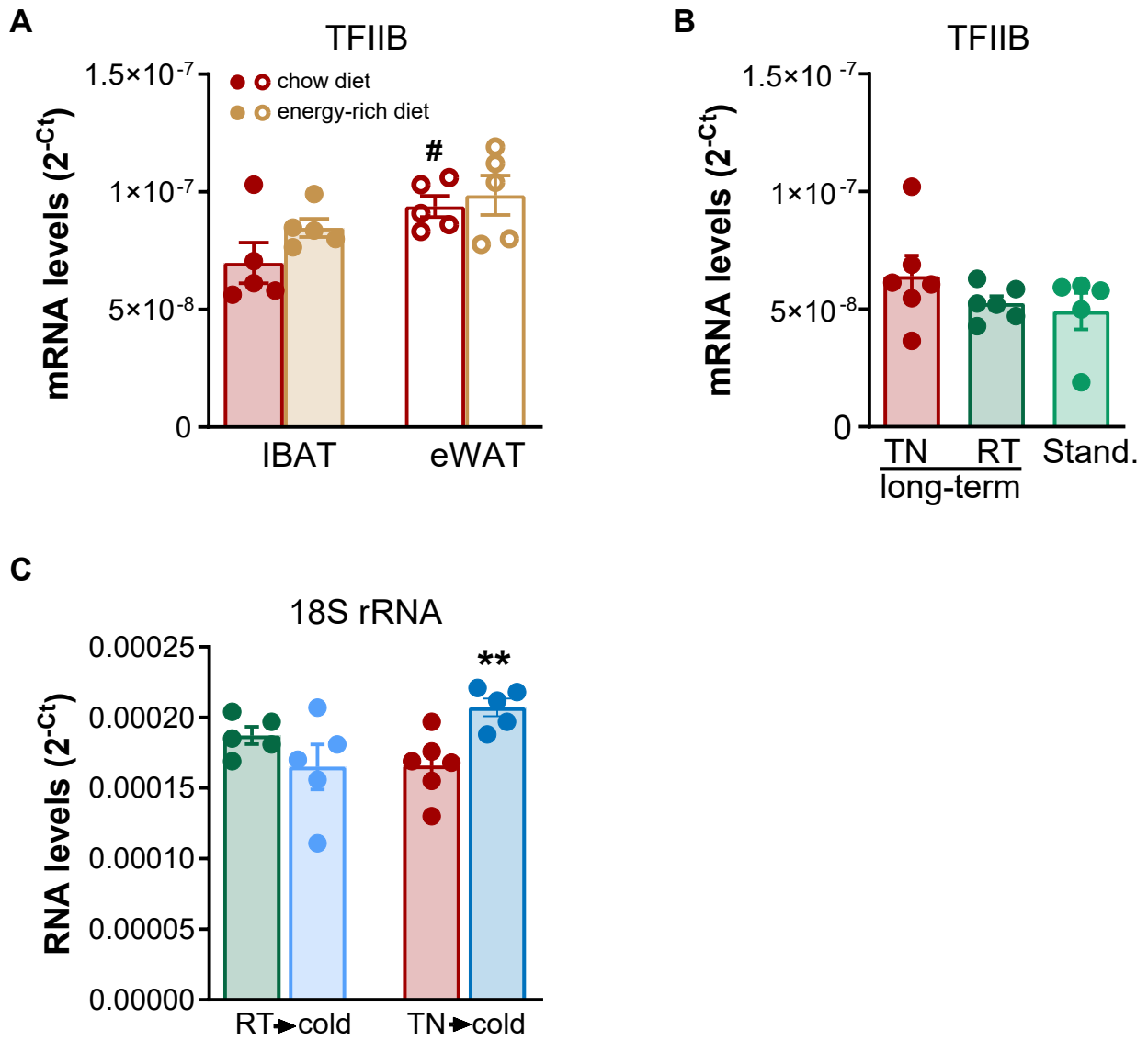


# Supplementary Figure 1



**Supplementary Figure 1.** Reference gene expression in adipose tissues. Values are antilog-transformed Ct values ( $2^{-Ct}$ ) presented as means  $\pm$  S.E.

