

# Trace Amounts of Antibiotic is Detrimental to the Health of Weaned Pigs

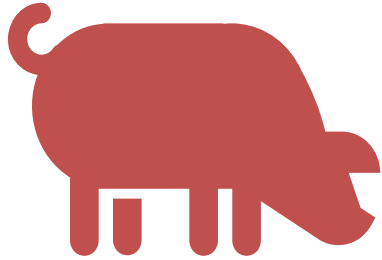
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**Department of Animal Science  
University of California, Davis**





# Outline



**Challenges in  
swine industry**



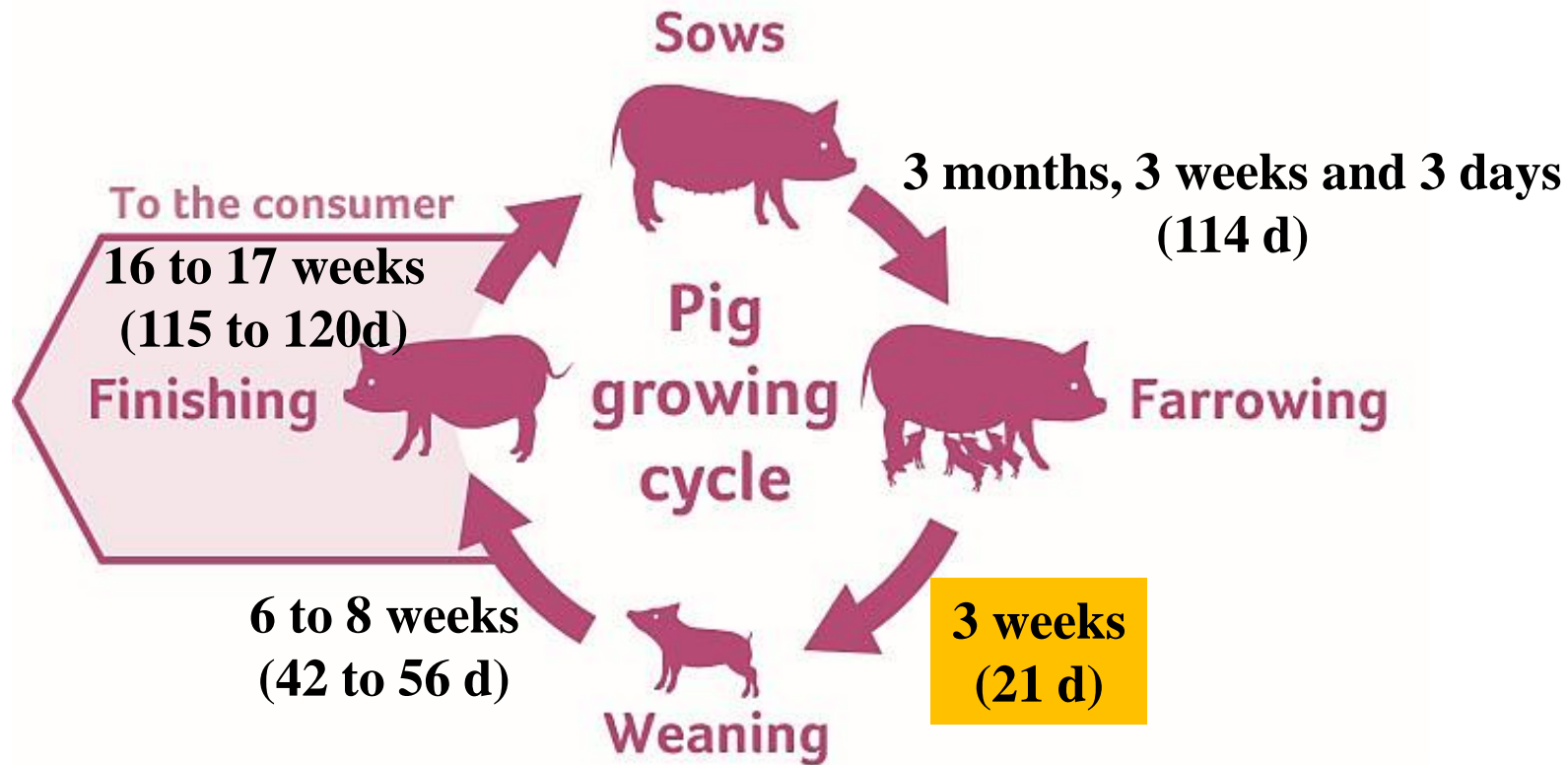
**In-feed antibiotics  
& Risk**



**Research:  
Part 1 & 2**



# Life cycle of a market pig





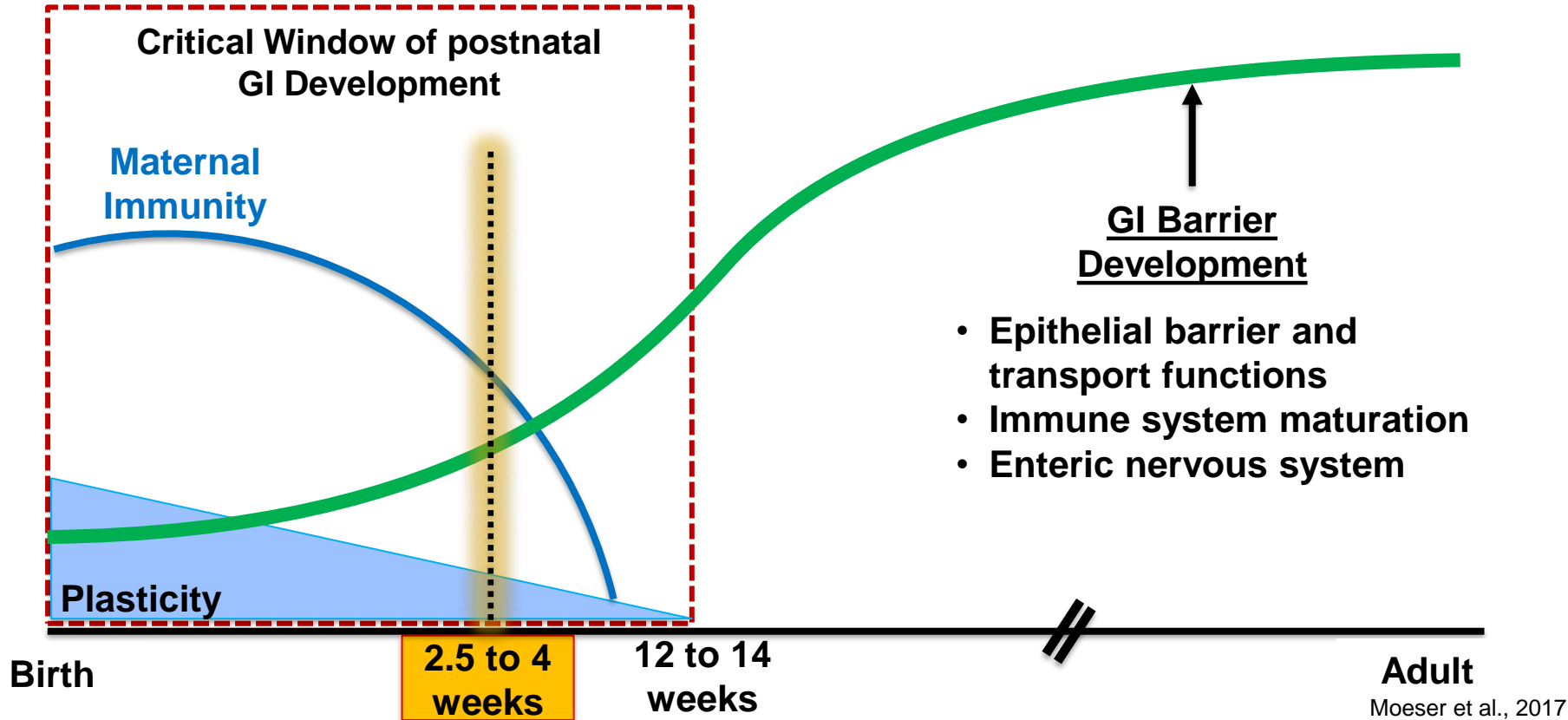
# Weaning stress

- Environmental changes
- Transportation stress
- Abrupt transition of diet
- Increased exposure to pathogens





