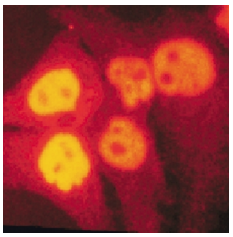
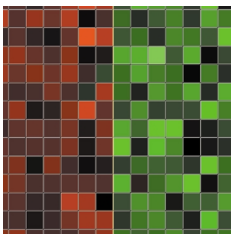
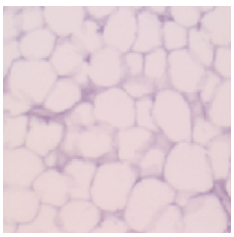


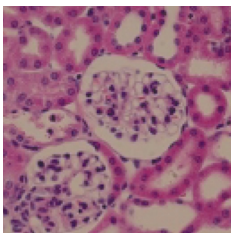
Stat3: tight import-export regulations. STATs, upon phosphorylation by cytokine receptors, translocate to the nucleus where they function as transcriptional regulators. Subsequent nuclear export ensures that the signal is transient and renders the STATs available for further rounds of signaling. Christian Schindler and colleagues have focused on the cellular whereabouts of Stat3. Their study (pages 553–559) — together with similar findings for Stat1 — supports a model in which two mechanisms exist to promote nuclear import of STATs: a rapid one in response to receptor activation, and a second, phosphorylation-independent one, which is active in unstimulated cells. The latter pathway leads to nuclear accumulation of low levels of STATs in resting cells. For Stat3, there appears to be an active export pathway in resting cells as well, which opposes nuclear accumulation. This tight control suggests that regulation in resting cells of Stat3 target genes — which remain to be identified — is important.



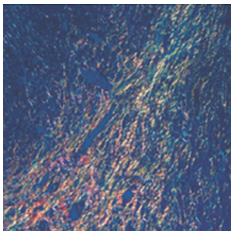
Expression profile of Hodgkin lymphoma cells. Hodgkin lymphoma is characterized by the presence of malignant Hodgkin and Reed-Sternberg cells in the affected lymph nodes. These cells, most frequently derived from germinal center B cells, but sometimes from T cells, have a heterogeneous and poorly characterized phenotype. Attempting a systematic large-scale characterization of the disease-specific cells, Ralf Küppers and colleagues have compared their expression profiles with those of normal and malignant B cells (pages 529–537). Cell lines derived from Hodgkin patients clustered as a distinct entity, irrespective of their B or T cell origin, and their expression profile was most similar to EBV-transformed B cells and cell lines derived from diffuse large B cell lymphomas. A number of genes expressed specifically in the Hodgkin-derived lines have potential as diagnostic markers. Future experiments are necessary to determine whether the Hodgkin-specific genes play a role in the pathogenesis of the disease and could be targets for therapeutic intervention.



Pref-1 and adipogenesis. The balance of signals experienced by preadipocytes influences whether these cells undergo adipogenesis. In addition to deriving from the endocrine system, these signals originate from the preadipocytes themselves or operate as part of a feedback loop involving mature adipocytes. Having previously cloned *Pref-1*, a gene expressed in preadipocytes but not mature adipocytes, Hei Sook Sul and colleagues now report (pages 453–461) that transgenic mice expressing the Pref-1 extracellular domain in adipocytes exhibited a decrease in total fat pad weight and a reduction in adipocyte markers, as well as hypertriglyceridemia, impaired glucose tolerance, and decreased insulin resistance. The same was true for mice expressing the transgene exclusively in the liver, suggesting that Pref-1 can function in an endocrine manner and that the resulting loss of adipocyte function triggers metabolic abnormalities.



Histone acetylation and autoimmune disease. Systemic lupus erythematosus (SLE) is associated with changes in cytokine patterns which are thought to contribute to the immunopathogenesis seen in patients and mouse models of the disease. In MRL-*lpr/lpr* mice, which mimic some aspects of the human disease, activated splenic T cells produce elevated levels of specific cytokines that drive the aberrant immune response. Having previously shown that histone deacetylase inhibitors (HDIs) can alter cytokine expression in human SLE T cells, Nilamadhab Mishra and colleagues report now (pages 539–552) that HDI treatment of splenocytes from MRL-*lpr/lpr* mice resulted in downregulation of Th1 and Th2 cytokines without apparent effects on general gene expression. Moreover, MRL-*lpr/lpr* mice treated with HDIs showed an amelioration of their autoimmune symptoms, especially of glomerulonephritis. These preliminary results are encouraging and warrant further exploration of the therapeutic potential of HDIs in lupus and other autoimmune diseases.



ECM organization and resistance to tumor growth. SPARC is a matricellular protein that modulates cellular interaction with the ECM during development, remodeling, and tissue repair. Interested in the contribution of endogenous SPARC to tumor growth and progression, E. Helene Sage and colleagues implanted tumors in SPARC-null ($SP^{-/-}$) mice and observed a substantial increase in tumor size compared to controls (pages 487–495). Given that tumor progression is dependent upon the growth of new blood vessels, the authors were surprised to find no difference in tumor vessel density or cell cycling between $SP^{-/-}$ and $SP^{+/+}$ mice. They did, however, observe faulty deposition of collagen — the major structural protein of the ECM — in $SP^{-/-}$ mice, which may lead to decreased mechanical resistance to tumor growth and transport. The data suggest the importance of SPARC in the development of the ECM and subsequent control of tumor growth.