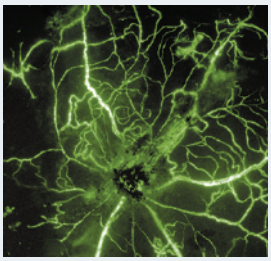
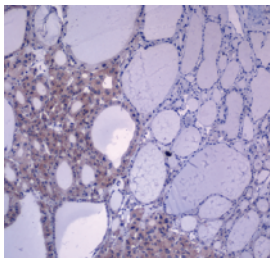
## An IGF-1 role for an eye disease



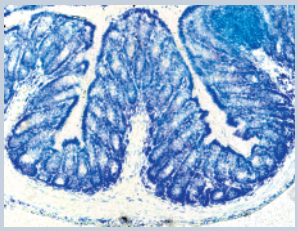
Human diabetic eye disease is the most common form of blindness. Currently no good model exists for studying this complication of long-term diabetes. Fatima Bosch and colleagues have developed a transgenic mouse overexpressing insulin-like growth factor 1 (IGF-1) in which the hallmarks of diabetic eye disease are mimicked (pages 1149–1157). IGF-1 has been a prime suspect in the pathogenesis of the disease, but the extent of its role remains unclear. Using this mouse model, the authors show that the local effects of ocular IGF-1 cause retinopathy characterized by vascular abnormalities and retinal detachment, rubeosis iridis, cataracts, and neovascular glaucoma. That the mice in this study were normoglycemic and normoinsulinemic emphasizes that the eye disease phenotype resulted specifically from local production of IGF-1. This model provides a useful tool for elucidating the mechanisms of diabetic eye disease as well as a method for assaying potential ocular therapies for long-term diabetic patients.

## SAGE-acious prediction of thyroid carcinoma



Current protocols for thyroid tumor diagnosis require thyroid surgery to distinguish follicular thyroid carcinoma (FTC) from benign follicular thyroid adenoma (FTA). Given the rise in the incidence of thyroid cancer, preoperative classification of FTC versus FTA would greatly improve selection of optimal treatment strategies. In addition, it would reduce health care costs by allowing patients to pursue more aggressive treatments for FTC cases and avoid unnecessary surgery for FTA. Using SAGE to screen for differentially expressed genes in FTA and FTC samples, Janete Cerutti, Gregory Riggins, and colleagues identified a set of candidate classification markers (pages 1234–1242). Further analysis with these genes by quantitative RT-PCR pinpointed four genes (*DDIT3*, *ARG2*, *ITM1*, and *C1orf24*) with statistically significant gene expression differences between FTC and FTA. They used these differentially expressed genes as predictive markers for carcinoma in a series of patient cases. RT-PCR analysis of patient samples for the markers successfully predicted tumor class with an accuracy of 83%, indicating the usefulness of this strategy for further development of preoperative diagnostic markers for FTC.

## Cannabinoid receptors spell relief



A variety of bowel diseases arise from enteric inflammation, infection, or trauma, including ulcerative colitis, Crohn disease, and irritable bowel syndrome. Relief from these disorders is in high demand, and the endogenous cannabinoid system is now a promising therapeutic target, according to a study by Beat Lutz and colleagues (pages 1202–1209). Using pharmacological agents to induce colonic inflammation, the researchers showed that mice lacking *CB1*, one of the two types of cannabinoid receptors, had more severe inflammatory responses than did wild-type mice. Blocking CB1 receptors with a CB1 antagonist yielded the same results, indicating that CB1 receptor action is required for protection from inflammation. Similarly, when wild-type mice with induced colitis were treated with a cannabinoid agonist, colonic inflammation was reduced. Further analysis revealed that the mechanism underlying this protective system is a localized response, as *CB1* transcription levels increased in neurons within the myenteric plexus after colitis induction. Electrophysiological studies also showed that $CB1^{-/-}$ mice with colonic inflammation displayed spontaneous action potentials that were not observed in wild-type mice. Together, these data point to the importance of the cannabinoid system as a protective means of physiologically counteracting the proinflammatory response.

## Metalloproteinases need their inhibitions

Hepatitis B virus (HBV) infection triggers a cellular response to viral antigens that initiates acute and chronic liver damage. Subsequent recruitment of antigen-nonspecific polymorphonuclear and mononuclear cells to the liver causes necrosis and heightens liver disease severity. This recruitment is induced by antigen-specific CTLs, but how this process is mediated is unknown. Luca G. Guidotti and colleagues investigated the potential roles for matrix metalloproteinases (MMPs) in facilitating this process (pages 1158–1167). Using a transgenic HBV mouse model, they monitored the expression and function of various MMPs. Antiviral CTL injection induced MMP-8 and MMP-9 activity, which was correlated with intrahepatic leukocyte (IHL) recruitment. To assay the functional effects of MMPs in their system, the researchers enhanced the expression of *TIMP-1*, a tissue inhibitor of MMPs, in the liver of HBV transgenic mice. Mice in which TIMP-1 inhibited MMP function were spared from CTL-induced severe liver damage. Moreover, amelioration of liver disease in these mice did not weaken the antiviral effects of CTLs. That MMP inhibition does not hamper antiviral activity but does minimize tissue damage may have important implications in HBV immunotherapy development.