

CHAPTER 8

THE ROLE OF INTESTINAL MICROBIOME IN THE HEALTH AND PRODUCTION OF COMMERCIAL POULTRY: A REVIEW

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ABSTRACT: The gastrointestinal tract (GIT) and the community of intestinal microorganisms play a crucial role in the health and functioning of birds, influencing nutrient absorption, strengthening the immune system, and protecting against diseases. Changes in the composition of this microbial community can negatively impact food efficiency, productivity, and bird welfare. The gastrointestinal compartments of birds are inhabited by complex bacterial communities, which recent studies have recognized as having fundamental roles in bird nutrition, physiology, and intestinal development. The intestinal microbiota can act as a protective barrier, adhering to the intestinal epithelial walls and reducing colonization by pathogenic bacteria. These bacteria produce beneficial compounds such as vitamins, short-chain fatty acids, and antimicrobial compounds, which provide nutrition and protection to the animal. However, the intestinal microbiome can also serve as a source of bacterial pathogens, posing a threat to public health. A healthy intestinal microbiota brings significant benefits, including effective competition against pathogens, immune system development, and the creation of protective barriers against undesirable microorganisms. On the other hand, the commensal microbiota also presents challenges, such as competition for energy and proteins in the proximal intestine and the generation of harmful metabolites. Despite the benefits, these processes increase the demand for energy and protein from the host, impacting bird growth performance. In summary, understanding and managing the intestinal microbiota is fundamental to sustainably promoting birds health and productivity. This study aims to analyze the influence of the intestinal microbiome on commercial poultry health and production, focusing on its effects on the immune system, digestion, and disease resistance.

KEYWORDS: intestinal health, symbiotic, probiotic

O PAPEL DO MICROBIOMA INTESTINAL NA SAÚDE E PRODUÇÃO DE AVES COMERCIAIS: UMA REVISÃO

RESUMO: O trato gastrointestinal (TGI) e a comunidade de microorganismos intestinais desempenham um papel crucial na saúde e funcionamento das aves, influenciando a absorção de nutrientes, fortalecimento do sistema imunológico e proteção contra doenças. Alterações na composição dessa comunidade microbiana podem impactar negativamente a eficiência alimentar, produtividade e bem-estar das aves. Os compartimentos gastrointestinais das aves são habitados por complexas comunidades bacterianas, que recentes estudos têm reconhecido como tendo papéis fundamentais na nutrição, fisiologia e desenvolvimento intestinal das aves. A microbiota intestinal pode agir como uma barreira protetora, fixando-se às paredes epiteliais do intestino e reduzindo a colonização por bactérias patogênicas. Essas bactérias produzem compostos benéficos, como vitaminas, ácidos graxos de cadeia curta e compostos antimicrobianos, que fornecem nutrição e proteção ao animal. No entanto, o microbioma intestinal também pode servir como fonte de patógenos bacterianos,

representando uma ameaça à saúde pública. Uma microbiota intestinal saudável traz benefícios significativos, incluindo competição eficaz contra patógenos, desenvolvimento do sistema imunológico e criação de barreiras protetoras contra microrganismos indesejáveis. Por outro lado, a microbiota comensal também apresenta desafios, como competição por energia e proteínas no intestino proximal, e geração de metabólitos prejudiciais. Apesar dos benefícios, esses processos aumentam a demanda por energia e proteína do hospedeiro, impactando o desempenho de crescimento das aves. Em suma, entender e gerenciar a microbiota intestinal é fundamental para promover a saúde e produtividade das aves de forma sustentável. Este estudo tem como objetivo analisar a influência do microbioma intestinal na saúde e na produção de aves comerciais, explorando seu impacto no sistema imunológico, na digestão e na resistência a doenças.

PALAVRAS-CHAVE: saúde intestinal, simbiótico, probiótico

INTRODUCTION

The health and proper functioning of the gastrointestinal tract (GIT) and the intestinal microorganism community are crucial for efficient nutrient absorption, strengthening the immune system, and protection against diseases. Changes in the composition of the microbial community in the GIT can impair feed efficiency, productivity, and poultry welfare (GASKINS; COLLIER; ANDERSON, 2002; KOHL, 2012). The gastrointestinal compartments of chickens are densely populated by complex microbial communities dominated by bacteria (FARKAS et al., 2022). Recent studies on interactions between the host and the intestinal bacterial microbiome of commercial poultry have been conducted, emphasizing the importance of the microbiome in the nutrition, physiology, and intestinal development of birds (FENG et al., 2023; NEMATHAGA et al., 2023).

