Mean ± SEM		WT	IL4/IL13$^{-/-}$	STAT6$^{-/-}$	IL4Rα$^{L/L}$	IL4Rα$^{L/L}$ LysM^{Cre}
Food [g hr^{-1}]	30ºC	0.14 ± 0.03	0.19 ± 0.02	0.16 ± 0.01	0.17 ± 0.02	0.13 ± 0.03
	22ºC	0.12 ± 0.01	0.12 ± 0.01	0.14 ± 0.03	0.13 ± 0.01	0.14 ± 0.01
	4ºC	0.39 ± 0.02	0.37 ± 0.10	0.31 ± 0.03	0.24 ± 0.04	0.21 ± 0.01
TG [mg dl^{-1}]	30ºC	152.1 ± 11.91	153.5 ± 18.22	174.8 ± 10.23	152.1 ± 23.83	102.5 ± 22.78
	22ºC	162.1 ± 14.38	164.6 ± 19.83	173.4 ± 23.63	148.9 ± 17.62	126.3 ± 19.05
	4ºC	127.3 ± 10.53	103.9 ± 15.45	123.7 ± 10.62	126.7 ± 38.73	105.3 ± 45.15
Cholesterol [mg dl^{-1}]	30ºC	91.74 ± 3.91	102.4 ± 5.37	105.9 ± 2.39	84.81 ± 16.76	91.29 ± 4.13
	22ºC	115.9 ± 8.47	113.3 ± 8.00	95.65 ± 11.35	98.44 ± 5.05	89.4 ± 5.68
	4ºC	115.5 ± 10.61	118.6 ± 6.19	113.3 ± 7.59	92.39 ± 4.77	84.12 ± 3.11
Body Weight [g]		21.44 ± 0.69	19.20 ± 0.42	20.26 ± 0.19	22.96 ± 0.40	21.77 ± 0.51
Weight Loss (%)		6.50 ± 2.19	3.41 ± 1.64 *	2.83 ± 1.79 **	7.38 ± 2.14	3.55 ± 1.21 **

Mean ± SEM		Liposome	Clodronate	C57BL/6J	C57BL/6J STAT6$^{-/-}$
Food [g hr^{-1}]	22ºC	0.14 ± 0.03	0.14 ± 0.01	0.096 ± 0.01	0.13 ± 0.01
	4ºC	0.23 ± 0.04	0.26 ± 0.02	0.21 ± 0.02	0.22 ± 0.02
TG [mg dl^{-1}]	22ºC	133.3 ± 6.66	131.1 ± 17.66	166.1 ± 14.89	170.5 ± 12.79
	4ºC	101.8 ± 2.53	123 ± 6.91	162.1 ± 11.01	157.9 ± 11.91
Cholesterol [mg dl^{-1}]	22ºC	104.3 ± 4.17	131.2 ± 5.05	94.87 ± 4.88	92.75 ± 2.99
	4ºC	111.3 ± 4.86	149.3 ± 7.41	86.21 ± 20.95	94.3 ± 5.16
Weight Loss (%)		7.84 ± 1.26 **	3.37 ± 2.61	7.30 ± 1.31 **	3.88 ± 1.16

Supplementary Table 1. Metabolic characteristics of mice exposed to a cold challenge.
*P < 0.05, **P < 0.01.

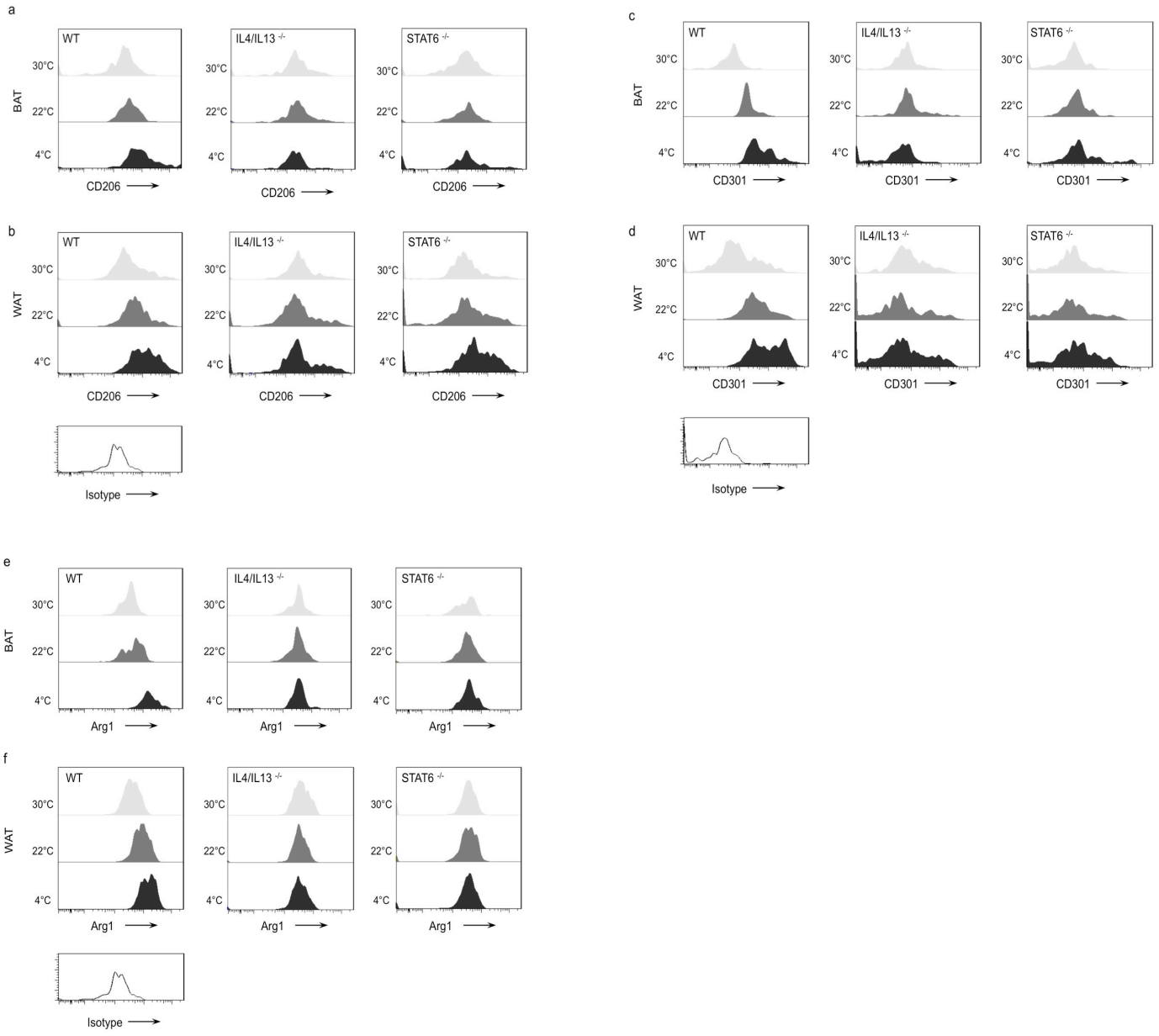
BAT [ng µg protein^{-1}]		IL4Rα$^{L/L}$	IL4Rα$^{L/L}$ LysM^{Cre}	Empty Liposome	Clodronate Liposome	C57BL/6J	C57BL/6J STAT6$^{-/-}$
Noradrenaline	22ºC	9.88 ± 3.31	7.35 ± 3.35	7.58 ± 1.63	8.51 ± 2.39	7.25 ± 1.68	7.97 ± 2.19
	4ºC	6.22 ± 1.91	1.64 ± 0.32 *	8.49 ± 1.86	3.16 ± 0.83 *	9.06 ± 1.25	1.29 ± 0.49 **
Adrenaline	22ºC	7.47 ± 1.73	7.09 ± 1.49	4.08 ± 1.56	5.56 ± 1.44	8.85 ± 2.94	3.75 ± 1.42
	4ºC	8.26 ± 0.65	4.08 ± 1.29 *	8.30 ± 1.89	1.34 ± 0.14 *	9.64 ± 2.76	1.34 ± 0.20 *
Dopamine	22ºC	7.13 ± 1.60	7.93 ± 1.65	8.28 ± 1.63	7.40 ± 1.03	8.45 ± 1.31	7.32 ± 1.33
	4ºC	6.51 ± 1.06	2.60 ± 0.94 *	6.26 ± 0.54	2.75 ± . 052 **	8.77 ± 1.41	1.06 ± 0.32 **
WAT [pg µg protein^{-1}]		**IL4Rα$^{L/L}$**	**IL4Rα$^{L/L}$ LysM^{Cre}**	**Empty Liposome**	**Clodronate Liposome**	**C57BL/6J**	**C57BL/6J STAT6$^{-/-}$**
Noradrenaline	22ºC	28.53 ± 6.82	20.87 ± 5.34	40.81 ± 6.80	43.04 ± 10.33	40.65 ± 8.41	42.03 ± 12.29
	4ºC	18.17 ± 2.57	6.25 ± 1.04 **	42.32 ± 7.77	20.00 ± 5.25 *	34.52 ± 5.27	19.33 + 2.34 *
Adrenaline	22ºC	38.77 ± 9.09	37.85 ± 7.83	26.73 ± 2.91	24.29 ± 3.98	25.79 ± 2.97	27.76 ± 3.27
	4ºC	32.98 ± 3.47	22.58 ± 2.09 *	25.71 ± 2.47	13.87 ± 2.41 *	28.64 ± 2.94	9.94 ± 1.61 **
Dopamine	22ºC	15.86 ± 6.80	20.12 ± 6.26	28.62 ± 8.72	13.8 ± 5.30	22.72 ± 6.38	9.64 ± 3.11
	4ºC	18.33 ± 3.22	3.72 ± 2.11**	26.92 ± 6.65	3.63 ± 0.34 *	23.62 ± 7.31	3.20 ± 0.99*

