

Supplementary Materials

Figure S1

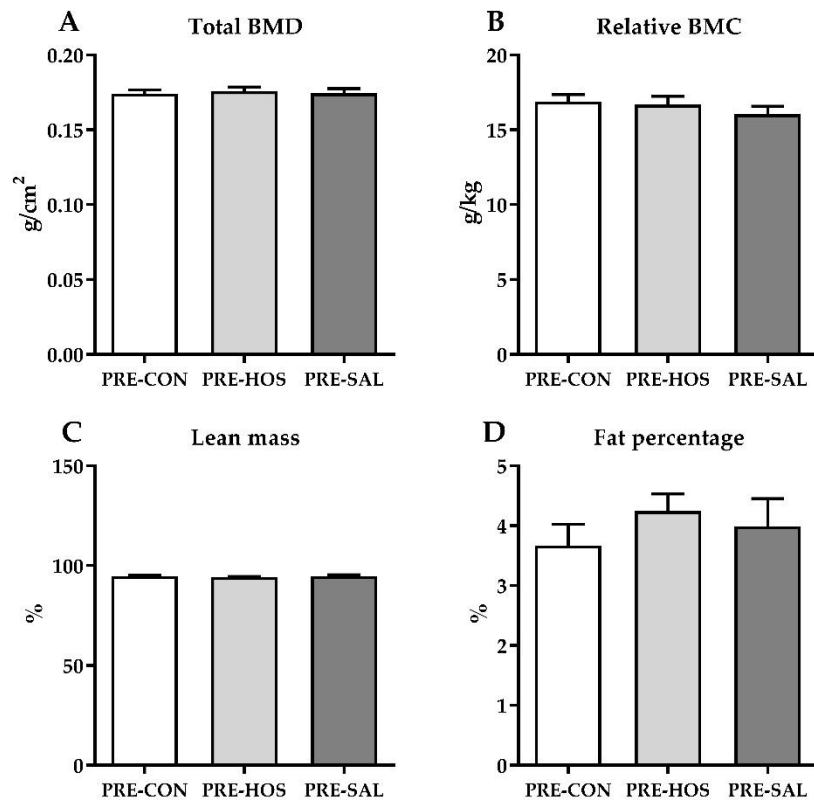


Figure S1. Dual Energy X-ray absorptiometry (DEXA) in preterm pigs (Experiment 1). (A) Bone mineral density (BMD, g/cm²), (B) bone mineral content (BMC, g/kg), (C) lean mass percentage and (D) fat percentage. Values are presented as mean $\pm$ SEM.

