Amino Acids as Functional Nutrients for Pig Health

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Currently, diets are formulated to optimize growth performance and profitability of pork production, however, with societal and legislative pressure to reduce antibiotic use in livestock agriculture, including in swine, there is an increased need to consider how diet impacts animal health as well as performance. This includes an evaluation of nutrient requirements during disease challenge in order to formulate diets that support proper gastrointestinal development and function and immune response during disease challenge in addition to growth performance. Pigs are continuously exposed to microbial pathogens and immune-stimulatory antigens that negatively impact animal productivity, with the impact on immune status likely a major factor in the observed gap between performance potential and observed performance under commercial conditions. This decrease in performance can have a substantial impact on profitability of producers. The continued sustainability of pork production will necessarily involve a re-evaluation of nutrient requirements and adjustment of diet formulation.

Impact of immune challenge on performance and nutrient utilization

The reduction in performance observed during disease challenge has largely been attributed to the observed drop in feed intake, however, recent meta-analyses have demonstrated that both reduction in nutrient supply (i.e., feed intake) and nutrient utilization (i.e., maintenance requirements) both contribute to reduced growth. The proportion with which feed intake and nutrient utilization impact performance is dependent on the specific immune challenge, with enteric bacterial infections having a greater impact on nutrient utilization while the negative effects of mycotoxins and respiratory disease are more due to decreased feed intake (Pastorelli et al., 2012; Rodrigues et al., 2021a).

In general, immune stimulation alters protein and amino acid metabolism and utilization, with amino acids redirected from growth towards supporting the immune response. This limits amino acid availability for growth which is further exacerbated by reduced feed intake. As a result, amino acid supply for the immune response is partially met through a catabolism

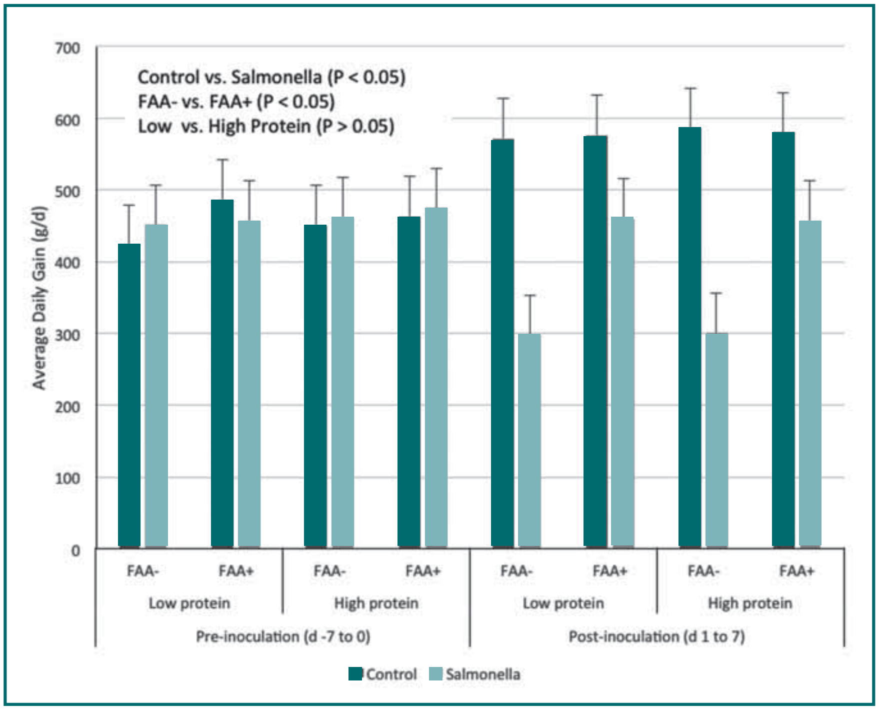

Figure 1. Growth performance of weaned pigs pre- and post-inoculation with saline (Control) or Salmonella and fed diets containing low or high protein (16.6 vs. 19.5%) with (FAA+) or without (FAA-) a functional amino acid blend supplying methionine, threonine, and tryptophan at 120% of NRC (2012) requirements for growth (n=8 pigs/treatment) Adapted from Rodrigues et al. (2021b).

of muscle protein. However, the amino acid profile of muscle protein differs significantly from that of protein involved in the immune response (Reeds et al., 1994). Overall, while it is true that immune challenge will result in a reduction in feed intake and, therefore, reduce growth and nutrient requirements for growth, it is likely that amino acid requirements (i.e., amino acid ratios to lysine) need to be adjusted during times of immune challenge based on determination of requirements in pigs during immune stimulation.