Supplementary Table 2. Catecholamine content of BAT and WAT in various strains of mice at 22 ºC and 4 ºC.

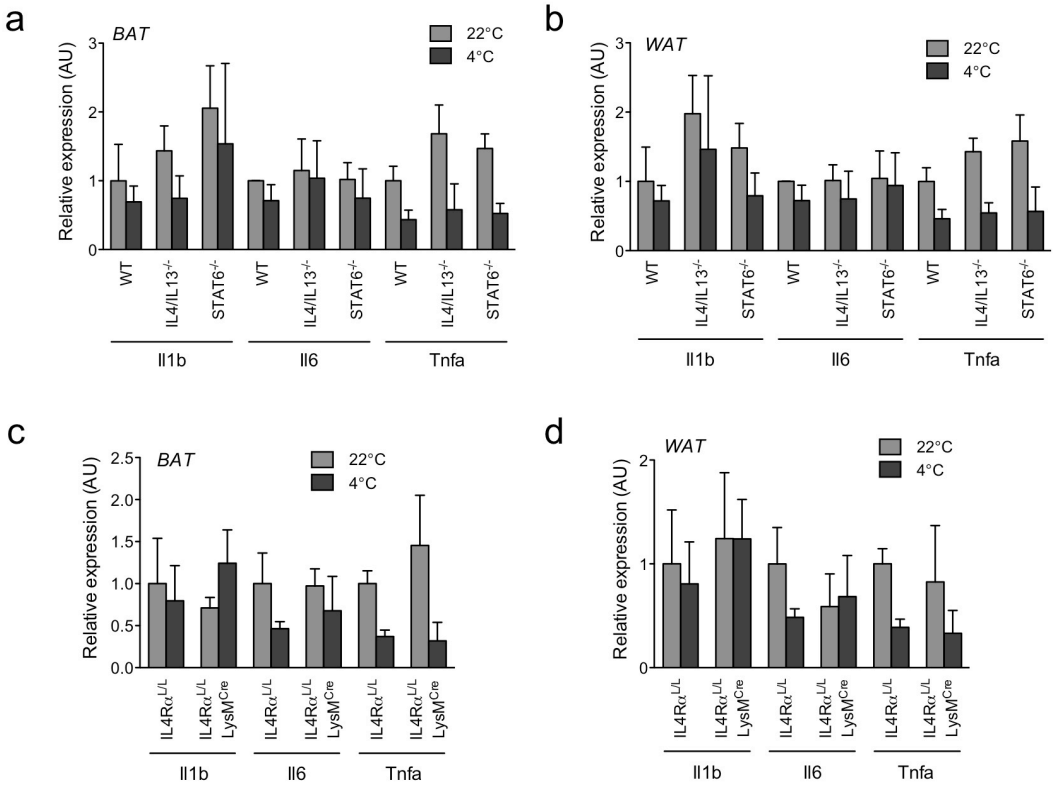
*P < 0.05, **P < 0.01.

Serum [ng ml^{-1}]		WT	IL4/IL13$^{-/-}$	STAT6$^{-/-}$	IL4R$^{L/L}$	IL4R$^{L/L}$ LysM^{Cre}
Noradrenaline	22ºC	14.38 ± 0.89	13.07 ± 0.74	14.81 ± 2.37	15.92 ± 1.73	16.21 ± 3.51
	4ºC	13.00 ± 0.46	12.34 ± 0.81	12.85 ± 2.50	14.51 ± 1.78	16.38 ± 4.16
Adrenaline	22ºC	22.23 ± 7.95	19.72 ± 4.7	27.99 ± 9.91	27.4 ± 3.81	24.69 ± 3
	4ºC	22.39 ± 6.39	24.9 ± 4.53	29.15 ± 7.24	29.96 ± 3.96	26.99 ± 3.01
Dopamine	22ºC	19.43 ± 1.28	17.20 ± 4.51	16.79 ± 3.11	13.71 ± 2.60	17.14 ± 3.42
	4ºC	14.98 ± 3.56	16.92 ± 1.42	13.21 ± 0.54	16.23 ± 6.91	20.43 ± 2.64
Liver [pg µg protein^{-1}]		WT	IL4/IL13$^{-/-}$	STAT6$^{-/-}$	IL4R$^{L/L}$	IL4R$^{L/L}$ LysM^{Cre}
Noradrenaline	22ºC	13.66 ± 4.30	13.49 ± 6.08	13.06 ± 4.92	12.8 ± 4.65	12.53 ± 4.89
	4ºC	18.7 ± 8.49	19.3 ± 10.91	18.57 ± 9.52	18.13 ± 9.49	17.51 ± 8.67
Adrenaline	22ºC	21.69 ± 8.28	19.86 ± 6.76	20.19 ± 7.22	13.73 ± 5.59	32.73 ± 18.51
	4ºC	33.01 ± 17.85	17.33 ± 5.97	28.45 ± 12.43	27.71 ± 5.77	28.98 ± 13.46
Dopamine	22ºC	18.24 ± 8.40	23.6 ± 15.32	24.2 ± 15.18	18.31 ± 5.72	18.7 ± 5.80
	4ºC	18.22 ± 6.93	22.18 ± 8.92	19.33 ± 4.45	14.51 ± 1.72	14.61 ± 2.68
Quadriceps [pg µg protein^{-1}]		WT	IL4/IL13$^{-/-}$	STAT6$^{-/-}$	IL4R$^{L/L}$	IL4R$^{L/L}$ LysM^{Cre}
Noradrenaline	22ºC	0.37 ± 0.33	0.66 ± 0.65	0.79 ± 0.47	2.87 ± 0.80	1.80 ± 0.94
	4ºC	0.43 ± 0.08	0.51 ± 0.29	0.64 ± 0.41	1.27 ± 0.82	1.13 ± 0.61
Adrenaline	22ºC	2.21 ± 0.91	2.65 ± 0.80	2.73 ± 1.06	0.74 ± 0.55	0.88 ± 0.89
	4ºC	0.92 ± 0.25	0.64 ± 0.16	1.03 ± 0.55	0.24 ± 0.11	0.62 ± 0.41
Dopamine	22ºC	0.37 ± 0.33	0.66 ± 0.65	0.79 ± 0.47	0.75 ± 0.55	0.89 ± 0.89
	4ºC	0.44 ± 0.07	0.50 ± 0.28	0.21 ± 0.11	0.24 ± 0.11	0.62 ± 0.42
Adrenal Gland [pg µg protein^{-1}]		WT	IL4/IL13$^{-/-}$	STAT6$^{-/-}$	IL4R$^{L/L}$	IL4R$^{L/L}$ LysM^{Cre}
Noradrenaline	22ºC	50.84 ± 27.14	44.39 ± 3.95	33.82 ± 12.26	50.20 ± 25.95	35.87 ± 11.67
	4ºC	45.17 ± 8.32	39.52 ± 4.89	37.44 ± 4.76	43.27 ± 7.63	39.76 ± 5.00
Adrenaline	22ºC	20.82 ± 7.26	22.14 ± 4.66	19.9 ± 3.77	26.62 ± 11.43	22.95 ± 5.51
	4ºC	22.12 ± 3.51	17.23 ± 2.53	19.25 ± 2.67	18.04 ± 2.75	18.12 ± 2.45
Dopamine	22ºC	20.4 ± 5.85	18.45 ± 4.81	21.56 ± 1.34	23.95 ± 8.44	26.14 ± 3.83
	4ºC	17.16 ± 1.34	13.99 ± 3.06	19.06 ± 2.08	25.14 ± 2.65	19.19 ± 3.81

