

**Table S1.** Oligonucleotides for real-time RT-PCR.

<b>mRNA targets</b>	<b>Descriptions</b>	<b>Sense</b>	<b>Antisense</b>
<i>NOX-1</i>	NOX-1 subunit of NADPH oxidase	TCTTGCTGGTTGACACTGC	TATGGGAGTGGGAATCTTG
<i>NOX-4</i>	NOX-4 subunit of NADPH oxidase	ACAGTCTGGCTTACCTTCG	TTCTGGGATCCTCATTCTGG
<i>p22phox</i>	p22phox subunit of NADPH oxidase	GCGGTGTGGACAGAAGTACC	CTTGGGTTTAGGCTCAATGG
<i>p47phox</i>	p47phox subunit of NADPH oxidase	CCCAGCGACAGATTAGAAGC	TGGATTGCCTTTGAGTCAGG
<i>Occludin</i>	occludin	AGCCTGGGCAGTCGGGTTGA	ACACAGACCCAGAGCGGCA
<i>ZO-1</i>	zonula occludens-1	GCCAGCCAGTCCGCCTCTG	AGGGTCCC GGTTGGTG
<i>MUC-2</i>	Mucin 2	CGATCACCACCATTGCCACTG	ACCACCATTACCACCACCTCAG
<i>MUC-3</i>	Mucin 3	CACAAAGGCAAGAGTCCAGA	ACTGTCCTTGGTGTCTGAATG
<i>IL18</i>	Interleukin 18	ACCGCAGTAATACGGAGCAT	CAGTCTGGTCTGGGATTCGT
<i>MCT1</i>	Monocarboxylate transporter 1	GAAAACTCAAGTCCAAGAGTCT	TTTCATTGTCTTCTGGGCTTCT
<i>MCT4</i>	Monocarboxylate transporter 4	TCAGGAGGCAAGCTGCTGGACGCAA	AGTTGCCAGCAGCAGCACAAAGGA
<i>TLR-4</i>	toll-like receptor-4	GCCTTTCAGGGAATTAAGTCC	AGATCAACCGATGGACGTGTAA
<i>GAPDH</i>	Glyceraldehyde-3-Phosphate Dehydrogenase	GTCGGTGTGAACGGATTT	ATGGGTTTCCCGTTGATG

**Table S2.** Body and organ weights and cardiac and renal indices.

	<b>WKY</b>	<b>SHR</b>	<b>LC40</b>	<b>BFM</b>	<b>Butyrate</b>	<b>Acetate</b>
	<b>(n = 10)</b>	<b>(n = 10)</b>	<b>(n = 10)</b>	<b>(n = 10)</b>	<b>(n = 10)</b>	<b>(n = 10)</b>
<b>BW (g)</b>	402.0 ± 9.4	405.7 ± 8.9	387.9 ± 17.2	373.0 ± 15.3	395.4 ± 11.4	374.6 ± 14.4
<b>HW (g)</b>	1.12 ± 0.03	1.26 ± 0.04**	1.25 ± 0.04	1.17 ± 0.03	1.26 ± 0.03	1.19 ± 0.7
<b>LVW (g)</b>	0.76 ± 0.02	0.94 ± 0.02**	0.90 ± 0.03	0.87 ± 0.02#	0.92 ± 0.02	0.87 ± 0.05
<b>KW (g)</b>	1.26 ± 0.05	1.21 ± 0.03	1.22 ± 0.07	1.16 ± 0.04	1.18 ± 0.02	1.16 ± 0.06
<b>HW/TL (mg/cm)</b>	206 ± 5	244 ± 5**	235 ± 6	222 ± 4#	231 ± 4#	224 ± 7#
<b>LVW/TL (mg/cm)</b>	143 ± 4	180 ± 4*	167 ± 4#	165 ± 4##	168 ± 3#	166 ± 6#
<b>KW/TL (mg/cm)</b>	238 ± 8	228 ± 6	232 ± 11	220 ± 7	223 ± 4	224 ± 9

BW, body weight; HW, heart weight; LVW, left ventricle weight; KW, kidney weight, TL, Tibia length. Values are expressed as mean ± SEM of n rats. # P<0,05 y ##P<0,01 vs WKY y \*P<0,05 vs SHR-control.

**Table S3.** Effects of *Lactobacillus fermentum* CECT5716 (LC40), *Bifidobacterium breve* CECT7263 (BFM), acetate and butyrate treatments in spontaneously hypertensive rats (SHR) on phyla changes in the gut microbiota.

