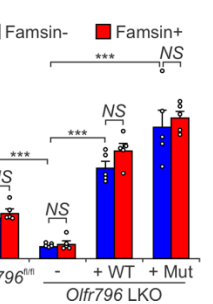
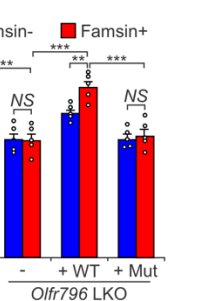
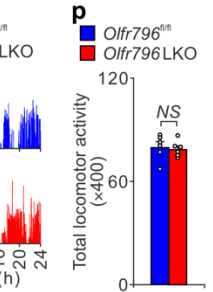
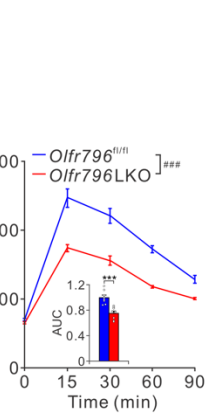
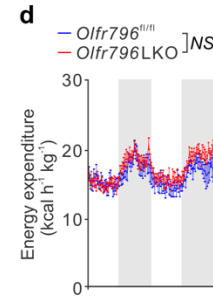
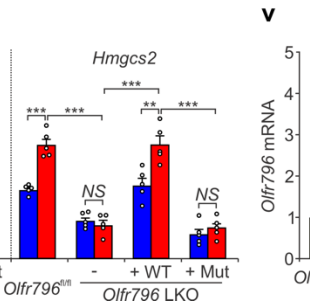
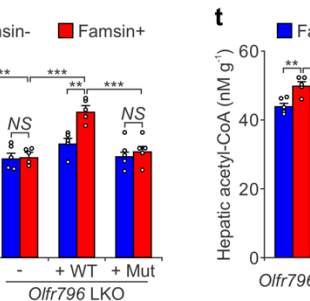
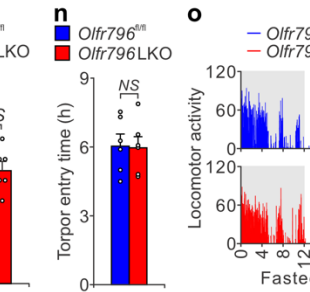
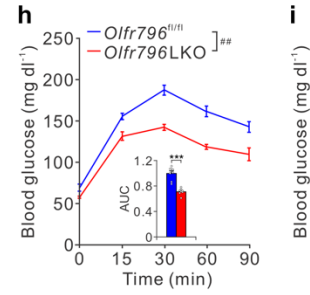
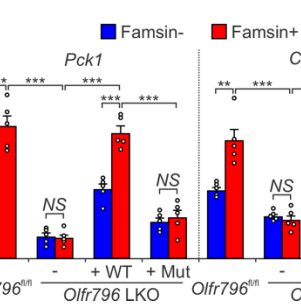
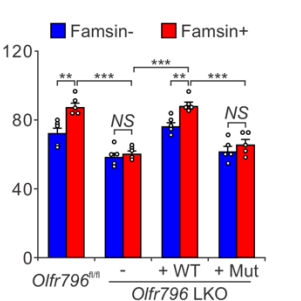
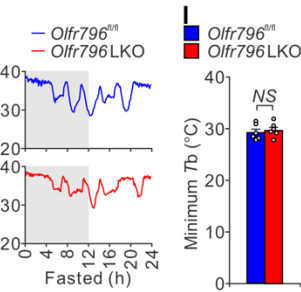
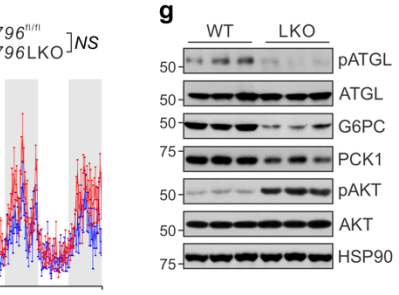


