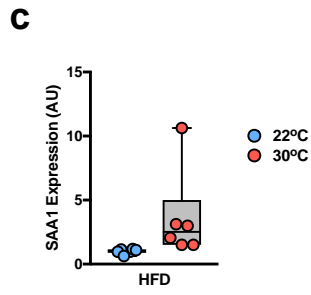
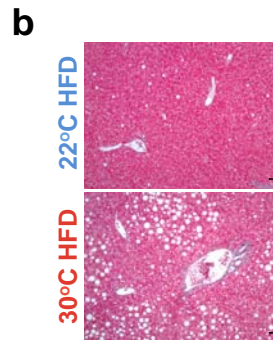
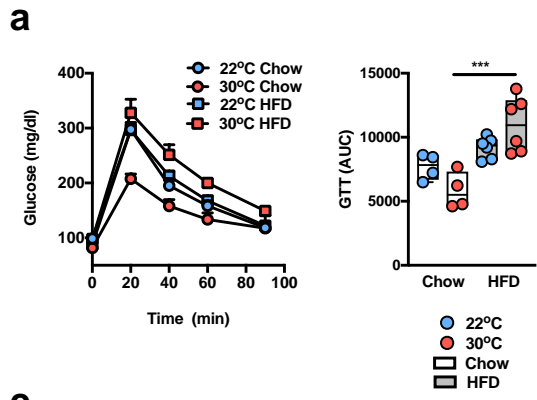


Supp Fig 11



**Supp Fig 12**

**a**

**Table 1a Ts vs Tn PBMCs in Chow Fed Mice**

**Supplement to Figure 1c**

**A = Decreased inflammatory response**

**B = Increased susceptibility to infection**

**C = Decreased acute inflammation**

Gene Name	Fold Change	Log Fold Chang	p-value	Associated Pathway
Ccr2	-2.900268	-1.5361862	0.0179735	A, B, C
S100a9	-3.9386005	-1.9776831	0.0010768	A, C
Mmp19	-3.5310318	-1.8200898	0.01617527	A, C
Sele	-2.1671202	-1.1157792	0.1969843	A, B, C
Selp	-5.3711905	-2.425242	0.27060795	A, B, C
Fpr2	-3.1194942	-1.6413121	0.0179063	A, B, C
Clec4d	-4.0024166	-2.0008714	0.1282988	A, C
Mmp2	-2.9483821	-1.5599235	0.5034918	A
Spp1	-2.0498734	-1.0355347	0.0785838	A, B, C
Cysltr1	-2.6501172	-1.4060562	0.01161632	A, C
Tnfrsf11a	-2.299639	-1.2014074	0.05569378	A, C
Cd14	-2.3607728	-1.2392592	0.12847532	A, B, C
Cebpd	-2.9350784	-1.553399	0.03184895	A
Ccr1	-6.9453616	-2.7960498	0.05346816	A, C
Il1b	-2.1949959	-1.1342182	0.00162273	A, C
Il1r1	-2.256751	-1.1742473	4.52E-04	A, C
Il6	-3.610195	-1.8520766	0.12287884	A, B, C
Nlrp12	-2.782047	-1.4761468	0.0777145	A, C
Ptafr	-2.3166058	-1.2120125	0.11318901	A
Ptgdr	-2.2381516	-1.1623077	0.28921354	A, C
Ptgs1	-4.4043546	-2.1389306	0.29489788	A
Clec4e	-5.236093	-2.3884907	3.11E-04	A, C
Cers6	-2.0422053	-1.0301279	0.01177411	A
Lbp	-15.296995	-3.9351764	0.01348366	A, B, C
Ecm1	-3.1597195	-1.6597965	0.2930402	A, C
S1pr3	-3.8994565	-1.963273	0.16772528	A, C
Ednrb	-4.345838	-2.1196344	0.3942885	A, C
Ltc4s	-3.3450212	-1.7420154	0.52104604	A, C
Aicda	-6.6319103	-2.7294245	0.2532547	B
Bpifa1	-34.406723	-5.1046185	0.18959704	B
Mmp8	-5.7030334	-2.5117295	0.02418746	B
Fpr1	-3.0620682	-1.6145064	0.05993914	A
Msr1	-3.5590317	-1.8314848	0.08937913	B
Slc16a2	-2.064818	-1.0460145	0.41816664	B
Slpi	-5.138603	-2.3613763	0.2985094	B
Marco	-2.9889517	-1.5796396	0.5811841	B
Gbp3	-1.2843655	-0.36105585	0.01599239	B
Gpc3	-6.992956	-2.8059025	0.02658532	B
C1qa	-2.7704086	-1.4700987	0.50132746	B
C3	-2.7789478	-1.4745387	0.0182416	B
C4a	-4.980624	-2.3163266	0.17424007	B
C5ar1	-2.3440626	-1.229011	0.13113089	B
Cd5l	-4.0239587	-2.0086155	0.34872347	B
Tlr5	-5.115588	-2.3549001	0.01195425	B
Cfh	-2.7807312	-1.4754642	0.0563215	B
Padi4	-2.2842767	-1.1917374	0.3320089	B
Vsig4	-2.0757298	-1.0536187	0.62382525	B
Vwf	-2.5577865	-1.3548958	0.090023	B
Rbpj	-1.2285191	-0.29692027	0.1118677	B
Cxcr2	-2.7580562	-1.4636518	0.04135978	B
Dlg2	-3.9399412	-1.9781741	0.27481955	B
Jam3	-7.921922	-2.9858506	0.02596029	B
Dusp3	-2.2197046	-1.1503677	0.00344865	B
Lcn2	-3.122755	-1.6428194	0.07775574	B