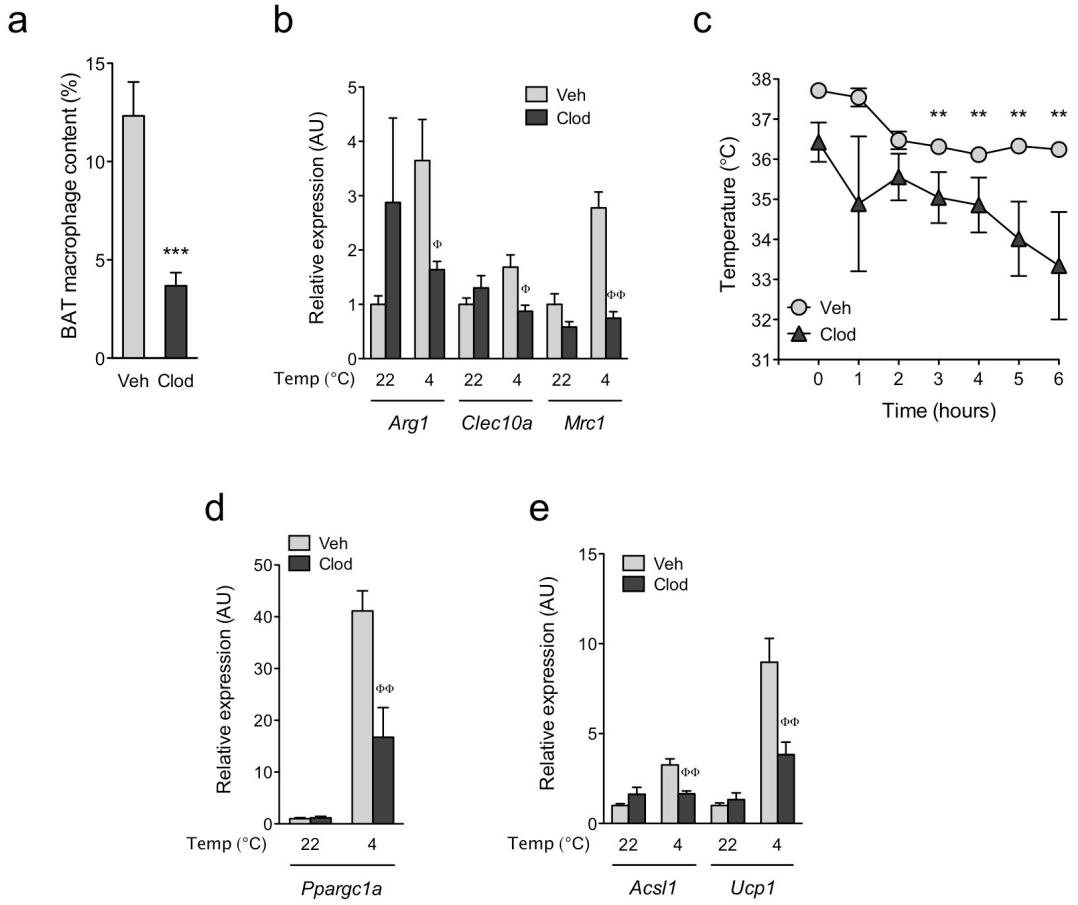
Supplementary Table 3. Catecholamine content of tissues in various strains of mice at 22 ºC and 4 ºC.



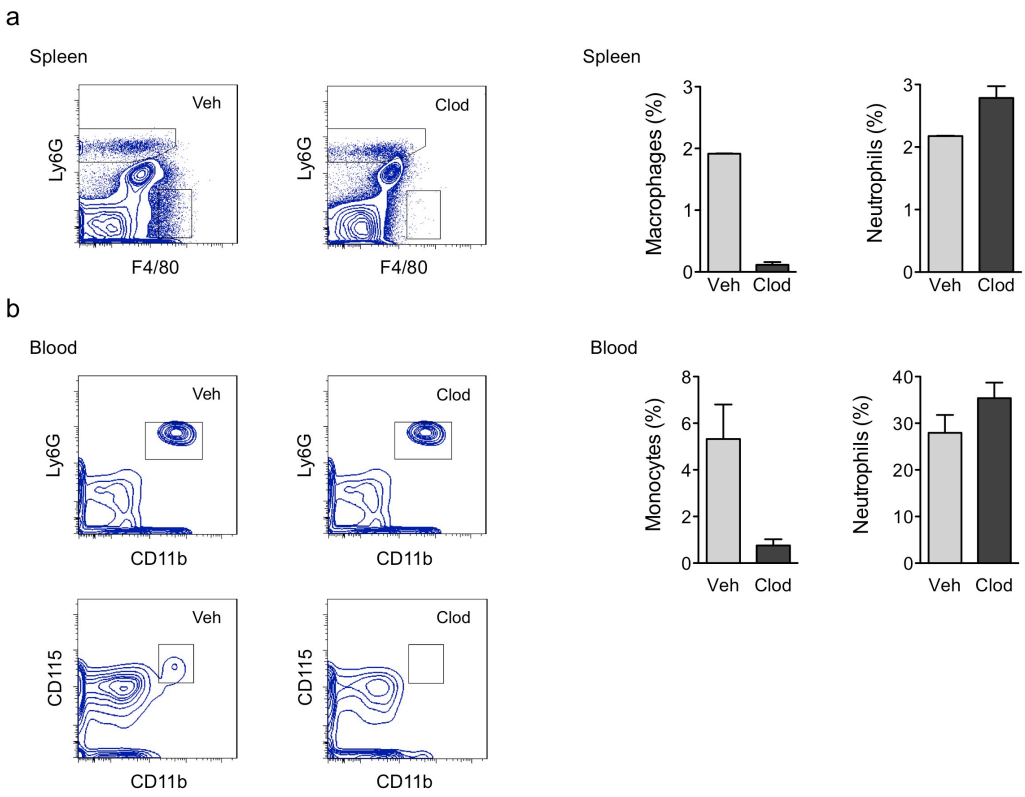
Supplementary Figure 1. Expression of alternative activation markers in adipose tissue macrophages. **a, b,** Representative FACS plots of CD206 in BAT (a) and WAT (b) macrophages of WT, IL4/IL13$^{-/-}$, and STAT6$^{-/-}$ mice housed at 30 ºC, 22 ºC or 4 ºC. **c, d,** Representative FACS plots of CD301 in BAT (c) and WAT (d) macrophages of WT, IL4/IL13$^{-/-}$, and STAT6$^{-/-}$ mice housed at 30 ºC, 22 ºC or 4 ºC. **e, f,** Representative FACS plots of Arg1 in BAT (e) and WAT (f) macrophages of WT, IL4/IL13$^{-/-}$, and STAT6$^{-/-}$ mice housed at 30 ºC, 22 ºC or 4 ºC.



