Journal of Animal Science, 2022, **100**, 1–14
https://doi.org/10.1093/jas/skac166
Advance access publication 7 May 2022
Animal Health and Well Being

Influence of yeast-based pre- and probiotics in lactation and nursery diets on nursery pig performance and antimicrobial resistance of fecal *Escherichia coli*

Jenna A. Chance,[†] Joel M. DeRouchey,[†] Raghavendra G. Amachawadi,[‡,1] Victor Ishengoma,[‡] Tiruvoor G. Nagaraja,[**] Robert D. Goodband,[†] Jason C. Woodworth,[†] Mike D. Tokach,[†] Qing Kang,[$] Joseph A. Loughmiller,[¶] Brian Hotze,[¶] and Jordan T. Gebhardt[**]

[†]Department of Animal Sciences and Industry, Kanas State University, Manhattan, KS 66506-0201, USA
[‡]Department of Clinical Sciences, College of Veterinary Medicine, Kansas State University, Manhattan, KS 66506-0201, USA
[$]Department of Statistics, College of Arts and Sciences, Kansas State University, Manhattan, KS 66506-0201, USA
[¶]Phileo by Lesaffre, Milwaukee, WI 53214-1552, USA
[**]Department of Diagnostic Medicine/Pathobiology, College of Veterinary Medicine, Kanas State University, Manhattan, KS 66506-0201, USA
[1]Corresponding author: agraghav@vet.ksu.edu

Abstract

Two experiments were conducted to determine the impact of various combinations of yeast-based direct fed microbials (DFM) in diets fed to nursery pigs weaned from sows fed lactation diets with or without yeast additives. In Exp. 1, 340 weaned pigs, initially 5.1 kg ± 0.02, were used to evaluate previous sow treatment (control vs. yeast additives) and nursery diets with or without added yeast-based DFM on growth performance and antimicrobial resistance (AMR) patterns of fecal *Escherichia coli*. Treatments were arranged in a 2 × 2 factorial with main effects of sow treatment (control vs. yeast-based pre- and probiotic diet; 0.10% ActiSaf Sc 47 HR+ and 0.025% SafMannan, Phileo by Lesaffre, Milwaukee, WI) and nursery treatment (control vs. yeast-based pre- and probiotic diet; 0.10% ActiSaf Sc 47 HR+, 0.05% SafMannan, and 0.05% NucleoSaf from days 0 to 7, then concentrations were decreased by 50% from days 7 to 24) with 5 pigs per pen and 17 replications per treatment. Progeny from sows fed yeast additives had increased ($P < 0.05$) average daily gain (ADG) from days 0 to 24 and days 0 to 45. However, pigs that were fed yeast additives for the first 24 d in the nursery tended to have decreased days 0 to 45 ADG ($P = 0.079$). Fecal *E. coli* isolated from pigs from the sows fed yeast group had increased ($P = 0.034$) resistance to nalidixic acid and a tendency for increased resistance to ciprofloxacin ($P = 0.065$) and gentamicin ($P = 0.054$). Yet, when yeast additives were added in the nursery, there was reduced ($P < 0.05$) fecal *E. coli* resistance to azithromycin and chloramphenicol. In Exp. 2, 330 weaned pigs, initially 5.8 kg ± 0.03, were used to evaluate diets with two different combinations of DFM on growth performance. Treatments were arranged in a 2 × 3 factorial with main effects of sow treatment (same as described in Exp. 1) and nursery treatment (control; YCW, 0.05% of SafMannan from days 0 to 38 and NucleoSaf at 0.05% from days 0 to 10 and 0.025% from days 10 to 24; or DFM, 0.10% MicroSaf-S from days 0 to 38 and NucleoSaf at 0.05% from days 0 to 10 and 0.025% from days 10 to 24) with 6 pigs per pen and 8 to 10 replications per treatment. From days 0 to 10 post-weaning, progeny of sows fed yeast additives had increased ($P < 0.05$) ADG and G:F. In conclusion, feeding sows yeast through lactation improved offspring growth performance in the nursery. Although feeding live yeast and yeast extracts reduced nursery pig performance in Exp. 1, feeding DFM improved growth later in the nursery period in Exp. 2.

Lay Summary

Feeding sows a diet containing live yeast and yeast extract from day 110 of gestation through weaning resulted in progeny that were heavier at weaning and had increased average daily gain and average daily feed intake throughout the nursery period. However, feeding yeast additives to pigs only in the nursery tended to reduce average daily gain. Fecal *E. coli* isolates from offspring that were fed yeast showed tendency towards antimicrobial resistance among fecal *E. coli* isolates to nalidixic acid, ciprofloxacin, and gentamicin. Yet, feeding live yeast and yeast extracts in the nursery phase may reduce the antimicrobial resistance of fecal *E. coli* to azithromycin and chloramphenicol.

Key words: antimicrobial resistance, *Bacillus*, growth, live yeast, nursery pigs, yeast extract

Abbreviations: ADFI, average daily feed intake;ADG, average daily gain;AMR, antimicrobial resistance;ATCC, American Type Culture Collection;BW, body weight;CFU, colony-forming unit;CLSI, Clinical and Laboratory Standards Institute;CP, crude protein;DFM, direct-fed microbial;ETEC, enterotoxigenic *E. coli*;G:F, gain-to-feed ratio/feed efficiency;ME, metabolizable energy;MIC, minimal inhibitory concentration;NARMS, National Antimicrobial Resistance Monitoring System;NRC, National Research Council;NE, net energy;PCR, polymerase chain reaction;PWD, post-weaning diarrhea;SCFA, short-chain fatty acid;SEM, standard error of the mean;SID, standardized ileal digestible;STTD, standardized total tract digestible;WHO, World Health Organization

Received April 28, 2022 Accepted May 3, 2022.

Introduction

The post-weaning period is one of the most stressful periods in a pig's life. Separation from the sow, transitioning from a liquid to solid diet, and a new environment with new pen-mates are contributing factors that lead to the post-weaning growth lag and diarrhea (PWD; Pluske, 2013). During this time, it is common for the colonization of enterotoxigenic *E. coli* (ETEC) in the gut which is one of the main causes for PWD (Fairbrother et al., 2005). Antibiotics were used for many years to help control the occurrences of PWD caused by ETEC; however, the ban of antibiotics for growth promotion purposes in the EU in 2006 (Regulation (EC) No. 1831/2003) and the implementation of the veterinary feed directive in the United States in 2017 (FD&C Act (21 U. S. C. 354 (a) (1))) have led to research in alternative strategies to help mitigate the negative effects that follow weaning.

Yeast-based pre- and probiotics, also known as direct fed microbials (DFM), have been considered an alternative of interest because of their potential to positively modulate gut microflora which may lead to improved immunity, nutrient digestion and absorption, and growth performance (Bajagai et al., 2016). These beneficial attributes may be heightened during a stressful stage of life, such as weaning. Supplementing live yeast (*Saccharomyces cerevisiae*) and/or yeast extracts derived from *S. cerevisiae* following weaning has alleviated the shedding of ETEC, shortened diarrhea occurrences, and improved nursery body weight (BW; Stuyven et al., 2009; Trckova et al., 2014). Lu et al. (2019) recently reported that feeding *S. cerevisiae* through gestation and lactation improved ADG, increased BW, and improved gross energy digestibility of offspring in the nursery.

There are little data exploring the impacts of feeding live yeast and yeast extracts in late gestation through lactation and its impact on subsequent offspring growth performance and antimicrobial susceptibilities of fecal *E. coli* in the nursery. Our hypothesis was that the addition of yeast-based DFM would provide additive growth, from both the sow and nursery supplementation, and may lessen the instances of antimicrobial resistance (AMR) of antibiotics that are meaningful to human and animal medicine in nursery pigs.

Materials and Methods

General

The Kansas State University Institutional Animal Care and Use Committee (IACUC # 4506.6) approved the protocols used in two experiments to evaluate various yeast-based DFM supplementation when pigs were weaned from sows fed a diet with or without yeast additives. Both studies were conducted at the Kansas State University Swine Teaching and Research Center in Manhattan, KS. A single nursery room was used in Exp. 1 and Exp. 2 was conducted between two identical nursery rooms. All nursery rooms utilized are completely enclosed, environmentally controlled, and mechanically ventilated. Each pen contained a 4-hole, dry self-feeder and a nipple waterer to provide ad libitum access to feed and water. Pens (1.3 × 1.3 m) had metal tri-bar floors and allowed approximately 0.34 m^2/pig in Exp. 1 and 0.28 m^2/pig in Exp. 2.

Experiment 1

Animals and treatment structure

The objective of Exp. 1 was to evaluate the live yeast *S. cerevisiae* strain NCYC Sc 47 and yeast-based prebiotics derived from *S. cerevisiae* on nursery pigs weaned from sows fed a diet with or without yeast additives on growth performance and antimicrobial susceptibilities of *E. coli* isolated from nursery pig fecal matter. A total of 340 weaned pigs (DNA 241 × 600, DNA; initially 5.1 ± 0.03 kg BW), offspring of sows fed either a control diet or a diet containing yeast-based pre- and probiotics from day 110 of gestation through weaning, were used in a 45-d nursery study. Only ten weaned pigs (7 from control litters and 3 from yeast additive litters) were not included in the nursery study to maintain an even number of replications per treatment and/or because of poor health. Pigs within the same sow treatment were kept together and allotted to pens, which were then allotted to treatment with 5 pigs per pen and 17 replications per treatment in a completely randomized design.

Dietary treatments were arranged in a 2 × 2 factorial with main effects of sow treatment (control vs. yeast additives; 0.10% ActiSaf Sc 47 HR+ and 0.025% SafMannan; Phileo by Lesaffre, Milwaukee, WI) and nursery treatment (control vs. yeast additives; 0.10% ActiSaf Sc 47 HR+, 0.05% SafMannan, and 0.05% NucleoSaf from days 0 to 7 and then concentrations were lowered by 50% from days 7 to 24). Thus, half of the pigs from each sow group were fed either a control diet or a diet with yeast additives. The live yeast *Saccharomyces cerevisiae* strain NCYC Sc 47 (ActiSaf Sc 47 HR+) served as the yeast-based probiotic. The yeast-based prebiotics included a yeast cell wall fraction with concentrated mannan-oligosaccharides and β-glucans from *S. cerevisiae* (SafMannan) and a yeast extract containing ≥ 6% unbound nucleotides from *S. cerevisiae* (NucleoSaf).

