1 **TITLE PAGE**

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| **Author** | Hyuck Kim[1, #], Dongcheol Song[1], Kyeongho Jeon[1], Jinmo Yang[1], Hyohyun Yu[1], Wankyu Lee[2], Sangmyeong Lee[2], Kwangwon Seo[2], Jaeyun Jung[3], Joeun Kim[4], Yohan Choi[4], Yongdae Jeong[4], Soojin Sa[4], Poongyeon Lee[5], Soyoung Choi[5], Won Yun[6], Jinho Cho[1, *] |
| **Affiliation** | [1] Department of Animal Science, Chungbuk National University, Cheongju, Republic of Korea, 28644<br>[2] College of Veterinary Medicine, Chungbuk National University, Cheongju, Republic of Korea, 28644<br>[3] Department of Biochemistry, College of Medicine, Chungbuk National University, Cheongju, Republic of Korea, 28644<br>[4] Swine Science Division, National Institute of Animal Science, Rural Development Administration, Cheonan, Republic of Korea, 31000<br>[5] Animal Biotechnology and Genomics Division, National Institute of Animal Science, Wanju, Republic of Korea, 55365<br>[6] Central Research Institute, Woosung Feed Co., Ltd, Daejeon 34379, Korea |
| **ORCID (for more information, please visit https://orcid.org)** | Hyuck Kim / harrck85@naver.com (https://orcid.org/0000-0002-5280-0734)<br>Dongcheol Song / paul741@daum.net (https://orcid.org/0000-0002-5704-603X)<br>Kyeongho Jeon / jeonkh1222@gmail.com (https://orcid.org/0000-0003-2321-3319) |

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|---|---|
| | Jinmo Yang / mike000315@gmail.com (https://orcid.org/0009-0007-4272-3441)<br>Hyohyun Yu / dbgygus123@naver.com (https://orcid.org/0009-0004-7633-8013)<br>Wankyu Lee / wklee@cbnu.ac.kr / (https://orcid.org/0000-0001-5087-6359)<br>Sangmyeong Lee / smlee@cbnu.ac.kr / (https://orcid.org/0000-0002-3624-3392)<br>Kwangwon Seo / vetskw16@cbnu.ac.kr / (https://orcid.org/0000-0003-1620-4916)<br>Jaeyun Jung / 3036best1@gmail.com / (https://orcid.org/0000-0001-5002-9846)<br>Joeun Kim / kjektw@korea.kr (https://orcid.org/0000-0002-1935-2132)<br>Yohan Choi / cyh6150@korea.kr (https://orcid.org/0000-0003-4710-4731)<br>Yongdae Jeong / yongdaejeong@korea.kr (https://orcid.org/0000-0002-1985-583X)<br>Soojin Sa / soojinsa@korea.kr (https://orcid.org/0000-0002-2634-5109)<br>Poongyeon Lee / pylee@korea.kr (https://orcid.org/0000-0003-2447-0392)<br>Soyoung Choi / csy7pp@korea.kr (https://orcid.org/0000-0003-0045-3758)<br>Won Yun / wyoun@woosung.kr (https://orcid.org/0000-0002-1835-2640)<br>Jinho Cho / jinhcho@cbnu.ac.kr (http://orcid.org/0000-0001-7151-0778) |
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| **Authors' contributions**<br>Please specify the authors' role using this form. | [#] *These authors contributed equally to this work*<br>Conceptualization: Kim H, Lee WK, Cho JH<br>Data curation: Kim H, Song DC, Kim JE<br>Formal analysis: Jeon KH, Yang JM, Yu HH<br>Methodology: Choi YH, Jeong YD, Sa SJ, Lee PY, Choi SY<br>Software: Lee SM, Seo KW, Jung JY<br>Validation: Kim H, Jeon KH, Song DC<br>Investigation: Cho JH, Yun W<br>Writing - original draft: Kim H, Yun W, Cho JH<br>Writing - review & editing: Kim H, Song DC, Jeon KH, Yang JM, Yu HH, Lee WK, Lee SM, Seo KW, Jung JY, Kim JE, Choi YH, Jeong YD, Sa SJ, Lee PY, Choi SY, Yun W, Cho JH |
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3 **CORRESPONDING AUTHOR CONTACT INFORMATION**

| **For the corresponding author (responsible for correspondence, proofreading, and reprints)** | **Fill in information in each box below** |
|---|---|
| First name, middle initial, last name | Jinho Cho |
| Email address – this is where your proofs will be sent | jinhcho@chungbuk.ac.kr |
| Secondary Email address | |

| | |
|---|---|
| Address | Department of Animal Science, Chungbuk National University, Cheongju, Republic of Korea, 28644 |
| Cell phone number | +82-10-8014-8580 |
| Office phone number | +82-43-261-2544 |
| Fax number | +82-43-273-2240 |