Figure S2

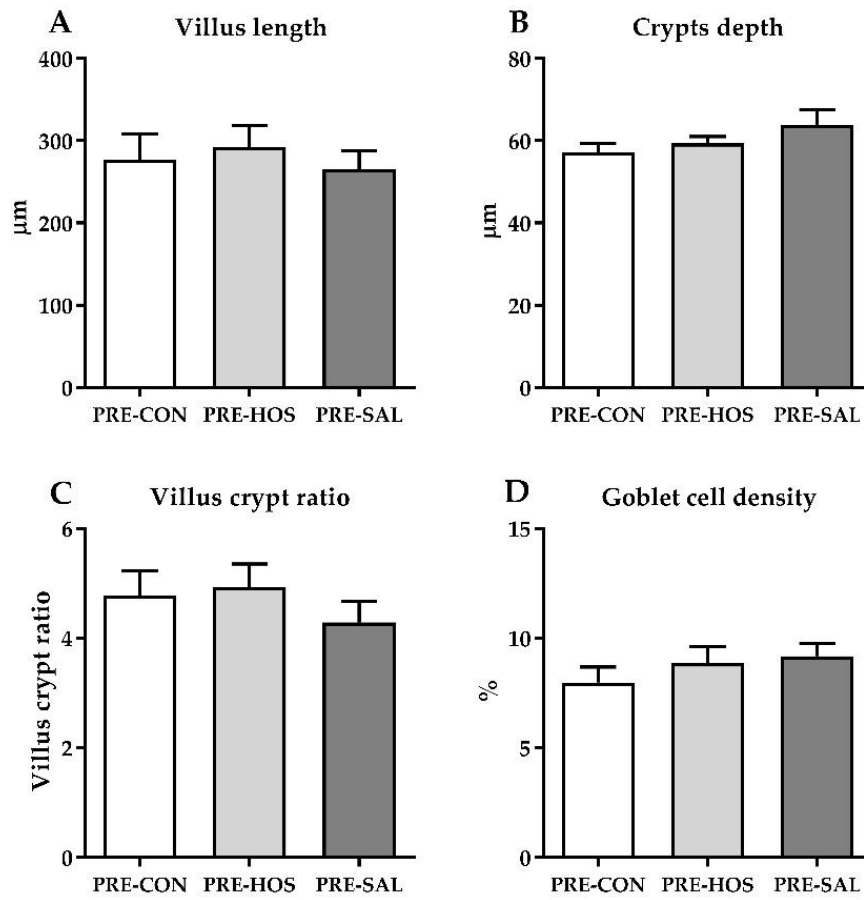


Figure S2. Gut structure in preterm pigs (Experiment 1). (A) Villus height, (B) crypt depth, and (C) villus/crypt ratio in the distal part of the small intestine. (D) Goblet cell density in colon. Values are presented as mean $\pm$ SEM.

Table S1

Organ weights at day 19 in preterm pigs (Experiment 1).

Relative organ weights (g/kg body weight)	PRE-CON	PRE-HOS	PRE-SAL
Proximal small intestine	15.0 $\pm$ 2.9	14.6 $\pm$ 2.8	14.2 $\pm$ 3.2
Middle small intestine	14.5 $\pm$ 3.3	13.9 $\pm$ 3.1	14.4 $\pm$ 3.5
Distal small intestine	16.7 $\pm$ 3.5	15.6 $\pm$ 2.6	15.4 $\pm$ 3.2
Stomach	7.6 $\pm$ 1.3	7.1 $\pm$ 1.0	7.1 $\pm$ 1.2
Colon	16.1 $\pm$ 7.7	15.6 $\pm$ 4.1	18.3 $\pm$ 10.1
Liver	22.3 $\pm$ 5.2	23.2 $\pm$ 6.5	23.1 $\pm$ 5.2
Spleen	1.9 $\pm$ 1.1	2.2 $\pm$ 1.2	2.2 $\pm$ 0.9
Heart	6.2 $\pm$ 1.0	6.3 $\pm$ 1.1	6.1 $\pm$ 1.0
Lungs	14.4 $\pm$ 2.2	16.8 $\pm$ 4.5	16.0 $\pm$ 5.0
Kidneys	7.4 $\pm$ 1.2	7.3 $\pm$ 1.3	6.9 $\pm$ 1.4
Adrenals	0.25 $\pm$ 0.06	0.22 $\pm$ 0.04	0.21 $\pm$ 0.06 [§]
Brain	27.8 $\pm$ 10.0	27.0 $\pm$ 7.9	24.2 $\pm$ 8.0

Expressed as relative weights as g/kg body weight. [§] indicates difference between PRE-CON and PRE-SAL. Values are presented as mean $\pm$ SD.

Table S2

Hematology measured at day 1, 10 and 19, respectively, in preterm pigs (Experiment 1).

