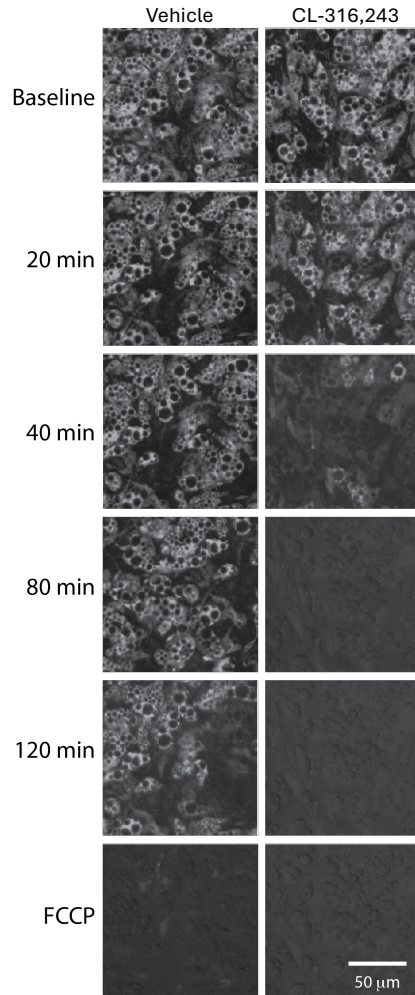


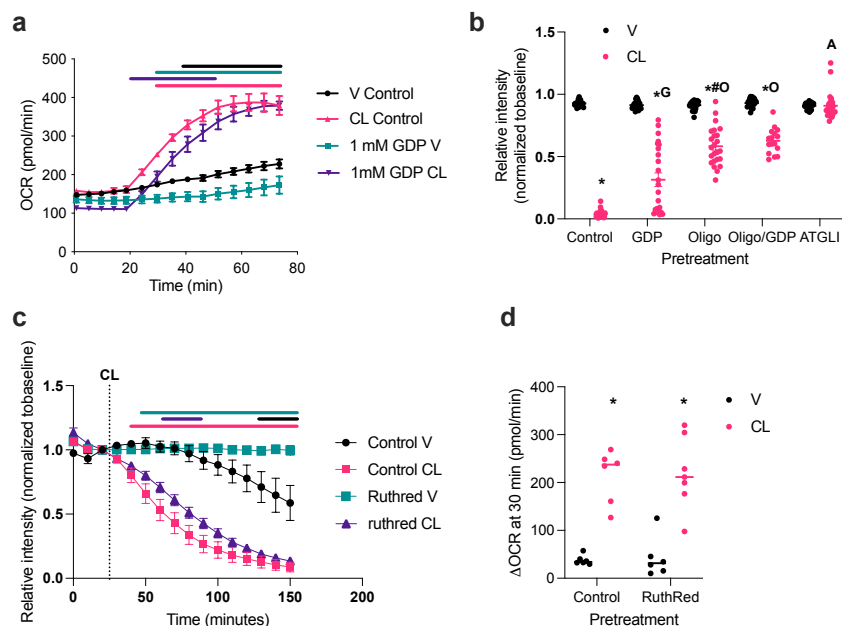
Extended data: Fatty acids promote uncoupled respiration via AAC in white adipocytes

