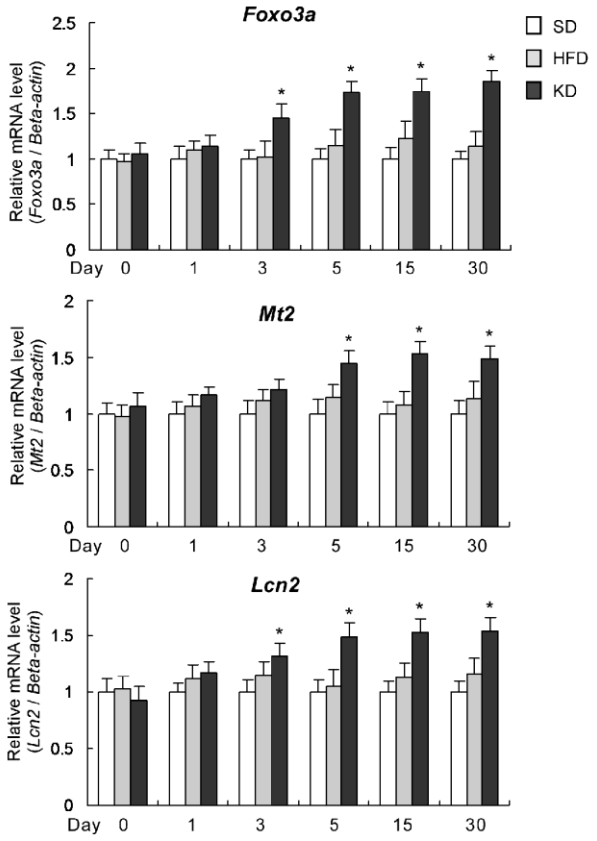
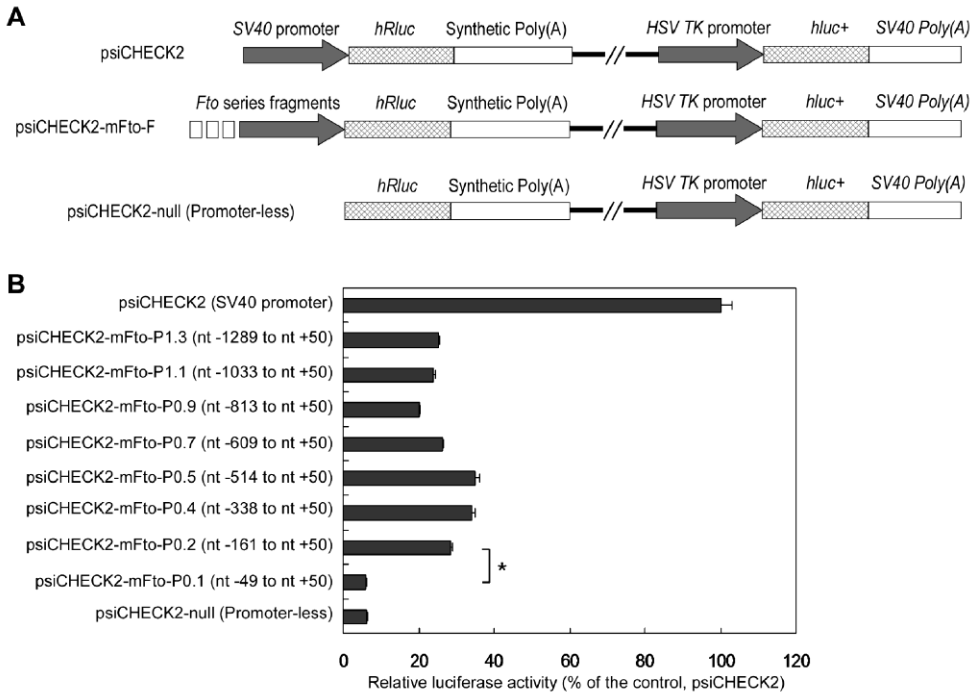
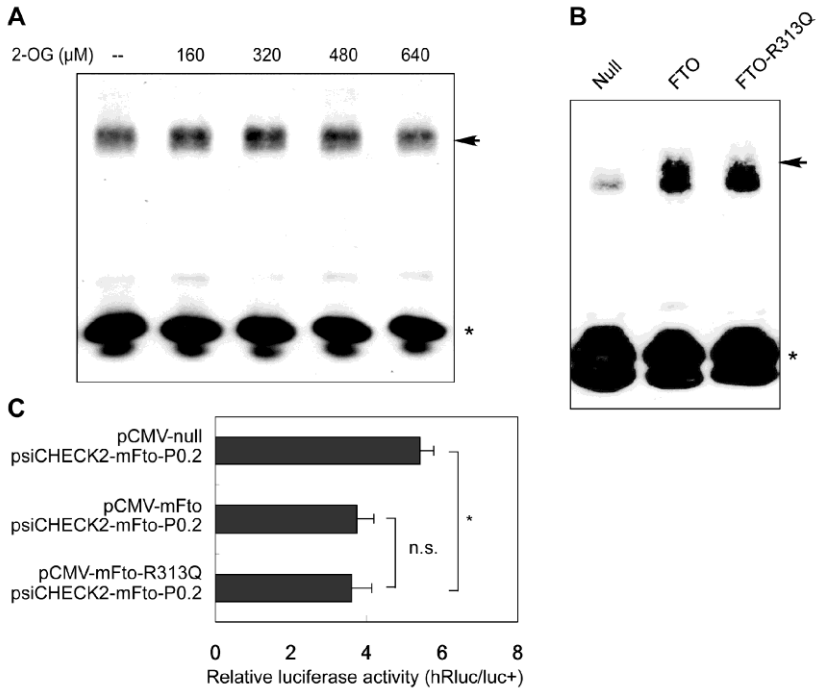