**Abstract**

This study was conducted to evaluate whether weaning weight (WW) at 28 d of age could serve as an indicator of postweaning robustness by comparing growth performance, nutrient digestibility, blood profiles, and intestinal morphology of pigs differing in body weight (BW). Among a total of 124 pigs, 74 pigs corresponding to the upper and lower 30% of the WW distribution were selected and assigned to heavy BW (HBW) and light BW (LBW) groups, respectively, and monitored until d 56 of age. In this study, the HBW group showed higher ($p < 0.05$) body weight, average daily gain, and apparent total tract digestibility of dry matter, crude protein, and gross energy than the LBW group. Differences in intestinal morphology were observed, HBW group exhibiting higher ($p < 0.05$) villus height (VH), villus width (VW) and villus height to crypt depth ratio (VH:CD). Blood profiles indicated elevated ($p < 0.05$) cortisol, tumor necrosis factor-α, interleukin-6, and interleukin-10 levels in LBW group, reflecting enhanced systemic stress and inflammatory activation. Correlation analysis further demonstrated positive associations between WW and growth performance and nutrient digestibility, VH, VW and VH:CD while showing negative correlations with inflammatory and stress markers. These results indicate that WW is closely linked to postweaning physiological responses and serve as a practical predictor of robustness, digestive capacity, and growth potential during the nursery phase.

**Keyword:** Weaning weight, Robustness, Nutrient digestibility, Cytokines, Intestinal morphology

## INTRODUCTION

Weaning is a critical transition in pig production, marked by sudden changes in diet, environment, and social dynamics, which can stress piglets [1, 2]. Environmental stressors such as maternal separation, regrouping, and new housing can suppress immunity. Additionally, nutritional stress is exacerbated by immature digestive capacity, which includes low enzyme secretion and underdeveloped intestinal structures [3]. As a result, undigested nutrients in the hindgut may ferment, producing short-chain fatty acids as well as harmful metabolites such as ammonia, hydrogen sulfide, and biogenic amines [4]. Their excessive production leads to intestinal atrophy, diarrhea, inflammation, and reduced growth performance. Excessive production results in intestinal atrophy, diarrhea, inflammation, and decreased growth performance [5, 6].

To mitigate these negative effects, we have utilized nutritional strategies such as functional feed additives, optimized dietary formulations, and effective management practices, resulting in improved gut health and growth performance [7]. Nevertheless, variability in post-weaning growth remains evident among pigs raised under similar management and nutritional conditions [8]. Previous studies have reported that when pigs were assigned to pens based on body weight (BW) categories (light, medium, and heavy), the coefficient of variation of BW for each treatment increased until day 21 post-weaning [9]. This variation highlights differences in robustness: some pigs adapt effectively to the post-weaning environment and maintain consistent growth, while others show reduced growth and impaired physiological responses [10, 11]. Robustness during the nursery period is recognized as a crucial factor influencing overall performance and health in swine production [12]. Weaning weight (WW) is often suggested as a straightforward and effective predictor of future performance. Previous studies have shown that heavier pigs at weaning experience greater post-weaning growth and feed utilization compared to their lighter counterparts [13, 14] (Colson et al., 2006; Leliveld et al., 2013). However, most previous studies have concentrated on the immediate post-weaning period, and there is limited information available regarding the physiological indicators that account for individual differences in growth performance during the mid-to-late nursery phase [15].

This study aimed to determine whether weaning weight (WW) can serve as an indicator of postweaning robustness by examining growth performance, nutrient digestibility, blood immune and stress markers, and intestinal morphology in pigs with varying body weights at weaning. To achieve this, pigs were classified into the upper and lower 30% of the WW distribution at 28 days old and monitored until 56 days old, which corresponds to the mid-to-late nursery phase. We hypothesized that pigs with higher WW would show enhanced digestive capacity, improved immune and stress profiles, and more developed intestinal morphology compared

to those with lower WW. Additionally, correlation analyses were performed to explore the relationships between WW and subsequent physiological responses, thereby evaluating the potential of WW as a practical predictor of robustness during the nursery period.

## MATERIALS AND METHODS

The animal experimental protocols used in this study were approved by the Institutional Animal Care and Use Committee of the National Institute of Animal Science (NIAS), Korea (Approval number: NIAS2025-0027).

### Experimental animals and treatment

A total of 124 crossbred [(Landrace × Yorkshire) × Duroc] pigs [initial BW of 7.34 ± 2.21] were weaned at 28 d of age and reared under identical management conditions. All pigs had *ad libitum* access to a single-phase nursery diet throughout the entire experimental period (from 28 d to 56 d of age). All diets were formulated to meet or exceed the National Research Council (NRC, 2012) requirement and fed during the experiment. At 28 d, pigs were ranked by BW, and 74 pigs were selected for the experiment, comprising the heaviest 30 % (n = 37) and the lightest 30 % (n = 37) of the population. Each treatment group consisted of 6 pens, with 6 to 7 pigs randomly assigned to each pen. These pigs were then classified into two categories according to BW: HBW (heavy BW, top 30 %; 9.18 ±0.64) and LBW (light BW, bottom 30%; 5.50 ± 1.64).

