting the stage for sensitive antigen recognition. This structure may play an important role in immune surveillance by CTL and implies unique regulatory mechanisms in CTL that are not shared with helper T cells.



Male/female differences? It's all in your head. Diabetic hyperglycemia increases brain damage after cerebral ischemia. The underlying mechanisms remain unclear but may involve increased apoptosis. While previous studies showed female diabetic mice suffered less brain damage following cerebral hypoxia-ischemia than male diabetic mice, Susan Vannucci and colleagues here investigate the effects of estrogen, an established neuroprotectant, on ischemic recovery (pages 85–95). Female diabetic and nondiabetic mice were ovariectomized (OVX) and treated with estrogen replacement or vehicle prior to hypoxia. OVX increased ischemic damage in nondiabetic mice, and estrogen replacement reduced tissue injury in association with enhanced expression of antiapoptotic gene expression. Diabetic mice showed significantly more damage, and there was no detectable protection afforded by estrogen replacement therapy. Such impaired wound healing is analogous to that seen in peripheral tissues but has never before been considered as part of the pathophysiology of ischemic stroke in the context of diabetes.