Animal Journal

Review: A systematic review of the effects of functional amino acids on small intestine barrier function and immunity in piglets

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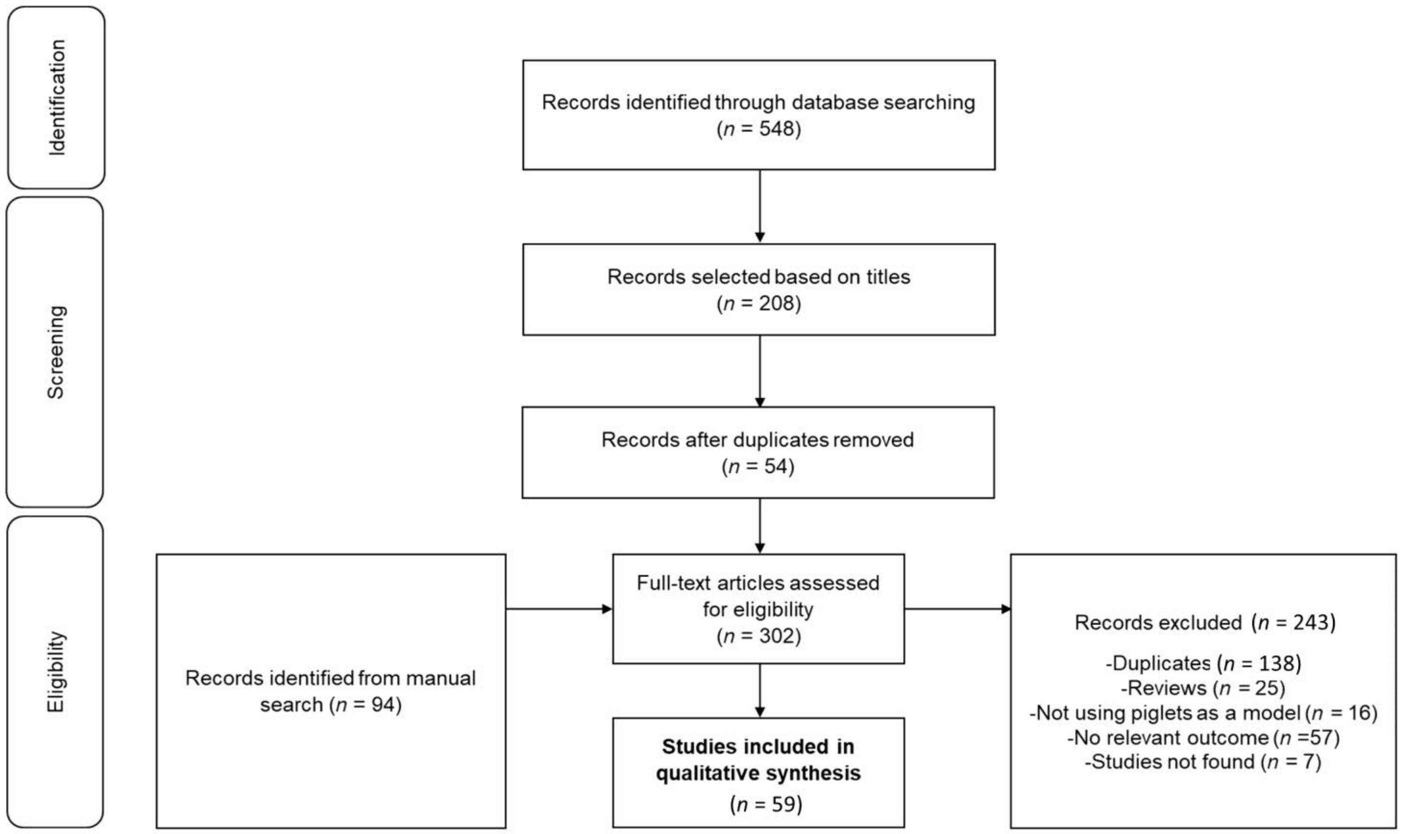

Supplementary Figure 1. Flow chart for the selection of the articles to evaluate the effects of functional amino acids on small intestine barrier function and immunity in piglets

Supplementary Table 1. Complete list of articles obtained from the literature search on the effects of amino acids on small intestine barrier function and immunity in piglets.