The intestinal microbiota can form a protective barrier by attaching to the epithelial walls of enterocytes, thus reducing the opportunity for colonization by pathogenic bacteria (KHAN et al., 2021). These bacteria produce vitamins, short-chain fatty acids, organic acids, antimicrobial compounds, and triglycerides, and induce non-pathogenic immune responses, providing nutrition and protection to the animal (PAN; YU, 2014). Conversely, the intestinal microbiome can also be a source of bacterial pathogens such as *Salmonella* and *Campylobacter*, which can spread to humans or act as a reservoir for antibiotic resistance and transmission, posing a serious threat to public health (JUN-XION, 2016).

A healthy intestinal microbiota brings both benefits and costs to the host. Primary benefits offered by commensal microbiota include effective competition against pathogens or non-native microorganisms, as well as contributions to host nutrition (DIBNER; RICHARDS, 2005). Additionally, commensal microbiota can promote the development of the immune system, including different components such as the mucosal layer, intestinal epithelial cells, intestinal immune cells, and lamina propria (SHAKOURI; IJI; MIKKELSEN; COWIESON, 2009). These tissues play a crucial role in creating barriers between the host and microbes, as well as combating undesirable intestinal microorganisms (OAKLEY et al., 2014).

On the other hand, commensal microbiota also presents challenges for the host. In proximal intestinal segments such as the gizzard and small intestine, microorganisms compete with the host for energy and proteins. In both proximal and distal intestines, microbes generate potentially harmful metabolites, such as amino acid catabolites, and degrade bile acids, which can negatively affect bird growth and fat digestibility, respectively (GASKINS; COLLIER; ANDERSON, 2002).

In the presence of microbiota, the intestinal mucus layer increases mucin production and the rate of epithelial cell turnover, ensuring lubrication of the gastrointestinal tract and preventing the invasion of microorganisms into the host intestinal epithelial cells (ARIYADI, B.; HARIMURTI, 2015). Furthermore, the intestinal immune system is more robust and secretes immunoglobulin A (IgA), which specifically binds to bacterial components, aiding in regulating bacterial composition in the gut (GUTZEIT; MAGRI; CERUTTI, 2014). Despite its benefits, these processes increase the host's demand for energy and protein, which can influence bird growth performance (SUZUKI; NAKAJIMA, 2014).

Considering these factors, this study aims to analyze the impact of the intestinal microbiome on the health and production of commercial poultry, exploring its influence on the immune system, digestion, and disease resistance.

THE FUNCTION OF THE GASTROINTESTINAL MICROBIOTA

The entire gastrointestinal tract (GIT) of chickens is colonized by complex microbial communities, composed of viruses, protozoa, fungi, bacteria, and archaea (WEI; MORRISON; YU, 2013). The set of interactions between the avian microbiome and the host has been extensively studied by many researchers (KUMAR et al., 2018; KOGUT, 2017; YITBAREK, A. et al 2018; WARD, T.L. et al. 2019), given that such factors play important roles in the physiology, intestinal morphology, and nutrition of birds (KOGUT et al., 2018).

A balanced intestinal microbiota brings benefits and costs to the host. The main attributions given by the balanced microbiota include the reduction of pathogenic or non-native bacteria through competitive exclusion mechanisms, stimulation of the birds' immune system, and contributions to the host's nutrient metabolism (DIBNER; RICHARDS, 2005). Previous studies have established that conventionally raised animals are less susceptible to pathogenic microorganisms compared to germ-free animals (AL-ASMAKH; ZADJALI, 2015).

Additionally, symbiotic microbiota can stimulate the development of the immune system, including stimulation of intestinal mucosa, intestinal immune cells (T cells, immunoglobulin-producing cells, and phagocytic cells), and lamina propria. These tissues constitute barriers between bacteria and the host, assisting in combating undesirable intestinal microorganisms (OAKLEY et al., 2014). In the distal portion of the avian intestine, the microbiota also produces energy and nutrients such as amino acids, short-chain fatty

acids (SCFAs), vitamins, and amino acids from undigested food, which are eventually available to the host (DIBNER; RICHARDS, 2005). These SCFAs have bacteriostatic components capable of eliminating pathogenic bacteria such as *Salmonella spp* and *Clostridium perfringens* (RICKE, 2003). SCFAs are also a source of energy for animals and can increase stimulation for the proliferation of intestinal epithelial cells, thus increasing the gastrointestinal absorption area (DIBNER; RICHARDS, 2005).