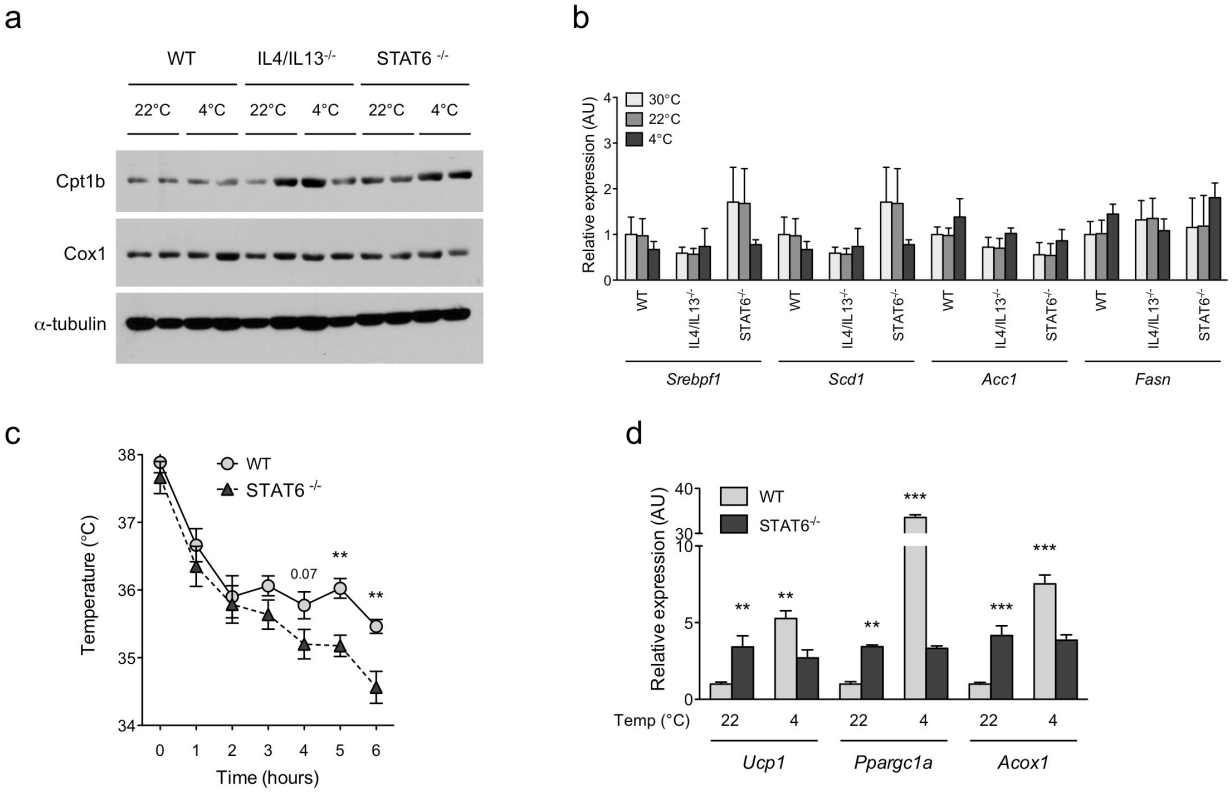
Supplementary Figure 2. Expression of inflammatory genes representative of classical macrophage activation in adipose tissue. **a, b** BAT (a) and WAT (b) from WT, IL4/IL13$^{-/-}$, and STAT6$^{-/-}$ mice housed at 30 ºC, 22 ºC or 4 ºC were analyzed by real-time PCR for expression of *Il1*, *Il6*, and *Tnfa* (n=4 per temperature). **c, d** BAT (c) and WAT (d) from IL4R$\alpha^{L/L}$ and IL4R$\alpha^{L/L}$LysM^{Cre} mice housed at 30 ºC, 22 ºC, and 4 ºC were analyzed by real-time PCR for expression of *Il1*, *Il6*, and *Tnfa* (n=4 per temperature).



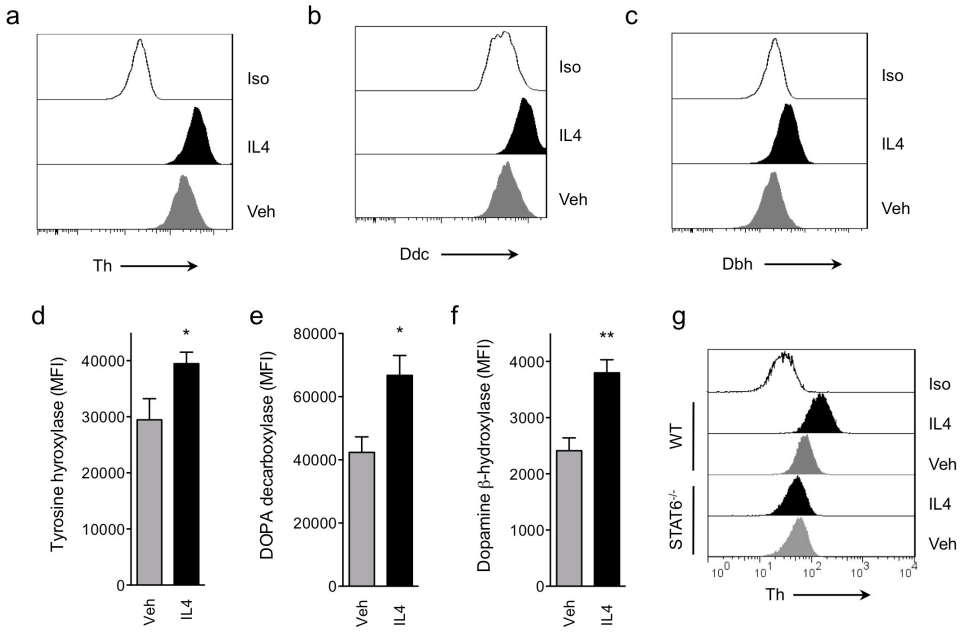
Supplementary Figure 3. Macrophages are required for adaptation to cold temperatures. **a,** BAT macrophage content in mice treated with empty (Veh) or clodronate-containing (Clod) liposomes (n=13-15 per treatment). **b,** Real-time PCR analysis of alternative activation markers in BAT of mice treated with Veh or Clod and then housed at 22 ºC and 4 ºC (n=5 per treatment and temperature). **c,** Core body temperature of mice treated with Veh or Clod after exposure to 4 ºC (n=7-8 per treatment). **d, e,** Real-time PCR analysis of *Ppargc1a* (d), *Ucp1, and Acsl1*(e) in BAT of mice treated with Veh or Clod and housed at 22 ºC or 4 ºC (n=4-5 per treatment and temperature). **P < 0.01, ***P < 0.001 compared to Veh. ΦP < 0.05, ΦΦP < 0.01 compared to Veh at 4 °C.



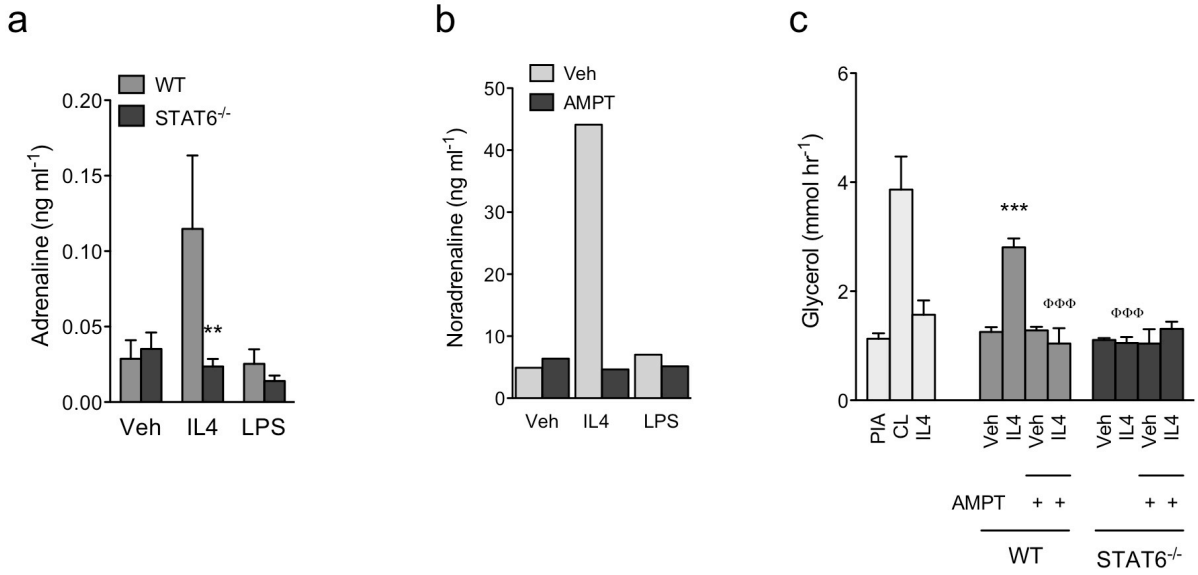
Supplementary Figure 4. Depletion of macrophages and monocytes by clodronate-containing liposomes. **a,** Representative FACS plots *(left)* and frequencies *(right)* of Ly6G$^+$ neutrophils and F4/80$^+$ macrophages in total splenocytes from mice treated with empty (Veh) or clodronate-containing (Clod) liposomes (n=2-3 per treatment). **b,** Representative FACS plots *(left)* and frequencies *(right)* of Ly6G$^+$ neutrophils and CD115$^+$ monocytes in total white blood cells from mice treated with Veh or Clod (n=2-3 per treatment).