Titles	Author	Year	Challenge	AA tested	Supplementation (%)	Duration (d)	n per group	Age (d)	BW (kg)
Antioxidant status and inflammatory response in weanling piglets fed diets supplemented with arginine and zinc	Bergeron	2013	Yes, LPS (d12)	L-Arginine	1	12	7--9	20	6.43
Effects of creep feeding and supplemental glutamine or glutamine plus glutamate (Aminogut) on pre- and post-weaning growth performance and intestinal health of piglets	Cabrera	2013	No	L-Glutamine	1	42	15	14	6.5
Asparagine improves intestinal integrity, inhibits TLR4 and NOD signaling, and differently regulates p38 and ERK1/2 signaling in weanling piglets after LPS challenge.	Chen	2016	Yes, LPS (d21)	L-Asparagine	0.5 or 1	21	6	35	8.87
l-Methionine supplementation maintains the integrity and barrier function of the small-intestinal mucosa in post-weaning piglets	Chen	2014	No	L-Methionine	0.12	14	6	28	7.3
Can nutraceuticals affect the structure of intestinal mucosa? Qualitative and quantitative microanatomy in L-glutamine diet-supplemented weaning piglets	Domeneghini	2006	No	L-Glutamine	0.5	28	8	21	5.07
Structural patterns of swine ileal mucosa following L-glutamine and nucleotide administration during the weaning period An histochemical and histometrical study	Domeneghini	2004	No	L-Glutamine	0.5	28	4	21	4.97
Glutamine supplementation improves intestinal barrier function in a weaned piglet model of Escherichia coli infection	Ewaschuk	2010	No	L-Glutamine	4.4	14	10	21	5--10
Intestinal development of early-weaned piglets receiving diets supplemented with selected amino acids or polyamines	Ewtushik	2000	No	L-Arginine or L-Glutamate	0.93 and 6.51	12	7	12.5	3.94
Dietary tryptophan and threonine supply to 28 days old weaned piglets	Fernández	2009	No	L-Tryptophan	0.4, 0.7, 1.2	28	60	28	8.1

AA: tested amino acids; d = days; n per group = numebrs of animals per group; BW= initial body weight; LPS=Lipopolysaccharides; DON=Deoxynivalenol; NA= not available

Titles	Author	Year	Challenge	AA tested	Supplementation (%)	Duration (d)	n per group	Age (d)	BW (kg)
Effects of Alpha-Ketoglutarate on Glutamine Metabolism in Piglet Enterocytes in Vivo and in Vitro	He	2016	No	L-Glutamine	1	14	7	28	6
Effects of different dietary tryptophan : lysine ratios and sanitary conditions on growth performance, plasma urea nitrogen, serum haptoglobin and ileal histomorphology of weaned pigs	Jayaraman	2016	No	L-Tryptophan	0.2, 0.5, 0.7, 0.9	14	18	21	7.36
Evaluating the behavior, growth performance, immune parameters, and intestinal morphology of weaned piglets after simulated transport and heat stress when antibiotics are eliminated from the diet or replaced with L-glutamine	Johnson	2017	Yes (Transport and heat stress)	L-Glutamine	0.5	14	20	21	5.6
Effects of supplemental L-tryptophan on serotonin, cortisol, intestinal integrity, and behavior in weanling piglets	Koopmans	2006	No	L-Tryptophan	0.5	20	36	25	NA
Effect of Dietary Glutamine Supplement on Performance and Intestinal Morphology of Weaned Pigs	Lee	2003	No	L-Glutamine	0.5 or 1 or 1.5	28	4--8	21	5.95
Tryptophan increases intestinal permeability and decreases intestinal tight junction protein expression in weanling piglets	Li	2016	No	L-Tryptophan	0.1	14	7	21	6.5
Dietary arginine supplementation alleviates intestinal mucosal disruption induced by Escherichia coli lipopolysaccharide in weaned pigs	Liu	2008	Yes, LPS (d16)	L-Arginine	1	18	18	21	5.78
Dietary L-arginine Supplementation Improves Intestinal Function in Weaned Pigs after an Escherichia coli Lipopolysaccharide Challenge	Liu	2009	Yes, LPS (d16)	L-Arginine	0.5 or 1	18	18	21	5.78
Dietary Leucine Supplementation Improves the Mucin Production in the Jejunal Mucosa of the Weaned Pigs Challenged by Porcine Rotavirus	Mao	2015	Yes, porcine rotavirus (d11)	L-Leucine	1	17	6	21	NA
Dietary supplementation of aspartate enhances intestinal integrity and energy status in weanling piglets after lipopolysaccharide challenge	Pi	2014	Yes, LPS (d19)	L-Aspartate	0.5 or 1	20	6	21	8.9

AA: tested amino acids; d = days; n per group = numebrs of animals per group; BW= initial body weight; LPS=Lipopolysaccharides; DON=Deoxynivalenol; NA= not available