On the other hand, beneficial microbiota incurs costs for the host. In the small intestine and gizzard, microorganisms compete with the host for energy and protein (BARKO et al., 2017). In both the proximal and distal intestines, bacteria produce toxic metabolites and catabolize bile acids, which can reduce bird growth and decrease fat digestibility (GASKINS; COLLIER; ANDERSON, 2002). In the presence of diverse microbiota, the intestinal mucus layer increases mucin secretion and turnover of epithelial cells, thereby keeping the gastrointestinal tract lubricated while preventing microorganisms from invading avian intestinal epithelial cells (SHIRA; FRIEDMAN, 2018).

The more developed intestinal immune system secretes IgA, which specifically binds to bacterial antigenic determinants, helping to regulate the bacterial composition in the intestine (SUZUKI; NAKAJIMA, 2014).

An imbalanced intestinal microbiota is often referred to as dysbiosis, which can be conceptualized as a qualitative and quantitative imbalance of the normal microbiota in the small intestine, which may lead to adverse reactions in the GI tract, including decreased intestinal barrier function (such as reduction of intestinal villi) and poor nutrient digestion, thus increasing the risk of colonization by pathogenic bacteria that may cause an inflammatory response. Both infectious and non-infectious stress conditions can lead to dysbiosis. Infectious causes include bacterial, viral, coccidial challenges, or toxic metabolites such as toxins produced by bacteria like *Clostridium perfringens*. Non-infectious agents include factors of nutritional imbalances, environmental stress, mycotoxins, and host genetic or enzymatic dysfunction (TEIRLYNCK et al., 2011).

The gastrointestinal microbiota can also be classified as mucosal microbiota and luminal microbiota. The composition of mucosa-related microbiota is influenced by various host factors such as expression of specific adhesion sites on the enterocyte membrane, immunoglobulin secretion, and mucin production ratio. The composition of luminal microbiota is established by available nutrients, food passage rate, and the presence of antimicrobial substances. Mucosal microbiota and luminal-associated microbiota also mutually influence each other; therefore, it is of paramount importance to consider that diet can modify both mucosal and luminal microbiota and consequently influence intestinal health (JEURISSEN SHI et al., 2002).

Studies have already compared the taxonomic composition of these two partitions in birds and highlighted how variability changes according to the food or additive in bird diets (AWAD et al., 2016; METZLER-ZEBELI et al., 2019; PARASKEUAS; MOUNTZOURIS,

2019). However, studies on the metabolic functions of these two microbial habitats have not yet been evidenced. Nevertheless, the ongoing study of variations between luminal and mucosal bacterial communities and studies on metabolic functions of the microbiota of each partition are of great importance for a better understanding of the modulation of the intestinal microbiota in birds. Additionally, the study of the bacterial community linked to the mucosa is fundamental to understanding the host mucosal responses, as all changes in mucosal immunity may have implications for the health and productive performance of birds (BORDA-MOLINA et al., 2016).

COMPOSITION OF THE GASTROINTESTINAL MICROBIOTA

The small intestine (duodenum, jejunum, and ileum) of birds primarily functions in the digestion and absorption of nutrients from food (SOUSA et al., 2015). Alongside these microenvironments of the small intestine, other areas such as the esophagus, crop, proventriculus, and gizzard harbor microbial colonies that perform important functions in the growth, health, and productive performance of the animal (CHRISTOFOLI et al., 2020).

The composition of the gastrointestinal tract microbiota in laying hens differs among segments, and its composition reflects the physicochemical changes of different microenvironments (Figure 1). The pH of the compartment, growth substrates, redox potential, antibacterial secretions, and host and microbiota metabolites directly influence the colonization efficiency of microorganisms in intestinal segments. Segments of the proximal part of the intestine are characterized by low pH, which selects for acid-tolerant bacteria and eliminates most pathogenic microorganisms (THOMPSON; HINTON, 1997).

