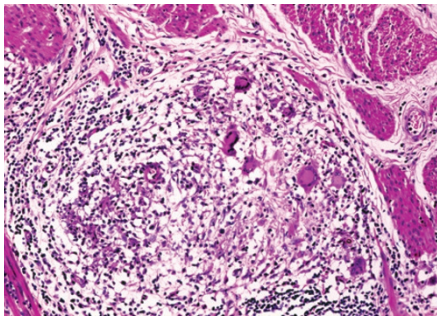


Biophoto Associates / Science Source

phase of the study (31% response rate at week 6 versus 26% with placebo), but it had a positive effect on remission rates (39% at week 52 versus 22% with placebo).

On the basis of this therapeutic effect, vedolizumab may become the latest biologic agent to join the list of approved medications to treat inflammatory bowel disease.—*JCL*

■ MYELOPROLIFERATIVE DISEASE

Leukemic cells hijack the niche

A new study shows that leukemic stem cells that propagate myeloproliferative disorders can harness stromal cells in the bone marrow niche to favor their own function and induce fibrosis while impairing normal hematopoiesis (*Cell Stem Cell*, **13**, 285–299).

Koen Schepers *et al.* showed that endosteal stromal cells, found at the bone surface of the bone marrow, can give rise to osteoblastic cells, which can then maintain hematopoietic stem cells. Using a mouse model of human chronic myelogenous leukemia, the authors showed that disease development in these mice resulted in expansion of osteoblastic cells and bone marrow fibrosis, which is often found in humans with myeloproliferative disorders. Cell–cell interactions and factors released by leukemic stem cells induced stromal cells to overproduce cells of the osteoblastic lineage, but these cells had an inflammatory phenotype that supported leukemic hematopoiesis and myelofibrosis at the expense of normal hematopoietic activity. The authors also investigated the genes involved in this process in myeloproliferative osteoblastic cells. Compared with control osteoblastic cells, they detected an increased expression of genes driving extracellular matrix organization and inflammatory responses, which are probably involved in tissue remodeling, and a downregulation of genes involved in maintaining normal hematopoiesis.

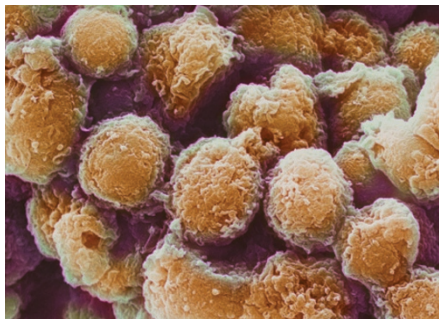
Although future studies should address the exact molecular underpinnings of these findings and their relevance in people with myeloproliferative disease, the results further our understanding of how leukemic cells exploit the bone marrow niche to reinforce leukemic growth at the expense of normal hematopoiesis.—*CP*

■ INFLAMMATION

Monocytes on the clock

Diurnal variations in inflammatory monocyte recruitment help control infection and metabolic disease, reports a recent study in *Science* (doi:10.1126/science.1240636).

Ajay Chawla and his colleagues found that in mice kept on a 12-h light-dark cycle, the number of inflammatory monocytes recruited to the inflamed peritoneum showed oscillatory changes, peaking 8 h after lights are turned on then decreasing thereafter. The authors found that when they infected mice with *Listeria monocytogenes* at this time point of 8 h, when monocyte numbers are at a peak, there was a reduced bacterial burden and a more robust adaptive immune response than in mice infected at 0 h of the cycle.



David McCarthy / Science Source

The researchers then generated mice with myeloid-specific deletion of the circadian gene *Bmal1*. This disrupted the oscillatory variation in monocyte recruitment, resulting in increased recruitment of monocytes to inflammatory sites and a higher mortality rate in response to *L. monocytogenes* infection compared to that observed in wild-type mice. When these myeloid-specific *Bmal1*-knockout mice were fed a high-fat diet, they gained more weight and had a greater accumulation of macrophages and adaptive immune cells in adipose tissue than wild-type mice. Together, these findings suggest that diurnal variations in inflammatory monocyte recruitment are important for both acute and chronic inflammatory conditions. —*KDS*

Written by Victoria Aranda, Eva Chmielnicki, Kevin Da Silva, Juan Carlos López, Carolina Pola & Meera Swami

New from NPG

Microbiota-liberated host sugars facilitate post-antibiotic expansion of enteric pathogens
Ng, K.M. *et al. Nature* doi:10.1038/nature12503 (1 September)
The pathogens *Salmonella enterica* serovar Typhimurium and *Clostridium difficile* take advantage of host carbohydrates liberated by the actions of the microbiota, allowing them to expand in the mouse gut. Antibiotic treatment disrupted the host microbiota and increased the free amounts of pathogen-utilized carbohydrate, promoting expansion of the pathogenic bacteria.

Modified mRNA directs the fate of heart progenitor cells and induces vascular regeneration after myocardial infarction
Zangi, L. *et al. Nat. Biotechnol.* doi:10.1038/nbt.2682 (8 September)
Injection of a synthetic modified RNA encoding vascular endothelial growth factor-A improves heart function and survival in a mouse model of myocardial infarction.

A *de novo* gain-of-function mutation in SCN11A causes loss of pain perception
Leipold, E. *et al. Nat. Genet.* doi:10.1038/ng.2767 (15 September)
The authors identified a *de novo* missense mutation in the gene *SCN11A*, encoding a sodium channel, in people who cannot experience pain. They find that mice carrying this mutation show reduced sensitivity to pain and show that the mutation mediates its effects through a gain-of-function mechanism.

IL-27 acts on DCs to suppress the T cell response and autoimmunity by inducing expression of the immunoregulatory molecule CD39
Mascanfroni, I.D. *et al. Nat. Immunol.* doi:10.1038/ni.2695 (1 September)
Signaling by interleukin-27 (IL-27) in mouse dendritic cells suppresses T cell responses and the development of experimental autoimmune encephalomyelitis, a mouse model of multiple sclerosis. These effects of IL-27 were partly mediated by its induction of CD39.

Brain tumor initiating cells adapt to restricted nutrition through preferential glucose uptake
Flavahan, W.A. *et al. Nat. Neurosci.* doi:10.1038/nn.3510 (1 September)
Nutrient restriction is shown to increase the survival of a population of cancer stem cells. These cells take up glucose efficiently by increasing their expression of the glucose transporter Glut3. Blocking Glut3 expression in the tumor-initiating cells reduced their growth and tumor progression when transplanted into mice.