**b**

**Table 1b Ts vs Tn Liver in Chow Fed Mice**

**Supplement to Supplementary Figure 3f**

**A = Metabolism of lipids and lipoprotein**

**B = Fatty acid metabolic pathway**

**C = Positive regulation of fatty acid oxidation**

Gene Name	Fold Change	Log Fold Chang	p-value	Associated Pathway
Mgll	2.263733	1.1787038	0.00213764	A, B
Chat	2.1188455	1.0832783	0.01085947	A
Pex11a	2.6956837	1.4306512	0.00267294	A
Fabp1	2.518476	1.332551	0.01452876	A, B, C
Lpin1	9.916864	3.309884	0.03805904	A, B
Gpd2	2.9046128	1.5383458	0.04214943	A
Pnpla2	2.1270788	1.0888735	0.00152263	A
G0s2	2.284056	1.1915979	0.02547845	A
Ppara	2.0650632	1.046186	0.04076514	A, B, C
Cpt1a	2.1424978	1.0992937	0.00830894	A, B, C
Ppargc1b	3.6117263	1.8526886	0.00190269	A
Trib3	3.6351936	1.8620322	0.00677629	A, B
Prkd1	3.4745681	1.7968336	0.00992504	A
Acot4	2.8300936	1.5008497	0.00610927	B
Acot2	5.1152916	2.3548164	0.01852117	B
Por	2.4115312	1.2699494	0.01191301	B
Acot1	4.9764776	2.315125	0.02481512	B
Ehhadh	3.8523538	1.9457402	0.04431824	B