# Gastrointestinal (GI) tract development during weanling





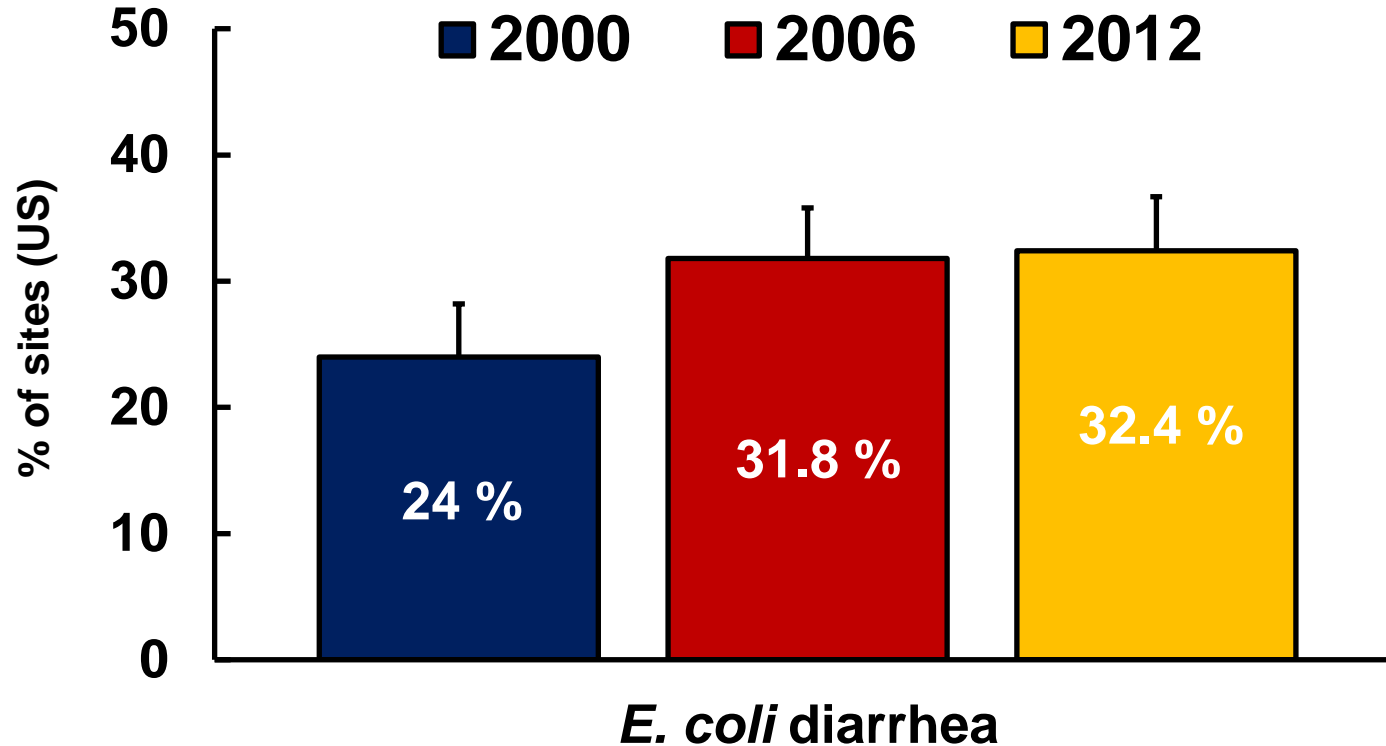
# Post-weaning diarrhea in pigs

- One of the most serious threats for the swine industry
- Usually associated with proliferation of enterotoxigenic *E. coli* (ETEC)
  - ✓ F4 (K88)
  - ✓ F18





