Table S1. Baseline Characteristics of Mitochondrial Bioenergetics Study Subjects.

	Study[a]	Abdomen Oxytherm Study
All		
	Number Male/Female	11 (3/8)
	Age	47.5 ± 4.3
	BMI	25.2 ± 0.8
Summer		
	Number Male/Female	5 (1/4)
	Age	46 ± 8.5
	BMI	24.1 ± 1.2
Winter		
	Number Male/Female	6 (2/4)
	Age	48.7 ± 4.5
	BMI	26.2 ± 0.9

[a]Baseline characteristics of subjects in the mitochondrial bioenergetics study. Note that all five of the summer subjects were also involved in the cold study presented in Table 1. Data are presented as means ± SEM.

Table S2. Effect of Mirabegron on Weight, Blood Pressure, and Heart Rate.

Study[a]	Weight (kg)	Systolic BP mm Hg	Diastolic BP mm Hg	Heart Rate (bpm)
Mirabegron Pre	93.2 ± 3.2	131.2 ± 6.2	81.3 ± 2.1	66 ± 1.6
Mirabegron Post	92.8 ± 3.3	128.0 ± 6.5	82.8 ± 5.1	69 ± 2.0
P[b]	0.70	0.44	0.80	0.40

[a]Data are presented as means ± SEM. [b]Paired, two-tailed student's t-test (n=6).

Table S3. Primer sequences.

Gene	Forward	Reverse
UCP1	AGGTCCAAGGTGAATGCCC	TTACCACAGCGGTGATTGTTC
TMEM26	ATGGAGGGACTGGTCTTCCTT	CTTCACCTCGGTCACTCGC
PGC1α	TCTGAGTCTGTATGGAGTGACAT	CCAAGTCGTTCACATCTAGTTCA
ACTB	GAGCACAGAGCCTCGCCTTT	CGCGGCGATATCATCATCCAT
PP1A	CCCACCGTGTTCTTCGACAT	GCTGTCTTTGGGACCTTGTCT
PP1B	AAGTCACCGTCAAGGTGTATTTT	TGCTGTTTTTGTAGCCAAATCCT
TBP	CCCGAAACGCCGAATATAATCC	AATCAGTGCCGTGGTTCGTG
TUBB	ACCAACCTACGGGGATCTGAA	TTGACTGCCAACTTGCGGA
UBC 9	CTGGAAGATGGTCGTACCCTG	GGTCTTGCCAGTGAGTGTCT
MT-ND1	GGGCTACTACAACCCTTCGC	TGGTGAGAGCTAAGGTCGGG
MT-ND4	CATAATCGCCCACGGGCTTA	GGTAAGGCGAGGTTAGCGAG
MT-ND6	ATTCCCCCGAGCAATCTCAAT	CGGGAGGATCCTATTGGTGC
CYPB	CCTCTCCGAACGCAACATGAA	CTTTGGGCCCCTTCTTCTTCT
BECN1	GAAGTTTTCCGGCGGCTAC	CCGTCACCCAAGTCCGGT
NEB 1	GGCACCTCTTGATATGCTCC	TATGCCTTCTTGGCAAGGTCC

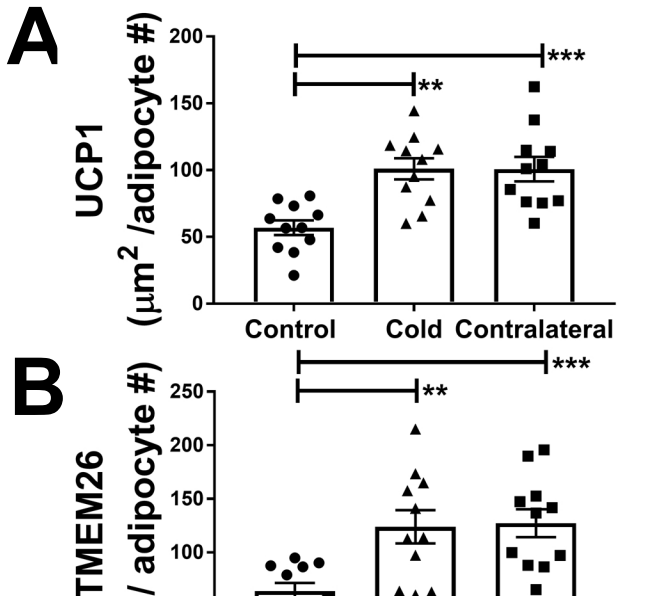

Figure S1. Repeated cold exposure induces uncoupling protein 1 (UCP1) and transmembrane protein 26 (TMEM26) in human abdomen subcutaneous white adipose tissue (SC WAT). An ice pack was applied to the abdomen for 30 min each day for 10 consecutive days. SC WAT was isolated and subjected UCP1 and TMEM26 immunohisto chemistry as described in Methods. A and B) UCP1 and TMEM26 expression was determined as described in Methods. The data are expressed as area of UCP1 (A) or TMEM26 (B) staining (μm^2) per adipocyte number. The data were analyzed by a repeated measures MANOVA as described in Methods. Data represent means ± SEM (n=11); **P<0.01; ***P<0.001.