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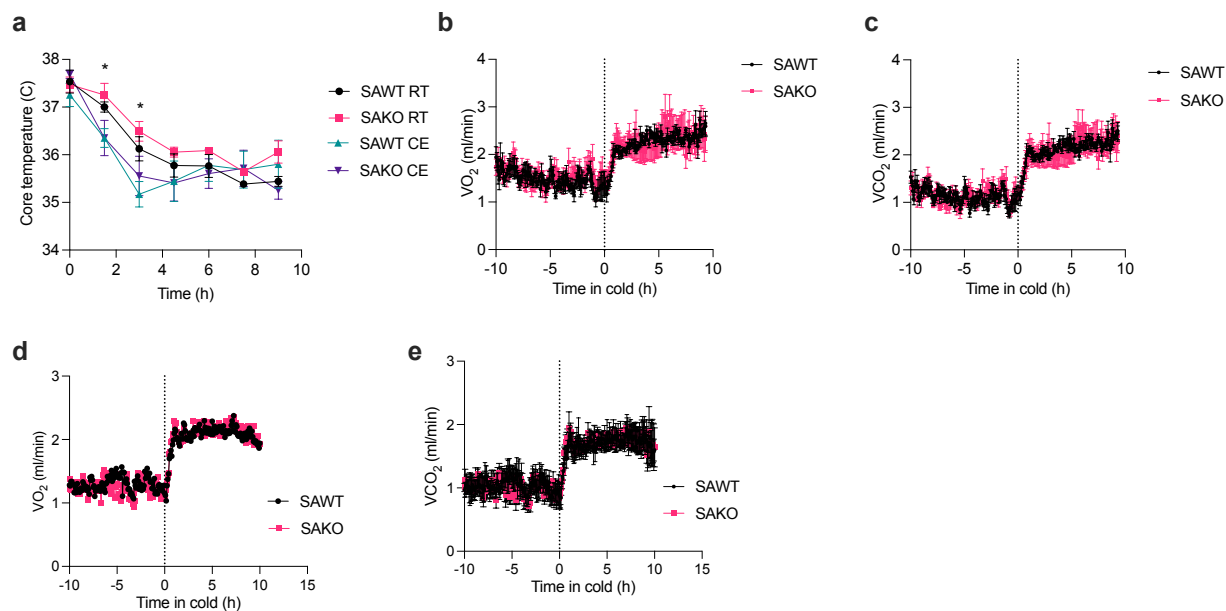


Extended data 1: Mitochondrial membrane potential staining with TMRM.

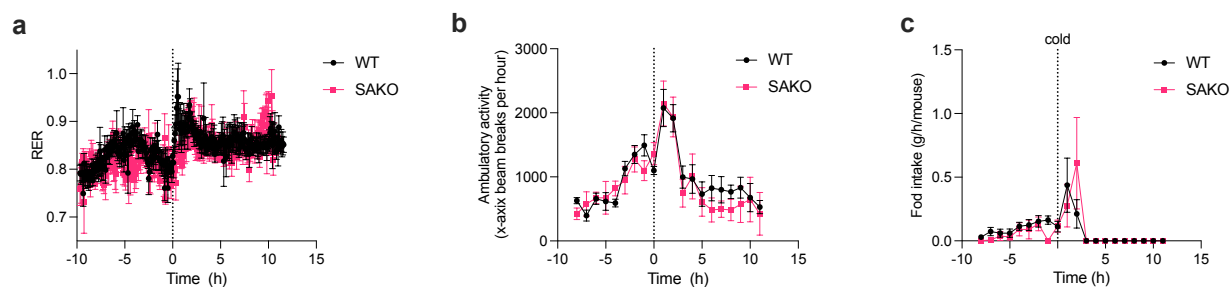
Tetramethylrhodamine, methyl ester, perchlorate (TMRM) staining imaged with an imageXpress MICRO Confocal Automated High-Content Analysis System to visualize live mitochondria membrane potential. After baseline images were collected, 100 nM CL-316,243 or vehicle control was added at time zero and imaging continued. The last image was taken after the addition of 1 μM FCCP. Scale bar = 50 μm.



