



**Supplementary Figure S1.** Different eCBome tone in the jejunum and the ileum of ob/ob and db/db mice. **(A)** Concentrations of the eCBome-related mediators in the jejunum and ileum, respectively (fmol/mg wet tissue weight), measured by HPLC-MS/MS. **(B)** mRNA expression of receptors and metabolic enzymes for 2-monoacylglycerols and N-acylethanolamines in the jejunum and the ileum, respectively, measured by qPCR-based TaqMan Open Array. Data are presented as the mean  $\pm$  S.E.M of  $n=7-10$ . \*  $P \leq 0.05$ , \*\*  $P \leq 0.01$ , \*\*\*  $P \leq 0.005$ , \*\*\*\*  $P \leq 0.001$ . For mRNA expression, relative units were calculated versus the mean of the CT ob mice values set at 1. Data were analyzed by one-way ANOVA followed by Tukey's post hoc test. Abbreviations: see supplementary Table S1 and Table S2.

**Supplementary Table S1.** Endocannabinoid and related lipid mediator abbreviations.

<b>Symbol</b>	<b>Endocannabinoids name</b>
<b>2-AG</b>	1(3)- and 2-arachidonoyl-glycerol
<b>AEA</b>	<i>N</i> -arachidonoyl-ethanolamine
<b>DHEA</b>	<i>N</i> -docosahexanoyl-ethanolamine
<b>2-DHG</b>	1(3)- and 2-docosahexaenoyl-glycerol
<b>DPA</b>	docosapentaenoic acid (n-3)
<b>2-DPG</b>	1(3)- and 2-docospentaenoyl-glycerol (n-3)
<b>EPEA</b>	<i>N</i> -eicosapentanoyl-ethanolamine
<b>EPA</b>	eicosapentaenoic acid
<b>2-EPG</b>	2-eicosapentaenoyl-glycerol
<b>15-HEPE</b>	15-hydroxyeicosapentaenoic acid
<b>18-HEPE</b>	18-hydroxyeicosapentaenoic acid
<b>13-HODE</b>	13-hydroxyoctadecadienoic acid
<b>13-HODE-G</b>	13-hydroxyoctadecadienoyl-glycerol
<b>11-HETE</b>	11-hydroxyeicosatetraenoic acid
<b>13(S)-HOTre</b>	13S-hydroxy-9Z,11E,15Z-octadecatrienoic acid
<b>12-HEPE</b>	12-hydroxyeicosapentaenoic acid
<b>15-HEPE</b>	15-hydroxyeicosapentaenoic acid
<b>14-HDHA</b>	14-hydroxydocosahexaenoic acid
<b>17-HDHA</b>	14-hydroxydocosahexaenoic acid
<b>LA</b>	Linoleic acid
<b>LEA</b>	<i>N</i> -linoleoyl-ethanolamine
<b>2-LG</b>	1(3)- and 2-linoleoyl-glycerol
<b>SEA</b>	<i>N</i> -stearoyl-ethanolamine
<b>OEA</b>	<i>N</i> -oleoyl-ethanolamine
<b>2-OG</b>	1(3)- and 2-oleoyl-glycerol
<b>PEA</b>	<i>N</i> -palmitoyl-ethanolamine
<b>2-PG</b>	2-palmitoyl-glycerol
<b>NAGly</b>	<i>N</i> -arachidonoyl glycine
<b>PGD<sub>2</sub></b>	Prostaglandin D <sub>2</sub>
<b>PGE<sub>2</sub></b>	Prostaglandin E <sub>2</sub>

