Nutritional intervention for the intestinal development and health of weaned pigs

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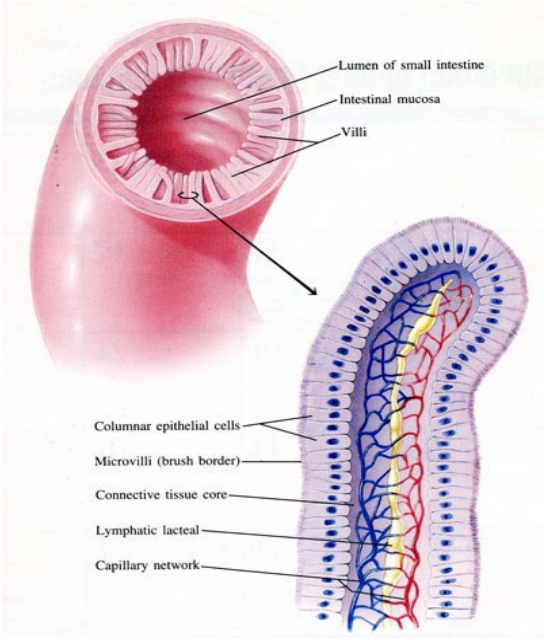
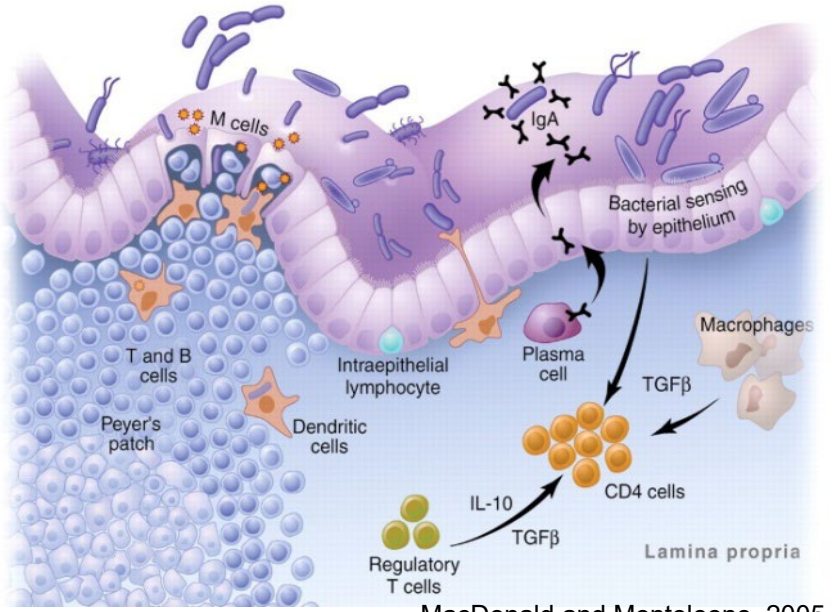
Outline

- 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

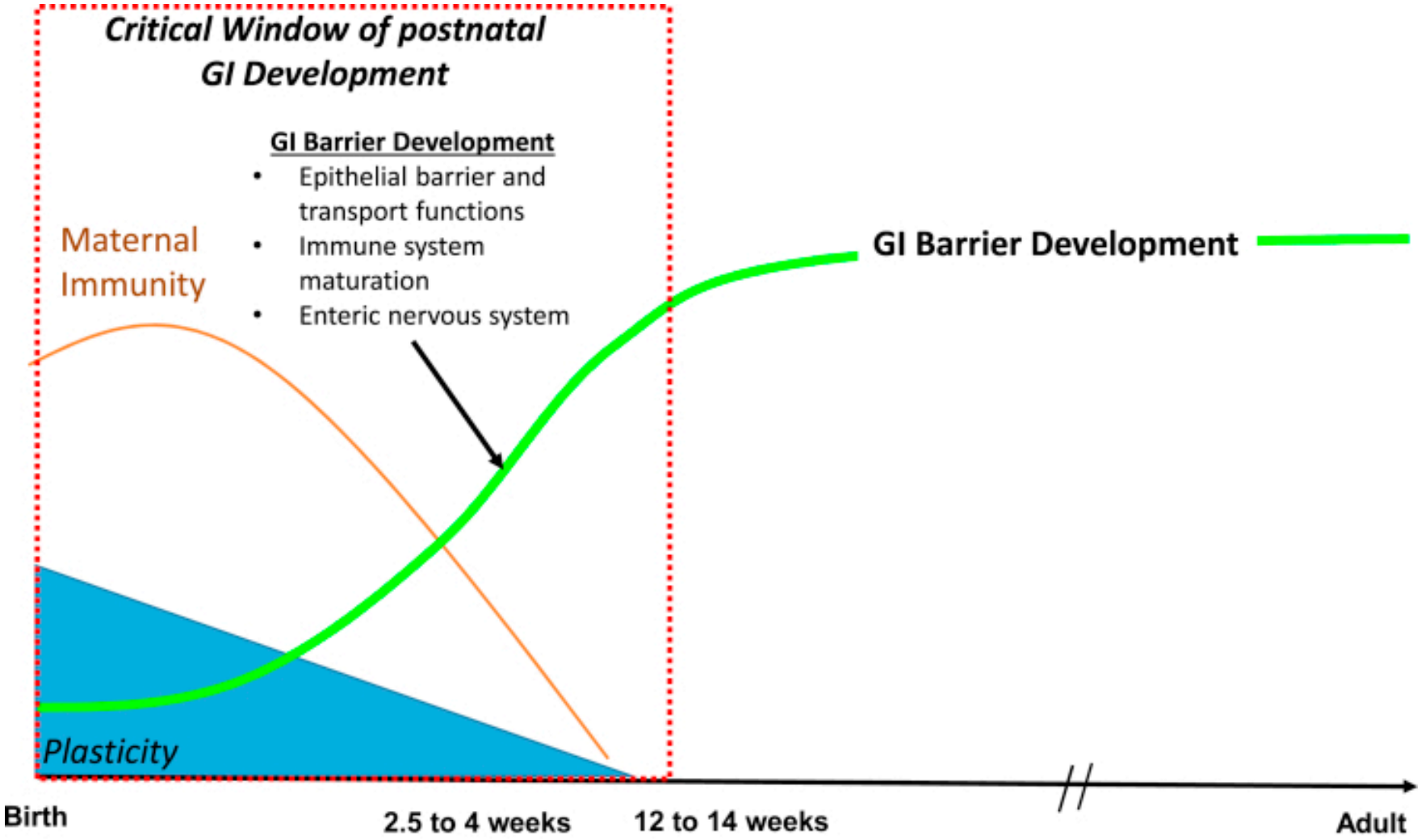
- Digestion and absorption of nutrients
- Physical barrier against pathogenic agents
- Large immune organ
- Nutrient chemo-sensing





