

**SUPPLEMENTAL TABLES**Table S1: Genotyping primers

<b>Gene</b>	<b>Forward</b>	<b>Reverse</b>	<b>Amplicon (bp)</b>	<b>Annealing Temperature (°C)</b>
<i>Stx1a</i>	GCT GCA GAA GCA AGA GAA CC	CAG CCA TAC AAA AAC CAC CA	WT: 404 Flox: 239	50.0
<i>Cre</i>	CAA GCC TGG CTC GAC GGC C	CGC GAA CAT CTT CAG GTT CT	390	50.0
<i>Gcg/GFP</i>	AAT TGA GCT CAT TTG GAC TGC C	CTT GCC GTA GGT GGC ATC G	210	50.0
<i>GFP/GFP</i>	CTG GTA GTG GTC GGC GAG C	GTT CAG CGT GTC CGG CGA G	470	50.0

Table S2: Antibody table

<b>Sample</b>	<b>Antigen</b>	<b>Primary Antiserum</b>	<b>Secondary Antiserum</b>
Ileal Tissue	Syntaxin1a	Rabbit anti-syn1a, 1:500 (Abcam cat#41453)	AlexaFluor488-goat anti-rabbit IgG, 1:150 (Life Technologies)
	GLP-1	Mouse anti-GLP-1, 1:400 (Abcam cat # 23472)	AlexaFluro555-goat anti-mouse IgG, 1:150 (Life Technologies)
AMIC Culture	Syntaxin1a	Rabbit anti-syn1a, 1:1000 (Abcam cat#41453)	AlexaFluor488-goat anti-rabbit IgG, 1:150 (Life Technologies)
	GLP-1	Mouse anti-GLP-1, 1:200 (Abcam cat # 23472)	AlexaFluro555-goat anti-mouse IgG, 1:150 (Life Technologies)

Table S3: qRT-PCR Primer/Probes (all from Applied Biosystems)

<b>Transcript</b>	<b>Product number</b>	<b>Exons targeted</b>
<i>Gcg</i>	Mm00801714_m1	5-6
<i>H3f3a</i>	Mm01612808_g1	3-4
<i>Stx1a</i>	Mm004444008_m1	1-2
<i>Stx1b</i>	Mm01275274_m1	1-2
<i>Stx2</i>	Mm04229900_m1	2-3
<i>Stx3</i>	Mm01197689_m1	6-7
<i>Stx4</i>	Mm00436827_m1	5-6

## SUPPLEMENTAL MATERIALS

### Supplemental Figure Legends

Figure S1: Body weight (**A**), small intestinal weight (**B**) and small intestinal weight normalized to body weight (**C**) in the male vs. female control and IE-syn1a KO mice shown in Figure 2. All data are shown as mean  $\pm$  SD.

Figure S2: Blood glucose (**A**), and plasma insulin (**B**) levels in the male vs. female control and IE-syn1a KO mice shown in Figure 3. All data are shown as mean  $\pm$  SD.

Figure S3: Plasma GLP-1 (**A**), and GIP (**B**) levels in the male vs. female control and IE-syn1a KO mice shown in Figure 3. All data are shown as mean  $\pm$  SD.

Figure S4: (**A-B**) Male C57Bl/6 mice were administered ileal AdV-RFP (control) or AdV-iCre followed by intra-ileal administration of OEA 2 d later, and determination of mucosal *Stx1a* mRNA transcript levels (**A**) and plasma GLP-1 levels (**B**; n=3-4). (**C-D**) AMIC cultures from male C57Bl/6 mice were treated with AdV-RFP (control) or AdV-iCre for 2 d, followed by 2 hr treatment with vehicle (basal), forskolin plus IBMX or OEA for 2 hr, and determination of cell *Stx1a* mRNA transcript levels (**C**) and GLP-1 content in the media and cells (**D**; n=4). All data are shown as mean  $\pm$  SD.

