Science Signaling
AAAS

stke.sciencemag.org/cgi/content/full/12/610/eaax0715/DC1

Supplementary Materials for

Hypusine biosynthesis in β cells links polyamine metabolism to facultative cellular proliferation to maintain glucose homeostasis

Esther M. Levasseur, Kentaro Yamada, Annie R. Piñeros, Wenting Wu, Farooq Syed, Kara S. Orr, Emily Anderson-Baucum, Teresa L. Mastracci, Bernhard Maier, Amber L. Mosley, Yunlong Liu, Ernesto Bernal-Mizrachi, Laura C. Alonso, Donald Scott, Adolfo Garcia-Ocaña, Sarah A. Tersey, Raghavendra G. Mirmira*

*Corresponding author. Email: mirmira@uchicago.edu

Published 3 December 2019, *Sci. Signal.* **12**, eaax0715 (2019)
DOI: 10.1126/scisignal.aax0715

This PDF file includes:

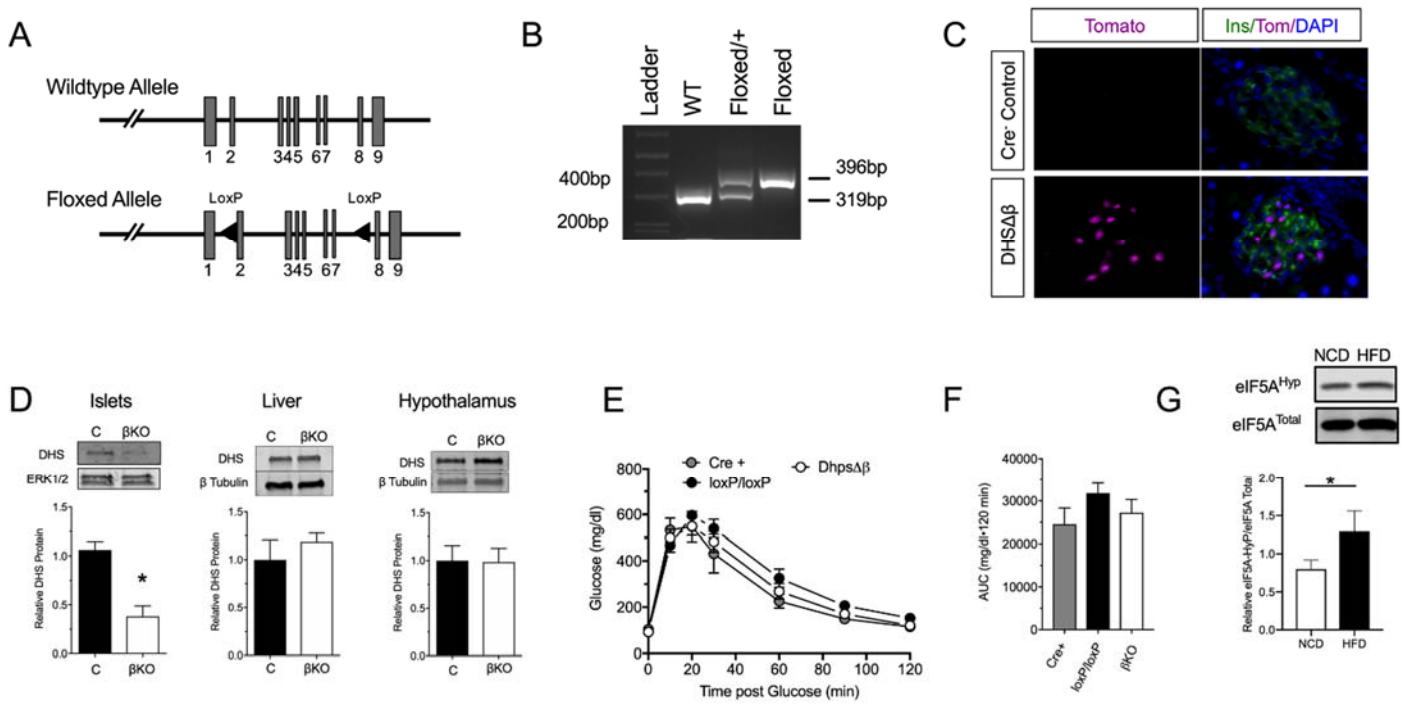

Fig. S1. β Cell–specific deletion of *Dhps* and its effect on glucose homeostasis. (***A***) Schematic representations of the wild-type and mutant (*loxp*) alleles corresponding to the mouse *Dhps* gene. Numbers and gray rectangles indicate positions of exons and "LoxP" indicates position of the Cre recombinase recognition sequence. (***B***) 2% agarose gel showing PCR amplification from genomic DNA of the floxed mutant allele (396 base-pair band) and wild-type allele (319 base-pair band). (***C***) Representative images of tomato fluorescent protein (red) in control (*loxP/+, Cre-*) and *Dhps*$^{\Delta\beta}$ crossed to *Gt(ROSA)26Sor* mice and stained for Insulin (Ins*,* green) and nuclei (DAPI, blue) 2 weeks after administration of tamoxifen to induce deletion of *Dhps*. (***D***) Immunoblot analysis from cell lysate isolated from islets, liver, and hypothalamus 2 weeks after administration of tamoxifen. N=3 mice per group. (***E***) Results of intraperitoneal glucose tolerance tests performed 2 weeks following administration of tamoxifen in male mice. N=8 mice for *loxP/loxP* control group, N=5 mice for Cre+ control group, and N=14 mice for *Dhps*$\Delta\beta$ group. (***F***) Area under the curve (AUC) of glucose tolerance tests in ***E***. (***G***) Immunoblot analysis from cell lysate isolated from islets of mice fed a normal chow diet (N=3 mice) or a high fat diet (N=5 mice). Data are presented as mean ±SEM; **p*-value <0.05.