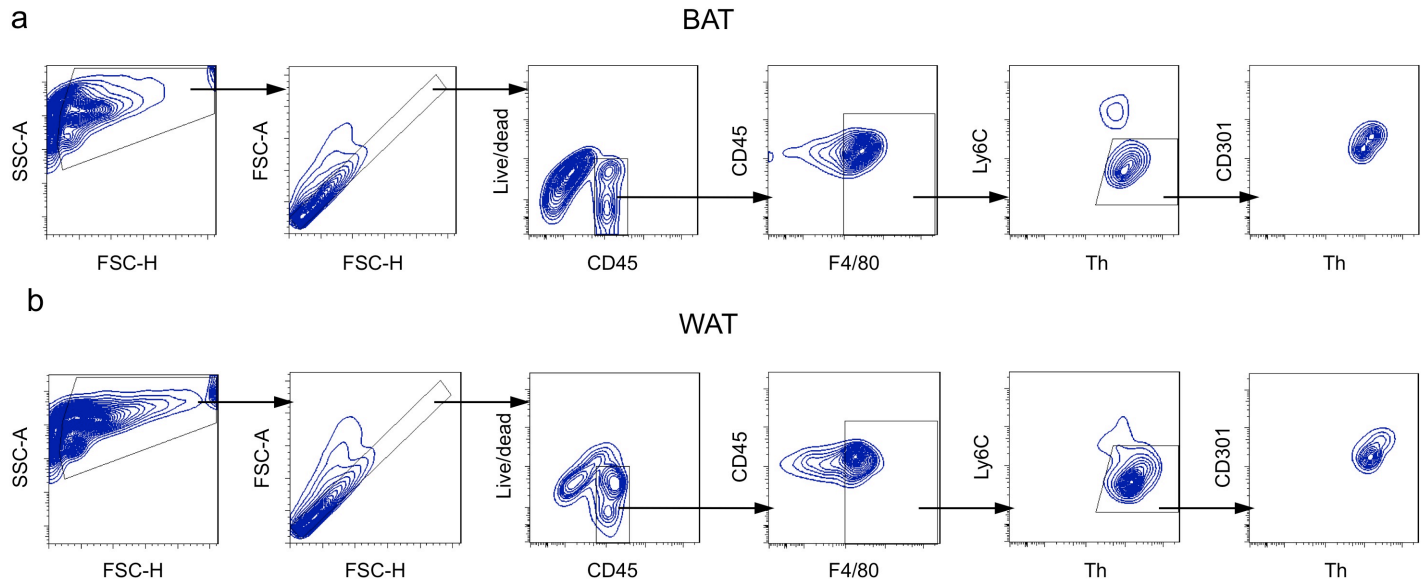
Supplementary Figure 5. a, Immunoblot analysis of muscle cpt1 (Cpt1b) and cytochrome c oxidase (Cox1) in solelus muscles of WT, IL4/IL13$^{-/-}$, and STAT6$^{-/-}$ mice housed at 22 ºC or 4 ºC. **b,** Expression of lipogenic genes in liver of WT, IL4/IL13$^{-/-}$, and STAT6$^{-/-}$ mice housed at 30 ºC, 22 ºC or 4 ºC (n=3 per genotype and temperature). **c, d,** Core body temperature of C57BL/6J WT and STAT6$^{-/-}$ mice housed at 4 ºC for 6 hours (n=5 per genotype and temperature). **d,** Real-time PCR of *Acox1, Ppargc1a,* and *Ucp1* mRNA levels in BAT of C57BL/6J WT and STAT6$^{-/-}$ mice housed at 22 ºC and 4 ºC (n=5 per genotype and temperature). **P < 0.01, ***P < 0.001 comparison between WT and STAT6$^{-/-}$ at the same temperature.



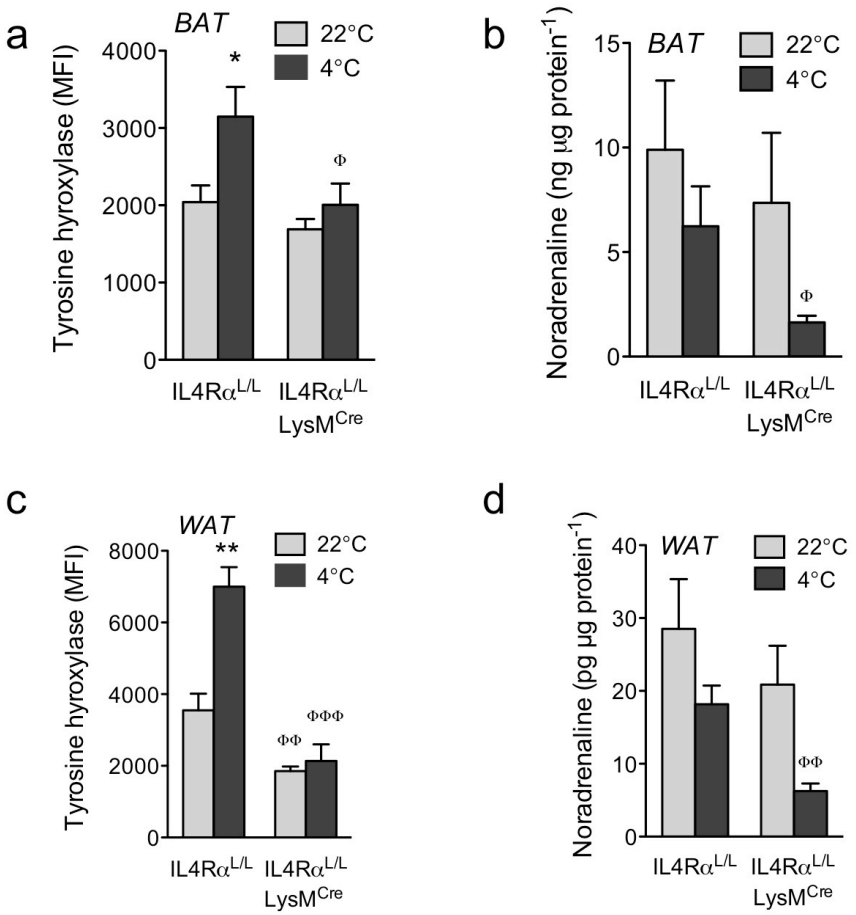
Supplementary Figure 6. Alternative activation induces expression of catecholamine synthesizing enzymes in macrophages. a-c, Representative FACS plots demonstrating intracellular staining for tyrosine hydroxylase (Th), dopa decarboxylase (Ddc), and dopamine β-hydroxylase (Dbh) in wild type peritoneal macrophages treated with vehicle (Veh) or IL4 (10 $ngml^{-1}$). Background staining was quantified using an appropriate isotype (Iso) control antibody. **d-f,** Th (d), Ddc (e), and Dbh (f) expression in wild type peritoneal macrophages stimulated with vehicle (Veh) or IL4 (10 $ngml^{-1}$) for 24 hours (n=5 per condition). **g,** Representative FACS plots of tyrosine hydroxylase expression in WT and $STAT6^{-/-}$ peritoneal macrophages treated with IL4 (10 $ngml^{-1}$). *P<0.05, **P < 0.01 compared to Veh.



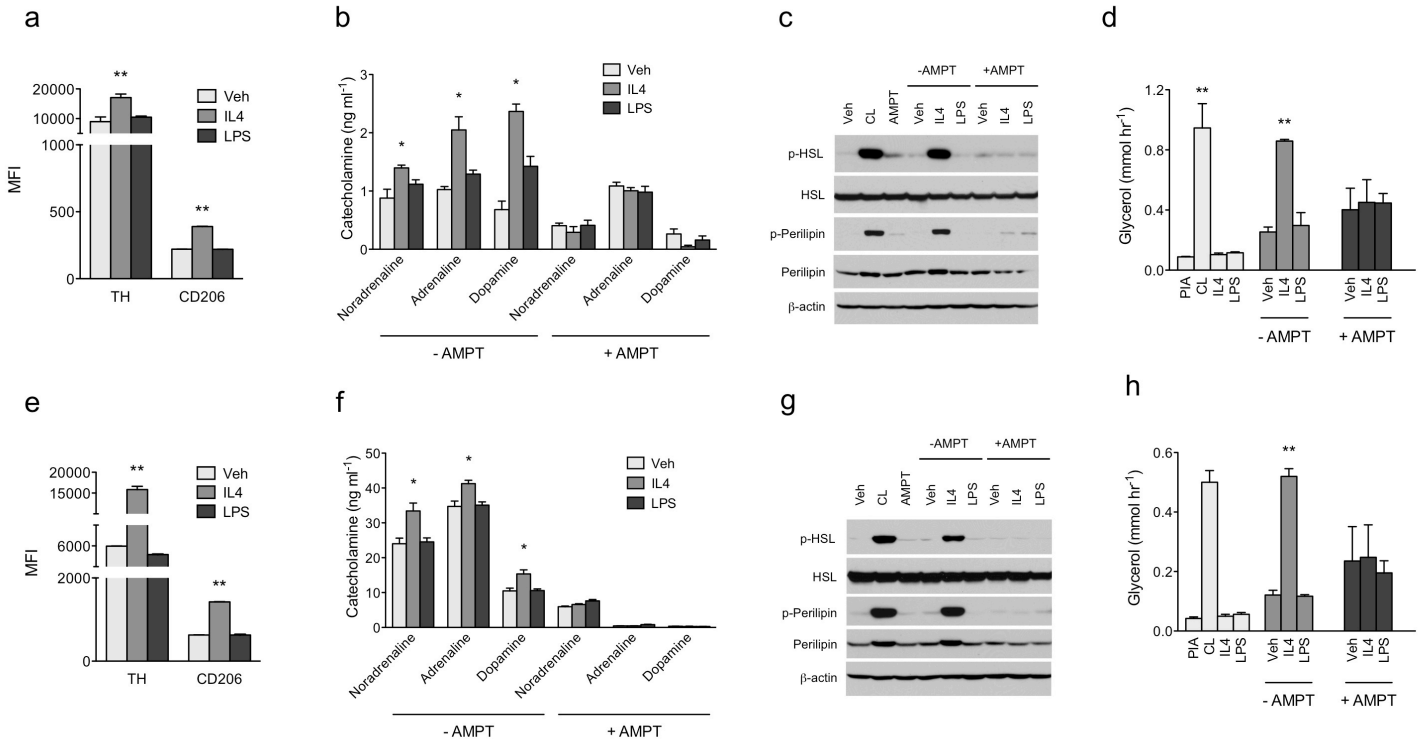
Supplementary Figure 7. Macrophage conditioned medium regulates lipolysis. a, Adrenaline secretion by WT and STAT6-/- bone marrow-derived macrophages (BMDMs) stimulated with IL4 or LPS (n=5 per genotype and condition). **b,** Noradrenaline production by IL4-treated BMDMs in the presence or absence of α-methyl-p-tyrosine (AMPT 2 mM, Sigma). **c,** Glycerol release by 3T3-L1 adipocytes after treatment with PIA, CL, IL4 or macrophage conditioned medium (± IL4 and AMPT) for 6 hours, n=4-6 per genotype and condition. ***P < 0.001 compared to WT with Veh. ΦΦΦP < 0.001 compared to WT with IL4.



