

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

ID_number	Year of collection	Age (year)	Gender	Serum		Plasma		Muscle Tissue		Adipose Tissue		Muscle tissue RNA		Adipose tissue RNA		
				S	W	S	W	S	W	S	W	S	W	S	W	
w0825	2011	4	F			X	X									
w0904		3	F			X	X									
w1004		2	M			X	X									
w1011	2012	3	F	Mix1	Mix1											
w1017		3	F													
w1104		2	F													
w1105		2	F													
w1110		2	F													
w1104	2013	3	F	Mix2	Mix2									X		
w1105		3	F			X	X									
w1110		3	F			X	X									X
w1204		2	M			X	X									X
w1207		2	M			X	X								X	X
w1209		2	F			X	X									X
w1303	2014	2	F	Mix3	Mix3										X	
w1304		2	F									X	X			
w1305		2	F													X
w1316		2	M									X	X			X
w1317		2	M								X	X	X	X		
w1404	2016	3	M	Mix4	Mix4			X	X	X	X	X	X	X	X	
w1407		3	F							X	X	X	X	X	X	
w1509		2	F					X	X			X	X	X	X	
w1511		2	F									X	X		X	
w1512		2	F									X	X			
w1509	2017	3	F	Mix5	Mix5					X	X					
w1601		2	M							X	X	X	X			X
w1608		2	F					X	X							X
w1610		2	M					X	X							X
w1604	2018	3	F	Mix6	Mix6					X	X					
w1701		2	F													
w1709		2	F													
w1710		2	F					X	X							
<b>N = 28</b>		<b>2,4 ± 0,09</b>	<b>Sex ratio : 9M/26F</b>	<b>n = 6</b>	<b>n = 6</b>	<b>n = 8</b>	<b>n = 8</b>	<b>n = 5</b>	<b>n = 5</b>	<b>n = 6</b>	<b>n = 6</b>	<b>n = 8</b>	<b>n = 8</b>	<b>n = 5</b>	<b>n = 13</b>	

A total of 28 bears were included in this study, and all were captured both in February during winter hibernation (W) and in June during summer active period (S). Among them 4 bears (w1104, w1105, w1110 and w1509) were included two consecutive years. Serum mixes were prepared as followed: for a given year, 50  $\mu$ l of summer serum from each bear of the year was pooled to obtain the summer mix. In parallel, 50  $\mu$ l of winter serum from the same bears was pooled to obtain the winter mix. A total of 6 summer and winter paired mixes were obtained. Plasma was collected at the two time points (S and W) from 8 individual animals. Muscle and adipose tissues collected at the two time points (S and W) from respectively 5 and 6 individual animals. Total RNAs were obtained from muscle and adipose tissues collected at the two time points (S and W). For the muscle tissue, RNAs were obtained from 8 individual animals, while for adipose tissue, RNAs were obtained from 5 bears in summer and 13 bears in winter (only 4 paired samples from individual animals). N: number of bears, n: number of samples.