MacDonald and Monteleone, 2005

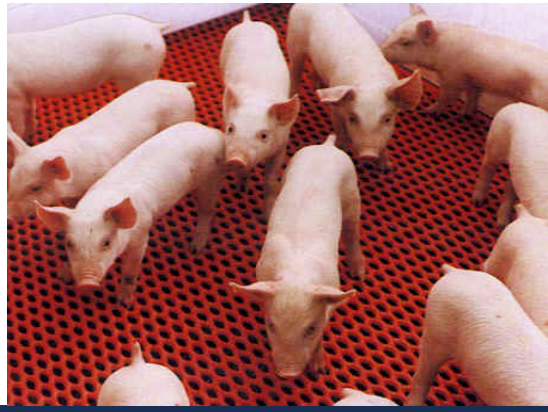
Focus on the GUT of weaning pigs



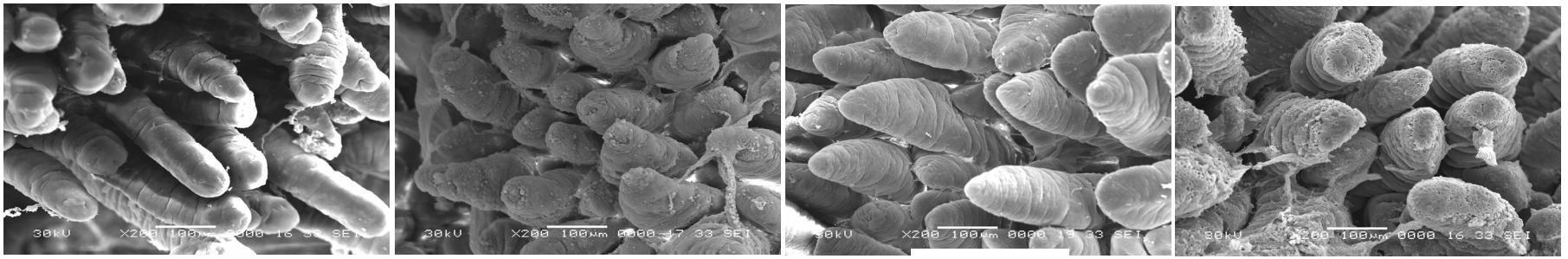
Moeser et al., 2017

Weaning stress

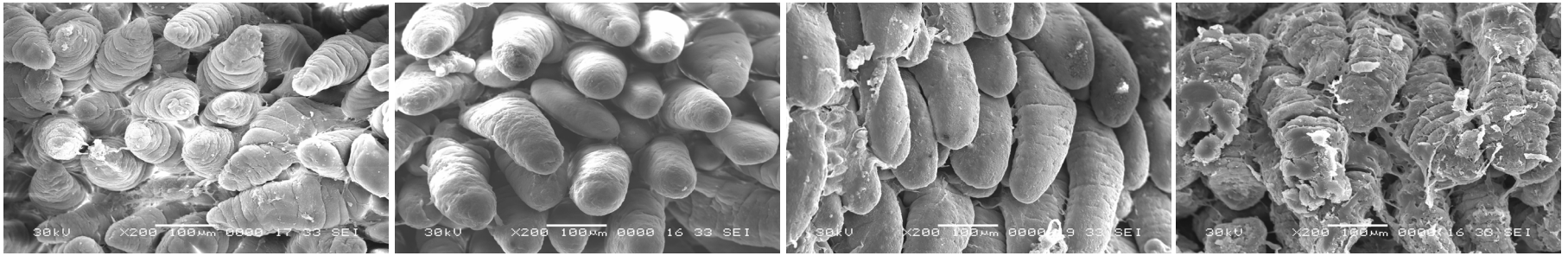
- Maternal separation
- Environmental change
- Increased exposure to pathogens
- Social hierarchy stress
- Move to solid feed
- Transportation stress



Weaning stress on intestinal morphology



d1 d7 d14 d21

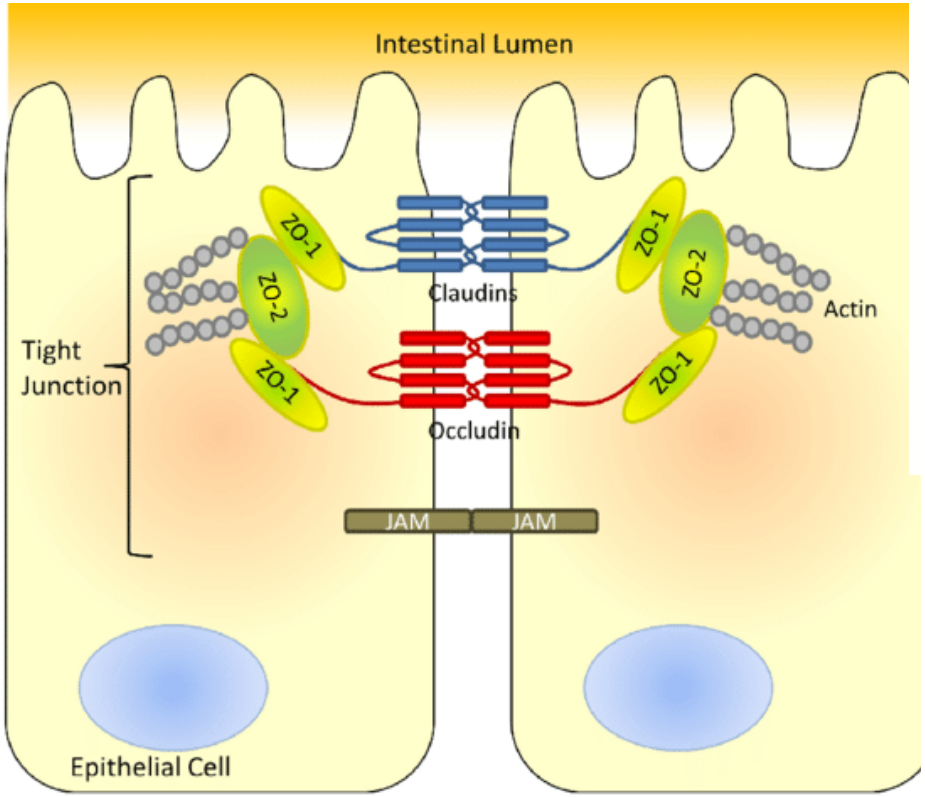


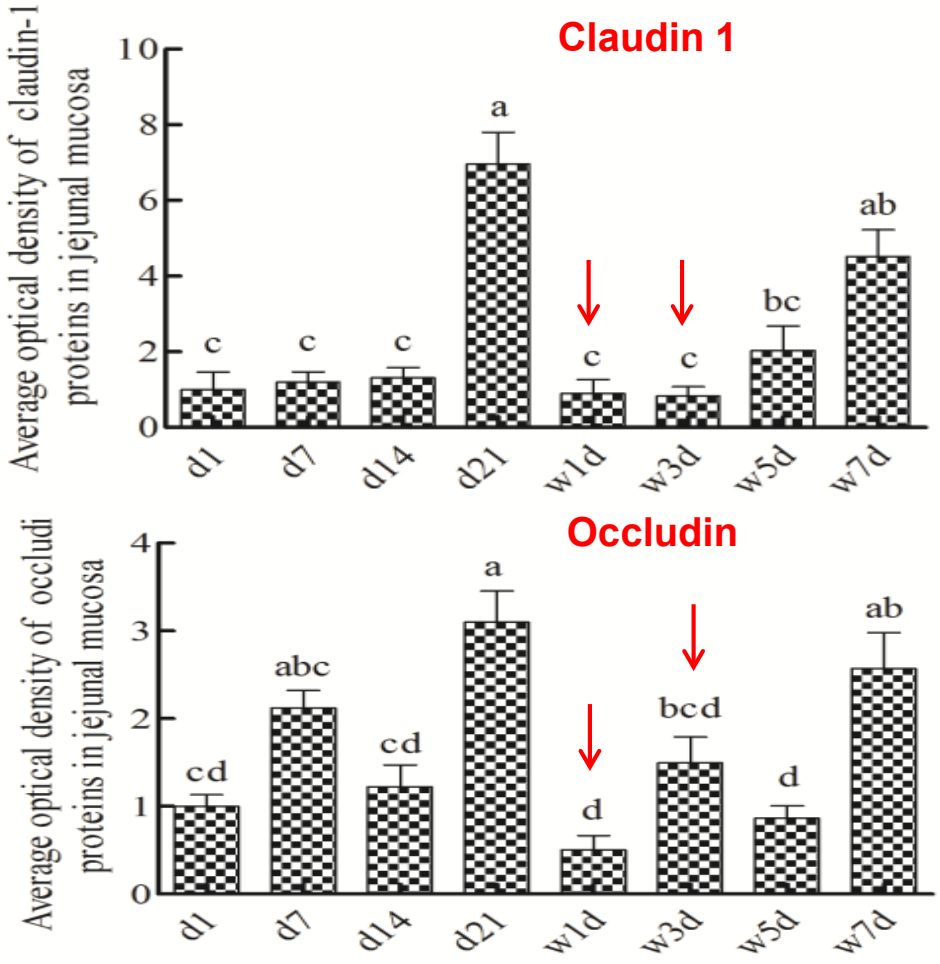
w1d w3d w5d w7d

- **Pre-weaning: d 1 to 21, villi surface was increased**
- **Post-weaning: reduced villi number and folding**