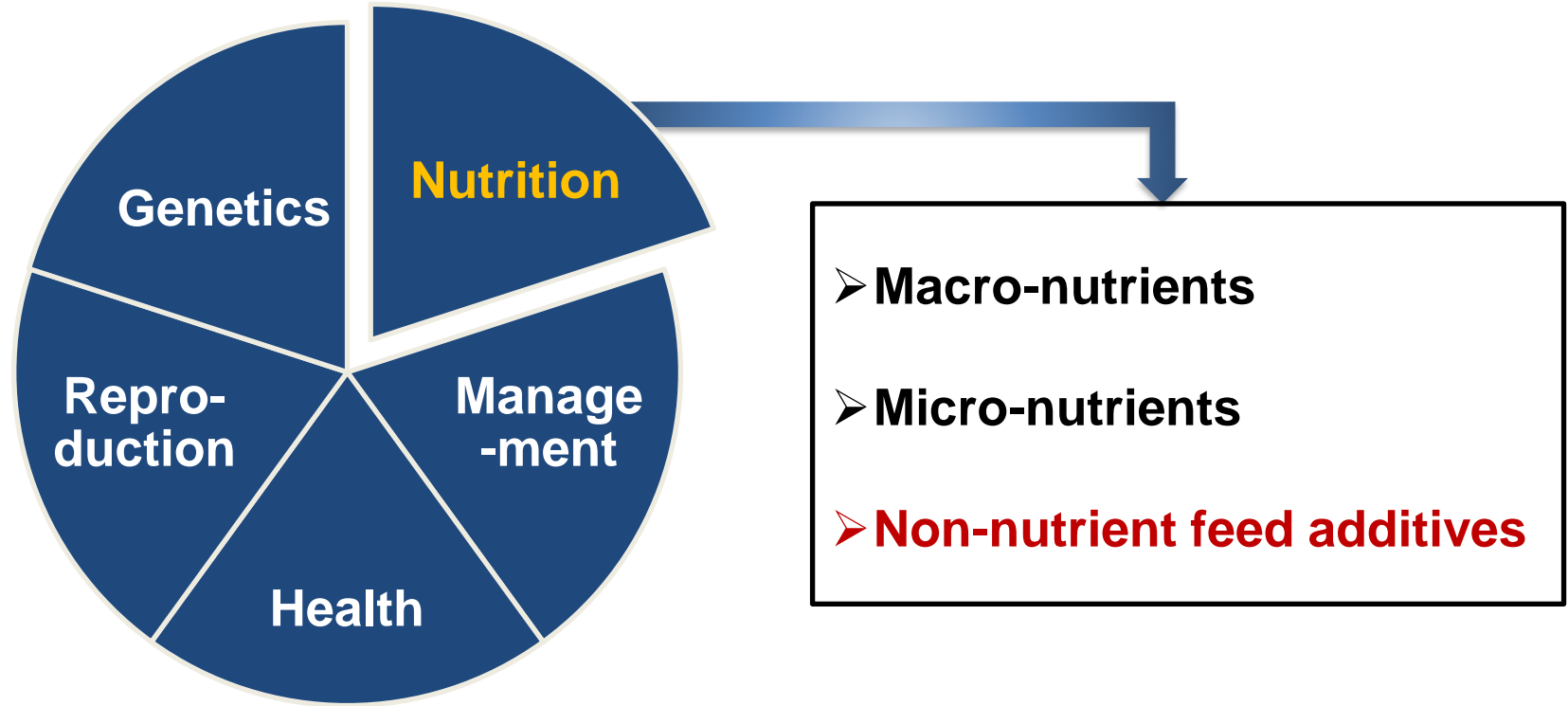
# Post-weaning ETEC diarrhea morbidity



Source: USDA, Swine 2012 Part III: Changes in the U.S. Swine Industry, 1995–2012



# Swine (Livestock) production technologies



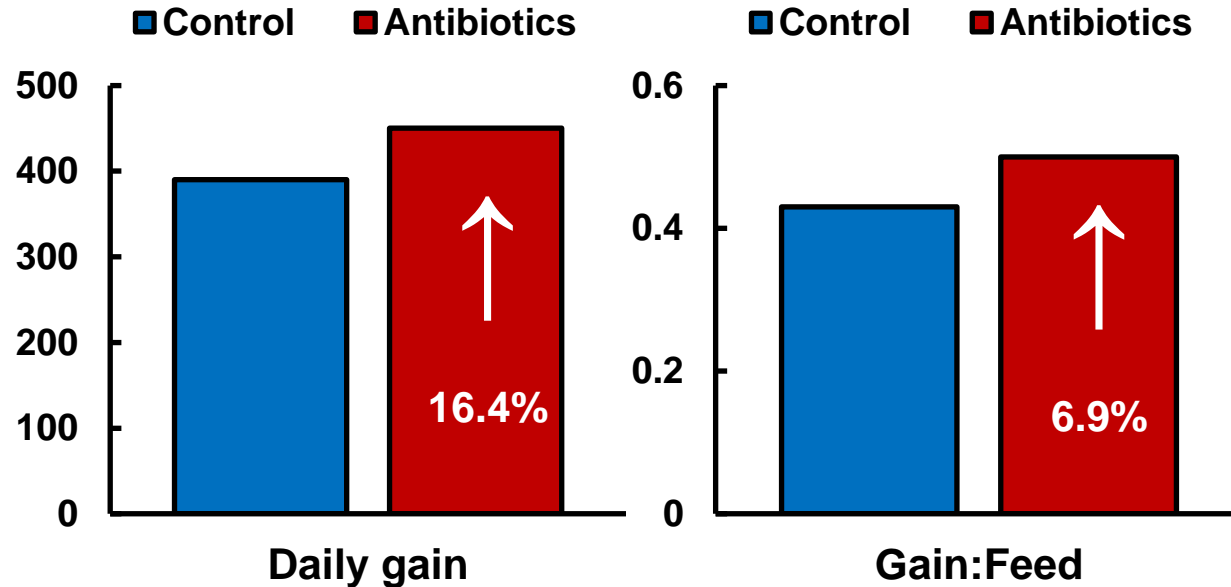


# Antibiotics use in livestock

## Efficacy of antibiotics as growth promoters for weaned pigs (7-25 kg)

### ➤ Antimicrobial substances active against bacteria

- Disease prevention
- Disease treatment
- Growth promotion

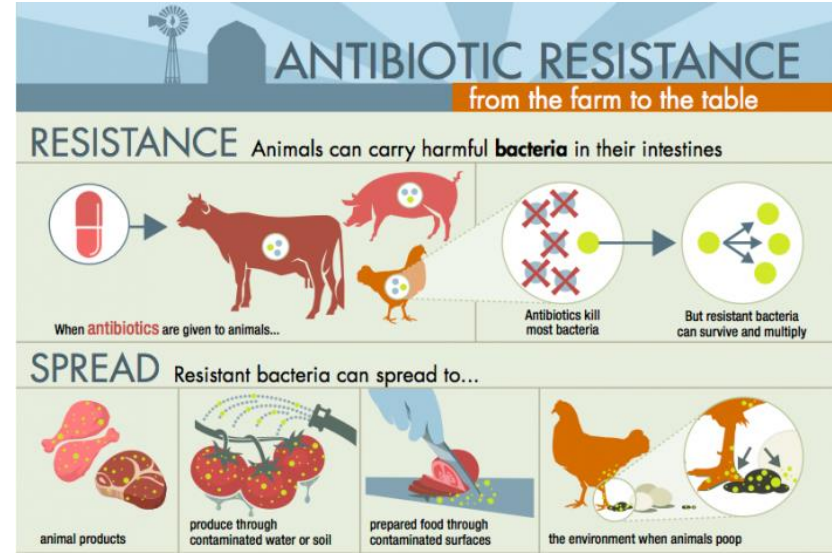


Zimmerman, 1986



# Antibiotics as growth promoter in animal diets poses risk

- Emergence of antibiotic resistance
- Banned in the European Union since 2006
- Also banned in the United States since 2017
- Alternatives to antibiotic are highly demanded



<https://fairfarmsnow.org>



# Trace levels of antibiotics: A global health hazard

- Manure
- Surface water
- Soil
- Air
- Dust
- Farm environment





# Adverse effects of trace levels of antibiotics

- Toxicity
- Mutagenicity
- Carcinogenicity
- Hypersensitivity
- Antibiotic resistance



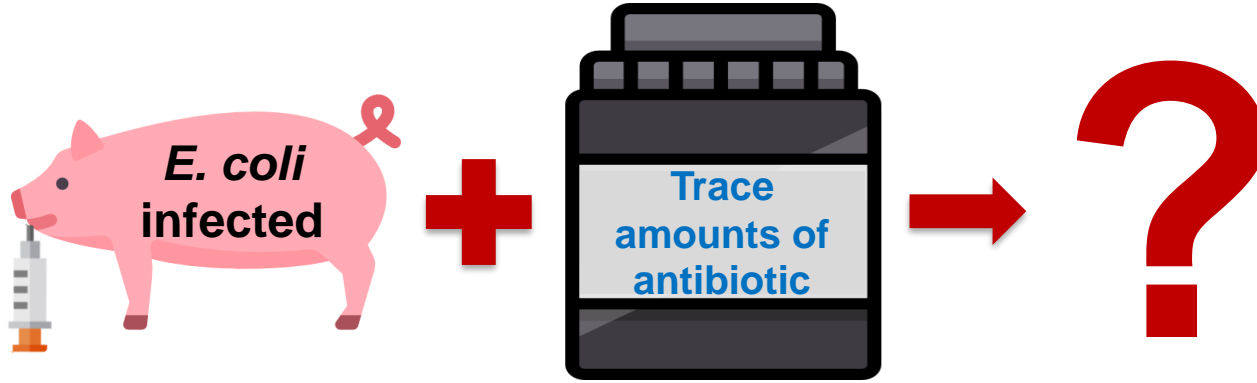
Young animals are more sensitive!