Diet preparation

Pigs were fed experimental phase 1 diets from placement until day 7 and then offered experimental phase 2 diets from days 7 to 24 (Table 1). A common phase 3 diet without live yeast or yeast extracts was fed to all pigs from days 24 to 45. Phase 1 diets were formulated to 1.40% standardized ileal digestible (SID) Lys and phase 2 and 3 diets were formulated to 1.35% SID Lys. All other nutrients were formulated to meet or exceed National Research Council (NRC, 2012) requirement estimates. Phase 1 and 2 diets were manufactured at the Kansas State University O.H. Kruse Feed Technology Innovation Center (Manhattan, KS) and the common phase 3 diet was manufactured by a commercial feed mill (Hubbard Feeds; Beloit, KS). All three phases were fed in meal form. Pens of pigs were weighed, and feed disappearance recorded weekly during the course of this study to determine average daily gain (ADG), average daily feed intake (ADFI), and gain-to-feed ratio (G:F).

Chemical analysis

Phase 1 and 2 diet samples were collected at manufacturing and phase 3 diets were collected from every fourth 23-kg bag using a feed probe to obtain a representative sample for each respective diet and phase. Complete diet samples were stored at −20 °C until they were homogenized, subsampled, and submitted for analysis. Samples per dietary treatment were analyzed (Analabs; Fulton, IL; method 997.02; AOAC International, 1998) for active live yeast in phase 1 (Control: 2,000 CFU/g vs. Yeast: 19,000,000 CFU/g) and phase 2 (Control: 1,000 CFU/g vs. Yeast: 8,000,000 CFU/g) diets.

Table 1. Diet composition (as-fed basis)[1,2]

Item	Exp. 1			Exp. 2		
	Phase 1	Phase 2	Phase 3	Phase 1	Phase 2	Phase 3
Ingredients, %						
Corn	44.36	57.40	64.73	44.15	56.75	64.75
Soybean meal, 46.5% CP	18.12	26.35	31.30	18.20	25.85	31.30
Whey powder	25.00	10.00	–	25.00	10.00	–
Fish meal	4.50	–	–	4.50	2.00	–
Enzymatically treated soybean meal[3]	3.75	2.00	–	3.75	–	–
Corn oil	1.50	–	–	1.50	1.50	–
Calcium carbonate	0.30	0.90	0.85	0.30	0.63	0.85
Monocalcium phosphate, 21% P	0.48	1.10	1.00	0.48	0.85	1.00
Salt	0.30	0.55	0.60	0.30	0.55	0.60
L-Lys-HCl	0.43	0.51	0.52	0.43	0.51	0.52
DL-Met	0.22	0.22	0.21	0.22	0.22	0.21
L-Thr	0.18	0.21	0.22	0.18	0.22	0.22
L-Trp	0.07	0.06	0.06	0.07	0.06	0.06
L-Val	0.13	0.14	0.13	0.13	0.15	0.13
L-Ile	–	–	–	–	0.02	–
Vitamin premix[4]	0.25	0.25	–	–	–	–
Vitamin premix with phytase[5]	–	–	0.25	0.25	0.25	0.25
Trace mineral premix[6]	0.15	0.15	0.15	0.15	0.15	0.15
Zinc oxide	–	–	–	0.40	0.27	–
Phytase[7]	0.08	0.08	–	–	–	–
DFM[8,9]	±	±	–	±	±	±
Total	100	100	100	100	100	100
	Exp. 1			Exp. 2		
	Phase 1	Phase 2	Phase 3	Phase 1	Phase 2	Phase 3
Calculated analysis						
SID amino acids, %						
Lys	1.40	1.35	1.35	1.40	1.35	1.35
Ile:Lys	56	55	55	56	55	55
Leu:Lys	109	112	114	109	110	114
Met:Lys	38	36	36	38	37	36
Met and Cys:Lys	57	57	57	57	57	57
Thr:Lys	63	63	63	63	63	63
Trp:Lys	20.6	20.2	20.3	20.6	20.0	20.3
Val:Lys	69	69	69	69	69	69
His:Lys	32	34	36	32	34	36
Total Lys, %	1.54	1.48	1.49	1.54	1.49	1.49
ME, kcal/kg	3,425	3,282	3,278	3,419	3,373	3,280
NE, kcal/kg	2,582	2,440	2,421	2,577	2,529	2,423
SID Lys:NE, g/Mcal	5.42	5.53	5.57	5.43	5.34	5.57
CP, %	20.9	20.5	21.2	20.9	20.3	21.2
Ca, %	0.69	0.77	0.69	0.69	0.70	0.69
P, %	0.68	0.66	0.61	0.68	0.64	0.61
STTD P, %	0.63	0.58	0.50	0.63	0.57	0.50

[1]In Exp. 1, phase 1 diets were fed from days 0 to 7 (approximately 5.1 to 5.5 kg BW) and phase 2 diets were fed from days 7 to 24 (approximately 5.5 to 11.9 kg BW). A common diet, without yeast additives, was fed during phase 3 from days 24 to 45 (approximately 11.9 to 27.1 kg BW).
[2]In Exp. 2, phase 1 diets were fed from days 0 to 10 (approximately 5.8 to 6.7 kg BW), phase 2 diets were fed from days 10 to 24 (approximately 6.7 to 13.3 kg BW), and phase 3 diets were fed from days 24 to 38 (approximately 13.3 to 21.5 kg BW).
[3]HP 300, Hamlet Protein, Findlay, OH.
[4]Provided per kg of premix: 1,653,465 IU vitamin A; 661,386 IU vitamin D; 17,637 IU vitamin E; 1,322 mg vitamin K; 13.2 mg vitamin B12; 19,841 mg niacin; 11,023 mg pantothenic acid; 3,307 mg riboflavin.
[5]Ronozyme HiPhos GT 2700 (DSM Nutritional Products, Parsippany, NJ) provided 2,027 FTU/kg in phases 1 and 2 and 1,250 FTU/kg in phase 3 with an expected STTD P release of 0.16% in phases 1 and 2 and 0.14% in phase 3. Provided per kg of premix: 1,653,465 IU vitamin A; 661,386 IU vitamin D; 17,637 IU vitamin E; 1,322 mg vitamin K; 13.2 mg vitamin B12; 19,841 mg niacin; 11,023 mg pantothenic acid; 3,307 mg riboflavin.
[6]Provided per kg of premix: 73 g Zn from Zn sulfate; 73 g Fe from iron sulfate; 22 g Mn from manganese oxide; 11 g Cu from copper sulfate; 0.2 g I from calcium iodate; 0.2 g Se from sodium selenite.
[7]Ronozyme HiPhos 2700 (DSM Nutritional Products, Parsippany, NJ) provided 918 FTU/lb and an estimated release of 0.16% STTD P.
[8]In Exp. 1, DFM included 0.10% ActiSaf Sc 47 HR+, 0.05% SafMannan, and 0.05% NucleoSaf in phase 1 diets and then concentrations were lowered by 50% in phase 2 diets (Phileo by Lesaffre, Milwaukee, WI).
[9]In Exp 2, YCW was a yeast-extract blend with SafMannan (0.05% in phases 1, 2, and 3) and NucleoSaf (0.05% in phase 1, 0.025% in phase 2, and 0% in phase 3) or DFM was a *Bacillus* spp. and yeast-extract blend of MicroSaf-S, (0.10% in phases 1, 2, and 3) and NucleoSaf (0.05% in phase 1, 0.025% in phase 2, and 0% in phase 3). SafMannan, NucleoSaf, and MicroSaf-S; Phileo by Lesaffre, Milwaukee, WI.

Fecal collection

Fecal samples were collected on days 5, 24, and 45 of the experiment for isolation and determination of antimicrobial susceptibility and resistance profiles of *E. coli*. Fecal samples were collected directly from the rectum of the same three randomly selected pigs from each pen and pooled by pen to form one composite sample. Fecal samples were collected using a sterile, single-use cotton tipped applicator (Fisher Healthcare, Pittsburgh, PA) and were kept in a zipper storage bag and kept on ice until delivered on the same day of collection to the laboratory at the Kansas State University College of Veterinary Medicine for antimicrobial susceptibility testing.

E. coli isolation and antimicrobial susceptibility testing.

One gram of fecal sample was suspended in 9 mL of phosphate-buffered saline for bacterial isolation. Fifty microliters of the fecal suspension were then spread-plated onto a MacConkey agar (Becton Dickinson, Sparks, MD) for the selective isolation of *E. coli*. The lactose-fermenting colonies were picked from each MacConkey agar and then individually streaked onto a blood agar plate (Remel, Lenexa, KS) and incubated at 37 °C for 24 h. Indole test was carried out first and indole-positive isolates were subjected for polymerase chain reaction (PCR) identification of *uidA* and *clpB* genes for species confirmation of *E. coli*. The conformed *E. coli* isolates were stored in cryo-protect beads (Cryocare, Key Scientific Products, Round Rock, TX) at −80 °C.

Antimicrobial susceptibility testing was conducted on one *E. coli* isolate per fecal sample obtained on days 5, 24, and 45. Briefly, the microbroth dilution method as outlined by the Clinical and Laboratory Standards Institute (CLSI, 2018, Table 2) was used to determine the minimal inhibitory concentrations (MIC) of antibiotics and to classify each isolate as susceptible, intermediate, or resistant according to the breakpoints established for each antimicrobial. The antimicrobials evaluated included: amoxicillin/clavulanic acid 2:1 ratio, ampicillin, azithromycin, cefoxitin, ceftiofur, ceftriaxone, chloramphenicol, ciprofloxacin, gentamicin, nalidixic acid, streptomycin, sulfisoxazole, tetracycline, and trimethoprim/sulfamethoxazole.

Experiment 2

Animals and treatment structure

The objective of Exp. 2 was to evaluate feeding diets with two different combinations of *Bacillus* spp. and yeast extracts derived from *S. cerevisiae* on nursery pigs weaned from sows fed a diet with or without yeast additives on nursery pig growth performance. A total of 330 weaned pigs (DNA 241 × 600, DNA; initially 5.8 ± 0.03 kg BW), progeny of sows fed either a control diet or a diet containing yeast additives from days 110 of gestation through weaning, were used in a 38-d nursery study. Only twelve weaned pigs (6 pigs from each sow treatment) were not included in the nursery study due to being either an unthrifty needing extra care or pigs that were well above the average weight at weaning. Pigs within the same sow treatment were randomly allotted to pens, pens were then allotted to treatment with 6 pigs per pen and 8 to 10 replications per treatment.

Dietary treatments were fed in three phases and arranged in a 2 × 3 factorial with main effects of sow treatment (control vs. yeast additives; 0.10% ActiSaf Sc 47 HR+ and 0.025% SafMannan; Phileo by Lesaffre, Milwaukee, WI) and nursery treatment (control; YCW, 0.05% of SafMannan from days 0 to 38 and NucleoSaf at 0.05% from days 0 to 10 and 0.025% from days 10 to 24; or DFM, 0.10% MicroSaf-S from days 0 to 38; and NucleoSaf at 0.05% from days 0 to 10 and 0.025% from days 10 to 24; SafMannan, NucleoSaf, and MicroSaf-S; Phileo by Lesaffre, Milwaukee, WI).