Titles	Author	Year	Challenge	AA tested	Supplementation (%)	Duration (d)	n per group	Age (d)	BW (kg)
Maintenance of villous height and crypt depth in piglets by providing continuous nutrition after weaning	Pluske	1996	No	L-Glutamine	2	5	8	28	8.9
Increased levels of standardized ileal digestible threonineattenuate intestinal damage and immune responses inEscherichia coli K88+challenged weaned piglets	Ren	2014	No	L-Threonine	0.75-1.11	18	6	21	7.34
Effect of High Dietary Tryptophan on Intestinal Morphology and Tight Junction Protein of Weaned Pig	Tossou	2016	No	L-Tryptophan	0.15 or 0.75	22	12	NA	8.26
A tryptophan-enriched diet improves feed intake and growth performance of susceptible weanling pigs orally challenged with Escherichia coli K88	Trevisi	2009	Yes, E. Coli (d4)	L-Tryptophan	0.10	23	11--15	21	6.5
Effect of added dietary threonine on growth performance, health, immunity and gastrointestinal function of weaning pigs with differing genetic susceptibility to Escherichia coli infection and challenged with E. coli K88ac	Trevisi	2014	Yes, E. coli (d7)	L-Threonine	0.05	13	12	24	7.7
Gene expression is altered in piglet small intestine by weaning and dietary glutamine supplementation	Wang	2008	No	L-Glutamine	1	7	12	21	5.93
Glutamine Enhances Tight Junction Protein Expression and Modulates Corticotropin- Releasing Factor Signaling in the Jejunum of Weanling Piglets	Wang	2014	No	L-Glutamine	1	7	12	21	6.68
Asparagine attenuates intestinal injury, improves energy status and inhibits AMP-activated protein kinase signalling pathways in weaned piglets challenged with Escherichia coli lipopolysaccharide.	Wang	2015	Yes,LPS (d19)	L-Asparagine	0.5-1	20	6	35	8.9
Aspartate attenuates intestinal injury and inhibits TLR4 and NODs/NF-κB and p38 signaling in weaned pigs after LPS challenge.	Wang	2016	Yes, LPS (d21)	L-Aspartate	0.5-1	21	6	35	8.92
Dietary glutamine supplementation prevents jejunal atrophy in weaned pigs	Wu	1996	No	L-Glutamine	1	14	10	21	NA

AA: tested amino acids; d = days; n per group = numebrs of animals per group; BW= initial body weight; LPS=Lipopolysaccharides; DON=Deoxynivalenol; NA= not available

Titles	Author	Year	Challenge	AA tested	Supplementation (%)	Duration (d)	n per group	Age (d)	BW (kg)
Dietary supplementation with L-arginine or N-carbamylglutamate enhances intestinal growth and heat shock protein-70 expression in weanling pigs fed a corn- and soybean meal-based diet.	Wu	2010	No	L-Arginine	0.6	7	28	21	5.56
Effects of alanyl-glutamine supplementation on the small intestinal mucosa barrier in weaned piglets	Xing	2016	No	L-Glutamine	0.34	28	60	35	10.01
Dietary L-arginine supplementation enhances intestinal development and expression of vascular endothelial growth factor in weanling piglets	Yao	2011	No	L-Arginine	1	7	10	21	5.3
Effect of glutamine and spray-dried plasma on growth performance, small intestinal morphology, and immune responses of K88-challenged weaned pigs	Yi	2005	Yes, E. Coli (d12)	L-Glutamine	2	14	8--10	17	5.32
Effects of Dietary Supplementation with Glutamate and Aspartate on Diquat-Induced Oxidative Stress in Piglets	Yin	2015	Yes, diquat (d5)	L-Aspartate or L-Glutamate	2	7	6	NA	9.92
Antioxidant status and expression of inflammatory genes in gut and liver of piglets fed different dietary methionine concentrations	Zeitz	2016	No	L-Methionine	0.04 or 0.08	21	15	NA	11
Dietary Arginine Supplementation Affects Microvascular Development in the Small Intestine of Early-Weaned Pigs	Zhan	2008	No	L-Arginine	0.7 or 1.2	10	8	14	5
Effects of Dietary Glutamine and Glutamate Supplementation on Small Intestinal Structure, Active Absorption and DNA, RNA Concentrations in Skeletal Muscle Tissue of Weaned Piglets during d 28 to 42 of Age	Liu	2002	No	L-Glutamate	1	14	24	28	NA
L-Glutamate Supplementation Improves Small Intestinal Architecture and Enhances the Expressions of Jejunal Mucosa Amino Acid Receptors and Transporters in Weaning Piglets	Lin	2014	No	L-Glutamate	1 or 2	28	60	35	8.91
Intestinal growth and morphology is associated with the increase in heat shock protein 70 expression in weaning piglets through supplementation with glutamine	Zhong	2011	No	L-Glutamine	6	14		21	6.5