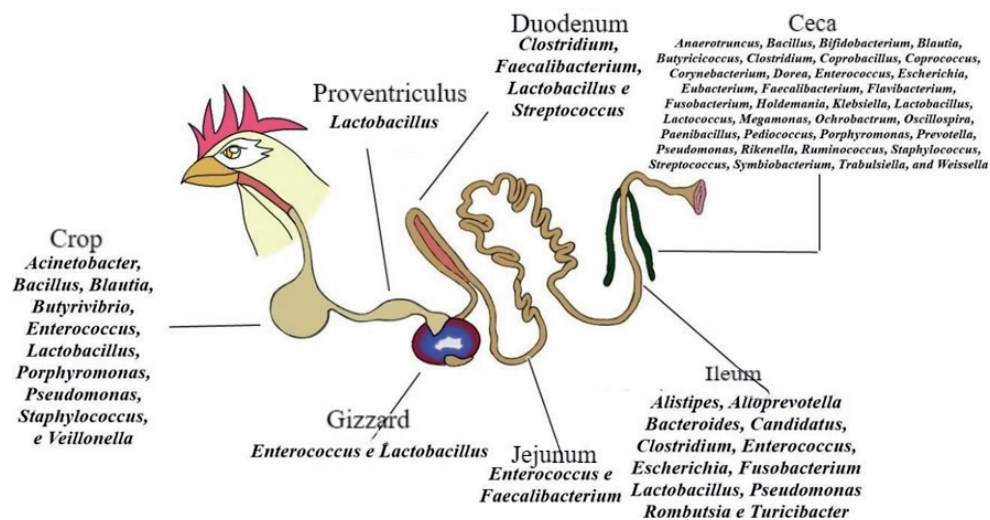


Figure 1. The composition of predominant microorganisms and the variation in diversity of the gastrointestinal microbiota in different segments of birds. Adapted from (KHAN et al., 2020).

The crop is responsible for storing food during periods without food and for moistening the food before enzymatic digestion, harboring approximately 10^8 to 10^9 bacteria per gram of crop contents (KIEROŃCZYK et al., 2016; YEOMAN et al., 2012). The crop microbiota is predominantly dominated by *Bacillus*, *Blautia*, *Enterococcus*, *Lactobacillus*, *Pseudomonas*, and *Staphylococcus* (SAXENA et al., 2016). Lactic acid-producing bacteria, such as *Lactobacillus*, can almost entirely colonize this segment, reducing their proportion along the GI tract (CHRISTOFOLI et al., 2020). The proventriculus is considered the true stomach of birds. The proventriculus is the part of the GI tract that secretes hydrochloric acid and pepsin, aiding in chemical digestion and chyme production, while the gizzard acts as a mechanical function on food (BEDFORD, 2006).

Together, such organs harbor fewer bacteria due to the acidity of the environment (REHMAN et al., 2007). The gizzard has approximately 10^7 to 10^8 bacteria per gram of chyme. Predominant bacterial populations in the chicken gizzard include *Enterobacteriaceae* and *Lactobacillus* (YEOMAN et al., 2012). Within what has been reported, in the proventriculus, the microorganism population is 10^4 to 10^6 CFU/g of bacteria. The proventricular microbiota of birds is dominated by *Lactobacillus*, similar to the gizzard, but unlike the crop, *Lactobacillus* does not adhere to the proventricular epithelium (FULLER; TURVEY, 1971; OAKLEY et al., 2014).

The small intestine of birds is divided into three different segments: the duodenum, jejunum, and ileum. The duodenum has a short transit time with a low pH, which functions to activate enzymes. Pancreatic and biliary secretions aid in digestion, ultimately diluting the chyme and limiting the number of bacteria capable of colonizing the GI tract (REHMAN et al., 2007). It is observed that the duodenal microbiota of birds consists mainly of *Clostridia*, *Streptococcus*, *Enterobacteria*, and *Lactobacillus* (WAITE; TAYLOR, 2015).

Therefore, as the chyme enters the jejunum and ileum, there is a decrease in digestive enzyme activities, and bile acids are unconjugated, thereby facilitating bacterial colonization with increased pH in the following portions (REHMAN et al., 2007), with the jejunum inhabited by *Lactobacillus*, *Streptococcus*, and *Proteobacteria*, and the ileum by *Lactobacillus*, *Enterococcus*, *Bifidobacterium*, *Bacteroides*, *Streptococcus*, *Clostridium*, *Fusobacterium*, and *Coliforms*. The jejunum and ileum have approximately 10^8 to 10^9 bacteria per gram of digestive matter, while the duodenum has 10^3 to 10^5 (STANLEY; HUGHES; MOORE, 2014).

