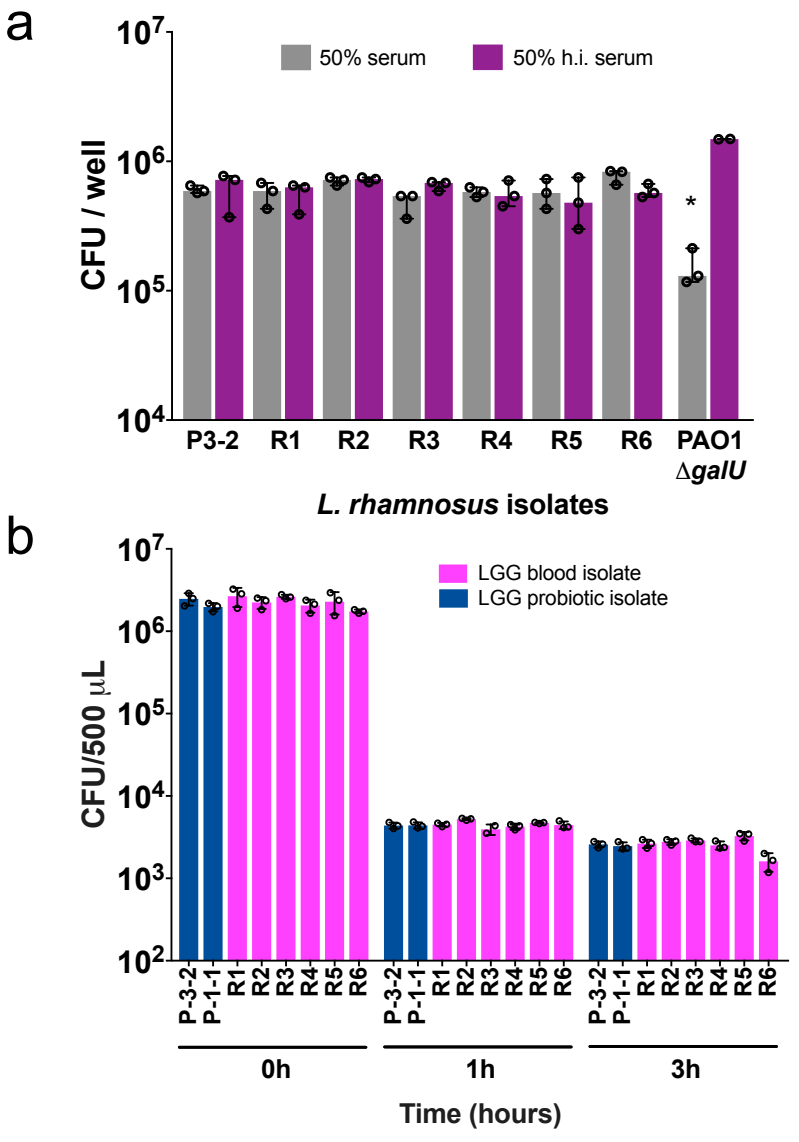

Supplementary Figure 1. Bacterial survival in human serum and whole blood are similar among the probiotic and blood isolates. (a) Survival in human serum of *L. rhamnosus* GG probiotic control strain without SNPs (P3-2) and blood *L. rhamnosus* isolates (R1-R6). The concentrations of serum tested were 50% vs. 50% heat-inactivated (h.i.). The bars show the medians. Error bars indicate interquartile ranges. *P = 0.0448 for 50% serum vs. 50% h.i. serum by Kruskal-Wallis test followed by Dunn's multiple comparisons test. Results shown are representative of 2 independent experiments. PAO1 Δ*galU* is a *Pseudomonas aeruginosa galU* mutant, an LPS-rough, serum-sensitive strain (positive control). (b) Survival in human whole blood of probiotic strains without SNPs (P3-2) or with the CcmA SNP (P1-1), and blood isolates (R1-R6). The bars show the means of 3 technical replicates. Error bars indicate SD. P = 0.1893 (t_{1h}/t_{0h}) and P = 0.1901 (t_{3h}/t_{0h}) by ANOVA test followed by Dunnett's multiple comparison test of survival indices at 1 and 3 hours compared to time 0, using the probiotic P3-2 as control. Results shown are representative of 2 independent experiments performed on different days using blood from two different donors. Px-y where x = probiotic batch number and y = isolate number.

