LETTER

Phenotypic Discrepancies in Acetyl-CoA Carboxylase 2-deficient Mice

Abu-Elheiga *et al.* (1) reported that whole-body deletion of acetyl-CoA carboxylase 2 (ACC2) prevented high-fat/high-carbohydrate diet-induced hepatic steatosis and insulin resistance. This report and their previous studies (2–4) differ from our findings in a separate line of $Acc2^{-/-}$ mice. Our mice display increased fatty acid oxidation; however, they do not have increased energy expenditure, altered body weight, or adiposity, nor are they protected from diet-induced insulin resistance and hepatic steatosis (5). Abu-Elheiga and colleagues suggested three reasons for these disparate findings: our use of C57BL/6 mice of pure genetic background *versus* their use of mixed and unmixed 129 backgrounds, differences in diet composition and duration, and our use of Cre to mediate *ACC2* deletion. However, in contrast to a statement in their article, our mice did not express Cre. The Cre gene was bred out of our mice after germ-line deletion of $Acc2^{-/-}$ was achieved, as stated in our study (5). Another key difference is that their $Acc2^{-/-}$ mice overexpress hypoxanthine-guanine phosphoribosyltransferase (HPRT) (4). HPRT plays a central role in nucleotide biosynthesis through the purine salvage pathway. Based upon their reported cloning strategy, HPRT is expressed only in their knock-out mice, but not in their WT mice (4); thus, it is conceivable that this contributes to their phenotype. Until the effect of HPRT overexpression on energy metabolism is resolved in properly controlled mice, this remains one of the key differences between our studies.

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DOI 10.1074/jbc.O112.356915

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ADDITIONS AND CORRECTIONS

THE JOURNAL OF BIOLOGICAL CHEMISTRY VOL. 287, NO. 24, p. 20468, June 8, 2012

VOLUME 287 (2012) PAGE 15801
DOI 10.1074/jbc.A112.356915

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Dr. Cooney's first name was listed incorrectly. His correct name is shown above.