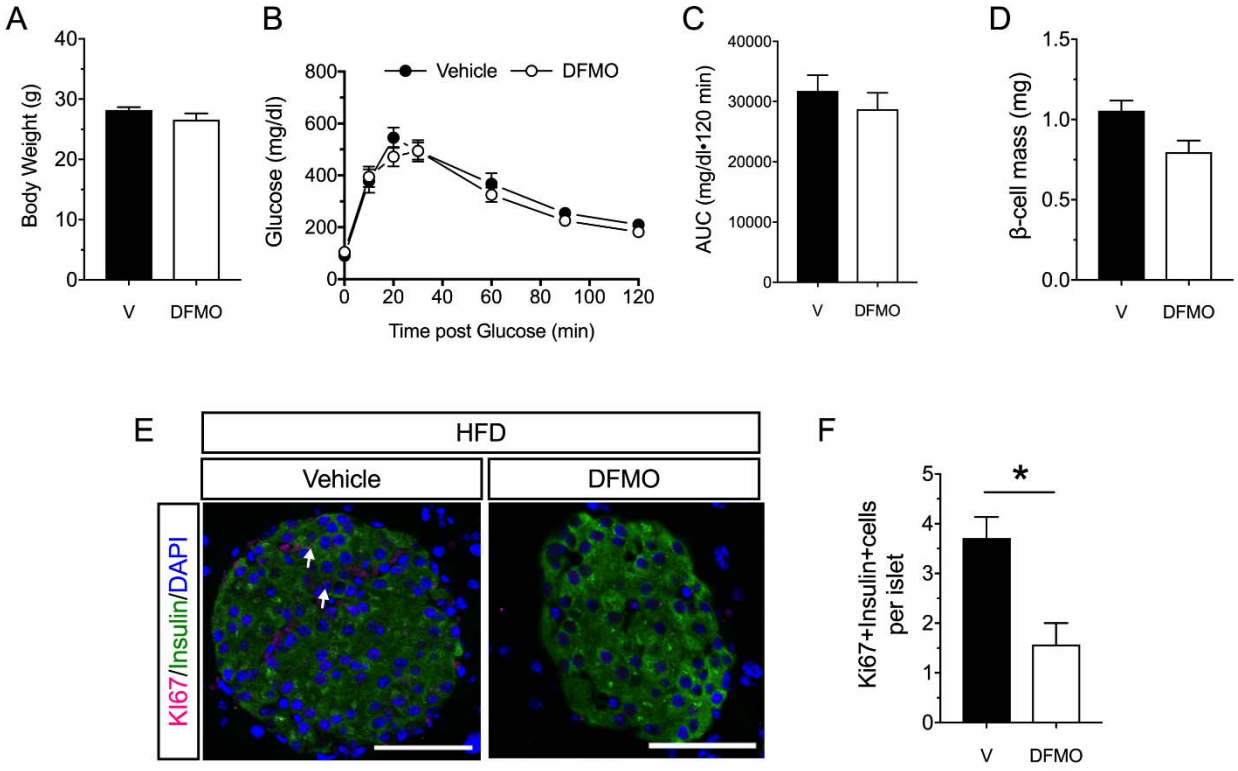

Fig. S2. ODC inhibition attenuates HFD-induced β cell proliferation. *C57BL/6J* mice were treated for 1 week with HFD and either 1% DFMO in the drinking water or water alone. (***A***) Body weight at the end of diet, N=5 mice per group. (***B***) Glucose tolerance test after 1 week of diet, N=5 mice per group. (***C***) Area under the curve (AUC) of glucose tolerance tests in *B*. (***D***) β-cell mass, N=3 animals per group. (***E***) Representative images of pancreata stained for Ki67 (arrows, magenta), insulin (green), and nuclei (DAPI, blue). Scale bar, 50 μm. (***F***) Quantification of Ki67 in insulin positive cells shown in *E*, N=5 mice per group. Data presented as mean +/- SEM; * p-value < 0.05.