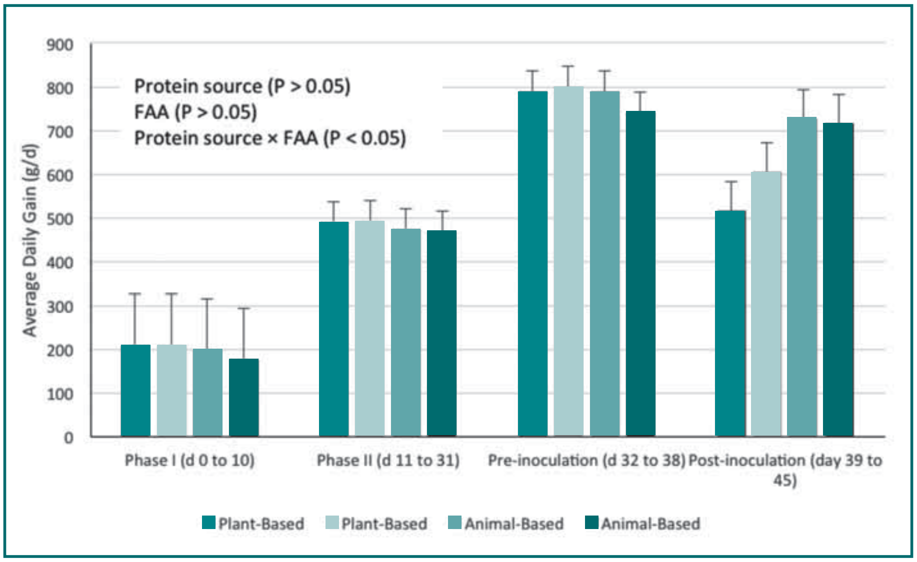

Figure 2. Growth performance of weaned pigs fed nursery diets containing either plant-based or animal-based protein sources and with (FAA+ or without (FAA-) a functional amino acid blend supplying methionine, threonine, and tryptophan at 120% of NRC (2012) requirements for growth. On d 32, piglets were placed on a common grower diet and inoculated with Salmonella Typhimurium on d 39 (n=8 pigs/treatment) (Rodrigues et al., 2022b).

Functional amino acids and pig health

Based on the amino acid profile of immune system components, glutamine, arginine, threonine, and the aromatic and sulfur amino acids would appear to play key roles in the immune response (Reeds and Jahoor, 2001). Therefore, supplementation with these amino acids during immune challenge, above the requirements for growth during, may be of benefit in mitigating the negative effects of immune challenge. Indeed, previous studies have demonstrated an increased requirement for growth for methionine and cysteine (Rakhshandeh et al., 2010; Litvak et al., 2013), threonine (Jayaraman et al., 2015; Wellington et al., 2018; McGilvray et al., 2019), and tryptophan (De Ridder et al., 2012) in response to immune stimulation. It is important to note, however, that amino acid requirements to maximize growth, with or without immune challenge, may differ from those required to maximize other outcomes, such as components of the immune response. This was demonstrated in a recent meta-analysis where it was demonstrated that dietary amino acid content above those for maximum growth result in improvements in key physiological responses, such as milk yield, litter size, immune response, and intestinal permeability (Ramirez-Camba and Levesque, 2023). So while we tend to base our diet decisions on growth performance, and the majority of immune stimulation requirements studies focus on growth, this may not be an appropriate outcome if optimizing pig health is the goal. The term 'functional amino acids' has been used to describe those amino acids supplemented in the diet for their roles beyond those for protein synthesis (i.e., lean gain). In the context of health, these include amino acids with significant roles in gastrointestinal health (e.g., barrier function) and immune response (e.g., antioxidant balance, acute phase response).

