COMMENT ON USSAR ET AL.

Regulation of Glucose Uptake and Enteroendocrine Function by the Intestinal Epithelial Insulin Receptor. Diabetes 2017;66:886–896

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Diabetes 2017;66:e5 | DOI: 10.2337/db17-0099

It was with great disappointment that I read the recently published article by Ussar et al. (1). Although the authors did a commendable job in characterizing the intestinal phenotypes of male intestinal epithelial insulin receptor and IGF-I insulin receptor knockout mice (VILIRKO and VILIGFRKO, respectively) as compared with floxed control animals, they failed to include female animals as well as an essential control group, namely, the villin-cre mice. It is recognized that the mice used in the current study expressed villin-cre constitutively. However, inducible villin-cre mice have been reported to have a distinct intestinal phenotype (2), and toxic effects of cre expression have been well established for other mouse cell types, such as the pancreatic β-cell (3). These findings necessitate routine examination of cre mice alone as a control. This issue of essential controls was also nicely highlighted in a recent opinion piece by Drucker (4). I therefore call upon the editors and the reviewers of *Diabetes* to ensure that all studies in accepted manuscripts on genetic mouse models are carefully controlled, using not only male and female age- and sex-matched littermates but also both the flox and cre animals used to generate the model as well as controls for the method of induction in inducible models (i.e., vehicle vs. tamoxifen for all control and knockout genotypes). Although this imposes an increased cost and time burden on the investigator(s), it will also aid in ensuring the reliability of the reported findings.

Duality of Interest. P.L.B. has been supported by an operating grant from Novo Nordisk A/S. No other potential conflicts of interest relevant to this article were reported.

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