Wang et al., 2016

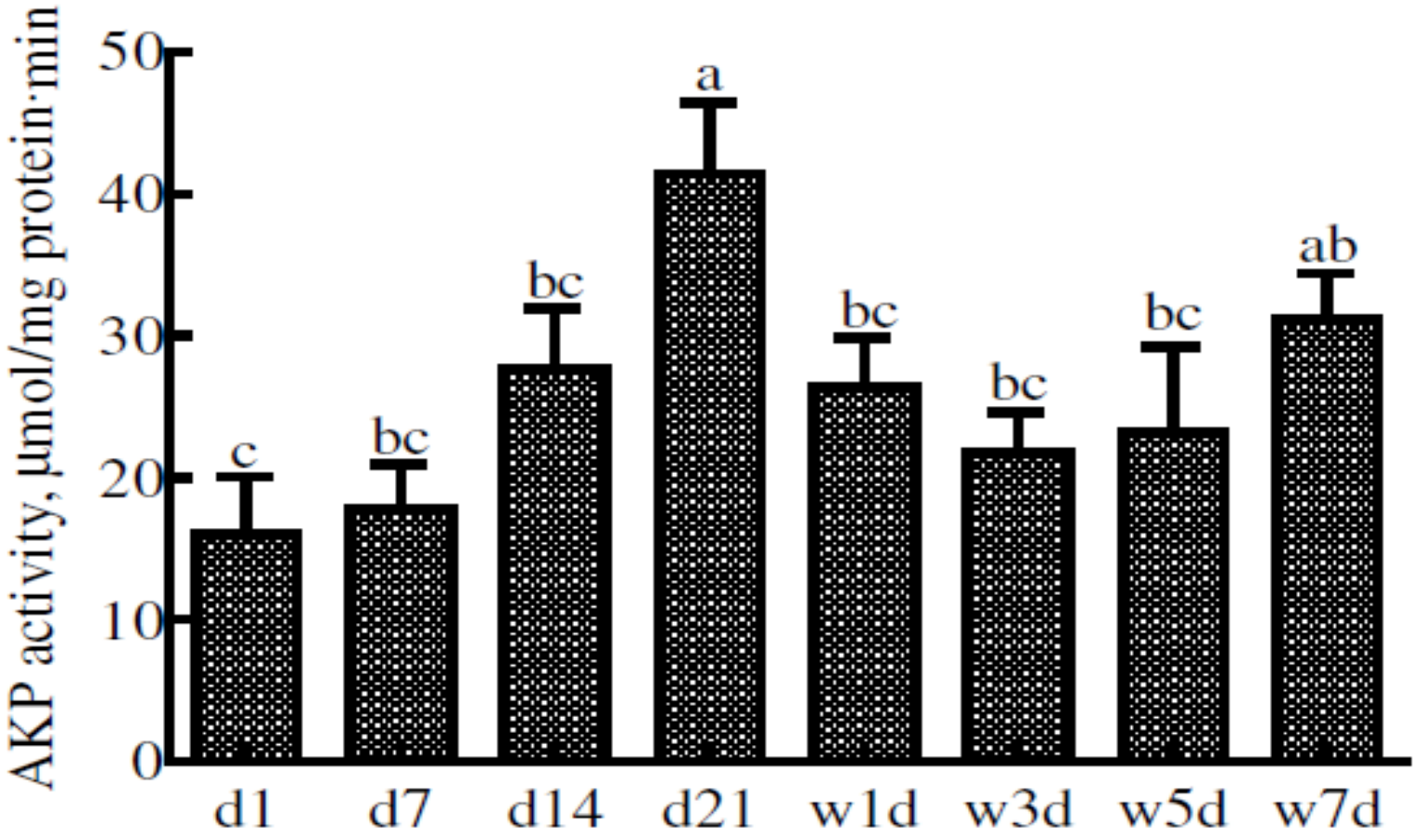
Weaning stress on intestinal barrier function





Neunlist et al., 2013; Wang et al., 2016

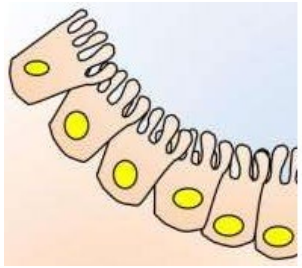
Weaning stress on intestinal barrier function, cont.



Wang et al., 2016

Weaning stress on intestinal microbial dysbiosis

Intestinal cells



Renewal and apoptosis

Nutrient pool

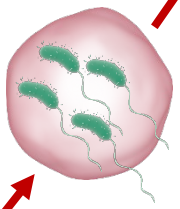
Proteins and peptides
Lipids
Nucleic acids
Carbohydrates