Figure S5: Body weight (**A**), small intestinal weight (**B**) and small intestinal weight normalized to body weight (**C**) in the male vs. female control and Venus-IE-syn1a-KO mice shown in Figure 5. All data are shown as mean  $\pm$  SD.

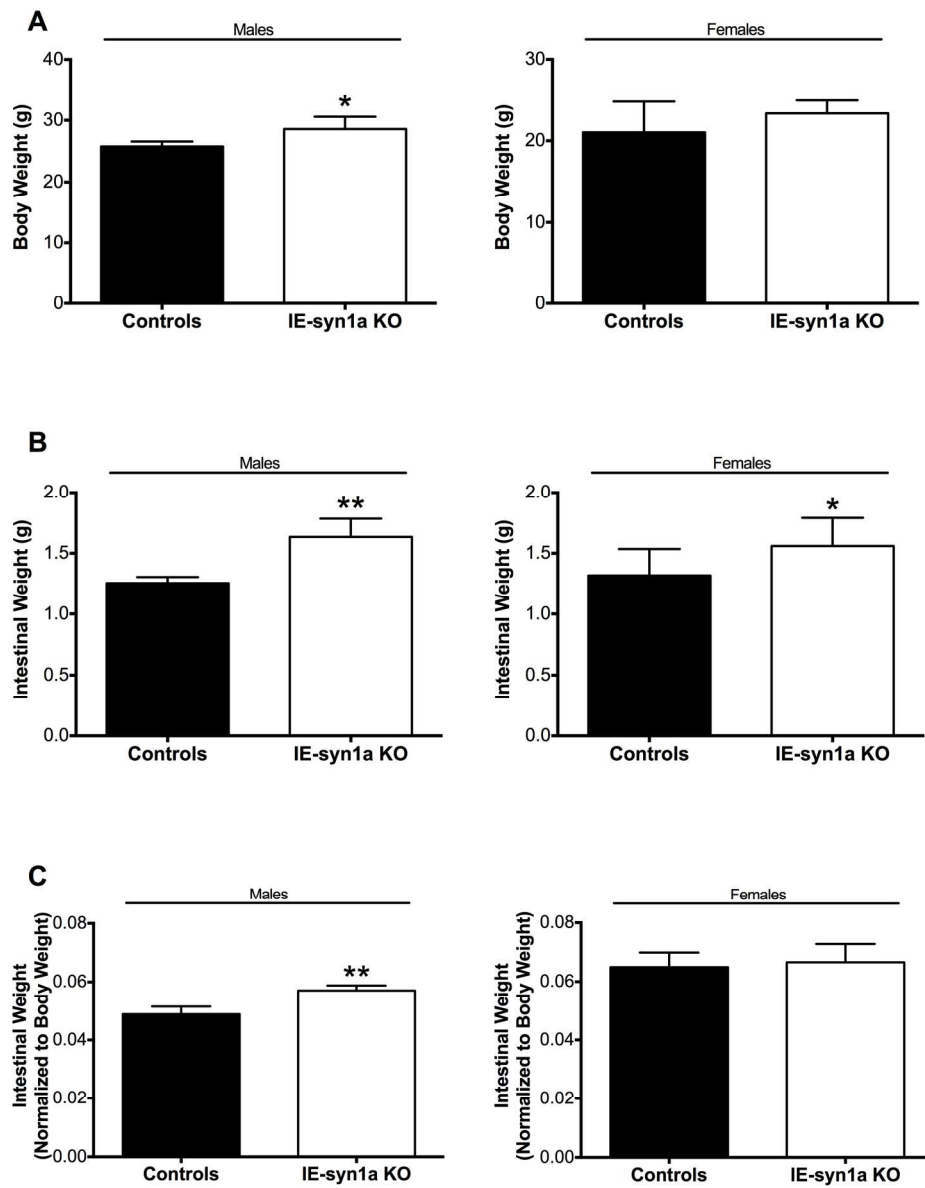
Figure S6: Blood glucose levels in the male vs. female control and Venus-IE-syn1a KO mice shown in Figure 5. All data are shown as mean  $\pm$  SD.