Day 1	PRE-CON	PRE-HOS	PRE-SAL
WBC ($\times 10^9/L$)	2.6 ± 0.6	2.8 ± 0.4	2.7 ± 0.4
RBC ($\times 10^{12}/L$)	4.2 ± 0.4	4.3 ± 0.4	4.3 ± 0.4
Hemoglobin (mmol/L)	5.5 ± 0.4	5.6 ± 0.5	5.7 ± 0.5
Hematocrit (L/L)	0.29 ± 0.02	0.29 ± 0.02	0.30 ± 0.02
Platelets ($\times 10^9/L$)	107 ± 29	113 ± 45	$132 \pm 57^{\S}$
Neutrophils ($\times 10^9/L$)	0.7 ± 0.2	0.7 ± 0.3	0.7 ± 0.2
Lymphocytes ($\times 10^9/L$)	1.8 ± 0.5	1.9 ± 0.4	1.8 ± 0.4
Monocytes ($\times 10^9/L$)	0.08 ± 0.04	0.07 ± 0.05	0.12 ± 0.24
Eosinophils ($\times 10^9/L$)	0.03 ± 0.02	0.02 ± 0.01	0.02 ± 0.02
Basophils ($\times 10^9/L$)	0.02 ± 0.02	0.02 ± 0.01	0.02 ± 0.02
Day 10			
WBC ($\times 10^9/L$)	5.5 ± 1.3	5.4 ± 1.6	5.6 ± 1.2
RBC ($\times 10^{12}/L$)	4.4 ± 0.7	4.4 ± 0.6	4.3 ± 0.9
Hemoglobin (mmol/L)	5.1 ± 1.1	5.0 ± 0.8	5.0 ± 1.1
Hematocrit (L/L)	0.3 ± 0.1	0.3 ± 0.03	0.3 ± 0.05
Platelets ($\times 10^9/L$)	281 ± 124	303 ± 125	331 ± 156
Neutrophils ($\times 10^9/L$)	2.8 ± 0.8	2.7 ± 1.1	2.7 ± 0.8
Lymphocytes ($\times 10^9/L$)	2.4 ± 0.7	2.4 ± 0.7	2.5 ± 0.6
Monocytes ($\times 10^9/L$)	0.13 ± 0.06	0.11 ± 0.05	0.13 ± 0.08
Eosinophils ($\times 10^9/L$)	0.10 ± 0.03	0.11 ± 0.05	0.11 ± 0.03
Basophils ($\times 10^9/L$)	0.01 ± 0.01	0.02 ± 0.02	0.03 ± 0.03
Day 19			
WBC ($\times 10^9/L$)	10.3 ± 3.5	8.7 ± 5.9	8.9 ± 5.2
RBC ($\times 10^{12}/L$)	4.8 ± 0.7	4.6 ± 0.7	4.5 ± 0.7
Hemoglobin (mmol/L)	5.0 ± 0.8	4.8 ± 0.6	4.8 ± 0.7
Hematocrit (L/L)	0.26 ± 0.05	0.25 ± 0.04	0.24 ± 0.05
Platelets ($\times 10^9/L$)	378 ± 210	333 ± 184	299 ± 193
Neutrophils ($\times 10^9/L$)	6.0 ± 2.9	4.9 ± 5.0	5.6 ± 4.3
Lymphocytes ($\times 10^9/L$)	3.6 ± 1.1	3.3 ± 1.2	2.7 ± 1.3
Monocytes ($\times 10^9/L$)	0.3 ± 0.2	0.2 ± 0.1	0.2 ± 0.2
Eosinophils ($\times 10^9/L$)	0.15 ± 0.05	0.14 ± 0.14	0.11 ± 0.14
Basophils ($\times 10^9/L$)	0.04 ± 0.05	0.03 ± 0.03	0.03 ± 0.03

Abbreviations: WBC, white blood cells; RBC, red blood cells. § indicates difference between PRE-CON and PRE-SAL. Values are presented as mean $\pm$ SD.

Table S3

Organ weights at day 19 in near-term pigs (Experiment 2).

