

Figure S1. Infant birth information, screening activity, and total abundance of peptides from individual proteins for each intestinal peptide extract. Peptide abundances from each intestinal sample are sorted by protein from highest to lowest mean abundance. Bovine milk proteins are labeled with a (B) in the legend and are filled with a dotted pattern. PIgR, polymeric immunoglobulin receptor; BSSL, bile salt-stimulated lipase. ¹ GA units are wk/day. ² + Indicates the sample stimulated growth of the bacteria, - indicates the sample inhibited growth, and no symbol indicates the sample was inactive.

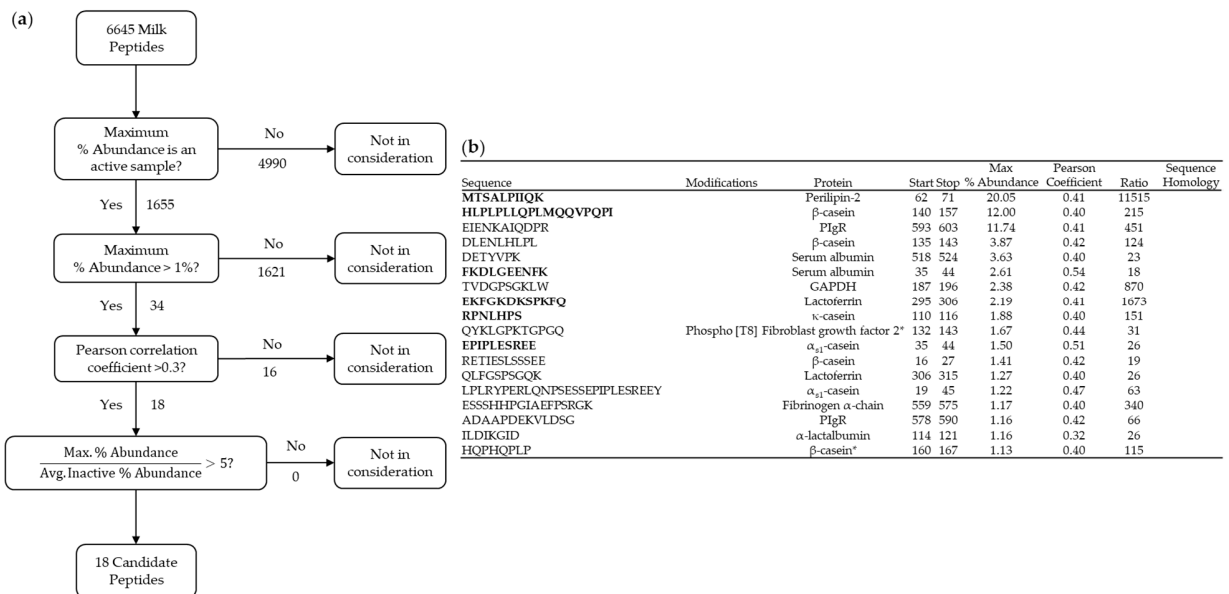


Figure S2. (a) Flow diagram of criteria and thresholds by which peptides with potential antimicrobial activity against *Staphylococcus aureus* were excluded from selection for activity testing. (b) List of peptides from which candidate peptides (in bold font) were selected for synthesis and activity testing.