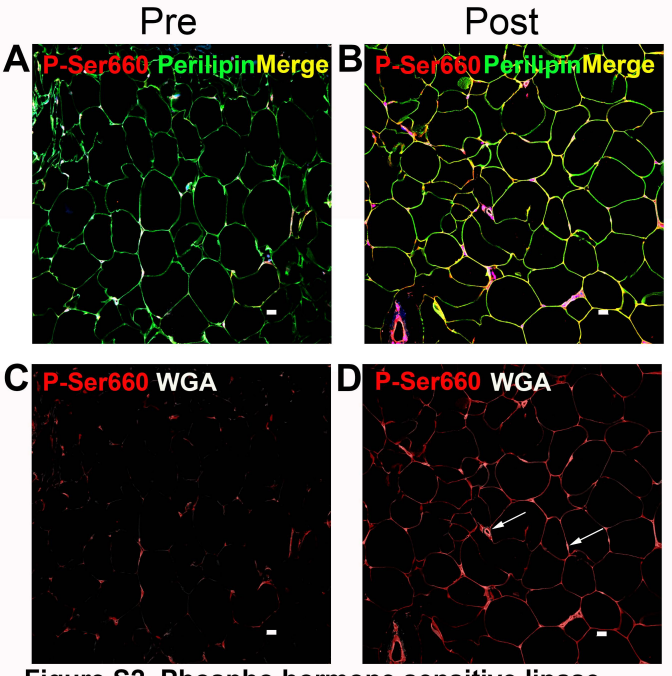

Figure S2. Phospho hormone sensitive lipase (HSL) serine^{660} (P-Ser660) staining colocalizes with perilipin and endothelial cells. An overlay of phospho-HSL serine^{660} staining (red) from Figure 8 with perilipin (green) and wheat germ agglutinin (WGA; white) is shown (scale bar: 10 μm). A and B) phospho-HSL serine^{660} and perilipin (yellow indicates overlapping staining). C and D) An overlay of phospho-HSL serine^{660} staining (red) with WGA (white) from A and B is shown. Arrows point to examples of overlap of phospho-HSL serine^{660} staining with endothelial cells in capillaries.

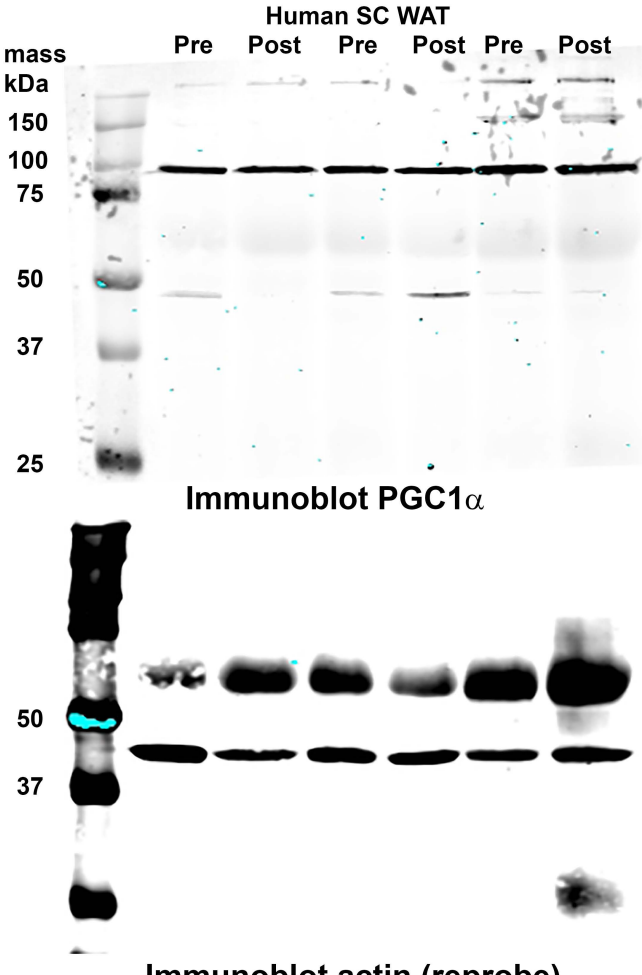

Figure S3. Uncropped immunoblots of peroxisome proliferator-activated receptor gamma co-activator 1-alpha (PGC1α) and actin. The uncropped immunoblots of human subcutaneous white adipose tissue before and after mirabegron treatment from the Figure 8E inset are shown. Reprobing with actin antibody resulted in a non specific band and a band at 45 KDa, the correct molecular mass of actin.