Relative organ weights (g/kg body weight)	TERM-CON	TERM-NAT	P-value
Proximal small intestine	14.2 ± 1.7	11.7 ± 1.6	**
Middle small intestine	11.2 ± 1.2	11.8 ± 1.7	*

Distal small intestine	15.2 ± 1.4	15.7 ± 1.8	
Stomach	7.0 ± 1.0	6.1 ± 1.9	
Colon	24.5 ± 8.9	12.8 ± 3.8	**
Liver	24.9 ± 3.8	26.0 ± 2.6	
Spleen	2.9 ± 0.6	5.2 ± 1.6	***
Heart	6.5 ± 0.5	6.4 ± 0.8	
Lungs	13.4 ± 1.9	16.6 ± 4.5	*
Kidneys	8.3 ± 1.2	7.2 ± 0.5	
Adrenals	0.20 ± 0.03	0.12 ± 0.02	***
Brain	23.6 ± 4.4	11.0 ± 4.9	***

Expressed as relative weights as g/kg body weight. Values are presented as mean ± SD.

Table S4

Small intestinal brush border enzyme activity and colonic microbial metabolite concentrations in near-term pigs (Experiment 2)

Brush border enzymes¹ (U/g)	TERM-CON	TERM-NAT	P-value
Sucrase	0.29 ± 0.17	10.4 ± 2.46	***
Maltase	3.35 ± 1.30	27.0 ± 8.04	***
Lactase	2.72 ± 2.12	53.2 ± 9.83	***
Aminopeptidase N	2.43 ± 0.56	8.44 ± 2.24	***
Aminopeptidase A	1.31 ± 0.51	5.61 ± 0.93	***
Dipeptidyl peptidase IV	0.89 ± 0.24	3.77 ± 0.68	***
Microbial metabolites (mmol/L)			
Acetic acid	65.9 ± 34.9	183.1 ± 103.5	**
Propionic acid	0.68 ± 0.74	26.3 ± 16.3	***
Butyric acid	1.87 ± 1.45	9.39 ± 7.01	***
Valeric acid	0.09 ± 0.20	4.34 ± 2.50	***
Propanediol	1.00 ± 0.93	2.15 ± 2.55	
Methyl Butanoic Acid	0.07 ± 0.04	1.56 ± 0.77	***
Lactate	41.5 ± 38.9	4.37 ± 12.3	**
Σ (SCFA and lactate)	111 ± 589	231 ± 131	

¹Day 19 brush border enzyme activity in the middle part of the small intestine. Values are presented as mean ± SD.

Table S5

Hematology measured at day 1, 10 and 19, respectively in near-term pigs (Experiment 2)							
	Day 1	Day 10		P-value	Day 19		P-value
	TERM-CON	TERM-CON	TERM-NAT		TERM-CON	TERM-NAT	
WBC ($\times 10^9/L$)	4.0 $\pm$ 1.0	6.6 $\pm$ 1.9	15.0 $\pm$ 6.7	**	6.6 $\pm$ 3.0	8.8 $\pm$ 6.0	
RBC ($\times 10^{12}/L$)	5.2 $\pm$ 0.5	5.8 $\pm$ 0.7	4.9 $\pm$ 0.6	**	5.3 $\pm$ 0.7	4.7 $\pm$ 0.7	*
Hemoglobin (mmol/L)	6.3 $\pm$ 0.6	6.4 $\pm$ 0.6	5.8 $\pm$ 0.6	**	5.7 $\pm$ 0.7	4.5 $\pm$ 1.1	**
Hematocrit (L/L)	0.34 $\pm$ 0.03	0.3 $\pm$ 0.03	0.3 $\pm$ 0.03		0.30 $\pm$ 0.04	0.24 $\pm$ 0.05	**
Platelets ($\times 10^9/L$)	205 $\pm$ 45	208 $\pm$ 80	539 $\pm$ 151	***	201 $\pm$ 128	527 $\pm$ 297	**
Neutrophils ($\times 10^9/L$)	2.0 $\pm$ 0.8	3.0 $\pm$ 1.4	8.4 $\pm$ 6.6	*	2.7 $\pm$ 1.9	4.4 $\pm$ 3.6	
Lymphocytes ($\times 10^9/L$)	1.9 $\pm$ 0.5	3.2 $\pm$ 1.4	5.8 $\pm$ 2.0	**	3.4 $\pm$ 1.2	3.8 $\pm$ 4.3	
Monocytes ($\times 10^9/L$)	0.07 $\pm$ 0.06	0.19 $\pm$ 0.09	0.42 $\pm$ 0.15	***	0.3 $\pm$ 0.2	0.2 $\pm$ 0.3	
Eosinophils ($\times 10^9/L$)	0.03 $\pm$ 0.04	0.04 $\pm$ 0.05	0.04 $\pm$ 0.03		0.05 $\pm$ 0.05	0.06 $\pm$ 0.05	
Basophils ($\times 10^9/L$)	0.01 $\pm$ 0.01	0.02 $\pm$ 0.01	0.10 $\pm$ 0.06	***	0.04 $\pm$ 0.02	0.11 $\pm$ 0.29	

