

Supplementary Table S1: Characteristics of brown bears included in the study

ID_number	Year of collection	Age (year)	Gender	Serum Lipidomic	Plasma	Adipose Tissue	Muscle	Muscle tissue RNA
w0825	2011	4	F		X			
w0904		3	F		X			
w1004		2	M		X			
w1011	2012	3	F	Mix1				
w1017		3	F					
w1104		2	F					
w1105		2	F					
w1110		2	F					
w1104	2013	3	F	Mix2				
w1105		3	F		X			
w1110		3	F		X			
w1204		2	M		X			
w1207		2	M		X			
w1209		2	F		X			
w1303	2014	2	F	Mix3				
w1304		2	F					X
w1305		2	F					
w1316		2	M					X
w1317		2	M			X		X
w1404	2016	3	M	Mix4		X	X	X
w1407		3	F			X		X
w1509		2	F				X	X
w1511		2	F					X
w1512		2	F					X
w1509	2017	3	F	Mix5		X		
w1601		2	M			X	X	
w1608		2	F					X
w1610		2	M					X
w1604	2018	3	F	Mix6		X		
w1701		2	F					
w1709		2	F					
w1710		2	F				X	
N = 28		2,4 ± 0,09	Sex ratio : 9M/26F	n = 6	n = 8	n = 6	n = 5	n = 8

A total of 28 bears were included in this study, and all were captured both in February during winter hibernation and in June during summer active period. Among them 4 bears (w1104, w1105, w1110 and w1509) were included two consecutive years. Samples were collected at the two time points and

all analysis were performed on winter and summer paired samples. For serum lipidomic analysis, serum from all bears captured in years 2012 to 2018 were pooled to obtain the 6 winter and summer mixes. Plasma, adipose tissue and muscle samples were obtained from individual bears for endocannabinoids quantification in plasma and tissues, as muscle samples for gene expression. N: number of bears, n: number of paired samples.

Supplementary Table S2: Serum fatty acids (FAs) concentrations (mmol/L) in winter hibernating (WBS) and summer active (SBS) bears.

Fatty acid	WBS	SBS	FC W/S	pvalue
14:0 (<i>myristic acid</i>)	0.41 ± 0.04	0.16 ± 0.01	2,57	4,31E-04
14:1 (<i>myristoleic acid</i>)	0.08 ± 0.01	0.02 ± 0.00	4,80	8,86E-04
15:0 (<i>pentadecanoic acid</i>)	0.07 ± 0.01	0.06 ± 0.01	1,12	1,68E-01
16:0 (<i>palmitic acid</i>)	6.99 ± 0.52	2.49 ± 0.17	2,80	1,13E-04
16:1 n-9 (<i>hypogeic acid</i>)	0.18 ± 0.02	0.17 ± 0.02	1,04	7,37E-01
16:1 n-7 (<i>palmitoleic acid</i>)	0.67 ± 0.06	0.22 ± 0.03	2,98	2,12E-05
18:0 (<i>stearic acid</i>)	3.79 ± 0.16	2.45 ± 0.14	1,54	3,91E-04
18:1 n-9c (<i>oleic acid</i>)	7.99 ± 0.63	4.70 ± 0.31	1,70	9,35E-04
18:1 n-7 (<i>vaccenic acid</i>)	0.89 ± 0.08	0.34 ± 0.03	2,62	3,81E-04
18:2 n-6c (<i>linoleic acid</i>)	4.04 ± 0.33	2.38 ± 0.17	1,70	6,74E-04
18:3 n-6 (<i>gamma-linolenic acid</i>)	0.05 ± 0.02	0.05 ± 0.01	1,10	7,05E-01
18:3 n-3 (<i>alpha-linolenic acid</i>)	0.15 ± 0.02	0.30 ± 0.06	0,49	7,35E-02
20:0 (<i>arachidonic acid</i>)	0.12 ± 0.01	0.11 ± 0.00	1,07	3,00E-01
20:1 n-9 (<i>gondoic acid</i>)	0.05 ± 0.01	0.04 ± 0.01	1,21	2,13E-01
20:2 n-6 (<i>eicosadienoic acid</i>)	0.32 ± 0.07	0.17 ± 0.05	1,91	3,00E-01
20:3 n-6 (<i>dihomo-gamma-linolenic acid</i>)	0.18 ± 0.01	0.09 ± 0.01	2,02	2,68E-02
20:4 n-6 (<i>arachidonic acid</i>)	1.86 ± 0.18	1.70 ± 0.26	1,09	1,94E-01
22:0 (<i>behenic acid</i>)	0.10 ± 0.01	0.06 ± 0.00	1,69	3,95E-03
22:1 n-9 (<i>erucic acid</i>)	0.02 ± 0.00	0.02 ± 0.00	1,32	3,39E-01
20:5 n-3 (<i>eicosapentaenoic acid</i>)	0.10 ± 0.02	0.38 ± 0.01	0,26	9,32E-03
22:5 n-3 (<i>docosapentaenoic acid</i>)	0.43 ± 0.05	0.16 ± 0.02	2,72	8,56E-04
22:6 n-3 (<i>docosahexaenoic acid</i>)	0.32 ± 0.07	0.08 ± 0.02	3,81	7,03E-03
24:0 (<i>lignoceric acid</i>)	0.11 ± 0.03	0.08 ± 0.03	1,47	7,37E-02
24:1 n-9 (<i>nervonic acid</i>)	0.21 ± 0.03	0.09 ± 0.02	2,48	1,15E-02
TOTAL	28.82 ± 1.71	15.99 ± 1.09	1,80	1,01E-04
<i>SFA</i>	11.59 ± 0.70	5.42 ± 0.31	2,14	1,15E-04
<i>MUFA</i>	10.09 ± 0.71	5.59 ± 0.33	1,80	3,36E-04
<i>PUFA</i>	7.14 ± 0.63	4.98 ± 0.57	1,43	5,21E-04
<i>n-3 FA</i>	0.94 ± 0.12	0.73 ± 0.14	1,30	8,19E-02
<i>n-6 FA</i>	6.20 ± 0.51	4.25 ± 0.45	1,46	2,09E-04

