

Supplementary Materials

Comparative Genomic and Metabolomic Characterization of *Lactiplantibacillus plantarum* LP140 and *Bifidobacterium breve* BB010 Reveals Distinct Metabolic Signatures Relevant to the Gut–Brain Axis

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Table S1. Comparison of PGAP and Bakta annotation outputs for the analyzed genomes. PGAP was used as the public-reference annotation framework, whereas Bakta served as a complementary local re-annotation layer for pathway-centered functional screening. The two pipelines were broadly consistent in overall genome description, but differed in CDS counts, pseudogene calls, and selected non-coding or accessory features.

Strain	Annotation pipeline	Genome size (bp)	GC (%)	Replicons	Genes total	CDSs total	Protein-coding CDSs / CDSs excluding pseudogenes*	Pseudogenes	tRNAs	rRNAs	ncRNAs	tmRNA	CRISPR arrays	Notes
<i>B. breve</i> BB010	PGAP v6.10	2,274,113	58.6	1	1,952	1,887	1,805	82	53	9	3	0	2	Public reference annotation associated with NCBI submission
<i>B. breve</i> BB010	Bakta v1.10.4	2,274,113	58.6	1	—	1,862	1,855	7	53	9	2	1	3	Local functional re-annotation used for downstream pathway analysis
<i>L. plantarum</i> LP140	PGAP v6.6	3,371,266	44.4	6	3,243	3,149	3,106	43	74	16	4	0	0	Public reference annotation associated with the previously published genome
<i>L. plantarum</i> LP140	Bakta v1.6.0	3,371,266	44.4	6	—	3,193	3,185	8	75	16	9	1	0	Local re-annotation used for harmonized comparative functional analysis

*For PGAP, the value corresponds to protein-coding CDSs reported directly by the pipeline. For Bakta, the value corresponds to CDSs excluding pseudogenes, calculated from the Bakta summary output.

Table S2. Diagnostic genes and pathway support in *B. breve* BB010 and *L. plantarum* LP140 Public PGAP / GenBank annotations were used as the primary identifiers, whereas Bakta annotations served as a complementary functional layer. KEGG Orthology assignments and KEGG Mapper Reconstruction were performed on Bakta-derived protein sets and were used as pathway-level support for final interpretation.

Category	Trait / pathway	Diagnostic gene / enzyme	BB010 PGAP	BB010 Bakta	LP140 PGAP	LP140 Bakta	KO / KEGG	Role	Interpretation
Vitamins/co factors	B1	<i>thiM</i>	AC0YDK_06655	BB01_01317 <i>thiM</i>	LP140_00465	<i>thiM</i>	BB010 partial; LP140 salvage complete	thiamine salvage	LP140 stronger
Vitamins/co factors	B1	<i>thiC</i>	AC0YDK_06660	BB01_01318 <i>thiC</i>	—	—	BB010 partial; LP140 de novo incomplete	HMP-P synthase	mainly BB010 support
Vitamins/co factors	B1	<i>thiD</i>	AC0YDK_06670	BB01_01320 <i>thiD</i>	LP140_00470	<i>thiD</i>	BB010 partial; LP140 salvage complete	HMP/PMP kinase	LP140 stronger
Vitamins/co factors	B2	<i>fmnP/ribU</i>	AC0YDK_06735	BB01_01333 <i>fmnP/ribU</i>	LP140_08200	<i>fmnP</i>	BB010 weak; LP140 near-complete	riboflavin uptake/support	LP140 stronger
Vitamins/co factors	B3 / NAD	<i>pncB</i>	AC0YDK_02030	BB01_00406 <i>pncB</i>	LP140_02345	<i>pncB</i>	BB010 complete; LP140 partial	NAD branch	BB010 stronger
Vitamins/co factors	B5	canonical B5 genes	—	incomplete	—	incomplete	partial / partial	pantothenate biosynth.	weak in both
Vitamins/co factors	CoA from B5	<i>coaD</i>	AC0YDK_02005	BB01_00401 <i>coaD</i>	LP140_09240	<i>coaD</i>	BB010 near-complete; LP140 complete	CoA biosynth.	LP140 stronger