**c**

	<i>Olf796<sup>fl/fl</sup></i>	<i>Olf796<sup>LKO</sup></i>	Mice (no.)
Body weight (g)	25.84 ± 0.96	26.43 ± 0.73	8
Fat mass (%)	6.87 ± 0.59	7.01 ± 0.79	8
Food intake (g day <sup>-1</sup> )	4.44 ± 0.19	4.47 ± 0.10	8
Water intake (g day <sup>-1</sup> )	3.49 ± 0.18	3.32 ± 0.12	8
Blood glucose (mg dl <sup>-1</sup> , fed)	155.48 ± 9.08	153.68 ± 4.02	8
Blood glucose (mg dl <sup>-1</sup> , fasted)	86.18 ± 2.37	70.20 ± 1.44***	8
Plasma TGs (mg dl <sup>-1</sup> , fed)	80.48 ± 9.93	81.70 ± 11.74	8
Plasma TGs (mg dl <sup>-1</sup> , fasted)	90.74 ± 11.86	127.66 ± 14.29	8
Hepatic TGs (mg g <sup>-1</sup> , fed)	10.78 ± 1.31	9.62 ± 1.00	8
Hepatic TGs (mg g <sup>-1</sup> , fasted)	53.29 ± 5.74	50.37 ± 4.80	8
Plasma cholesterol (mg dl <sup>-1</sup> , fed)	98.44 ± 5.89	105.93 ± 5.31	8
Hepatic cholesterol (mg g <sup>-1</sup> , fed)	1.80 ± 0.09	1.82 ± 0.05	8
Plasma insulin (ng ml <sup>-1</sup> , fed)	1.13 ± 0.12	0.93 ± 0.11	8
Plasma insulin (ng ml <sup>-1</sup> , fasted)	0.126 ± 0.005	0.126 ± 0.006	8
Hepatic glycogen (mg g <sup>-1</sup> , fed)	34.11 ± 1.68	29.46 ± 1.98	8
Hepatic glycogen (mg g <sup>-1</sup> , fasted)	0.20 ± 0.03	0.21 ± 0.03	8
β-Hydroxybutyrate (mM, fasted)	1.44 ± 0.14	1.01 ± 0.05*	8
Hepatic acetyl-CoA (nM g <sup>-1</sup> , fasted)	50.53 ± 1.18	36.79 ± 1.34***	8



**Supplementary information, Fig. S6. Effect of *Olfir796* liver-specific knockout on metabolism.**

**a** Generation of *Olfir796* liver-specific knockout (LKO) mice. **b-c** Effect of *Olfir796* LKO on *Olfir796* mRNA levels (**b**) and metabolic parameters (**c**) including body weight, fat mass, food intake, water intake, blood glucose, plasma TGs, hepatic TGs, plasma total cholesterol, hepatic cholesterol, plasma insulin levels, hepatic glycogen, blood glucose, plasma  $\beta$ -hydroxybutyrate and hepatic acetyl-CoA in 8-10-week-old male mice. Data are shown as mean  $\pm$  s.e.m. Comparison of different groups was carried out using unpaired two-tailed Student's *t*-test. \* $p < 0.05$ , \*\*\* $p < 0.001$ . NS, no statistical significance. **d-f** Effect of *Olfir796* LKO on energy expenditure (**d**), RER (**e**) and movement (**f**) in 8-10-week-old male mice. The white and grey backgrounds indicate 12-hr periods of light and darkness, respectively. Data are shown as mean  $\pm$  s.e.m. Comparison of different groups was carried out using two-way ANOVA followed by Tukey's test. NS, no statistical significance.  $n = 8$  mice. **g** Immunoblots showing the effect of *Olfir796* knockout on hepatic lipolysis and gluconeogenesis. **h-j** Pyruvate tolerance test (**h**), glucose tolerance test (**i**) and insulin tolerance test (**j**) results from fasted WT and *Olfir796* LKO mice. The relative area under the curve (AUC) is shown in the inset of each panel. Data are shown as mean  $\pm$  s.e.m. Comparison of different groups was carried out using two-way ANOVA followed by Tukey's test (curve data, # $p < 0.05$ , ## $p < 0.01$ , ### $p < 0.001$ ) or unpaired two-tailed Student's *t*-test (AUC data, \*\*\* $p < 0.001$ ).  $n = 8$  mice. **k-q** Effect of *Olfir796* LKO on torpor evaluated by core body temperature (*T<sub>b</sub>*, **k**), minimum *T<sub>b</sub>* (**l**), torpor frequency (number of torpor bouts, **m**), torpor entry time (**n**), locomotor activity (**o**), relative total locomotor activity (**p**) and starvation resistance (**q**) of fasted 8-week-old male mice. Failure of starvation resistance was judged as *T<sub>b</sub>*  $< 28$  °C following a quick decrease in *T<sub>b</sub>* below the environmental temperature. The white and grey backgrounds (**k** and **o**) indicate 12-hr periods of light and darkness, respectively. Data are shown as mean  $\pm$  s.e.m. Comparison of different groups was carried out using unpaired two-tailed Student's *t*-test (**l-n** and **p**) or log-rank test (**q**). \* $p < 0.05$ . NS, no statistical significance.  $n = 6$  mice. **r-v** Effect of WT OLFR796 or its mutant (Mut; R187D, R195D and E197A) on blood glucose (**r**), plasma  $\beta$ -hydroxybutyrate (**s**), hepatic acetyl-CoA (**t**), relative mRNA levels of genes involved in lipid oxidation (*Cpt1a*), ketogenesis (*Hmgcs2*) and gluconeogenesis (*G6pc*, *Pck1*) (**u**) and relative expression of *Olfir796* (**v**) from liver extracts of overnight fasted 8-10-week-old male mice treated with (Famsin+) or without (Famsin-) famsin. 400  $\mu\text{g kg}^{-1}$  famsin was intraperitoneally injected after 4 hr fasting. Data are shown as mean  $\pm$  s.e.m. Comparison of different groups was carried out using two-way ANOVA followed by Tukey's test. \*\* $p < 0.01$ , \*\*\* $p < 0.001$ . NS, no statistical significance.  $n = 5$  mice.