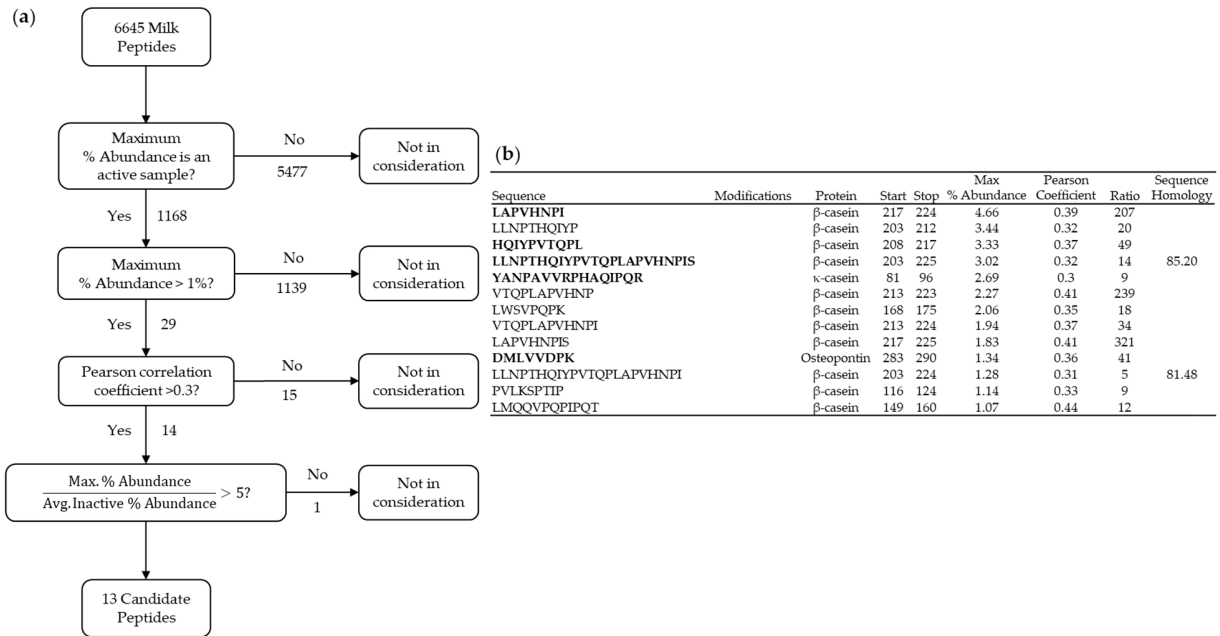


Figure S3. (a) Flow diagram of criteria and thresholds by which peptides with potential bifidogenic activity for *Bifidobacterium infantis* were excluded from selection for activity testing. (b) List of peptides from which candidate peptides (in bold font) were selected for synthesis and activity testing.

Table S1. List of known bioactive peptides in the infant intestinal samples.

Peptide	Species	Parent Protein	Location	Function
ENLHLPLP	Both	β -casein	(137–144)	ACE-inhibitory
NLHLPLP	Both	β -casein	(138–144)	ACE-inhibitory
ENLHLPLPLL	Both	β -casein	(146–155)	ACE-inhibitory
NLHLPLPLL	Both	β -casein	(147–155)	ACE-inhibitory
FFVAPFPEVFGK	Bovine	α_{s1} -casein	(38–49)	ACE-inhibitory
FVAPFPEVFG	Bovine	α_{s1} -casein	(39–48)	ACE-inhibitory
FPEVFGK	Bovine	α_{s1} -casein	(43–49)	ACE-inhibitory
IGSENSEKTTMP	Bovine	α_{s1} -casein	(201–212)	ACE-inhibitory
ALNEINQFYQK	Bovine	α_{s2} -casein	(96–106)	ACE-inhibitory
AMKPWIQPK	Bovine	α_{s2} -casein	(204–212)	ACE-inhibitory
LVYPPGPI	Bovine	β -casein	(73–81)	ACE-inhibitory
MPFPKYVPEP	Bovine	β -casein	(124–133)	ACE-inhibitory
VENLHLPLPLL	Bovine	β -casein	(145–155)	ACE-inhibitory
LLYQEPVLGPPVRGPFPIIV	Bovine	β -casein	(206–224)	ACE-inhibitory
QEPVLGPPVRGPFPIIV	Bovine	β -casein	(209–224)	ACE-inhibitory
EPVLGPPVRGPFPI	Bovine	β -casein	(210–221)	ACE-inhibitory
VLGPPVRGPFPI	Bovine	β -casein	(212–221)	ACE-inhibitory
LDIQKVAGTW	Bovine	β -lactoglobulin	(28–37)	ACE-inhibitory
DAQSAPLRVY	Bovine	β -lactoglobulin	(49–58)	ACE-inhibitory
FSDKIAK	Bovine	κ -casein	(39–45)	ACE-inhibitory
HPHPHLSF	Bovine	κ -casein	(119–126)	ACE-inhibitory
DKIYPSFQPQPLIYP	Human	β -casein	(53–67)	ACE-inhibitory
IYPSFQPQPLIYP	Human	β -casein	(55–67)	ACE-inhibitory
FQPQPLIYP	Human	β -casein	(59–67)	ACE-inhibitory
TVYTKGRVMP	Human	β -casein	(107–116)	ACE-inhibitory
LTDLENLHLPL	Human	β -casein	(133–142)	ACE-inhibitory
LENLHLPLP	Human	β -casein	(136–144)	ACE-inhibitory
YANPAVVRP	Human	κ -casein	(81–89)	ACE-inhibitory
IKHQGLPQEV	Bovine	α_{s1} -casein	(21–30)	Antimicrobial
LRLKKYKVPQL	Bovine	α_{s1} -casein	(114–124)	Antimicrobial
SDIPNPIGSENSEK	Bovine	α_{s1} -casein	(195–208)	Antimicrobial
TKKTKLTEEEKNRL	Bovine	α_{s2} -casein	(163–176)	Antimicrobial
IQPKTKVIPYVR	Bovine	α_{s2} -casein	(209–220)	Antimicrobial
TKVIPYVRYL	Bovine	α_{s2} -casein	(213–222)	Antimicrobial
TEDELQDKIHPF	Bovine	β -casein	(56–67)	Antimicrobial
PVVVPPFLQPE	Bovine	β -casein	(96–106)	Antimicrobial
VLPVPQKAVPYPQR	Bovine	β -casein	(185–198)	Antimicrobial
YQEPVLGPPVRGPFPI	Bovine	β -casein	(206–220)	Antimicrobial
GLDIQKVAGT	Bovine	β -lactoglobulin	(27–36)	Antimicrobial
AASDISLLDAQSAPLR	Bovine	β -lactoglobulin	(41–56)	Antimicrobial