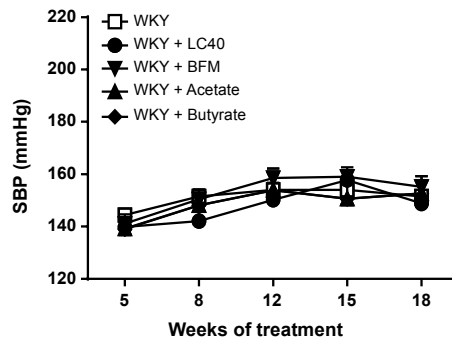
	WKY	SHR	LC40	BFM	Butyrate	Acetate
Phylum	(n = 6)	(n = 5)	(n = 6)	(n = 6)	(n = 5)	(n = 5)
<b>Tenericutes</b>	0.5 ± 0.2	0.7 ± 0.3	0.3 ± 0.2	0.3 ± 0.1	0.6 ± 0.2	0.4 ± 0.2
<b>Actinobacteria</b>	0.1 ± 0.0	0.3 ± 0.2	0.3 ± 0.1	0.2 ± 0.1	0.1 ± 0.0	0.1 ± 0.1
<b>Verrucomicrobia</b>	0.4 ± 0.2	0.4 ± 0.1	0.5 ± 0.5	0.1 ± 0.0#	0.6 ± 0.5	0.9 ± 0.5
<b>Proteobacteria</b>	0.6 ± 0.2	0.6 ± 0.2	0.4 ± 0.1	0.7 ± 0.2	0.4 ± 0.1	1.3 ± 0.6
<b>Bacteroidetes</b>	36.1 ± 2.5	22.8 ± 2.4**	30.6 ± 4.4	36.6 ± 5.5#	37.7 ± 4.5#	38.5 ± 5.5#
<b>Firmicutes</b>	61.0 ± 2.5	72.3 ± 2.9*	67.7 ± 4.5	61.6 ± 5.3	60.5 ± 4.6#	58.0 ± 5.1#
<b>Cyanobacteria</b>	0.0 ± 0.0	0.1 ± 0.0	0.0 ± 0.0#	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
<b>Others</b>	1.2 ± 0.6	2.7 ± 1.4	0.2 ± 0.1	0.5 ± 0.3	0.0 ± 0.0	0.6 ± 0.6

Values are expressed as mean ± SEM. \*P< 0.05 and \*\*P<0.01 compared with the Wistar Kyoto (WKY) group. #P< 0.05 compared with the non-treated SHR group.

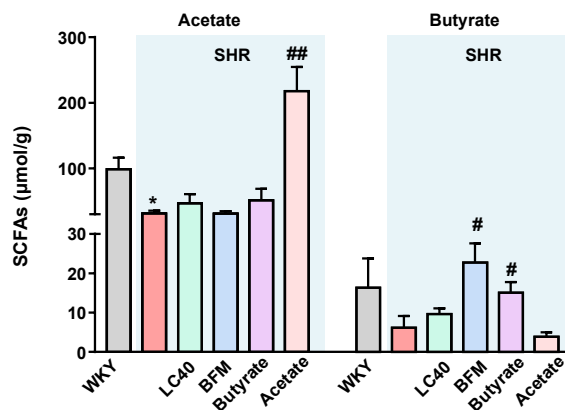
**Table S4.** Effects of *Lactobacillus fermentum* CECT5716 (LC40), *Bifidobacterium breve* CECT7263 (BFM), acetate and butyrate treatments in spontaneously hypertensive rats (SHR) on plasma metabolites expressed as relative units.

	WKY	SHR	LC40	BFM	Butyrate	Acetate
Phylum	(n = 10)	(n = 10)	(n = 9)	(n = 10)	(n = 10)	(n = 10)
Valine+Propionate	64.3±6.3	79.3±3.2*	77.2±6.2	75.1±4.0	83.4±4.3	76.4±3.71
Leucine	58.9±5.4	72.7±2.4*	70.4±3.6	68.5±3.2	73.7±2.9	68.2±3.5
Creatinine	20.8±1.7	25.6±1.2*	27.9±3.2	25.8±1.1	31.0±2.4#	28.9±2.5
Glucose	102.6±5.5	145.8±7.3**	143.2±10.3	137.9±4.5	146.0±5.8	152.1±9.0
Phenylalanine	2.2±0.5	3.6±0.2*	2.6±0.5#	2,4±0.6#	2.9±0.6	2,9±0.7
-(CH <sub>2</sub> )n-	22.6±1.7	18.5±1.2*	18.5±1.0	22.0±1.2	18.6±1.0	18.8±0.9
-CH <sub>2</sub> -CH <sub>2</sub> -CH=CH-	51.7±4.5	39.9±2.5*	39.2±3.4	39.4±1.4	37.7±2.2	37.6±5.8
-CH=CH-CH <sub>2</sub> -CH=CH-	23.3±2.3	17.9±1.4*	17.6±2.0	17.4±1.0	15.8±1.3	14.5±1.7