Delay the growth & recovery  
from diseases



# Central Idea & Objective



To investigate the potential detrimental effects of trace amounts of antibiotics on weaned pigs experimentally infected with a pathogenic *E. coli*



# Part 1) Trace amounts of antibiotic exacerbated diarrhea and systemic inflammation of weaned pigs infected with a pathogenic *E. coli*

->Published; Journal of Animal Science (2021)



Journal of Animal Science, 2021, Vol. 99, No. 3, 1–13

doi:10.1093/jas/skab073

Advance Access publication March 6, 2021

Received: 8 January 2021 and Accepted: 2 March 2021

Non Ruminant Nutrition

## NON RUMINANT NUTRITION

### Trace amounts of antibiotic exacerbated diarrhea and systemic inflammation of weaned pigs infected with a pathogenic *Escherichia coli*

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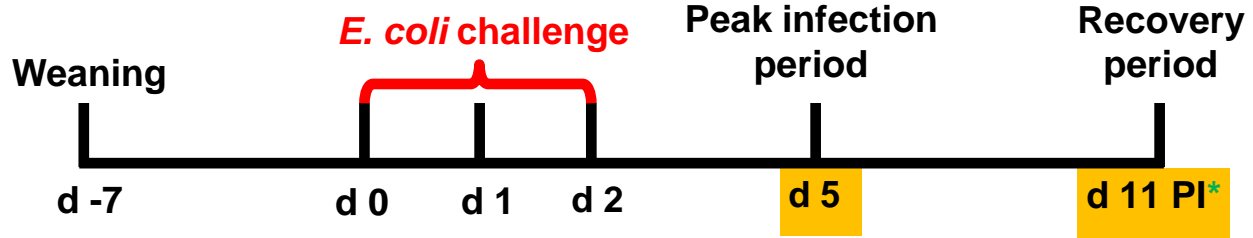
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## Abstract

The experiment was conducted to investigate the effects of trace amounts of antibiotic on growth performance, diarrhea, systemic immunity, and intestinal health of weaned pigs experimentally infected with an enterotoxigenic *Escherichia coli*. Weaned pigs ( $n = 34$ ,  $6.88 \pm 1.03$  kg body weight [BW]) were individually housed in disease containment rooms and randomly allotted to one of the three dietary treatments: nursery basal diet (CON) and two additional diets supplemented with 0.5 or 50 mg/kg carbadox to the nursery basal diet (TRA or REC), respectively. The experiment lasted 18 d with 7 d before and 11 d after the first *E. coli* inoculation. The *E. coli* F18 inoculum was orally provided to all pigs with a dose of  $10^{10}$  colony-forming unit (CFU)/3 mL for three consecutive days. Fecal and blood samples were collected on day 0 before inoculation and days 2, 5, 8, and 11 postinoculation (PI) to test the percentage of  $\beta$ -hemolytic coliforms in total coliforms and complete blood cell count, respectively. Sixteen pigs were euthanized on day 5 PI, whereas the remaining pigs were euthanized at the end of the experiment to collect the jejunal and ileal mucosa and mesenteric lymph node for gene expression and bacterial translocation, respectively. Pigs in REC had greater ( $P < 0.05$ ) final BW and lower ( $P < 0.05$ ) overall frequency of diarrhea compared with pigs in the CON and TRA groups. Pigs in TRA had the lowest ( $P < 0.05$ ) average daily gain and feed efficiency from day 0 to 5 PI, highest ( $P < 0.05$ ) percentage of  $\beta$ -hemolytic coliforms in fecal samples on days 2 and 5 PI, and greatest ( $P < 0.05$ ) bacterial colonies in mesenteric lymph nodes on day 11 PI compared with pigs in the CON and REC groups. Pigs in TRA had the greatest ( $P < 0.05$ ) neutrophils on day 5 PI and higher ( $P < 0.05$ ) white blood cell counts and lymphocytes than other groups on day 11 PI. Pigs in TRA had the greatest ( $P < 0.05$ ) serum C-reactive protein on days 2 and 5 PI and serum tumor necrosis factor- $\alpha$  on day 5 PI, compared with pigs in the CON and REC groups. Pigs fed REC had increased ( $P < 0.05$ ) mRNA expression of zona occludens-1 (ZO-1) and occludin (OCLN) and reduced ( $P < 0.05$ ) interleukin-1 beta (IL1B), interleukin-6 (IL6), and tumor necrosis factor- $\alpha$  (TNF $\alpha$ ) in ileal mucosa on day 5 PI, compared with the CON, whereas TRA upregulated ( $P < 0.05$ ) mRNA expression of IL1B, IL6, and cyclooxygenase-2 (COX2) in the ileal mucosa on day 11 PI, compared with the REC. In conclusion, trace amounts of antibiotic may exacerbate the detrimental effects of *E. coli* infection on pig performance by increasing diarrhea and systemic inflammation of weaning pigs.

**Key words:** carbadox, diarrhea, enterotoxigenic *Escherichia coli*, gut health, immunity, weaned pigs

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➤ Pathogenic F18 *E. coli* challenge (LT, STb, SLT-2); oral inoculation,  $10^{10}$  cfu/dose with 3 doses

Control diet (CON)

Trace amounts of antibiotic (LOW)  
Control diet + 0.5 mg/kg Carbadox

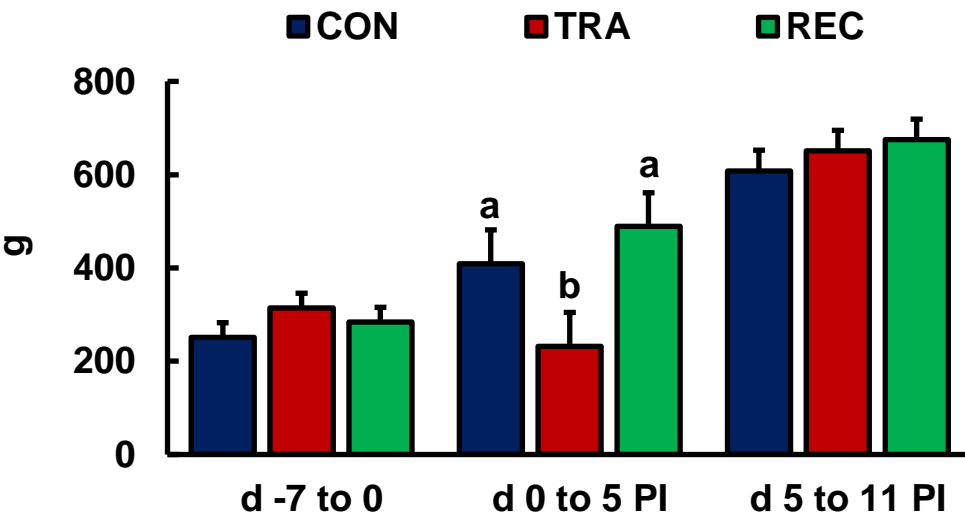
Recommended dose of antibiotic (REC)  
Control diet + 50 mg/kg Carbadox