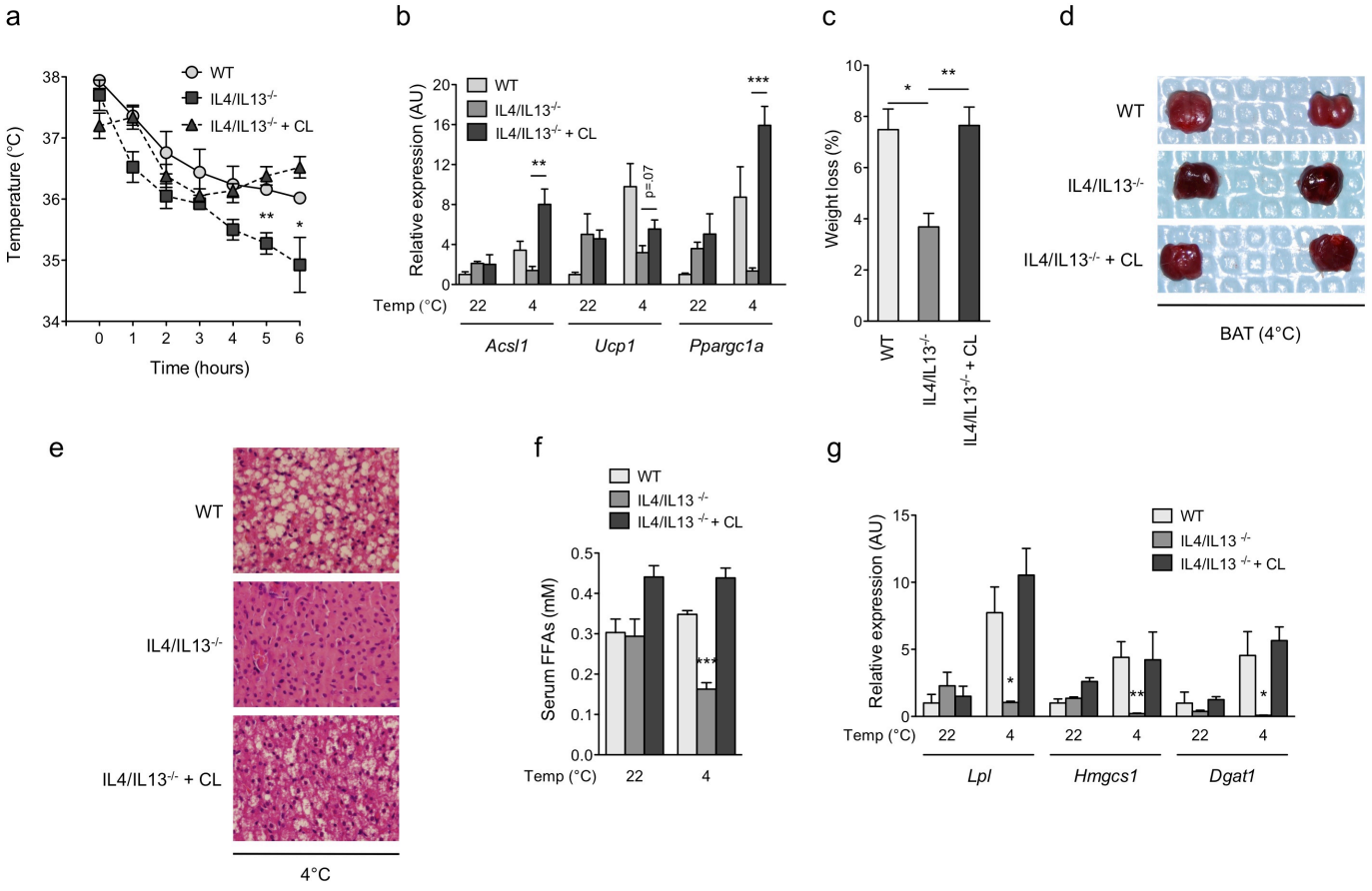
Supplementary Figure 8. Flow cytometric gating strategy for tyrosine hydroxylase expression in adipose tissue macrophages. a, b, Stromal vascular fractions were isolated from BAT (a) and WAT (b), and gated for side- and forward-scatter (SSC/FSC), doublets, and live cells prior to the analysis of the $CD45^{+}F4/80^{+}$ macrophages. Tyrosine hydroxylase (Th) co-localizes with CD301 in BAT and WAT macrophages.



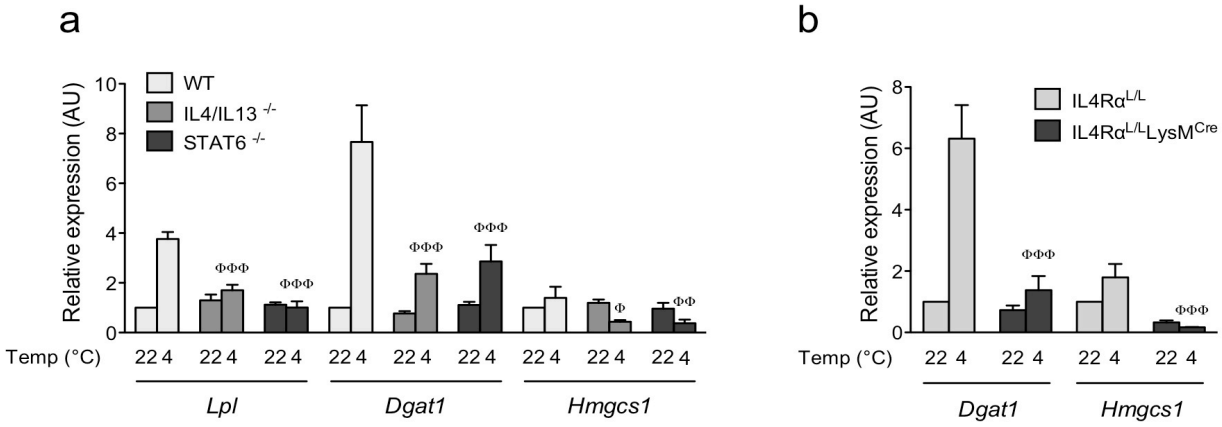
Supplementary Figure 9. Tyrosine hydroxylase expression and catecholamine production by alternatively activated adipose tissue macrophages. a, c, Tyrosine hydroxylase expression in BAT (a) and WAT (c) macrophages of IL4Rα$^{L/L}$ and IL4Rα$^{L/L}$LysM^{Cre} mice housed at 22 ºC or 4 ºC (n=4-5 per genotype and temperature). **b, d,** Noradrenaline content of BAT (b) and WAT (d) of IL4Rα$^{L/L}$ and IL4Rα$^{L/L}$LysM^{Cre} mice at various temperatures (n=4-5 per genotype and temperature). **P < 0.01 comparison of values at 22ºC and 4 ºC in IL4Rα$^{L/L}$ mice. ΦP < 0.05, ΦΦP < 0.01, ΦΦΦP < 0.001 comparison between IL4Rα$^{L/L}$ and IL4Rα$^{L/L}$LysM^{Cre} mice at the same temperature.



