

# Comment on: Turban et al. Optimal Elevation of $\beta$ -Cell 11 $\beta$ -Hydroxysteroid Dehydrogenase Type 1 Is a Compensatory Mechanism That Prevents High-Fat Diet–Induced $\beta$ -Cell Failure. *Diabetes* 2012;61:642–652

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**T**urban et al. (1) recently reported a surprise finding that moderately elevated 11 $\beta$ -hydroxysteroid dehydrogenase type 1 (11 $\beta$ -HSD1) expression in the pancreatic  $\beta$ -cells promoted a compensation against high-fat (HF) diet–induced  $\beta$ -cell failure because glucocorticoids are well established to impair insulin secretion and cause  $\beta$ -cell death and insulin resistance in key insulin targets. Rather than accepting the U-shaped dose response, nongenomic (glucocorticoid receptor–independent) mechanism, or even mineralocorticoid receptor–mediated effect, a simpler approach is to question the model. While we have no reason to doubt the data integrity, the evidence used to establish HF diet–induced  $\beta$ -cell failure was far from convincing. Although an established procedure of using a 58% fat diet to feed mice for 12 weeks was used, wild-type mice did not become obese by gaining any weight, there was no elevation in fasting blood glucose and serum insulin levels (Table 1), and no significant decrease in glucose-stimulated insulin secretion caused by HF diet and measured by area

under the curve (Fig. 2C, first two columns in ref. 1), leading one to question the authors' statement that "HF-fed KsJ mice ... showed markedly attenuated GSIS [glucose-stimulated insulin secretion] indicative of  $\beta$ -cell failure and ... (Fig. 2B and C)" (1). The HF feeding experiment has clearly failed to cause obesity and insulin resistance versus our previously published findings (2); there was no obvious sign of  $\beta$ -cell failure. How could one compensate a nonfailure?

#### ACKNOWLEDGMENTS

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#### REFERENCES

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