### Analysis items and measurements

#### Growth performance

All pigs weighed at d 28 and 56 to estimate BWG. The BWG was calculated as the current week's BW and subtracted from the BW of the previous week for each.

#### Fecal score

The diarrhea scores were individually recorded at 08:00 a.m. and 5:00 p.m. by the same person during the entire experimental period. The diarrhea scores were as follows: 0 (normal feces), 1 (soft feces), 2 (mild diarrhea), and 3 (severe diarrhea). Scores were calculated as the average diarrhea score for each period per treatment group by summing the average daily diarrhea scores of each pig.

**Nutrient digestibility**

Apparent total tract digestibility (ATTD) of dry matter (DM), crude protein (CP), and gross energy (GE) were determined using chromic oxide (0.2%) as an inert indicator by Fenton and Fenton (1979) method. Pigs were fed diets mixed with chromic oxide from 3 days before the end of the experiment. Fresh excreta samples were collected from all pigs in each pen. At the same time, those diet samples were also collected. Fresh fecal and diet samples were stored in a freezer at −20 °C immediately after collection. At the end of the experiment, fecal samples were dried at 70 °C for 72 h and then crushed on a 1 mm screen. All diet and fecal samples were then analyzed for DM following the procedures by the AOAC (2007). The CP and GE content were analyzed by using the dumas (Rapid MAX N-Exceed, Elementar, Langenselbold, Germany) and bomb calorimeter (Parr 6400 Bomb Calorimeter, Parr Instrument, Moline, IL, USA), respectively. Chromium levels were determined via UV absorption spectrophotometry (UV-1201, Shimadzu, Kyoto, Japan) using Williams et al. [16] method. For calculating the ATTD of the nutrients, we used the following equation: Digestibility = $1 - [(Nf \times Cd)/ (Nd \times Cf)] \times 100$, where Nf = concentration of nutrient in fecal, Nd = concentration of nutrients in the diet, Cd = concentration of chromium in the diet, and Cf = concentration of chromium in the fecal.

**Blood profile**

At the end of the experiment, blood samples were collected from the jugular vein of all pigs. At the time of collection, blood samples were collected into vacuum tubes containing $K_3$EDTA for complete blood count analysis, and nonheparinized tubes for serum analysis, respectively. After collecting, serum samples were centrifuged at 3,000 × g for 20 min at 4 °C. The white blood cell (WBC), basophil, neutrophil, and lymphocyte levels in the whole blood were measured using an automatic blood analyzer (ADVIA 120, Bayer, NY, USA). The inflammatory cytokine such as interleukin-6 (IL-6), interleukin-10 (IL-10) and TNF-α was measured using commercially available ELISA kits (Quantikine, R&D systems, Minneapolis, MN, USA) and the absorbance was measured at 450 nm. The cortisol level was measured using radioimmunoassay Coat-A-Count cortisol kits (Catalog number-TKCO5, Siemens Medical Solution Diagnostics, USA).

**Intestinal morphology**

After blood sampling at the end of the experiment, all pigs were anesthetized with 0.1 mL succipharm (50 mg suxamethonium chloride, Komipharm International Co., Ltd., Shieung, Korea) after blood sampling and subsequently euthanized by exsanguination. After euthanization, intestinal tissues of about 10 cm from the ileum (close to the ileocecal junction) were collected. Among the collected intestine samples, samples for intestinal morphology analysis were washed with 10% neutral buffered formalin (Sigma-Aldrich, St. Louis, MO, USA), fixed, and stored refrigerated until staining for analysis. The fixed intestinal segments were dehydrated and embedded in paraffin. Cross sections of a thickness of 5 μm were sectioned and stained with hematoxylin and eosin (H&E) for measuring intestinal morphology. The slides were examined using an Olympus IX51 inverted phase-contrast microscope. Intestinal morphological measurements of VH, crypt depth (CD), and villus height to crypt depth ratio (VH:CD) were calculated for the mean value of six well-orientated villus and crypts, respectively.