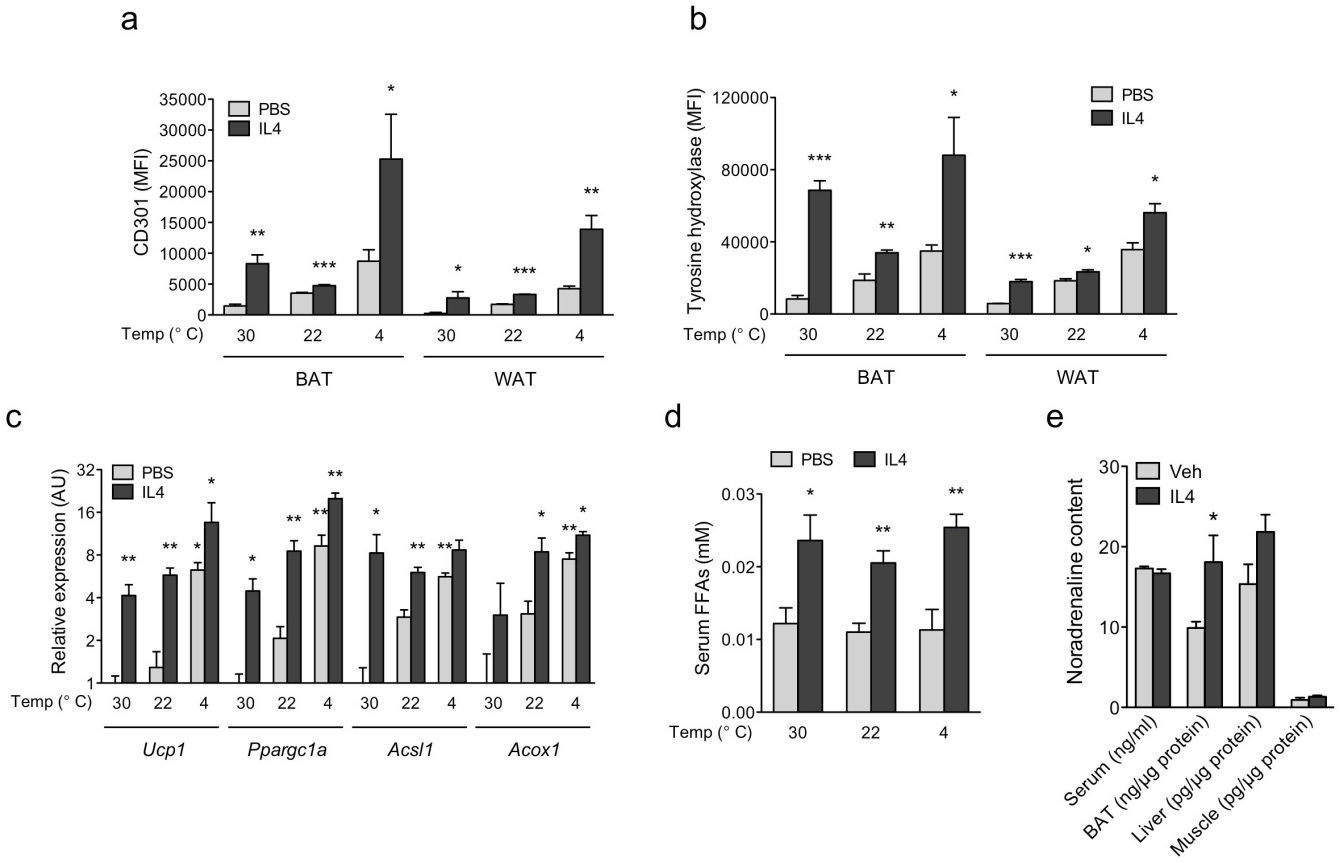
Supplementary Figure 10. Human monocytes and macrophages produce catecholamines. **a, e,** Expression of tyrosine hydroxylase and CD206 in primary monocytes (a) and human macrophage cell line U937 (e) treated with vehicle (Veh), IL4 (10 $ngml^{-1}$), or lipopolysaccharide (LPS, 10 $ngml^{-1}$), n=4-5 per condition. **b, f,** Catecholamine secretion by primary monocytes (b) and human macrophage cell line U937 (f) stimulated with IL4 or LPS, (± AMPT), n=4 per condition. **c, g,** Immunoblot analysis for phosphorylated-HSL and total HSL, phosphorylated-perilipin and total perilipin in 3T3-L1 adipocytes treated with PIA (1 mM), CL-316243 (1 mM), IL4 (10 $ngml^{-1}$), primary monocyte (c) or U937 cell (g) conditioned medium (± IL4 and AMPT) for 15 min. PIA (N6-phenylisopropyl adenosine), AMPT (a-methyl-p-tyrosine). **d, h,** Glycerol release by 3T3-L1 adipocytes after 6h treatment with PIA, CL, IL4, primary monocyte (d) or U937 cell (h) conditioned medium (n=5 per condition). *P < 0.05, **P < 0.01 compared to Veh.



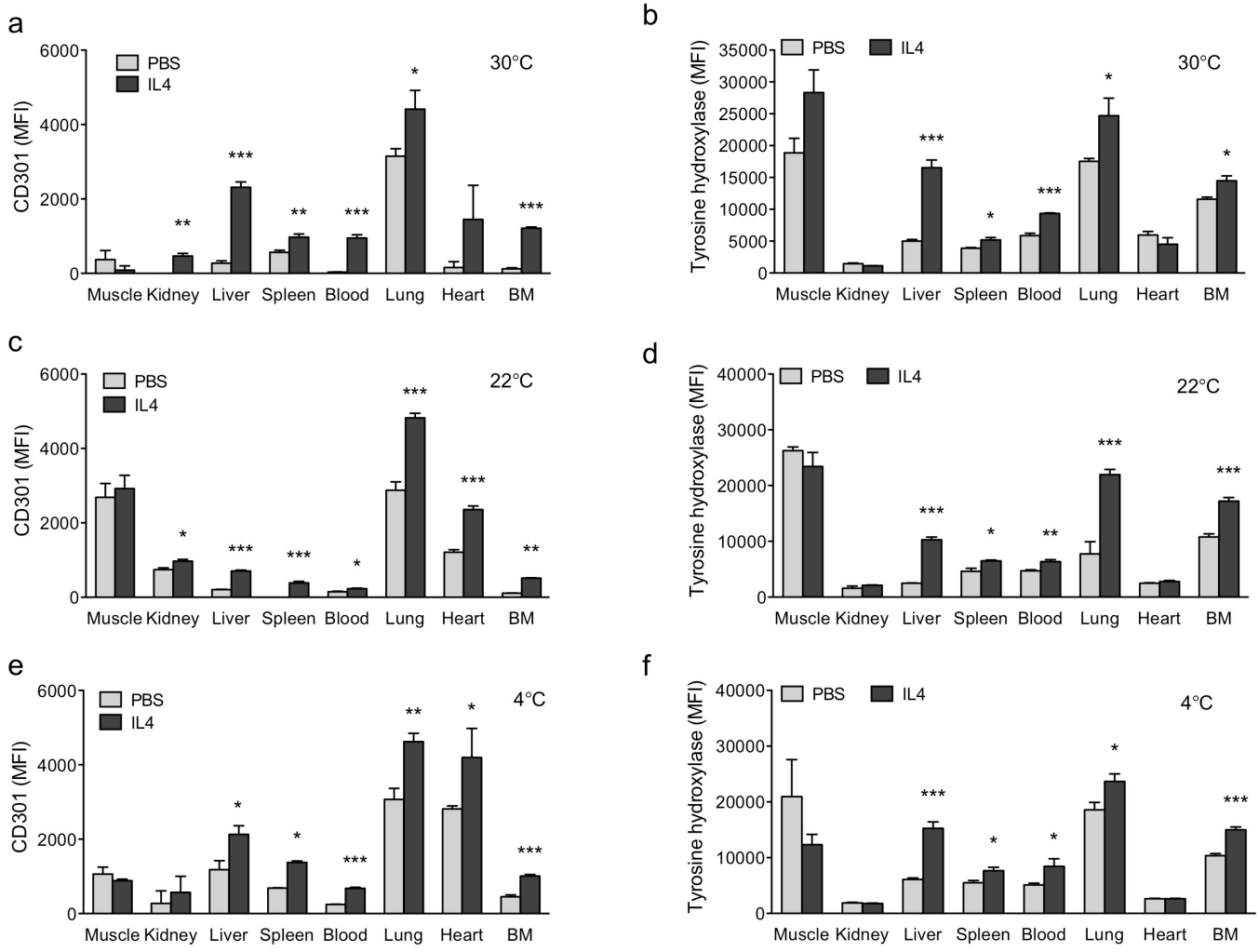
Supplementary Figure 11. Characteristics of IL4/IL13$^{-/-}$ mice treated with β3-adrenergic agonist CL-316243. a, Core body temperature of WT, IL4/IL13$^{-/-}$ and IL4/IL13$^{-/-}$ mice treated with CL-316243 (n=5 per genotype and treatment). **b,** Real-time PCR analysis of thermogenic genes in BAT of WT, IL4/IL13$^{-/-}$ and IL4/IL13$^{-/-}$ mice treated with CL-316243 (n=4-5 per genotype and treatment). **c,** Cold (4 °C) induced weight loss in WT, IL4/IL13$^{-/-}$ and IL4/IL13$^{-/-}$ mice treated with CL-316243 (n=4-5 per genotype and treatment). **d-e,** Representative histology of BAT from WT, IL4/IL13$^{-/-}$ and IL4/IL13$^{-/-}$ mice treated with CL-316243 after exposure to 4 °C; gross (d) and haematoxylin and eosin stained sections (e). **f**, Serum free fatty acid (FFA) levels in WT, IL4/IL13$^{-/-}$, and IL4/IL13$^{-/-}$ mice treated with CL-316243 housed at 22 ºC or 4 ºC (n=4-5 per condition and genotype). **g,** Real-time PCR of lipogenic genes (*Lpl, Dgat1, Hmgcs1)* in BAT of WT, IL4/IL13$^{-/-}$, and IL4/IL13$^{-/-}$ mice treated with CL-316243 housed at 22 ºC or 4 ºC (n=4-5 per genotype and temperature). *P < 0.05, **P < 0.01, *** P < 0.001 compared to WT.



