



## SUPPLEMENTARY ONLINE DATA

## Reduction in BACE1 decreases body weight, protects against diet-induced obesity and enhances insulin sensitivity in mice

Paul J. MEAKIN\*<sup>1</sup>, Alex J. HARPER†<sup>1,2</sup>, D. Lee HAMILTON\*, Jennifer GALLAGHER\*, Alison D. McNEILLY‡, Laura A. BURGESS\*, Lobke M. VAANHOLT§, Kirsten A. BANNON\*, Judy LATCHAM†, Ishrut HUSSAIN†<sup>3</sup>, John R. SPEAKMAN§, David R. HOWLETT†<sup>4</sup> and Michael L.J. ASHFORD\*<sup>5</sup>

\*Division of Cardiovascular and Diabetes Medicine, Medical Research Institute, Ninewells Hospital and Medical School, University of Dundee, Dundee DD1 9SY, Scotland, U.K., †Neuroscience Centre of Excellence for Drug Discovery, GlaxoSmithKline R&D, New Frontiers Science Park, Harlow CM19 5AW, U.K., ‡Division of Neuroscience, University of Dundee, Medical Research Institute, Dundee DD1 9SY, Scotland, U.K., and §Aberdeen Centre for Energy Regulation and Obesity, Institute of Biological and Environmental Sciences, University of Aberdeen, Aberdeen AB24 2TZ, Scotland, U.K.

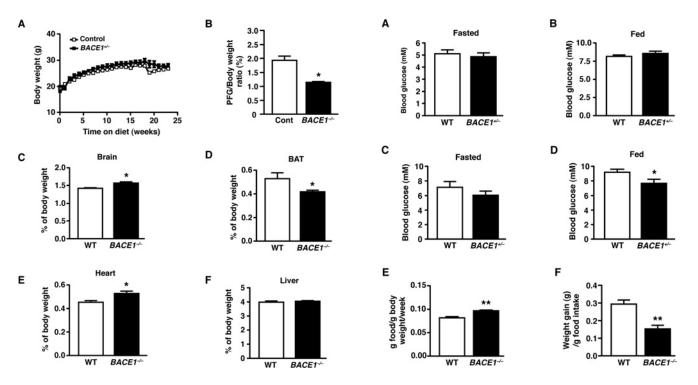


Figure S1  $\,$  Body mass of BACE1  $^{+/-}$  , and tissue mass of BACE1  $^{-/-}$  mice compared with their WT littermates

(A) Body mass curves of age-matched WT littermates with  $BACE1^{+/-}$  mice fed on a regular chow diet and monitored over a period of 24 weeks from 9 weeks of age. Results are means  $\pm$  S.E.M. from 7–8 animals of each genotype. The relative masses (expressed as the percentage of total body mass) of perigenital fat (B), brain (C), BAT (D), heart (E) and liver (F) for WT and  $BACE1^{-/-}$  mice are shown. Results are means  $\pm$  S.E.M. from 5–7 animals of each genotype.  $^*P < 0.05$ .

Figure S2 Comparison of the effects of diet on WT, BACE1 $^{+/-}$  and BACE1 $^{-/-}$  mice

Fasted (**A**) and fed (**B**) blood glucose levels of 8-month-old male mice of the indicated genotypes fed on a regular chow diet (n=6–10). Fasted (**C**) and fed (**D**) blood glucose levels of 10-month-old mice of the indicated genotypes fed on an HFD for 20 weeks. (**E**) Food intake per mouse per week normalized by body mass (relative food intake) for mice of the indicated genotypes fed on an HFD. (**F**) BACE $^{-/-}$  mice on a HFD have decreased feed efficiency compared with the WT controls. Results are means  $\pm$  S.E.M. from 11–14 animals of each genotype. \*\*P < 0.01,\*P < 0.05.

<sup>&</sup>lt;sup>1</sup> These authors contributed equally to this work.

<sup>&</sup>lt;sup>2</sup> Present address: Lilly Research Laboratories, Eli Lilly & Co., Erlwood Manor, Sunninghill Road, Windlesham, GU20 6PH. U.K.

<sup>&</sup>lt;sup>3</sup> Present address: Merck Serono S.A., Chemin des Mines 9, 1202 Geneva, Switzerland

<sup>&</sup>lt;sup>4</sup> Present address: Wolfson Centre for Age-Related Diseases, King's College London, London SE1 1UL, U.K.

<sup>&</sup>lt;sup>5</sup> To whom correspondence may be addressed (email m.l.j.ashford@dundee.ac.uk).

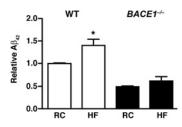


Figure S3  $\,$  A 20-week HFD was shown to increase levels of A $\beta_{x\text{-}42}$  in the cerebral cortices of WT mice, but not BACE1 $^{-/-}$  mice

Results from an ELISA showing the level of A $eta_{x\text{-}42}$  (normalized to mean WT, normal chow diet amount) in the cerebral cortices of WT and BACE $^{-/-}$  mice fed on a regular chow (RC) diet or an HFD. WT, n=5; BACE $^{-/-}$ , n=6. Results are means  $\pm$  S.E.M. \*P<0.05.

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