*E. coli*  
challenged

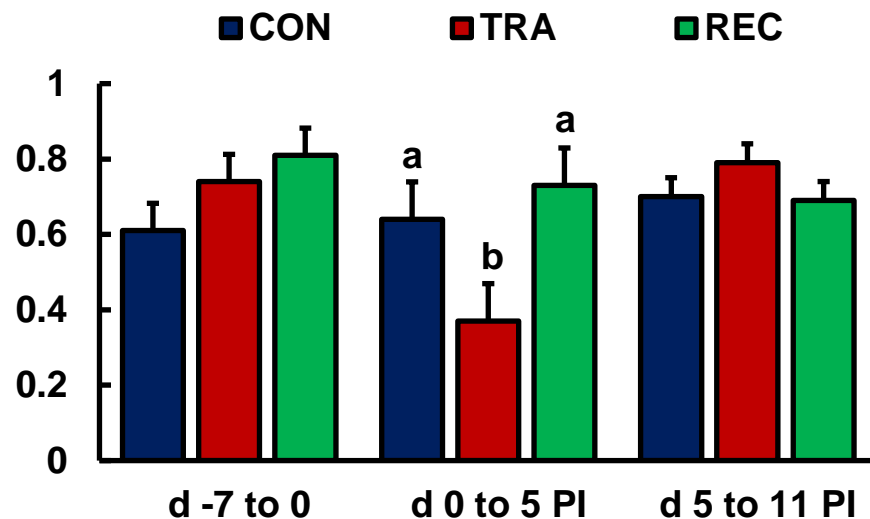


# Trace amounts of antibiotic reduced growth performance

## Average daily gain



## Gain:Feed



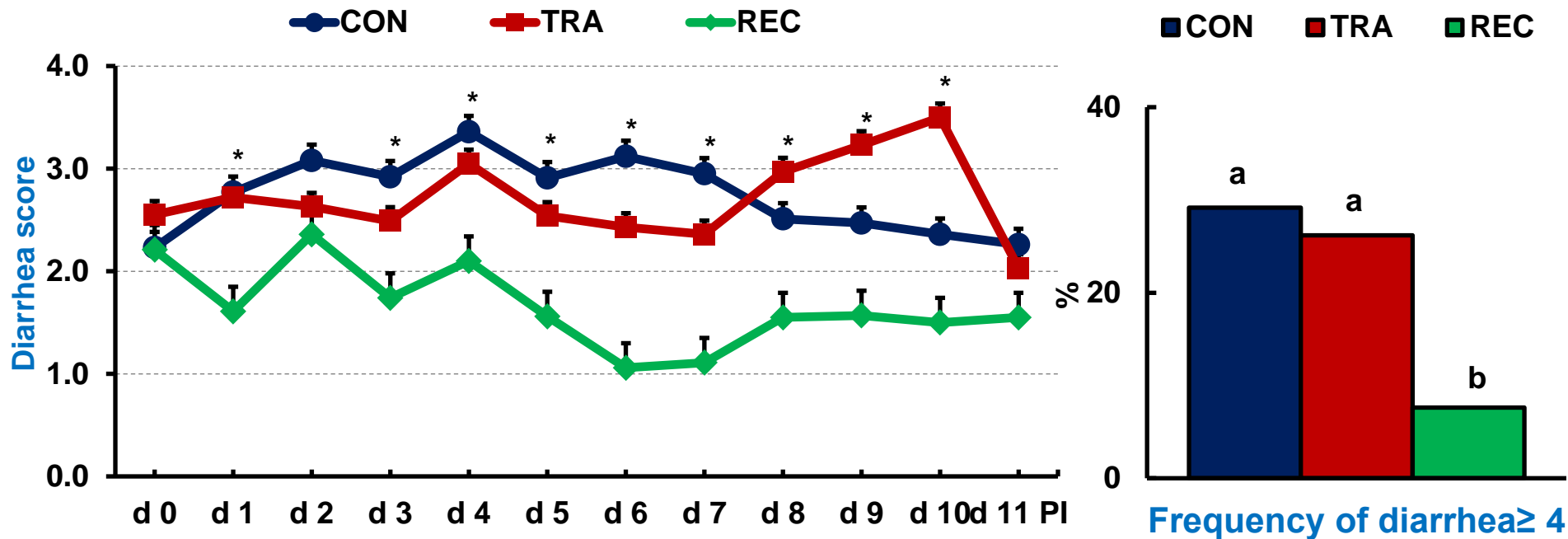
**TRA**= 0.5 mg/kg Carbadox

**REC**= 50 mg/kg Carbadox

PI=post-inoculation



# Trace amounts of antibiotic exacerbated the severity of diarrhea



TRA= 0.5 mg/kg Carbadox

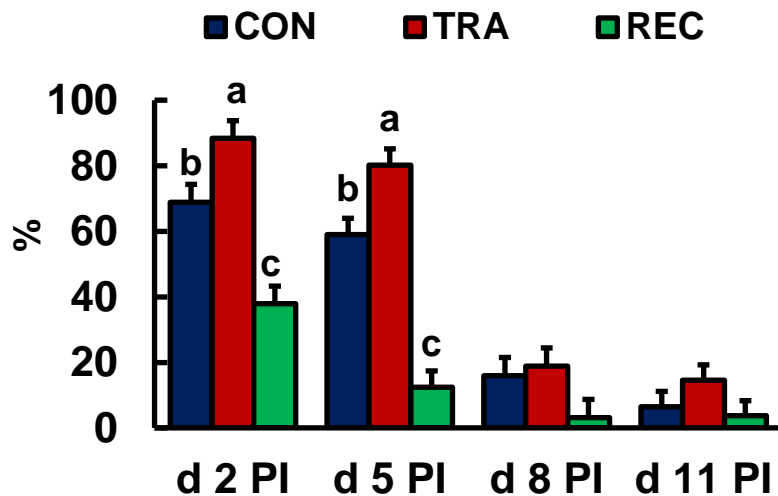
REC= 50 mg/kg Carbadox

PI=post-inoculation

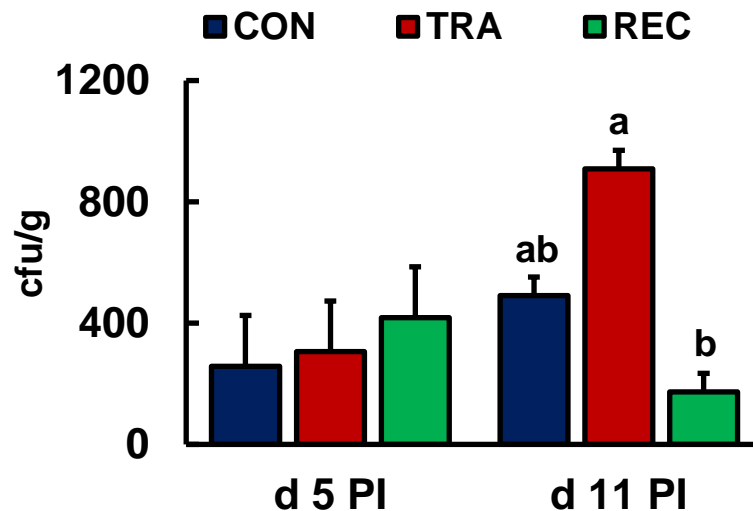


# Trace amounts of antibiotic worsened the *E. coli* infection

## $\beta$ -hemolytic coliforms in feces



## Bacterial translocation in mesenteric lymph node



TRA= 0.5 mg/kg Carbadox