Vitamins/co factors	CoA from B5	<i>coaE</i>	AC0YDK_03895	BB01_00769 <i>coaE</i>	LP140_06565	<i>coaE</i>	BB010 near-complete; LP140 complete	CoA biosynth.	LP140 stronger
Vitamins/co factors	B6 / PLP	<i>pdxS</i>	AC0YDK_02745	BB01_00546 <i>pdxS</i>	—	—	BB010 complete; LP140 partial	PLP synthase	BB010 stronger
Vitamins/co factors	B6 / PLP	<i>pdxT</i>	AC0YDK_02750	BB01_00547 <i>pdxT</i>	—	—	BB010 complete; LP140 partial	PLP synthase	BB010 stronger
Vitamins/co factors	B7	<i>bioY</i>	AC0YDK_08700	BB01_01722 <i>bioY</i>	LP140_01415	<i>bioY</i>	no complete module	biotin uptake	uptake only
Vitamins/co factors	B7	<i>birA</i>	AC0YDK_08705 <i>birA</i> -like	BB01_01723 <i>birA</i>	LP140_01420	<i>birA</i>	no complete module	biotin ligase	uptake/usage only
Vitamins/co factors	B9 / THF	<i>folE</i>	AC0YDK_07630	BB01_01510 <i>folE</i>	LP140_14220	<i>folE</i>	near-complete / near-complete	THF biosynth.	strong but incomplete in both
Vitamins/co factors	B9 / THF	<i>folP</i>	AC0YDK_07625	BB01_01509 <i>folP</i>	LP140_14205	<i>folP</i>	near-complete / near-complete	THF biosynth.	strong but incomplete in both
Vitamins/co factors	B9 / THF	<i>folD</i>	—	BB01_00767 <i>folD</i>	LP140_06960	<i>folD</i>	near-complete / near-complete	C1/THF metabolism	supports THF network
Vitamins/co factors	B9 / THF	<i>folA</i>	AC0YDK_07790	BB01_01540 <i>folA</i>	LP140_08125	<i>folA</i>	near-complete / near-complete	DHFR step	late THF support
Vitamins/co factors	B9 precursor	<i>pabA</i>	AC0YDK_00370	BB01_00079 <i>pabA</i>	LP140_07200	<i>pabA</i>	near-complete / near-complete	pABA branch	precursor support
Vitamins/co factors	B12	canonical B12 genes	—	—	—	—	not supported / not supported	cobalamin biosynth.	unsupported in both
AA / related	Ser	<i>serA</i>	AC0YDK_06450	BB01_01275 <i>serA</i>	—	weaker support	BB010 complete; LP140 partial	Ser biosynth.	BB010 stronger
AA / related	Met	<i>metA, metF, metB</i>	AC0YDK_01590 (<i>metA</i>) AC0YDK_02705 (<i>metB</i>) AC0YDK_04990 (<i>metF</i>)	BB01_00317 <i>metA</i> , BB01_00538 <i>metB</i>	—	strong support	complete / complete	Met biosynth.	strong in both
AA / related	Val/Ile	<i>ilvB, ilvH, ilvC</i>	AC0YDK_01975 (<i>ilvH</i> / <i>ilvN</i> -like) AC0YDK_01980 (<i>ilvB</i>), AC0YDK_00590/AC0YDK_0059 5 (<i>ilvC</i> -like)	BB01_00395 <i>ilvH</i> , BB01_00396 <i>ilvB</i> , BB01_00121/00122 <i>ilvC</i>	—	weaker support	complete / partial	BCAA biosynth.	BB010 stronger

Category	Trait / pathway	Diagnostic gene / enzyme	BB010 PGAP	BB010 Bakta	LP140 PGAP	LP140 Bakta	KO / KEGG	Role	Interpretation
AA / related	Leu	<i>leuA, leuB</i>	AC0YDK_00895 (<i>leuA</i>) AC0YDK_02430 (<i>leuB</i>)	BB01_00179 <i>leuA</i> , BB01_00484 <i>leuB</i>	—	—	weaker support	complete / partial	Leu biosynth. BB010 stronger
AA / related	Lys	<i>lysC, asd, dapA, dapB</i>	C0YDK_00795 (<i>lysC</i>), AC0YDK_00805 (<i>asd</i>), AC0YDK_02550 (<i>dapA</i>), AC0YDK_02545 (<i>dapB</i>)	BB01_00160 <i>lysC</i> , BB01_00162 <i>asd</i> , BB01_00172 <i>dapA</i> , BB01_00507 <i>dapB</i>	V2P12_08000, V2P12_09055, V2P12_11490	—	strong support	complete / near-complete	Lys biosynth. strong in both
AA / related	Arg/Orn	orn/arg enzymes	AC0YDK_03520 AC0YDK_03525	strong support	V2P12_02125, V2P12_02130	—	strong support	complete / complete	Glu→Orn→Arg strong in both
AA / related	Pro	<i>putP/proP</i> + pathway	AC0YDK_00295 (<i>putP</i> -like)	BB01_00064 <i>putP</i> , BB01_01358 <i>proP</i>	—	—	strong support	complete / complete	Pro biosynth./transport strong in both