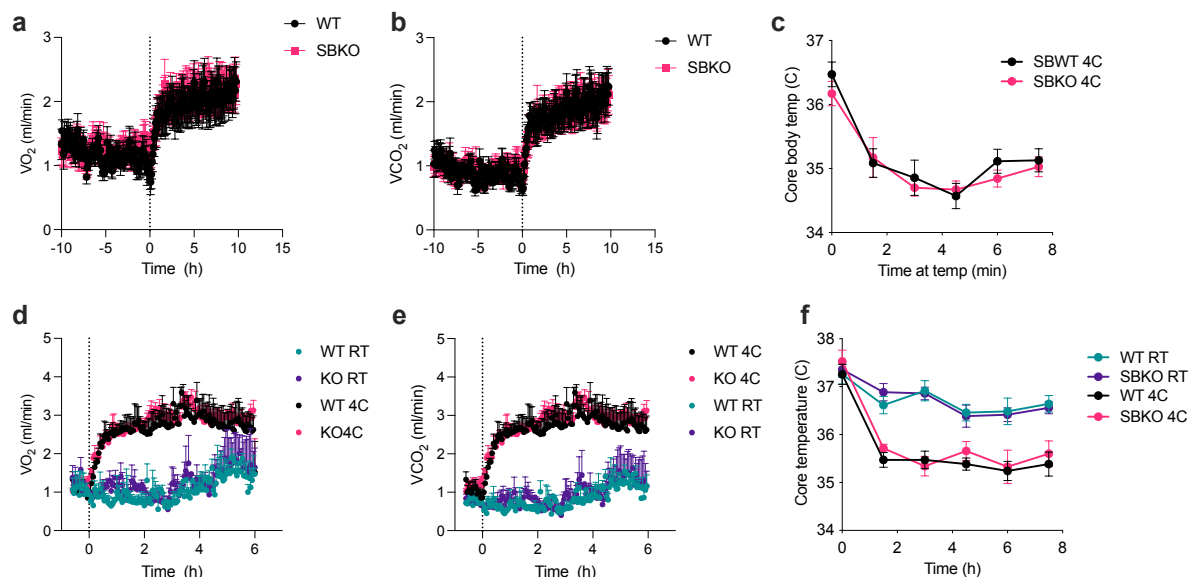
Extended data 2: Effects of GDP and ruthenium red on oxidative metabolism and membrane potential. **a**, OCR in primary adipocytes pretreated with 1 mM GDP or V, then stimulated with 100 nM CL or V in port A. Pink: p-val < 0.05 V control vs. CL control, black: V control vs. V GDP, purple: p-val < 0.05 CL control vs. CL GDP, and teal: p-val < 0.05 V GDP vs. CL GDP at the time points beneath the line. n = 6. **b**, Baseline normalized TMRM straining in primary adipocytes pretreated with 1 mM GDP or V 50 minutes after stimulation with 100 nM CL or V. *p-val < 0.05 V vs. CL, #p-val < 0.05 vs. CL control, °p-val < 0.05 GDP vs control, °p-val < 0.05 Oligo vs. control, ^p-val < 0.05 ATGLi vs. control. n = 16-24. **c**, Baseline normalized TMRM straining in primary adipocytes pretreated with 1 mM ruthenium red (Ruthred) or V then stimulation with 100 nM CL or V. Pink: p-val < 0.05 V control vs. CL control, black: V control vs. V Ruthred, purple: p-val < 0.05 CL control vs. CL GDP, and teal: p-val < 0.05 V Ruthred vs. CL Ruthred at the time points beneath the line. n = 6. **d**, Change in OCR from baseline to 30 minutes after stimulation with V or 50 nM CL in primary adipocytes pretreated with Ruthred or V. *p-val < 0.05 V vs. CL. n = 6-7.



Extended data 3: Normal diet fed SAKO mice exhibit no defect in cold tolerance. **a**, Core body temperature during acute cold exposure (CE) or room temperature controls (RT) in normal diet fed male SAKO and SAWT. *p-val < 0.05 RT vs cold. n = 5. **b** and **c**, Oxygen consumption (VO₂) (b) and carbon dioxide production (VCO₂) (c) of normal diet fed male SAWT and SAKO mice at 30 °C then transitioned to 5 °C (cold) at time zero. n = 5. **d**, and **e**, VO₂ (d) and VCO₂ (e) of normal diet fed female SAWT and SAKO mice at 30 °C then transitioned to 5 °C (cold) at time zero. n = 5.