**Supplementary Table S2.** List of the genes analyzed by qPCR based TaqMan Open Array and their function.

<b>Gene symbol</b>	<b>Gene name</b>	<b>Function</b>
<i>Cacna1b</i>	calcium channel, voltage-dependent, T type, alpha 1B subunit	receptor
<i>Cacna1h</i>	calcium channel, voltage-dependent, T type, alpha 1H subunit	receptor
<i>Cnr1</i>	cannabinoid receptor 1	receptor
<i>Cnr2</i>	cannabinoid receptor 2	receptor
<i>Gpr119</i>	G protein-coupled receptor 119	receptor
<i>Gpr18</i>	G protein-coupled receptor 18	receptor
<i>Gpr55</i>	G protein-coupled receptor 55	receptor
<i>Ppara</i>	peroxisome proliferator activated receptor alpha	receptor
<i>Pparg</i>	peroxisome proliferator activated receptor gamma	receptor
<i>Ptgfr</i>	prostaglandin F receptor	receptor
<i>Trpv1</i>	transient receptor potential cation channel, subfamily V, member 1	ligand-activated channel
<i>Trpv2</i>	transient receptor potential cation channel, subfamily V, member 2	ligand-activated channel
<i>Trpv4</i>	transient receptor potential cation channel, subfamily V, member 4	ligand-activated channel
<i>Abhd4</i>	abhydrolase domain containing 4	anabolic enzyme for NAEs
<i>Akr1b3</i>	aldo-keto reductase family 1, member B3 (aldose reductase)	anabolic enzyme for prostamides, catabolic enzyme for AEA and 2-AG
<i>Fam213b</i>	family with sequence similarity 213, member B	anabolic enzyme for prostamides, catabolic enzyme for AEA and 2-AG
<i>Gde1</i>	glycerophosphodiester phosphodiesterase 1	anabolic enzyme for NAEs
<i>Gdpd1</i>	glycerophosphodiester phosphodiesterase domain containing 1	anabolic enzyme for NAEs
<i>Hrasls5</i>	HRAS-like suppressor family, member 5	anabolic enzyme for NAEs
<i>Inpp5d</i>	inositol polyphosphate-5-phosphatase D	anabolic enzyme for NAEs
<i>Napepld</i>	N-acyl phosphatidylethanolamine-specific phospholipase D-like enzyme	anabolic enzyme for NAEs
<i>Pla2g5</i>	phospholipase A2, group V	AA-releasing enzyme possibly involved in phospholipid remodeling and hence biosynthesis of eCB precursors
<i>Ptgs2</i>	prostaglandin-endoperoxide synthase 2	anabolic enzyme for prostamides, catabolic enzyme for AEA and 2-AG
<i>Ptpn22</i>	protein tyrosine phosphatase, non-receptor type 22 (lymphoid)	anabolic enzyme for AEA
<i>Ptges</i>	prostaglandin E synthase	anabolic enzyme for prostamides, catabolic enzyme for AEA and 2-AG
<i>Comt</i>	catechol-O-methyltransferase	catabolic enzyme for N-acyl-dopamines
<i>Faah</i>	fatty acid amide hydrolase	catabolic enzyme for NAEs, primary fatty acid amides, N-acyl-taurines and N-acyl-glycines
<i>Naaa</i>	N-acylethanolamine acid amidase	catabolic enzyme for saturated NAEs
<i>Pam</i>	peptidylglycine alpha-amidating monooxygenase	anabolic enzyme for primary fatty acid amides, catabolic enzyme for N-acyl-glycines
<i>Dagla</i>	diacylglycerol lipase, alpha	anabolic enzyme for 2-acylglycerols

<b><i>Daglb</i></b>	diacylglycerol lipase, beta	anabolic enzyme for 2-acylglycerols
<b><i>Dgke</i></b>	diacylglycerol kinase, epsilon	anabolic/catabolic enzyme for 2-acylglycerols
<b><i>Enpp2</i></b>	ectonucleotide pyrophosphatase/phosphodiesterase 2	autotaxin- a LysoPLD: produces LPA.
<b><i>Pla1a</i></b>	phospholipase A1 member A	anabolic enzyme for 2-acylglycerols
<b><i>Plcb1</i></b>	phospholipase C, beta 1	anabolic enzyme for 2-acylglycerols
<b><i>Abhd12</i></b>	abhydrolase domain containing 12	catabolic enzyme for monacylglycerols
<b><i>Abhd16a</i></b>	abhydrolase domain containing 16	catabolic enzyme for monacylglycerols
<b><i>Abhd6</i></b>	abhydrolase domain containing 6	catabolic enzyme for monacylglycerols
<b><i>Agk</i></b>	acylglycerol kinase	catabolic enzyme for monacylglycerols
<b><i>Alox12</i></b>	arachidonate 12-lipoxygenase	catabolic enzyme for AEA and 2-AG
<b><i>Alox15</i></b>	arachidonate 15-lipoxygenase	catabolic enzyme for AEA and 2-AG
<b><i>Ces1d</i></b>	carboxylesterase 1D	catabolic enzyme for monoacylglycerols
<b><i>Ces2h</i></b>	carboxylesterase 2H	catabolic enzyme for monoacylglycerols
<b><i>Mgl1 (Magl)</i></b>	monoglyceride lipase	catabolic enzyme for monoacylglycerols
<b><i>Mogat1</i></b>	monoacylglycerol O-acyltransferase 1	catabolic enzyme for monoacylglycerols
<b><i>Ppt1</i></b>	palmitoyl-protein thioesterase 1	catabolic enzyme for 2-AG
<b><i>Gapdh</i></b>	glyceraldehyde-3-phosphate dehydrogenase	reference gene
<b><i>Hprt</i></b>	hypoxanthine guanine phosphoribosyl transferase	reference gene
<b><i>Rps13</i></b>	ribosomal protein S13	reference gene
<b><i>Tbp</i></b>	TATA box binding protein	reference gene

**Supplementary Table S3.** qPCR primer sequences for the targeted mouse genes.

Gene symbol	Gene name	Forward Primer sequence (5'-3')	Reverse Primer sequence (5'-3')
<i>Rorgt2</i>	Retinoid orphan receptor gamma t	GAAATGTTGTTGACCCCTCT	TCATACCCAAACCCCATAAAC
<i>Il17a</i>	Interleukin 17a	AAGGCCCTCAGACTACCTCAA	TTCCCAGATCACAGAGGGATATCTA
<i>Rpl19</i>	Ribosomal Protein L19	GAAGGTCAAAGGGAATGTGTTCA	CCTTGTCTGCCTTCAGCTTGT