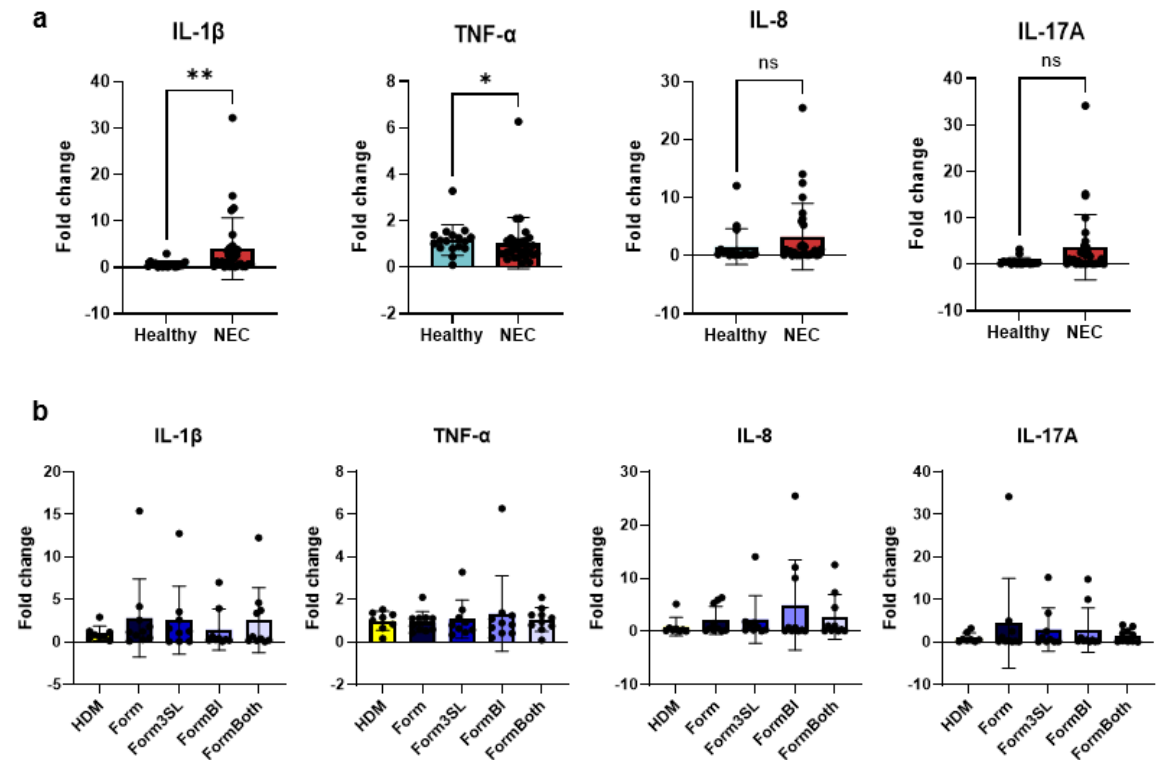
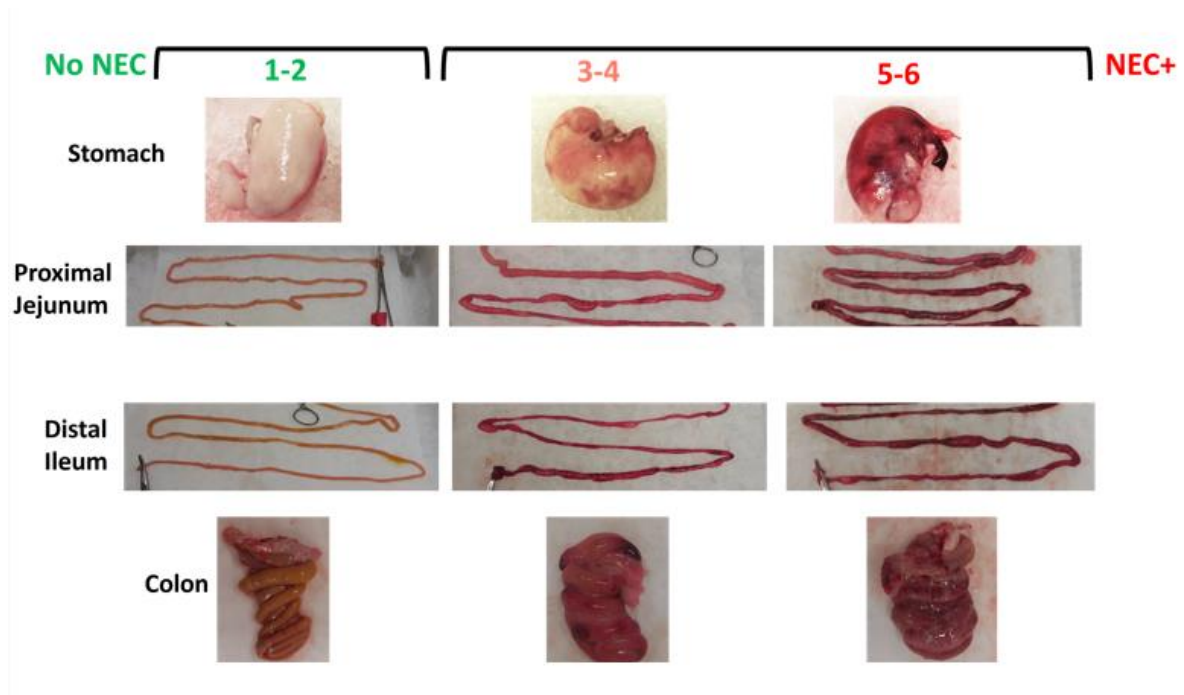


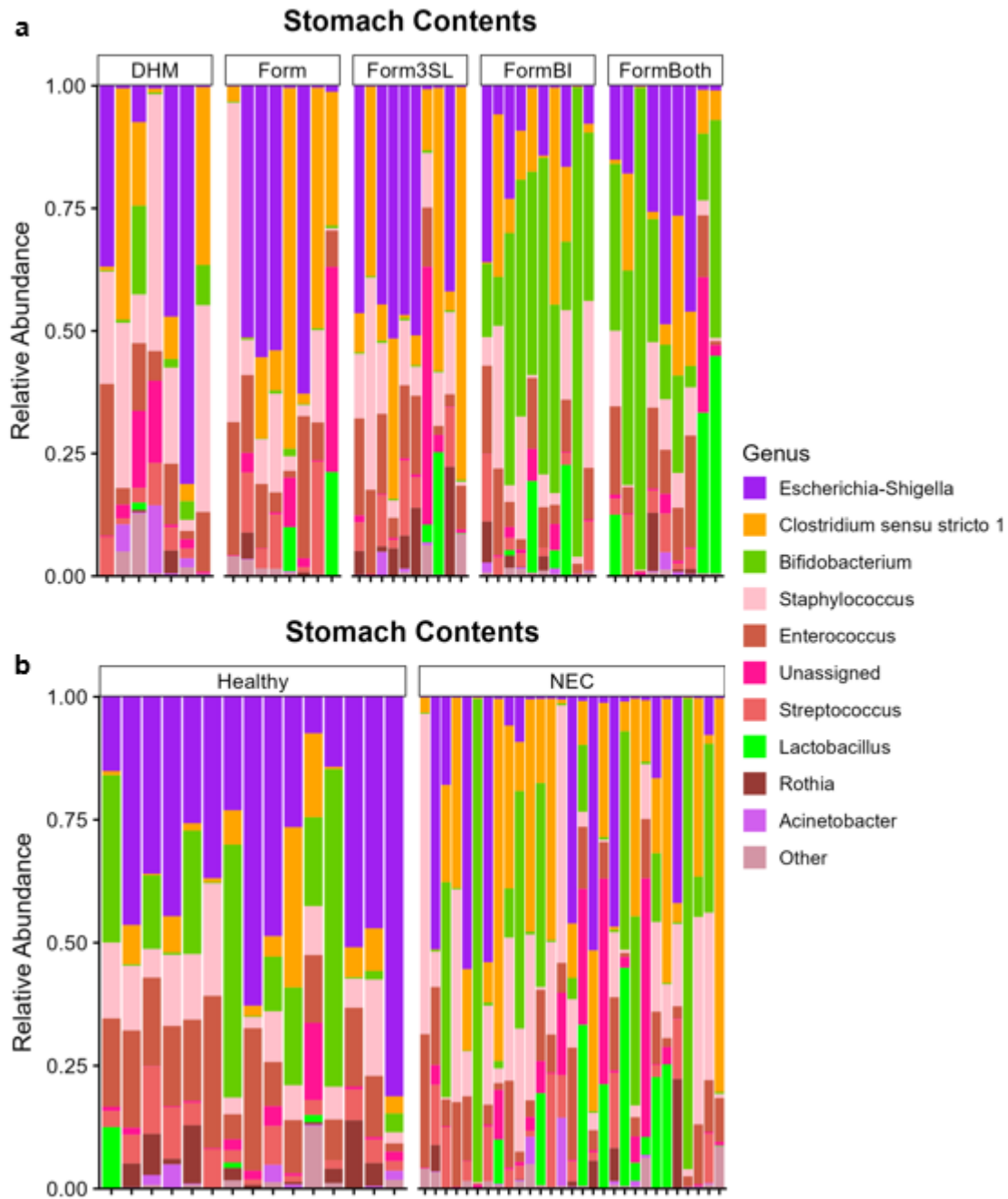
Supplementary Figure S1. Phenotypic study outcomes. **(a)** Gross severity score by intestinal segment. P-value was determined using a Two-way ANOVA, Tukey's multiple comparisons test; **:p-value \leq 0.01 between DHM and FormBoth. **(b)** Histological severity score by intestinal segment.



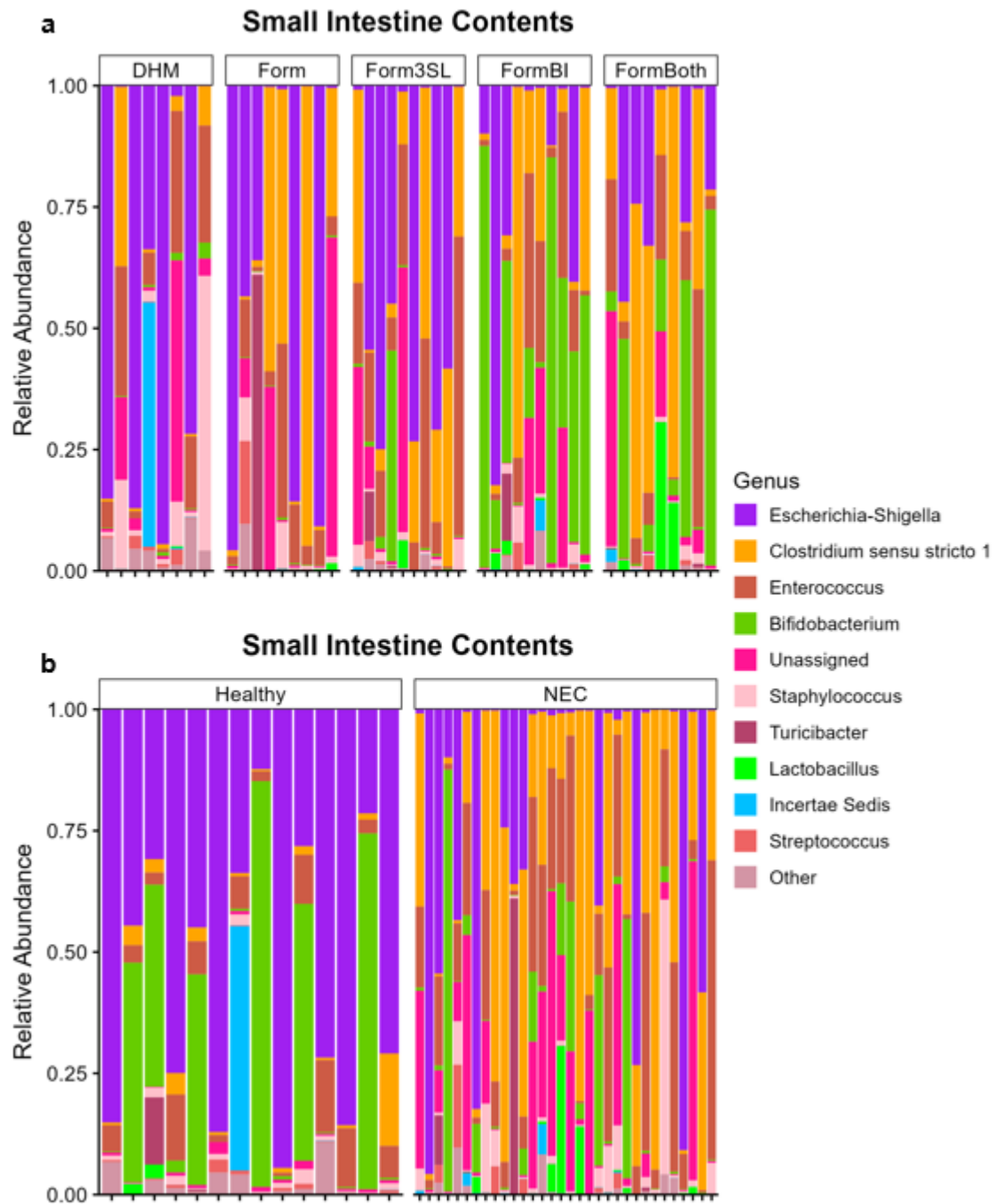
Supplementary Figure S2. Pro-inflammatory cytokine expression analysis in distal ileum tissue. **(a)** Fold change in expression of IL-1 β , TNF- α , IL-8, and IL-7a