Table 2. Resistance breakpoints and evaluated concentrations for antimicrobials of National Antimicrobial Resistance Monitoring System Gram-negative bacteria panel (CMV3AGNF; WHO, 2018)[1]

Antimicrobial	WHO classification[2]	Susceptible breakpoints, µg/mL	Intermediate breakpoints, µg/mL	Resistant breakpoint, µg/mL
Amoxicillin:clavulanic acid 2:1 ratio	Critically important	≤ 8/4	16/8	≥ 32/16
Ampicillin	Critically important	≤ 8	16	≥ 32
Azithromycin	Critically important	≤ 16	N/A[3]	≥ 32
Cefoxitin	Highly important	≤ 8	16	≥ 32
Ceftiofur	Critically important	≤ 2	4	≥ 8
Ceftriaxone	Critically important	≤ 1	2	≥ 4
Chloramphenicol	Highly important	≤ 8	16	≥ 32
Ciprofloxacin	Critically important	≤ 0.06	≥ 0.12	≥ 0.12
Gentamicin	Critically important	≤ 4	8	≥ 16
Nalidixic acid	Critically important	≤ 16	N/A	≥ 32
Streptomycin	Critically important	≤ 16	N/A	≥ 32
Sulfisoxazole	Highly important	≤ 256	N/A	≥ 512
Tetracycline	Highly important	≤ 4	8	≥ 16
Trimethoprim/sulfamethoxazole 1:19 ratio	Highly important	≤ 2/38	N/A	≥ 4/76

[1]Breakpoints established by Clinical and Laboratory Standards Institute (CLSI, 2018) which are categorized as susceptible (treatable), intermediate (possibly treatable with higher doses), and resistant (not treatable). MIC values greater than the susceptible breakpoint but lower than the resistant breakpoint were considered intermediate.
[2]World Health Organization (WHO) categorization of antimicrobials according to importance for human medicine (WHO, 2018).
[3]N/A, not applicable. The National Antimicrobial Resistance Monitoring System has not established breakpoints; therefore, there is no Clinical and Laboratory Standards Institute resistant breakpoint.

Thus, one third of the pigs from each sow group were fed either a control diet, a diet with the YCW additives, or a diet with the DFM additives. Direct fed microbial 1 included a yeast cell wall fraction with concentrated mannan-oligosaccharides and β-glucans from *S. cerevisiae* (SafMannan) and DFM 2 included a blend of *Bacillus* spp. and a yeast cell wall fraction (MicroSaf-S). Both YCW and DFM included a yeast extract containing ≥6% unbound nucleotides from *S. cerevisiae* (NucleoSaf). A respiratory disease challenge occurred from approximately days 8 to 20 of the study; thus, removals were recorded and analyzed.

Diet preparation

Pigs were fed phase 1 diets from placement until day 10, phase 2 diets were fed from days 10 to 24, and phase 3 diets fed from days 24 to 38. Phase 1 diets were formulated to 1.40% SID Lys and phase 2 and 3 diets were formulated to 1.35% SID Lys. All other nutrients were formulated to meet or exceed NRC (2012) requirement estimates. The phase 1 control diet was manufactured by a commercial feed mill (Hubbard Feeds; Beloit, KS) and then YCW and DFM were added at their respective amounts for phase 1 and mixed at the O.H. Kruse Feed Technology Innovation Center (Manhattan, KS). All phase 2 and 3 diets were manufactured by the same commercial feed mill with the DFM added at the expense of corn. Feed samples were collected from every fourth, 23 kg bag using a feed probe to obtain a representative sample for each respective diet and phase. All three phases were fed in meal form. Pens of pigs were weighed, and feed disappearance recorded weekly to determine ADG, ADFI, and G:F.

Statistical analysis

In both experiments, growth performance data were analyzed using the *nlme* package of R (Version 4.0.0, R Foundation for Statistical Computing, Vienna, Austria) as a completely randomized design with pen as the experimental unit. Fixed effects included sow treatment, nursery treatment, and their interaction. Nursery room served as the random effect in Exp. 2. The main effects of sow treatment and nursery treatment, as well as their interactions, were tested. In Exp. 2, the proportion of pigs removed from test pens was analyzed using a binomial distribution using a logit link function. Differences between treatments were considered significant at $P \leq 0.05$ and marginally significant at $0.05 < P \leq 0.10$.

In Exp. 1, the MIC data of each antimicrobial were analyzed using a linear mixed model. Fixed effects of the model included sow diet, nursery pig diet, sampling day, and their second- and third-order interactions. Pen was included in the model as a random effect. The variance-covariance structure of pen was taken as either compound symmetry, first-order autoregressive or unstructured according to the model fitting criteria. To better satisfy model assumptions, data underwent natural log transformation before statistical modeling. Treatment effect was assessed via back-transformed least squares means, i.e., geometric means of the MIC values. Statistical analysis was performed using Statistical Analysis Software (SAS version 9.4; Cary, NC) PROC MIXED with option DDFM=KR in the MODEL statement. Comparisons were carried out using the two-sided test. No multiplicity adjustment was applied.

RESULTS

Experiment 1

Growth performance

There were no interactions observed between sow treatment and nursery treatment for any growth performance criteria. In phase 1 (days 0 to 7), there were no main effects ($P > 0.30$) observed for ADG, ADFI, or G:F for sow or nursery treatments (Table 3). Pigs weaned from sows fed the yeast-based pre- and probiotics entered the nursery at a heavier BW ($P < 0.001$; 5.0 vs. 5.2 kg) compared to offspring from the control sows. There was statistical difference ($P < 0.001$) in day 7 BW with offspring from sows fed the yeast-based pre- and probiotics having a heavier BW at the end of phase 1.

In phase 2 (days 7 to 24) and for the overall experimental period (days 0 to 24), progeny from sows fed the yeast-based pre- and probiotics had increased ($P < 0.05$) ADG, ADFI, and day 24 BW; however, there was no evidence for difference ($P = 0.162$) in G:F. There was no statistical difference ($P > 0.10$) observed for nursery dietary treatment on any growth criteria.

During the common period (days 24 to 45), there were main effects ($P < 0.05$) of both sow and nursery treatments on ADG. Offspring from sows fed the yeast-based pre- and probiotics had increased ($P = 0.003$) ADG, heavier ($P < 0.001$) day 45 BW, and a tendency ($P = 0.057$) for increased ADFI compared to progeny from sows fed the control diet. Pigs fed the control diet in the nursery had increased ($P = 0.011$) ADG and a tendency ($P = 0.060$) for increased ADFI compared to those fed the diet containing live yeast and yeast extracts. There was no evidence for statistical difference ($P > 0.10$) in G:F for sow or nursery treatment.

For the overall period (days 0 to 45), progeny from sows fed the yeast-based products had increased ($P < 0.05$) BW, ADG, ADFI, and improved G:F compared to pigs from sows fed the control diet. There was a tendency for increased ($P = 0.079$) ADG and increased ($P = 0.086$) BW for pigs fed the control diet in the nursery compared to those fed the yeast-based pre- and probiotics. There was no statistical difference ($P > 0.10$) in ADFI or G:F for nursery treatment.

Antimicrobial susceptibilities

A three-way interaction of sow treatment × nursery treatment × sampling day was observed ($P < 0.05$) for ciprofloxacin, gentamicin, sulfisoxazole, and trimethoprim/sulfamethoxazole (Table 4). *E. coli* isolated from feces of piglets from sows fed yeast-based pre- and probiotics through the nursery had reduced ($P = 0.044$) MIC values to ciprofloxacin on day 45 with a tendency ($P = 0.081$) for reduced resistance on day 24 compared to piglets from the same sow treatment group but fed a control nursery diet. However, there was evidence for a marginal increase ($P = 0.061$) in MIC values of *E. coli* to ciprofloxacin on day 5 from progeny of sows fed yeast which were also fed live yeast-based pre- and probiotics in the nursery. For gentamicin, MIC values of fecal *E. coli* isolated from piglets of the yeast-supplemented sow and yeast nursery treatment were higher ($P = 0.021$) on day 5 but lower ($P = 0.018$) on day 24 compared to the yeast-supplemented sow and control nursery treatment. On day 45, *E. coli* isolated from feces collected from progeny of the control sows that were then fed yeast-based pre- and probiotics in the nursery had lower ($P = 0.005$) MIC values to sulfisoxazole compared to pigs that were also from the control sow group but fed a control

Table 3. Main effects of yeast-fed sows and yeast-fed nursery pigs on growth performance of nursery pigs, Exp. 1[1]

Item	Sow treatment[2]		SEM	*P*	Nursery treatment[3]		SEM	*P*
	Control	Yeast			Control	Yeast		
BW, kg								
d 0	5.00	5.21	0.024	< 0.001	5.11	5.09	0.024	0.507
d 7	5.37	5.61	0.049	0.001	5.51	5.46	0.049	0.516
d 24	11.44	12.27	0.149	< 0.001	11.92	11.80	0.149	0.569
d 45	26.36	27.79	0.251	< 0.001	27.38	26.76	0.251	0.086
Phase 1 (days 0 to 7)								
ADG, g	50	53	5.6	0.719	54	50	5.6	0.604
ADFI, g	113	119	4.5	0.351	118	114	4.5	0.585
G:F, g/kg	416	406	40.2	0.858	430	391	40.2	0.497
Phase 2 (days 7 to 24)								
ADG, g	357	388	6.8	0.002	375	370	6.8	0.653
ADFI, g	496	529	10.3	0.026	517	508	10.3	0.530
G:F, g/kg	721	737	8.1	0.162	727	730	8.1	0.781
Experimental period (days 0 to 24)								
ADG, g	266	289	5.7	0.006	280	275	5.7	0.560
ADFI, g	383	408	8.0	0.031	400	391	8.0	0.479
G:F, g/kg	695	711	7.6	0.153	703	703	7.6	0.974
Phase 3 common diet (days 24 to 45)								
ADG, g	708	738	6.8	0.003	735	710	6.8	0.011
ADFI, g	1,072	1,103	11.5	0.057	1,104	1,072	11.5	0.060
G:F, g/kg	661	669	3.7	0.123	667	663	3.7	0.446
Overall (days 0 to 45)								
ADG, g	471	496	5.2	0.001	490	477	5.2	0.079
ADFI, g	703	729	8.7	0.037	725	708	8.7	0.163
G:F, g/kg	671	681	3.6	0.040	677	675	3.6	0.599