As indicated above, while past research has indicated alterations in nutrient metabolism, specifically of amino acids, the effect of supplementation of amino acids for pig robustness has only recently received significant attention. Supplementation of individual functional amino acids has been shown to improve growth performance of pigs under immune challenge. Wellington et al. (2018) demonstrated an increase in the threonine requirement in immune stimulated pigs and then further demonstrated (Wellington et al., 2019) that threonine supplementation resulted in improved growth performance of growing pigs fed high fibre diets during Salmonella challenge, most likely through support of improved gut barrier function (i.e., mucin production). Likewise, Koo et al. (2020) observed that increasing threonine content resulted in improved gut integrity (i.e., goblet cell density, tight junction gene expression) in pigs with induced intestinal inflammation as a result of being fed a 'simple' diet. Koo et al. (2021) also demonstrated improved immune status in pigs housed in unsanitary conditions when fed valine-supplemented diets. An improvement in growth performance was also observed by Jayaraman et al. (2015) and Trevisi et al. (2015) in pigs housed in unsanitary conditions or challenged with E. coli, respectively, when fed diets containing supplemental threonine and Le Floc'h et al. (2009) observed improved growth performance in weaned pigs provided supplemental tryptophan when housed in unsanitary conditions.

> "There are a number of dietary strategies that can be used to improve pig robustness."

More recent work has examined the use of a blend of functional amino acids on growth performance and immune status in weaned and growing pigs. For example, Rodrigues et al. (2021b) fed grower pigs diets containing either a standard amino acid profile (NRC, 2012) or one in which threonine, methionine, and tryptophan were supplemented at 120% of the requirements for growth. Pigs fed the amino acid blend had improved growth performance and immune status (e.g., increased serum albumin and glutathione, reduced serum haptoglobin and superoxide dismutase) when challenged with Salmonella than their unsupplemented counterparts. The same amino acid profile improved growth performance and immune status (i.e.,

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acute phase response, antioxidant balance) in Salmonella-challenged nursery pigs (Rodrigues et al., 2021b). Likewise, Valini et al. (2023), using the same amino acid blend, observed improved growth performance and immune status, including reduced body temperature and Salmonella shedding, and improved average daily gain, body weight, and nutrient utilization in grower pigs that were challenged with Salmonella and housed in unsanitary conditions. Rodrigues et al. (2021b) also observed decreased fecal myeloperoxidase, an indication of reduced intestinal damage, with the amino acid blend, indicating a role of these amino acids in supporting gut health during an enteric pathogen challenge. The effectiveness of supplementation with this amino acid blend may be dependent on specific conditions, as van der Meer et al. (2016) showed improved immune status but limited effect on growth performance in wean to finish pigs under low sanitary conditions even though the same amino acids were supplemented at the same level as Rodrigues et al. (2021b).