in healthy vs NEC piglets. **(b)** Fold change in expression of IL-1 β , TNF- α , IL-8, and IL-7a in all treatment groups (HDM (n= 8), Form (n=10), Form3SL (n=9), FormBoth (n=10), FormBI (n=9)).



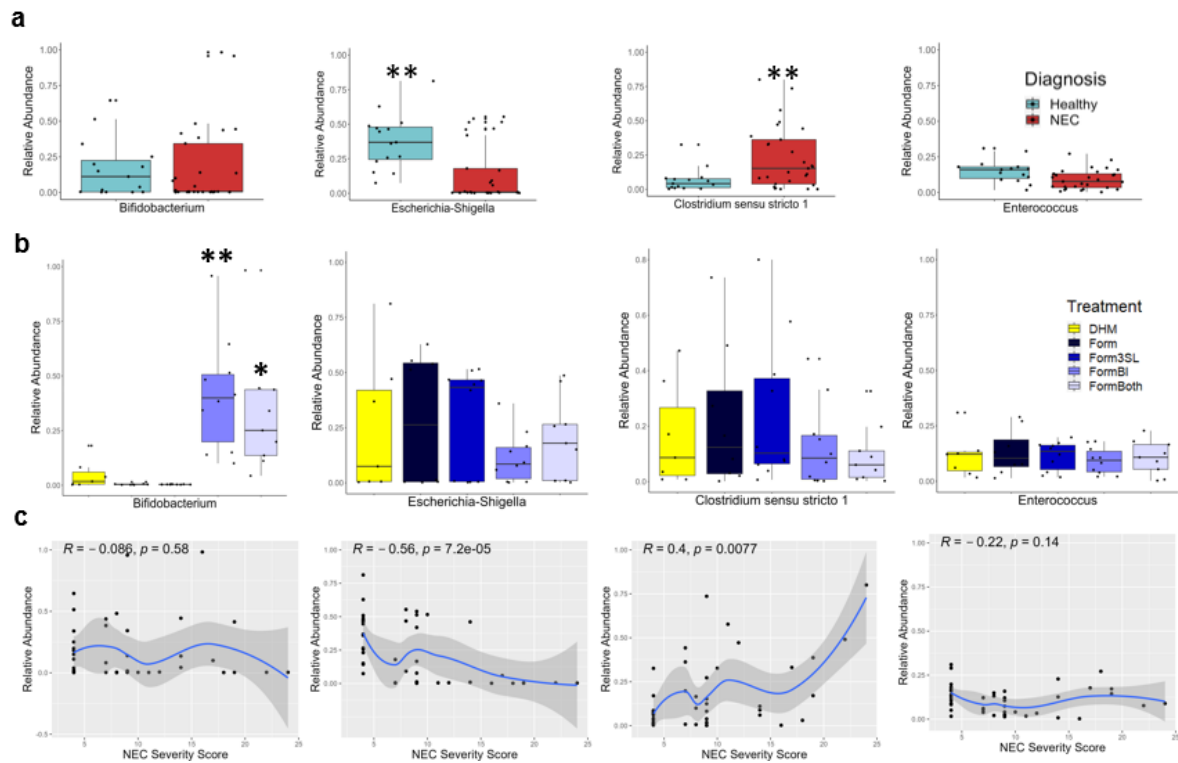
Supplementary Figure S3. Representative images and scoring of gross NEC severity score.



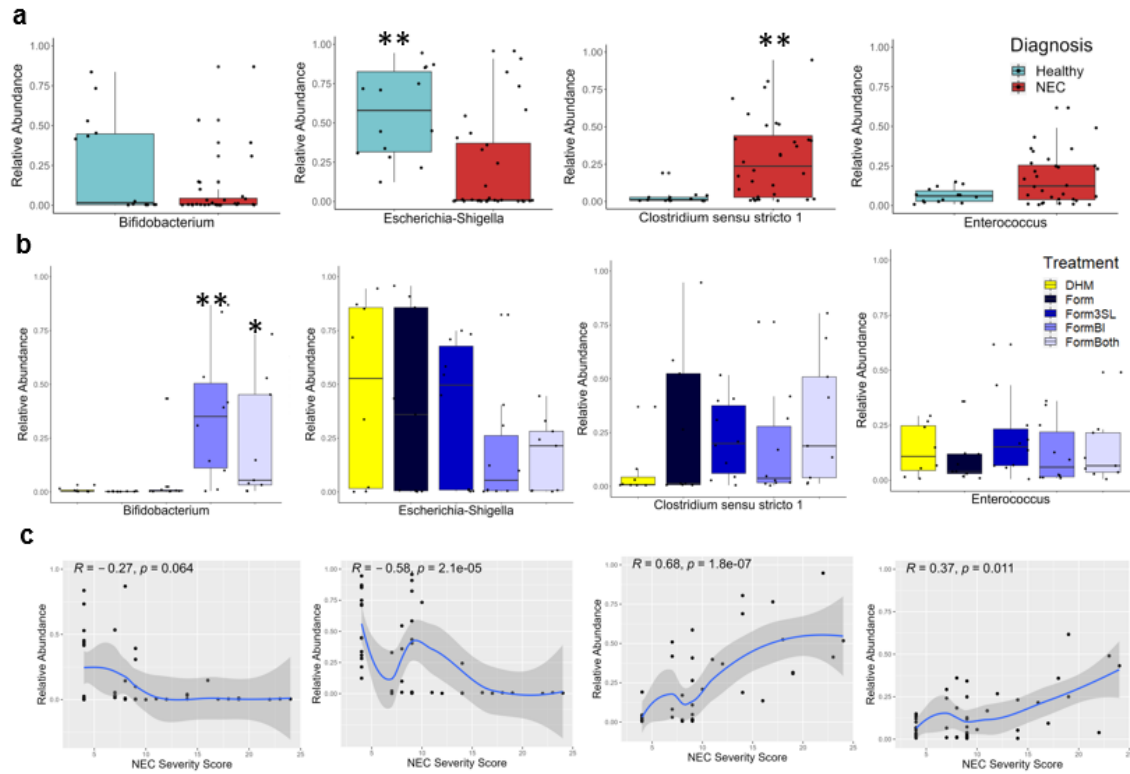
Supplementary Figure S4. Relative abundance by 16S sequencing of top 10 genera in stomach contents. (a) Relative abundance of top 10 genera in all treatment groups (DHM (n=9), Form (n=8), Form3SL (n=9), FormBI (n=11), and FormBoth (n=10)). (b) Relative abundance of top 10 genera in NEC (n=31) vs healthy (n=15) piglets.