Lipidomic analysis were performed in bear serum as described in Material and Methods. Data are expressed in concentrations (mmol/L) of individual fatty acids. Data are represented as mean ± SEM of separate extractions and quantifications from the seven bear serum mixes. FC W/S : fold change from winter / summer ratios, MUFA : monounsaturated fatty acids, PUFA : polyunsaturated fatty acids, SBS : summer bear serum, SFA : saturated fatty acids, WBS : winter bear serum. Student t-test was used for season comparison and generation of p values (below 0.05 in bold).

Supplementary Table S3: Serum fatty acids (FAs) relative proportions (mol %) in winter hibernating (WBS) and summer active (SBS) bears.

Fatty acid	WBS	SBS	FC W/S	pvalue
14:0 (<i>myristic acid</i>)	1.38 ± 0.07	1.00 ± 0.09	1.38	8,82E-03
14:1 (<i>myristoleic acid</i>)	0.27 ± 0.02	0.11 ± 0.02	2.60	1,15E-03
15:0 (<i>pentadecanoic acid</i>)	0.24 ± 0.02	0.39 ± 0.02	0.62	3,40E-03
16:0 (<i>palmitic acid</i>)	24.18 ± 0.51	15.64 ± 0.45	1.55	1,91E-05
16:1 n-9 (<i>hypogeic acid</i>)	0.62 ± 0.06	1.08 ± 0.06	0.57	2,56E-03
16:1 n-7 (<i>palmitoleic acid</i>)	2.32 ± 0.13	1.42 ± 0.18	1.63	1,24E-04
18:0 (<i>stearic acid</i>)	13.22 ± 0.28	15.41 ± 0.45	0.86	1,71E-03
18:1 n-9c (<i>oleic acid</i>)	27.72 ± 1.47	29.52 ± 1.33	0.94	1,47E-01
18:1 n-7 (<i>vaccenic acid</i>)	3.12 ± 0.31	2.19 ± 0.27	1.42	8,47E-03
18:2 n-6c (<i>linoleic acid</i>)	14.08 ± 0.94	14.89 ± 0.44	0.95	3,66E-01
18:3 n-6 (<i>gamma-linolenic acid</i>)	0.18 ± 0.05	0.29 ± 0.03	0.61	2,40E-02
18:3 n-3 (<i>alpha-linolenic acid</i>)	0.50 ± 0.05	1.85 ± 0.38	0.27	1,47E-02
20:0 (<i>arachidonic acid</i>)	0.42 ± 0.02	0.71 ± 0.02	0.59	5,30E-06
20:1 n-9 (<i>gondoic acid</i>)	0.19 ± 0.03	0.28 ± 0.05	0.67	1,03E-01
20:2 n-6 (<i>eicosadienoic acid</i>)	1.05 ± 0.26	0.91 ± 0.14	1.15	7,85E-01
20:3 n-6 (<i>dihomo-gamma-linolenic acid</i>)	0.67 ± 0.04	0.63 ± 0.04	1.07	5,31E-01
20:4 n-6 (<i>arachidonic acid</i>)	6.41 ± 0.37	10.36 ± 0.81	0.62	9,45E-04
22:0 (<i>behenic acid</i>)	0.35 ± 0.03	0.38 ± 0.04	0.92	9,17E-02