AA: tested amino acids; d = days; n per group = numebrs of animals per group; BW= initial body weight; LPS=Lipopolysaccharides; DON=Deoxynivalenol; NA= not available

Titles	Author	Year	Challenge	AA tested	Supplementation (%)	Duration (d)	n per group	Age (d)	BW (kg)
Effects of glutamine on growth performance of weanling piglets	Zou	2006	No	L-Glutamine	1	20	30	21	5
Feed supplementation with arginine and zinc on antioxidant status and inflammatory response in challenged weanling piglets	Bergeron	2017	Yes, LPS (d5, d12)	L-Arginine	1	14	12	34	7.39
Effects of Dietary Serine Supplementation on Intestinal Integrity, Inflammation and Oxidative Status in Early-Weaned Piglets	Zhou	2018	No	L-Serine	0.2	28	14	35	6.5
L-Cysteine protects intestinal integrity, attenuates intestinal inflammation and oxidant stress, and modulates NF-iB and Nrf2 pathways in weaned piglets after LPS challenge	Song	2016	Yes, LPS (d19)	L-Cysteine	0.25 or 0.5	20		41	6.72
Effect of L-arginine on intestinal mucosal immune barrier function in weaned pigs after Escherichia coli LPS challenge	Zhu	2012	Yes, LPS (d16)	L-Arginine	0.5	18	6		5.53
Effects of Glutamine on Growth Performance and Small Intestine Villus Height in Weanling Pigs	Kitt	2002	No	L-Glutamine	1	18	16	39	NA
l-Isoleucine Administration Alleviates Rotavirus Infection and Immune Response in the Weaned Piglet Model	Mao	2018	Yes (Rotavirus, d15)	L-Isoleucine	0.68	18	7	39	6.5
Effects of Supplemental Glutamine on Growth Performance,Plasma Parameters and LPS-induced Immune Response of Weaned Barrows after Castration	Hsu	2012	No	L-Glutamine	2	25	24		8.18
L-tryptophan Enhances Intestinal Integrity in Diquat- Challenged Piglets Associated with Improvement of Redox Status and Mitochondrial Function	Liu	2019	Yes (diquat, d7)	L-Tryptophan	0.15	21	10	46	8.66
Glutamate alleviates intestinal injury, maintains mTOR and suppresses TLR4 and NOD signaling pathways in weanling pigs challenged with lipopolysaccharide	Qin	2018	Yes, LPS (d12)	L-Glutamate	1 or 2		6		NA

AA: tested amino acids; d = days; n per group = numebrs of animals per group; BW= initial body weight; LPS=Lipopolysaccharides; DON=Deoxynivalenol; NA= not available

Titles	Author	Year	Challenge	AA tested	Supplementation (%)	Duration (d)	n per group	Age (d)	BW (kg)
Optimal Dietary True Ileal Digestible Threonine for Supporting the Mucosal Barrier in Small Intestine of Weanling Pigs	Wang	2010	No	L-Threonine	0.37 or 0.52 or 0.74	21		35	6.79
Effects of oral supplementation with glutamate or combination of glutamate and N-carbamylglutamate on intestinal mucosa morphology and epithelium cell proliferation in weanling piglets	Wu	2015	No	L-Glutamate	1	20	6	41	5.56
Therapeutic Effects of Glutamic Acid in Piglets Challenged with Deoxynivalenol	Wu	2014	Yes (DON, d0)	L-Glutamate	2	37	7	NA	12.23
The effects of dietary sulfur amino acids on serum biochemical variables, mucosal amino acid profiles, and intestinal inflammation in weaning piglets	Liu	2019	No	L-Methionine	0.63or 0.74 or 0.85 or 0.96	14	8	21	
Dietary Glutamic Acid Modulates Immune Responses and Gut Health of Weaned Pigs	Kyoung	2020	No	L-Glutamate	0.5	38	48	28	8.1
Replacing dietary antibiotics with 0.20% l-glutamine and synbiotics following weaning and transport in pigs	McConn	2020	Yes (long transport 12h)	L-Glutamine	0.2	14/35/68	20	19	5.86
Effects of Zinc Oxide and Arginine on the Intestinal Microbiota and Immune Status ofWeaned Pigs Subjected to High Ambient Temperature	Yoon	2020	High temperature	L-Arginine	0.6	14	30	28	10.45
Low-protein diets supplemented with glutamic acid or aspartic acid ameliorate intestinal damage in weaned piglets challenged with hydrogen peroxide	Chen	2021	10% H_2O_2	L-Glutamate	1 or 2	14	20	28	10.96
Glycine regulates mucosal immunity and the intestinal microbial composition in weaned piglets	Ji	2021	No	L-Glycine	0.5 or 1 or 2	7	32	21	6.8
Dietary Tryptophan Levels Impact Growth Performance andIntestinal Microbial Ecology in Weaned Piglets via Tryptophan Metabolites and Intestinal Antimicrobial Peptides	Rao	2021	No	L-Tryptophan	0.2 or 0.28 or 0.35	28	10	28	5.42