**c**

**Table 1c Ts vs Tn Liver in HFD Fed Mice**

**Supplement to Figure 2o**

**A = Collagen Formation**

**B = Positive regulation of apoptosis signaling pathway**

**C = Top 200 marker genes up-regulated in the 'proliferation' subclass of HCC**

Gene Name	Fold Change	Log Fold Chang	p-value	Associated Pathway
Col4a5	2.595481	1.3760018	0.02289232	A
Col9a2	3.503366	1.8087417	0.02282644	A
Adams14	2.2215497	1.1515664	0.00680651	A
Agtr2	2.0226696	1.0162606	0.0129051	B
Ngfr	2.0322323	1.0230653	0.020088	B
Srpx	2.1963255	1.1350919	0.02551001	B
Nck2	2.0141392	1.0101633	0.03370601	B
Osm	2.8813698	1.5267549	0.02944854	B
Ppp3cc	2.104037	1.07316	0.00375977	B
Sox4	2.7958655	1.483295	0.01094856	C
Cdkn3	3.391282	1.7618308	0.03137689	C
Hk2	2.7739832	1.471959	0.01099649	C
Ddr1	2.311051	1.208549	0.02099115	C
Ect2	2.9456124	1.5585676	0.03136202	C
Cdk1	2.443331	1.2888494	0.01801695	C
Kif18b	2.1213937	1.0850123	0.01129002	C

**d**

**Table 1d Ts vs Tn PBMCs in Chow Fed Mice**

**Supplement to Figure 4a and 5a**

**A = Cytokines and inflammatory response**

**B = Positive regulation of TLR signaling**

**C = Cellular Response to LPS**

**D = Positive regulation of TLR4 signaling**

**E = Increased IL-17 secretion**

Gene Name	Fold Change	Log Fold Chang	p-value	Associated Pathway
Il5	7.01585	2.810618	0.03999559	A
Il10	4.8075986	2.2653165	0.09900788	A, C
Il15	2.1603541	1.1112678	0.23251489	A
Lbp	2.7008667	1.4334224	0.59380835	B, C, D
Tlr5	2.5381804	1.3437946	0.31909248	B, C
Ly96	2.7357821	1.4519533	0.07607134	C
Nr1d1	-1.623939	-0.6994975	0.37599245	C
Cyp17a1	12.413165	3.633799	0.02596169	C
Ltf	2.0185776	1.013339	0.36580375	B, C, B
Il1rn	2.6822443	1.4234406	0.03462122	D
Nfil3	2.4986777	1.3211648	0.03562596	D
Rag1	3.612676	1.8530678	0.28290012	D
Il17rc	1.9096935	0.9333411	0.42264974	D

## Supp Table 1

## Supplementary Figure Legends

**Supplementary Figure 1.** Thermoneutral housing does not alter basal immune cell numbers and composition. **(a-d)** 6 week old WT C57BL/6 male mice were housed at  $T_S$  (22°C) or  $T_N$  (30°C) conditions for a minimum of 3 weeks. **(a)** Total cell number, percent of hematopoietic stem and progenitor cells, and percent of lymphoid and myeloid cells in the bone marrow ( $n = 3$  per group). **(b)** Total white blood cell number and levels of circulating immune cells ( $n = 7$  per group). **(c)** Total cell number and cellular composition in the spleen ( $n = 6$  per group at  $T_S$ , 5 per group at  $T_N$ ). **(d)** Total cell number and cellular composition in the thymus ( $n = 6$  per group at  $T_S$ , 5 per group at  $T_N$ ). Blue denotes  $T_S$  (22°C); Red denotes  $T_N$  (30°C). **(a, c and d)** A single experiment. **(b)** A representative of 2 individual experiments. **(a-d)** Student's *t*-test.

**Supplementary Figure 2.** Thermoneutral housing's effect on adipose tissue, glucose metabolism, cholesterol and triglyceride levels. **(a-i)** 6 week-old WT C57BL/6 male mice were housed at  $T_S$  (22°C) or  $T_N$  (30°C) conditions for 24 weeks and fed a chow or HFD. **(a)** Representative epididymal white adipose tissue histology ( $n = 3$  mice per group) by H&E staining at 20x magnification. Scale bars, 100µm. **(b)** Immune cell (CD45<sup>+</sup>) infiltration to epididymal white adipose tissue ( $n = 6$  per group at  $T_S$ , 5 per group at  $T_N$ ). **(c)** Mean fluorescent intensity (MFI) of Ly6c expression by CD11b+F4/80+ macrophages in white adipose tissue ( $n = 4$  per group at  $T_S$ , 5 per group at  $T_N$ ). **(d)** Glucose tolerance test and area under the curve after 14 weeks of diet ( $n = 8$  per group). **(e)**