[1]A total of 340 pigs (initial BW of 5.1 ± 0.03 kg) were used in a 45-d nursery trial with 5 pigs per pen and 34 pens per treatment. Pigs were weaned at approximately 19 d of age and allotted to treatment in completely randomized design. Dietary treatments were arranged in a 2 × 2 factorial with main effects of sow treatment (control or yeast additives) and nursery pig treatment (control or yeast additives). All interactions, $P > 0.10$.
[2]Sow treatment consisted of providing a control diet or a yeast-based pre- and probiotic diet supplemented with ActiSaf Sc 47 HR+ at 0.10% and SafMannan at 0.025% (Phileo by Lesaffre, Milwaukee, WI) from day 110 of gestation until weaning.
[3]Nursery treatment consisted of providing a control diet or a yeast-based pre- & probiotic diet supplemented with 0.10% ActiSaf Sc 47 HR+, 0.05% SafMannan, and 0.05% NucleoSaf in phase 1 diets and then concentrations were lowered by 50% in phase 2 diets (Phileo by Lesaffre, Milwaukee, WI).

diet in the nursery. Fecal *E. coli* had lower ($P = 0.004$) MIC values on day 5 to trimethoprim/sulfamethoxazole from the control sow and yeast nursery treatment compared to the control sow and control nursery treatment. All fecal *E. coli* isolates had lower MIC values for ciprofloxacin, gentamicin, sulfisoxazole, and trimethoprim/sulfamethoxazole and thus would be classified as susceptible. There were no further three- or two-way interactions observed; thus, the main effects of sow treatment, nursery treatment, and sampling day were explored (Table 5).

The dams of the pigs used in this study had increased ($P < 0.001$) fecal *E. coli* resistance to tetracycline at weaning compared to at the entry into the farrowing house, regardless of dietary treatment (Chance et al., unpublished data). Interestingly, this effect carried over into the nursery. All fecal *E. coli* isolates had significantly ($P < 0.001$) higher MIC values to tetracycline on day 5 post-weaning which then decreased on day 24 and then slightly increased on day 45. Regardless of the dietary treatment combination, all *E. coli* isolates were resistant to tetracycline on day 5 but were intermediate on days 24 and 45. Fecal *E. coli* isolates were susceptible or intermediate for the remaining 13 antimicrobials at all three sampling times (days 5, 24, and 45), regardless of the sow or nursery dietary inclusion of live yeast and yeast extracts.

E. coli isolated from feces of the progeny of sows fed yeast-based pre- and probiotics had increased ($P = 0.034$) MIC values to nalidixic acid and a tendency for increased resistance to ciprofloxacin ($P = 0.065$) and gentamicin ($P = 0.054$). Fecal *E. coli* isolates had reduced resistance to azithromycin ($P = 0.037$) and chloramphenicol ($P = 0.031$) when live yeast and yeast extracts were supplemented in the nursery. Again, all fecal *E. coli* isolates were susceptible or intermediate for each antimicrobial as tetracycline was the only antibiotic that displayed resistance in this study.

There was evidence for decreased ($P < 0.05$) resistance over time in fecal *E. coli* for azithromycin, cefoxitin, and streptomycin regardless of yeast-based pre- and probiotic supplementation in the sow or nursery treatment. Axomicillin:clavulanic acid, chloramphenicol, and trimethoprim/sulfamethoxazole had increased ($P < 0.10$) MIC values from days 5 to 24 and then reduced MIC values from days 24 to 45. This differed from gentamicin, nalidixic acid, and tetracycline which had reduced ($P < 0.10$) resistance from days 5 to 24 and then an increase in MIC values from days 24 to 45.

Table 4. Interactive effects of yeast-fed sows and yeast-fed nursery pigs over time on antimicrobial susceptibilities of nursery pig fecal *Escherichia coli* according to National Antimicrobial Resistance Monitoring System (CLSI, 2018) established breakpoints, Exp. 1[1,2]

Item	Sow treatment[2]/Nursery treatment[3]				*P*						
	Control		Yeast								
	Control	Yeast	Control	Yeast	Sow	Nursery	Day	Sow × Nursery	Sow × Day	Nursery × Day	Sow × Nursery × Day
Amoxicillin:clavulanic acid 2:1 ratio[5]					0.455	0.389	0.024	0.389	0.438	0.656	0.849
d 5	4.9 ± 1.1	5.1 ± 1.1	6.3 ± 1.3	6.0 ± 1.3							
d 24	6.8 ± 1.5	8.0 ± 1.7	10.2 ± 2.2	8.0 ± 1.7							
d 45	6.8 ± 1.5	5.5 ± 1.2	6.3 ± 1.3	4.5 ± 1.0							
Ampicillin					0.925	0.85	0.191	0.220	0.697	0.226	0.856
d 5	7.7 ± 2.2	9.0 ± 2.5	7.7 ± 2.2	7.4 ± 2.1							
d 24	7.4 ± 2.1	11.1 ± 3.1	10.2 ± 2.9	12.0 ± 3.4							
d 45	7.7 ± 2.2	6.8 ± 1.9	9.0 ± 2.5	4.3 ± 1.2							
Azithromycin					0.291	0.037	0.034	0.480	0.484	0.909	0.328
d 5	5.1 ± 0.46	5.1 ± 0.46	5.3 ± 0.48	4.5 ± 0.41							
d 24	4.5 ± 0.32	4.0 ± 0.28	4.5 ± 0.32	4.5 ± 0.32							
d 45	4.2 ± 0.24	4.0 ± 0.23	4.9 ± 0.28	4.2 ± 0.24							
Cefoxitin					0.434	0.372	0.006	0.823	0.352	0.543	0.781
d 5	10.2 ± 2.0	8.3 ± 1.6	9.4 ± 1.8	9.8 ± 1.9							
d 24	8.0 ± 1.5	8.0 ± 1.5	10.6 ± 2.1	11.1 ± 2.1							
d 45	7.4 ± 1.4	6.0 ± 1.2	7.4 ± 1.4	5.3 ± 1.0							
Ceftiofur					0.438	0.877	0.962	0.485	0.708	0.374	0.073
d 5	0.96 ± 0.30	0.64 ± 0.20	0.69 ± 0.22	1.70 ± 0.53							
d 24	0.92 ± 0.29	0.88 ± 0.28	0.96 ± 0.30	1.08 ± 0.34							
d 45	0.92 ± 0.29	0.92 ± 0.29	1.28 ± 0.40	0.61 ± 0.19							
Ceftriaxone					0.687	0.762	0.279	0.481	0.194	0.519	0.509
d 5	0.42 ± 0.19	0.48 ± 0.21	0.82 ± 0.36	1.13 ± 0.50							
d 24	1.04 ± 0.46	1.13 ± 0.50	0.96 ± 0.43	0.88 ± 0.39							
d 45	0.69 ± 0.31	0.78 ± 0.35	0.96 ± 0.43	0.33 ± 0.15							
Chloramphenicol					0.299	0.031	<0.001	0.136	0.966	0.180	0.701
d 5	9.0 ± 0.97	7.1 ± 0.76	9.0 ± 0.97	6.5 ± 0.70							
d 24	9.4 ± 1.01	11.1 ± 1.19	10.2 ± 1.09	8.7 ± 0.93							
d 45	7.4 ± 0.79	7.1 ± 0.76	7.4 ± 0.79	6.3 ± 0.67							
Ciprofloxacin[6]					0.065	0.557	0.790	0.291	0.419	0.495	0.010
d 5	0.020 ± 0.0043	0.015 ± 0.0032	0.018 ± 0.0040	0.033 ± 0.0071							
d 24	0.015 ± 0.0032	0.017 ± 0.0037	0.029 ± 0.0062	0.017 ± 0.0037							
d 45	0.018 ± 0.0038	0.025 ± 0.0053	0.028 ± 0.0060	0.015 ± 0.0032							
Gentamicin[7]					0.054	0.638	< 0.001	0.736	0.379	0.065	0.045
d 5	0.96 ± 0.210	0.89 ± 0.194	0.96 ± 0.210	2.00 ± 0.437							
d 24	0.48 ± 0.086	0.48 ± 0.086	0.72 ± 0.129	0.39 ± 0.070							

Table 4. Continued

Item	Sow treatment[2]/Nursery treatment[3]										
	Control		Yeast		*P*						
	Control	Yeast	Control	Yeast	Sow	Nursery	Day	Sow × Nursery	Sow × Day	Nursery × Day	Sow × Nursery × Day
d 45	0.72 ± 0.071	0.61 ± 0.060	0.78 ± 0.077	0.67 ± 0.065							
Nalidixic acid					0.034	0.648	0.075	0.648	0.061	0.551	0.201
d 5	2.0 ± 0.45	2.0 ± 0.45	3.1 ± 0.71	4.2 ± 0.94							
d 24	2.2 ± 0.13	2.1 ± 0.13	2.4 ± 0.15	2.1 ± 0.13							
d 45	2.2 ± 0.35	3.0 ± 0.49	2.9 ± 0.47	2.5 ± 0.40							
Streptomycin					0.493	0.600	< 0.001	0.444	0.147	0.391	0.393
d 5	14.2 ± 3.23	21.3 ± 4.86	13.1 ± 2.98	16.0 ± 3.65							
d 24	7.1 ± 2.56	12.5 ± 4.53	11.6 ± 4.17	8.3 ± 3.01							
d 45	6.5 ± 1.68	4.7 ± 1.21	9.0 ± 2.32	9.0 ± 2.32							
Sulfisoxazole[8]					0.881	1.000	0.363	0.159	0.989	0.416	0.035
d 5	67 ± 20	78 ± 24	69 ± 21	85 ± 26							
d 24	48 ± 15	64 ± 20	57 ± 17	57 ± 17							
d 45	109 ± 33	32 ± 10	44 ± 14	78 ± 24							
Tetracycline					0.540	0.624	< 0.001	0.223	0.580	0.985	0.645
d 5	25.1 ± 3.7	30.7 ± 4.5	26.1 ± 3.9	18.8 ± 2.8							
d 24	6.8 ± 1.5	7.4 ± 1.7	8.3 ± 1.9	6.5 ± 1.5							
d 45	8.7 ± 2.1	8.3 ± 2.0	8.3 ± 2.0	8.3 ± 2.0							
Trimethoprim/sulfamethoxazole 1:19 ratio[5,9]					0.781	0.304	0.069	0.973	0.415	0.208	0.042
d 5	0.42 ± 0.126	0.12 ± 0.036	0.24 ± 0.074	0.24 ± 0.074							
d 24	0.28 ± 0.083	0.37 ± 0.111	0.30 ± 0.091	0.21 ± 0.063							
d 45	0.12 ± 0.036	0.18 ± 0.055	0.22 ± 0.068	0.18 ± 0.055							

