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Control of whole-body insulin sensitivity. The AMP-activated protein kinase (AMPK) has been proposed as a fuel sensor that mediates the cellular response to nutritional variation. Of several existing AMPK isoforms, AMPKα2 is thought to be physiologically active in skeletal muscle. Benoit Viollet and colleagues have generated mice lacking AMPKα2. As they report (pages 91–98), the mutants are normal with respect to body composition and food intake, but exhibit reduced glucose tolerance. The latter is associated with reduced insulin release and decreased insulin sensitivity of peripheral tissues. However, the metabolic function of mutant isolated skeletal muscle and pancreatic islets is normal, suggesting that the origin of the glucose intolerance is located elsewhere. The authors speculate that AMPKα2 exerts its function as a fuel sensor by modulating the activity of the sympathetic nervous system.

SHP-1 and allergic airway inflammation. The tyrosine phosphatase SHP-1 functions as a negative regulator of several signal transduction pathways, including those downstream of the T cell and IL-4 receptors. As both of these pathways are thought to be critical for successful Th2 cell development, Toshinori Nakayama and colleagues examined the role of SHP-1 in general Th1 and Th2 cell development, and in Th2-dependent allergic responses. As reported on pages 109–119, they found that heterozygous *motheaten* mutants, which lack one copy of SHP-1, exhibited elevated levels of Th2 differentiation and Th2-specific cytokine production upon stimulation when compared with wild-type mice. *Motheaten* heterozygous mice also showed increased allergic responses in an allergic airway inflammation model, suggesting that SHP-1 may function as a negative regulator in the development of allergic responses such as asthma.

Cannabinoids inhibit skin carcinomas. Basal and squamous cell carcinomas, collectively referred to as nonmelanoma skin cancers, are two of the most common malignancies diagnosed in humans. Manuel Guzmán and colleagues have previously shown that cannabinoids can induce the regression of murine gliomas in vivo through activation of the widely expressed CB cannabinoid receptors. On pages 43–50, these authors now demonstrate that CB1, and a second cannabinoid receptor CB2, are expressed in both normal skin and nonmelanoma skin tumors of mice and humans. Administration of CB agonists significantly inhibited skin tumor growth in mice. Two underlying mechanisms seem to be responsible: cannabinoid-treated tumors showed an increase in the number of apoptotic cells, and a decrease in the expression of pro-angiogenic factors such as VEGF and angiopoietin 2. While this suggests that cannabinoids may be utilized in the treatment of skin tumors, further studies will need to investigate their utility as topical therapeutics.