Table S1: Demographic and clinical data of VLBW human subjects included in Figure 1A and Figure S1.

Feed	Formula					Human milk				
ID in Sup Fig 1a	F1	F2	F3	F4	F5	HM1	HM2	HM3	HM4	HM5
Sex (M/F)	M	F	M	F	F	F	F	F	F	M
Race (African-American AA /White W/Asian A/Other/Prefers not to indicate or unknown)	AA	W	AA	AA	W	A	W	W	W	W
Ethnicity (Hispanic H/Not Hispanic NH/not known-prefers not to indicate)	NH	NH	NH	NH	NH	NH	NH	NH	NH	NH
Gestational age at birth (weeks.days)	28.5	29.3	29.0	28.5	30.5	28.3	27.2	29.1	27.6	28.0
Weight at birth - grams	1070	1330	1360	970	1340	950	1048	1190	1080	1020
Apgar scores at 1 minute of age	1	4	5	6	7	5	4	1	5	1
Apgar scores at 5 minute of age	6	6	7	6	8	7	6	3	9	3
Apgar scores at 10 minutes of age (X= not available)	6	9	x	6	x	x	x	3	x	6
NEC (yes/no)	no	no	no	no	no	no	no	no	no	no
Bloodstream infection (yes/no)	no	no	no	no	no	no	no	no	no	no

Table S2: *E. coli* used in the studies, MLST, source and lethality in mice following gavage of EGFRi treated mice.

Designation in text	*adk*	*fumC*	*gyrB*	*icd*	*mdh*	*purA*	*recA*	ST	Day of life on which blood positive culture was obtained, or stool was sampled	Birthweight (g)	Gestational age at birth (weeks.days)	Lethality in mouse model
Bloodstream isolates												
BSI-A[1]	21	35	27	6	5	5	4	69	21	790	28.0	75%
BSI-B	53	40	47[2]	13	36	28	29	131	10	670	24.0	100%
BSI-C[1]	34	36	28	25	25	28	4	70	34	800	26.0	100%
BSI-D	37	38[3]	19	37	17	8	26	421	32	650	23.5	50%
BSI-E	53	40	47	13	36	28	29	131	8	1110	26.2	0%
BSI-F[4]	37	38	19	37	17	11	26	95	9	810	24.4	50%
Stool isolates												
C1	20	24	19	13	23	16	17	35	442	2583	37.1	0%
C2	100	22	2	6	286	5	39	n/a	451	930	25.7	0%

[1]Isolates BSI-A and BSI-C are from Cases 3 and 5, respectively, in previous work (1)

[2]Isolate BSI-B differs from *gyrB* allele 47 by a single nucleotide variant.

[3]Isolate BSI-D differs from *fumC* allele 38 by a single nucleotide variant.

[4]This isolate originated at the Children's Hospital of Oklahoma University. All other isolates originated from cohorts at St. Louis Children's Hospital.

Sequence typing (ST) by multilocus seqeuence typing was performed according to (2)