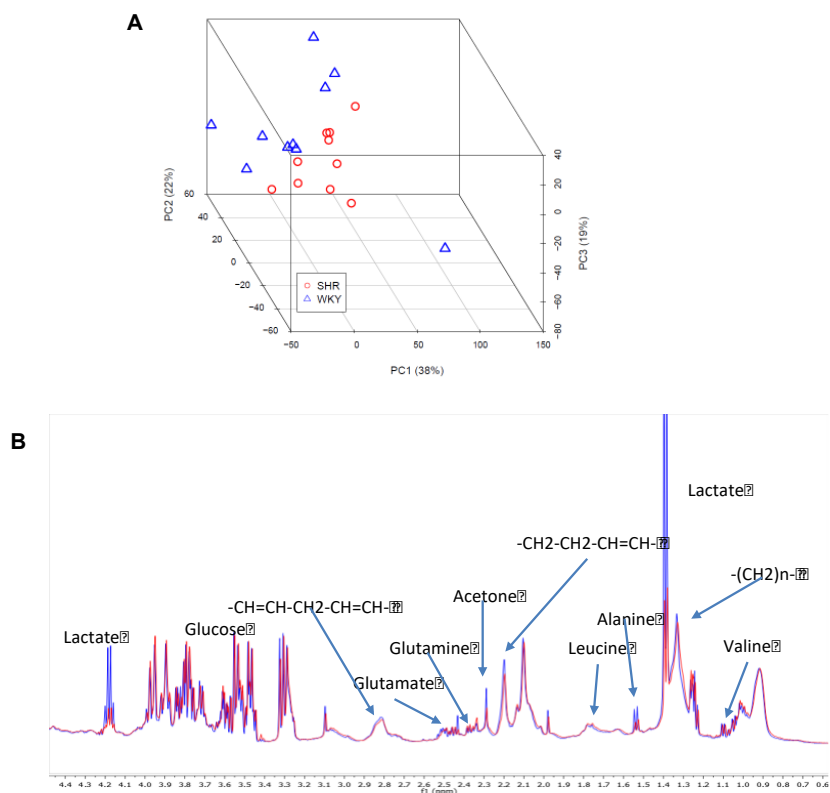
Values are expressed as mean ± SEM. \*P< 0.05 and \*\*P<0.01 compared with the Wistar Kyoto (WKY) group. #P< 0.05 compared with the non-treated SHR group.



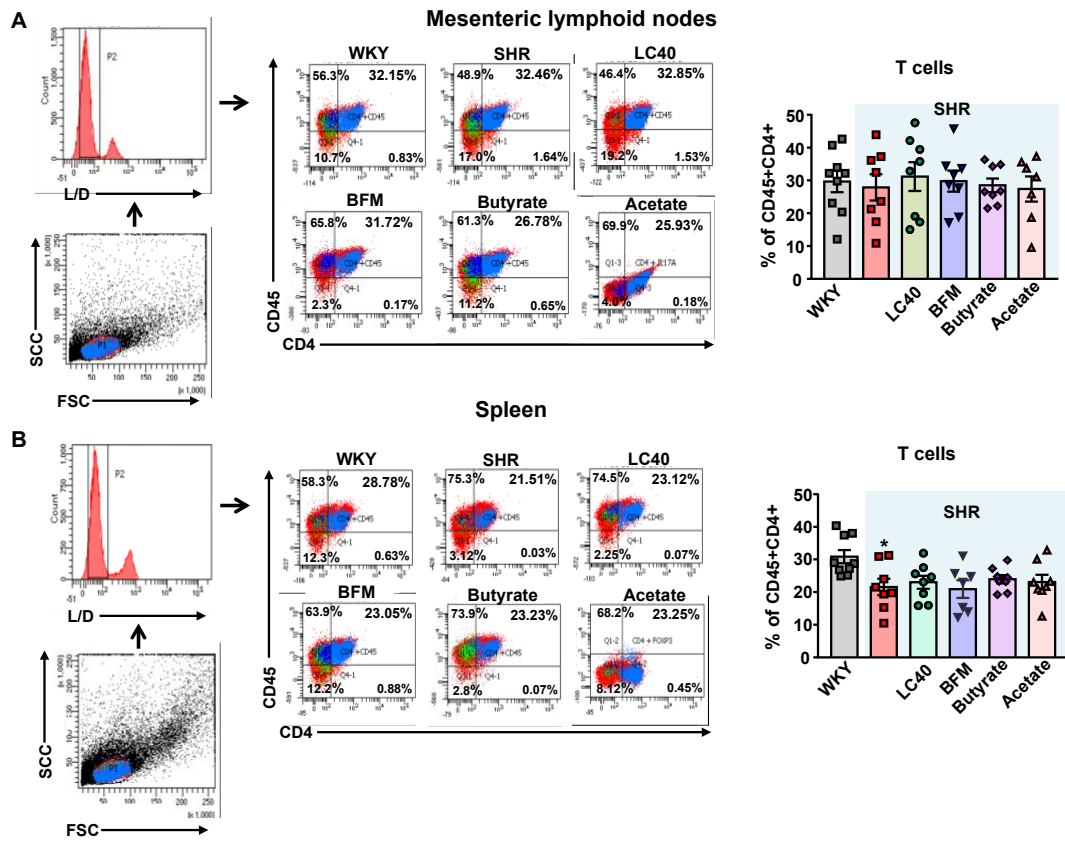
**Figure S1.** Effects Probiotic treatments in blood pressure in Wistar Kyoto rats (WKY). Time course of systolic blood pressure (SBP), measured by tail-cuff plethysmography in all experimental groups. Results are shown as mean  $\pm$  SEM (n = 6). LC40, *Lactobacillus fermentum* CECT5716; BFM, *Bifidobacterium breve* CECT7263.