AA / related	His	histidine enzymes	AC0YDK_06530 AC0YDK_06535	near-complete	V2P12_11020, V2P12_11055, V2P12_11070	—	complete	near-complete / complete	His biosynth. LP140 stronger
AA / related	Trp	<i>trpA, trpD, trpE</i>	AC0YDK_05405 AC0YDK_05970 AC0YDK_05545	partial	V2P12_07075, V2P12_07080, V2P12_07090, V2P12_07095	—	complete	partial / complete	Trp biosynth. LP140 stronger
AA / related	GABA biosynth.	glutamate decarboxylase	—	no major GAD locus	V2P12_14435	LP140_14645 <i>gadA</i>	—	BB010 weak; LP140 partial	Glu→GABA LP140 stronger
AA / related	GABA export	canonical <i>gadC</i> / non-canonical transporter	—	—	V2P12_12995 <i>yjeM</i>	LP140_13185 <i>yjeM</i>	—	canonical <i>gadC</i> absent; LP140 partial	putative GABA transport LP140 partial, non-canonical
Organic acids	Lactate	<i>ldh</i>	AC0YDK_05140, AC0YDK_06475	BB01_01015 <i>ldh</i> , BB01_01280 <i>ldh</i>	multiple PGAP loci	multiple <i>ldh</i> -like copies	—	complete / complete	pyruvate→lactate strong in both
Organic acids	Acetate	<i>pta, ackA</i>	AC0YDK_03995 (<i>pta</i>), AC0YDK_03990 (<i>ackA</i> -like)	BB01_00789 <i>pta</i> , BB01_00788 <i>ackA</i>	V2P12_03720; V2P12_00865, V2P12_01260, V2P12_09665	—	supported	complete / complete	PTA-AK route strong in both
Organic acids	Succinate	<i>ppc, pyc, pckA, fum, sdh/frd</i> -like	AC0YDK_00285, AC0YDK_04165	BB01_00062 <i>ppc</i> + limited support	V2P12_09115, V2P12_14425, V2P12_04975	—	broader support	partial / near-complete	reductive C4 branch LP140 stronger
Organic acids	Propionate	PDO / propionyl-CoA genes	—	—	—	—	—	not supported / not supported	propionate pathway unsupported in both
Organic acids	Butyrate	<i>buk, ptb</i> , butyryl-CoA genes	—	—	—	—	—	not supported / not supported	butyrate pathway unsupported in both
Sugars	Lactose/galactose	<i>lacY, lacZ, lacS/galP/rafP, lacE/F/G</i>	AC0YDK_00045, AC0YDK_00050, AC0YDK_02130, AC0YDK_02655, AC0YDK_07720	BB01_01528 <i>lacS/galP/rafP</i> , BB01_01529 <i>lacZ</i> , BB01_00301–00303 <i>lacE/F/G</i>	V2P12_04265, V2P12_06040, V2P12_11875, V2P12_14625, V2P12_14695	—	robust support	complete / complete	uptake + hydrolysis strong in both
Bile salt	BSH	<i>bsh</i>	AC0YDK_04995	direct BSH support	V2P12_14940	LP140_15155 <i>bsh</i>	—	complete / complete	bile salt deconjugation present in both
Poly amine	Polyamine turnover	transport / antiporter genes	—	BB01_00338–00341, BB01_00542	—	—	weaker support	partial / partial	transport/turnover turnover > de novo in both
Biogenic amine	Histamine biosynth.	<i>hdc</i>	—	—	—	—	—	not supported / not supported	histamine formation unsupported in both
Biogenic amine	Tyramine biosynth.	<i>tyrDC/tdc</i>	—	—	—	—	—	not supported / not supported	tyramine formation unsupported in both

Table S3. Complete numerical dataset underlying the exploratory Biocrates MxP® Quant 500 analysis shown in Fig. 2. Raw concentration values (μM) in uninoculated medium control (C_{control}) and cell-free spent medium (C_{CFSM}), together with calculated net changes ($\Delta = C_{\text{CFSM}} - C_{\text{control}}$) and \log_2 fold-changes ($\log_2\text{FC}$), corresponding to the exploratory dataset visualized in Fig. 2. The Biocrates dataset was acquired as a single exploratory measurement per strain/condition ($n = 1$) and is provided for hypothesis generation and strain prioritization only.