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

Fatty acid	WBS	SBS	FC W/S	pvalue	Adjusted p value (BH)
<i>C14:0 (myristic acid)</i>	0.41 ± 0.04	0.16 ± 0.01	2.57	4.31E-04	<b>1.44E-03</b>
<i>C14:1 (myristoleic acid)</i>	0.08 ± 0.01	0.02 ± 0.00	4.80	8.86E-04	<b>2.00E-03</b>
<i>C15:0 (pentadecanoic acid)</i>	0.07 ± 0.01	0.06 ± 0.01	1.12	1.68E-01	2.19E-01
<i>C16:0 (palmitic acid)</i>	6.99 ± 0.52	2.49 ± 0.17	2.80	1.13E-04	<b>8.63E-04</b>
<i>C16:1 n-9 (hypogeic acid)</i>	0.18 ± 0.02	0.17 ± 0.02	1.04	7.37E-01	7.37E-01
<i>C16:1 n-7 (palmitoleic acid)</i>	0.67 ± 0.06	0.22 ± 0.03	2.98	2.12E-05	<b>6.36E-04</b>
<i>C18:0 (stearic acid)</i>	3.79 ± 0.16	2.45 ± 0.14	1.54	3.91E-04	<b>1.44E-03</b>
<i>C18:1 n-9 (oleic acid)</i>	7.99 ± 0.63	4.70 ± 0.31	1.70	9.35E-04	<b>2.00E-03</b>
<i>C18:1 n-7 (vaccenic acid)</i>	0.89 ± 0.08	0.34 ± 0.03	2.62	3.81E-04	<b>1.44E-03</b>
<i>C18:2 n-6 (linoleic acid)</i>	4.04 ± 0.33	2.38 ± 0.17	1.70	6.74E-04	<b>1.84E-03</b>
<i>C18:3 n-6 (gamma-linolenic acid)</i>	0.05 ± 0.02	0.05 ± 0.01	1.10	7.05E-01	7.29E-01
<i>C18:3 n-3 (alpha-linolenic acid)</i>	0.15 ± 0.02	0.30 ± 0.06	0.49	7.35E-02	1.05E-01
<i>C20:0 (arachidic acid)</i>	0.12 ± 0.01	0.11 ± 0.00	1.07	3.00E-01	3.33E-01
<i>C20:1 n-9 (gondoic acid)</i>	0.05 ± 0.01	0.04 ± 0.01	1.21	2.13E-01	2.56E-01
<i>C20:2 n-6 (eicosadienoic acid)</i>	0.32 ± 0.07	0.17 ± 0.05	1.91	3.00E-01	3.33E-01
<i>C20:3 n-6 (dihomo-gamma-linolenic acid)</i>	0.18 ± 0.01	0.09 ± 0.01	2.02	2.68E-02	<b>4.23E-02</b>
<i>C20:4 n-6 (arachidonic acid)</i>	1.86 ± 0.18	1.70 ± 0.26	1.09	1.94E-01	2.43E-01
<i>C20:5 n-3 (eicosapentaenoic acid)</i>	0.10 ± 0.02	0.38 ± 0.01	0.26	9.32E-03	<b>1.64E-02</b>
<i>C22:0 (behenic acid)</i>	0.10 ± 0.01	0.06 ± 0.00	1.69	3.95E-03	<b>7.90E-03</b>
<i>C22:1 n-9 (erucic acid)</i>	0.02 ± 0.00	0.02 ± 0.00	1.32	3.39E-01	3.63E-01
<i>C22:5 n-3 (docosapentaenoic acid)</i>	0.43 ± 0.05	0.16 ± 0.02	2.72	8.56E-04	<b>2.00E-03</b>
<i>C22:6 n-3 (docosahexaenoic acid)</i>	0.32 ± 0.07	0.08 ± 0.02	3.81	7.03E-03	<b>1.32E-02</b>
<i>C24:0 (lignoceric acid)</i>	0.11 ± 0.03	0.08 ± 0.03	1.47	7.37E-02	1.05E-01
<i>C24:1 n-9 (nervonic acid)</i>	0.21 ± 0.03	0.09 ± 0.02	2.48	1.15E-02	<b>1.92E-02</b>
<b>TOTAL</b>	<b>28.82 ± 1.71</b>	<b>15.99 ± 1.09</b>	<b>1.80</b>	1.01E-04	<b>8.63E-04</b>
SFA	11.59 ± 0.70	5.42 ± 0.31	2.14	1.15E-04	<b>8.63E-04</b>
MUFA	10.09 ± 0.71	5.59 ± 0.33	1.80	3.36E-04	<b>1.44E-03</b>
PUFA	7.14 ± 0.63	4.98 ± 0.57	1.43	5.21E-04	<b>1.56E-03</b>
n-3 PUFA	0.94 ± 0.12	0.73 ± 0.14	1.30	8.19E-02	1.12E-01
n-6 PUFA	6.20 ± 0.51	4.25 ± 0.45	1.46	2.09E-04	<b>1.25E-03</b>

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 twelve 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. **Paired Student t-test** was used for season comparison and generation of p values. **The Benjamini-Hochberg (BH) correction for multiple comparison was used to obtain the adjusted p values** (below 0.05 in bold).

