that at the site of viral replication, chronic infections showed an accumulation of Eomes^{hi} CD8^{+} T cells and depletion of T-bet^{hi} cells relative to resolved infections. These observations suggest that these two subsets of CD8^{+} T cells may also be relevant to control of chronic viral infections in humans.—*MS*

■ NEUROSCIENCE

Seizures after surgery

Tranexamic acid (TXA) and ε-aminocaproic acid (EACA), two antifibrinolytic drugs used to minimize blood loss during surgery, can cause seizures. A recent study (*J. Clin. Invest.* **122**, 4654–4666, 2012) identifies glycine-receptor inhibition as a possible mechanism for this side effect and suggests a possible way to prevent it.

TXA and EACA bear some structural similarity to glycine, inhibition of which triggers epilepsy. Might both compounds promote seizures by interfering with glycine-mediated neurotransmission? Studying mouse neurons and brain slices, Irene Lecker *et al.* found that, indeed, both drugs competitively antagonize glycine receptors. Moreover, the concentration of TXA in the cerebrospinal fluid of patients undergoing surgery was similar to concentrations with inhibitory potency *in vitro*.

As patients treated with TXA and EACA often experience seizures after coming out of anesthesia, the authors went on to show that the anesthetics isoflurane and propofol reduced the inhibitory effect of the antifibrinolytic drugs. This observation raises the possibility of using these general anesthetics to prevent TXA- and EACA-induced epileptic activity.—*JCL*

■ INFLAMMATION

Stemming colitis

Myeloid cells accumulate in the intestine in mouse models of colitis, but how this aberrant increase occurs and what part it plays in the disease are unclear. Griseri *et al.* now report that altered hematopoiesis is responsible for the increased myeloid cell number and is a pathogenic in colitis (*Immunity* doi:10.1016/j.immuni.2012.08.025).

In colitic mice, the researchers found increased proliferation of hematopoietic stem cells (HSCs) and skewing of common myeloerythroid progenitors toward granulocyte-monocyte progenitors (GMPs) in the bone marrow and spleen. Highly proliferative GMPs were also found in the colon, and the authors propose that these changes in hematopoietic subsets account for the increased numbers of neutrophils and inflammatory monocytes seen in the spleen and colon of mice with colitis. Although granulocyte colony–stimulating factor (G-CSF) and granulocyte-macrophage colony–stimulating factor (GM-CSF) (key cytokines in granulocyte and monocyte differentiation) did not induce accumulation of GMPs in the mouse colon, GM-CSF blockade prevented the increase in GMPs and reduced the severity of colitis. Moreover, transfer of GMPs from colitic mice enhanced disease in secondary recipients.

The researchers further showed that interferon-γ (IFN-γ), which is produced by colitogenic T cells and can induce HSC proliferation, was responsible for the increase in HSCs in bone marrow in their model of colitis. The authors describe a model in which interleukin-23 induces IFN-γ and GM-CSF production by T and other cells, which trigger, respectively, HSC proliferation and increased GMP recruitment and proliferation and differentiation in the colon, thereby contributing to intestinal inflammation. Their findings uncover a pathogenic role for hematopoietic stem and progenitor cells in experimental colitis.—*AF*

■ HEMATOPOIETIC SYSTEM

Piquing platelet production

The bone marrow produces millions of platelets every hour. Lin Zhang *et al.* now find that platelet production in mice requires signaling by the lipid mediator sphingosine 1-phosphate (*J. Exp. Med.* **209**, 2165–2181, 2012).

In the last steps of platelet production, megakaryocytes extend pseudopods, termed proplatelets, into the lumen of bone marrow sinusoids. Platelets are then shed from the tips of the proplatelets into the blood. The researchers showed that both of these steps are controlled by sphingosine 1-phosphate signaling through the sphingosine 1-phosphate receptor S1pr1 on megakaryocytes. Proplatelet extension requires a transendothelial gradient of sphingosine 1-phosphate, and platelet shedding occurs in response to the high concentrations of sphingosine 1-phosphate in the blood.

A drug that acts on sphingosine 1-phosphate receptors, fingolimod, is approved for the treatment of multiple sclerosis. Pointing to the potential clinical utility of targeting sphingosine 1-phosphate signaling for treating thrombocytopenia, the authors showed that treating mice with fingolimod accelerated platelet shedding and resulted in increased platelet counts.—*MB*

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New from NPG

CCR5 is a receptor for Staphylococcus aureus leukotoxin ED
Alonzo III, F. *et al. Nature* doi:10.1038/nature11724 (13 December 2012)
The authors identify C-C chemokine receptor type 5 (CCR5) as a cellular receptor for the *Staphylococcus aureus* leukotoxin ED (LukED), showing that it is needed for killing of cells by this toxin. In addition, they used CCR5 antagonists, such as the HIV drug maraviroc, to block LukED-dependent killing.

A role for Schwann cell-derived neuregulin-1 in remyelination
Stassart, R.M. *et al. Nat. Neurosci.* doi:10.1038/nn.3281 (9 December 2012)
The authors found that peripheral nerve remyelination after injury is more efficient in mice overexpressing neuregulin-1 (NRG1) type III or type I than in wild-type mice. Nerve injury induced the expression of NRG1 type I in Schwann cells. Moreover, mice lacking Nrg1 in Schwann cells showed normal primary myelination but impaired remyelination as they aged, suggesting a key role for NRG1 in myelination control.

Large-scale association analysis identifies new risk loci for coronary artery disease
The CARDIoGRAMplusC4D Consortium. *Nat. Genet.* doi:10.1038/ng.2480 (2 December 2012)
The researchers performed a case-control association analysis for coronary artery disease (CAD), allowing them to identify 15 new risk loci and taking the total number of susceptibility loci for this disease to 46. They also carried out a network analysis of candidate genes involved in CAD, highlighting the importance of pathways linked to lipid metabolism and inflammation.

Nitric oxide controls the immunopathology of tuberculosis by inhibiting NLRP3 inflammasome-dependent processing of IL-1β
Mishra, B.B. *et al. Nat. Immunol.* doi:10.1038/ni.2474 (18 November 2012)
Using a mouse model of *Mycobacterium tuberculosis* infection in which replication of the bacterium was controlled exogenously, the authors found that nitric oxide deactivated the assembly of the NLRP3 inflammasome. They suggest this mechanism is important for tempering detrimental innate inflammatory responses during persistent infection.