Strain	Class	Metabolite	C_{control} [μM]	C_{CFSM} [μM]	Δ [μM]	$\log_2\text{FC}$
<i>B. breve</i> BB010	Alkaloids	Trigonelline	0.846	0.938	0.092	0.149
<i>L. plantarum</i> LP140	Alkaloids	Trigonelline	0.846	0.909	0.063	0.104
<i>B. breve</i> BB010	Amine Oxides	TMAO	0.0075	0.0075	0	0
<i>L. plantarum</i> LP140	Amine Oxides	TMAO	0.0075	0.0075	0	0
<i>B. breve</i> BB010	Aminoacids	Ala	3268	4132	864	0.338
<i>L. plantarum</i> LP140	Aminoacids	Ala	3268	2940	-328	-0.153
<i>B. breve</i> BB010	Aminoacids	Arg	641	798	157	0.316
<i>L. plantarum</i> LP140	Aminoacids	Arg	641	729	88	0.186
<i>B. breve</i> BB010	Aminoacids	Asn	584	658	74	0.172
<i>L. plantarum</i> LP140	Aminoacids	Asn	584	245	-339	-1.253
<i>B. breve</i> BB010	Aminoacids	Asp	814	964	150	0.244
<i>L. plantarum</i> LP140	Aminoacids	Asp	814	418	-396	-0.962
<i>B. breve</i> BB010	Aminoacids	Gln	7.09	336	328.91	5.567
<i>L. plantarum</i> LP140	Aminoacids	Gln	7.09	24.7	17.61	1.801
<i>B. breve</i> BB010	Aminoacids	Glu	2500	2676	176	0.098
<i>L. plantarum</i> LP140	Aminoacids	Glu	2500	1439	-1061	-0.797
<i>B. breve</i> BB010	Aminoacids	Gly	5129	6317	1188	0.301
<i>L. plantarum</i> LP140	Aminoacids	Gly	5129	5653	524	0.14
<i>B. breve</i> BB010	Aminoacids	His	159	250	91	0.653
<i>L. plantarum</i> LP140	Aminoacids	His	159	138	-21	-0.204
<i>B. breve</i> BB010	Aminoacids	Ile	763	963	200	0.336
<i>L. plantarum</i> LP140	Aminoacids	Ile	763	712	-51	-0.1
<i>B. breve</i> BB010	Aminoacids	Leu	1949	1961	12	0.009
<i>L. plantarum</i> LP140	Aminoacids	Leu	1949	1779	-170	-0.132
<i>B. breve</i> BB010	Aminoacids	Lys	468	674	206	0.526
<i>L. plantarum</i> LP140	Aminoacids	Lys	468	453	-15	-0.047
<i>B. breve</i> BB010	Aminoacids	Met	163	311	148	0.932
<i>L. plantarum</i> LP140	Aminoacids	Met	163	213	50	0.386
<i>B. breve</i> BB010	Aminoacids	Phe	745	833	88	0.161
<i>L. plantarum</i> LP140	Aminoacids	Phe	745	404	-341	-0.883
<i>B. breve</i> BB010	Aminoacids	Pro	457	603	146	0.4
<i>L. plantarum</i> LP140	Aminoacids	Pro	457	600	143	0.393
<i>B. breve</i> BB010	Aminoacids	Ser	945	1106	161	0.227
<i>L. plantarum</i> LP140	Aminoacids	Ser	945	453	-492	-1.061
<i>B. breve</i> BB010	Aminoacids	Thr	850	1058	208	0.316
<i>L. plantarum</i> LP140	Aminoacids	Thr	850	695	-155	-0.29
<i>B. breve</i> BB010	Aminoacids	Trp	154	179	25	0.217
<i>L. plantarum</i> LP140	Aminoacids	Trp	154	114	-40	-0.434
<i>B. breve</i> BB010	Aminoacids	Tyr	250	326	76	0.383
<i>L. plantarum</i> LP140	Aminoacids	Tyr	250	85.7	-164.3	-1.545
<i>B. breve</i> BB010	Aminoacids	Val	1092	1482	390	0.441
<i>L. plantarum</i> LP140	Aminoacids	Val	1092	1323	231	0.277
<i>B. breve</i> BB010	Aminoacids Related	1-Met-His	0.49	0.843	0.353	0.783
<i>L. plantarum</i> LP140	Aminoacids Related	1-Met-His	0.49	0.708	0.218	0.531
<i>B. breve</i> BB010	Aminoacids Related	3-Met-His	0.584	0.882	0.298	0.595
<i>L. plantarum</i> LP140	Aminoacids Related	3-Met-His	0.584	0.814	0.23	0.479
<i>B. breve</i> BB010	Aminoacids Related	5-AVA	2.01	2.03	0.02	0.014