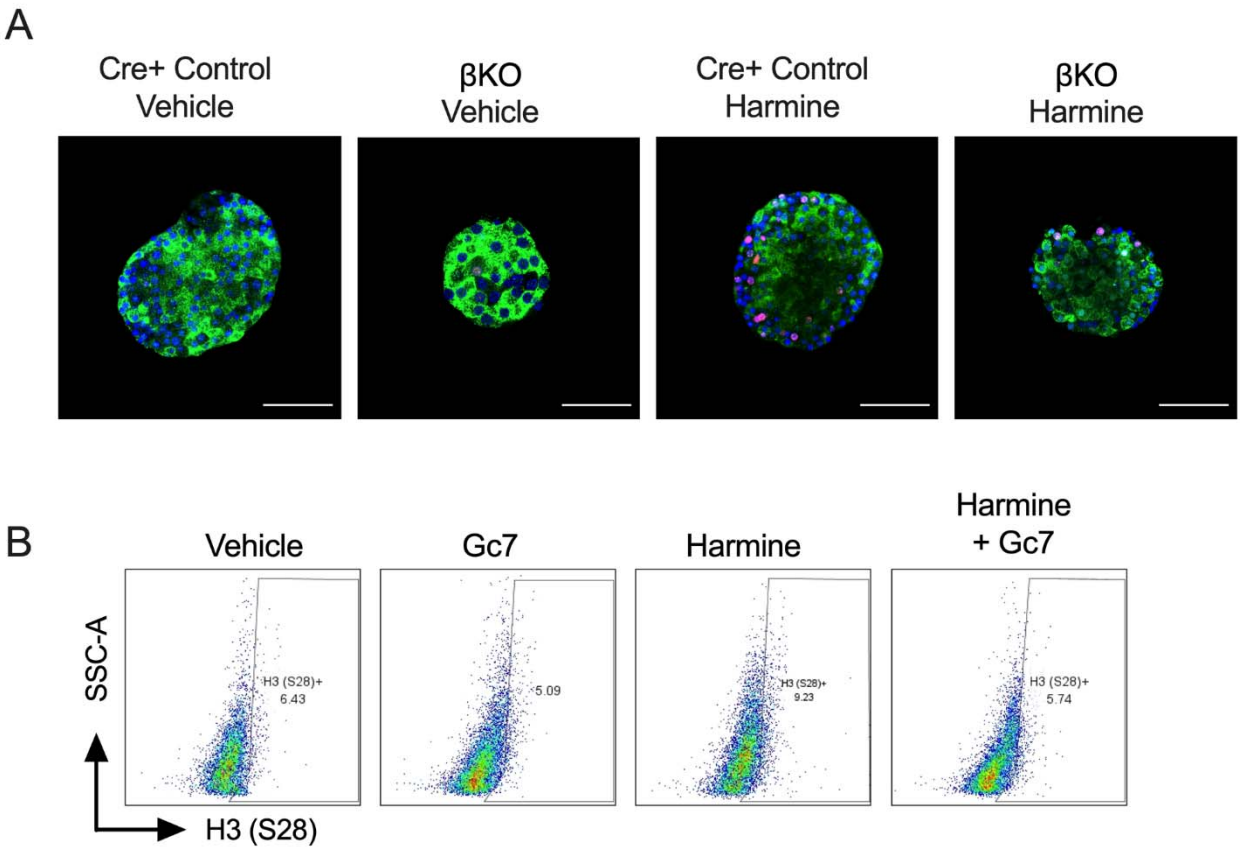

Fig. S3. DHPS inhibition attenuates harmine-induced β cell proliferation in mouse islets. (***A***) Representative images of Cre+ control or DhpsΔβ mouse islets treated with harmine for 48 hours and stained with PCNA (magenta), insulin (green), or DAPI (blue, nuclei). N=3 mice per group. (***B***) Male CD1 mouse islets were treated with harmine and/or an inhibitor of DHPS, Gc7. Representative flow cytometry analyses of phospho-histone H3 