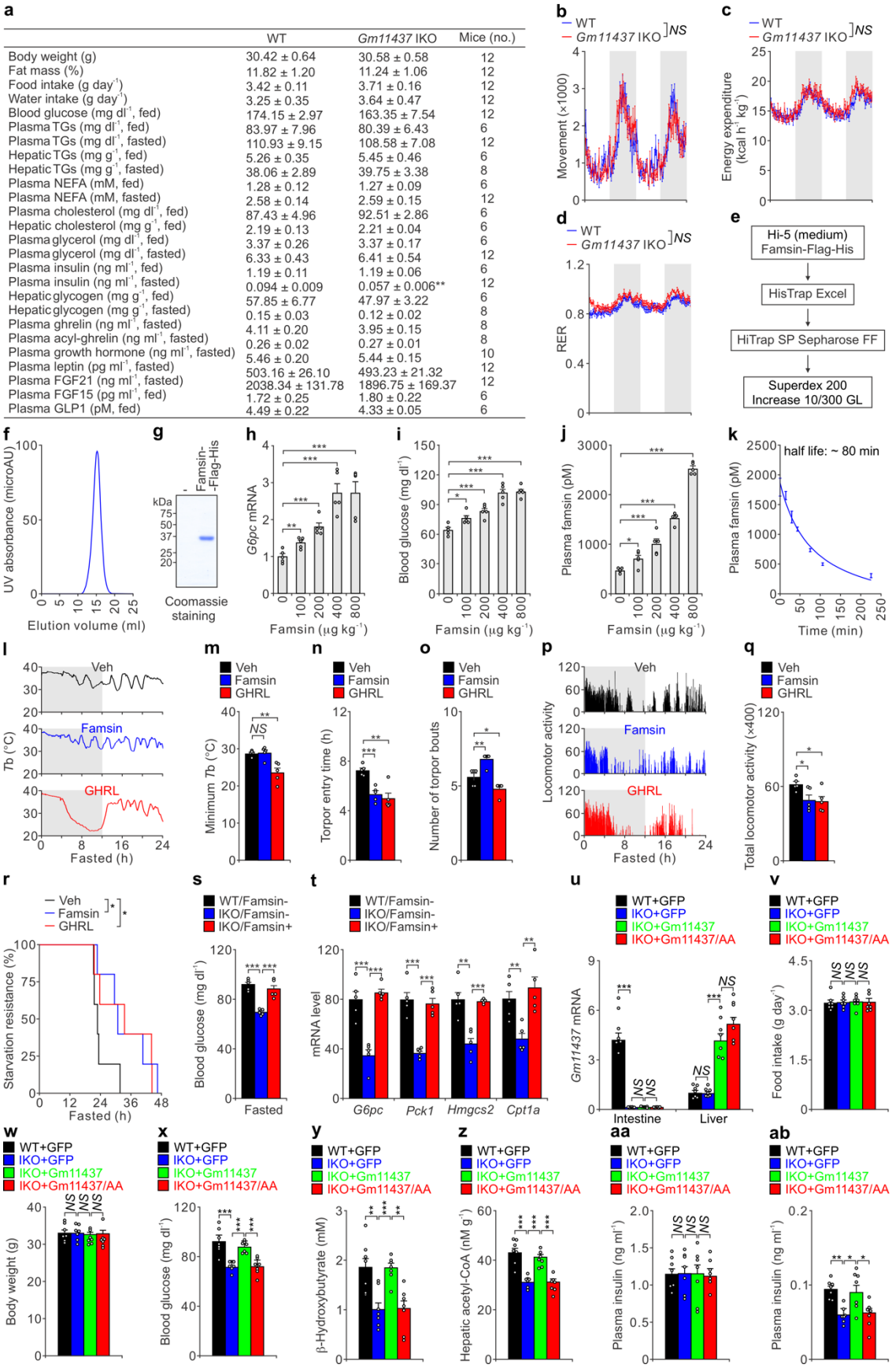
a

	WT	*Gm11437* IKO	Mice (no.)