Figure S7: Representative 2-photon images of full and compound fusion events using SRB (red) and Venus (green), as visualized in the respective cells shown in Figure 6A.

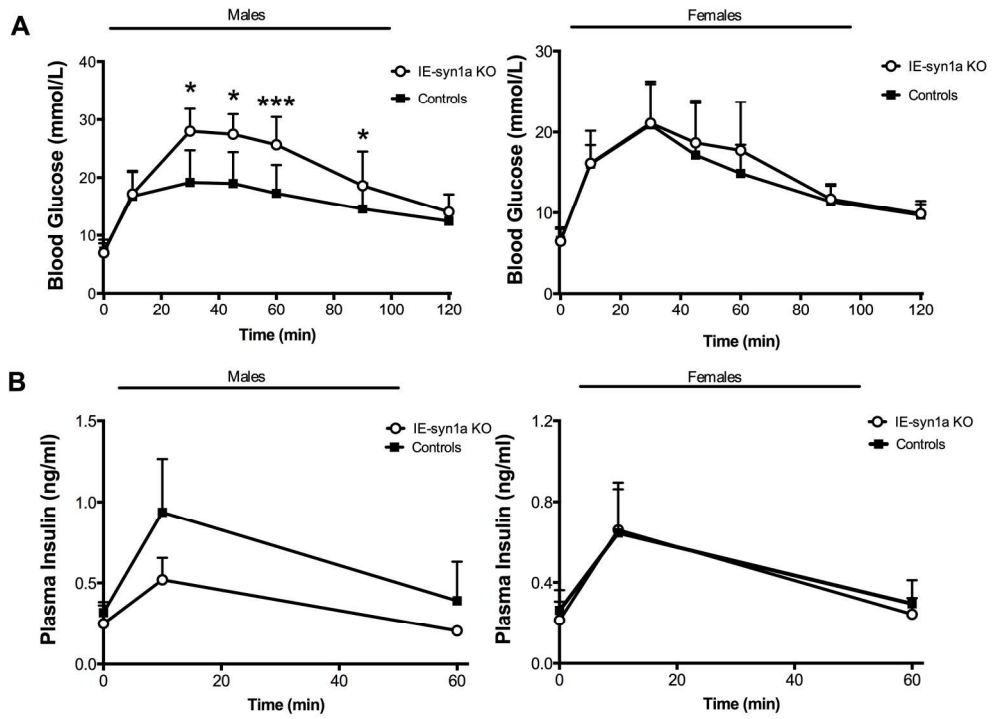
Supplemental Video 1: Full-field view of a Venus<sup>+</sup> L-cell (green) surrounded by unlabelled cells. Forskolin was added at t = 30 sec. Note the large granule size and multiple fusion events occurring in a single neighbouring cell (arrow), consistent with the known properties of mast cells. The same video is submitted in both .avi and .mp4 format.

Supplemental Video 2: Single granule, full fusion event at t = 577.8 sec in the membrane of a Venus<sup>+</sup> L-cell. The same video is submitted in both .avi and .mp4 format.