Table S1 (cont.)

Peptide	Species	Parent Protein Location	Function
IIEKTKIPAVF	Bovine	β -lactoglobulin (89–100)	Antimicrobial
FSDKIAK	Bovine	κ -casein (39–45)	Antimicrobial
MAIPPKNQDKTEIPTINT	Bovine	κ -casein (127–145)	Antimicrobial
LLNQELLLNPTHQIYPV	Human	β -casein (197–213)	Antimicrobial
QELLLNPTHQIYPVTQPLAPVHNPISV	Human	β -casein (200–226)	Antimicrobial
QVVPYPQ	Human	β -casein (182–188)	Antioxidant
YLGYLEQLLR	Bovine	α 1-casein (106–115)	Anxiolytic
ALKALPMHIR	Bovine	β -lactoglobulin (155–164)	Cell-proliferative
RETIESLSSESSEESITEYK	Human	β -casein (16–33)	Cell-proliferative
SPTIPFFDPQIPK	Human	β -casein (120–132)	Cell-proliferative
LIVTQTMK	Bovine	β -lactoglobulin (17–24)	Cytotoxic
LPQNIPPLT	Bovine	β -casein (85–93)	DPP-IV-inhibitory
LKPTPEGDL	Bovine	β -lactoglobulin (62–70)	DPP-IV-inhibitory
LKPTPEGDL	Bovine	β -lactoglobulin (62–71)	DPP-IV-inhibitory
INNQFLPYPY	Bovine	κ -casein (72–81)	DPP-IV-inhibitory
VYVEELKPTPEGDLEILLQK	Bovine	β -lactoglobulin (57–76)	Hypocholesterolemic
LYQEPVLGVPVRGPFPIIV	Bovine	β -casein (207–224)	Immunomodulatory
YVPFPGPI	Bovine	β -casein (74–81)	PEP-inhibitory
ALPMHIR	Bovine	β -lactoglobulin (158–164)	ACE-inhibitory Cell-proliferative
FALPQYLK	Bovine	α 2-casein (189–196)	ACE-inhibitory Antioxidant
IQKVAGTW	Bovine	β -lactoglobulin (28–35)	ACE-inhibitory DPP-IV-inhibitory
LKALPMH	Bovine	β -lactoglobulin (156–162)	ACE-inhibitory DPP-IV-inhibitory
PYVRYL	Bovine	α 2-casein (217–222)	ACE-inhibitory Antimicrobial Antioxidant
RELEELNVPGEIVESLSSESITR	Bovine	β -casein (16–40)	Caseinophosphopeptide Immunomodulatory
TPEVDDEALEK	Bovine	β -lactoglobulin (141–151)	Antimicrobial DPP-IV-inhibitory
VKEAMAPK	Bovine	β -casein (113–120)	Antimicrobial Antioxidant
VLVLDTDYK	Bovine	β -lactoglobulin (108–116)	Antimicrobial DPP-IV-inhibitory
YVPFPGPIP	Bovine	β -casein (74–83)	ACE-inhibitory Antioxidant
WSVPQPK	Human	β -casein (169–175)	ACE-inhibitory Antioxidant

Table S1 (cont.)

Peptide	Species	Parent Protein Location	Function
YQEPVLGPVR	Bovine	β -casein (208–217)	ACE-inhibitory Immunomodulatory
YQEPVLGPVRGPFPIIV	Bovine	β -casein (208–224)	ACE-inhibitory Antimicrobial Antithrombin Immunomodulatory
YQKFPQY	Bovine	α s2-casein (105–111)	ACE-inhibitory Antioxidant