Body weight (g)	30.42 ± 0.64	30.58 ± 0.58	12
Fat mass (%)	11.82 ± 1.20	11.24 ± 1.06	12
Food intake (g day^{-1})	3.42 ± 0.11	3.71 ± 0.16	12
Water intake (g day^{-1})	3.25 ± 0.35	3.64 ± 0.47	12
Blood glucose (mg dl^{-1}, fed)	174.15 ± 2.97	163.35 ± 7.54	12
Plasma TGs (mg dl^{-1}, fed)	83.97 ± 7.96	80.39 ± 6.43	6
Plasma TGs (mg dl^{-1}, fasted)	110.93 ± 9.15	108.58 ± 7.08	12
Hepatic TGs (mg g^{-1}, fed)	5.26 ± 0.35	5.45 ± 0.46	6
Hepatic TGs (mg g^{-1}, fasted)	38.06 ± 2.89	39.75 ± 3.38	8
Plasma NEFA (mM, fed)	1.28 ± 0.12	1.27 ± 0.09	6
Plasma NEFA (mM, fasted)	2.58 ± 0.14	2.59 ± 0.15	12
Plasma cholesterol (mg dl^{-1}, fed)	87.43 ± 4.96	92.51 ± 2.86	6
Hepatic cholesterol (mg g^{-1}, fed)	2.19 ± 0.13	2.21 ± 0.04	6
Plasma glycerol (mg dl^{-1}, fed)	3.37 ± 0.26	3.37 ± 0.17	6
Plasma glycerol (mg dl^{-1}, fasted)	6.33 ± 0.43	6.41 ± 0.54	12
Plasma insulin (ng ml^{-1}, fed)	1.19 ± 0.11	1.19 ± 0.06	6
Plasma insulin (ng ml^{-1}, fasted)	0.094 ± 0.009	0.057 ± 0.006**	12
Hepatic glycogen (mg g^{-1}, fed)	57.85 ± 6.77	47.97 ± 3.22	6
Hepatic glycogen (mg g^{-1}, fasted)	0.15 ± 0.03	0.12 ± 0.02	8
Plasma ghrelin (ng ml^{-1}, fasted)	4.11 ± 0.20	3.95 ± 0.15	8
Plasma acyl-ghrelin (ng ml^{-1}, fasted)	0.26 ± 0.02	0.27 ± 0.01	8
Plasma growth hormone (ng ml^{-1}, fasted)	5.46 ± 0.20	5.44 ± 0.15	10
Plasma leptin (pg ml^{-1}, fasted)	503.16 ± 26.10	493.23 ± 21.32	12
Plasma FGF21 (ng ml^{-1}, fasted)	2038.34 ± 131.78	1896.75 ± 169.37	12
Plasma FGF15 (pg ml^{-1}, fed)	1.72 ± 0.25	1.80 ± 0.22	6
Plasma GLP1 (pM, fed)	4.49 ± 0.22	4.33 ± 0.05	6



Supplementary information, Fig. S3. Effect of *Gm11437* knockout on metabolism.