22:1 n-9 (<i>erucic acid</i>)	0.08 ± 0.01	0.10 ± 0.00	0.78	2,92E-01
20:5 n-3 (<i>eicosapentaenoic acid</i>)	0.31 ± 0.03	2.14 ± 0.16	0.15	1,65E-02
22:5 n-3 (<i>docosapentaenoic acid</i>)	1.47 ± 0.08	0.97 ± 0.06	1.51	8,96E-04
22:6 n-3 (<i>docosahexaenoic acid</i>)	1.11 ± 0.22	0.51 ± 0.09	2.17	2,17E-02
24:0 (<i>lignoceric acid</i>)	0.41 ± 0.12	0.54 ± 0.21	0.77	2,89E-01
24:1 n-9 (<i>nervonic acid</i>)	0.76 ± 0.13	0.56 ± 0.12	1.35	1,01E-01
SFA	40.21 ± 0.46	34.08 ± 1.14	1,18	9,31E-04
MUFA	35.04 ± 1.52	35.22 ± 1.57	0,99	8,75E-01
PUFA	24.75 ± 1.42	30.70 ± 1.59	0,81	1,62E-03
n-3 FA	3.23 ± 0.29	4.40 ± 0.66	0,73	5,97E-02
n-6 FA	21.52 ± 1.17	26.30 ± 1.02	0,82	2,20E-03

Lipidomic analysis were performed in bear serum as described in Material and Methods. Data are expressed in molar percentage (mol %) of total circulating lipids, reflecting proportions of individual fatty acids. Data are represented as mean ± SEM of separate extractions and quantifications from the seven bear serum mixes. FC W/S : fold change from winter / summer ratios, MUFA : monounsaturated fatty acids, PUFA : polyunsaturated fatty acids, SBS : summer bear serum, SFA : saturated fatty acids, WBS : winter bear serum. Student t-test was used for season comparison and generation of p values (below 0.05 in bold).

Supplementary Table S4 : List of primers used for RT-qPCR

Gene		Primer
Ua.TBP	Forward	5'- AGACCATTGCACTTCGTGCC -3'
	Reverse	5'- CCTGTGCACACCATTTTCCC -3'
Ua.CNR1	Forward	5'- GTTGCCGAGGGAGCTTCTCC -3'
	Reverse	5'- TGTCGGCAAGGCCATCTAGG -3'
Ua.CNR2	Forward	5'- AACTCAACATGTCGGCAGCC -3'
	Reverse	5'- CCATACCCAGCGTCTCTCC -3'
Ua.NAPEPLD	Forward	5'- TTTGACCTTGCAGCTATTCC -3'
	Reverse	5'- GATTCTCCATGCTTCAAGAC -3'
Ua.FAAH	Forward	5'- AAGCAACATACCCCATGCTC -3'
	Reverse	5'- GGTCACGAAATCACCTTTG -3'
Ua.DAGLA	Forward	5'- CACGTGGTCCACAACCCACC -3'
	Reverse	5'- AGGTGCTCATGCAGCATGGC -3'
Ua.DAGLB	Forward	5'- GTGCTGCTGTGTCGGGAAGG -3'
	Reverse	5'- GGCACCAGATCTGTGTCTGA -3'
Ua.MGLL	Forward	5'- GCGTGCTCTCTCGGAATAAG -3'
	Reverse	5'- TTGCCGAAGCACACCTTCAG -3'