Table S3: Virulence factors present in BSI-A, BSI-C, C-1, and C-2

Gene	Primer Forward	Primer Reverse	Reference	BSI-A	BSI-C	C1	C2
afa/draBC	GGCAGAGGGCCGGCAACAGGC	CCCGTAACGCGCCAGCATCTC	(3)				
afa8	CTAACTTGCCATGCTGTGACAGTA	TTATCCCCTGCGTAGTTGTGAATC	(4)				
astA	VirulenceFinder[1]		(5)				
bmaE	ATGGCGCTAACTTGCCATGCTG	AGGGGGACATATAGCCCCCTTC	(3)				
clbB	GCGCATCCTCAAGAGTAAATA	GCGCTCTATGCTCATCAACC	(6)				
clbN	GTT TTG CTC GCC AGA TAG TCA TTC	CAG TTC GGG TAT GTG TGG AAG G	(7)				
clpG	GGGCGCTCTCTCCTTCAAC	CGCCCTAATTGCTGGCGAC	(4)				
cnf1	AAGATGGAGTTTCCTATGCAGGAG	CATTCAGAGTCCTGCCCTCATTATT	(3)				
cvaC	CACACACAAACGGGAGCTGTT	CTTCCCGCAGCATAGTTCCAT	(3)				
f17	VirulenceFinder [1]		(5)				
fimH	TGCAGAACGGATAAGCCGTGG	GCAGTCACCTGCCCTCCGGTA	(3)				
fliC	CCGAATTCATGGCACAAGTCATTAATAC	CCGAATTCTTAACCCTGCAGTAGAGACA	(8)				
fliC H7	GCGCTGTCGAGTTCTATCGAGC	CAACGGTGACTTTATCGCCATTCC	(8)	x [2]	x [2]	x [2]	
focG	CAGCACAGGCAGTGGATACGA	GAATGTCGCCTGCCCATTGCT	(3)				
fyuA	TGATTAACCCCGCGACGGGAA	CGCAGTAGGCACGATGTTGTA	(3)		x		
gafD	TGTTGGACCGTCTCAGGGCTC	CTCCCGGAACTCGCTGTTACT	(3)				
hlyA	AACAAGGATAAGCACTGTTCTGGCT	ACCATATAAGCGGTCATTCCCGTCA	(3)				
hlyD	GCCGTCTGAAGGTGCGTCCGTCATCAC	GCGATTTCTTGGGCCAGGGCATTGTCG	(7)				
hlyE	AATATTTGTCGCTGC	TGTCAACAGGTAACTCTC	(9)		x [2]	x [2]	x [2]

hra	TCACTTGCAGACCAGCGTTTC	GTAACTCACACTGCTGTCACCT	(7)				
ibeA	AGGCAGGTGTGCGCCGCGTAC	TGGTGCTCCGGCAAACCATGC	(3)			x	
iss	VirulenceFinder [1]		(5)	x		x	x[3]
iutA	GGCTGGACATCATGGGAACTGG	CGTCGGGAACGGGTAGAATCG	(3)	x			
kpsMT II	GCGCATTTGCTGATACTGTTG	CATCCAGACGATAAGCATGAGCA	(3)				
kpsMT III	TCCTCTTGCTACTATTCCCCCT	AGGCGTATCCATCCCTCCTAAC	(3)				
kpsMT K1	TAGCAAACGTTCTATTGGTGC	CATCCAGACGATAAGCATGAGCA	(3)				
kpsMT K15	ACG GAT TCA CGA CAA AGC TC	GGC AAA TAT CGC TTG GGT TA	(7)				
kpsMT K2	GCGCATTTGCTGATACTGTTG	AGGTAGTTCAGACTCACACCT	(10)	x [2]			
kpsMT K5	CAGTATCAGCAATCGTTCTGTA	CATCCAGACGATAAGCATGAGCA	(3)				
malx	GGACATCCTGTTACAGCGCGCA	TCGCCACCAATCACAGCCGAAC	(7)				
nfaE	GCTTACTGATTCTGGGATGGA	CGGTGGCCGAGTCATATGCCA	(3)				
ompT	TCATCCCGGAAGCCCTCACTACT	TAGCGTTTGCTGCACTGGCTTCTGAT	(7)				
PAI	GGACATCCTGTTACAGCGCGCA	TCGCCACCAATCACAGCCGAAC	(3)				
papAH	ATGGCAGTGGTGTCTTTTGGTG	CGTCCCACCATACGTGCTCTTC	(3)	x [2]			
papC	GTGGCAGTATGAGTAATGACCGTTA	ATATCCTTTCTGCAGGGATGCAATA	(3)				
papEF	GCAACAGCAACGCTGGTTGCATCAT	AGAGAGAGCCACTCTTATACGGACA	(3)				
papG							
II,III	CTGTAATTACGGAAGTGATTTCTG	ACTATCCGGCTCCGGATAAACCAT	(3)	x [2]			
I	CTGTAATTACGGAAGTGATTTCTG	TCCAGAAATAGCTCATGTAACCCG	(3)				
allele I	TCGTGCTCAGGTCCGGAATTT	TGGCATCCCCCAACATTATCG	(3)				

