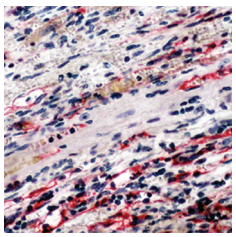
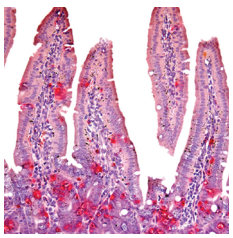
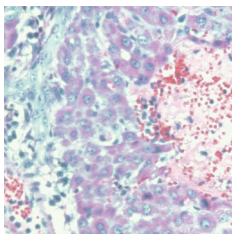
**Regulatory T cells keep GVHD in check.** Using large numbers of immunoregulatory $CD4^+CD25^+$ T cells with allogeneic hematopoietic stem cell transplantation holds great promise in treating graft versus host disease (GVHD). José Cohen and colleagues now describe a method to circumvent the difficulty of obtaining enough freshly purified $CD4^+CD25^+$ regulatory T cells to have a therapeutic effect (pages 1688–1696). The authors performed regulatory T cell expansion ex vivo by stimulation with allogeneic antigen-presenting cells, which has the additional effect of producing alloantigen-specific regulatory T cells. Regulatory T cells specific for recipient-type alloantigens, but not irrelevant regulatory T cells, controlled GVHD while favoring immune reconstitution. Preferential survival of specific regulatory T cells was observed in the grafted animals. This work may be useful in the design of future clinical trials relying on the use of $CD4^+CD25^+$ regulatory T cells to control GVHD.



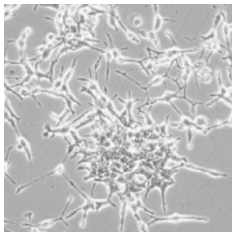
**Not just angiogenesis: a role for VEGF in immunity.** Though VEGF is expressed in allografts undergoing rejection, its function in the rejection process has not been defined. David Briscoe and colleagues elucidate the role of VEGF in two transplantation models (pages 1655–1665). In vitro, VEGF enhanced endothelial expression of monocyte chemoattractant protein–1 and IL-8, and in combination with IFN-γ, VEGF synergistically induced endothelial production of the T cell chemoattractant IFN-inducible protein–10. In vivo, anti-VEGF inhibited T cell infiltration of allografts and acute rejection in mice transplanted with fully MHC mismatched donor hearts. While VEGF expression was increased in allografts, neovascularization was not associated with acute rejection. Thus, VEGF appears to be functional in acute allograft rejection via its effects on leukocyte trafficking. These observations provide mechanistic insight into the proinflammatory function of VEGF in immunity.



**Mast cells to blame for allergic diarrhea.** While exposure to food allergens is often associated with diarrhea in humans, knowledge of the cell types and mediators involved in the process is still limited. Marc Rothenberg and colleagues use a murine model of oral allergen–induced intestinal inflammation accompanied by strong Th2-associated humoral and cellular responses (pages 1666–1677). Mice had dose-dependent acute diarrhea associated with increased intestinal permeability, eosinophilia, and mastocytosis. Depletion of mast cells completely abrogated intestinal mastocytosis and blocked the allergic diarrhea. Furthermore, allergic diarrhea was dependent upon synergistic signaling induced by serotonin and platelet-activating factor (PAF), but not histamine. Evidence from IL-5/eotaxin–deficient mice indicated that the numerous eosinophils present in the intestines did not contribute to the diarrhea observed in this model. These results demonstrate that oral allergen–induced diarrhea associated with experimental Th2 intestinal inflammation is largely mast cell, serotonin, and PAF dependent.



**Hepatoprotection with FXR.** In cholestasis, failure to rid hepatocytes of bile constituents results in toxicity. It follows that treatments that enhance the ability of cells to rid themselves of these products will decrease toxicity. Stacey Jones and colleagues describe a hepatoprotective effect by a potent and selective agonist of farnesoid X receptor (FXR) in two rat models of cholestasis (pages 1678–1687). In both models, rats that received the agonist showed significant reductions in serum markers of liver damage accompanied by improvements in liver histology. Treatment with the FXR agonist increased expression of the bile transporters, bile salt export pumps, and multidrug resistance–related protein 2 and repressed key genes involved in bile acid biosynthesis. FXR agonists may provide hepatoprotection in conditions of cholestasis both by increasing the capacity for bile excretion from the hepatoctye and decreasing bile acid biosynthesis.



***c-myc* causes hormones to lose control.** Treating prostate cancer becomes problematic when the tissue no longer responds to antihormonal treatment. The mechanisms underlying the change from androgen dependence to independence are poorly understood. Based on data showing amplification of *c-myc* in androgen-independent prostate cancer, David Bernard and colleagues studied the ability of *c-myc* to confer androgen-independent prostate cancer cell growth (pages 1724–1731). Ectopic expression of *c-myc* allowed human androgen-dependent prostate cancer cells to grow without androgen stimulation and to keep their tumorigenic activity in androgen-depleted conditions. Analysis of signaling pathways showed that *c-myc* is regulated by the androgen receptor, is required for androgen-dependent growth and, following ectopic expression, can induce androgen-independent growth. In addition, *c-myc* downregulation slowed the growth of androgen-independent tumor cell lines. These results suggest a physiological role for *c-myc* in prostate cancer.