AA: tested amino acids; d = days; n per group = numebrs of animals per group; BW= initial body weight; LPS=Lipopolysaccharides; DON=Deoxynivalenol; NA= not available

Supplementary Table 2. The effect of the supplementation of amino acids on the epithelial barrier and digestion of post weaning pigs.

Amino acid	Gobet cells	Mucin 1	Mucin 2	Caspase 3
L-Arginine	duo: → (0.6% Wu et al., 2010); il: ↑28% (0.6% Wu et al., 2010)			duo: ↓ 19% (0.6% Wang et al., 2021)
L-Aspargine				jej: → (0.5%, Chen et al., 2016)→ (1%, Chen et al., 2016); il: ↓52%, (0.5%, Chen et al., 2016) ↓41% (1%, Chen et al., 2016)
L-Aspartate				jej: → (0.5% Wang et al., 2016) → (1% Wang et al., 2016); il: ↓56% (0.5% Wang et al., 2016)↓56% (1% Wang et al., 2016)
L-Cysteine				jej: ↑(NA)(0.25% Song et al., 2016)↑(NA)(0.5% Song et al., 2016); il: →(0.25% Song et al., 2016)→(0.5% Song et al., 2016)
L-Glutamate	duo:↑45% (0.5 Kyoung et al., 2020); jej: →(2%, Wu et al.,2014)↓36%(2%, Wu et al.,2014)↑56% (0.5 Kyoung et al.,	jej: ↑10% (0.5 Kyoung et al., 2020)		

The percentage following the arrow represents the percentage difference with the control diet.The percentage shown inside the square bracket represents the dose of supplemental amino acid included in the diet; duo= duodenum; jej= jejunum; il=ileum; → = similar to the control; ↑ = increased significantly relative to the control; ↓ = decreased significantly relative to the control.

Amino acid	Gobet cells	Mucin 1	Mucin 2	Caspase 3
L-Glutamine		jej: →(0.34% Xing et al., 2016);	jej: ↑(NA)(0.34% Xing et al., 2016)	jej: ↓79%(3.42mmol/kg, Hynes et al., 2009)
L-Glycine		jej: ↑10% (2% Ji et al., 2021)		
L-Leucine	jej:→ (1% Mao et al., 2015)↑89% (1% Mao et al., 2015); il:→ (1% Mao et al., 2015)	jej↑35% (1% Mao et al., 2015)↑51% (1% Mao et al., 2015)	jej:→ (1% Mao et al., 2015)→ (1% Mao et al., 2015)	
L-Methionine				↓ (NA)(0.12%Chen et al., 2014)
L-Threonine		jej:→(0.05% Trevisi et al., 2014)		jej:→(0.05% Trevisi et al., 2014)
L-Tryptophan	duo, jej and il:→ (0.15%, Tossou et al., 2016)→ (0.75%, Tossou et al., 2016)			

The percentage following the arrow represents the percentage difference with the control diet.The percentage shown inside the square bracket represents the dose of supplemental amino acid included in the diet; duo= duodenum; jej= jejunum; il=ileum; → = similar to the control; ↑ = increased significantly relative to the control; ↓ = decreased significantly relative to the control.

Amino acid	Severity of diarrhea	Transepithelial resistance	Zonulin
L-Arginine	→ (2.4%, Gookin et al., 2008) ↑ (NA) (d3) (2.4%, Gookin et al., 2008) ↓61% (0.6% Wang et al., 2021) → (0.6% Wu et al., 2010) → (1%Yao et al., 2011) ↓57%(0.7%, Zhan et al., 2008) ↑ 70%	il: → (2.4%, Gookin et al., 2008)→ (2.4%, Gookin et al., 2008)	
L-Aspargine			
L-Aspartate			il: → (1%, Chen et al., 2021)
L-Cysteine		jej: ↑21%(0.25% Song et al., 2016)↑22%(0.5% Song et al., 2016); il: →(0.25% Song et al., 2016)→(0.5% Song et al., 2016)	jej and il: →(0.25% Song et al., 2016)→(0.5% Song et al., 2016)
L-Glutamate			jej: ↑(NA)(2%, Liu et al., 2003); il: → (2% Chen et al., 2021)

The percentage following the arrow represents the percentage difference with the control diet.The percentage shown inside the square bracket represents the dose of supplemental amino acid included in the diet; duo= duodenum; jej= jejunum; il=ileum; → = similar to the control; ↑ = increased significantly relative to the control; ↓ = decreased significantly relative to the control.