Glucose tolerance test and area under the curve after 20 weeks of diet ( $n = 8$  per group). (f) Insulin tolerance test after 22 weeks of diet ( $n = 8$  per group). (g) Hepatic cholesterol levels ( $n = 4$  per group). (h) Serum triglyceride levels ( $n = 4$  per group). (i) Serum cholesterol levels ( $n = 8$  per group). Blue denotes  $T_S$  ( $22^\circ\text{C}$ ); Red denotes  $T_N$  ( $30^\circ\text{C}$ ). A representative of 2 individual experiments. Throughout  $*P < 0.05$ ,  $**P < 0.01$ ,  $***P < 0.001$ ,  $****P < 0.0001$ . (b-i) One way ANOVA with *post hoc* Tukey's test. (c) Student's *t*-test.

**Supplementary Figure 3. Thermoneutral housing alters hepatic gene expression.** (a-d) 6 week-old WT C57BL/6 male mice were housed at  $T_S$  ( $22^\circ\text{C}$ ) or  $T_N$  ( $30^\circ\text{C}$ ) conditions for 24 weeks and fed a chow or HFD. (a) Expression of the indicated lipid mediator genes in the liver ( $n = 4$  per group) of chow fed mice. (b) Expression of the indicated chemokine genes in the liver ( $n = 4$  per group) of chow fed mice. (c) Expression of the indicated fibrosis marker genes in the liver ( $n = 4$  per group) of chow fed mice. (d) Trichrome staining in liver of HFD fed mice ( $n = 4$  mice per group) at 10x magnification. Scale bars,  $250\mu\text{m}$ . (e) Heatmap of differential hepatic gene expression in mice housed at  $T_S$  or  $T_N$  and fed a chow or HFD for 8 weeks, as determined by RNAseq ( $n = 2$  per group). (f) Upregulated gene expression pathways determined by RNASeq analysis comparing mice fed chow diet and housed at  $T_S$  or  $T_N$  ( $n = 2$  per group). (g) Cytomap of relevant altered ontologies in livers of HFD fed  $T_N$ -housed or  $T_S$ -housed mice. Blue denotes  $T_S$  ( $22^\circ\text{C}$ ); Red denotes  $T_N$  ( $30^\circ\text{C}$ ). (a-c) Data

represents mean + s.e.m. **(a-e)** A single experiment. Throughout  $*P < 0.05$ ,  $**P < 0.01$ ,  $***P < 0.001$ ,  $****P < 0.0001$ . **(b-d)** Student's *t*-test.

**Supplementary Figure 4.** Thermoneutral housing exacerbates obesity and NAFLD progression in the AKR strain of inbred mice. **(a-k)** 6 week-old AKR male mice were housed at  $T_S$  (22°C) or  $T_N$  (30°C) and fed HFD for 18 weeks ( $n = 3$  per group). **(a)** Weight gain. **(b)** Epididymal, inguinal and perirenal white adipose tissue weights. **(c)** Liver weight. **(d)** Hepatic triglyceride levels. **(e)** Representative liver histology ( $n = 3$  mice per group) by H&E staining at 20x and 40x magnification Scale bars, 100µm (left) and 50µm (right). **(f)** NAFLD activity score. **(g)** Expression of the indicated chemokine genes in the liver **(h)** Percent of hepatic CD11b<sup>+</sup>F4/80<sup>+</sup> immune cells. **(i)** Serum ALT levels. **(j)** Expression of the indicated fibrosis marker genes in the liver. **(k)** Trichrome staining in liver of HFD fed mice ( $n = 3$  mice per group) at 10x magnification. Scale bars, 250µm. Percent Trichrome positive pixels. Blue denotes  $T_S$  (22°C); Red denotes  $T_N$  (30°C). For bar graph, data represents mean + s.e.m. **(a-k)** a single experiment. Throughout  $*P < 0.05$ ,  $**P < 0.01$ ,  $***P < 0.001$ ,  $****P < 0.0001$ . **(a-d and f-k)** Student's *t*-test.