<i>L. plantarum</i> LP140	Aminoacids Related	5-AVA	2.01	2.15	0.14	0.097
<i>B. breve</i> BB010	Aminoacids Related	AABA	8.03	7.52	-0.51	-0.095
<i>L. plantarum</i> LP140	Aminoacids Related	AABA	8.03	7.42	-0.61	-0.114
<i>B. breve</i> BB010	Aminoacids Related	ADMA	0.93	1.76	0.83	0.92
<i>L. plantarum</i> LP140	Aminoacids Related	ADMA	0.93	0.838	-0.092	-0.15
<i>B. breve</i> BB010	Aminoacids Related	Ac-Orn	1.14	1.8	0.66	0.659
<i>L. plantarum</i> LP140	Aminoacids Related	Ac-Orn	1.14	1.61	0.47	0.498
<i>B. breve</i> BB010	Aminoacids Related	Anserine	5.31	6.41	1.1	0.272
<i>L. plantarum</i> LP140	Aminoacids Related	Anserine	5.31	4.81	-0.5	-0.143
<i>B. breve</i> BB010	Aminoacids Related	BABA	0.358	0.313	-0.045	-0.194
<i>L. plantarum</i> LP140	Aminoacids Related	BABA	0.358	0.456	0.098	0.349
<i>B. breve</i> BB010	Aminoacids Related	Betaine	275	316	41	0.2
<i>L. plantarum</i> LP140	Aminoacids Related	Betaine	275	307	32	0.159
<i>B. breve</i> BB010	Aminoacids Related	Carnosine	17.7	21.2	3.5	0.26
<i>L. plantarum</i> LP140	Aminoacids Related	Carnosine	17.7	18.4	0.7	0.056
<i>B. breve</i> BB010	Aminoacids Related	Cit	19.7	40.3	20.6	1.033
<i>L. plantarum</i> LP140	Aminoacids Related	Cit	19.7	22.4	2.7	0.185
<i>B. breve</i> BB010	Aminoacids Related	Creatinine	79.3	98.7	19.4	0.316
<i>L. plantarum</i> LP140	Aminoacids Related	Creatinine	79.3	133	53.7	0.746

Strain	Class	Metabolite	C _{control} [μM]	C _{CFSM} [μM]	Δ [μM]	log ₂ FC
<i>B. breve</i> BB010	Aminoacids Related	Cystine	0.0025	0.0025	0	0
<i>L. plantarum</i> LP140	Aminoacids Related	Cystine	0.0025	0.0025	0	0
<i>B. breve</i> BB010	Aminoacids Related	DOPA	0.665	0.793	0.128	0.254
<i>L. plantarum</i> LP140	Aminoacids Related	DOPA	0.665	0.503	-0.162	-0.403
<i>B. breve</i> BB010	Aminoacids Related	HArg	0.254	0.261	0.007	0.039
<i>L. plantarum</i> LP140	Aminoacids Related	HArg	0.254	0.582	0.328	1.196
<i>B. breve</i> BB010	Aminoacids Related	Kynurenine	0.001	0.001	0	0
<i>L. plantarum</i> LP140	Aminoacids Related	Kynurenine	0.001	0.001	0	0
<i>B. breve</i> BB010	Aminoacids Related	Met-SO	250	116	-134	-1.108
<i>L. plantarum</i> LP140	Aminoacids Related	Met-SO	250	60.9	-189.1	-2.037
<i>B. breve</i> BB010	Aminoacids Related	Nitro-Tyr	0.005	0.005	0	0
<i>L. plantarum</i> LP140	Aminoacids Related	Nitro-Tyr	0.005	0.005	0	0
<i>B. breve</i> BB010	Aminoacids Related	Orn	27.5	36	8.5	0.389
<i>L. plantarum</i> LP140	Aminoacids Related	Orn	27.5	38.6	11.1	0.489
<i>B. breve</i> BB010	Aminoacids Related	PAG	0.003	0.003	0	0
<i>L. plantarum</i> LP140	Aminoacids Related	PAG	0.003	0.003	0	0
<i>B. breve</i> BB010	Aminoacids Related	PheAlaBetaine	0.005	0.005	0	0
<i>L. plantarum</i> LP140	Aminoacids Related	PheAlaBetaine	0.005	0.005	0	0
<i>B. breve</i> BB010	Aminoacids Related	ProBetaine	0.549	0.787	0.238	0.52
<i>L. plantarum</i> LP140	Aminoacids Related	ProBetaine	0.549	0.722	0.173	0.395
<i>B. breve</i> BB010	Aminoacids Related	SDMA	2.15	6.13	3.98	1.512