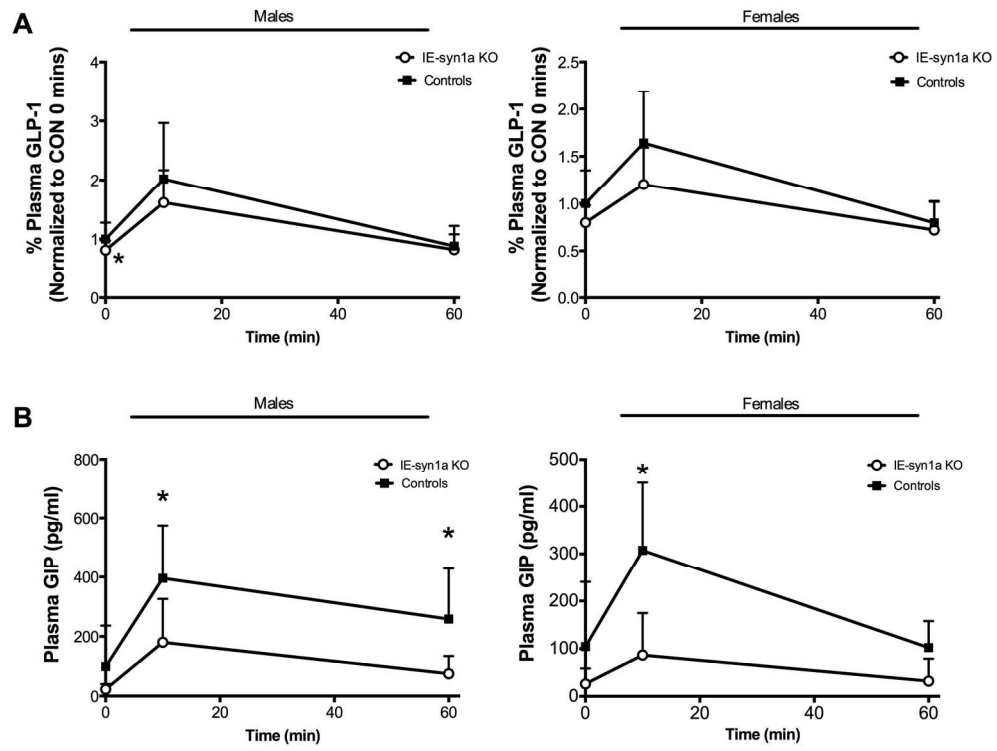
Supplemental Video 3: Multi-granular, compound fusion event at t = 129.3 – 255.3 sec in the membrane of a Venus<sup>+</sup> L-cell. The same video is submitted in both .avi and .mp4 format.