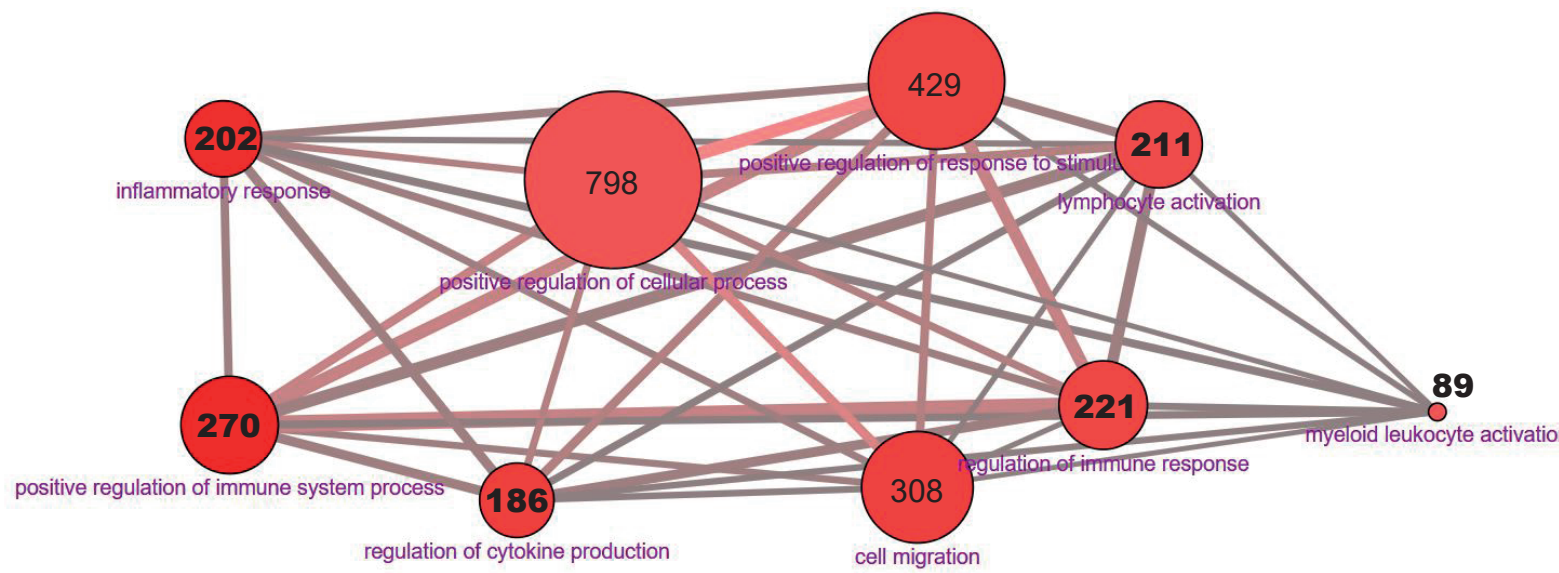
**(A)** TFIIB gene expression levels in adipose depots presented in Figure 2. #  $P < 0.05$ ; significant difference between IBAT and eWAT by Student's unpaired t-test.

**(B)** TFIIB gene expression levels in adipose depots presented in Figures 3B-F. No significant difference between groups by one-way ANOVA.

**(C)** 18S rRNA expression levels in adipose depots presented in Figures 6B-E, 7B-E and 7G.

\*\*  $P < 0.01$ ; significant difference between cold and thermoneutral temperature.

# Supplementary Figure 2



Node label color	Node size (# genes)	Node color (p value)	Edge width (% shared genes)	Edge color (genes from input)
The node label color denotes the type of the gene sets:	207 genes	$p < 10^{48}$	1%	383
<b>neighborhood-based set</b>	1065 genes	$p < 10^{24}$	50%	191
<b>manually curated pathway</b>	5487 genes	$p = 1.0$	100%	0
<b>Gene Ontology category</b>				
<b>protein complex</b>				

**Supplementary Figure 2.** Visualization of the top 9 Gene Ontology pathways upregulated in IBAT of both physiologically humanized and long-term thermoneutral mice versus mice exposed to standard conditions. The numbers within the nodes denote how many of the 2401 commonly upregulated genes are found in each node. Pathways related to inflammation are highlighted in bold.