**Supplementary Figure 5.** Adrenalectomy removes the inhibition of NAFLD progression associated with thermostressed housing. **(a-m)** 6 week-old WT C57BL/6 male mice with surgically removed adrenal glands were housed at  $T_S$  (22°C) or  $T_N$  (30°C) and fed chow ( $n = 4$  per group) or HFD ( $n = 4$  per group at  $T_S$



and  $n = 5$  per group at  $T_N$ ) for 16 weeks. **(a)** Weight gain. **(b)** Epididymal white adipose tissue weight. **(c)** Inguinal white adipose tissue weight. **(d)** Perirenal white adipose tissue weight. **(e)** Liver weight. **(f)** Hepatic triglyceride levels. **(g)** Representative liver histology ( $n = 4$  mice per group) by H&E staining at 20x and 40x magnification. Scale bars, 100 $\mu$ m (left and middle) and 50 $\mu$ m (right). **(h)** Expression of the indicated lipid mediator genes in the liver. **(i)** Expression of the indicated chemokine genes in the liver. **(j)** Percent of hepatic CD11b<sup>+</sup>F4/80<sup>+</sup> immune cells. **(k)** Expression of the indicated chemokine genes in the liver. **(l)** Serum ALT levels. **(m)** Fold change in ALT levels as compared to non-adrenalectomized C57BL/6 mice fed HFD for 16 weeks at the same temperature. Blue denotes  $T_S$  (22°C); Red denotes  $T_N$  (30°C). For bar graphs, data represents mean + s.e.m. **(a-m)** A single experiment. Throughout  $*P < 0.05$ ,  $**P < 0.01$ ,  $***P < 0.001$ ,  $****P < 0.0001$ . **(a-f, k and l)**. One way ANOVA with *post hoc* Tukey's test. **(h-j and m)** Student's *t*-test.

**Supplementary Figure 6.** Thermoneutral housing in intestinal epithelial resistance and kinetic modulation of intestinal microbiome composition. **(a,b)** 6 week-old WT C57BL/6 male mice ( $n = 8$  per group) were housed at  $T_S$  (22°C) or  $T_N$  (30°C) conditions for 24 weeks and fed a chow or HFD. **(a)** Representative intestinal histology ( $n = 4$  mice per group) by H&E staining at 20x magnification. Scale bar, 100 $\mu$ m. **(b)** Trans-epithelial resistance ( $n = 4$  per group). **(c-e)** Kinetic phyla level analysis of  $T_S$  and  $T_N$  mice fed chow or HFD. Mice were separated into  $T_S$  or  $T_N$  rooms, housed for 2 weeks and fed chow, prior to being separated

into a chow or HFD fed groups (c) Microbiome upon arrival, before room separation. (d) Microbiome after two-week acclimation. (e) Microbiome after 12 weeks of chow or HFD feeding. (f-k) Relative abundance of all microbiome phyla after 24 weeks ( $n = 8$  mice per group). (f) Percent composition of actinobacteria. (g) Percent composition of bacteroidetes. (h) Percent composition of firmicutes. (i) Percent composition of proteobacteria. (j) Percent composition of tenericutes. (k) Percent composition of verrucomicrobia. Blue denotes  $T_S$  (22°C); Red denotes  $T_N$  (30°C). (a-b) A representative of 2 experiments. (c-k) A single experiment. (b and f-k)  $*P < 0.05$ ,  $**P < 0.01$ ,  $***P < 0.001$ ,  $****P < 0.0001$ . One way ANOVA with *post hoc* Tukey's test.