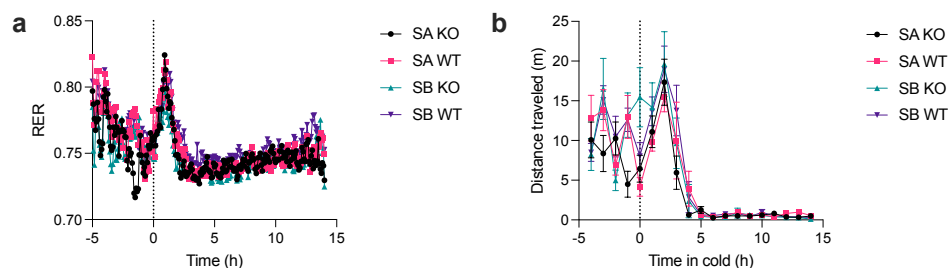


Extended data 4: RER and activity in SAWT and SAKO. Respiratory exchange ratio (a), ambulatory activity (b), and food intake (c) in in obese thermoneutral adapted male SAWT and SAKO mice at 30 °C then transitioned to cold at time zero. n = 15 SAWT and 9 SAKO.

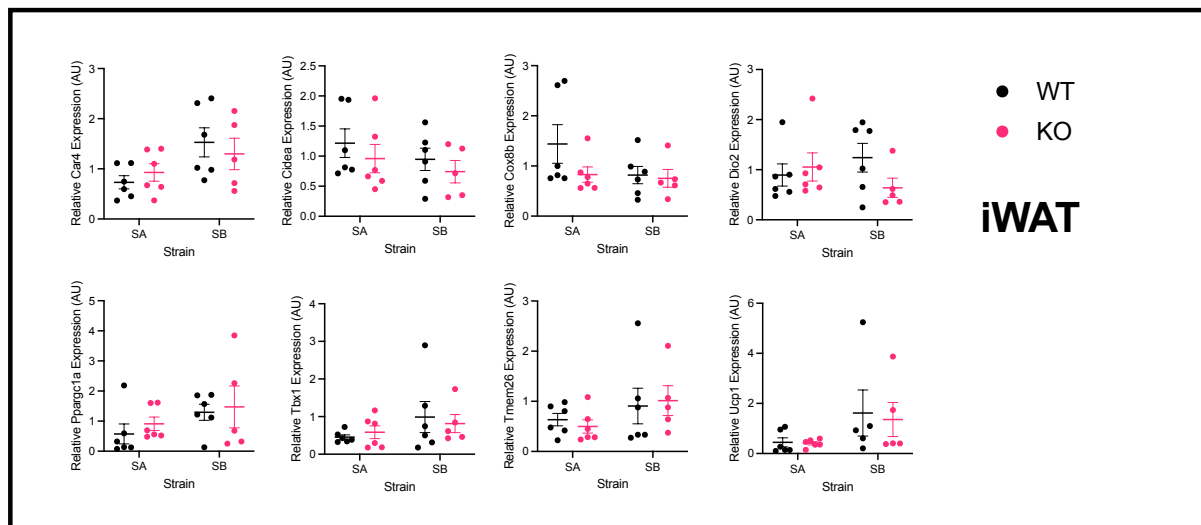
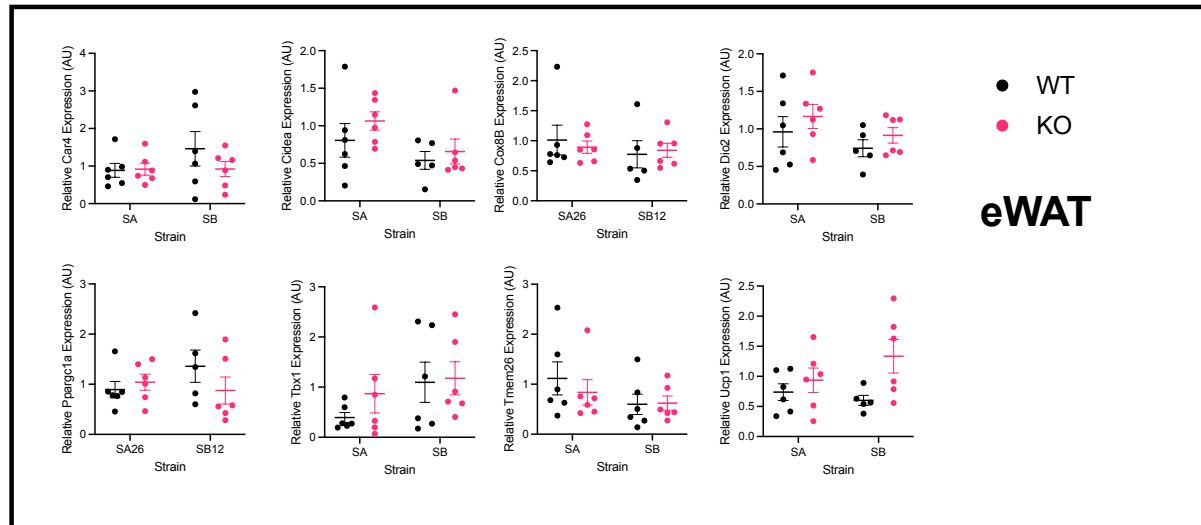


