Revisiting Lessons from the C57BL/6J Mouse

To the Editor: We were delighted to see the article by Watson et al. on “Differential regulation of leptin expression and function in A/J vs. C57BL/6J mice during diet-induced obesity” that was recently published in the American Journal of Physiology (AJP; Am J Physiol Endocrinol Metab 279: E356–E365, 2000).

The following is an abstract of the article discussed in the subsequent letter:

Watson, Patricia M., Scott P. Commins, Rudolph J. Beiler, Heather C. Hatcher, and Thomas W. Gettys. Differential regulation of leptin expression and function in A/J vs. C57BL/6J mice during diet-induced obesity. Am J Physiol Endocrinol Metab 279: E356–E365, 2000.—Obesity-resistant (A/J) and obesity-prone (C57BL/6J) mice were weaned onto low-fat (LF) or high-fat (HF) diets and studied after 2, 10, and 16 wk. Despite consuming the same amount of food, A/J mice on the HF diet deposited less carcass lipid and gained less weight than C57BL/6J mice over the course of the study. Leptin mRNA was increased in white adipose tissue (WAT) in both strains on the HF diet but to significantly higher levels in A/J compared with C57BL/6J mice. Uncoupling protein 1 (UCP1) and UCP2 mRNA were induced by the HF diet in brown adipose tissue (BAT) and WAT of A/J mice, respectively, but not in C57BL/6J mice. UCP1 mRNA was also significantly higher in retroperitoneal WAT of A/J compared with C57BL/6J mice. The ability of A/J mice to resist diet-induced obesity is associated with a strain-specific increase in leptin, UCP1, and UCP2 expression in adipose tissue. The findings indicate that the HF diet does not compromise leptin-dependent regulation of adipocyte gene expression in A/J mice and suggest that maintenance of leptin responsiveness confers resistance to diet-induced obesity.

References


To the Editor: The studies reported in our recent article (6) were motivated by the pioneering work of Drs. Surwit and Collins in the area of dietary obesity. In particular, we wanted to explore the mechanism underlying their recent observation that high-fat diets induce a short-lived but larger than predicted increase in serum leptin in obesity-resistant compared with obesity-prone mice (see Fig. 3D of Ref. 5). This involved replicating their experimental design, and at the behest of the referees, we provided basic observations about growth, fat deposition, food intake, and serum profiles to demonstrate that there was a common basis for comparing our findings with those published by the authors. We were particularly interested in the effect of high-fat diets on leptin expression, and found that leptin mRNA was significantly higher in obesity-resistant compared with obesity-prone mice at all time points during the study (Table 2 of Ref. 6). This differs from Surwit et al., who found that, after 6 wk on the
high-fat diet, serum leptin in obesity-resistant mice was either similar to or lower than levels in obesity-prone mice. On the basis of our recent work showing that leptin inhibits its own expression through central modulation of sympathetic tone (1,2), we tested the hypothesis that differences in inhibitory regulation were responsible for diet-induced differences in leptin expression between the mouse strains. This was done by acutely treating mice of each strain with a selective β3-adrenergic receptor agonist after various times on the high-fat diet and evaluating the ability of the agonist to downregulate leptin mRNA. We found significant differences in the way leptin was regulated between the strains (Fig. 3 of Ref. 6) that were unrelated to any change in β3-adrenergic receptor expression or function in white adipose tissue. These findings are novel and likely related to observations from others showing that transcriptional regulation of gene expression by β-agonists differs in adipocytes from A/J and C57BL/6J mice (3, 4). The challenge that lies ahead will be in defining the molecular basis for this difference and relating it to the relative propensity of mice from these two strains to become obese. The studies of Drs. Surwit and Collins have led the way in demonstrating the utility of this model system for studying diet-induced obesity and defining the role of the adipocyte in the process.

REFERENCES


Thomas W. Gettys
Departments of Medicine and Biochemistry and Molecular Biology
Medical University of South Carolina
Charleston, SC 29425