

**Supplementary Figure 1.** 7 week old control male mice were put in CLAMS apparatus and fed standard chow or HFrD for a total of 7 days, including 2 days acclimation period. Littermate LiChKO mice were fed HFrD only (n = 4-6 per group). Oxygen consumption (**A**), carbon dioxide production (**B**), respiratory exchange ratio (**C**), heat production (**D**) and ambulatory activity (**E**) were measured for 5 consecutive days, and averaged values for a 24 hour period are presented. P values were obtained using 1-way ANOVA, \*P < 0.05 compared with control on chow; # P < 0.05 compared with control on HFrD.



**Supplementary Figure 2.** Cumulative food intake was measured in mice described in Supplementary Figure 1 for 5 consecutive days. P values were obtained using 1-way ANOVA, # P < 0.05 compared with control on HFrD.



**Supplementary Figure 3. Confirmation of nuclear versus cytosolic fractionation for SREBPF1 blots.** The top panel is blotted for GAPDH and the bottom panel is blotted for LMNB1.



**Supplementary Figure 4. Fructose is more potent than in glucose in activating ChREBP signaling in small intestine.** 8 week old female C3H/HeJ mice were fasted for 5 hours, then gavaged with water, glucose or fructose (4 g/kg of body weight) and sacrificed 100 min later. Intestinal gene expression was measured by qPCR, (n = 6 per group). P values were obtained using 1-way ANOVA, \*P < 0.05 compared with water; # P < 0.05 compared between glucose and fructose treatment.

	Forward	Reverse
ChREBP-alpha	AGCATCGATCCGACACTCAC	TTGTTCAGCCGGATCTTGTC
ChREBP-beta	TCTGCAGATCGCGTGGAG	CTTGTCCCGGCATAGCAAC
Pklr	CATCCCTGCCTTGATCATCT	TATCGACTCAGAGCCTGTGG
Fasn	GCTGCGGAAACTTCAGGAAAT	AGAGACGTGTCACTCCTGGACTT
G6pc	GTGTCCAGGACCCACCAATA	ACTGTGGGCATCAATCTCCT
Khk	GGACAGTGCAGGAGTTGGAT	GGACATCATCAATGTGGTGG
Aldob	GCTGGGCAATTTCAGAGAGC	GAGGACTCTTCCCCTTTGCT
Slc2a5	GAGCCCCTCGTAGGTTTTTC	TCCAGACTTCTGGTTGGAATC
Slc2a2	TGTCTCTGTGCTGCTTGTG	ACTCATCCAGGTGAACTTATCC
Tkfc	AGCACACCCTTCCACAGAAT	CGGCATCTCAGAGCAGAAG
Atf6	CATGTGGTGAATGTGCTGCC	CACAGCGATATCCGAACCCA
Xbp1s	GAGTCCGCAGCAGGTG	GTGTCAGAGTCCATGGGA
Xbp1t	GAGCAGCAAGTGGTGGATTT	CCGTGAGTTTTCTCCCGTAA
Bbc3	TACGAGCGGCGGAGACAAG	GTGTAGGCACCTAGTTGGGC
Srebf2	CCCTATTCCATTGACTCTGAGC	GAGTCCGGTTCATCCTTGAC
Hmgcs1	TTCAAAGGAAGTGACCCAGG	GGTCTGATCCCCTTTGGTG
Hmgcr	CACAATAACTTCCCAGGGGT	GGCCTCCATTTAGATCCG
Sqle	GATGGGCATTGAGACCTTCT	TTTAAAAGAGCCCGACAGGA
Cd68	GCTTATAGCCCAAGGAACAGAG	CTGTAGGTGTCATCGTGAAGGA
Tnfa	GATCGGTCCCCAAAGGGATG	TGAGGGTCTGGGCCATAGAA

Supplementary Table 1. qPCR primers