The ceca contributes to various functions in avian physiology, such as nitrogen recycling, water absorption, and electrolytes. The cecal microbiota is capable of food fermentation and synthesizing metabolites such as SCFAs, which can then be used by the host. The intestinal segment has the highest bacterial density in birds; this segment has a cecal content pH ranging from 6.0 to 7.0 and a bacterial concentration of 10^{10} to 10^{12} CFU/g and can be colonized by *Lactobacillus*, *Bacteroides*, *Proteobacteria*, *Bacillus*, *Clostridium*, *Bifidobacterium*, *Fecalibacterium*, *Ruminococcus*, *Eubacterium*, and *Fusobacterium* (STANLEY; HUGHES; MOORE, 2014; SVIHUS, 2014).

MICROBIAL COMPOSITION ACCORDING TO AGE

The structure of the microbiota undergoes several changes throughout the life of birds due to modifications in metabolic function and cell density (SHANG et al., 2018). Differences in microbiota structure change with age, which, in turn, alters modulation and mechanisms in the intestine. Structure refers to total population density, the main community colonizing the microenvironment, the native population, and how these microorganisms interact with each other. In a favorable scenario, this balanced population structure can exclude pathogenic bacterial populations. Intestinal stability reduces the possibility of dysbiosis, resulting in a healthy microbiota (FEYE et al., 2020). The intestinal microbiota rapidly increases from the 1st to the 3rd day, and around the 7th day, most microorganisms inhabiting the mature microbiota are already present; therefore, the number of colonies varies weeks before stabilizing. Two weeks after hatching, *Oscillopira* and *Ruminococcus* bacteria significantly increase their population, whereas the number of *Enterococcus* is reduced (BALLOU et al., 2016). When comparing chickens at 8 and 30 weeks of age, it is observed that bacteria of the *Firmicutes* and *Bacteroidetes* genera become more abundant in the GI tract (CUI et al., 2017). Evaluating the effect of age on laying hens from 1 to 60 weeks old on the composition of the intestinal microbiota, it was observed that *Bacteroidetes*, *Firmicutes*, and *Proteobacteria* formed the vast majority of the microbiota population at all evaluated stages (VIDENSKA et al., 2014). These data show that gram-negative bacteria dominate the intestine in younger birds, while *Firmicutes* become more prevalent in the later stage of the laying hen cycle (KHAN et al., 2020).

As chickens age, the intestinal barrier is compromised due to changes in the composition of the intestinal microbiota, and studies indicate that reducing microbiota variation may trigger dysbiosis in older birds, thus requiring the use of intestinal microbiota balancers (BALLOU et al., 2016; MALIK et al., 2019; XU et al., 2016).

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CONCLUSION

In recent years, significant advances have been made in understanding the taxonomic composition of the gastrointestinal microbiome and its impact on intestinal health. However, there is a growing recognition of the need to expand our knowledge about the crucial role that the microbiome plays in the nutrition, health, disease, and productivity of birds. To advance in this direction, future studies need to adopt integrative approaches, combining data from genomics, transcriptomics, proteomics, and metabolomics. This holistic approach will allow for a more comprehensive understanding of the interactions between intestinal microorganisms and their hosts.

By better understanding the complex interactions between the microbiome and its host, we will be able to develop more targeted and effective interventions to promote intestinal health in birds. This includes modifying the metabolic pathways associated with the microbiome, which may open up new opportunities for innovative therapeutic and preventive interventions.

