Nutritional intervention for the intestinal development and health of weaned pigs

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Outline

• Weaning stress on intestinal development and health
• How to define a healthy gut
• Nutritional intervention
  • Functional amino acids
  • Short chain fatty acids
• Take home message
Focus on the GUT

• Digestion and absorption of nutrients
• Physical barrier against pathogenic agents
• Large immune organ
• Nutrient chemo-sensing

MacDonald and Monteleone, 2005
Focus on the GUT of weaning pigs

Critical Window of postnatal GI Development

GI Barrier Development
- Epithelial barrier and transport functions
- Immune system maturation
- Enteric nervous system

Maternal Immunity
Plasticity

Birth 2.5 to 4 weeks 12 to 14 weeks Adult

Moeser et al., 2017
Weaning stress

- Maternal separation
- Environmental change
- Increased exposure to pathogens
- Social hierarchy stress
- Move to solid feed
- Transportation stress
Weaning stress on intestinal morphology

- Pre-weaning: d1 to 21, villi surface was increased
- Post-weaning: reduced villi number and folding

Wang et al., 2016
Weaning stress on intestinal barrier function

Neunlist et al., 2013; Wang et al., 2016
Weaning stress on intestinal barrier function, cont.
Weaning stress on intestinal microbial dysbiosis

Intestinal cells

Renewal and apoptosis

Nutrient pool
- Proteins and peptides
- Lipids
- Nucleic acids
- Carbohydrates
  - Ethanolamine
  - Fucose

Proliferation and breakdown

Microbial communities

Intestinal inflammation
Diseases

Immune cells
Intracellular proliferation

Pathogenic bacteria
- ETEC
- EHEC
- Salmonella

Gut microflora dysbiosis
Loss of bacterial diversity

Stahl et al., 2011; Thiennimitr et al., 2011; Xiong et al., 2019
Weaning stress on intestinal mucosal immunity

- Weaning induces a transient gut inflammation in pigs
  - Enhanced pro-inflammatory cytokines
  - Increased intestinal CD4+ and CD8+ T lymphocytes
  - Up-regulated matrix metalloproteinase
  - Down-regulated MHC I expression
  - Reduced secretory IgA

McCracken et al., 1999; Pié et al., 2004
Weaning stress on intestinal oxidative status

Yin et al., 2014
Focus on the GUT of weaning pigs

Compromised intestinal barrier development and function
- Increased intestinal permeability
- Increased immune cell activity and numbers
- Hyperactive enteric nervous system
- Increased oxidation

Moeser et al., 2017
How to define a healthy gut

• Effective nutrient digestion and absorption
• Effective waste excretion

Overall, should be concomitant with optimal performance
(the absence of diseases)

• A functional and protective gut immunity
• A minimal activation of stress/neural pathways

Pluske et al., 2018
Nutritional strategies

• Optimization of feed formulation
• Utilization of low protein diet in post-weaning period
• Enhancement of feed processing and manufacturing
• Supplementation of feed additives
Feed additives

• Improvement of nutrient digestion and absorption (i.e. exogenous enzymes)

• Regulation gut microbiota to more favorable bacterial species (i.e. prebiotics & probiotics)

• Immune modulation to enhance disease resistance of weaned pigs (i.e. β-glucan, phytochemicals)
Two examples

- Functional amino acids
- Short chain fatty acids
Functional amino acids

• Indispensable amino acids vs. dispensable amino acids

• Functional amino acids
  • Extra benefits to the host beyond the nutrient contribution
  • Arginine family (glutamate, glutamine, proline)
  • Aromatic amino acids (tryptophan, phenylalanine, tyrosine)
Arginine family

Wu et al., 2007
Arginine family

• Substrates for tissue protein synthesis

• Regulate
  • Cellular signaling
  • Hormone synthesis and secretion (insulin, glucagon, etc.)
  • Endothelial function, vasodilation, blood flow
  • Nutrient metabolism
  • Intestinal integrity and function
  • Immune function and health

Wu et al., 2007
• Oral administration of proline enhanced protein expression of ornithine decarboxylase (ODC) activity in jejunum, ileum, and colon

Tan et al., 2017
• Oral administration of proline enhanced the expression of proteins involved in tight junction barrier of weaned pigs