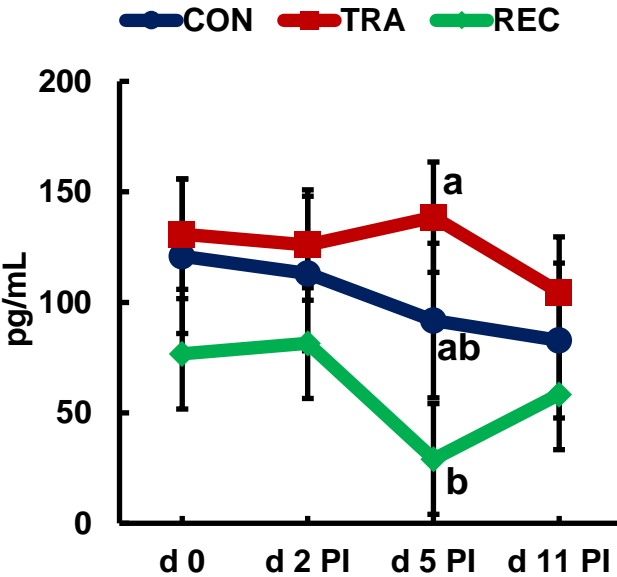
REC= 50 mg/kg Carbadox

PI=post-inoculation

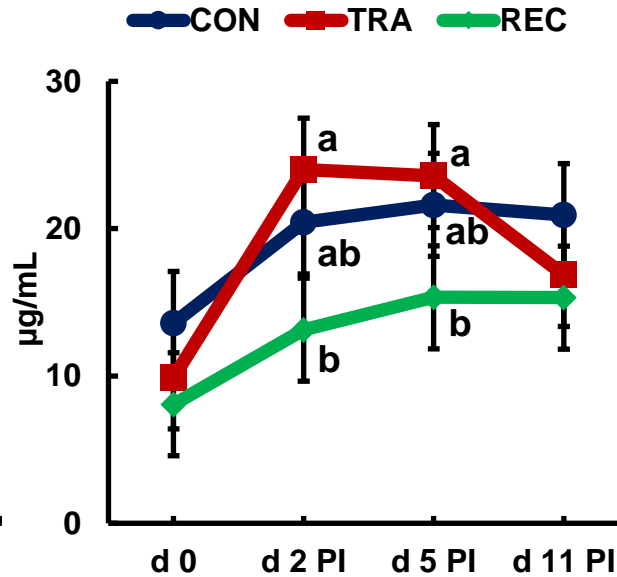


# Trace amounts of antibiotic elevated systemic inflammatory markers

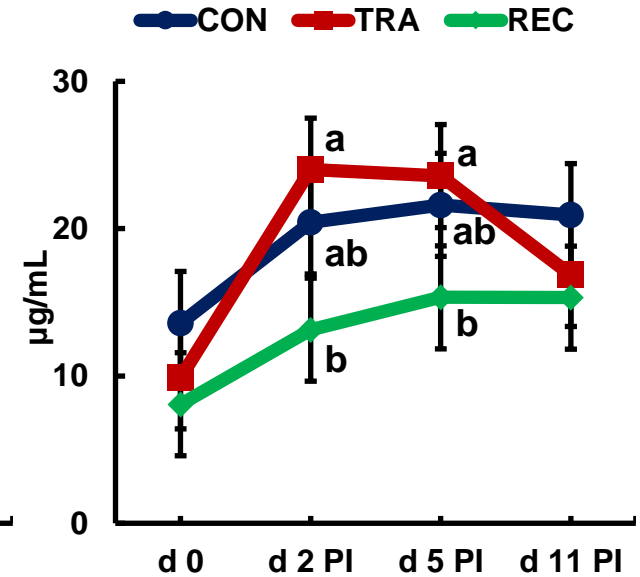
## TNF- $\alpha$



## C-reactive protein

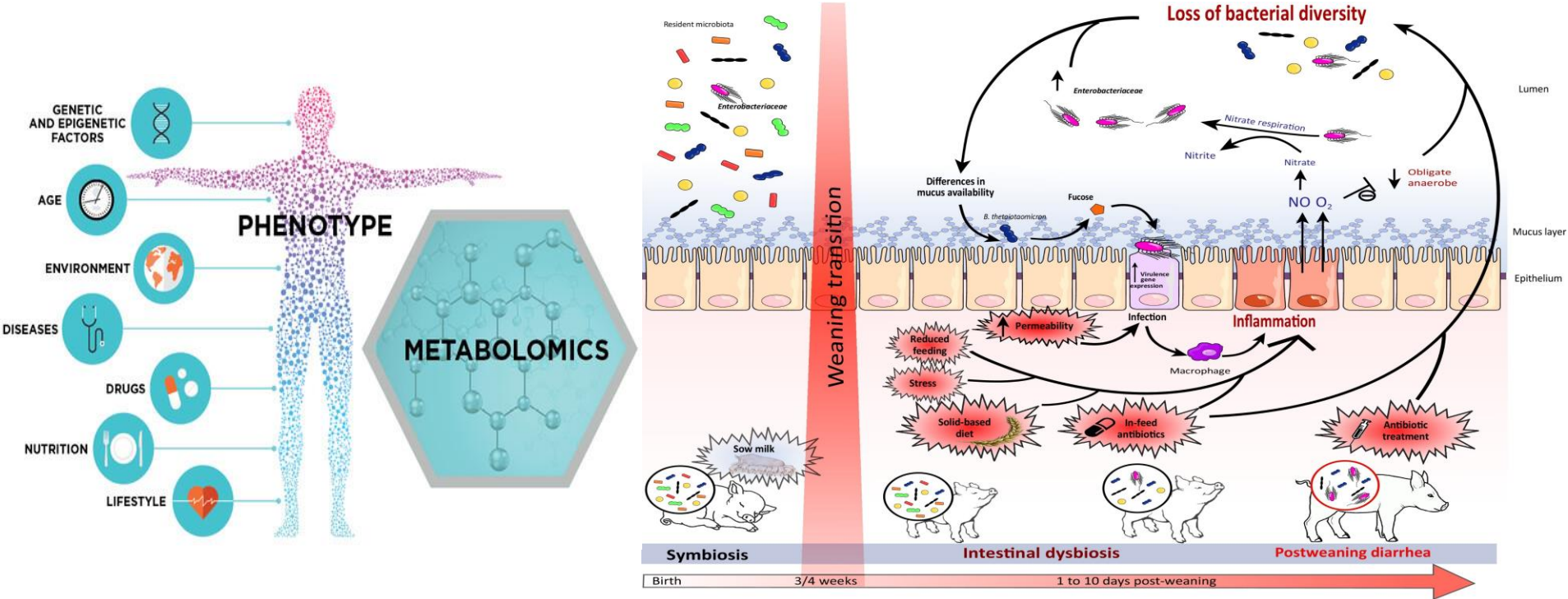


## Haptoglobin





# Part 2) Trace amounts of antibiotic altered metabolomic and microbial profiles of weaned pigs infected with a pathogenic *E. coli*



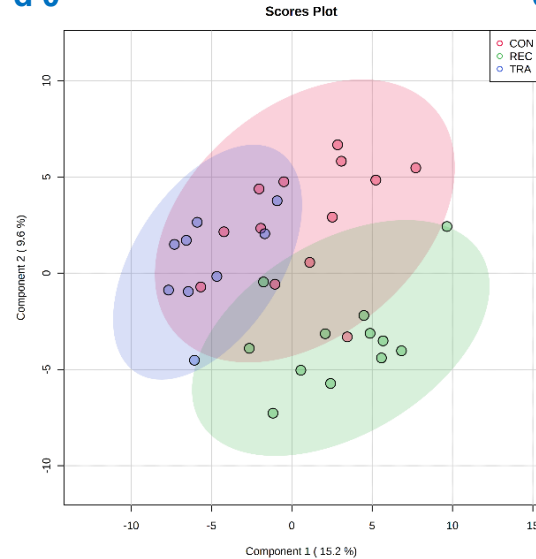
Trends in Microbiology

Gresse et al. (2017); Metabolomic Technologies Inc.

