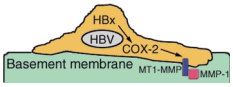
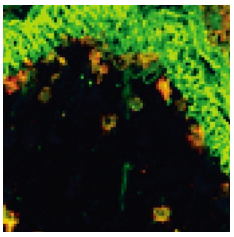
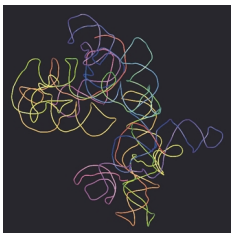


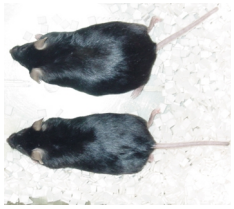
Mechanism of HBV-mediated metastasis. Chronic hepatitis B virus (HBV) infection is a major risk factor for hepatocellular carcinoma, a cancer associated with recurrent intrahepatic metastasis and poor prognosis. HBx is the only viral gene product consistently present in hepatic tumor cells, and previous work has focused mainly on its potential role in tumor development. Manuel López-Cabrera and colleagues, in contrast, have studied the role of HBx in metastasis. As they report on pages 1831–1838, HBx expression induces tumor cell invasion in vitro and in vivo. The invasive phenotype is associated with increased levels of cyclooxygenase-2 (COX-2) and matrix metalloproteinases and can be blocked by COX-2 inhibitors. HBx, a transcriptional activator, upregulates COX-2 expression at the mRNA and protein levels. These results suggest that HBx plays a direct role in the late stages of hepatocellular carcinoma.



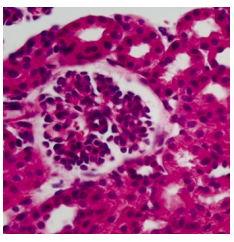
Integrins and intestinal inflammation. Inflammatory bowel diseases are associated with chronic inflammation of the intestinal tract. Affected tissue is characterized by dense leukocyte infiltrate, and therapeutic strategies to interfere with adhesion molecules necessary for leukocyte migration and activation are under investigation. Antonin de Fougerolles and colleagues have focused on the collagen-binding integrin $\alpha1\beta1$, which is expressed on the surface of activated T cells and monocytes. They report (pages 1773–1782) that lack of $\alpha1\beta1$ integrin or its blockage with antibody attenuated disease in a mouse model of colitis. This effect occurred independently of lymphocytes, and $\alpha1\beta1$-expressing monocytes were identified as a key cell type involved in the development of colitis in this model. These results underscore the importance of innate immunity in addition to the interaction of leukocytes with the extracellular matrix in regulating local inflammatory responses.



Ribozymes to the rescue. Modified versions of the *Tetrahymena* group I intron ribozyme have been used previously to repair defective proteins in cultured cells, but the general applicability and efficiency of the process is still unclear. In an article beginning on page 1783, Alfred George, Jr., and colleagues demonstrate that ribozyme-mediated *trans*-splicing can repair a mutant chloride channel mRNA transcript. The ribozyme they engineered catalyzed *trans*-splicing of a 4 kb–long restorative exon (compared with 1.1 kb, the largest exon *trans*-spliced previously), and the repaired mRNA product is translated into a functional channel. While this is the first demonstration of complete restoration of protein function using *trans*-splicing ribozymes, the efficiency of the *trans*-splicing reaction remains a critical issue. Overall repair efficiency in the study was low, but detailed analysis revealed a striking heterogeneity among individual cells. Future experiments will need to explain that heterogeneity and might suggest ways to increase overall efficiency.



Histamine H3 receptors and body-weight homeostasis. Histamine has numerous functions in the mammalian immune, digestive, and nervous systems. Previous studies suggested that histamine may regulate food intake, a function most likely mediated by H3 receptors in the hypothalamus. Hidehito Kotani and colleagues have directly tested this hypothesis by generating and analyzing mice lacking H3 receptors. As they report (pages 1791–1799), the mutant animals are mildly obese, have increased food intake and adipodisity, and also have reduced energy expenditure. In addition, they have increased levels of plasma leptin and insulin, exhibit resistance to both hormones, and show decreased levels of histamine and increased histamine turnover in the hypothalamic and thalamic brain regions. These results demonstrate a critical role of H3 receptors in the control of body weight in mice.



Mopping up xenoantibodies. Pig cells, unlike those of humans and Old World primates, express a specific trisaccharide (αGal) on their surfaces, and antibody-mediated destruction of donor tissues is a major hurdle of pig-to-primate organ transplantation. One way to avoid this problem is to sequester the circulating αGal antibodies and thus prevent them from binding to and destroying the donor tissue. Andreas Katopodis and colleagues developed a soluble αGal-polylysine conjugate (called GAS914) that effectively competes with cell-surface αGal for antibody binding. On pages 1869–1877 the authors report that in different monkey species, injections of GAS914 drastically reduced the levels of circulating αGal antibodies and anti-pig cytotoxicity. The conjugate binds to circulating antibodies, and the complex is quickly metabolized and excreted without apparent acute or chronic toxicity. The GAS backbone may be a promising scaffold to which to attach other antigens for the antigen-specific removal of antibodies in vivo.