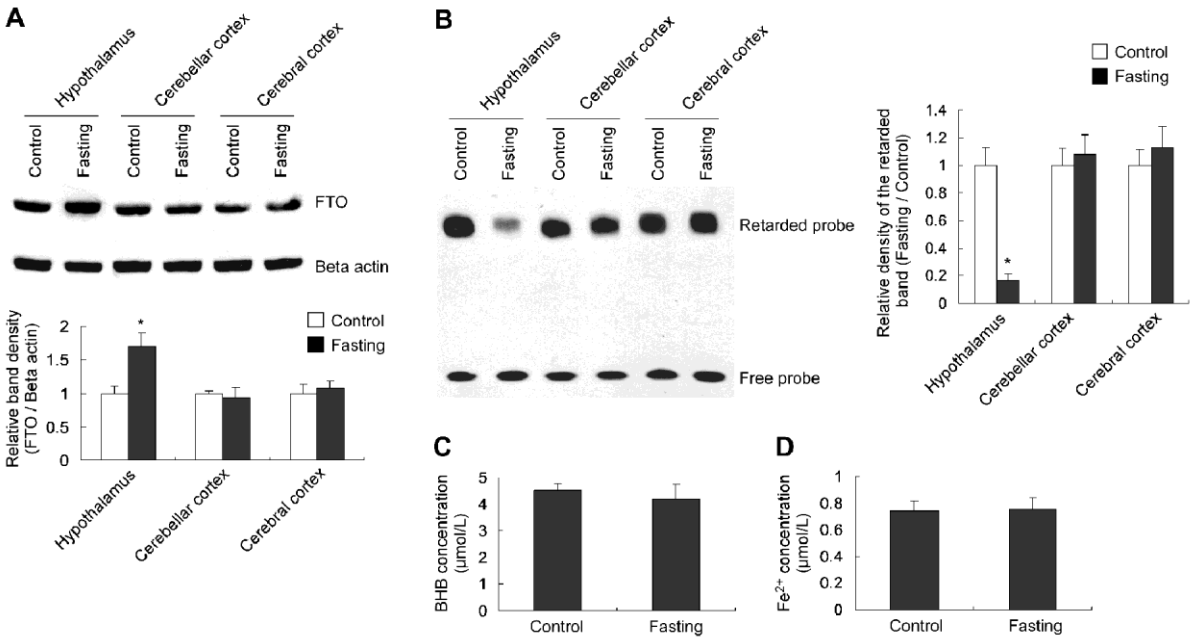
Supplementary Figure S1 Increase of *Foxo3a*, *Mt2* and *Lcn2* genes' transcriptions in the hypothalamus of KD-mice. The qPCR showed that the mRNA levels of *Foxo3a*, *Mt2* and *Lcn2* genes in the mice after 3- to 30-day ketogenic (KD) diet significantly increased compared with those in the standard-diet (SD) mice. The mRNA levels of the target genes were normalized to the mRNA levels of *β-actin*. The relative mRNA levels at all time points in the SD mice were normalized as "1". n=5, **P* < 0.001, compared with the mRNA levels at the same time point in the SD mice.



Supplementary Figure S2 Identification of the *Fto* minimal functional promoter in N1E-115 cells. **(A)** Schematic of the reporter constructs used to determine the minimal functional promoter and upstream regulatory regions. **(B)** Luciferase analysis showing the minimal functional promoter (P0.2: nt -161 to nt +50). n=10, **P* < 0.001.



Supplementary Figure S3 2-oxoglutarate (2-OG) is not essential for FTO's function as a transcriptional repressor. **(A)** EMSA showing no effect of 2-oxoglutarate (2-OG) on the FTO's binding to the core promoter. The arrow shows the retarded probes. The star shows the free probes. **(B)** EMSA showing no alteration of the binding ability of the mutant FTO-R313Q, an essential site for 2-OG binding, compared with the wild-type FTO. **(C)** Luciferase assays showing no alteration in the promoter activity between that the mutant FTO-R313Q and the wild-type. n = 10, $*P < 0.001$.



Supplementary Figure S4 Upregulation of FTO and increase in the FTO's binding to its own promoter in the hypothalamus of 48-hr fasting mice. **(A)** Western blot showing a significant increase of the FTO protein levels in the hypothalamus of the 48-hr fasting mice, but not in cerebellar cortex and cerebral cortex. n = 3, *P<0.0001. **(B)** ESMA assays showing a significant decrease of the FTO's binding capability to its own promoter in the hypothalamus of the 48-hr fasting mice, but not in cerebellar cortex and cerebral cortex. n = 3, *P<0.001. **(C-D)** No alteration of BHB and Fe^{2+} levels in the hypothalamus of the 48-hr fasting mice, compared with the control mice. n = 5.