Amino acid	Severity of diarrhea	Transepithelial resistance	Zonulin
L-Glutamine	→ (0.5%, Lee et al., 2003)→(1%, Lee et al., 2003)→(1.5%, Lee et al., 2003)→ (2% Yi2005)↓ (NA) (1% Zou2006)	jej: →(4.4%, Ewaschuk et al., 2010)	jej:→(1% Wang et al., 2014)↑(NA)(0.34% Xing et al., 2016)→ (0.2% McConnon et al., 2020); il: → (0.2% McConnon et al., 2020)
L-Glycine	→ (0.5% Ji et al., 2021)→ (1% Ji et al., 2021)→ (2% Ji et al., 2021)		
L-Leucine	→ (1% Mao et al., 2015)↓41% (1% Mao et al., 2015)		
L-Methionine	jej:→(0.12%Chen et al., 2014)	jej:↑(NA)(0.12%Chen et al., 2014)	jej:→(0.04% Zeitz et al., 2016)→ (0.08% Zeitz et al., 2016)
L-Threonine	↓5%(1.2% Fernández et al., 2009)→(0.05% Trevisi et al., 2014)		
L-Tryptophan	→ (0.4, 0.7%, Fernández et al., 2009)→(0.10%Trevisi et al., 2009; not sus.)→(0.10%Trevisi et al., 2009; susc)	jej:↑NA (0.15%, Yan et al., 2019)	jej: → (0.15%, Tossou et al., 2016)↓(NA) (0.75%, Tossou et al., 2016); il: ↓NA (0.1%, Li et al., 2016)↓NA (0.1%, Li et al., 2016)↑NA (0.15%, Yan et al., 2019)

The percentage following the arrow represents the percentage difference with the control diet.The percentage shown inside the square bracket represents the dose of supplemental amino acid included in the diet; duo= duodenum; jej= jejunum; il=ileum; → = similar to the control; ↑ = increased significantly relative to the control; ↓ = decreased significantly relative to the control.

Amino acid	Occludin	Claudin-1	Claudin-2	Claudin-3
L-Glutamine	jej: → (4.4%, Ewaschuk et al., 2010)↑(NA)(1% Wang et al., 2014)↑(NA)(0.34% Xing et al., 2016)	jej:↑(NA)(1% Wang et al., 2014)→(0.34% Xing et al., 2016)→ (0.2% McConnon et al., 2020); il: → (0.2% McConnon et al., 2020)	jej:→ (4.4%, Ewaschuk et al., 2010)↑(NA)(1% Wang et al., 2014)	↑(1% Wang et al., 2014)
L-Glycine			jej:↓50% (2% Ji et al., 2021)	
L-Leucine				
L-Methionine	jej:↑(NA)(0.12%Chen et al., 2014)→(0.04% Zeitz et al., 2016)→ (0.08% Zeitz et al., 2016)			→ (0.12%Chen et al., 2014)→(0.04% Zeitz et al., 2016)→ (0.08% Zeitz et al., 2016)
L-Threonine				
L-Tryptophan	jej: → (0.15%, Tossou et al., 2016)↓(NA) (0.75%, Tossou et al., 2016)↑NA (0.15%, Yan et al., 2019); il: → (0.1%, Li et al., 2016)↓NA (0.1%, Li	jej:→ (0.15%, Tossou et al., 2016)→ (0.75%, Tossou et al., 2016)→ (0.15%, Yan et al., 2019); il: → (0.1%, Li et al., 2016)↓NA (0.1%, Li et al., 2016)→ (0.75%, Tossou et al., 2016)		

The percentage following the arrow represents the percentage difference with the control diet.The percentage shown inside the square bracket represents the dose of supplemental amino acid included in the diet; duo= duodenum; jej= jejunum; il=ileum; → = similar to the control; ↑ = increased significantly relative to the control; ↓ = decreased significantly relative to the control.