Ethanolamine
Fucose

Proliferation and breakdown

Microbial communities

Pathogenic bacteria
ETEC, EHEC, Salmonella



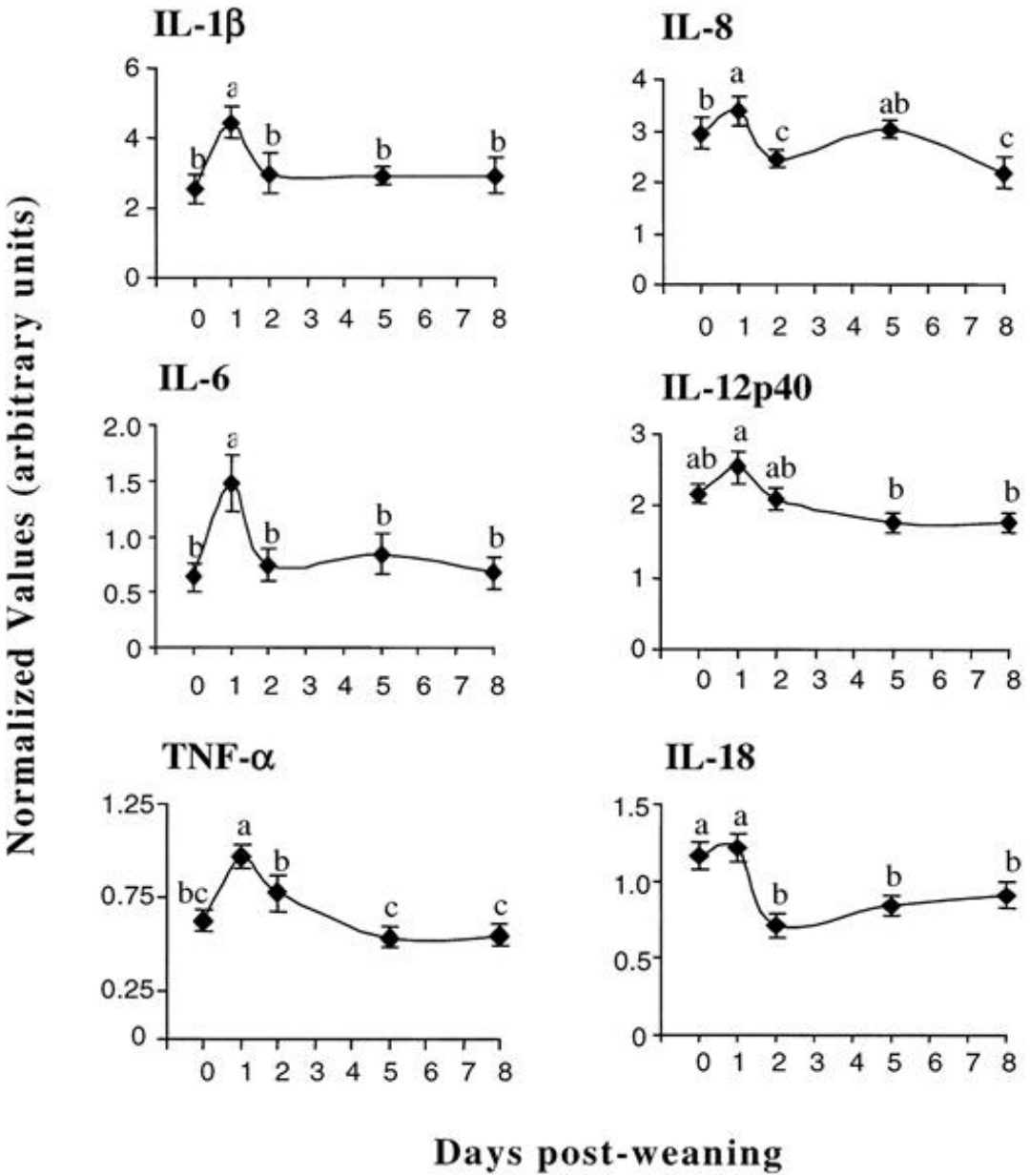
Immune cells
Intracellular proliferation