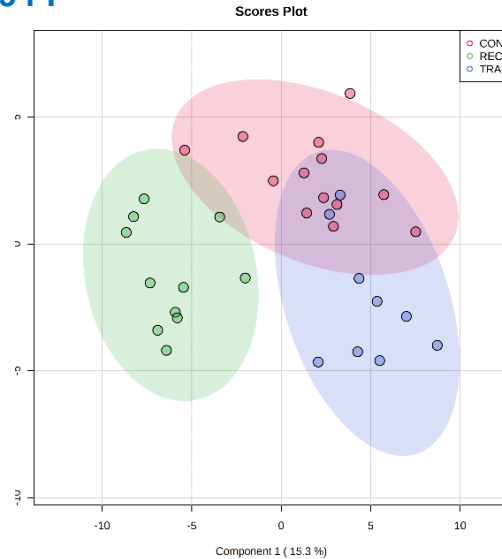


# Partial Least Squares Discriminant Analysis (PLS-DA) 2D score plot of the metabolites in serum showed separated clusters between trace amounts of antibiotic and label-recommended dose of antibiotic groups

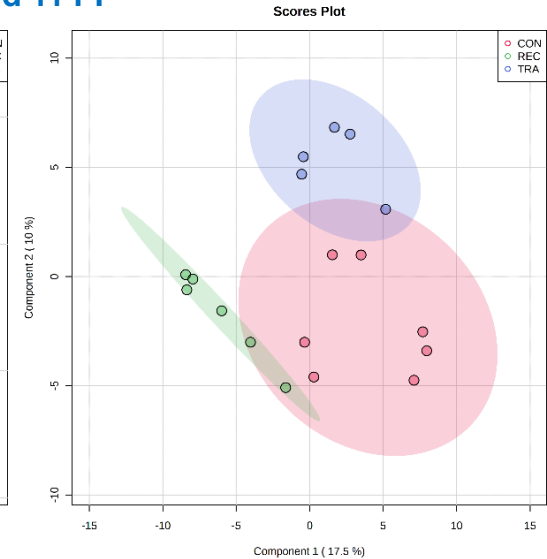
d 0



d 5 PI



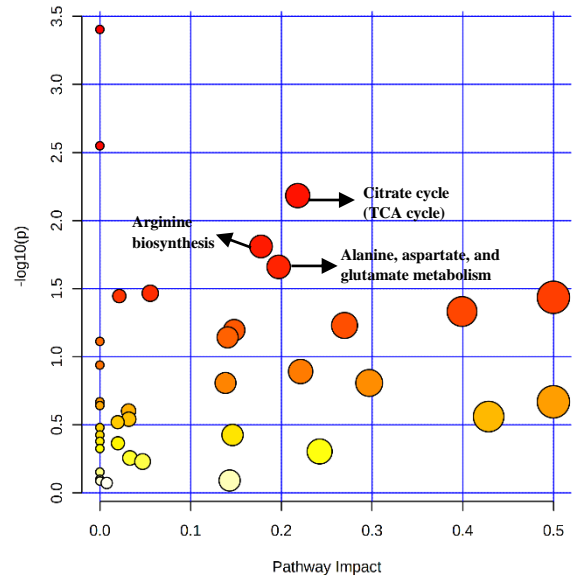
d 11 PI



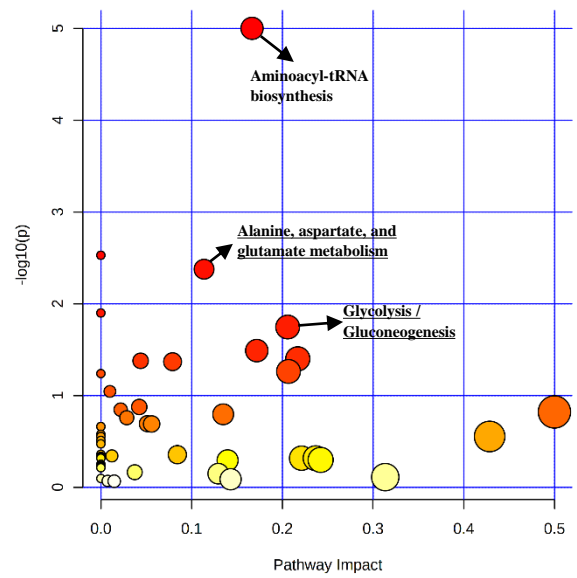


# Significantly changed pathways in serum between trace amounts of antibiotic and label-recommended dose of antibiotic groups

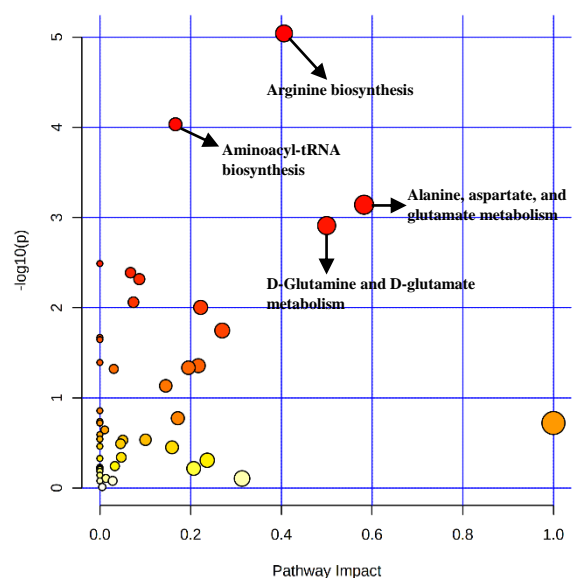
d 0



d 5 PI



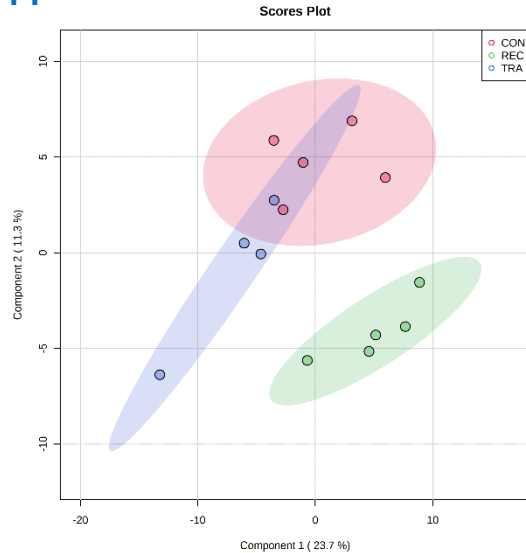
d 11 PI



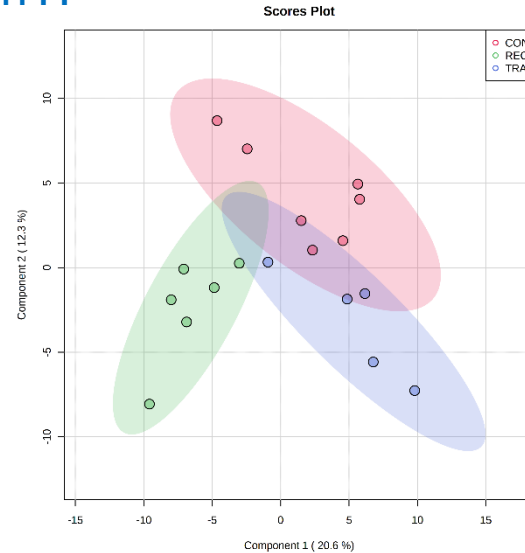


# Partial Least Squares Discriminant Analysis (PLS-DA) 2D score plot of the metabolites in colon digesta showed separated clusters between trace amounts of antibiotic and label-recommended dose of antibiotic groups