<i>L. plantarum</i> LP140	Aminoacids Related	SDMA	2.15	9.64	7.49	2.165
<i>B. breve</i> BB010	Aminoacids Related	Sarcosine	6.66	6.66	0	0
<i>L. plantarum</i> LP140	Aminoacids Related	Sarcosine	6.66	6.91	0.25	0.053
<i>B. breve</i> BB010	Aminoacids Related	Taurine	26.1	25.6	-0.5	-0.028
<i>L. plantarum</i> LP140	Aminoacids Related	Taurine	26.1	24	-2.1	-0.121
<i>B. breve</i> BB010	Aminoacids Related	alpha-AAA	1.98	2.97	0.99	0.585
<i>L. plantarum</i> LP140	Aminoacids Related	alpha-AAA	1.98	2.51	0.53	0.342
<i>B. breve</i> BB010	Aminoacids Related	c4-OH-Pro	32.7	27.6	-5.1	-0.245
<i>L. plantarum</i> LP140	Aminoacids Related	c4-OH-Pro	32.7	30.3	-2.4	-0.11
<i>B. breve</i> BB010	Aminoacids Related	t4-OH-Pro	76.7	94.8	18.1	0.306
<i>L. plantarum</i> LP140	Aminoacids Related	t4-OH-Pro	76.7	69.8	-6.9	-0.136
<i>B. breve</i> BB010	Bile Acids	CA	0.001	0.001	0	0
<i>L. plantarum</i> LP140	Bile Acids	CA	0.001	0.001	0	0
<i>B. breve</i> BB010	Bile Acids	CDCA	0.0015	0.0015	0	0
<i>L. plantarum</i> LP140	Bile Acids	CDCA	0.0015	0.0015	0	0
<i>B. breve</i> BB010	Bile Acids	DCA	0.0005	0.0005	0	0
<i>L. plantarum</i> LP140	Bile Acids	DCA	0.0005	0.0005	0	0
<i>B. breve</i> BB010	Bile Acids	GCA	0.004	0.002	-0.002	-1.00
<i>L. plantarum</i> LP140	Bile Acids	GCA	0.004	0.0005	-0.0035	-3.00
<i>B. breve</i> BB010	Bile Acids	GCDCA	0.0005	0.0005	0	0
<i>L. plantarum</i> LP140	Bile Acids	GCDCA	0.0005	0.0005	0	0
<i>B. breve</i> BB010	Bile Acids	GDCA	0.001	0.001	0	0
<i>L. plantarum</i> LP140	Bile Acids	GDCA	0.001	0.001	0	0
<i>B. breve</i> BB010	Bile Acids	GLCA	0.0005	0.0005	0	0
<i>L. plantarum</i> LP140	Bile Acids	GLCA	0.0005	0.0005	0	0
<i>B. breve</i> BB010	Bile Acids	GLCAS	0.0005	0.0005	0	0
<i>L. plantarum</i> LP140	Bile Acids	GLCAS	0.0005	0.0005	0	0
<i>B. breve</i> BB010	Bile Acids	GUDCA	0.0005	0.001	0.0005	1.00
<i>L. plantarum</i> LP140	Bile Acids	GUDCA	0.0005	0.0005	0	0
<i>B. breve</i> BB010	Bile Acids	TCA	0.006	0.001	-0.005	-2.585
<i>L. plantarum</i> LP140	Bile Acids	TCA	0.006	0.002	-0.004	-1.585
<i>B. breve</i> BB010	Bile Acids	TCDCa	0.0005	0.0005	0	0
<i>L. plantarum</i> LP140	Bile Acids	TCDCa	0.0005	0.0005	0	0
<i>B. breve</i> BB010	Bile Acids	TDCA	0.0005	0.0005	0	0
<i>L. plantarum</i> LP140	Bile Acids	TDCA	0.0005	0.0005	0	0
<i>B. breve</i> BB010	Bile Acids	TLCA	0.0005	0.0005	0	0
<i>L. plantarum</i> LP140	Bile Acids	TLCA	0.0005	0.0005	0	0
<i>B. breve</i> BB010	Bile Acids	TrpBetaine	0.002	0.002	0	0
<i>L. plantarum</i> LP140	Bile Acids	TrpBetaine	0.002	0.002	0	0
<i>B. breve</i> BB010	Biogenic Amines	Dopamine	0.001	0.001	0	0
<i>L. plantarum</i> LP140	Biogenic Amines	Dopamine	0.001	0.001	0	0
<i>B. breve</i> BB010	Biogenic Amines	GABA	59.7	60.7	1	0.024
<i>L. plantarum</i> LP140	Biogenic Amines	GABA	59.7	148	88.3	1.31
<i>B. breve</i> BB010	Biogenic Amines	Histamine	0.69	0.541	-0.149	-0.351
<i>L. plantarum</i> LP140	Biogenic Amines	Histamine	0.69	0.508	-0.182	-0.442