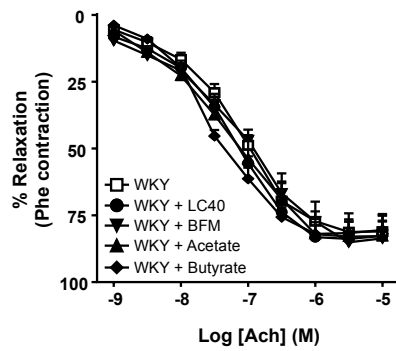
**Figure S2.** Effects Probiotic treatments in short-chain fatty acids (SCFAs) level in feces of spontaneously hypertensive rats (SHR). Acetate and butyrate content in feces from all experimental groups measured by GC. Results are shown as mean  $\pm$  SEM (n = 5 - 6). \*P < 0.05 compared with WKY group. #P < 0.05 and ##P < 0.01 compared with the non-treated SHR group. LC40, *Lactobacillus fermentum* CECT5716; BFM, *Bifidobacterium breve* CECT7263.



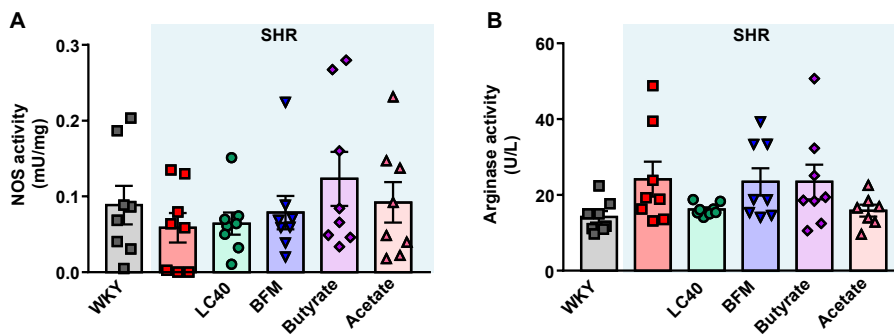
**Figure S3.** Plasma metabolome of Wistar Kyoto rats (WKY) and spontaneously hypertensive rats (SHR). **(A)** PCA scoring performed on  $^1\text{H}$  NMR spectra of plasma samples from WKY (triangles) and SHR (open circles) rats. **(B)** Representative part of  $^1\text{H}$  NMR spectra of plasma samples from WKY (blue) and SHR (red).



**Figure S4.** Effects of probiotics treatments on percentage of total T cells in mesenteric lymph nodes and spleen of spontaneously hypertensive rats (SHR). Total T cells in mesenteric lymphoid nodes (A) and spleen (B) in Wistar Kyoto (WKY) and SHR groups. Results are shown as mean  $\pm$  SEM (n = 7-10). \*P < 0.05 compared with WKY group. LC40, *Lactobacillus fermentum* CECT5716 (LC40); BFM, *Bifidobacterium breve* CECT7263.



**Figure S5.** Effects of probiotic treatments in endothelial function in Wistar Kyoto rats (WKY). Vascular relaxant responses induced by acetylcholine (Ach), in endothelium-intact aortae pre-contracted by phenylephrine (Phe) in all experimental groups. Results are shown as mean  $\pm$  SEM (n = 6). LC40, *Lactobacillus fermentum* CECT5716; BFM, *Bifidobacterium breve* CECT7263.



**Figure S6.** Effects of probiotics treatments on aortic nitric oxide synthase (NOS) activity (A) and arginase activity (B) in spontaneously hypertensive rats (SHR). Results are shown as mean  $\pm$  SEM. LC40, *Lactobacillus fermentum* CECT5716 (LC40); BFM, *Bifidobacterium breve* CECT7263.