a Effect of *Gm11437* knockout on metabolic parameters including body weight, fat mass, food intake, water intake, blood glucose, hepatic triglycerides (TGs) and cholesterol, hepatic glycogen, plasma triglycerides (TGs), NEFAs, cholesterol, glycerol and various hormones in 8-10-week-old male mice. Data are shown as mean ± s.e.m. Comparison of different groups was carried out using unpaired two-tailed Student's *t*-test. **p < 0.01. **b-d** Effect of *Gm11437* knockout on movement (**b**), energy expenditure (**c**) and respiratory exchange ratio (RER, **d**) in 8-10-week-old male mice. The white and grey backgrounds (**b-d**) indicate 12-hr periods of light and darkness, respectively. Data are shown as mean ± s.e.m. Comparison of different groups was carried out using two-way ANOVA followed by Tukey's test. *NS*, no statistical significance. n = 12 mice. **e** Schematic showing the purification procedure for famsin-Flag-His from Hi-5 cell medium. **f** A representative chromatogram from size exclusion chromatography of famsin-Flag-His purified from Hi-5 cells. microAU, micro-ultraviolet absorbance at 280 nm. **g** Coomassie staining showing purified famsin-Flag-His separated by SDS-PAGE. **h-i** Effect of different doses of famsin-Flag-His on hepatic *G6pc* mRNA (**h**) and blood glucose (**i**). Five 8-10-week-old male mice were used for measurement. Famsin was intraperitoneally injected after 4 hr fasting, and blood glucose and hepatic *G6pc* mRNA was measured at 8 hr after administration. Data are shown as mean ± s.e.m. Comparison of different groups was carried out using one-way ANOVA followed by Tukey's test. *p < 0.05, **p < 0.01, ***p < 0.001. n = 5 mice. **j-k** Plasma famsin levels of 8-week-old male mice after intraperitoneal injection of different doses (**j**) or after an intraperitoneal injection of 400 μg kg^{-1} (**k**). Data are shown as mean ± s.e.m. Comparison of different groups was carried out using one-way ANOVA followed by Tukey's test (**j**). *p < 0.05, ***p < 0.001. n = 5 mice. **l-r** Effect of famsin or ghrelin (GHRL) on torpor evaluated by core body temperature (*T*b, **l**), minimum *T*b (**m**), torpor entry time (**n**), torpor frequency (number of torpor bouts, **o**), locomotor activity (**p**), relative total locomotor activity (**q**) and starvation resistance (**r**) of fasted 8-week-old male mice. Failure of starvation resistance was judged as *T*b < 28 ºC following a quick decrease in *T*b below the environmental temperature. Famsin (400 μg kg^{-1}) or GHRL (4000 μg kg^{-1}) was intraperitoneally injected after 4 hr fasting. Data are shown as mean ± s.e.m. Comparison of different groups was carried out using one-way ANOVA followed by Tukey's test (**m-o** and **q**) or log-rank test (**r**). *p < 0.05, **p < 0.01, ***p < 0.001. *NS*, no statistical significance. n = 5 mice. **s-t** Effect of Gm11437 IKO and famsin on blood glucose (**s**) and relative mRNA levels of genes involved in lipid oxidation (*Cpt1a*), ketogenesis (*Hmgcs2*) and gluconeogenesis (*G6pc*, *Pck1*) in liver extracts (**t**) from overnight-fasted mice. 400 μg kg^{-1} famsin was intraperitoneally injected after 4 hr fasting, and mRNA was measured at 8 hr after administration. Data are shown as mean ± s.e.m. Comparison of different groups was carried out using one-way ANOVA followed by Tukey's test. **p < 0.01, ***p < 0.001. n = 5 mice. **u** qPCR results showing expression of Gm11437 in intestinal and liver extracts from 8-10-week-old WT or *Gm11437* IKO male mice after adenoviral administration of GFP, Gm11437 or Gm11437/AA. Data are shown as mean ± s.e.m. Comparison of different groups was carried out using one-way ANOVA followed by Tukey's test. ***p < 0.001. *NS*, no statistical significance. n = 7 mice. **v-ab** Effect of adenoviral-expressed WT Gm11437 or Gm11437/AA on food intake (**v**), body weight (**w**), blood glucose after overnight fasting (**x**), plasma β-hydroxybutyrate after overnight fasting (**y**) and hepatic acetyl-CoA after overnight fasting (**z**) and plasma insulin during feeding (**aa**) or overnight fasting (**ab**) of 8-week-old male mice. Data are shown as mean ± s.e.m. Comparison of different groups was carried out using one-way ANOVA followed by Tukey's test. *p < 0.05, **p < 0.01, ***p < 0.001. *NS*, no statistical significance. n = 7 mice.