**Supplementary Table 1.** Primer sequences

<b>Gene</b>	<b>Forward (5' - 3')</b>	<b>Reverse (5' - 3')</b>
<i>Cx3cr1</i>	AAGTTCCCTTCCCATCTGCT	CAAAATTCTCTAGATCCAGTTCAGG
<i>Adgre1</i>	GGAGGACTTCTCCAAGCCTATT	AGGCCTCTCAGACTTCTGCTT
<i>Lgals3</i>	GCCTACCCCAAGTGCTCCT	GGTCATAGGGCACCCTCA
<i>Cd68</i>	CGGTGGAATACAATGTGTCCT	GATGAATTCTGCGCCATGA
<i>Fcgr1</i>	TGTGGCTTCTAACAACCTCTGCT	ACAGCCTTGGTGGCATTAAAC
<i>Tnfa</i>	TCTTCTCATTCTGCTTGTGG	GGTCTGGGCCATAGAACTGA
<i>Ccl2</i>	CATCCACGTGTTGGCTCA	GATCATCTTGCTGGTGAATGAGT
<i>Mrc1</i>	CAAACCTGGGGGAAAGGCTAT	TTGCCACCAATCACAACTACA
<i>Mrc2</i>	TACAGCTCCACGCTATGGATT	CACTCTCCCAGTTGAGGTACT
<i>Clec10a</i>	TGAGAAAGGCTTTAAGAACTGGG	GACCACCTGTAGTGATGTGGG
<i>Spp1</i>	CCCGGTGAAAGTGACTGATT	ATCTGGGTGGAGGCTGTAA
<i>Pgc1a</i>	GAAAGGGCCAAACAGAGAGA	GTAAATCACACGGCGCTCTT
<i>Ucp1</i>	GGCCTCTACGACTCAGTCCA	TAAGCCGGCTGAGATCTTGT
<i>Dio2</i>	CTGCGCTGTGTCTGGAAC	GGAATTGGGAGCATCTTCAC
<i>Elovl3</i>	GCCTCTCATCCTCTGGTCCT	TGCCATAAACTTCCACATCCT
<i>TH</i>	GCTACCGAGAGGACAGCATT	CACGGGCAGACAGTAGACC
<i>18S</i>	AGTCCCTGCCCTTTGTACACA	CGATCCGAGGGCCTCACTA
<i>TFIIB</i>	TGGAGATTTGTCCACCATGA	GAATTGCCAAACTCATCAAACT

**Supplementary Table 2.** A multiple linear regression analysis P values and  $\beta$  values for influence of age and temperature on the expression of thermogenesis-related and macrophage marker genes

Gene	P values		$\beta$ values	
	Age	temperature	age	temperature
<i>Ucp1</i>	< 0.01	< 0.01	-123.8	-120.7
<i>Pgc1a</i>	0.9918	< 0.001	0.00	-0.57
<i>Cx3cr1</i>	0.6107	0.1433	0.02	0.07
<i>Adgre1</i>	0.5440	< 0.05	0.28	1.19
<i>Lgals3</i>	0.7998	< 0.001	0.78	19.90
<i>Cd68</i>	0.7278	< 0.01	0.58	5.71
<i>Fcgr1</i>	0.9459	< 0.001	0.09	6.00
<i>Tnfa</i>	0.1963	< 0.001	0.14	0.45
<i>Ccl2</i>	0.9328	< 0.01	0.08	3.60
<i>Mrc1</i>	0.1436	< 0.05	0.47	0.81
<i>Mrc2</i>	< 0.05	< 0.05	0.29	-0.31
<i>Clec10a</i>	0.8919	< 0.01	0.11	2.26
<i>Spp1</i>	0.9950	<0.05	0.02	7.99