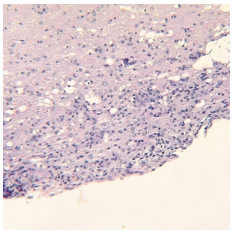
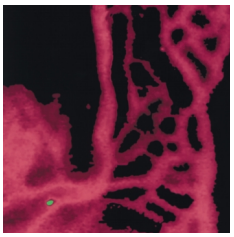
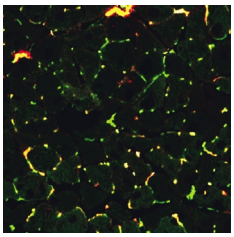


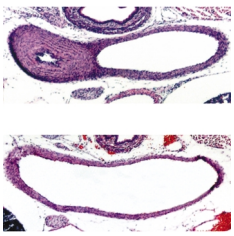
The partial truth on IL-12 and EAE. IL-12 is a pro-inflammatory mediator and has been implicated as a key player in experimental autoimmune encephalitis (EAE), an animal model for multiple sclerosis. Elevated IL-12 levels have also been reported in multiple sclerosis patients. IL-12 is a heterodimer consisting of two subunits, p40 and p35. Burkhard Becher and colleagues have examined the roles of the two subunits in EAE and report (pages 493–497) that it is not IL-12 itself that is essential for the development of the disease phenotype. Mice lacking p35 (and thus unable to produce IL-12) are highly susceptible to EAE. In contrast, and consistent with earlier findings, mice devoid of p40 are resistant. The authors speculate that another p40-containing cytokine is critical to EAE development, and data on their favorite candidate, IL-23, are eagerly awaited.



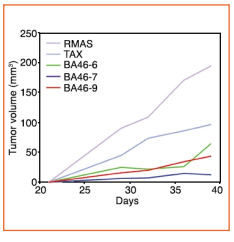
Homing of hematopoeitic progenitors. Hematopoietic progenitor cells are found primarily in the bone marrow, and this is where external progenitors end up after intravenous injection. Paul Frenette and colleagues examined the mechanisms underlying this homing behavior using sophisticated microscopy to follow human progenitor cells in mutant mice. As they report, beginning on page 559, the same molecules that are known to guide leukocytes to sites of inflammation throughout the body are also involved in the homing of progenitor cells to the bone marrow. In mice lacking P and E selectin, human progenitor cells failed to undergo rolling on bone marrow endothelium and extravasation into the bone marrow compartment. The researchers also observed a difference in rolling efficiency between progenitors derived from adult human peripheral blood and those from cord blood. This might be due to the lack of functional P selectin ligands on a subset of neonatal progenitors. If confirmed by future studies, this would raise the possibility of improving the homing of cord-blood–derived progenitor cells, and possibly their reconstituting potential.



Angiogenesis alternatives. Having previously reported the angiogenic effects of exogenous nicotine, John Cooke and collaborators describe on pages 527–536 the first endogenous cholinergic pathway for angiogenesis, mediated by nicotinic acetylcholine receptors (nAChRs) on the surface of epithelial cells. Selective inhibition of these receptors on cultured endothelial cells significantly reduced new vessel formation and revealed that the effect is primarily mediated by the α7-nAChR receptor isoform. Pharmaceutical inhibition of nAChRs or genetic disruption of α7-nAChR reduced inflammatory and ischemia-induced angiogenesis and suppressed tumor growth in a mouse lung cancer model. These results implicate the cholinergic system in physiological and pathological angiogenesis and suggest new ways for pro- and anti-angiogenic therapeutic intervention.



COX-1 inhibition prolongs gestation. Premature birth, a major contributor to infant mortality, can be delayed by cyclooxygenase (COX) inhibitors. A potentially serious side effect in the fetus or neonate is the altered closure of the ductus arteriosus, which can contribute to respiratory distress and congestive heart failure. Beginning on page 549, Robert Langenbach and colleagues investigate the role that the two COX isoforms, COX-1 and COX-2, play in vessel closure and labor delay in mice. Inhibition of COX-2 during pregnancy had no effect on preventing labor, but adversely affected closure of the ductus arteriosus. Chronic inhibition of COX-1, in contrast, effectively delayed labor without adverse effects, suggesting selective COX-1 inhibition as an alternative strategy for delaying premature labor without the neonatal complications associated with nonselective COX inhibitors.



A target for breast cancer immunotherapy. The development of cancer vaccines depends on the identification of tumor-associated antigens that can induce effective immune responses. Most antigens identified early on were associated with melanomas, and some of them have been shown to induce anti-tumor responses in patients. Identification of carcinoma-associated antigens has been less straightforward, but recent technical advances have led to the discovery of a number of promising candidates. One such candidate is lactadherin, a human milk fat globule membrane protein that is overexpressed in a large fraction of breast cancers. In an article beginning on page 453, Lea Eisenbach and colleagues report the identification of antigenic peptides derived from lactadherin. The peptides elicited specific cytotoxic lymphocyte activity in mice and stimulated cytotoxic activity in lymphocytes from breast cancer patients, suggesting these molecules as potential peptide vaccines for breast cancer.