Intestinal inflammation Diseases

Gut microflora dysbiosis
Loss of bacterial diversity

Stahl et al., 2011; Thiennimitr et al., 2011; Xiong et al., 2019

Middle of the small intestine

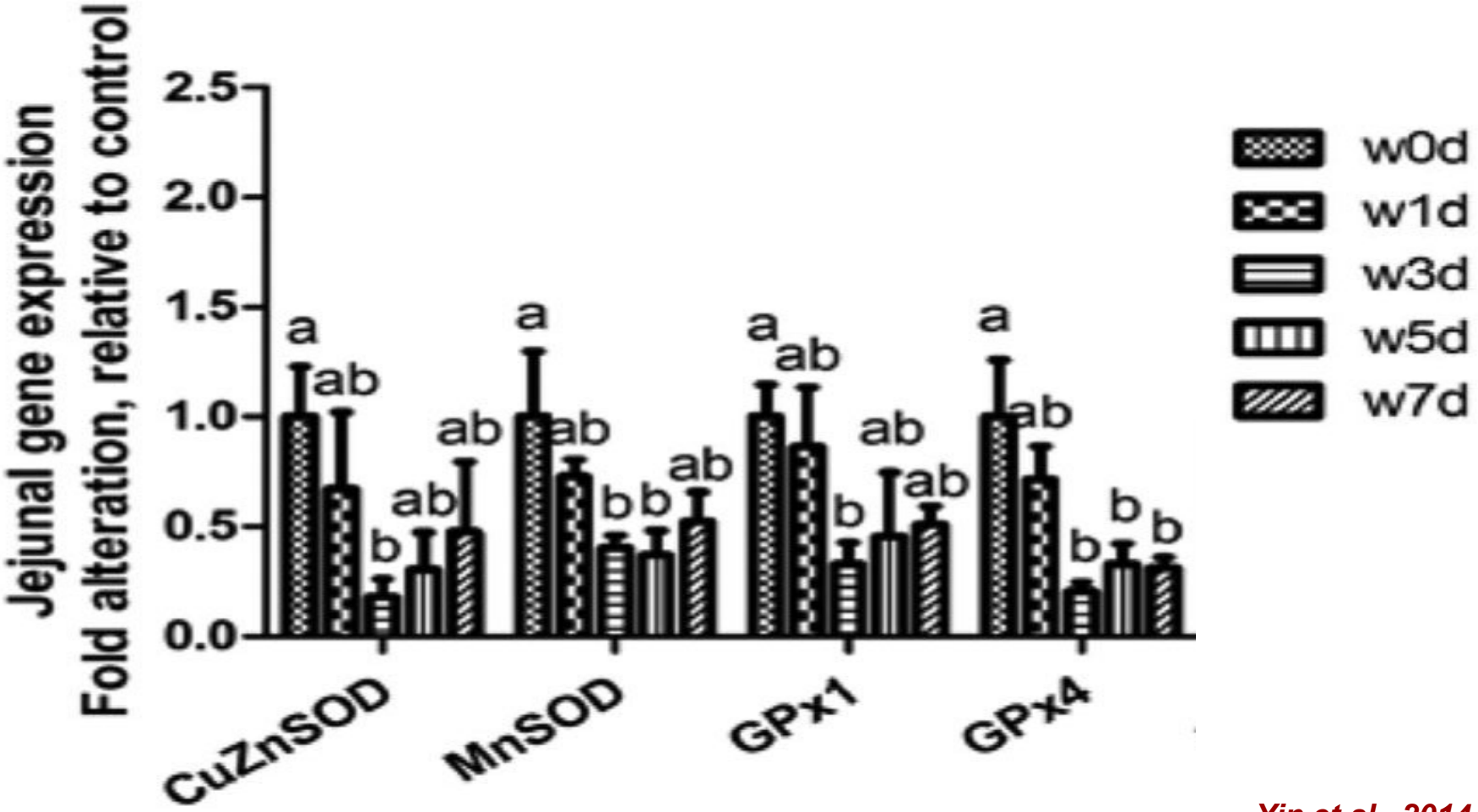


Weaning stress on intestinal mucosal immunity

- **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**

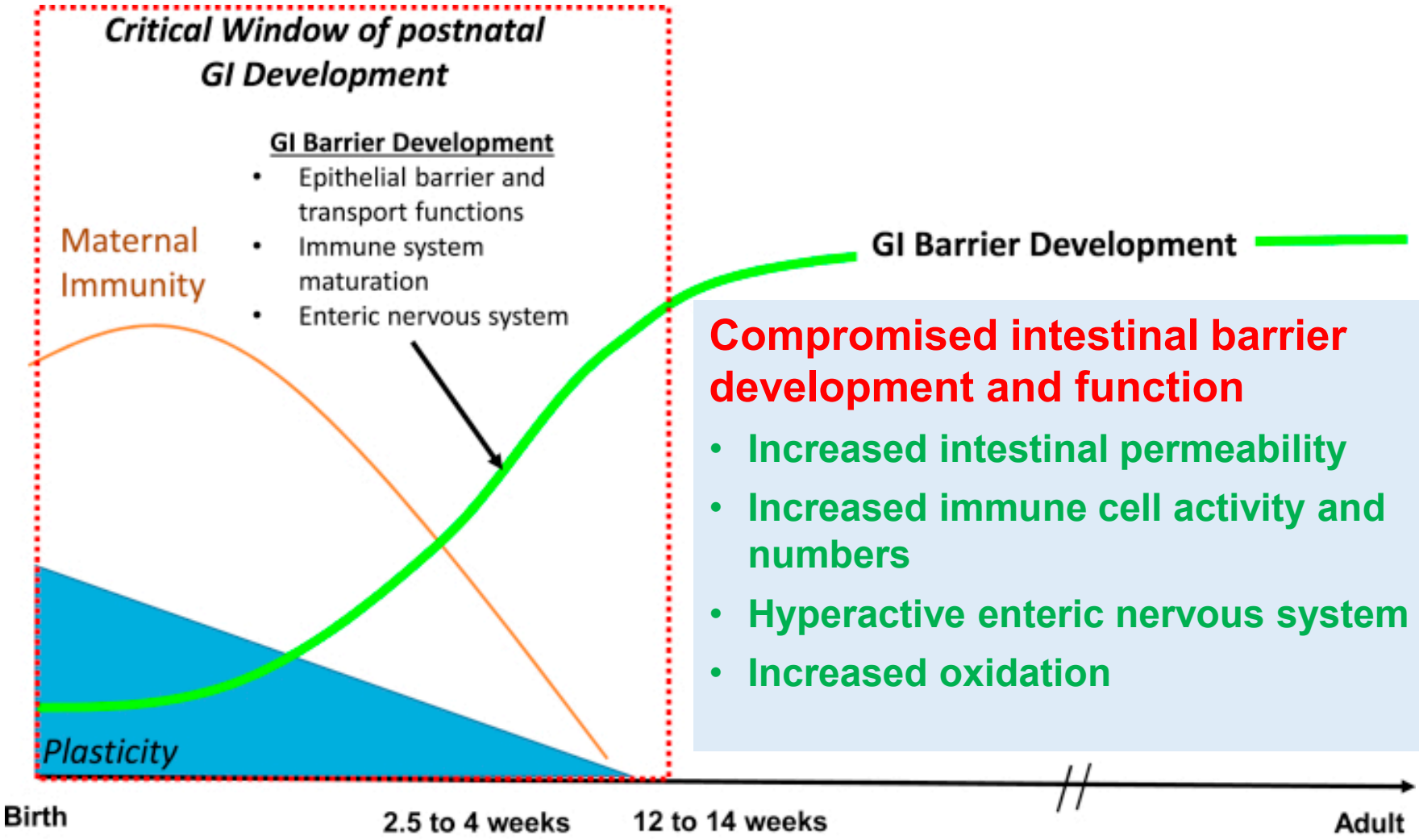
McCracken et al., 1999; Pié et al., 2004

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)