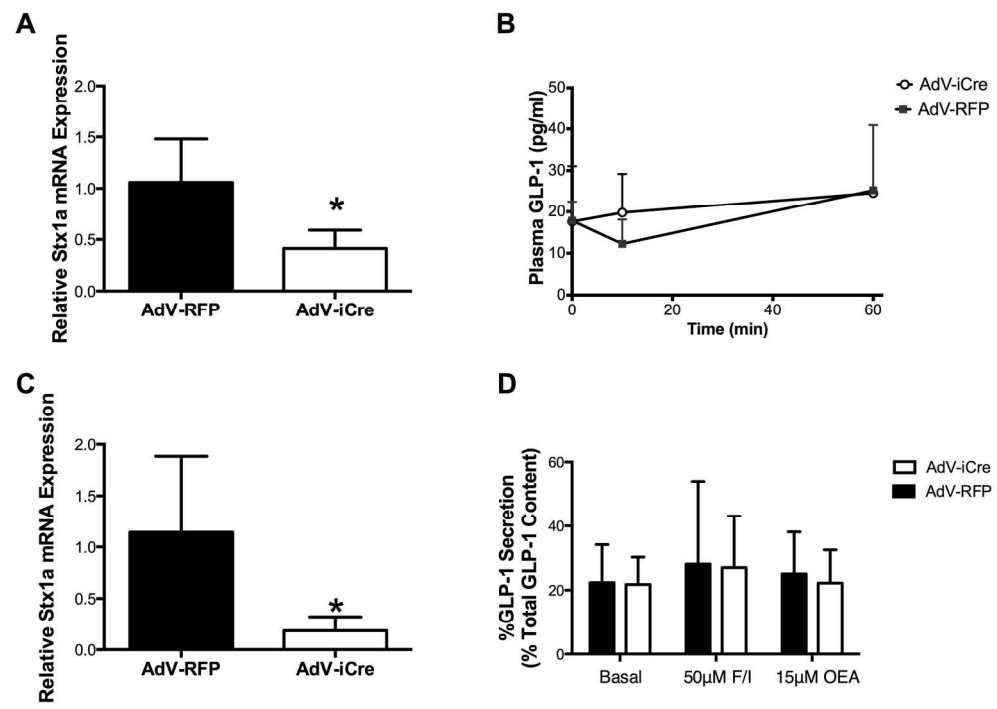
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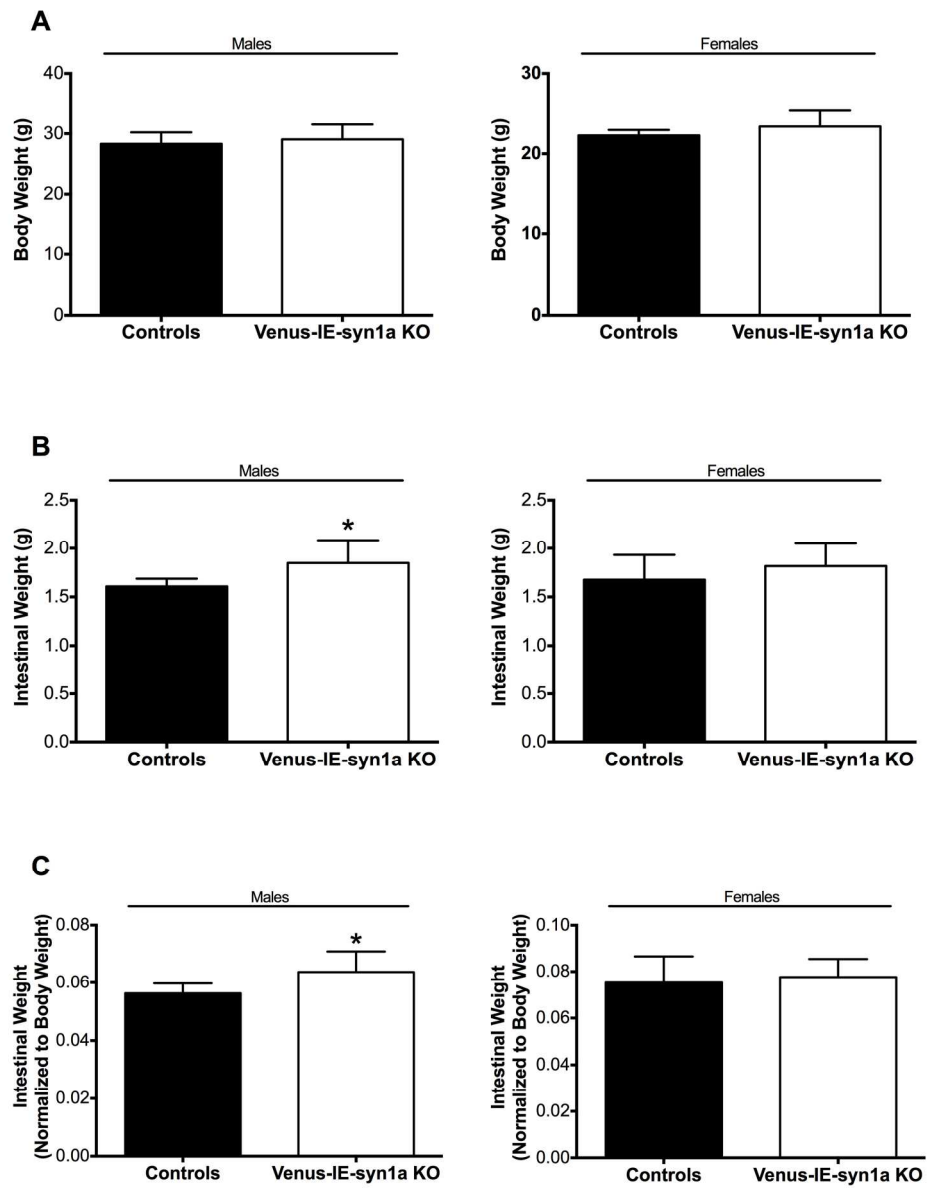