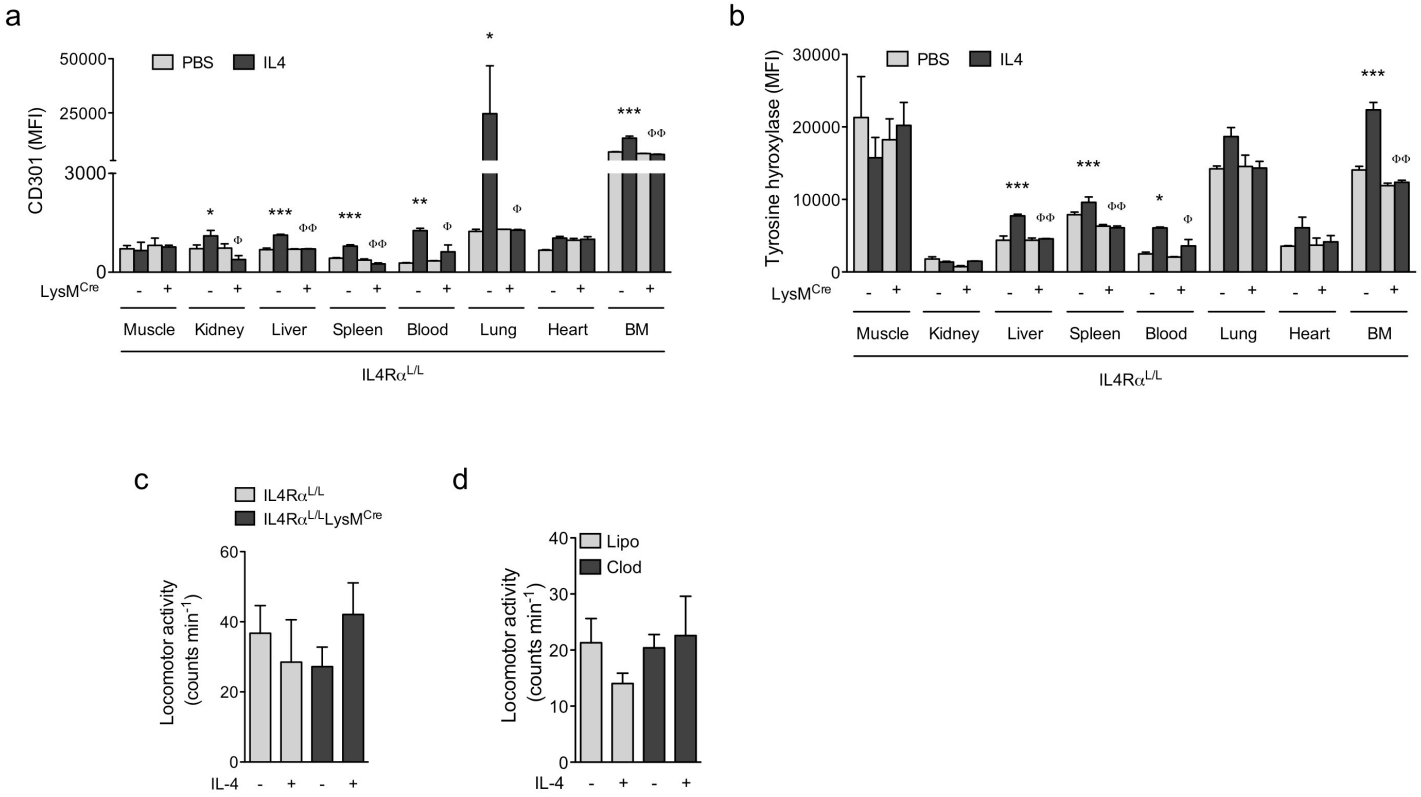
Supplementary Figure 12. Cold challenge induces lipogenic gene expression in brown adipose tissue. a, Real-time PCR of lipogenic genes (*Lpl, Dgat1, Hmgcs1)* in BAT of WT, IL4/IL13$^{-/-}$, and STAT6$^{-/-}$ mice housed at 22 ºC or 4 ºC (n=4-5 per genotype and temperature). **b,** Real-time PCR of lipogenic genes (*Dgat1, Hmgcs1)* in BAT of IL4Rα$^{L/L}$ and IL4Rα$^{L/L}$LysM^{Cre} mice housed at 22 ºC or 4 ºC (n=4-5 per genotype and temperature). ΦP < 0.05, ΦΦP < 0.01, ΦΦΦP < 0.001 compared to WT or IL4Rα$^{L/L}$ at 4 ºC.



Supplementary Figure 13. Effects of IL4 in wild type mice housed at various temperatures. a, b, Expression of alternative activation marker CD301 (a) and tyrosine hydroxylase (b) in adipose tissue macrophages of WT mice injected with vehicle (Veh) or IL4 at 30 °C, 22 °C or 4°C (n=4-5 per condition). **c,** Real-time RT-PCR analysis of thermogenic genes (*Acox1, Acsl1, Ppargc1a*, and *Ucp1*) in BAT of WT mice treated with Veh or IL4 for 6h at various temperatures (n=4-5 per condition). **d,** Serum free fatty acid (FFA) levels of WT mice treated with Veh or IL4 for 6h at 30°C, 22°C, and 4°C (n=4-5 per condition). **e,** Noradrenaline content of serum and various tissues 30 minutes after injection of IL4. *P < 0.05, **P < 0.01, *** P < 0.001 compared to Veh.



Supplementary Figure 14. Expression of CD301 and tyrosine hydroxylase in wild type mouse tissues at various temperatures. a, c, e, Expression of CD301 was quantified by flow cytometry in wild type mice 6 hours after administration of vehicle (Veh) or IL4 at 30°C (a), 22°C (c), and 4°C (e) (n=4-5 per condition). **b, d, f,** Tyrosine hydroxylase expression was quantified in mouse tissue macrophages by flow cytometry 6 hours after injection of vehicle (Veh) or IL4 at 30°C (d), 22°C (e), and 4°C (f) (n=4-5 per condition). Bone marrow (BM). *P < 0.05, **P < 0.01, *** P < 0.001 compared to Veh.



Supplementary Figure 15. Effects of IL4 in IL4Rα$^{L/L}$ and IL4Rα$^{L/L}$LysM^{Cre} mice. **a, b,** Expression of CD301 (a) and tyrosine hydroxylase (b) in tissue macrophages of IL4Rα$^{L/L}$ and IL4Rα$^{L/L}$LysM^{Cre} mice treated with vehicle (Veh) or IL4 at 22°C (n=4-5 per genotype and condition). **c, d,** Locomotor activity of IL4Rα$^{L/L}$ and IL4Rα$^{L/L}$LysM^{Cre} mice (c), and liposome (Lipo) or clodronate-containing liposome (Clod) treated mice (d) after IL4 injection (n=7-8 per genotype and condition). *P < 0.05, **P < 0.01, ***P < 0.001 compared to IL4Rα$^{L/L}$ with Veh. ΦP < 0.05, ΦΦP < 0.01, ΦΦΦP < 0.001 compared to IL4Rα$^{L/L}$ with IL4.