**Statistical analysis**

All statistical analyses were conducted using JMP Pro software (version 16.0.0; SAS Institute Inc., Cary, NC, USA). Mixed model analyses were performed using the Fit Model platform in JMP Pro. Growth performance, fecal score and the ATTD of nutrients were analyzed using the pen as the experimental unit (n = 6 per treatment), with the weaning weight (WW) category included as a fixed effect and replicate as a random effect. For blood profiles and intestinal morphology, the individual pig served as the experimental unit (n = 37 per treatment), and pen was included as a random effect to account for the non-independence of pigs housed within the same pen. Least squares means (LSMeans) and their standard error means were reported for all response variables, and pairwise comparisons were conducted based on LSMeans. Pearson correlation coefficients were calculated to evaluate the relationship between WW and subsequent measurements. Correlation analysis for ATTD was conducted using pen means, whereas correlations for growth performance, blood profiles, and intestinal morphology were based on individual pig data. The correlations were visualized using GraphPad Prism 9 software (GraphPad Software, San Diego, CA, USA). Differences were considered statistically significant at $p \leq 0.05$, and tendencies were considered at $0.05 < p \leq 0.10$.

## RESULTS

### Growth performance

BW and average daily gain (ADG) of pigs classified by WW are presented in Table 2. At the start of the experiment (d 0), the HBW group showed a higher BW than the LBW group ($p < 0.05$). This difference remained significant at d 28 and d 56 ($p < 0.05$). Similarly, ADG from d 28 to 56 was greater in the HBW group than in the LBW group ($p < 0.05$).

### Fecal score

The fecal score was not statistically different between each treatment ($p > 0.05$; Fig 1). The LBW group showed the higher proportion of score 2 (11.00 %), which is considered as diarrhea compared to the HBW group.

### Nutrient digestibility

Nutrient digestibility in pigs classified by WW is presented in Table 3. The HBW group showed a higher ($p < 0.05$) digestibility of DM, CP, and GE than the LBW group. Specifically, DM digestibility was 2.15% higher in the HBW group, while CP and GE digestibility were 4.14% and 1.38% higher, respectively.

### Blood profiles

The blood profiles of pigs classified by WW are presented in Table 4. The LBW group showed a higer ($p < 0.05$) concentrations of white blood cells (WBC) and cortisol than the HBW group. The LBW group showed a higher ($p < 0.05$) proinflammatory cytokines including TNF-α, IL-6 and IL-10 than the HBW group.

### Intestinal morphology

The intestinal morphology of pigs classified by WW is presented in Table 5. The HBW group showed a higher ($p < 0.05$) villus height (VH), villus width (VW) and villus height to crypt depth ratio (VH:CD) than the LBW group.

### Correlation analysis

The correlations between WW and other measurements are presented in Figs. 1–4. The WW had positive correlations with the BW at 56 d (r = 0.908; $p < 0.001$) and ADG at 28 to 56 d (r = 0.908; $p < 0.001$) (Fig 1).

The WW had positive correlations with the DM digestibility (r = 0.833; $p < 0.001$), CP digestibility (r = 0.897; $p < 0.001$) and GE digestibility (r = 0.772; $p = 0.003$) (Fig 2). The WW had negative correlations with the WBC (r = -0.600; $p < 0.001$), cortisol (r = -0.544; $p < 0.001$), TNF-α (r = -0.478; $p < 0.001$), IL-6 (r = -0.382; $p = 0.006$) and IL-10 (r = -0.448; $p = 0.001$) (Fig 3). The WW had positive correlations with the VH at 56 d (r = 0.282; $p = 0.047$), VW at 56 d (r = 0.450; $p = 0.001$), and VH:CD at 56 d (r = 0.250; $p = 0.080$) (Fig 4).

## Discussion

In the present study, the HBW group demonstrated better nutrient digestibility and intestinal morphology compared to the LBW group. These differences were associated with lower levels of circulating stress and inflammatory markers, as well as a more favorable immune profile in the HBW group. Together, these findings suggest that body weight (BW) at weaning is a significant factor influencing postweaning physiological responses and subsequent growth potential, supporting earlier reports that initial BW at weaning has a lasting impact on performance during the nursery period.

Throughout the experimental period, the BW and ADG of the HBW group remained consistently higher than those of the LBW group. This indicates that heavier pigs at weaning have a greater capacity for growth after weaning. This aligns with previous studies showing that pigs weaned at a higher BW possess more developed gastrointestinal tracts and increased digestive enzyme activities, which aid in their rapid adaptation to solid diets [17, 18]. In contrast, the LBW group exhibited lower ADG due to their relatively immature digestive systems and limited capacity to cope with post-weaning stressors [19, 20]. Also, in this study, the strong correlation between WW and BW at day 56 (r = 0.908) highlights the close relationship between WW and subsequent growth. These findings suggest that ensuring adequate WW can establish a favorable growth pattern during the nursery phase and may serve as a practical indicator of early-life development and productivity. Therefore, preweaning interventions that promote uniform and sufficient BW, such as litter management and nutritional support, are essential for optimizing nursery performance [21]. Differences in nutrient digestibility between the HBW and LBW groups were evident, with the HBW group exhibiting greater ATTD of DM, CP and GE. This suggests that pigs with higher WW utilize dietary nutrients more efficiently than those in the LBW group. Additionally, in the current study, nutrient digestibility demonstrated a strong association with WW, and among the digestibility indices, CP showed the greatest difference between the HBW and LBW groups. Weaning-stressed piglets exhibited immature intestinal development, characterized by insufficient mucosal integrity, reduced VH, and