<i>B. breve</i> BB010	Biogenic Amines	PEA	1.09	0.518	-0.572	-1.073
<i>L. plantarum</i> LP140	Biogenic Amines	PEA	1.09	0.463	-0.627	-1.235
<i>B. breve</i> BB010	Biogenic Amines	Putrescine	2.09	2.35	0.26	0.169
<i>L. plantarum</i> LP140	Biogenic Amines	Putrescine	2.09	3.21	1.12	0.619
<i>B. breve</i> BB010	Biogenic Amines	Serotonin	0.0005	0.0005	0	0
<i>L. plantarum</i> LP140	Biogenic Amines	Serotonin	0.0005	0.0005	0	0
<i>B. breve</i> BB010	Biogenic Amines	Spermidine	4.22	6.13	1.91	0.539
<i>L. plantarum</i> LP140	Biogenic Amines	Spermidine	4.22	0.796	-3.424	-2.406

Strain	Class	Metabolite	C _{control} [μ M]	C _{CFSM} [μ M]	Δ [μ M]	log ₂ FC
<i>B. breve</i> BB010	Biogenic Amines	TMCA	0.004	0.003	-0.001	-0.415
<i>L. plantarum</i> LP140	Biogenic Amines	TMCA	0.004	0.0015	-0.0025	-1.415
<i>B. breve</i> BB010	Biogenic Amines	beta-Ala	5.27	4.39	-0.88	-0.264
<i>L. plantarum</i> LP140	Biogenic Amines	beta-Ala	5.27	2.88	-2.39	-0.872
<i>B. breve</i> BB010	Carboxylic Acids	AconAcid	9.08	768	758.92	6.402
<i>L. plantarum</i> LP140	Carboxylic Acids	AconAcid	9.08	11.8	2.72	0.378
<i>B. breve</i> BB010	Carboxylic Acids	DiCA(12:0)	0.005	0.005	0	0
<i>L. plantarum</i> LP140	Carboxylic Acids	DiCA(12:0)	0.005	0.005	0	0
<i>B. breve</i> BB010	Carboxylic Acids	DiCA(14:0)	0.001	0.001	0	0
<i>L. plantarum</i> LP140	Carboxylic Acids	DiCA(14:0)	0.001	0.001	0	0
<i>B. breve</i> BB010	Carboxylic Acids	HipAcid	0.005	0.005	0	0
<i>L. plantarum</i> LP140	Carboxylic Acids	HipAcid	0.005	0.005	0	0
<i>B. breve</i> BB010	Carboxylic Acids	Lac	3234	14470	11236	2.162
<i>L. plantarum</i> LP140	Carboxylic Acids	Lac	3234	145059	141825	5.487
<i>B. breve</i> BB010	Carboxylic Acids	OH-GlutAcid	85.4	22.8	-62.6	-1.905
<i>L. plantarum</i> LP140	Carboxylic Acids	OH-GlutAcid	85.4	55.6	-29.8	-0.619
<i>B. breve</i> BB010	Carboxylic Acids	Spermine	0.62	0.633	0.013	0.03
<i>L. plantarum</i> LP140	Carboxylic Acids	Spermine	0.62	1.12	0.5	0.853
<i>B. breve</i> BB010	Cresols	Suc	501	597	96	0.253
<i>L. plantarum</i> LP140	Cresols	Suc	501	2094	1593	2.063
<i>B. breve</i> BB010	Fatty Acids	FA 12:0	28	20.8	-7.2	-0.429
<i>L. plantarum</i> LP140	Fatty Acids	FA 12:0	28	59.6	31.6	1.09
<i>B. breve</i> BB010	Fatty Acids	FA 14:0	214	167	-47	-0.358
<i>L. plantarum</i> LP140	Fatty Acids	FA 14:0	214	1062	848	2.311
<i>B. breve</i> BB010	Fatty Acids	FA 16:0	175	175	0	0
<i>L. plantarum</i> LP140	Fatty Acids	FA 16:0	175	175	0	0
<i>B. breve</i> BB010	Fatty Acids	FA 18:0	175	175	0	0
<i>L. plantarum</i> LP140	Fatty Acids	FA 18:0	175	175	0	0
<i>B. breve</i> BB010	Fatty Acids	FA 18:1	0.05	0.05	0	0
<i>L. plantarum</i> LP140	Fatty Acids	FA 18:1	0.05	0.05	0	0
<i>B. breve</i> BB010	Fatty Acids	FA 18:2	0.015	0.015	0	0
<i>L. plantarum</i> LP140	Fatty Acids	FA 18:2	0.015	0.015	0	0
<i>B. breve</i> BB010	Fatty Acids	FA 20:1	0.015	0.015	0	0
<i>L. plantarum</i> LP140	Fatty Acids	FA 20:1	0.015	0.015	0	0
<i>B. breve</i> BB010	Fatty Acids	FA 20:2	0.05	0.05	0	0