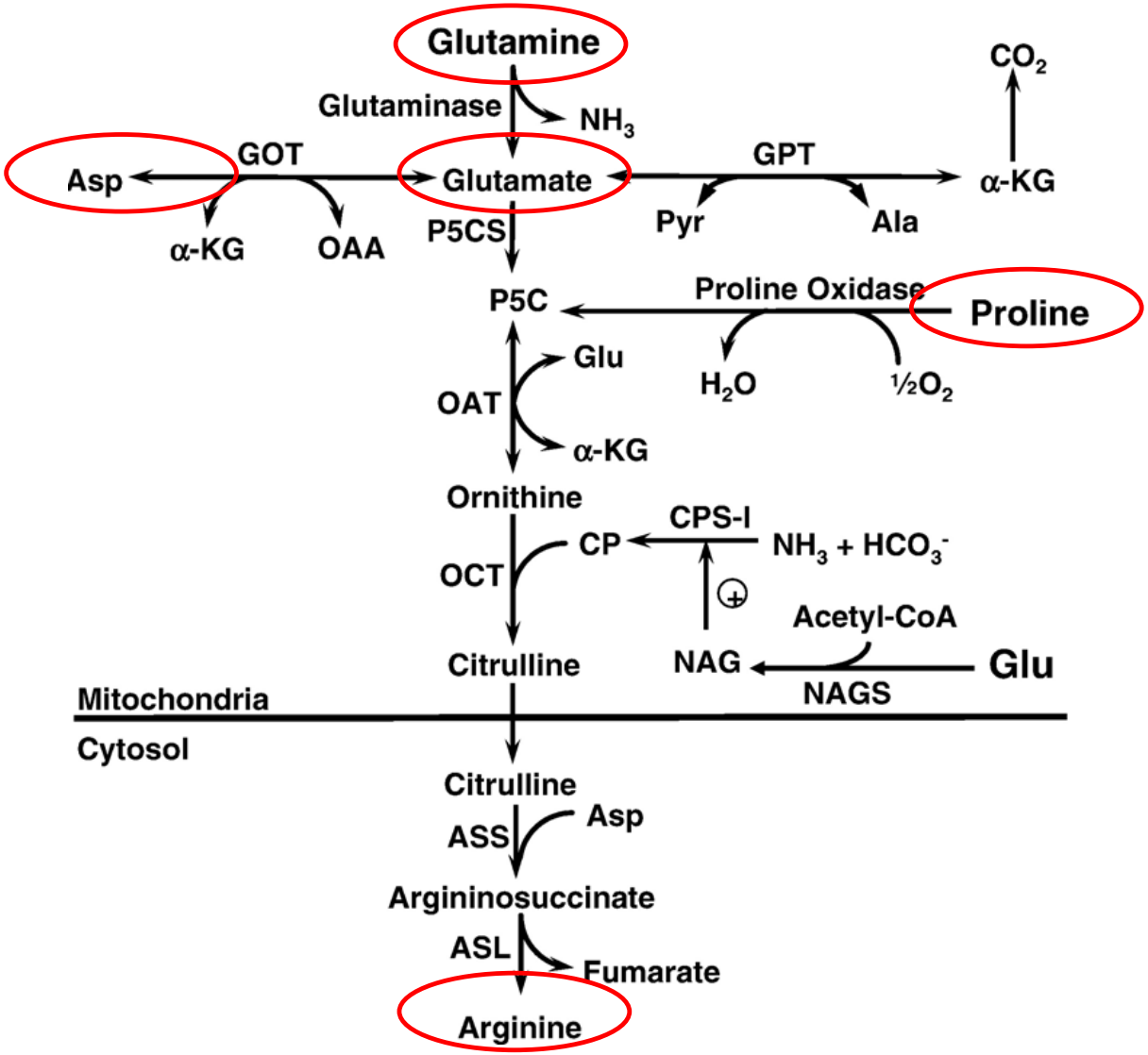
Two examples

- 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



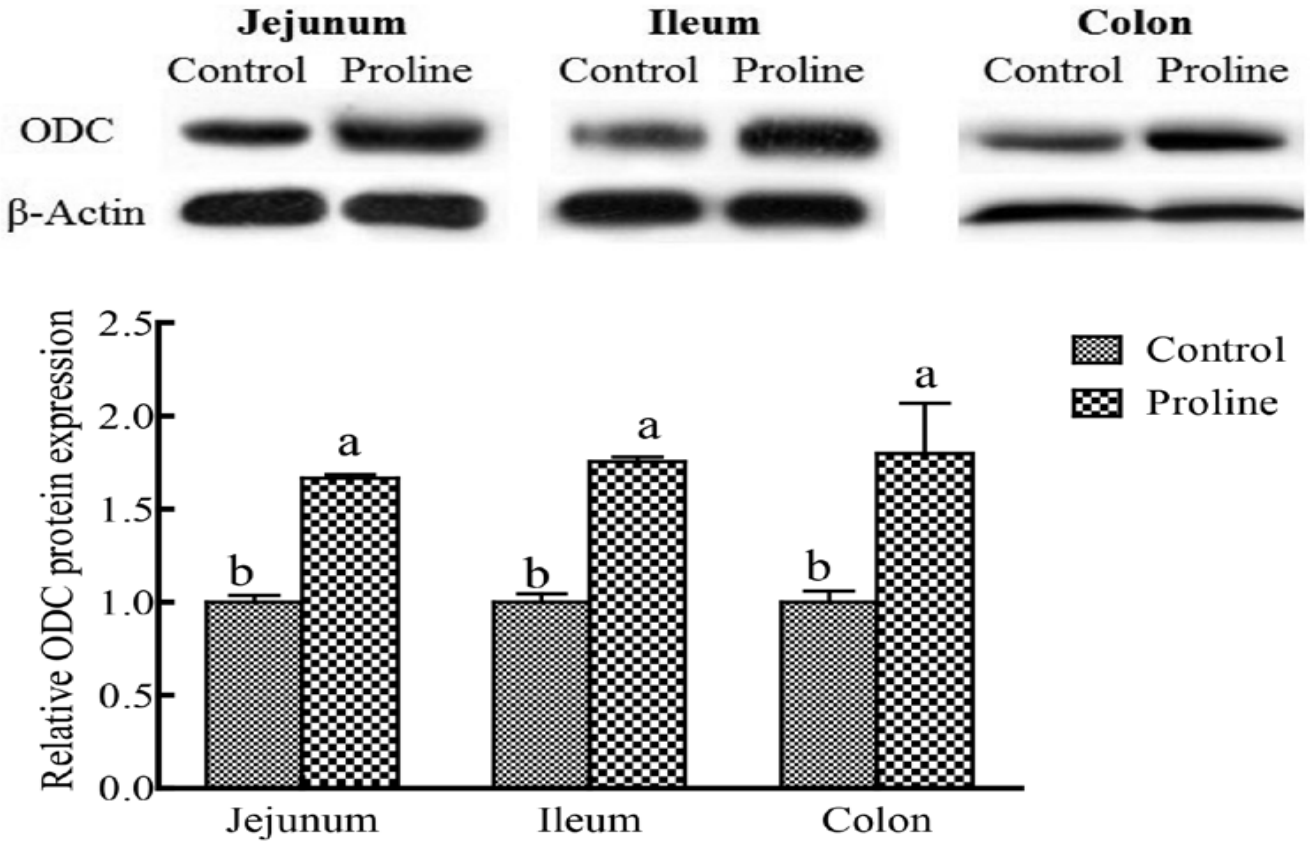
Wu et al., 2007

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

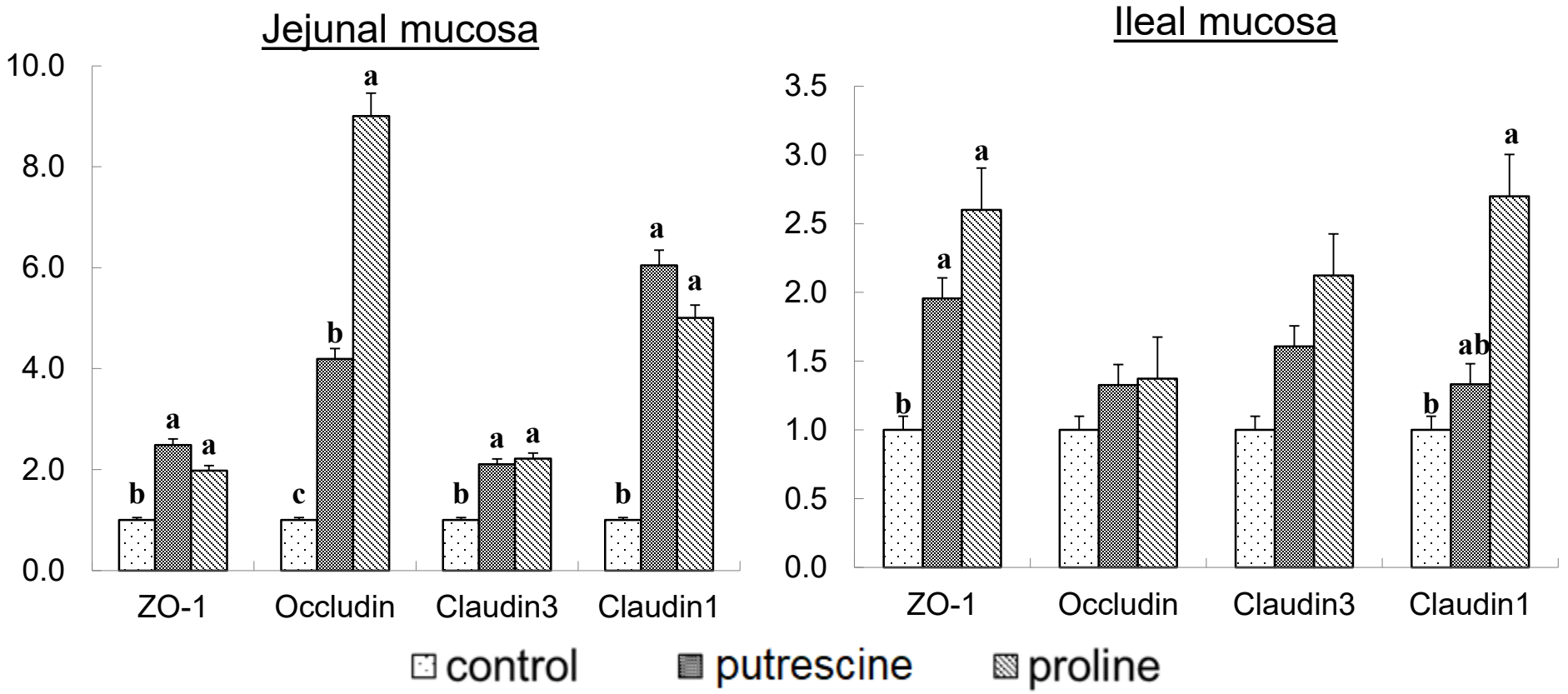
Proline



- **Oral administration of proline enhanced protein expression of ornithine decarboxylase (ODC) activity in jejunum, ileum, and colon**

Tan et al., 2017

Proline



- **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

Serum, pg/mL	Saline		LPS	
	Basal diet	TPT diet	Basal diet	TPT diet
IL1β	254^{c}	215^{c}	1384^{a}	793^{b}
IL6	17.1^{c}	9.4^{c}	270^{a}	132^{b}
IL8	98^{c}	96^{c}	1076^{a}	674^{b}
IL12	115^{c}	102^{c}	497^{a}	310^{b}
GM-CSF	154^{b}	113^{c}	189^{a}	161^{b}
TNFα	0.06^{c}	0.07^{c}	326^{a}	171^{b}
IL4	317^{b}	660^{a}	167^{c}	291^{b}
TGFβ1	897^{a}	883^{a}	416^{c}	623^{b}

