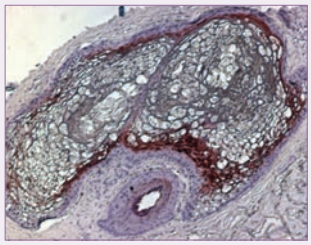
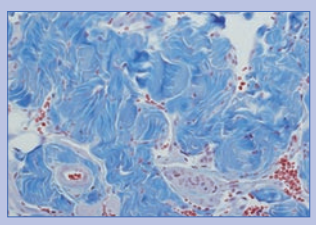
How 13-*cis* retinoic acid combats acne

13-*cis* retinoic acid (13-*cis* RA; also known as isotretinoin) is the most potent agent available for the treatment of acne. Use of the drug is limited due to teratogenic side effects, however, and there is no available alternative with comparable efficacy. Little is known about the mechanism by which 13-*cis* RA treats acne, but it is hoped that understanding this mechanism will lead to development of a therapeutic alternative to this drug. In this issue, Nelson and colleagues (pages 1468–1478) have described that 13-*cis* RA induces apoptosis in human sebaceous glands in vivo and that this effect is mediated by increased expression of the gene lipocalin 2, which encodes neutrophil gelatinase–associated lipocalin (NGAL). The authors found increased immunolocalization of NGAL in the sebaceous glands of individuals with acne following treatment with 13-*cis* RA. Recombinant NGAL also induced apoptosis in cells cultured from human sebocytes. Furthermore, apoptosis in response to 13-*cis* RA was inhibited in the presence of siRNA to lipocalin 2. These data led the authors to suggest that the apoptotic effect of 13-*cis* RA is mediated by NGAL and that agents that selectively induce NGAL expression in human sebaceous glands might provide a new approach to treating individuals with acne.



High levels of adenosine linked to priapism

Priapism — prolonged penile erection in the absence of sexual interest — is common in male individuals with sickle cell disease (SCD). It is considered a medical emergency because it is associated with ischemia-mediated erectile tissue damage, which can result in erectile dysfunction and impotence. However, the development of effective treatment and prevention approaches has been limited by poor understanding of the molecular mechanisms underlying priapism. Some insight has now been provided by Mi and colleagues (pages 1491–1501), who have shown that male mice lacking adenosine deaminase (ADA) exhibit priapism and that this could be corrected by ADA therapy. Consistent with these data suggesting that high levels of adenosine are associated with priapism, genetic and pharmacologic studies indicated that high levels of adenosine induced priapism through stimulation of the A_{2B} adenosine receptor ($A_{2B}R$) in ADA-deficient mice. Because increased adenosine signaling through the $A_{2B}R$ was also shown to contribute to priapism in SCD transgenic mice, a well-accepted mouse model of the disorder, the authors suggest that approaches to either reduce adenosine levels or block $A_{2B}R$ activation might provide new ways to treat priapism.



Dopamine stops endothelial progenitor cell mobilization

Angiogenesis and/or neovascularization is important for the growth, progression, and metastasis of malignant tumors, and recent evidence has indicated that mobilization of endothelial progenitor cells (EPCs) from the bone marrow might be crucial for neovascularization in several tumor types. In this issue, Chakroborty and colleagues (pages 1380–1389) have identified the neurotransmitter dopamine (DA) as a regulator of EPC mobilization from the bone marrow of mice. Decreased levels of DA in the bone marrow were associated with increased mobilization of EPCs in mice bearing sarcomas, and administration of DA inhibited this mobilization. The ability of DA to inhibit EPC mobilization from the bone marrow was mediated via the DA D_2 receptor expressed by the EPCs. Activation of the DA D_2 receptor was shown to suppress VEGFA-induced ERK1/ERK2 phosphorylation, which resulted in decreased synthesis of MMP9, a critical regulator of EPC mobilization. These data led the authors to suggest that DA and DA D_2 receptor agonists, which are widely used in the clinic for the treatment of several conditions including Parkinson disease and shock might provide new approaches to the treatment of cancer.

Dissecting differences between genetic causes of Bardet-Biedl syndrome

Bardet-Biedl syndrome (BBS) is a heterogeneous genetic disorder characterized by many features, including obesity and an increased risk of hypertension and cardiovascular disease. To date, mutations in 12 BBS genes have been identified as causing BBS; however, little is known about the mechanisms underlying the metabolic and cardiovascular disorders in individuals with these mutations. In this issue, Rahmouni and colleagues (pages 1458–1467) have dissected these mechanisms in three mouse models of BBS: *Bbs2*$^{-/-}$, *Bbs4*$^{-/-}$, and *Bbs6*$^{-/-}$ mice. In all three mouse strains, obesity was associated with hyperleptinemia, increased appetite, and low locomotor activity. Furthermore, administration of exogenous leptin failed to decrease body weight and appetite, indicating that leptin resistance accounts for the obesity observed in the mouse models of BBS. Resistance to the metabolic effects of leptin was associated with a defect in proopiomelanocortin neurons in the hypothalamus. However, only *Bbs2*$^{-/-}$ mice were resistant to the effects of leptin on renal sympathetic activity and arterial pressure. As a consequence, whereas *Bbs4*$^{-/-}$ and *Bbs6*$^{-/-}$ mice developed hypertension, *Bbs2*$^{-/-}$ mice did not. These data provide clues to explain why some, but not all, BBS-causing mutations are associated with hypertension in humans.