Abbreviations: WBC, white blood cells; RBC, red blood cells. Values are presented as mean $\pm$ SD.

Table S6

Serum and CSF biochemistry measured at day 19 in near-term pigs (Experiment 2)

Serum	TERM-CON	TERM-NAT	P-value
Albumin (g/L)	15.39 $\pm$ 1.74	27.47 $\pm$ 6.27	***
Total protein (g/L)	25.14 $\pm$ 1.87	42.31 $\pm$ 5.80	***
Alkaline phosphatase (U/L)	878 $\pm$ 334	3335 $\pm$ 1427	***
Alanine aminotransferase (U/L)	30.86 $\pm$ 5.17	31.42 $\pm$ 9.13	
Total bilirubin (μ mol/L)	2.56 $\pm$ 0.98	3.09 $\pm$ 1.09	
Cholesterol (mmol/L)	1.75 $\pm$ 0.32	3.21 $\pm$ 0.52	***
Creatinine (μ mol/L)	47.64 $\pm$ 7.37	76.92 $\pm$ 11.41	***
Creatine kinase (U/L)	222 $\pm$ 110	584 $\pm$ 226	***
Iron (μ mol/L)	9.09 $\pm$ 3.28	5.87 $\pm$ 7.04	*
Phosphate (mmol/L)	2.50 $\pm$ 0.34	3.12 $\pm$ 0.67	*
Aspartate aminotransferase (U/L)	28.50 $\pm$ 5.49	37.25 $\pm$ 9.37	*
Blood urea nitrogen (mmol/L)	4.25 $\pm$ 3.09	3.40 $\pm$ 0.80	
Gamma-glutamyl transferase (U/L)	18.00 $\pm$ 4.84	26.58 $\pm$ 7.72	**
Calcium (mmol/L)	2.41 $\pm$ 0.13	2.91 $\pm$ 0.18	***
Magnesium (mmol/L)	0.80 $\pm$ 0.05	1.07 $\pm$ 0.17	***
Sodium (mmol/L)	139.5 $\pm$ 2.3	148.0 $\pm$ 5.9	***
Potassium (mmol/L)	4.03 $\pm$ 0.44	4.10 $\pm$ 0.67	
Lactate (mmol/L)	1.49 $\pm$ 0.45	3.54 $\pm$ 5.10	
Glucose (mmol/L)	6.25 $\pm$ 2.01	8.74 $\pm$ 3.92	
CSF			
Albumin (mg/L)	8.99 $\pm$ 3.01	26.08 $\pm$ 10.06	***
Total protein (mg/L)	144.7 $\pm$ 33.0	222.0 $\pm$ 60.4	**
Lactate (mmol/L)	1.90 $\pm$ 0.64	2.32 $\pm$ 1.46	

Glucose (mmol/L)	3.32 ± 0.96	3.75 ± 0.86
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Abbreviations: CSF, cerebrospinal fluid. Values are presented as mean ± SD.