allele I′a	CTACTATAGTTCATGCTCAGGTC	CTGACATCCTCCAACATTATCGA	(3)				
allele II	GGGATGAGCGGGCCTTTGAT	CGGGCCCCCAAGTAACTCG	(3)				
allele III	GGCCTGCAATGGATTTACCTGG	CCACCAAATGACCATGCCAGAC	(3)				
rfc	ATCCATCAGGAGGGGACTGGA	AACCATACCAACCAATGCGAG	(3)				
sfa/focDE	CTCCGGAGAACTGGGTGCATCTTAC	CGGAGGAGTAATTACAAACCTGGCA	(3)				
sfaS	GTGGATACGACGATTACTGTG	CCGCCAGCATTCCCTGTATTC	(3)				
traT	GGTGTGGTGCGATGAGCACAG	CACGGTTCAGCCATCCCTGAG	(3)	x	x		x
usp	ATGCTACTGTTTCCGGGTAGTGTGT	CATCATGTAGTCGGGGCGTAACAAT	(11)				
vat	GAACACAGTTCATCTGATCTCC	GAATATATCAAATTGGTCCCCC	(12)				
yfcV	ACATGGAGACCACGTTCACC	GTAATCTGGAATGTGGTCAGG	(13)				

[1] VirulenceFinder results were based on whole alignment to gene sequence, while all other genes were identified by in silico PCR with primer search from EMBOSS (14).