Supplementary Figure S5. Relative abundance by 16S sequencing of top 10 genera in small intestinal contents. **(a)** Relative abundance of top 10 genera present in small intestinal contents in all treatment groups (DHM (n=9), Form (n=8), Form3SL (n=9), FormBI (n=11), and FormBoth (n=10)). **(b)** Relative abundance of top 10 genera present in small intestinal contents in NEC (n=31) vs healthy (n=15) piglets.



Supplementary Figure S6. Relative abundance and correlation with disease severity of top 3 most abundant genera in stomach contents by 16S sequencing. (a) Relative abundance of Bifidobacterium, Escherichia-Shigella, Clostridium sensu stricto 1, and Enterococcus genera in colon contents by diagnosis; P-value was determined using a Wilcoxon rank sum exact test; **:p-value ≤ 0.01 healthy (n=15) vs NEC (n=31) (a). (b) Relative abundance of Bifidobacterium, Escherichia-Shigella, Clostridium sensu stricto 1, and Enterococcus genera in colon contents by treatment group; P-value was determined using Kruskal-Wallis multiple comparisons followed by p-value adjustment with the Benjamin-Hochberg method; **:p-value ≤ 0.01 Form and Form3SL vs DHM (b). (DHM (n=9), Form (n=8), Form3SL (n=9), FormBI (n=11), and FormBoth (n=10)). (c) Spearman correlation of relative abundance of Bifidobacterium, Escherichia-Shigella, Clostridium sensu stricto 1, and Enterococcus with total NEC severity score (n=46).



Supplementary Figure S7. Relative abundance and correlation with disease severity of top 3 most abundant genera in small intestinal contents by 16S sequencing. (a) Relative abundance of Bifidobacterium, Escherichia-Shigella, Clostridium sensu stricto 1, and Enterococcus genera in colon contents by diagnosis; P-value was determined using a Wilcoxon rank sum exact test; **:p-value ≤ 0.01 healthy (n=15) vs NEC (n=31) (a). (b) Relative abundance of Bifidobacterium, Escherichia-Shigella, Clostridium sensu stricto 1, and Enterococcus genera in colon contents by treatment group; P-value was determined using Kruskal-Wallis multiple comparisons followed by p-value adjustment with the Benjamin-Hochberg method; **:p-value ≤ 0.01 Form and Form3SL vs DHM (b). (DHM (n=9), Form (n=8), Form3SL (n=9), FormBI (n=11), and FormBoth (n=10)). (c) Spearman correlation of relative abundance of Bifidobacterium, Escherichia-Shigella, Clostridium sensu stricto 1, and Enterococcus with total NEC severity score (n=46).