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

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Turban et al. (1) recently reported a surprise finding that moderately elevated 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1) expression in the pancreatic β-cells promoted a compensation against high-fat (HF) diet–induced β-cell failure because glucocorticoids are well established to impair insulin secretion and cause β-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 β-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. 2*C*, 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 β-cell failure and … (Fig. 2*B* 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 β-cell failure. How could one compensate a nonfailure?

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**REFERENCES**

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