[1]A total of 340 pigs (initially 5.1 ± 0.03 kg) were used in a 45-d nursery trial with 5 pigs per pen and 17 pens per treatment. Pigs were weaned at approximately 19 d of age and allotted to treatment in completely randomized design. Dietary treatments were arranged in a 2 × 2 factorial with main effects of sow treatment (control or yeast-based probiotics) and nursery pig treatment (control or yeast-based probiotics). Data reported as geometric mean of MIC ± SEM.
[2]Fecal samples from the same 3 pigs/pen were collected on days 5, 24, and 45.
[3]Sow treatment consisted of providing a control diet or a yeast-based pre- and probiotic diet supplemented with ActiSaf Sc 47 HR+ at 0.10% and SafMannan at 0.025% (Phileo by Lesaffre, Milwaukee, WI) from day 110 of gestation until weaning. Sow fecal samples were collected on ~ day 110 of gestation and day 18 post-farrowing.
[4]Nursery treatment consisted of providing a control diet or a yeast-based pre- and probiotic diet supplemented with 0.10% ActiSaf Sc 47 HR+, 0.05% SafMannan, and 0.05% NucleoSaf in phase 1 diets and then concentrations were lowered by 50% in phase 2 diets (Phileo by Lesaffre, Milwaukee, WI).
[5]The MIC numerator of the ratio was reporter for the antimicrobial's amoxicillin:clavulanic acid 2:1 ratio and trimethoprim/sulfamethoxazole 1:19 ratio.
[6]A three-way interaction of sow treatment × nursery treatment × day was observed ($P = 0.010$). On day 24 ($P = 0.081$) and on day 45 ($P = 0.044$), pigs that were fed yeast in the nursery and came from the yeast sow group having reduced MIC values compared to nursery pigs fed a control diet who were also reared from sows fed yeast. There was marginal evidence on d 5 ($P = 0.061$) for the yeast sow group offspring fed yeast additives having increased MIC values compared to pigs fed a control diet who were also offspring of sows fed yeast.
[7]A three-way interaction of sow treatment × nursery treatment × day was observed ($P = 0.045$). MIC values of fecal *E. coli* isolated from pigs of the yeast sow and yeast nursery treatment being higher ($P = 0.021$) on day 5 but lower ($P = 0.018$) on day 24 compared to the yeast sow and control nursery treatment. There was no evidence for difference ($P > 0.10$) between dietary treatments on day 45.
[8]A three-way interaction of sow treatment × nursery treatment × day was observed ($P = 0.035$). On day 45, pigs that came from the control sow treatment and yeast nursery treatment had lower ($P = 0.005$) MIC values compared to pigs that were also from the control sow group but fed a control diet in the nursery. There was no evidence for difference ($P > 0.10$) between dietary treatments on day 5 or 24.
[9]A three-way interaction of sow treatment × nursery treatment × day was observed ($P = 0.042$). On day 5, pigs that came from the control sow treatment and yeast nursery treatment had lower ($P = 0.004$) MIC values compared to the control sow and control nursery treatment. There was no evidence for difference ($P > 0.10$) between dietary treatments on day 24 or 45.

Table 5. Main effects of yeast-fed sows, yeast-fed nursery pigs, and sampling time on antimicrobial susceptibilities of nursery pig fecal *Escherichia coli* according to National Antimicrobial Main Resistance Monitoring System (CLSI, 2018) established breakpoints, Exp. 1[1,2]

Item	Sow treatment[3]		*P*	Nursery treatment[4]		*P*	Day			
	Control	Yeast		Control	Yeast		5	24	45	*P*
Amoxicillin:clavulanic acid 2:1 ratio[5]	6.1 ± 0.51	6.7 ± 0.55	0.455	6.7 ± 0.56	6.1 ± 0.50	0.389	5.5 ± 0.59[a]	8.2 ± 0.87[b]	5.7 ± 0.61[a]	0.024
Ampicillin	8.2 ± 0.83	8.1 ± 0.82	0.925	8.2 ± 0.83	8.0 ± 0.81	0.850	7.9 ± 1.1	10.0 ± 1.4	6.7 ± 0.9	0.191
Azithromycin	4.5 ± 0.12	4.7 ± 0.13	0.291	4.7 ± 0.13	4.4 ± 0.12	0.037	5.0 ± 0.23[b]	4.4 ± 0.16[a]	4.3 ± 0.12[a]	0.034
Cefoxitin	7.9 ± 0.67	8.7 ± 0.74	0.434	8.7 ± 0.75	7.8 ± 0.67	0.372	9.4 ± 0.91[b]	9.3 ± 0.90[b]	6.5 ± 0.62[a]	0.006
Ceftiofur	0.87 ± 0.11	0.99 ± 0.12	0.438	0.94 ± 0.12	0.92 ± 0.11	0.877	0.92 ± 0.14	0.96 ± 0.15	0.90 ± 0.14	0.962
Ceftriaxone	0.71 ± 0.14	0.79 ± 0.15	0.687	0.78 ± 0.15	0.72 ± 0.14	0.762	0.66 ± 0.15	1.00 ± 0.22	0.65 ± 0.14	0.279
Chloramphenicol	8.4 ± 0.35	7.9 ± 0.33	0.299	8.7 ± 0.36	7.6 ± 0.32	0.031	7.8 ± 0.42[a]	9.8 ± 0.52[b]	7.0 ± 0.37[a]	< 0.001
Ciprofloxacin	0.018 ± 0.0015	0.022 ± 0.0018	0.065	0.021 ± 0.0017	0.019 ± 0.0016	0.557	0.021 ± 0.0022	0.019 ± 0.0020	0.021 ± 0.0022	0.790
Gentamicin	0.67 ± 0.047	0.81 ± 0.058	0.054	0.75 ± 0.053	0.72 ± 0.051	0.638	1.13 ± 0.124[c]	0.51 ± 0.045[a]	0.69 ± 0.034[b]	< 0.001
Nalidixic acid	2.2 ± 0.16	2.8 ± 0.20	0.034	2.4 ± 0.18	2.5 ± 0.19	0.648	2.7 ± 0.30[b]	2.2 ± 0.07[a]	2.6 ± 0.21[b]	0.075
Streptomycin	9.7 ± 1.1	10.9 ± 1.3	0.493	9.8 ± 1.2	10.7 ± 1.3	0.600	15.8 ± 1.8[b]	9.6 ± 1.7[a]	7.1 ± 0.9[a]	< 0.001
Sulfisoxazole	61.9 ± 7.9	63.6 ± 8.1	0.881	62.7 ± 8.0	62.7 ± 8.0	1.000	74.6 ± 11.4	56.1 ± 8.6	59.0 ± 9.0	0.363
Tetracycline	11.9 ± 0.93	11.1 ± 0.87	0.540	11.8 ± 0.92	11.2 ± 0.87	0.624	24.8 ± 1.83[b]	7.2 ± 0.82[a]	8.4 ± 1.03[a]	< 0.001
Trimethoprim/ Sulfamethoxazole[5]	0.22 ± 0.028	0.23 ± 0.029	0.781	0.25 ± 0.031	0.20 ± 0.026	0.304	0.23 ± 0.035[b]	0.28 ± 0.043[b]	0.17 ± 0.026[a]	0.069

[1]A total of 340 pigs (initially 5.1 ± 0.03 kg BW) were used in a 45-d nursery trial with 5 pigs per pen and 34 pens per treatment. Pigs were weaned at approximately 19 d of age and allotted to treatment in completely randomized design. Dietary treatments were arranged in a 2 × 2 factorial with main effects of sow treatment (control or yeast additives) and nursery pig treatment (control or yeast additives). Data reported as geometric mean of MIC ± SEM.
[2]Fecal samples from the same 3 pigs/pen were collected on days 5, 24, and 45.
[3]Sow treatment consisted of providing a control diet or a yeast-based pre- and probiotic diet supplemented with ActiSaf Sc 47 HR+ at 0.10% and SafMannan at 0.025% (Phileo by Lesaffre, Milwaukee, WI) from day 110 of gestation until weaning. Sow fecal samples were collected on ~ day 110 of gestation and d 18 post-farrowing.
[4]Nursery treatment consisted of providing a control diet or a yeast-based pre- and probiotic diet supplemented with 0.10% ActiSaf Sc 47 HR+, 0.05% SafMannan, and 0.05% NucleoSaf in phase 1 diets and then concentrations were lowered by 50% in phase 2 diets (Phileo by Lesaffre, Milwaukee, WI).
[5]The MIC numerator of the ratio was reporter for the antimicrobial's amoxicillin:clavulanic acid 2:1 ratio and trimethoprim/sulfamethoxazole.
[a,b]Superscripts signify a statistical difference of $P < 0.05$.

Experiment 2

There were no interactions observed between previous sow treatment and nursery treatment. Thus, the main effects of sow and nursery treatment are reported (Table 6).

In phase 1 (days 0 to 10), pigs weaned from sows fed yeast additives had increased ($P < 0.03$) ADG, ADFI, and G:F. Offspring from the sows fed yeast additives had lighter BW at weaning ($P < 0.001$) compared to the control sow's progeny; however, by day 10, there was no difference ($P = 0.753$) in nursery pig BW between the two sow treatments. There was no evidence for difference ($P > 0.10$) for nursery dietary treatment on any growth measurements from days 0 to 10. In phase 2 (days 10 to 24), there was no evidence ($P > 0.10$) for difference for either sow or nursery treatments on any of the response criteria.

In phase 3 (days 24 to 38), there was a tendency ($P = 0.090$) for increased ADFI for progeny of sows that were fed the control diet. There was no difference ($P > 0.10$) for previous sow treatment on ADG, G:F, or day 38 BW. Interestingly, pigs fed the DFM treatment in the nursery had increased ($P < 0.05$) ADG, G:F, and day 38 BW compared to the control treatment with pigs fed YCW intermediate.

For the overall period (days 0 to 38), a tendency ($P = 0.080$) was observed for improved G:F of offspring from sows fed yeast additives from day 110 of gestation through weaning. As mentioned previously, pigs fed the DFM treatment in the nursery had greater ($P < 0.05$) ending BW compared to the control treatment with pigs fed YCW intermediate. Regardless of dietary treatment, there was no difference ($P > 0.05$) in ADG or ADFI for the overall period. There was no evidence for statistical difference ($P > 0.10$) for the percentage of removals between treatments in this study.