REFERENCES

- AL-ASMAKH, M., & ZADJALI, F. **Use of Germ-Free Animal Models in Microbiota-Related Research.** *Journal Of Microbiology And Biotechnology*, [S.L.], v. 25, n. 10, p. 1583-1588, 2015. Disponível em: <https://doi.org/10.1016/j.anifeedsci.2014.07.008>.
- ARIYADI, B., & HARIMURTI, S. **Effect of indigenous probiotics lactic acid bacteria on the small intestinal histology structure and the expression of mucins in the ileum of broiler chickens.** *International Journal of Poultry Science*, v. 14, p. 276-278, 2015. Disponível em: <https://doi.org/10.3923/IJPS.2015.276.278>.
- AWAD, W. A. et al. **Age-Related Differences in the Luminal and Mucosa-Associated Gut Microbiome of Broiler Chickens and Shifts Associated with Campylobacter Jejuni Infection.** *Frontiers in Cellular and Infection Microbiology*, v. 6, 22 Nov. 2016. Disponível em: [https://doi.org/10.1011](https://doi.org/10.1011/jvim.14875).
- BALLOU, A. L. et al. **Development of the Chick Microbiome: How Early Exposure Influences Future Microbial Diversity.** *Frontiers in Veterinary Science*, v. 3, 20 Jan. 2016. Disponível em: <https://doi.org/10.1016/j.anifeedsci.2014.07.008>.
- BARKO, P., MCMICHAEL, M., SWANSON, K., & WILLIAMS, D. **The Gastrointestinal Microbiome: A Review.** *Journal of Veterinary Internal Medicine*, v. 32, p. 9-25, 2017. Disponível em: <https://doi.org/10.1111/jvim.14875>.
- BEDFORD, M. R. **Effect of non-starch polysaccharidases on avian gastrointestinal function.** In: *Avian gut function in health and disease*. Wallingford: CABI, 2006. p. 159–170. Disponível em: <https://doi.org/10.1093/jas/skac334>.
- BORDA-MOLINA, D. et al. **Insights into Broilers' Gut Microbiota Fed with Phosphorus, Calcium, and Phytase Supplemented Diets.** *Frontiers in Microbiology*, v. 7, 19 dez. 2016. Disponível em: <https://doi.org/10.1016/j.anifeedsci.2014.07.008>.
- CHRISTOFOLI, M. et al. **Microbiota intestinal benéfica e prejudicial na avicultura: Revisão.** *Research, Society and Development*, v. 9, n. 7, p. e43973667, 27 abr. 2020. Disponível em: <https://doi.org/10.1016/j.anifeedsci.2014.07.008>.
- CUI, Y. et al. **Age-Related Variations in Intestinal Microflora of Free-Range and Caged Hens.** *Frontiers in Microbiology*, v. 8, 11 Jul. 2017. Disponível em: <https://doi.org/10.1016/j.anifeedsci.2014.07.008>.
- DIBNER, J.J.; RICHARDS, J.D. **Antibiotic growth promoters in agriculture: history and mode of action.** *Poultry Science*, [S.L.], v. 84, n. 4, p. 634-643, apr. 2005. Disponível em: <http://dx.doi.org/10.1093/ps/84.4.634>.