Amino acid	Occludin	Claudin-1	Claudin-2	Claudin-3
L-Arginine				
L-Aspargine	jej: ↑81% (0.5%, Chen et al., 2016) ↑76% (1%, Chen et al., 2016); il: → (0.5%, Chen et al., 2016)→ (1%, Chen et al., 2016)	jej: ↑130% (0.5%, Chen et al., 2016) ↑122% (1%, Chen et al., 2016); il: → (0.5%, Chen et al., 2016)↑55%; (1%, Chen et al., 2016)		
L-Aspartate	jej: → (0.5% Wang et al., 2016)→ (1% Wang et al., 2016); il: → (0.5% Wang et al., 2016)→ (1% Wang et al., 2016)→ (1%, Chen et al., 2021)	jej: ↑64% (0.5% Wang et al., 2016)↑96% (1% Wang et al., 2016); il: → (0.5% Wang et al., 2016)→ (1% Wang et al., 2016		
L-Cysteine	jej and il: ↑(NA)(0.25% Song et al., 2016)↑(NA) (0.5% Song et al., 2016)	jej and il: ↑(NA)(0.25% Song et al., 2016)↑(NA) (0.5% Song et al., 2016)		
L-Glutamate	jej: ↑(NA)(2%, Liu et al., 2003)↑130% (0.5 Kyoung et al., 2020); il: →(2% Chen et al., 2021)	jej: → (2%, Liu et al., 2003)↑35%(1%, Qin et al., 2018)↑33%(2%, Qin et al., 2018)↑40% (0.5 Kyoung et al., 2020); il: → (1%, Qin et al., 2018)↑33%(2%, Qin et al., 2018)	jej: ↑30% (0.5 Kyoung et al., 2020)	jej: ↑10% (0.5 Kyoung et al., 2020)

The percentage following the arrow represents the percentage difference with the control diet.The percentage shown inside the square bracket represents the dose of supplemental amino acid included in the diet; duo= duodenum; jej= jejunum; il=ileum; → = similar to the control; ↑ = increased significantly relative to the control; ↓ = decreased significantly relative to the control.

Supplementary Table 3. The effect of the supplementation of amino acids on immunoglobulis and immune parameters of post weaning pigs.

Amino acid	sIgA	IgA	IgG	IgM	Intraepithelial lymphocyte
L-Arginine					
L-Cysteine					
L-Glutamate					jej and il: →(2%,Wu et al., 2014, nc); ↓15%(2%,Wu et al., 2014, c)
L-Glutamine	jej: ↑3% (0.34%,Xing et al., 2017, nc)		jej:→ (0.34%,Xing et al., 2017, nc)	jej: → (0.34%,Xing et al., 2017, nc)	

The percentage following the arrow represents the percentage difference with the control diet.The percentage shown inside the square bracket represents the dose of supplemental amino acid included in the diet; duo= duodenum; jej= jejunum; il=ileum; → = similar to the control; ↑ = increased significantly relative to the control; ↓ = decreased significantly relative to the control; c= challenge; nc= no challenge; NA = not available. Abbreviations: sIgA= secretory immunoglobulin A; IgA=Immunoglobulin A; IgG= immunoglobulin G; IgM= immunoglobuli M; IL= Interleukin; TNF-α = Tumor Necrosis Factor alpha.

Amino acid	sIgA	IgA	IgG	IgM	Intraepithelial lymphocyte
L-Glycine	jej:↑35% (2%,Ji et al., 2021, nc)				
L-Isoleucine					
L-Serine					
L-Threonine		jej: →(0.75-1.11%,Ren et al., 2014, nc) ; →(0.05%,Trevisi et al., 2015, c)	jej: →(0.75-1.11%,Ren et al., 2014, nc)	jej: → (0.75-1.11%, (Ren et al., 2014)) →(0.05%,Trevisi et al., 2015, c)	jej: ↑31%(0.75-1.11%,Ren et al., 2014, nc)
L-Tryptophan					duo, jej and il: → (NA) (0.75%, and 0.15%, (Tossou et al., 2017,

The percentage following the arrow represents the percentage difference with the control diet.The percentage shown inside the square bracket represents the dose of supplemental amino acid included in the diet; duo= duodenum; jej= jejunum; il=ileum; → = similar to the control; ↑ = increased significantly relative to the control; ↓ = decreased significantly relative to the control; c= challenge; nc= no challenge; NA = not available. Abbreviations: sIgA= secretory immunoglobulin A; IgA=Immunoglobulin A; IgG= immunoglobulin G; IgM= immunoglobuli M; IL= Interleukin; TNF-α = Tumor Necrosis Factor alpha.