limited secretion of digestive enzymes, all of which collectively diminish digestive capacity [22-24]. According to Engelsmann et al., [25] CP digestibility increased from approximately 60% at two weeks post-weaning to around 71% by week four as weaning stress diminished. In the present study, the CP digestibility of the HBW group reached 73.49%, consistent with this recovery phase. In contrast, the LBW group exhibited a lower CP digestibility of 69.35%, indicating a delayed recovery of digestive function. In addition, Yang et al. [26] reported DM and CP digestibility rates of 80.35% and 78.43%, respectively, in 8-week-old piglets. In contrast, Song et al. [27] documented a CP digestibility of 70.91% in piglets fed a corn-soybean meal diet. Compared to these values, the digestibility rates observed in the LBW group in the current study indicate a slower maturation of gastrointestinal function. Such limitations may decrease digestive resilience and nutrient utilization, leading to poorer growth during the nursery period [17, 28, 29].

Histomorphological analysis of the ileum revealed that the HBW group had higher VH and VW compared to the LBW group. The increased VH and VW indicate an expanded absorptive surface and a more mature epithelial lining [30, 31]. These structural advantages align with their higher nutrient digestibility. In contrast, increased crypt depth is often observed in cases of mucosal damage or inflammation, during which epithelial loss accelerates and compensatory cell proliferation increases [32-34]. Piglets experiencing weaning stress cannot regenerate epithelial cells at a rate that matches their loss. This results in shorter villi and increased crypt depth in animals adapting to the weaning transition [35]. However, crypt depth did not differ between the HBW and LBW groups, indicating that epithelial turnover and mucosal regeneration had already normalized in both groups by 8 weeks of age. Nevertheless, villus development was more advanced in the HBW group, suggesting that structural maturation of the mucosa continued to differ despite similar regeneration rates [36].Consequently, the mucosal architecture in the HBW group indicates a more competent intestine, with enhanced absorptive and barrier functions [37-39]. Overall, the BW-dependent differences in VH and VW at 8 weeks suggest that intestinal morphology is a structural component of post-weaning robustness. This interpretation is further supported by the positive correlations between WW and morphological indicators, which link early-life BW to long-term digestive potential.

WW exhibited moderate to negative correlations with key stress and inflammatory markers, including WBC ($r = –0.60$), cortisol ($r = –0.54$), TNF-α ($r = –0.48$), IL-6 ($r = –0.38$), and IL-10 ($r = –0.45$). These correlations suggest that lower WW is linked to increased systemic inflammation and stress responses. This trend is consistent with the reduced villus development seen in the LBW group, indicating immature mucosa and heightened intestinal

permeability, which may contribute to systemic inflammation [37-38]. In line with these associations, the LBW group exhibited higher concentrations of cortisol, TNF-α, and IL-6 compared to the HBW group. Previous studies have indicated that the LBW group is more vulnerable to inflammatory and oxidative stress, which can redirect nutrients towards immune activation and hinder growth performance [7, 40-42]. Cortisol suppresses immune function and slows the renewal of epithelial cells, and sustained elevated levels are known to weaken the intestinal barrier [43-45]. The physiological effects observed in the LBW group included reduced villus height, which suggests limited epithelial recovery and a less developed absorptive surface. Additionally, serum IL-10 concentrations were higher in the LBW group, indicating the activation of an anti-inflammatory regulatory pathway. IL-10 is crucial for restraining excessive immune activation, and its elevation typically reflects a compensatory mechanism aimed at counterbalancing increased inflammation [46, 47]. The concurrent elevation of pro-inflammatory cytokines (TNF-α, IL-6) and the anti-inflammatory cytokine (IL-10) in the LBW group suggests that these animals were experiencing an heightened inflammatory state, accompanied by an insufficient counter-regulatory response [48-50]. Despite the compensatory increase in IL-10, the LBW group continued to exhibit a higher inflammatory status and lower growth performance, suggesting that immune regulation had not been fully restored

## Conclusion

In conclusion, higher WW was closely associated with superior nutrient digestibility, advanced intestinal maturation, and a more resilient immune profile during the nursery period. These multifaceted findings provide robust evidence that WW serves as an integrative surrogate for post-weaning physiological robustness, rather than merely reflecting physical size. The consistent alignment between phenotypic growth and underlying biological markers including digestive capacity and inflammatory status substantiates the use of WW as a strategic and practical metric for identifying vulnerable piglets and implementing targeted nursery management. While further research is needed to explore metabolic links, this study establishes WW as a validated indicator for evaluating early-life resilience in commercial swine production.