<i>L. plantarum</i> LP140	Fatty Acids	FA 20:2	0.05	0.05	0	0
<i>B. breve</i> BB010	Fatty Acids	FA 20:3	0.05	0.05	0	0
<i>L. plantarum</i> LP140	Fatty Acids	FA 20:3	0.05	2.01	1.96	5.329
<i>B. breve</i> BB010	Fatty Acids	FA 20:4n-6 (AA)	0.02	0.02	0	0
<i>L. plantarum</i> LP140	Fatty Acids	FA 20:4n-6 (AA)	0.02	0.02	0	0
<i>B. breve</i> BB010	Fatty Acids	FA 20:5n-3 (EPA)	0.005	0.005	0	0
<i>L. plantarum</i> LP140	Fatty Acids	FA 20:5n-3 (EPA)	0.005	0.005	0	0
<i>B. breve</i> BB010	Fatty Acids	p-Cresol-SO4	0.494	0.398	-0.096	-0.312
<i>L. plantarum</i> LP140	Fatty Acids	p-Cresol-SO4	0.494	0.305	-0.189	-0.696
<i>B. breve</i> BB010	Hormones	AbsAcid	0.001	0.001	0	0
<i>L. plantarum</i> LP140	Hormones	AbsAcid	0.001	0.0005	-0.0005	-1.00
<i>B. breve</i> BB010	Hormones	Cortisol	0.0025	0.0025	0	0
<i>L. plantarum</i> LP140	Hormones	Cortisol	0.0025	0.0025	0	0
<i>B. breve</i> BB010	Hormones	Cortisone	0.0025	0.0025	0	0
<i>L. plantarum</i> LP140	Hormones	Cortisone	0.0025	0.0025	0	0
<i>B. breve</i> BB010	Hormones	FA 22:6n-3 (DHA)	0.0075	0.0075	0	0
<i>L. plantarum</i> LP140	Hormones	FA 22:6n-3 (DHA)	0.0075	0.0075	0	0
<i>B. breve</i> BB010	Indoles Derivatives	3-IAA	0.005	0.005	0	0
<i>L. plantarum</i> LP140	Indoles Derivatives	3-IAA	0.005	0.005	0	0
<i>B. breve</i> BB010	Indoles Derivatives	3-IPA	0.0015	0.0015	0	0
<i>L. plantarum</i> LP140	Indoles Derivatives	3-IPA	0.0015	0.0015	0	0
<i>B. breve</i> BB010	Indoles Derivatives	DHEAS	0.0075	0.0075	0	0
<i>L. plantarum</i> LP140	Indoles Derivatives	DHEAS	0.0075	0.0075	0	0
<i>B. breve</i> BB010	Indoles Derivatives	Ind-SO4	0.014	0.017	0.003	0.28
<i>L. plantarum</i> LP140	Indoles Derivatives	Ind-SO4	0.014	0.011	-0.003	-0.348
<i>B. breve</i> BB010	Nucleobases Related	Hypoxanthine	7.9	15	7.1	0.925
<i>L. plantarum</i> LP140	Nucleobases Related	Hypoxanthine	7.9	0.05	-7.85	-7.304
<i>B. breve</i> BB010	Nucleobases Related	Indole	2	2	0	0
<i>L. plantarum</i> LP140	Nucleobases Related	Indole	2	2	0	0
<i>B. breve</i> BB010	Other	Choline	39.6	47.1	7.5	0.25
<i>L. plantarum</i> LP140	Other	Choline	39.6	14.8	-24.8	-1.42
<i>B. breve</i> BB010	Vitamins & Cofactors	Xanthine	13.8	4.45	-9.35	-1.633
<i>L. plantarum</i> LP140	Vitamins & Cofactors	Xanthine	13.8	0.2	-13.6	-6.109

Figure S1. Baseline-corrected metabolite signatures in bacterial CFSM (targeted LC-MS/MS). Net changes are shown as $\Delta = C_{\text{CFSM}} - C_{\text{control}}$ after run-matched medium-only baseline correction within each analytical run (“test”). Points are individual tests; diamonds and bars denote mean \pm 95% CI ($n \geq 3$). q-values were obtained by BH-FDR correction across analytes within each strain (* $q < 0.05$, ** $q < 0.01$, *** $q < 0.001$). Panel groups: **(A)** Fermentation-derived carboxylic acids (SCFAs, lactate and related organic acids); **(B)** B vitamins and vitamers; **(C)** amino acids (incl. GABA); **(D)** polyamines and related biogenic amines.