[2] Only forward or reverse primer found

[3] 99.66% Identity

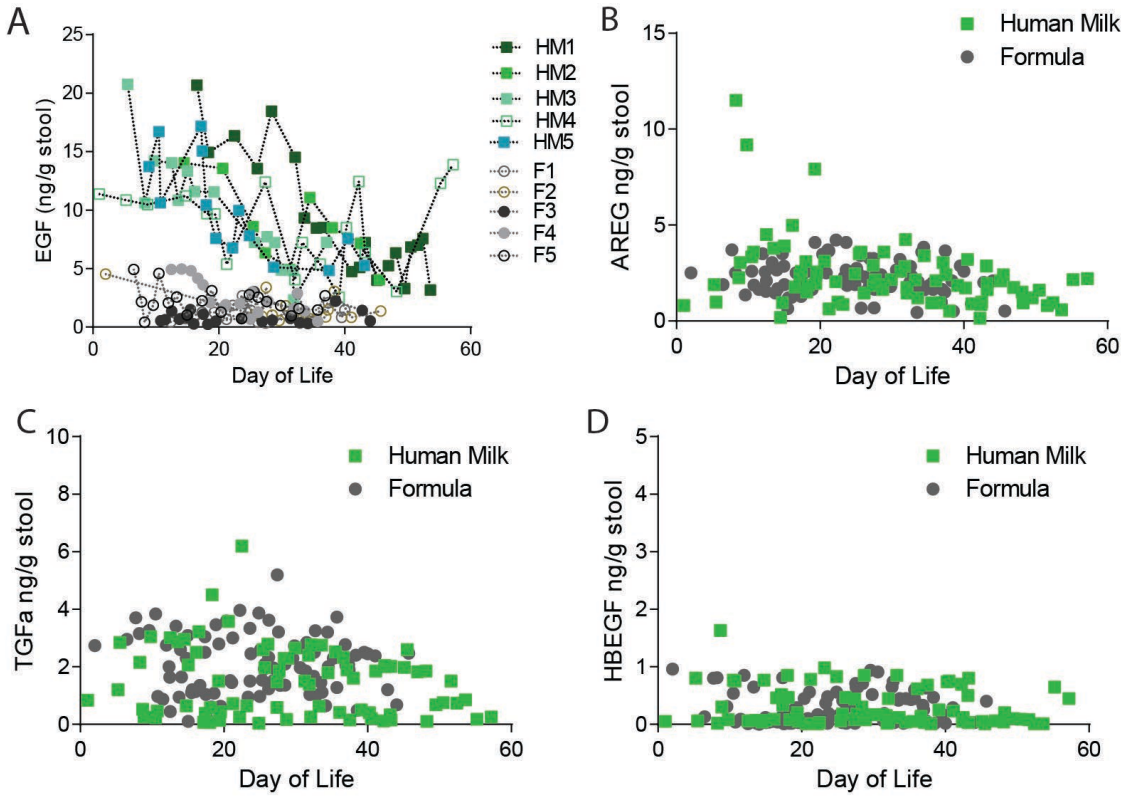

Figure S1: A) Concentration of EGF as measured by ELISA from the stool of individual VLBW children fed mother's own milk (green squares) or formula (gray circles), individuals denoted by connected line. B) Concentration of B) Amphiregulin (AREG), C) TGF-α , or D) Heparin-binding epidermal growth factor (HB-EGF) as measured by ELISA from the stool of VLBW children fed mother's own milk (green squares) or formula (gray circles).

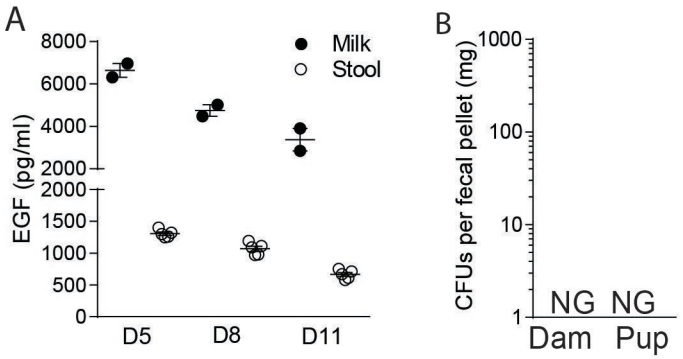

Figure S2: A) EGF concentration as measured by ELISA from the milk of lactating murine dam or stool from pups. B) CFUs of nalidixic acid resistant bacteria in fecal pellets from untreated breeding dams and pups, NG=no growth.

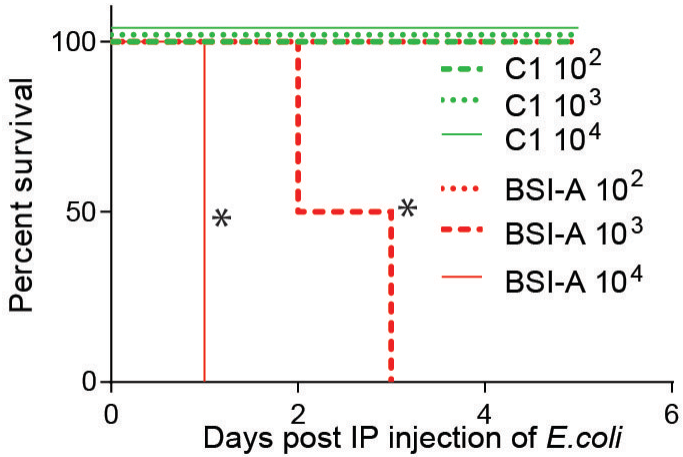

Figure S3: Kaplan-Meier survival curve of mice following of i.p. injection of *E. coli* strains. * denotes statistical significance, $p<0.05$ or less.