**Supplementary Figure 7.** Thermoneutral housing alteration of the intestinal microbiome extends past the phyla level. (a-c) 6 week-old WT C57BL/6 male mice were housed at  $T_S$  (22°C) or  $T_N$  (30°C) conditions for 24 weeks and fed a chow or HFD ( $n = 8$  per group). (a) LEfSe analysis generated cladogram displaying most differentially abundant taxa in  $T_S$  and  $T_N$  mice after 24 weeks of chow or HFD feeding. (b) LDA scores of differentially abundant taxa. (c) LEfSe analysis generated cladogram displaying most differentially abundant taxa in  $T_S$  and  $T_N$  mice after 24 weeks of HFD only. (a-c) A single experiment.

**Supplementary Figure 8.** Hepatic phenotype of mice treated with gram-negative antibiotics. (a-g) 6 week-old WT C57BL/6 male mice ( $n = 8$  per group) were housed at  $T_S$  (22°C) or  $T_N$  (30°C) and fed a HFD. After 8 weeks of HFD, mice

were mock-treated (Ctrl) or treated with antibiotics (Abx Tx) supplied in drinking water in addition to HFD exposure for additional 16 weeks. (a) Weight gain. (b) Epididymal white adipose tissue weight. (c) Inguinal white adipose tissue weight. (d) Perirenal white adipose tissue weight. (e) Liver weight. (f) Hepatic triglyceride levels. (g) Glucose tolerance test and area under the curve. Blue denotes  $T_S$  (22°C); Red denotes  $T_N$  (30°C). (a-g) A single experiment. Throughout  $*P < 0.05$ ,  $**P < 0.01$ ,  $***P < 0.001$ ,  $****P < 0.0001$ . (a-g) One way ANOVA with *post hoc* Tukey's test.

**Supplementary Figure 9.** Hepatic phenotype of  $TLR4^{fl/fl}Vav1-Cre^+$  mice. (a-g) 6 week-old male  $TLR4^{fl/fl}Vav1-Cre^-$  mice housed at 22°C ( $n = 9$  per group) and 30°C ( $n = 8$  per group), and  $TLR4^{fl/fl}Vav1-Cre^+$  mice housed at 22°C ( $n = 7$  per group) and 30°C ( $n = 5$  per group) were fed HFD for 24 weeks. (a) Weight gain. (b) Epididymal white adipose tissue weight. (c) Inguinal white adipose tissue weight. (d) Perirenal white adipose tissue weight. (e) Liver weight. (f) Hepatic triglyceride levels. (g) Glucose tolerance test and area under the curve. Blue denotes  $T_S$  (22°C); Red denotes  $T_N$  (30°C). (a-g) 2 combined experiments. Throughout  $*P < 0.05$ ,  $**P < 0.01$ ,  $***P < 0.001$ ,  $****P < 0.0001$ . (a-g) One way ANOVA with *post hoc* Tukey's test.

**Supplementary Figure 10.** LPS induction of IL-17 promoting cytokines and hepatic phenotype of the IL-17 axis deficient mice. (a-c) 6 week-old WT C57BL/6 male mice were housed at  $T_S$  (22°C) or  $T_N$  (30°C) conditions for 24 weeks and

fed a HFD ( $n = 3$  per group). BMDCs derived from these mice were then stimulated with LPS and cytokine levels were quantified, (a) IL-6 and (b) IL-1 $\beta$ . (c) Indicated gene expression in BMDCs. (d-j) 6 week old WT ( $n = 5$  per group), IL-17RA<sup>-/-</sup> ( $n = 4$  per group) and IL-17A<sup>-/-</sup> ( $n = 4$  per group) mice were housed at T<sub>N</sub> (30°C) for 24 weeks and fed a HFD. (d) Weight gain. (e) Epididymal white adipose tissue weight. (f) Inguinal white adipose tissue weight. (g) Perirenal white adipose tissue weight. (h) Hepatic triglyceride levels. (i) Glucose tolerance test and area under the curve. (j) Liver weight. Blue bars denote T<sub>S</sub> (22°C); Red bars denote T<sub>N</sub> (30°C). (a-c) A representative of 3 individual experiments. (d-j) A representative of 2 individual experiments. Throughout \* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ , \*\*\*\* $P < 0.0001$ . (a-c) Student's *t*-test. (d-j) One way ANOVA with *post hoc* Tukey's test.