- FARKAS, V. et al. **Microbiota Composition of Mucosa and Interactions between the Microbes of the Different Gut Segments Could Be a Factor to Modulate the Growth Rate of Broiler Chickens.** *Animals: an Open Access Journal from MDPI*, v. 12, 2022. Disponível em: <https://doi.org/10.3390/ani12101296>.
- FEYE, K. M. et al. **Influential factors on the composition of the conventionally raised broiler gastrointestinal microbiomes.** *Poultry Science*, v. 99, n. 2, p. 653–659, Feb. 2020. Disponível em: <https://doi.org/10.1016/j.anifeedsci.2014.07.008>.
- GASKINS, H. R.; COLLIER, C. T.; ANDERSON, D. B.. **ANTIBIOTICS AS GROWTH PROMOTANTS: mode of action.** *Animal Biotechnology*, [S.L.], v. 13, n. 1, p. 29-42, jul. 2002. Disponível em: <http://dx.doi.org/10.1081/abio-120005768>.
- GERRITSEN, J. et al. **Intestinal microbiota in human health and disease: the impact of probiotics.** *Genes & Nutrition*, v. 6, n. 3, p. 209–240, 27 ago. 2011. Disponível em: <http://dx.doi.org/10.1007/s12263-011-0229-7>.
- GUTZEIT, Cindy; MAGRI, Giuliana; CERUTTI, Andrea. **Intestinal IgA production and its role in host-microbe interaction.** *Immunological Reviews*, [S.L.], v. 260, n. 1, p. 76-85, 19 jun. 2014. Disponível em: <http://dx.doi.org/10.1111/imr.12189>.
- JEURISSEN SHI et al. **Parameters and techniques to determine intestinal health of poultry as constituted by immunity, integrity, and functionality.** *Current Issues in Intestinal Microbiology*, v. 1, p. 1–14, mar. 2002.
- KHAN, S. et al. **The Gut Microbiota of Laying Hens and Its Manipulation with Prebiotics and Probiotics To Enhance Gut Health and Food Safety.** *Applied and Environmental Microbiology*, v. 86, n. 13, 17 jun. 2020. Disponível em: <https://doi.org/10.1128/AEM.00600-20>.
- KHAN, I. et al. **Mechanism of the Gut Microbiota Colonization Resistance and Enteric Pathogen Infection.** *Frontiers in Cellular and Infection Microbiology*, v. 11, 2021. <https://doi.org/10.3389/fcimb.2021.716299>.
- KOHL, Kevin D. **Diversity and function of the avian gut microbiota.** *Journal Of Comparative Physiology B*, [S.L.], v. 182, n. 5, p. 591-602, 14 jan. 2012. <http://dx.doi.org/10.1007/s00360-012-0645-z.3>
- KOGUT, M.H. 2017. **Issues and consequences of using nutrition to modulate the avian immune response.** *Journal Of Applied Poultry Research*, [S.L.], v. 26, n. 4, p. 605-612, dez. Disponível em: <https://doi.org/10.3382/japr/pfx028>.
- KOGUT, Michael H. **The effect of microbiome modulation on the intestinal health of poultry.** *Animal Feed Science And Technology*, [S.L.], v. 250, p. 32-40, apr. 2019. Disponível em: <http://dx.doi.org/10.1016/j.anifeedsci.2018.10.008>.
- KUMAR, S. et al. **Effect of antibiotic withdrawal in feed on chicken gut microbial dynamics, immunity, growth performance and prevalence of foodborne pathogens.** *PLOS ONE*, v. 13, n. 2, p. e0192450, 14 feb. 2018. Disponível em: <https://doi.org/10.1371/journal.pone.0192450>.
- NEMATHAGA, Mishumo; SMITH, Rae M.; MALATJI, Dikeledi P. **Interactions between the helminth and intestinal microbiome in smallholder chicken farming systems.** *Frontiers in Veterinary Science*, v. 10, 2023. Disponível em: <https://doi.org/10.3389/fvets.2023.1309151>.

MALIK, J. K. et al. **Synbiotics in Animal Health and Production**. *Nutraceuticals in Veterinary Medicine*, p. 287–301, 2019. Disponível em: https://doi.org/10.1007/978-3-030-04624-8_20.

METZLER-ZEBELI, B. U. et al. **Feed Restriction Modifies Intestinal Microbiota-Host Mucosal Networking in Chickens Divergent in Residual Feed Intake**. *mSystems*, v. 4, n. 1, 26 fev. 2019. Disponível em: <https://doi.org/10.1128/msystems.00261-18>.

OAKLEY et al. **The chicken gastrointestinal microbiome**. *Fems Microbiology Letters*, [S.L.], v. 360, n. 2, p. 100-112, 13 out. 2014. <http://dx.doi.org/10.1111/1574-6968.12608>.

PAN, D., & YU, Z. **Intestinal microbiome of poultry and its interaction with host and diet**. *Gut Microbes*, v. 5, p. 108 - 119, 2014. <https://doi.org/10.4161/gmic.26945>.

PARASKEUAS, V.; MOUNTZOURIS, K. C. **Broiler gut microbiota and expressions of gut barrier genes affected by cereal type and phytogetic inclusion**. *Animal Nutrition*, v. 5, n. 1, p. 22–31, mar. 2019. Disponível em: <https://doi.org/10.1016/j.aninu.2018.11.002>.

REHMAN, H. U. et al. **Indigenous bacteria and bacterial metabolic products in the gastrointestinal tract of broiler chickens**. *Archives of Animal Nutrition*, v. 61, n. 5, p. 319–335, 31 out. 2007. Disponível em: <https://doi.org/10.1080/17450390701556817>.

RICKE, S. **Perspectives on the use of organic acids and short chain fatty acids as antimicrobials**. *Poultry Science*, v. 82, n. 4, p. 632–639, apr. 2003. Disponível em: <https://doi.org/10.1093/ps/82.4.632>.

SHANG, Y. et al. **Chicken Gut Microbiota: Importance and Detection Technology**. *Frontiers in Veterinary Science*, v. 5, 23 out. 2018. Disponível em: <https://doi.org/10.3389/fvets.2018.00254>.