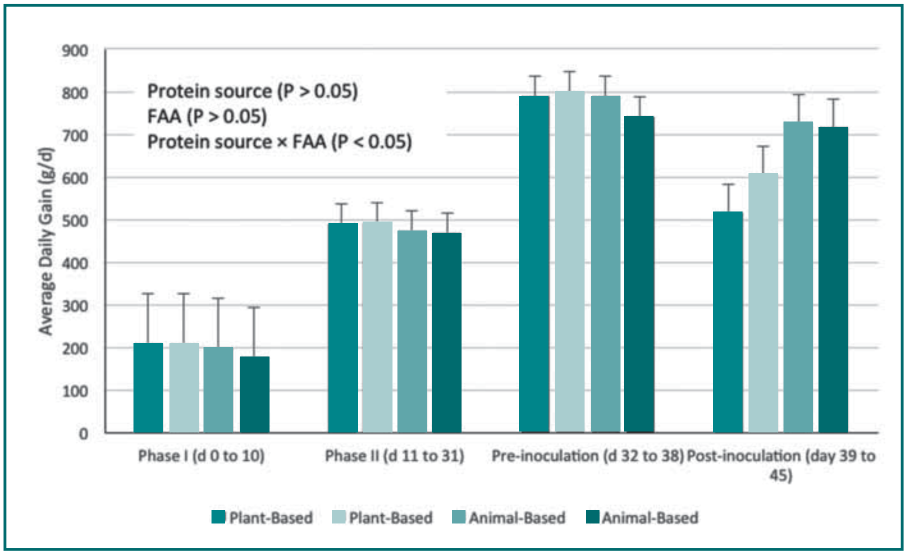

Figure 3. Growth performance of weaned pig pre- and post-inoculation with Salmonella and fed diets without (FAA-) or with a functional amino acid blend supplying methionine, threonine, and tryptophan at 120% of NRC (2012) requirements for growth during the post-inoculation period (FAA+0), for 1 week pre- and post-inoculation (FAA+1), or for 2 weeks pre- and 1 week post-inoculation (FAA+2) (n=8 pigs/treatment). Adapted from Rodrigues et al. (2021c).

Factors affected functional amino acid impact

The timing and duration of functional amino acid provision may impact the effectiveness of supplementation at improving performance and immune status. Rodrigues et al. (2021c) demonstrated a further increase in growth performance in pigs provided the blend of functional amino acids when the adaptation period prior to Salmonella infection was increased from 0 to 2 weeks (Fig. 3). Not all components of the immune response responded the same way to functional amino acids supplementation time, however, with acute phase response responding positively to a longer adaptation time while antioxidant balance did not. While there was no overall effect of amino acid supplementation, van der Meer et al. (2016) observed improved average daily gain in the nursery period and improved feed efficiency in the finisher period in pigs housed in unsanitary conditions. Moreover, the response to sanitary conditions was greater during the nursery period, indicating that supplementation may be more beneficial

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in the immediate post-weaned period. This is supported by Rodrigues et al. (2021a) who demonstrated that the negative impacts of disease challenge are greater in the nursery period than in grower-finisher pigs, potentially due to a more immature intestinal tract in this period. Schweer et al. (2019) and Jasper et al. (2020) were able to improve growth performance in pigs inoculated with PRRS virus by increasing lysine:energy ratio at the time of challenge, however, no improvement was observed if the adjustment was made post-challenge (Gabler, 2021).

Functional amino acid supplementation in the nursery period may also provide long-term benefits, as Rodrigues et al. (2022a) demonstrated improved growth in pigs that had received a supplemental functional amino acid blend in the nursery period but were fed a common grower diet at the time of Salmonella-challenged in unsanitary conditions. This blend of amino acids, however, was only partially able to attenuate the negative effect of disease challenge in low-birth weight pigs during the subsequent disease challenge. Other components in the diet may also affect functional amino acid effectiveness, as supplementation with the same blend of functional amino acids was able to improve performance of nursery pigs that had received a plant-based diet, however, provided no further benefit to those pigs that had received animal-based protein sources in the nursery (Fig. 2; Rodrigues et al., 2022b).

The appropriate intervention may be dependent on the type of challenge experienced, and is likely related to the specific immune response to different challenge types and the proportion of the decrease in performance that is due to either reduced feed intake or alterations in nutrient utilization (Rodrigues et al., 2021a, Pastorelli et al., 2012). For example, while nutrient adjustment was effective in PRRS infected pigs, this adjustment was not effective in pigs challenged with Mycoplasma hyopneumoniae (Jasper, 2020). This may also explain why the blend of functional amino acids was effective during an enteric pathogen challenge (Rodrigues et al., 2021bc) but had reduced effectiveness during a sanitary challenge (van der Meer et al., 2016).

Conclusions

Disease challenge can have a substantial negative effect on productivity and profitability of swine production, however, there are a number of dietary strategies that can be used to improve pig robustness. Functional amino acids have been investigated for their role during disease challenge and ability to support both the immune response and growth performance. While these have been shown to be effective under some circumstances (i.e., normal birth weight, enteric challenge), this is not always the case. Overall, adjustments to dietary amino acid content is another tool that can be incorporated into pig health programs. Dietary strategies to improve pig health should, however, be based on the specific circumstances and goals of the production unit.