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

Tan et al., 2017

Aromatic amino acids

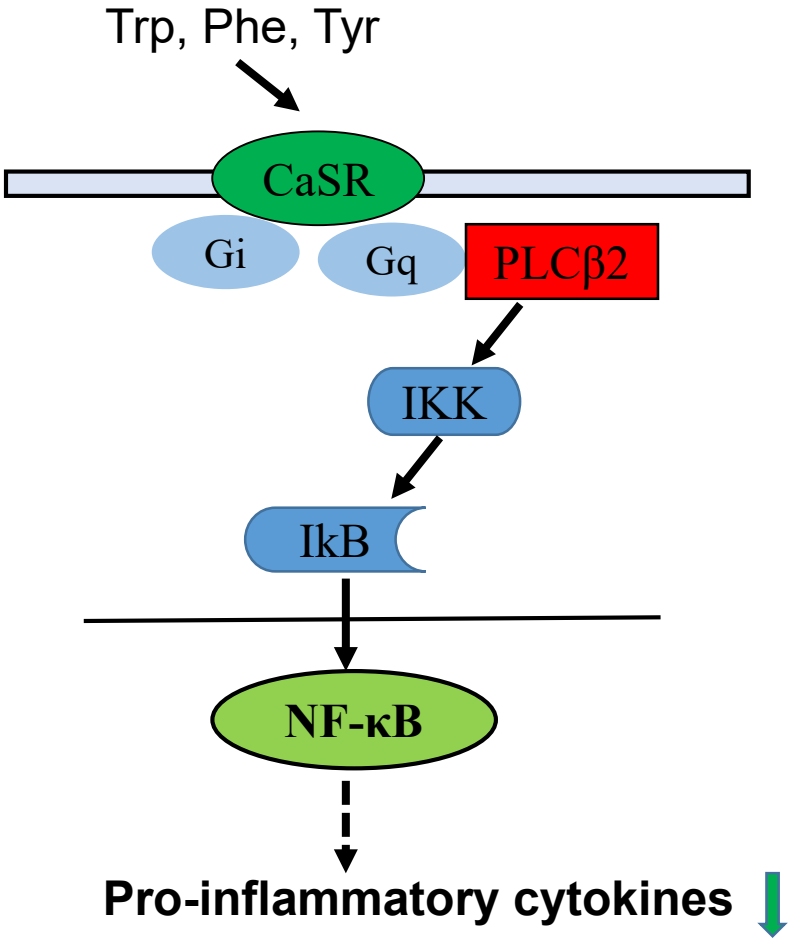
pig intestinal immunity

Gene expression	Saline		LPS	
	Basal diet	TPT diet	Basal diet	TPT diet
IL6	1^{ab}	0.76^{b}	1.41^{a}	0.44^{b}
IL12	1^{b}	0.91^{b}	1.71^{a}	0.37^{c}
IL18	1^{ab}	1.04^{ab}	1.52^{a}	0.47^{b}
TNFα	1^{a}	1.10^{a}	1.28^{a}	0.27^{b}
TGFβ	1^{c}	2.57^{ab}	1.93^{b}	3.10^{a}

Tan et al., 2017

Aromatic amino acids

Potential mechanisms

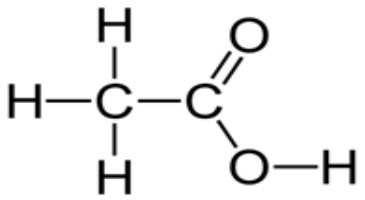


- **Dietary supplemented with aromatic amino acids increased CaSR and PLCβ2 protein expression levels**
- **But decreased p-NF-κB, IKKα/β, and IκB protein expression levels in the LPS-challenged piglets**

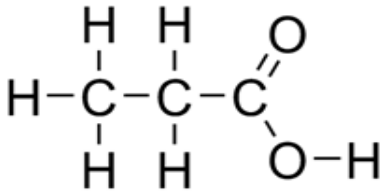
Tan et al., 2017

Short chain fatty acids

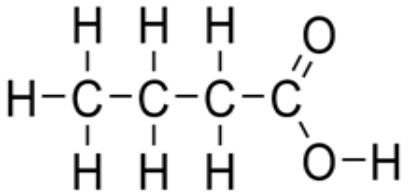
- Fatty acids with a chain of < 6 carbon atoms
  - Acetate, propionate, and butyrate
- Produced by microbial fermentation in the gastrointestinal tract of pigs
- Major fuel source for colonocytes (90% of butyrate)
- Derivatives: salts (Ca, Na), monobutyrin, tributyrin



Acetic acid (acetate)



Propionic acid (propionate)



Butyric acid (butyrate)

Short chain fatty acids

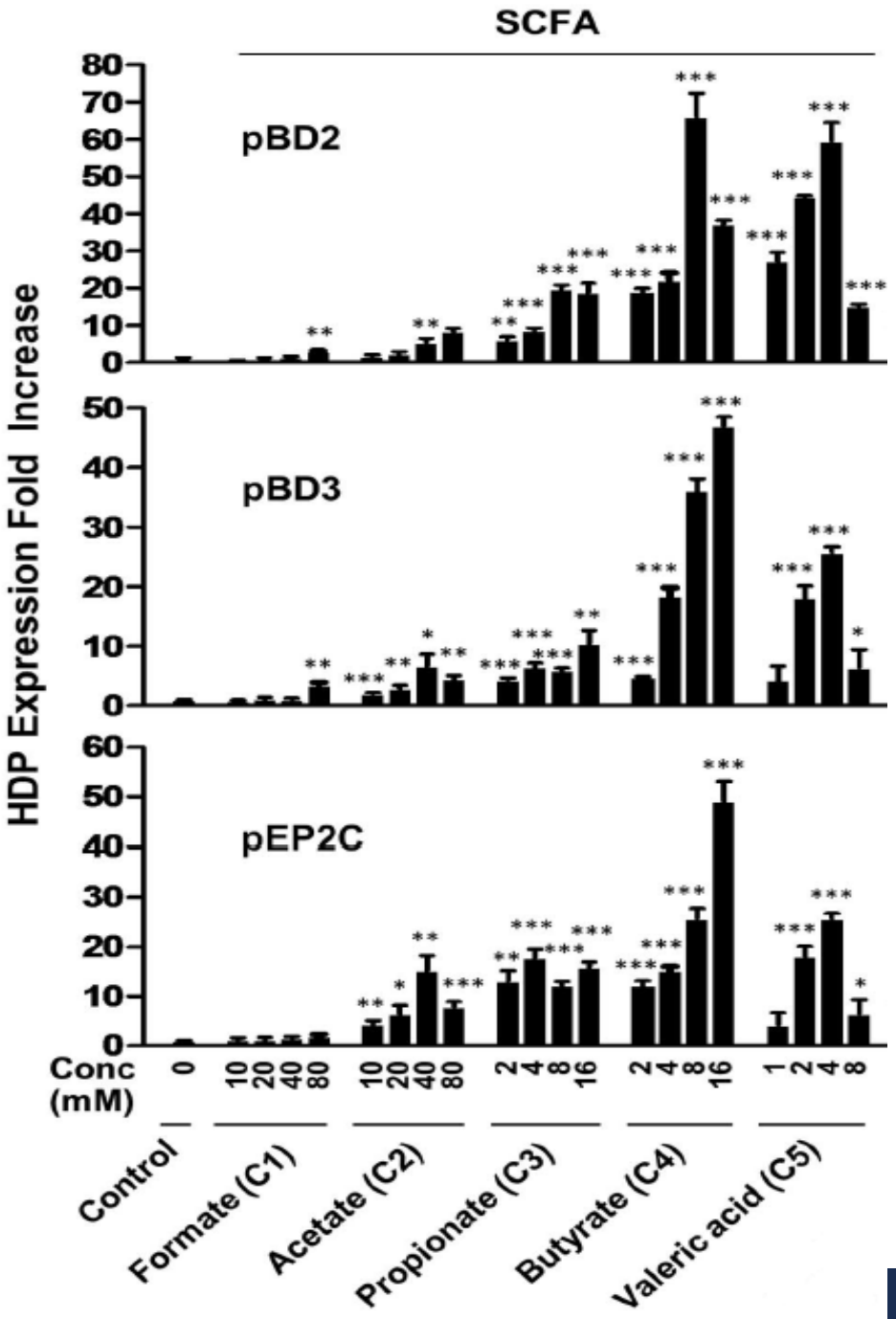
Antimicrobial effects of butyric acid

Gram-negative bacteria	MIC, mg/mL
E. coli, wild type	**2.3**
E. coli, F18	**2.5**
Salmonella Typhimurium, wild type	**2.7**
Salmonella Typhimurium, disease break	**2.6**
Campylobacter jejuni, wild type	**0.5**
Campylobacter jejuni, disease outbreak	**0.7**