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

Fatty acid	WBS	SBS	FC W/S	p value	Adjusted p value (BH)
<b>C14:0</b> ( <i>myristic acid</i> )	1.38 ± 0.07	1.00 ± 0.09	1.38	8.82E-03	<b>1.76E-02</b>
<b>C14:1</b> ( <i>myristoleic acid</i> )	0.27 ± 0.02	0.11 ± 0.02	2.60	1.15E-03	<b>4.93E-03</b>
<b>C15:0</b> ( <i>pentadecanoic acid</i> )	0.24 ± 0.02	0.39 ± 0.02	0.62	3.40E-03	<b>8.50E-03</b>
<b>C16:0</b> ( <i>palmitic acid</i> )	24.18 ± 0.51	15.64 ± 0.45	1.55	1.91E-05	<b>2.87E-04</b>
<b>C16:1 n-9</b> ( <i>hypogeic acid</i> )	0.62 ± 0.06	1.08 ± 0.06	0.57	2.56E-03	<b>6.98E-03</b>
<b>C16:1 n-7</b> ( <i>palmitoleic acid</i> )	2.32 ± 0.13	1.42 ± 0.18	1.63	1.24E-04	<b>1.24E-03</b>
<b>C18:0</b> ( <i>stearic acid</i> )	13.22 ± 0.28	15.41 ± 0.45	0.86	1.71E-03	<b>5.70E-03</b>
<b>C18:1 n-9</b> ( <i>oleic acid</i> )	27.72 ± 1.47	29.52 ± 1.33	0.94	1.47E-01	1.84E-01
<b>C18:1 n-7</b> ( <i>vaccenic acid</i> )	3.12 ± 0.31	2.19 ± 0.27	1.42	8.47E-03	<b>1.76E-02</b>
<b>C18:2 n-6</b> ( <i>linoleic acid</i> )	14.08 ± 0.94	14.89 ± 0.44	0.95	3.66E-01	4.07E-01
<b>C18:3 n-6</b> ( <i>gamma-linolenic acid</i> )	0.18 ± 0.05	0.29 ± 0.03	0.61	2.40E-02	<b>3.79E-02</b>
<b>C18:3 n-3</b> ( <i>alpha-linolenic acid</i> )	0.50 ± 0.05	1.85 ± 0.38	0.27	1.47E-02	<b>2.76E-02</b>
<b>C20:0</b> ( <i>arachidic acid</i> )	0.42 ± 0.02	0.71 ± 0.02	0.59	5.30E-06	<b>1.59E-04</b>
<b>C20:1 n-9</b> ( <i>gondoic acid</i> )	0.19 ± 0.03	0.28 ± 0.05	0.67	1.03E-01	1.34E-01
<b>C20:2 n-6</b> ( <i>eicosadienoic acid</i> )	1.05 ± 0.26	0.91 ± 0.14	1.15	7.85E-01	8.12E-01
<b>C20:3 n-6</b> ( <i>dihomo-gamma-linolenic acid</i> )	0.67 ± 0.04	0.63 ± 0.04	1.07	5.31E-01	5.69E-01
<b>C20:4 n-6</b> ( <i>arachidonic acid</i> )	6.41 ± 0.37	10.36 ± 0.81	0.62	9.45E-04	<b>4.73E-03</b>
<b>C20:5 n-3</b> ( <i>eicosapentaenoic acid</i> )	0.31 ± 0.03	2.14 ± 0.16	0.15	1.65E-02	<b>2.91E-02</b>
<b>C22:0</b> ( <i>behenic acid</i> )	0.35 ± 0.03	0.38 ± 0.04	0.92	9.17E-02	1.31E-01
<b>C22:1 n-9</b> ( <i>erucic acid</i> )	0.08 ± 0.01	0.10 ± 0.00	0.78	2.92E-01	3.37E-01
<b>C22:5 n-3</b> ( <i>docosapentaenoic acid</i> )	1.47 ± 0.08	0.97 ± 0.06	1.51	8.96E-04	<b>4.73E-03</b>
<b>C22:6 n-3</b> ( <i>docosahexaenoic acid</i> )	1.11 ± 0.22	0.51 ± 0.09	2.17	2.17E-02	<b>3.62E-02</b>
<b>C24:0</b> ( <i>lignoceric acid</i> )	0.41 ± 0.12	0.54 ± 0.21	0.77	2.89E-01	3.37E-01
<b>C24:1 n-9</b> ( <i>nervonic acid</i> )	0.76 ± 0.13	0.56 ± 0.12	1.35	1.01E-01	1.34E-01
SFA	40.21 ± 0.46	34.08 ± 1.14	1.18	9.31E-04	<b>4.73E-03</b>
MUFA	35.04 ± 1.52	35.22 ± 1.57	0.99	8.75E-01	8.75E-01
PUFA	24.75 ± 1.42	30.70 ± 1.59	0.81	1.62E-03	<b>5.70E-03</b>
n-3 PUFA	3.23 ± 0.29	4.40 ± 0.66	0.73	5.97E-02	8.96E-02
n-6 PUFA	21.52 ± 1.17	26.30 ± 1.02	0.82	2.20E-03	<b>6.60E-03</b>
DHA/AA	0.17 ± 0.03	0.05 ± 0.01	3.44	3.80E-03	<b>8.77E-03</b>