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**Table 1.** Composition of basal diets (as-fed-basis)

| Items | Content |
|---|---|
| Ingredients, % | |
| EP Corn | 46.25 |
| Soybean meal | 10.00 |
| Broken rice | 4.00 |
| Soy protein concentrate | 2.50 |
| Fermented soybean meal | 4.00 |
| Whey | 17.50 |
| Fish meal | 1.50 |
| Plasma protein | 4.00 |
| Soybean oil | 2.40 |
| Lactose | 4.00 |
| Ca-formate | 1.30 |
| Copra meal | 1.50 |
| Vitamin premix[1] | 0.20 |
| Mineral premix[2] | 0.25 |
| L-Methionine | 0.10 |
| L-Lysine | 0.40 |
| L-Threonine | 0.10 |
| Total | 100.00 |
| Calculated value | |
| NE, kcal/kg | 2,600.00 |
| CP, % | 19.20 |
| Lysine, % | 1.40 |
| Methionine, % | 0.40 |
| Ca, % | 0.50 |
| P, % | 0.45 |

[1]Provided per kg of complete diet: vitamin A, 9,000 IU; vitamin $D_3$, 1,620 IU; vitamin E, 35 IU; vitamin $B_{12}$, 40 μg; vitamin $B_2$, 6 mg; vitamin $B_6$, 3 mg; vitamin $K_3$, 2 mg; vitamin C, 100 mg; niacin, 50 mg; ca-pantothenate, 20 mg; biotin, 0.2 mg.
[2]Provided per kg of complete diet without zinc: Mn, 35 mg; Zn, 30 mg; Fe, 150 mg; Cu, 50 mg; I, 0.5 mg; Co, 0.15 mg; and Se, 0.2 mg.
Abbreviation: EP corn, extruded-pelleted corn; NE, net energy; CP, crude protein.

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**Table 2.** Growth performance of pigs classified by weaning weight

| Item | HBW | LBW | SE | *p*-value |
|---|---|---|---|---|
| BW, kg | | | | |
| d 28 | 9.18 | 5.50 | 0.204 | <0.001 |
| d 56 | 25.80 | 17.94 | 0.567 | <0.001 |
| ADG, kg/ d | 0.59 | 0.44 | 0.015 | <0.001 |

Abbreviation: HBW, pigs with high body weight at weaning (top 30% of the population); LBW, pigs with low body weight at weaning (bottom 30% of the population); BW, body weight; ADG, average daily gain; SE, standard error.

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**Table 3.** Nutrient digestibility of pigs classified by weaning weight on d 56

| Item | HBW | LBW | SE | *p*-value |
|---|---|---|---|---|
| DM | 79.85 | 77.70 | 0.575 | 0.024 |
| CP | 73.49 | 69.35 | 0.890 | 0.008 |
| GE | 79.70 | 78.32 | 0.435 | 0.049 |

Abbreviation: HBW, pigs with high body weight at weaning (top 30% of the population); LBW, pigs with low body weight at weaning (bottom 30% of the population); DM, dry matter; CP, crude protein; GE, gross energy; SE, standard error.

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**Table 4.** Blood profile of pigs classified by weaning weight on d 56

| Item | HBW | LBW | SE | *p*-value |
|---|---|---|---|---|
| WBC, $10^3$/μL | 15.40 | 21.46 | 1.068 | 0.010 |
| Cortisol, ng/mL | 27.96 | 32.32 | 0.656 | 0.003 |
| TNF-α, pg/mL | 61.35 | 89.04 | 6.136 | 0.023 |
| IL-6, pg/mL | 104.67 | 148.52 | 10.645 | 0.024 |
| IL-10, pg/mL | 27.35 | 44.97 | 3.587 | 0.015 |

Abbreviation: HBW, pigs with high body weight at weaning (top 30% of the population); LBW, pigs with low body weight at weaning (bottom 30% of the population); WBC, white blood cell; TNF-α, tumor necrosis factor-α; IL-6, interleukin-6; IL-10, interleukin-10; SE, standard error.

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**Table 5.** Intestinal morphology of pigs classified by weaning weight on d 56

| Item | HBW | LBW | SE | p-value |
|---|---|---|---|---|
| VH, μm | 446.05 | 394.88 | 11.532 | 0.019 |
| CD, μm | 268.79 | 273.61 | 7.539 | 0.705 |
| VW, μm | 166.41 | 138.22 | 6.762 | 0.027 |
| VH:CD | 1.75 | 1.50 | 0.054 | 0.020 |

Abbreviation: HBW, pigs with high body weight at weaning (top 30% of the population); LBW, pigs with low body weight at weaning (bottom 30% of the population); VH, villus height; CD, crypt depth; VW, villus width; VH:CD, villus height to crypt ratio; SE, standard error.