Gram-positive bacteria	MIC, mg/mL
Enterococcus faecalis	**2.0**
Clostridium perfringens	**1.2**
Streptococcus pneumonia	**1.0**
Streptococcus suis	**0.7**

MIC: minimal inhibitory concentration

Kovanda et al., 2019



Short chain fatty acids

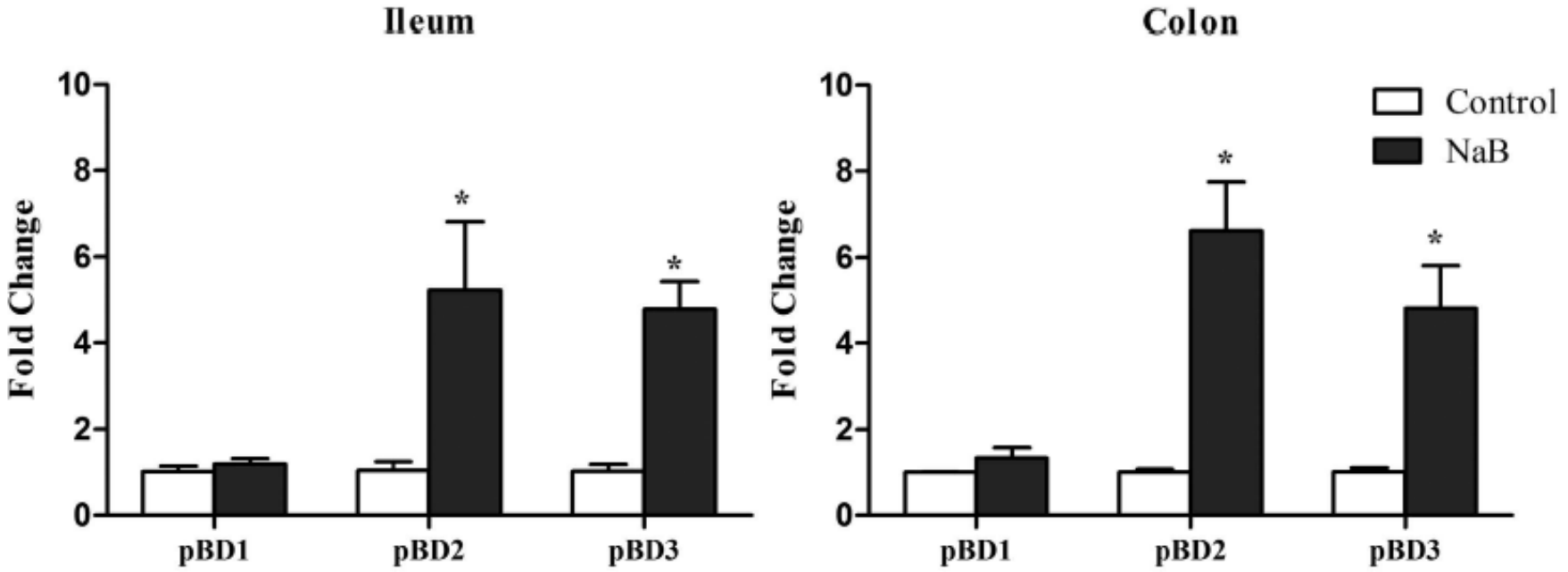
Host defense peptides, in vitro

- 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

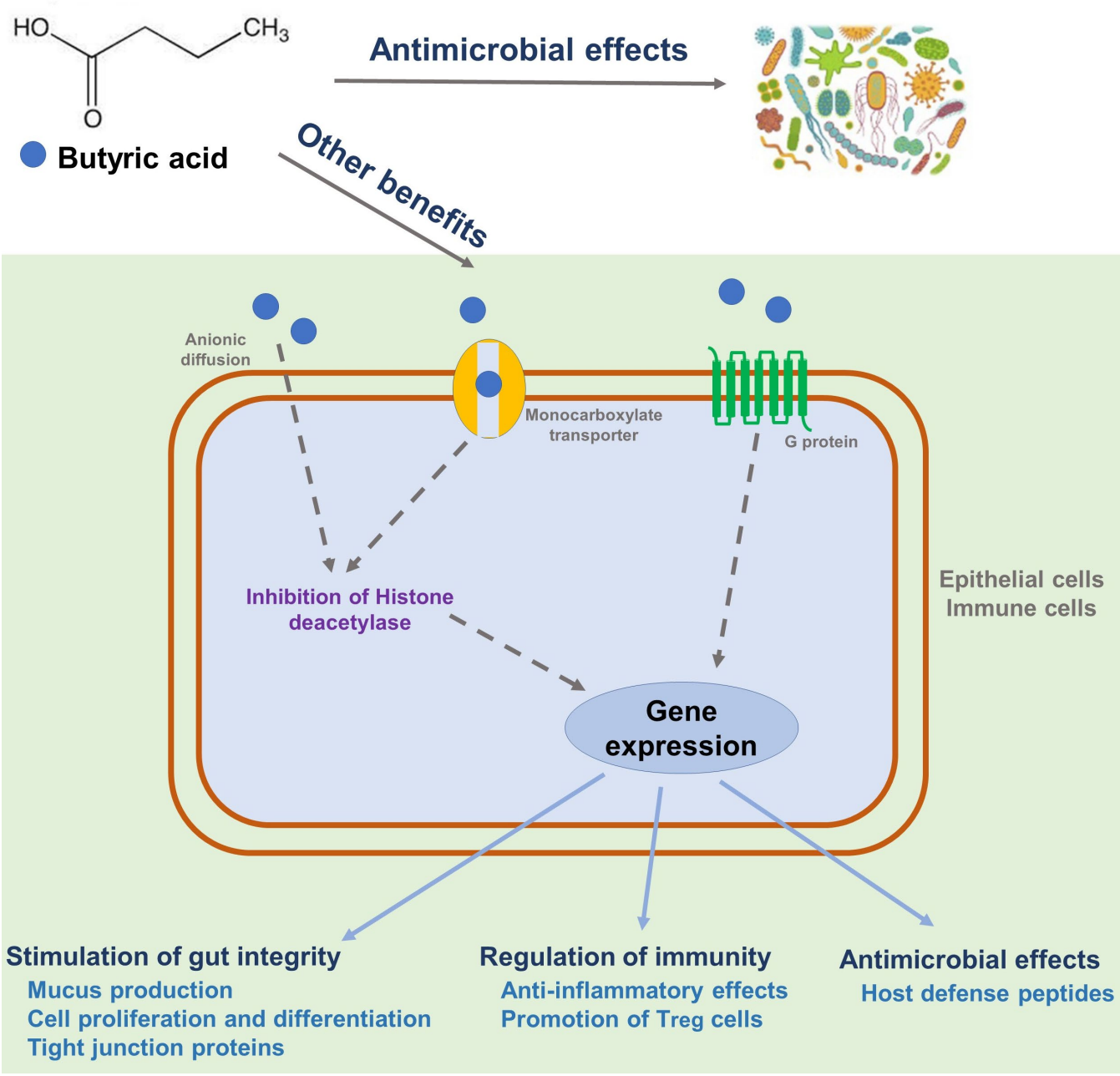
Short chain fatty acids

Host defense peptides, in vivo



- **Weaning pigs, 0.2% sodium butyrate, 10 days**

Xiong et al., 2016



Xiong et al., 2019

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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