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 twelve 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. Paired Student t-test was used for season comparison and generation of p values. The Benjamini-Hochberg (BH) correction for multiple comparison was used to obtain the adjusted 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'- CACGTGGTCCACAACCACCC -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'

**Supplementary Table S5 : Endocannabinoids (eCBs) and mRNA quantification in plasma and tissues in winter hibernating (W) and summer active (S) bears.**

<b><i>eCBs in plasma (ng/mL)</i></b>				
	<b>WBP</b>	<b>SBP</b>	<b>FC W/S</b>	<b>p value</b>
AEA	0,66 ± 0,06	1,06 ± 0,14	0,63	<b>1,14E-02</b>
2-AG	6,20 ± 0,51	6,67 ± 0,74	0,93	6,10E-01
OEA	24,02 ± 2,06	7,35 ± 1,09	3,27	<b>3,18E-04</b>
<b><i>eCBs in muscle tissue (pg/mg tissue)</i></b>				
	<b>WBM</b>	<b>SBM</b>	<b>FC W/S</b>	<b>p value</b>
AEA	0,58 ± 0,07	1,56 ± 0,38	0,37	6,45E-02
2-AG	28,05 ± 1,20	45,46 ± 2,67	0,62	<b>4,87E-03</b>
OEA	15,18 ± 1,06	16,55 ± 2,97	0,92	5,89E-01
<b><i>eCBs in adipose tissue (pg/mg tissue)</i></b>				
	<b>WBA</b>	<b>SBA</b>	<b>FC W/S</b>	<b>p value</b>
AEA	0,70 ± 0,06	1,58 ± 0,36	0,44	6,92E-02
2-AG	14,56 ± 0,90	129,89 ± 33,09	0,11	<b>1,69E-02</b>
OEA	12,87 ± 1,39	12,63 ± 3,29	1,02	9,40E-01
<b><i>Gene expression in muscle tissue (normalized to TBP)</i></b>				
	<b>WBM</b>	<b>SBM</b>	<b>FC W/S</b>	<b>p value</b>
CNR1	0.63 ± 0.15	1.00 ± 0.15	0,63	<b>3,40E-02</b>
CNR2	1.07 ± 0.23	1.00 ± 0.15	1,07	7,98E-01
FAAH	2.32 ± 0.45	1.00 ± 0.13	2,32	<b>1,23E-02</b>
MGLL	1.11 ± 0.13	1.00 ± 0.10	1,11	5,09E-01
DAGLA	0.41 ± 0.06	1.00 ± 0.23	0,45	<b>2,72E-02</b>
DAGLB	1.54 ± 0.14	1.00 ± 0.14	1,54	<b>1,07E-02</b>
NAPEPLD	0.77 ± 0.06	1.00 ± 0.11	0,77	7,03E-02
<b><i>Gene expression in adipose tissue (normalized to TBP)</i></b>				
	<b>WBA</b>	<b>SBA</b>	<b>FC W/S</b>	<b>p value</b>
CNR1	1.65 ± 0.39	1.00 ± 0.31	1,65	3,39E-01
CNR2	0.42 ± 0.05	1.00 ± 0.23	0,42	<b>2,24E-03</b>
FAAH	0.75 ± 0.10	1.00 ± 0.25	0,75	2,85E-01
MGLL	1.40 ± 0.15	1.00 ± 0.21	1,40	1,78E-01
DAGLA	0.94 ± 0.11	1.00 ± 0.24	0,94	8,12E-01
DAGLB	1.43 ± 0.06	1.00 ± 0.09	1,44	<b>2,08E-03</b>
NAPEPLD	0.75 ± 0.06	1.00 ± 0.07	0,75	<b>3,25E-02</b>

Quantification were performed as described in the Methods section. Data are expressed as Mean ± SEM. For gene expression, mRNA levels were normalized to TBP expression then expressed related to the summer values. Season differences were assessed using the Student paired t-test, except for gene expression in adipose tissue where unpaired t-test were used, and p values are reported.