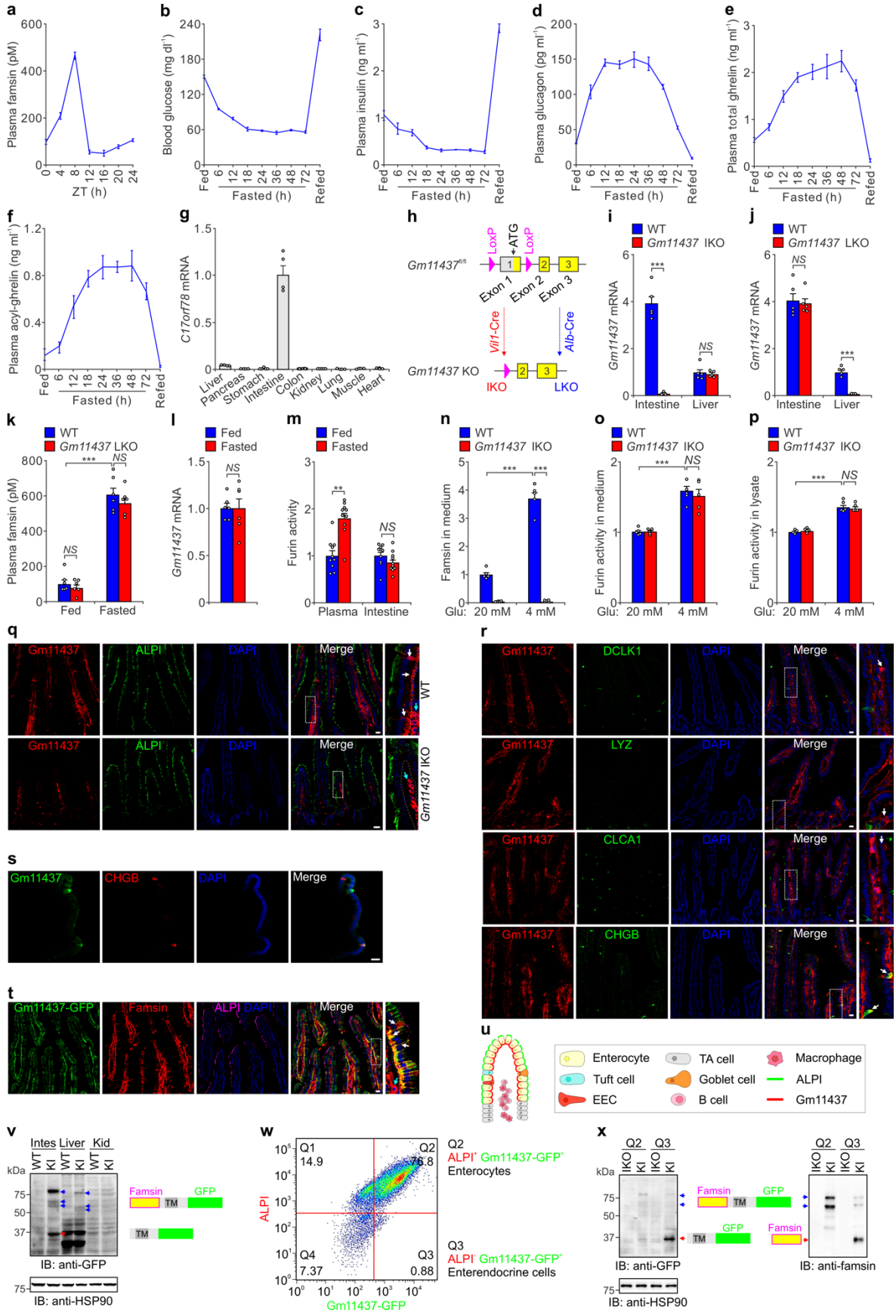
a
Plasma famsin (pM)
ZT (h)
b
Blood glucose (mg dl-1)
Fed
Fasted (h)
Refed
c
Plasma insulin (ng ml-1)
d
Plasma glucagon (pg ml-1)
e
Plasma total ghrelin (ng ml-1)
f
Plasma acyl-ghrelin (ng ml-1)
g
C17orf78 mRNA
Liver
Pancreas
Stomach
Intestine
Colon
Kidney
Lung
Muscle
Heart
h
Gm11437fl/fl
LoxP
ATG
Exon 1
Exon 2
Exon 3
Vil1-Cre
Alb-Cre
Gm11437 KO
IKO
LKO
i
WT
Gm11437 IKO
Gm11437 mRNA
Intestine
Liver
j
Gm11437 LKO
k
Plasma famsin (pM)
l
Fed
Fasted
m
Furin activity
Plasma
Intestine
n
Famsin in medium
Glu: 20 mM
4 mM
o
Furin activity in medium
p
Furin activity in lysate
q
Gm11437
ALPI
DAPI
Merge
WT
Gm11437 IKO
r
DCLK1
LYZ
CLCA1
CHGB
s
t
Gm11437-GFP
Famsin
u
Enterocyte
TA cell
Macrophage
Tuft cell
Goblet cell
ALPI
EEC
B cell
Gm11437
v
Intes
Liver
Kid
kDa
IB: anti-GFP
IB: anti-HSP90
TM
w
Q1
14.9
Q2
76.8
Q4
7.37
Q3
0.88
Q2
ALPI+ Gm11437-GFP+
Enterocytes
Q3
ALPI- Gm11437-GFP+
Enterendocrine cells
x
IKO
KI
IB: anti-famsin

Supplementary information, Fig. S2. Characterization of *Gm11437* knockout mice.