**Supplementary Figure 11.** Thermoneutrality-driven augmentation of hepatic SAA1 expression is linked to TLR4 and IL-17 axes. (a) Indicated gene expression in liver of 6 week-old WT C57BL/6 male mice housed at T<sub>S</sub> (22°C;  $n = 4$  per group) or T<sub>N</sub> (30°C;  $n = 5$  per group) for 24 weeks, fed a HFD. (b) Indicated gene expression in liver of 6 week old TLR4<sup>fl/fl</sup>Vav1-Cre<sup>+</sup> ( $n = 3$  per group) and control TLR4<sup>fl/fl</sup>Vav1-Cre<sup>-</sup> ( $n = 3$  per group) mice housed at T<sub>N</sub> (30°C) conditions for 24 weeks, on a HFD. (c) Indicated gene expression in liver of 6 week old WT ( $n = 5$  per group), IL-17RA<sup>-/-</sup> ( $n = 4$  per group) and IL-17A<sup>-/-</sup> ( $n = 3$  per group) mice housed at T<sub>N</sub> (30°C) for 24 weeks, on a HFD. Blue denotes T<sub>S</sub> (22°C); Red denotes T<sub>N</sub> (30°C). A single experiment. Throughout \* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P <$

0.001, \*\*\*\* $P < 0.0001$ . (a-b) Student's  $t$ -test. (c) One way ANOVA with *post hoc* Tukey's test.

**Supplementary Figure 12.** Thermoneutral housing removes the barrier to modeling obesity in female mice. (a-c) 6 week-old WT C57BL/6 female mice were housed at  $T_S$  (22°C) fed chow ( $n = 4$  per group) or HFD ( $n = 6$  per group) or housed at  $T_N$  (30°C) and fed chow ( $n = 4$  per group) or HFD ( $n = 6$  per group) for 24 weeks. (a) Glucose tolerance test and area under the curve from glucose tolerance test. (b) Trichrome staining in liver of HFD fed mice ( $n = 4$  mice per group) at 10x magnification. Scale bars, 250 $\mu$ m. (c) Indicated gene expression in liver of mice fed HFD. Blue denotes  $T_S$  (22°C); Red denotes  $T_N$  (30°C). Data represents mean + s.e.m. (a-c) A representative of 3 individual experiments. Throughout \* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ , \*\*\*\* $P < 0.0001$ . (a-b) One way ANOVA with *post hoc* Tukey's test. (c) Student's  $t$ -test.

**Supplementary Table 1.** Genes associated with pathways upregulated by temperature and diet changes. (a-d) Genes significantly upregulated in gene associated pathways depicted in figures ( $n = 2$  mice per group). (a) Genes associated with pathways depicted in Figure 1c. Genes are differentially expressed at least two-fold in PBMCs from  $T_N$  vs  $T_S$  chow fed mice. Negative fold change represents increased expression in  $T_S$  PBMCs. (b) Genes associated with pathways depicted in Supplemental Figure 3f. (c) Genes associated with pathways depicted in Figure 2o. Genes are differentially expressed at least two-

fold in the liver of  $T_N$  vs  $T_S$  HFD fed mice. Positive fold change represents increased expression in  $T_N$  liver. Genes are differentially expressed at least two-fold in the liver of  $T_N$  vs  $T_S$  chow fed mice. Positive fold change represents increased expression in  $T_N$  liver. **(d)** Genes associated with pathways depicted in Figures 4a and 5a. Genes are differentially expressed at least two-fold in PBMCs from  $T_N$  vs  $T_S$  HFD fed mice. Positive fold change represents increased expression in  $T_N$  PBMCs.