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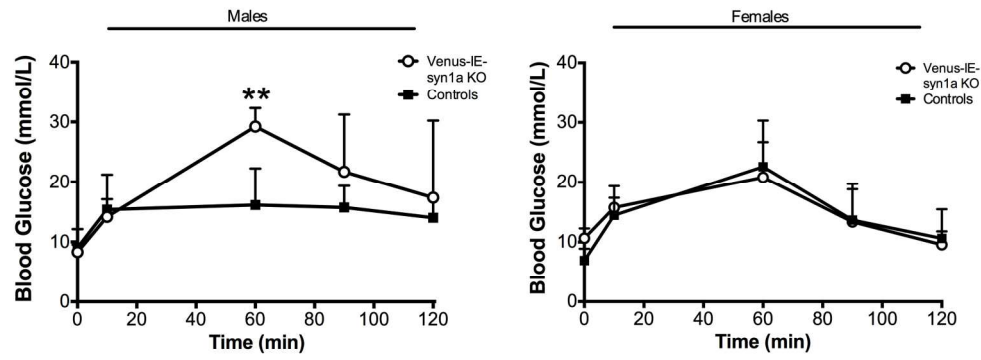


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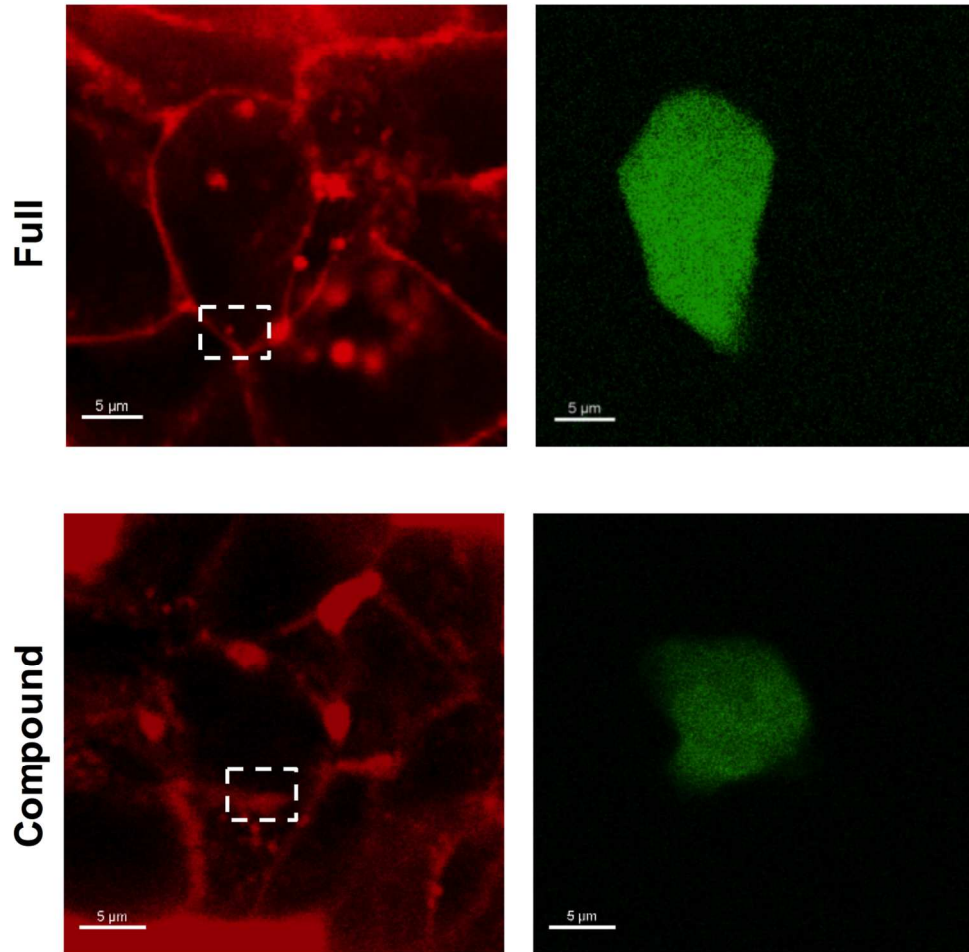




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175x65mm (300 x 300 DPI)



128x129mm (300 x 300 DPI)