Discussion

Probiotics are beneficial, live microorganisms that withstand the acidic pH of the stomach and reach the hindgut to manipulate microbial population and their activities. As reviewed by Liao and Nyachoti (2017) and Cameron and McAllister (2019), probiotics increase the desirable microbes in the gut while out-competing enteric pathogens, which can lead to increased short-chain fatty acid (SCFA) production, improved intestinal lining integrity, increased nutrient absorption, and ultimately improved growth. Most probiotics include bacteria,

Table 6. Main effects of yeast-fed sows and DFM-fed nursery pigs on growth performance of nursery pigs, Exp. 2[1]

Item	Sow treatment[2]		SEM	*P*	Nursery treatment			SEM	*P*
	Control	Yeast			Control	YCW[3]	DFM[4]		
BW, kg									
d 0	5.90	5.64	0.017	< 0.001	5.78	5.77	5.76	0.022	0.738
d 10	6.67	6.65	0.061	0.753	6.59	6.71	6.69	0.077	0.498
d 24	13.21	13.31	0.139	0.591	13.01	13.38	13.39	0.174	0.206
d 38	21.50	21.57	0.203	0.800	20.98[b]	21.71[ab]	21.92[a]	0.255	0.028
Phase 1 (days 0 to 10)									
ADG, g	75	100	5.9	0.003	81	90	92	7.4	0.508
ADFI, g	127	151	5.2	0.002	128	147	143	6.6	0.103
G:F, g/kg[5]	570	655	26.0	0.023	594	610	634	32.7	0.680
Phase 2 (days 10 to 24)									
ADG, g	458	460	7.0	0.815	447	463	467	8.7	0.235
ADFI, g	590	594	9.5	0.738	572	600	604	11.9	0.117
G:F, g/kg	778	775	5.9	0.772	783	773	774	7.5	0.547
Phase 3 (days 24 to 38)									
ADG, g	592	586	7.4	0.553	570[b]	595[ab]	604[a]	9.3	0.033
ADFI, g	900	875	10.2	0.090	876	893	893	12.8	0.533
G:F, g/kg	659	670	6.3	0.191	651[b]	666[ab]	677[a]	7.9	0.057
Overall (days 0 to 38)									
ADG, g	402	406	5.8	0.596	391	410	411	7.2	0.094
ADFI, g	575	573	7.5	0.811	560	584	579	9.4	0.173
G:F, g/kg	698	709	4.6	0.080	698	703	711	5.7	0.276
Removals, %	4.1	5.4	2.08	0.625	4.0	3.6	7.5	2.54	0.402

[1]A total of 330 pigs (initially 5.8 ± 0.03 kg BW) were used in a 38-d nursery trial with 6 pigs per pen and 16 to 20 pens per treatment. Pigs were weaned at approximately 19 d of age and allotted to treatment in completely randomized design. Dietary treatments were arranged in a 2 × 3 factorial with main effects of sow treatment (control or yeast additives) and nursery pig treatment (control, YCW, or DFM). All interactions, $P > 0.10$ unless otherwise noted.
[2]Sow treatment consisted of providing a control diet or a yeast-based pre- and probiotic diet supplemented with Actisaf Sc 47 HR+ at 0.10% and SafMannan at 0.025% (Phileo by Lesaffre, Milwaukee, WI) from day 110 of gestation until weaning.
[3]YCW was a yeast-extract blend with SafMannan (0.05% in phases 1, 2, and 3) and NucleoSaf (0.05% in phase 1, 0.025% in phase 2, and 0% in phase 3); Phileo by Lesaffre, Milwaukee, WI.
[4]DFM was a *Bacillus* spp. and yeast-extract blend of MicroSaf-S (0.10% in phases 1, 2, and 3) and NucleoSaf (0.05% in phase 1, 0.025% in phase 2 and 0% in phase 3); Phileo by Lesaffre, Milwaukee, WI.
[5]Sow × nursery interaction, $P = 0.081$.
[a,b]Superscripts signify a statistical difference of $P < 0.05$.

such as *Bacillus*, *Lactobacillus*, *Bifidobacterium*, and *Pediococcus* or yeast (*S. cerevisiae*; Stein and Kil, 2006; Cameron and McAllister, 2019). Although similar to probiotics, prebiotics are not live microorganisms. Instead, prebiotics function as a substrate, through fermentation and SCFA production, to selectively stimulate the favorable gut microorganisms (Gibson et al., 2004). Inulin, lactulose, fructo-olgosaccharides, and transgalacto-oligosaccharides can be easily fermented; thus, they are some of the most commonly used prebiotics in nursery pig diets (Gibson et al., 2004).

In Exp. 1, live *S. cerevisiae* strain NCYC Sc 47 was evaluated as the probiotic (ActiSaf Sc 47 HR+; Phileo by Lesaffre, Milwaukee, WI). We evaluated two yeast-based prebiotics in both Exp. 1 and Exp. 2, which included a yeast cell wall fraction with concentrated mannan-oligosaccharides and β-glucans (SafMannan; Phileo by Lesaffre, Milwaukee, WI) and a yeast extract containing ≥ 6% unbound nucleotides (NucleoSaf; Phileo by Lesaffre, Milwaukee, WI). The unique qualities of live yeast and yeast extracts are partially due to the β-glucans and α-mannans in the yeast cell wall and the fact that they also include free nucleotides (Avarima and Amariei et al., 2021). Some of the benefits from feeding nursery pigs live yeast (probiotic) and yeast extracts (prebiotic) include enhanced immunity (Perez-Sotelo et al., 2011; Zanello et al., 2011; Badia et al., 2012), minimized ETEC challenges (Kiarie et al., 2011; Che et al., 2017; Trevisi et al., 2017), adsorption of mycotoxins in the feed (Kogan and Kocher, 2007), and increased growth (Shen et al., 2009; Kiros et al., 2018).

In Exp. 2, YCW contained the same yeast extracts as in Exp. 1 (SafMannan and NucleoSaf) but did not contain a probiotic source. Direct fed microbial 2 contained a blend of *Bacillus* spp. and yeast extracts (MicroSaf-S and NucleoSaf; Phileo by Lesaffre, Milwaukee, WI). *Bacillus*-based probiotics are spores that can withstand the acidic pH of the stomach and high temperatures of pelleting making them one of the most utilized probiotics in swine diets (Stein and Kil, 2006). *Bacillus* spores germinate at the more neutral pH of the small intestine allowing for a higher likelihood for colonization and production of enzymes leading to an increase in SCFA (Smiricky-Tjardes et al., 2003). Increasing SCFA production in a young pig can lower the digesta pH, which becomes less hospitable for enteric pathogens and can lead to reduced occurrences of PWD (Pollmann et al., 1990; Bajagai et al., 2016).

Although feeding pre- and probiotics has promising results on growth performance in the nursery, there is still inconsistency in literature (Zimmerman et al., 2016). Many studies have observed increased ADG, ADFI, and BW when live *S. cerevisiae* and yeast extracts were fed in the nursery (Shen et al., 2009; Kiarie et al., 2011; Kiros et al., 2018). In contrast, we observed reduced ADG during the common (days 24 to 45) and overall (days 0 to 45) periods with little statistical impact on any of the remaining growth criteria when pigs were fed the live yeast *S. cerevisiae* and yeast extracts in Exp. 1. While growth performance was not different for pigs fed YCW, it was intermediate between control and DFM. Similarly, feeding live yeast and/or yeast extracts did not affect nursery pig growth performance in some studies (Perez-Sotelo et al., 2011; Trevisi et al., 2015). When pigs were fed a *Bacillus* spp. and yeast extract blend (DFM), they had improved ADG and G:F in phase 3 (days 24 to 38) and heavier end of nursery BW. When Lee et al. (2011) fed a yeast-*Bacillus* blend for 35 d post-weaning, they saw no added growth benefit from the inclusion of the probiotic blend.

Some literature does not report improvement in ADG, ADFI, or BW when *Bacillus* was included in nursery diets (Williams et al., 2018; Menegat et al., 2019; Wang et al., 2021); however, other studies report an improvement in G:F in the early nursery period (Cai et al., 2015; Wang et al, 2021). A possible explanation for the improvement in some growth performance criteria in Exp. 2 for DFM could be because there was a synergistic effect of the *Bacillus* spp. and the yeast cell wall fraction (MicroSaf-S), without the inclusion of the unbound nucleotides (NucleoSaf), which resulted in an improvement in the later nursery period, regardless of sow treatment. The results from both experiments further exemplify the variability in results when feeding pre- and probiotics in the nursery.

Some studies have observed an increase in sow ADFI during lactation when yeast products were included in the diet (Chance et al., unpublished data; Tan et al., 2021). It is generally observed that when sows have increased intake during lactation, they tend to wean heavier pigs (Eissen et al., 2003; Krahn et al., 2021). Even though our study and Tan et al. (2021) observed increased sow ADFI in lactation, they did not observe an improvement in litter or individual pig weaning weight. However, feeding sows yeast additives has shown to improve offspring immunity (Zanello et al., 2012; Gao et al., 2021), increase exposure to beneficial microorganisms through the sow feces (Hasan et al., 2018), and increase growth pre-weaning (Kim et al., 2008; Shen et al., 2011). These benefits may allow for the offspring to be more physiologically prepared for the stressful weaning period. In the present study, pigs were weaned from sows that were fed the live yeast *S. cerevisiae* strain NCYC Sc 47 (ActiSaf HR+; Phileo by Lesaffre, Milwaukee, WI) which served as the yeast-based probiotic from entry into the farrowing house (approximately ay 110 of gestation) through lactation. A yeast cell wall fraction with concentrated mannan-oligosaccharides and β-glucans derived from *Saccharomyces cerevisiae* (SafMannan; Phileo by Lesaffre, Milwaukee, WI) was also fed and considered a yeast-based prebiotic.

The immunological and microbiological benefits observed pre-weaning may be the main contributing factors to the improvement in growth post-weaning as a few studies have observed improved growth in the nursery when pigs were weaned from sows fed yeast. Both Lu et al. (2019) and Loughmiller et al. (2021) reported increased ADG and ADFI in the nursery when pigs were weaned from sows that were fed live yeast through gestation and lactation, which is consistent with the results from days 0 to 24 and 0 to 45 in Exp. 1 and days 0 to 10 in Exp. 2. Both of the present experiments showed the potential for improved G:F when pigs were weaned from sows supplemented with yeast which was consistent with Lu et al. (2019) but not with Loughmiller et al. (2021).