after 48 hours. N=5 mice for Vehicle, N=7 mice for Gc7, N=3 mice for Harmine, N=3 mice for Harmine + Gc7.

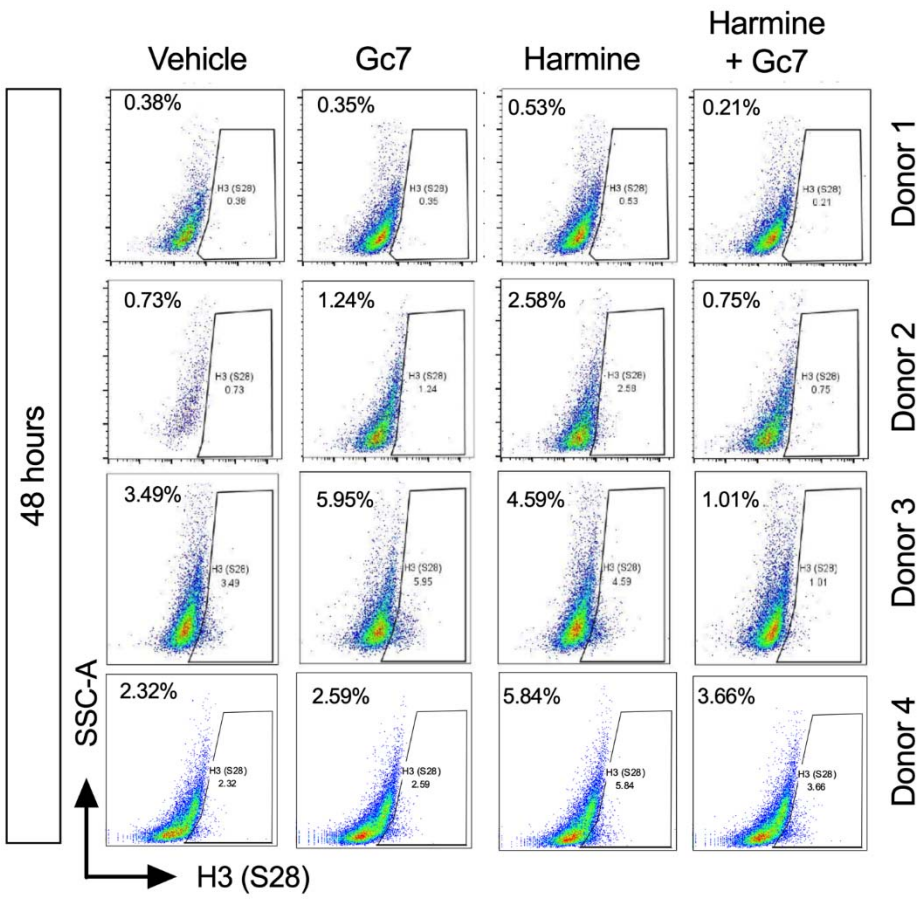

Fig. S4. DHPS inhibition decreases harmine-induced β cell proliferation in human islets. Human islets were treated with harmine and/or an inhibitor of DHPS, Gc7. Shown are flow cytometry analyses of phospho-histone H3 after 48 h of incubation. Data from a single technical replicate for each of 4 individual donors are presented**.**