Tan et al., 2017
# Aromatic amino acids

## pig systemic immunity

<table>
<thead>
<tr>
<th>Serum, pg/mL</th>
<th>Saline</th>
<th>LPS</th>
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</thead>
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<tr>
<td></td>
<td>Basal diet</td>
<td>TPT diet</td>
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<tr>
<td>IL1β</td>
<td>254&lt;sup&gt;c&lt;/sup&gt;</td>
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<td>102&lt;sup&gt;c&lt;/sup&gt;</td>
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<td>113&lt;sup&gt;c&lt;/sup&gt;</td>
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<td>TNFα</td>
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<td>660&lt;sup&gt;a&lt;/sup&gt;</td>
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<tr>
<td>TGFβ1</td>
<td>897&lt;sup&gt;a&lt;/sup&gt;</td>
<td>883&lt;sup&gt;a&lt;/sup&gt;</td>
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</table>

- Aromatic amino acids: Trp, Phe, Tyr, 1.5*NRC, 2012

Tan et al., 2017
# Aromatic amino acids
pig intestinal immunity

<table>
<thead>
<tr>
<th>Gene expression</th>
<th>Saline</th>
<th>LPS</th>
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<tr>
<td></td>
<td>Basal diet</td>
<td>TPT diet</td>
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<td>IL6</td>
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<td>2.57&lt;sup&gt;ab&lt;/sup&gt;</td>
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</tbody>
</table>

Tan et al., 2017
Aromatic amino acids

Potential mechanisms

- Dietary supplemented with aromatic amino acids increased CaSR and PLCβ2 protein expression levels
- But decreased p-NF-κB, IKKα/β, and IκB protein expression levels in the LPS-challenged piglets

Tan et al., 2017
Short chain fatty acids

- Fatty acids with a chain of < 6 carbon atoms
  - Acetate, propionate, and butyrate
- Produced by microbial fermentation in the gastrointestinal tract of pigs
- Major fuel source for colonocytes (90% of butyrate)
- Derivatives: salts (Ca, Na), monobutyrin, tributyrin

Acetic acid (acetate)  Propionic acid (propionate)  Butyric acid (butyrate)
Short chain fatty acids
Antimicrobial effects of butyric acid

<table>
<thead>
<tr>
<th>Gram-negative bacteria</th>
<th>MIC, mg/mL</th>
<th>Gram-positive bacteria</th>
<th>MIC, mg/mL</th>
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<tbody>
<tr>
<td><em>E. coli</em>, wild type</td>
<td>2.3</td>
<td><em>Enterococcus faecalis</em></td>
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<tr>
<td><em>E. coli</em>, F18</td>
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<td><em>Clostridium perfringens</em></td>
<td>1.2</td>
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<tr>
<td><em>Salmonella Typhimurium</em>, wild type</td>
<td>2.7</td>
<td><em>Streptococcus pneumonia</em></td>
<td>1.0</td>
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<tr>
<td><em>Salmonella Typhimurium</em>, disease break</td>
<td>2.6</td>
<td><em>Streptococcus suis</em></td>
<td>0.7</td>
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<tr>
<td><em>Campylobacter jejuni</em>, wild type</td>
<td>0.5</td>
<td></td>
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</tr>
<tr>
<td><em>Campylobacter jejuni</em>, disease outbreak</td>
<td>0.7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

MIC: minimal inhibitory concentration

Kovanda et al., 2019
Short chain fatty acids

Host defense peptides, in vitro

- Also known as antimicrobial peptides
- Defensins or cathelicidins
- Small, positively charged, and amphipathic
- Disturb cell membrane structure, penetrate into cells, regulate intracellular pathways, cause bacterial cell death

Zeng et al., 2013
Short chain fatty acids
Host defense peptides, in vivo

- Weaning pigs, 0.2% sodium butyrate, 10 days

Xiong et al., 2016
Take home message

A healthy gut is extremely important for weanling pigs

- Nutrient digestion & absorption
- Waste excretion
- Functional and protective gut barrier
- Stable & appropriate microbial community
- Functional and protective gut immunity
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http://animalnutr-ansci.faculty.ucdavis.edu/