To the best of our knowledge, there are no data following the offspring of sows fed a lactation diet with or with yeast on the antimicrobial resistance of gut bacteria. A sow treatment × nursery treatment × sampling day interaction was observed for gentamicin in the current study. This interaction revealed fecal *E. coli* from progeny of yeast-fed sows that were also fed yeast in the nursery had higher MIC on day 5 post-weaning but lower MIC on day 24 compared to pigs from the yeast-fed sows but fed a control diet in the nursery. Furthermore, offspring of sows fed yeast tended to have increased resistance to

gentamicin than offspring of sows fed the control diet in the farrowing house. It is important to note that, while there were statistical differences, all fecal *E. coli* were susceptible to gentamicin. Gentamicin is an aminoglycoside class antimicrobial, and it targets the 30s ribosomal subunit to prevent protein synthesis (Yoshizawa et al., 1998). It is commonly used to treat Gram-negative bacterial infections but can also be used to treat a select few Gram-positive bacteria in both humans and animals.

Ciprofloxacin and nalidixic acid are in the fluoroquinolone and quinolone antimicrobial classes. Ciprofloxacin is used as broad-spectrum antimicrobial and nalidixic acid, which was once used to treat primarily Gram-negative bacteria infections, is no longer used clinically (Crumplin and Smith, 1975; Davis et al., 1996). Ciprofloaxicin is widely used in human medicine; however, it is not approved for use in farm animals, but is used under extra label in companion animals. Fluoroquinolones prevent bacteria DNA synthesis by inhibiting the DNA gyrase enzyme resulting in cell death (Paton and Reeves, 1988). We observed a sow treatment × nursery treatment × sampling day interaction for ciprofloxacin. Fecal *E. coli* of offspring of yeast-fed sows that were fed yeast in the nursery appeared to have higher MIC on days 24 and 45 but lower MIC on day 5 compared to pigs also weaned from sows fed yeast and fed the control diet in the nursery. Furthermore, progeny of sows fed yeast in the farrowing house tended to have increased resistance to ciprofloxacin and nalidixic acid. However, regardless of sow treatment, all fecal *E. coli* were susceptible to ciprofloxacin and nalidixic acid at all sampling time points.

Sulfisoxazole and trimpethorim/sulfamethoxazole are broad-spectrum antibiotics and inhibit the dihydropteroate enzyme needed for folic acid synthesis, and folates are important cofactors for nucleic acid synthesis (Kapoor et al., 2017). Sulfisoxazole and trimpethorim/sulfamethoxazole are commonly used antibiotics in both human and livestock medicine. A sow treatment × nursery treatment × sampling day interaction was observed for both sulfisoxazole and trimpethorim/sulfamethoxazole in our study. Progeny of the control sows that were fed live yeast and yeast extracts in the nursery had lower MIC values to sulfisoxazole on day 45 and to trimpethorim/sulfamethoxazole on day 5 compared to offspring that were also from the control sows but were fed a control diet in the nursery. Once again, all fecal *E. coli* isolates were susceptible to both sulfisoxazole and trimpethorim/sulfamethoxazole regardless of treatment or sampling day.

Azithromycin is in the azalide family, a more specific class of macrolide antimicrobials (Bakheit et al., 2014). Chloramphenicol is a partially synthesized antibiotic from *Streptomyces venequelae* in the phenicol class (National Center for Biotechnology Information, 2021). Both azithromycin and chloramphenicol are broad-spectrum antibiotics that interfere with protein synthesis by binding to the 50s ribosomal subunit resulting in bacterial cell death (Bakheit et al., 2014; National Center for Biotechnology Information, 2021). However, azithromycin is commonly utilized in both humans and animals while chloramphenicol is rarely used in human medicine and prohibited in food animals. We observed a decrease in MIC values for the antimicrobial's azithromycin and chloramphenicol in nursery pig fecal *E. coli* w isolates when live yeast and yeast extracts were included in the diet. All MIC values were under the CLSI breakpoint for azithromycin and chloramphenicol and were considered either susceptible or intermediate. Adversely, the addition of the same combination of live yeast and yeast extracts used in Exp. 1 did not impact the resistance of fecal *E. coli* in nursery pigs (Chance et al., 2021). Using the same 14 antimicrobials evaluated in our study, Williams et al. (2018) also observed no difference in the resistance of fecal *E. coli* from nursery pigs that were fed a *bacillus*-based DFM or a blend of lactic acid producing DFM compared to pigs fed a control diet.

In conclusion, for Exp. 1, when sows were fed a live yeast and yeast extract from day 110 of gestation through weaning, their progeny were heavier at weaning and had increased ADG, ADFI, and heavier BW throughout the nursery period. However, feeding yeast additives in the nursery tended to reduce ADG and lower nursery ending BW. Offspring from sows that were fed yeast might increase the potential of fecal *E. coli* resistance to nalidixic acid, ciprofloxacin, and gentamicin. Yet, feeding live yeast and yeast extracts in the nursery may lessen the resistance of azithromycin and chloramphenicol of fecal *E. coli*. In Exp. 2, feeding yeast additives from day 110 of gestation through lactation improved progeny nursery growth performance from days 0 to 10 post-weaning and tended to improve overall G:F. Additionally, feeding DFM in nursery diets improved final BW and late nursery ADG and G:F compared to pigs not fed a DFM. Thus, in Exp. 2, the addition of yeast additives in sow diets had more impact on offspring's growth performance in the early nursery while the inclusion of DFMs in the nursery had more influence on growth later in the nursery.

Acknowledgments

Contribution no. 22-113-J of the Kansas Agricultural Experiment Station, Manhattan, 66506-0201. We would like to thank Phileo by Lesaffre, Milwaukee, WI, for providing the yeast additives and partial financial support of this study. This work was supported in part by the USDA National Institute of Food and Agriculture, Hatch/Multistate Project 1014385.

Conflict of Interest Statement

The authors declare no conflict of interest; however, Joseph A. Loughmiller and Brian Hotze are employees of Phileo by Lesaffre, the company who provided partial financial support for this project.

Literature Cited

AOAC International. 1998. *Official methods of analysis of AOAC International*. 8th ed. Assoc. Off. Anal. Chem., Arlington, VA.

Avarima, I., and S. Amariei. 2021. Spent brewer's yeast as a source of insoluble β-glucans. *Int. J. Mol. Sci.* 22:825. doi:10.3390/ijms22020825.

Badia, R., R. Lizardo, P. Martinez, I. Badiola, and J. Brufau. 2012. The influence of dietary locust bean gum and live yeast on some digestive immunological parameters of piglets experimentally challenged with *Escherichia coli*. *J. Anim. Sci.* 90:260–262. doi:10.2527/jas.53894.

Bajagai, Y., A. Klieve, P. Dart, and W. Bryden. 2016. *Probiotics in animal nutrition: production, impact and regulation*. FAO, Rome, Italy. http://www.fao.org/3/i5933e/i5933e.pdf

Bakheit, A. H. H., B. M. H. Al-Hadiya, and A. A. Abd-Elgalil. 2014. Azithromycin. *Profiles Drug Subst. Excip. Relat. Methodol.* 39:1–40. doi:10.1016/B978-0-12-800173-8.00001-5.

Cai, L., S. Indrakumar, E. Kiarie, and I. H. Kim. 2015. Effects of a multi-strain *Bacillus* species–based direct-fed microbial on growth performance, nutrient digestibility, blood profile, and gut health in nursery pigs fed corn–soybean meal–based diets. *J. Anim. Sci.* 93:43336–44342. doi:10.2527/jas.2015-9056.

Cameron, A., and T. A. McAllister. 2019. Could probiotics be the panacea alternative to the use of antimicrobials in livestock diets? *Benef. Microbes* 10:773–799. doi:10.3920/BM2019.0059.

Chance, J. A., J. M. DeRouchey, R. G. Amachawadi, V. Ishenhoma, T. G. Nagaraja, R. D. Goodband, J. C. Woodworth, M. D. Tokach, H. I. Calderon, Q. Kang, et al. 2021. Live yeast and yeast extracts with and without pharmacological levels of zinc on nursery pig growth performance and antimicrobial susceptibilities of fecal Escherichia coli. *J. Anim. Sci.* 99:1–10. doi:10.1093/jas/skab330.

Che, L., Q. Xu, C. Wu, Y. Luo, X. Huang, B. Zhang, E. Auclair, T. Kiros, Z. Fang, Y. Lin, et al. 2017. Effects of dietary live yeast supplementation on growth performance, diarrhoea severity, intestinal permeability and immunological parameters of weaned piglets challenged with enterotoxigenic *Escherichia coli* K88. *Br. J. Nutr.* 118:949–958. doi:10.1017/S0007114517003051.

Clinical and Laboratory Standards Institute (CLSI). 2018. *Performance standards for antimicrobial disk and dilution susceptibility tests for bacteria isolated from animals*. Approved standard, 5th ed. CLSI supplement VET08. CLSI, Wayne, PA.

Crumplin, G. C., and J. T. Smith. 1975. Nalidixic acid: an antibacterial paradox. *Antimic. Ag. Chemoth.* 8:251–261. doi:10.1128/AAC.8.3.251.

Davis, R., A. Markham, and J. A. Balfour. 1996. Ciprofloxacin. *Drugs* 51:1019–1074. doi:10.2165/00003495-199651060-00010.

Eissen, J. J., E. J. Apeldoorn, E. Kanis, M. W. A. Verstegen, and K. H. de Greef. 2003. The importance of a high feed intake during lactation of primiparous sows nursing large litters. *J. Anim. Sci.* 81:594–603. doi:10.2527/2003.813594x.

Fairbrother, J. M., E. Nadeau, and C. L. Gyles. 2005. *Escherichia coli* in postweaning diarrhea in pigs: an update on bacterial types, pathogenesis, and prevention strategies. *Anim. Heal. Res. Rev.* 6:17–39. doi:10.1079/AHR2005105.

Gao, L., C. Xie, X. Liang, Z. Li, B. Li, X. Wu, and Y. Yin. 2021. Yeast-based nucleotide supplementation in mother sows modifies the intestinal barrier function and immune response of neonatal pigs. *J. Anim. Nutr.* 7:84–93. doi:10.1016/j.aninu.2020.06.009.

Gibson, G. R., H. M. Probert, J. van Loo, R. A. Rastall, and M. B. Roberfroid. 2004. Dietary modulation of the human colonic microbiota: updating the concept of prebiotics. *Nutr. Res. Rev.* 17:259–275. doi:10.1079/NRR200479.

Hasan, S., S. Junnikkala, O. Peltoniemi, L. Paulin, A. Lyyski, J. Vuorenmaa, and C. Oliviero. 2018. Dietary supplementation with yeast hydrolysate in pregnancy influences colostrum yield and gut microbiota of sows and piglets after birth. *PLoS One* 13:e0197586. doi:10.1371/journal.pone.0197586.