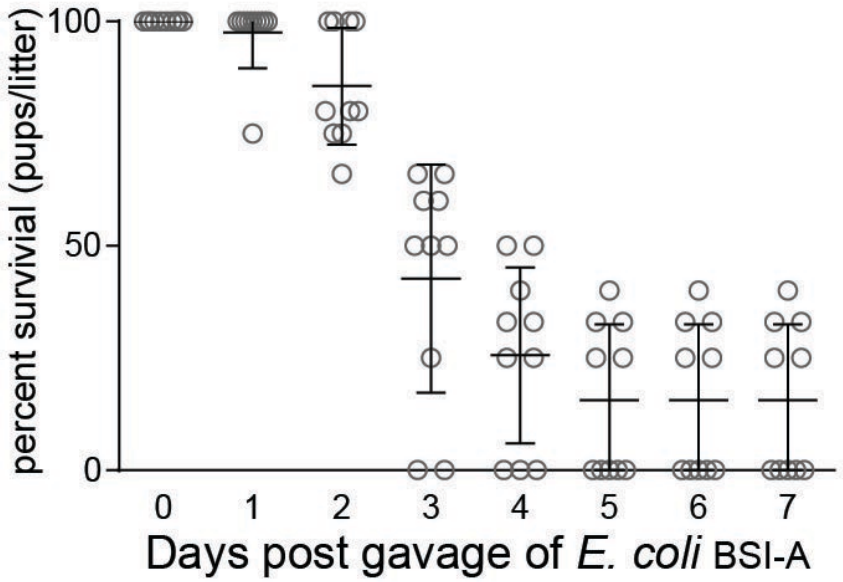

Figure S4: Percent surviving pups per litter post gavage of *E. coli* BSI-A^{NalR} in EGFRi treated mice. Each data point represents one litter measured repeatedly throughout the course of infection, and the percentage of surviving pups up to 7 days following gavage of *E. coli*. n=10 litters, with mean and SD plotted per group.

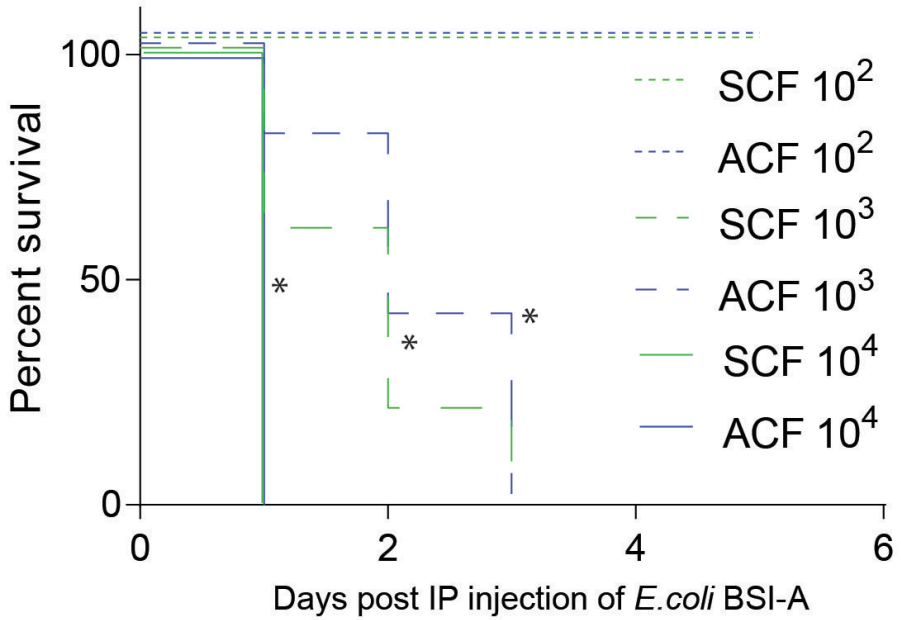

Figure S5: Kaplan-Meier survival curve of mice following of i.p. injection of *E. coli* BSI-A. * denotes statistical significance, $p<0.05$ or less.