SHAKOURI, M. D.; IJI, P. A.; MIKKELSEN, L. L.; COWIESON, A. J.. **Intestinal function and gut microflora of broiler chickens as influenced by cereal grains and microbial enzyme supplementation**. *Journal Of Animal Physiology And Animal Nutrition*, [S.L.], v. 93, n. 5, p. 647-658, 10 set. 2009. Disponível em: <http://dx.doi.org/10.1111/j.1439-0396.2008.00852.x>.

SHIRA, ENAV BAR; FRIEDMAN, AHARON. **Innate immune functions of avian intestinal epithelial cells: response to bacterial stimuli and localization of responding cells in the developing avian digestive tract**. *Plos One*, [S.L.], v. 13, n. 7, p. 13-28, 6 jul. 2018. Disponível em: <http://dx.doi.org/10.1371/journal.pone.0200393>.

SOUSA, D. C. et al. **Caracterização morfológica do trato gastrointestinal de frangos de corte dalinhagem Cobb 500®**. *Pesquisa Veterinária Brasileira*, v. 35, n. suppl 1, p. 61–68, dez. 2015. Disponível em: <https://doi.org/10.1590/S0100-736X2015001300011>.

STANLEY, D.; HUGHES, R. J.; MOORE, R. J. **Microbiota of the chicken gastrointestinal tract: influence on health, productivity and disease**. *Applied Microbiology and Biotechnology*, v. 98, n. 10, p. 4301–4310, 19 maio 2014. Disponível em: <https://doi.org/10.1007/s00253-014-5646-2>.

SUZUKI, Keiichiro; NAKAJIMA, Akira. **New aspects of IgA synthesis in the gut**. *International Immunology*, [S.L.], v. 26, n. 9, p. 489-494, 28 maio 2014. Disponível em: <http://dx.doi.org/10.1093/intimm/dxu059>.

SVIHUS, B. **Function of the digestive system**. *Journal of Applied Poultry Research*, v. 23, n. 2, p. 306–314, jun. 2014. Disponível em: <https://doi.org/10.3382/japr.2014-00937>.

TEIRLYNCK, E. et al. **Morphometric evaluation of “dysbacteriosis” in broilers.** Avian Pathology, v. 40, n. 2, p. 139–144, abr. 2011. Disponível em: <https://doi.org/10.1080/03079457.2010.543414>.

VIDENSKA, P. et al. **Succession and Replacement of Bacterial Populations in the Caecum of Egg Laying Hens over Their Whole Life.** PLoS ONE, v. 9, n. 12, p. e115142, 12 dez. 2014. Disponível em: <https://doi.org/10.1371/journal.pone.0115142>.

YEOMAN, C. J. et al. **The microbiome of the chicken gastrointestinal tract.** Animal health research reviews / Conference of Research Workers in Animal Diseases, v. 13, n. 1, p. 89-99, 2012. Disponível em: <https://doi.org/10.1017/S1466252312000138>.

YITBAREK, A. et al. **Gut microbiota modulates type I interferon and antibody-mediated immune responses in chickens infected with influenza virus subtype H9N2.** Beneficial Microbes, [S.L.], v. 9, n. 3, p. 417-427, 25 abr. 2018. Disponível em: <https://doi.org/10.3920/BM2017.0088>.

WAITE, D. W.; TAYLOR, M. W. **Exploring the avian gut microbiota: current trends and future directions.** Frontiers in Microbiology, v. 6, 3 jul. 2015. Disponível em: <https://doi.org/10.3389/fmicb.2015.00673>.

WARD, T.L. et al. **Antibiotics and Host-Tailored Probiotics Similarly Modulate Effects on the Developing Avian Microbiome, Mycobiome, and Host Gene Expression.** Mbio, [S.L.], v. 10, n. 5, p. 1-17, 29 out. 2019. Disponível em: <https://doi.org/10.1128/mbio.02171-19>.

WEI, S.; MORRISON, M.; YU, Z. **Bacterial census of poultry intestinal microbiome.** Poultry Science, v. 92, n. 3, p. 671–683, mar. 2013. Disponível em: <https://doi.org/10.3382/ps.2012-02822>.

XU, Y. et al. **High-throughput sequencing technology to reveal the composition and function of cecal microbiota in Dagu chicken.** BMC Microbiology, v. 16, n. 1, p. 259, 4 dez. 2016. Disponível em: <https://doi.org/10.1186/s12866-016-0877-2>.