Kapoor, G., S. Saigal, and A. Elongavan. 2017. Action and resistance mechanisms of antibiotics: a guide for clinicians. *J. Anaesthesiol. Clin. Pharmacol.* 33:300–305. doi:10.4103/joacp.JOACP_349_15.

Kiarie, E., S. Bhandari, M. Scott, D. O. Krause, and C. M. Nyachoti. 2011. Growth performance and gastrointestinal microbial ecology responses of piglets receiving *Saccharomyces cerevisiae* fermentation products after an oral challenge with *Escherichia coli* (K88). *J. Anim. Sci.* 89:1062–1078. doi:10.2527/jas.2010-3424.

Kim, S. W., M. Brandherm, M. Freeland, B. Newton, D. Cook, and I. Yoon. 2008. Effects of yeast culture supplementation to gestation and lactation diets on growth of nursing piglets. *Asian-Aust. J. Anim. Sci.* 21:1011–1014. doi:10.5713/ajas.2008.70438.

Kiros, T. G., H. Derakhshani, E. Pinloche, R. D'Inca, M. Jason, E. Auclair, E. Khafipour, and A. Van Kessel. 2018. Effect of live yeast *Saccharomyces cerevisiae* (ActiSaf Sc 47) supplementation on the performance and hindgut microbiota composition of weanling pigs. *Sci. Rep.* 8:5315–5328. doi:10.1038/s41598-018-23373-8.

Kogan, G., and A. Kocher. 2007. Role of yeast cell wall polysaccharides in pig nutrition and health protection. *Livest. Sci.* 109:161–165. doi:10.1016/j.livsci.2007.01.134.

Krahn, G., C. Eden, B. Altman, J. Spencer, and J. Lee. 2021. The power of pig data analytics to generate data-driven production decisions. *Proc. Am. Assoc. Swine Vet. 146. 52nd Annual meeting of the American Association of Swine Veterinarians*.

Lee, C. Y., J. W. Lim, Y. H. Ko, S. Y. Kang, M. J. Park, T. G. Ko, J. H. Lee, Y. Hyun, K. S. Jeong, and I. S. Jang. 2011. Intestinal growth and development of weanling pigs in response to dietary supplementation of antibiotics, phytogenic products and brewer's yeast plus *Bacillus* spores. *J. Anim. Sci. Tech.* 53:227–235. doi:10.5187/JAST.2011.53.3.227.

Liao, S. F., and M. Nyachoti. 2017. Using probiotics to improve swine gut health and nutrient utilization. *Anim. Nutr* 3:331–343. doi:10.1016/j.aninu.2017.06.007.

Loughmiller, J. A., G. Gourley, B. Hotze, J. Corley, E. Bruder, and F. Catunda. 2021. Effects of ActiSaf HR+ SC47 live yeast probiotic fed at two levels to sows on offspring performance before and after weaning. *Proc. Amer. Soc. Anim. Sci. 52nd Annual meeting of the American Association of Swine Veterinarians*.

Lu, H., P. Wilcock, O. Adeola, and K. M. Ajuwon. 2019. Effect of live yeast supplementation to gestating sows and nursery piglets on postweaning growth performance and nutrient digestibility. *J. Anim. Sci.* 97:2534–2540. doi:10.1093/jas/skz150.

Menegat, M. B., R. D. Goodband, J. M. DeRouchey, M. D. Tokach, J. C. Woodworth, and S. S. Dritz. 2019. Effects of *Bacillus subtilis* C-3102 on sow and progeny performance, fecal consistency, and fecal microbes during gestation, lactation, and nursery periods. *J. Anim. Sci.* 97:3920–2937. doi:10.1093/jas/skz236.

National Center for Biotechnology Information. 2021. PubChem Compound Summary for CID 5959, Chloramphenicol. https://pubchem.ncbi.nlm.nih.gov/compound/Chloramphenicol.

National Research Council. 2012. *Nutrient Requirements of Swine: Eleventh Revised Edition*. The National Academies Press, Washington, DC. doi:10.17226/13298.

Paton, J. H., and D. S. Reeves. 1988. Fluoroquinolone antibiotics. *Microbiol. Pharmacokinet. Clin. Use* 36:193–228. doi:10.2165/00003495-198836020-00004.

Perez-Sotelo, L., G. Vaughan, R. Fajardo, Y. Gonzalez, H. Monroy, and J. C. Vazquez. 2011. Modulator effects of dietary supplementation with *Saccharomyces Cerevisiae* on coliform counts, adaptive general immunologic response and growth-performance in pigs. *Indian J. Anim. Nutr.* 28:191–197.

Pluske, J. R. 2013. Feed- and feed additives-related aspects of gut health and development in weanling pigs. *J. Anim. Sci. Biotech.* 4:1. doi:10.1186/2049-1891-4-1.

Pollmann, D. S., D. M. Danielson, and E. R. Peo. 1990. Effects of microbial feed additives on performance of starter and growing-finishing pigs. *J. Anim. Sci.* 65:577–581. doi:10.2527/jas1980.513577x.

Shen, Y. B., J. A. Carroll, I. Yoon, R. D. Mateo, and S. W. Kim. 2011. Effects of supplementing *Saccharomyces cerevisiae* fermentation product in sow diets on performance of sows and nursing piglets. *J. Anim. Sci.* 89:2462–2471. doi:10.2527/jas.2010-3642.

Shen, Y. B., X. S. Piao, S. W. Kim, L. Wang, P. Liu, I. Yoon, and Y. G. Zhen. 2009. Effects of yeast culture supplementation on growth performance, intestinal health, and immune response of nursery pigs. *J. Anim. Sci.* 87:2614–2624. doi:10.2527/jas.2008-1512.

Smiricky-Tjardes, M. R., C. M. Grieshop, E. A. Flickinger, L. L. Bauer, and G. C. Fahey, Jr. 2003. Dietary galactooligosaccharides affect ileal and total-tract nutrient digestibility, ileal and fecal bacterial concentrations, and ileal fermentative characteristics of growing pigs. *J. Anim. Sci.* 81:2535–2545. doi:10.2527/2003.81102535x.

Stein, H. H., and D. Y. Kil. 2006. Reduced use of antibiotic growth promoters in diets fed to weanling pigs: Dietary tools, part 2. *Anim. Biotechnol.* 17:217–231. doi:10.1080/10495390600957191.

Stuyven, E., E. Cox, S. Vancaeneghem, S. Arnouts, P. Deprez, and B.M. Goddeeris. 2009. Effect of beta-glucans on an ETEC infection in

piglets. *Vet. Immunol. Immunopathol.* 128:6066. doi:10.1016/j.vetimm.2008.10.311.

Tan, C. W., J. Y. Li, Y. C. Ji, Y. Y. Yang, X. C. Zhao, M. X. Chen, Z. Q. Xin, L. J. Wen, Z. Y. Cui, G. Shu, et al. 2021. Effects of dietary supplementation of different amounts of yeast extract on oxidative stress, milk components, and productive performance of sows. *J. Ani. Feed Sci.* 247:114648. doi:10.1016/j.anifeedsci.2020.114648.

Trckova, M., M. Faldyna, P. Alexa, Z. S. Zajacova, E. Gopfert, D. Kumprechtova, E. Auclair, and R. D'Inca. 2014. The effects of live yeast *Saccharomyces cerevisiae* on postweaning diarrhea, immune response, and growth performance in weaned piglets. *J. Anim. Sci.* 92:767. doi:10.2527/jas2013-6793.

Trevisi, P., M. Colombo, D. Priori, L. Fontanesi, G. Galimberti, G. Calò, V. Motta, R. Latorre, F. Fanelli, M. Mezzullo, et al. 2015. Comparison of three patterns of feed supplementation with live *Saccharomyces cerevisiae* yeast on postweaning diarrhea, health status, and blood metabolic profile of susceptible weaning pigs orally challenged with *Escherichia coli* F4ac. *J. Anim. Sci.* 93:2225–2233. doi:10.2527/jas2014-8539.

Trevisi, P., R. Latorre, D. Priori, D. Luise, I. Archetti, M. Mazzoni, R. D'Inca, and B. P. 2017. Effect of feed supplementation with live yeast on the intestinal transcriptome profile of weaning pigs orally challenged with *Escherichia coli* F4. *Animal* 11:33–44. doi:10.1017/S1751731116001178.

Wang, X., T. Tsai, X. Wei, B. Zuo, E. Davis, T. Rehberger, S. Hernandez, E. J. M. Jochems, C. V. Maxwell, and J. Zhao. 2021. Effect of Lactylate and *Bacillus subtilis* on growth performance, peripheral blood cell profile, and gut microbiota of nursery pigs. *Microorg.* 9:803. doi:10.3390/microorganisms9040803.

Williams, H. E., M. D. Tokach, S. S. Dritz, J. C. Woodworth, J. M. DeRouchey, T. G. Nagaraja, R. D. Goodband, J. R. Pluske, K. Chitakasempornkul, N. M. Bello, et al. 2018. Effects of chlortetracycline alone or in combination with direct fed microbials on nursery pig growth performance and antimicrobial resistance of fecal *Escherichia coli*. *J. Anim. Sci.* 96:5166–5178. doi:10.1093/jas/sky370.

World Health Organization. 2018. *Critically important antimicrobials for human medicine—6th rev*. WHO Document Production Services, Geneva, Switzerland.

Zanello G., F. Meurens, M. Berri, C. Chevaleyre, S. Melo, E. Auclair, and H. Salmon. 2011. *Saccharomyces cerevisiae* decreases inflammatory responses induced by F4+ enterotoxigenic *Escherichia coli* in porcine intestinal epithelial cells. *Vet. Immunol. Immunopathol.* 141:133–138. doi:10.1016/j.vetimm.2011.01.018.

Zanello, G., F. Meurens, D. Serreau, C. Chevaleyre, S. Melo, M. Berri, R. D'Inca, E. Auclair, and H. Salmon. 2012. Effects of dietary yeast strains on immunoglobulin in colostrum and milk of sows. *J. Vet. Imm. Immunopath.* 152:20–27. doi:10.1016/j.vetimm.2012.09.023.

Zimmermann, J. A., M. L. Fusari, E. Rossler, J. E. Blajman, A. Romero-Scharpen, D. M. Astesana, C. R. Olivero, A. P. Berisvil, M. L. Signorini, M. V. Zbrun, et al. 2016. Effects of probiotics in swines growth performance: a meta- analysis of randomized controlled trials. *Anim. Feed Sci. Tech.* 219:280–293. doi:10.1016/j.anifeedsci.2016.06.021.

Yoshizawa, S., D. Fourmy, and J. D. Puglisi. 1998. Structural origins of gentamicin antibiotic action. *EMBO J.* 17:6437–6448. doi:10.1093/emboj/17.22.6437.