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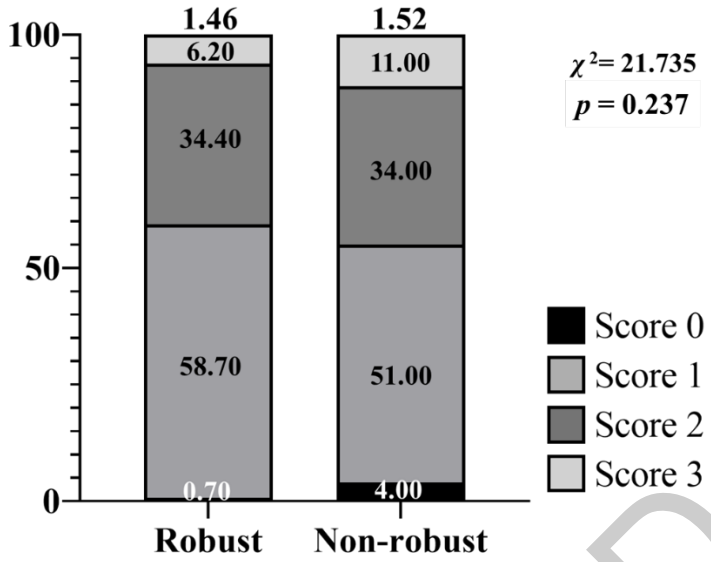



**Fig 1**. Fecal score of pigs classified by weaning weight. Score 0, normal feces; 1, soft feces; 2, mild diarrhea; 3, severe diarrhea. $\chi^2$= 21.735, $p$ = 0.237. Robust, pigs with high weaning weight (top 30% of the population); Non-robust, pigs with low weaning weight (bottom 30% of the population).

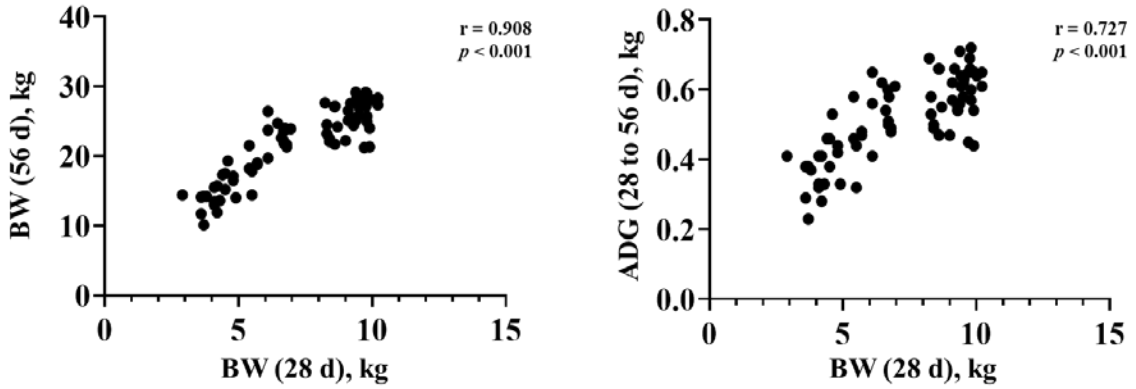



**Fig 2**. Pearson correlation coefficients between weaning weight and growth performance. BW, body weight; ADG, average daily gain.