a Diurnal rhythm of plasma famsin levels. ZT is the *Zeitgeber* time. Five 8-10-week-old male mice for each indicated time point were used for measurement. Data are shown as mean ± s.e.m. **b**-**f** Effect of *ad lib* feeding, fasting, or refeeding 1.5 hr after fasting on blood glucose levels (**b**), plasma insulin levels (**c**), plasma glucagon levels (**d**), plasma total ghrelin levels (**e**) and plasma acyl-ghrelin levels (**f**). Fasting was started at ZT0. Six 12-week-old male mice for each indicated time point were used for measurement. Data are shown as mean ± s.e.m. **g** qPCR results showing relative mRNA levels of *C17orf78* in different tissues from human. n = 3 (liver), n = 4 (pancreas, intestine, lung, muscle, heart), n = 5 (stomach), n = 6 (kidney), n = 7 (colon). Data are shown as mean ± s.e.m. **h** Generation of *Gm11437* intestine-specific knockout (IKO) or *Gm11437* liver-specific knockout (LKO) mice. **i**-**j** Relative mRNA levels of *Gm11437* in 8-10-week-old WT and IKO male mice (**i**) or WT and LKO male mice (**j**). Data are shown as mean ± s.e.m. Comparison of different groups was carried out using unpaired two-tailed Student's *t*-test. ***p < 0.001. *NS*, no statistical significance. n = 5 mice. **k** Plasma famsin levels in 8-10-week-old *Gm11437* WT and LKO male mice with *ad lib* feeding or overnight fasting. Data are shown as mean ± s.e.m. Comparison of different groups was carried out using two-way ANOVA followed by Tukey's test. ***p < 0.001. *NS*, no statistical significance. n = 6 mice. **l** Relative mRNA levels of intestine *Gm11437* in *ad lib* fed or overnight fasted 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. *NS*, no statistical significance. n = 6 mice. **m** Relative plasma and intestine furin activity in *ad lib* fed or overnight fasted 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. *NS*, no statistical significance. n = 10 mice. **n**-**p** Effect of glucose on secretion of famsin from intestinal organoids (**n**) and furin activity in medium (**o**) or lysate (**p**) of intestinal organoids. Glu: Glucose. Data are shown as mean ± s.e.m. Comparison of different groups was carried out using two-way ANOVA followed by Tukey's test. ***p < 0.001. *NS*, no statistical significance. n = 5. **q** Immunostaining results showing the expression of Gm11437 and ALPI (intestinal alkaline phosphatase, enterocyte marker) in intestinal sections from WT and *Gm11437* IKO mice. The enlarged images of the boxed areas are shown on the right. The white arrows indicate positive staining of Gm11437, and the cyan arrows indicate background signals in mesenchyme. Scale bars, 20 μm. **r** Immunostaining results showing the expression of Gm11437 and DCLK1 (doublecortin like kinase 1, Tuft cell marker), LYZ (lysozyme, Paneth cell marker), CLCA1 (chloride channel accessory 1, Goblet cell marker) or CHGB (chromogranin B, enteroendocrine cell marker) in intestinal sections from WT mice. The enlarged images of the boxed areas are shown on the right. The white arrows indicate positive staining of Gm11437. Scale bars, 20 μm. **s** Immunostaining results showing Gm11437 and CHGB (chromogranin B) in intestinal organoids. Scale bar, 20 μm. **t** Immunostaining results showing the expression of ALPI (intestinal alkaline phosphatase, enterocyte marker) and Gm11437 stained by famsin antibody or visualized by GFP in intestinal sections from Gm11437-GFP knock-in mice. The enlarged image of the boxed area is shown on the right. The white arrows indicate positive staining of Gm11437, and the cyan arrow indicates background signals in mesenchyme. Scale bars, 20 μm. **u** The small intestinal villi contain a variety of cell types, including enterocytes, EECs, tuft cells, goblet cells, and TA cells. ALPI (green) is localized to the brush border membrane of enterocytes, while Gm11437 (red) is localized to the basolateral membrane of enterocytes and EECs. B cells and macrophages result in the background staining signals in the mesenchyme. **v** Immunoblots showing cleavage of Gm11437 from intestinal extracts (Intes), liver extracts and kidney extracts (Kid) of *ad lib*-fed Gm11437-GFP knock-in mice. The blue arrowheads indicate full-length Gm11437-GFP, while the red arrowhead indicates the cleaved C-terminal product of Gm11437 detected by anti-GFP antibody. **w** Isolation of Gm11437-GFP-positive intestinal cells by flow cytometry. Q2 contains cells positive for both Gm11437 and ALPI, which should be enterocytes. Q3 contains cells positive for Gm11437 and negative for ALPI. Based on our previous results, the cells in Q3 should be enteroendocrine cells. **x** Immunoblots showing cleavage of Gm11437 and famsin production in isolated intestinal cells. In the left panel, the blue arrowheads indicate full-length Gm11437-GFP and the red arrowhead indicates the cleaved C-terminal product of Gm11437 detected by anti-GFP antibody. In the right panel, the blue arrowheads indicate full-length Gm11437-GFP and the red arrowhead indicates famsin detected by anti-famsin antibody.