Amino acid	IL-1β	IL-6	IL-8	IL-10	TNF-α
L-Arginine		duo: → (1%,Liu et al., 2008, c); jej: → (1%,Liu et al., 2008, c); → (0.6%,Yoon et al., 2020, c); il: → (1%,Liu et al., 2008, c)		jej:→ (1%,Bergero et al., 2014, nc)	duo: → (1%,Bergeron et al., 2014, nc); jej: ↓50% (1%,Liu et al., 2008, c); → (1%,Bergeron et al., 2014, nc); → (0.6%,Yoon et al., 2020, c); il:→ (1%,Bergeron et al., 2014, nc); → (1%,Liu et al., 2008, c); → (1%,Bergeron et al., 2014, c)
L-Cysteine		jej: ↓44% (0.25%,Song et al., 2016, c); ↓48%(0.5%,Song et al., 2016, c); il: ↓20%(0.25%,Song et al., 2016, c); ↓25%(0.5%,Song et al., 2016, c)	jej: ↓64%(0.25%,Song et al., 2016, c); ↓66%(0.5%,Song et al., 2016, c); il: ↓65%(0.25%,Song et al., 2016, c); ↓67%(0.5%,Song et al., 2016, c)		jej: ↓52%(0.25%,Song et al., 2016, c); ↓55%(0.5%,Song et al., 2016, c); il↓35%(0.25%, (Song et al., 2016, c) ↓40%(0.5%,Song et al., 2016) c)
L-Glutamate	jej: ↑15% (0.5%,Kyoung et al., 2021, nc)	jej: ↑10% (0.5%,Kyoung et al., 2021, nc)			il: ↓5% (0.5%,Kyoung et al., 2021, nc)
L-Glutamine	jej:→(4.4%,Ewaschuk et al., 2011, nc)	duo: → (4.4%,Ewaschuk et al., 2011, nc)	jej:→ (0.2%,McConn et al., 2020, c)	jej:→ (4.4%,Ewaschuk et al., 2011, nc)	duo: →(4.4%,Ewaschuk et al., 2011, nc); → (0.2%,McConn et al., 2020, c)

The percentage following the arrow represents the percentage difference with the control diet.The percentage shown inside the square bracket represents the dose of supplemental amino acid included in the diet; duo= duodenum; jej= jejunum; il=ileum; → = similar to the control; ↑ = increased significantly relative to the control; ↓ = decreased significantly relative to the control; c= challenge; nc= no challenge; NA = not available. Abbreviations: sIgA= secretory immunoglobulin A; IgA=Immunoglobulin A; IgG= immunoglobulin G; IgM= immunoglobuli M; IL= Interleukin; TNF-α = Tumor Necrosis Factor alpha.

Amino acid	IL-1β	IL-6	IL-8	IL-10	TNF-α
L-Glycine	jej: ↓40% (2%,Ji et al., 2021,, nc); il: → (2%,Ji et al., 2021, nc)	duo: → (2%,Ji et al., 2021, nc); jej:↓40% (2%,Ji et al., 2021, nc); il: → (2%,Ji et al., 2021, nc)	jej: → (2%,Ji et al., 2021, nc); il: → (2%,Ji et al., 2021, nc)		duo: ↓60% (2%,Ji et al., 2021, nc); jej: ↓40% (2%,Ji et al., 2021, nc); il: → (2%,Ji et al., 2021, nc)
L-Isoleucine	il: → (NA) (1%,Mao et al., 2018,				duo: ↑25% (1%,Mao et al., 2018, c) jej: → (NA) (1%,Mao et al., 2018, c and nc
L-Serine					jej: ↓ (NA)(0.2%,Zhou et al., 2018, nc); il: ↓ (NA)(0.2%,Zhou et al., 2018, nc)
L-Threonine	jej: ↓30%(1.11%,Ren et al., 2014, nc)	jej: ↑31%(0.75-1.11%,Ren et al., 2014, nc)			
L-Tryptophan					jej and il: → (0.20%, 0.28%; 0.35% (Rao et al., 2021, nc)

The percentage following the arrow represents the percentage difference with the control diet.The percentage shown inside the square bracket represents the dose of supplemental amino acid included in the diet; duo= duodenum; jej= jejunum; il=ileum; → = similar to the control; ↑ = increased significantly relative to the control; ↓ = decreased significantly relative to the control; c= challenge; nc= no challenge; NA = not available. Abbreviations: sIgA= secretory immunoglobulin A; IgA=Immunoglobulin A; IgG= immunoglobulin G; IgM= immunoglobuli M; IL= Interleukin; TNF-α = Tumor Necrosis Factor alpha.