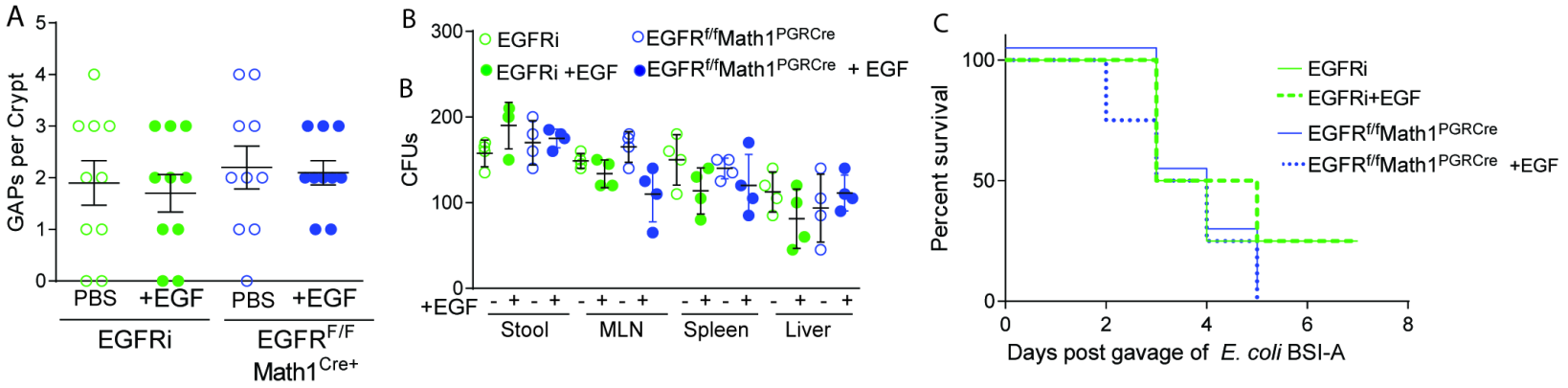

Figure S6: EGF does not rescue GAP formation, bacterial translocation, or sepsis in EGFRi treated mice or EGFR$^{f/f}$Math1^{PGRCre} mice. A) Counts of GAPs per colonic crypt in EGFRi treated mice or EGFR$^{f/f}$Math1^{PGRCre} mice gavaged with EGF or vehicle. B) CFUs in stool, mesenteric lymph node (MLN), spleen, and liver three days following gavage of 2x10^5 CFUs of *E. coli* BSI-A^{nalR} in conventionally reared EGFRi treated mice or EGFR$^{f/f}$Math1^{PGRCre} mice gavaged with EGF or vehicle. C) Survival of EGFRi treated mice or EGFR$^{f/f}$Math1^{PGRCre} mice gavaged with EGF or vehicle following gavage of 2x10^5 CFUs of *E. coli* BSI-A^{nalR}. n=4 mice per group in A-C.

Supplemental Methods:

Cohort description. Specimens were obtained from infants enrolled in a prospective cohort study performed to confirm or refute the hypothesis that bacterial dysbiosis precedes and increases the risk for necrotizing enterocolitis. Inclusion criteria for the participants consisted of birth weight ≤ 1500 g, admission to the NICUs at St. Louis Children's Hospital or Children's Hospital of Oklahoma University, Oklahoma City, OK, and expectation that the infant would survive the first week of life. Stools were stored briefly at 4°C in the respective neonatal intensive care units, after which they were frozen at −80°C until they were analyzed (15, 16), or used for culture (9).

In parallel, we stored all blood culture isolates from members of this cohort in nutrient broth with 15% glycerol. In a prior study, we sought and found bacteria in the stool that were isogenic with cognate bloodstream isolates, including BSI-A and BSI-C (from cases 5 and 7 in (9)) from patients hospitalized at St. Louis Children's Hospital. Additionally, we obtained stools from children who had been enrolled in the necrotizing enterocolitis study and discharged home from the St. Louis Children's Hospital using a courier service; *E. coli* strains C1 and C2 were isolated from these specimens (46). Details of the *E. coli* used in this study are provided in *Appendix* Tables S2 and S3.

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