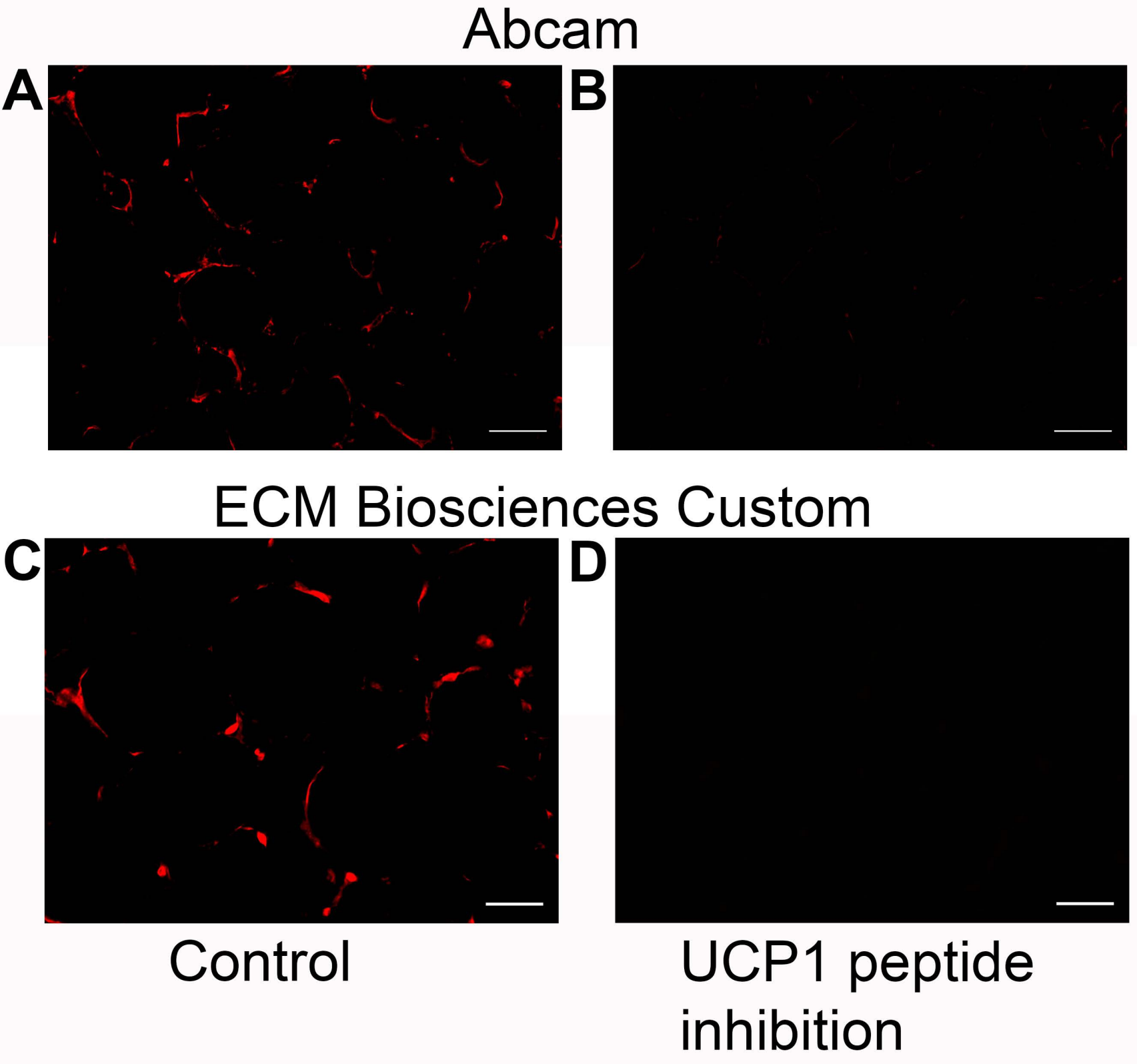

Figure S4. The reactivity of the Abcam and ECM biosciences uncoupling protein 1 (UCP1) antibodies is inhibited by UCP1 peptide. Thigh subcutaneous white adipose tissue from the cold treated leg of a lean research participant was stained with the indicated antibody with and without pre incubation with free UCP1 peptide (scale bar: 50 μm).