d 5 PI



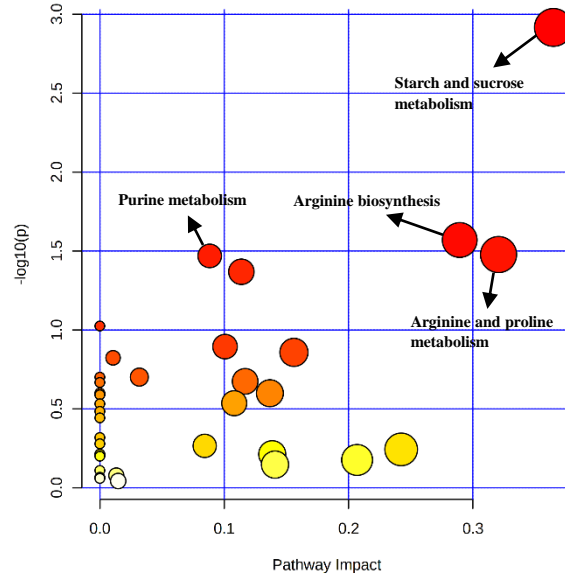
d 11 PI



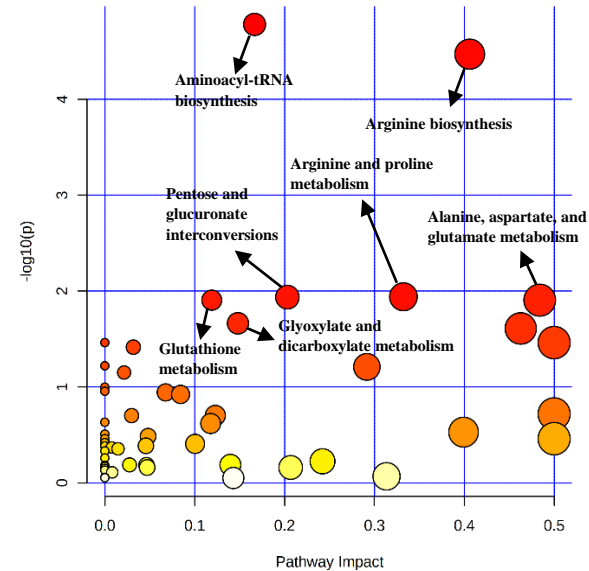


# Significantly changed pathways in colon digesta between trace amounts of antibiotic and label-recommended dose of antibiotic groups

d 5 PI

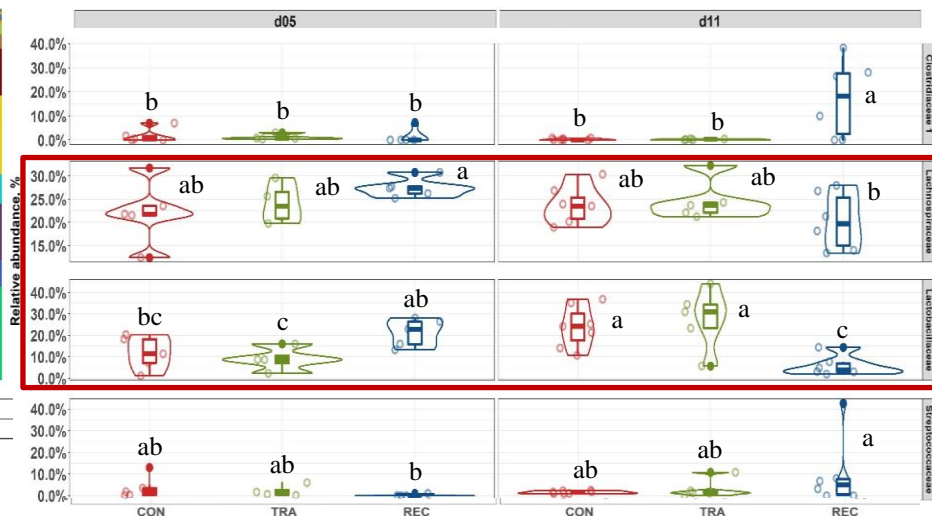
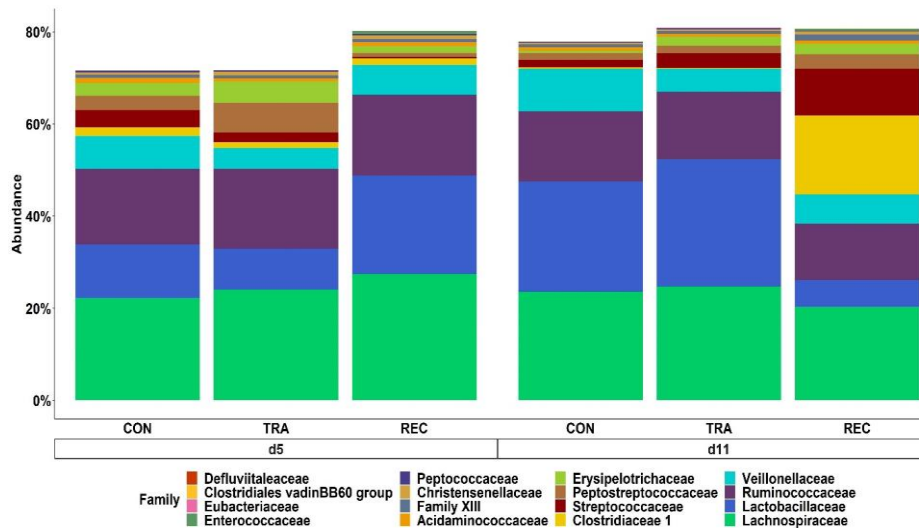


d 11 PI





# Relative abundance of Firmicutes family in colon digesta of pigs fed diets supplemented with different dose of antibiotic on d 5 and 11 post-inoculation



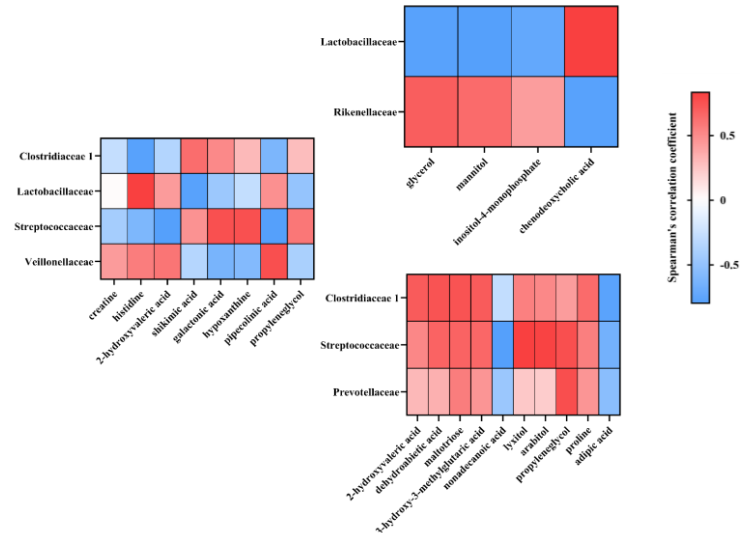


# Summary and Future Research (Chapter 2&3)

- ❖ Trace amounts of antibiotic have shown detrimental effects on growth performance and disease resistance of pigs challenged with ETEC F18, potentially by exacerbating systemic inflammation and altering metabolic and microbial profiles.

- ❖ On-going and future research

- ✓ RNA sequencing
- ✓ Correlation analysis
- ✓ Targeted-metabolomics
- ✓ Metagenomics





# Acknowledgements



**Comparative Animal Nutrition & Physiology Laboratory  
University of California, Davis**



*Journal of Animal Science*, 2021, Vol. 99, No. 3, 1–13

doi:10.1093/jas/skab073

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**Research project No. W4002**



**Thank you for your attention!**





**Thank you for your attention!**