Supplementary Table 1a. All cases of *Lactobacillus* bacteremia identified in ICU patients during the 5-year study period.

Case	Consecutive days receiving probiotic prior to bacteremia	Route of probiotic admin.	Age (y)	Hospital location at time of bacteremia	Year of bacteremia	Chronic conditions	*Lactobacillus* species by MALDI-TOF	*Lactobacillus rhamnosus* strain by WGS*
R1	89	Nasojejunal	2	ICP	2011	Mitochondrial disorder	*rhamnosus*	*LGG*
R2	Home medication	Jejunostomy	4	ICP	2012	Mitochondrial disorder	*rhamnosus*	*LGG*
R3	4	Gastrostomy	12	Medical/ Surgical ICU	2012	Cerebral palsy	*rhamnosus*	*LGG*
R4	12	Jejunostomy	1	Cardiac ICU	2013	Congenital heart disease	*rhamnosus*	*LGG*
R5	118	Gastrostomy	19	Medical ICU	2014	Cystic fibrosis	*rhamnosus*	*LGG*
R6	13	Gastrostomy	19	Medical/ Surgical ICU	2014	Cystic fibrosis	*rhamnosus*	*LGG*
N1	Not receiving probiotics		16	Medical/ Surgical ICU	2010	22q11 deletion, VCFS, s/p dental procedure	*acidophilus*	
N2	Not receiving probiotics		0.5	Medical ICU	2010	s/p BMT, GVHD	*plantarum*	

Abbreviations: ICP, intermediate care program; BMT, bone marrow transplant; GVHD, graft-versus-host disease; SBS, short bowel syndrome; FTT, failure to thrive; PN, parenteral nutrition; VCFS, velocardiofacial syndrome. *See Fig. 1a.

Supplementary Table 1b. All cases of *Lactobacillus* bacteremia identified in non-ICU patients during the 5-year study period.

Case	Consecutive days receiving probiotic prior to bacteremia	Route of probiotic admin.	Age (y)	Hospital location at time of bacteremia	Year of bacteremia	Chronic conditions	*Lactobacillus* species by MALDI-TOF	*Lactobacillus rhamnosus* strain by WGS*
N3	Not receiving probiotics		18	BMT unit	2009	BMT, GVHD	*casei*	
N4	Not receiving probiotics		1	Inpatient floor	2009	SBS, on PN	*plantarum*	
N5	Not receiving probiotics		1	Inpatient floor	2009	Cerebral Palsy	*rhamnosus*	CP006804
N6	Not receiving probiotics		0.4	Inpatient floor	2009	Prematurity, SBS	Unknown, isolate not available	
N7	Not receiving probiotics		3	Inpatient floor	2010	Retino-blastoma	*gasseri*	
N8	Not receiving probiotics		1	Emergency Department	2011	SBS, on PN	No ID by MALDI-TOF	
N9	Not receiving probiotics		0.7	Outpatient surgery clinic	2011	SBS, on PN	*rhamnosus*	CP006804
N10	Not receiving probiotics		7	BMT unit	2012	s/p BMT	*rhamnosus*	CP005485
N11	Not receiving probiotics		0.6	Inpatient floor	2013	FTT, on PN	*rhamnosus*	CP006804
N12	Not receiving probiotics		0.8	Inpatient floor	2013	SBS, on PN	*plantarum*	

Abbreviations: BMT, bone marrow transplant; GVHD, graft-versus-host disease; SBS, short bowel syndrome; FTT, failure to thrive; PN, parenteral nutrition. *See Fig. 1a.

Supplementary Table 5. Mutations unique to blood isolates of *Lactobacillus rhamnosus*.

Case	Gene ID	Type of mutation	Protein ID	AA position	Associated pathway
R1	*rpoB*	Non-synonymous	DNA directed RNA polymerase β -subunit	H487D	DNA transcription
R2	*pgm*	Synonymous	Phosphoglucomutase	V132	Pentose phosphate pathway
R2	*trxB* <> *pgm*	Intergenic	Thioredoxin reductase <> Phosphoglucomutase		
R3	*yhfS*	Synonymous	Putative acetyl-CoA C-acetyltransferase	G44	
R6	*rbsK*	Non-synonymous	Ribokinase	A259D	Pentose phosphate pathway