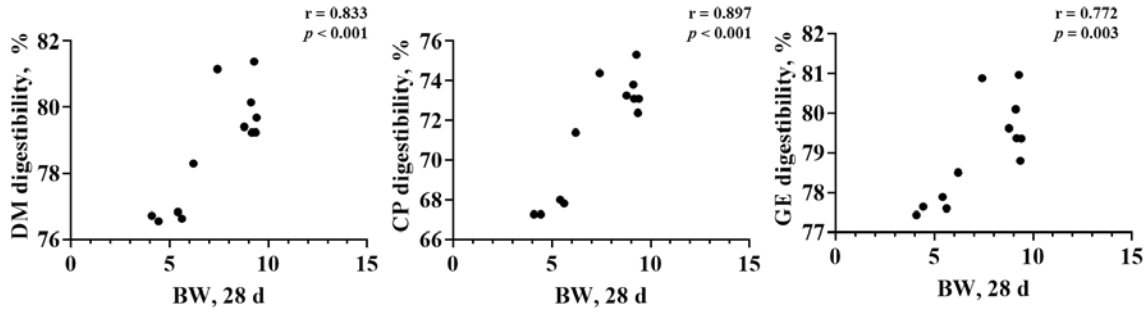
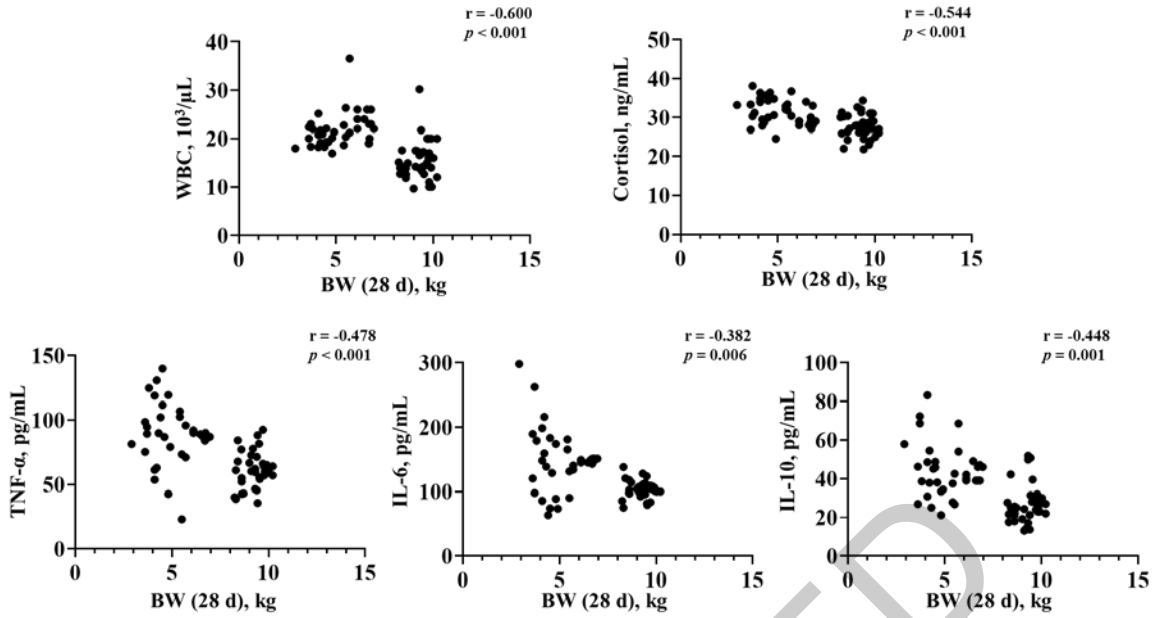



**Fig 3**. Pearson correlation coefficients between weaning weight and nutrient digestibility. DM, dry matter; CP, crude protein; GE, gross energy.




411
412 **Fig 4**. Pearson correlation coefficients between weaning weight and blood profiles. WBC, white blood cell; TNF-
413 α, tumor necrosis factor-α; IL-6, interleukin-6; IL-10, interleukin-10.
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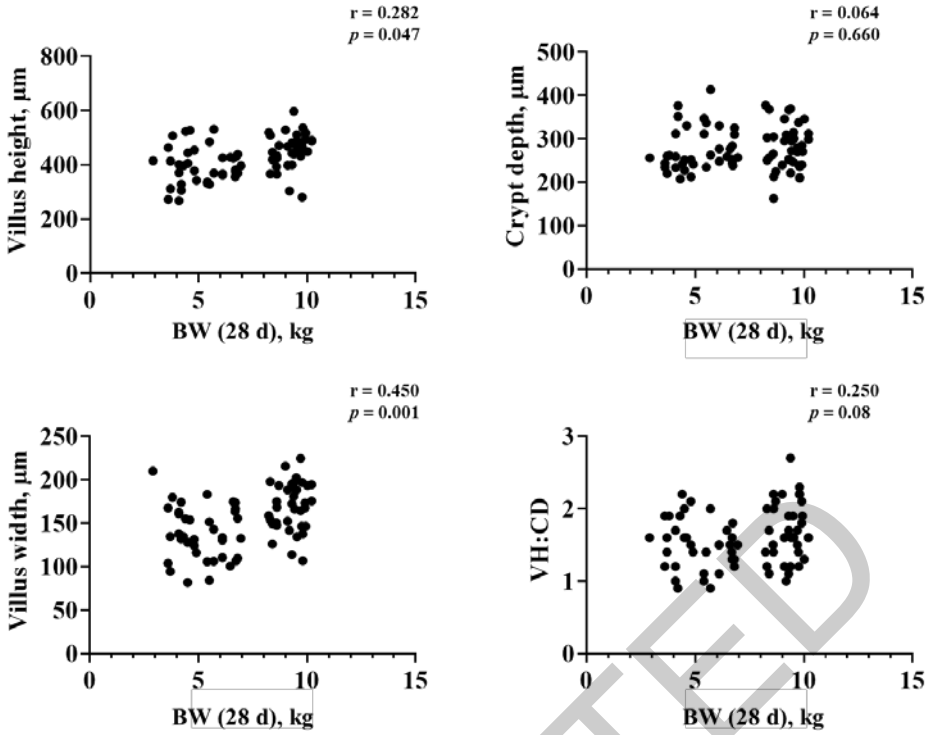


**Fig 5**. Pearson correlation coefficients between weaning weight and intestinal morphology. VH:CD, villus height to crypt depth ratio.