Extended data 5: SBKO mice do not exhibit cold sensitivity relative to SBWT controls.

a, and **b**, Oxygen consumption (VO_2) (**a**) and carbon dioxide production (VCO_2) (**b**) of normal diet fed male SBWT and SBKO mice at 30 °C then transitioned to 5 °C (cold) at time zero. $n = 7$ SBWT and 8 SBKO. **c**, Acute cold exposure in obese thermoneutral adapted male SBWT and SBKO mice. $n = 7$. **d** and **e**, VO_2 (**d**) and VCO_2 (**e**) of obese thermoneutral adapted male SAWT and SAKO mice at 30 °C then transitioned to 5 °C (cold) at time zero. $n = 2$ room temp and 4 cold exposed per genotype. Acute cold exposure in obese thermoneutral adapted female SBWT and SBKO mice with room temperature controls. $n = 7$.



Extended data 6: RER and activity in SAWT, SAKO, SBWT and SBKO mice. Respiratory exchange ratio (**a**) and ambulatory activity (**b**) in obese thermoneutral adapted male SAWT/KO and SBWT/KO mice at 30 °C then transitioned to cold at time zero. $n = 9-13$.



Extended data 7: Gene expression in Stat3 Knockout adipose tissues. Expression of various brown/beige associated genes in inguinal and epididymal white adipose tissue. No statically significant changes in gene expression were observed.

Extended data table 1: QPCR primer sequences

Gene	Forward sequence 5'→ 3'	Reverse sequence 5'→ 3'
<i>Arbp</i>	CAC TGG TCT AGG ACC CGA GAA	TAG CCA TCA AAC CTG TTG AGC
<i>Car4 F</i>	TACGTGGCCCCCTCTACTG	GCTGATTCTCCTTACAGGCTCC
<i>Cidea</i>	TGACATTCATGGGATTGCAGAC	GGCCAGTTGTGATGACTAAGAC
<i>Cox8b</i>	TGTGGGGATCTCAGCCATAGT	AGTGGGCTAAGACCCATCCTG
<i>Dio2</i>	AATTATGCCTCGGAGAAGACCG	GGCAGTTGCCTAGTGAAAGGT
<i>Ppargc1</i>	TATGGAGTGACATAGAGTGTGCT	CCACTTCAATCCACCCAGAAAG
<i>Tbx1</i>	CTGTGGGACGAGTTCAATCAG	TTGTCATCTACGGGCACAAAG
<i>Tmem26</i>	TTCCTGTTGCATTCCCTGGTC	GCCGGAGAAAGCCATTGT
<i>Ucp1</i>	AGGCTTCCAGTACCATTAGGT	CTGAGTGAGGCAAAGCTGATTT