

The gut–brain–mitochondria axis in heat-stressed poultry: Mechanisms and implications for health and productivity

Review Article

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Abstract: Heat stress remains a major constraint to global poultry production, with profound implications for bird health, welfare, and productivity. Exposure to elevated ambient temperatures disrupts thermoregulation, metabolism, immune competence, and behaviour, ultimately compromising performance and survival. Growing evidence indicates that the gut–brain–mitochondria axis (GBMA) represents a critical integrative network through which birds perceive, respond to, and adapt to thermal stress. Heat stress-induced impairment of intestinal barrier integrity, dysbiosis of the gut microbiota, and altered secretion of gut-derived metabolites and neuroactive compounds converge on neuroendocrine pathways, particularly the hypothalamic–pituitary–adrenal and sympathetic axes, thereby modulating appetite regulation, stress reactivity, and thermoregulatory behaviour. Concurrently, excessive production of reactive oxygen species and calcium imbalance in mitochondria-rich tissues disrupt mitochondrial dynamics and bioenergetics, promoting oxidative damage and apoptosis. This review synthesises current evidence on heat stress-induced disruption of the GBMA at multiple levels, including gut architecture and microbiota, neuroendocrine regulation, and mitochondrial function. We further highlight how maladaptive feedback loops involving inflammation and oxidative stress exacerbate physiological dysfunction, ultimately reducing productivity, resilience, and welfare in poultry.

Keywords: Gut–brain–mitochondria axis • Free radicals • Oxidative damage • Poultry • Heat stress

1. Introduction

Climate change has intensified the frequency and duration of heat events, thereby increasing welfare concerns and economic losses in poultry production systems worldwide. Heat stress remains one of the most critical environmental challenges affecting poultry production, particularly in tropical and arid regions where ambient temperature and humidity frequently exceed the thermoregulatory capacity of birds (Onagbesan et al., 2023; Oni et al., 2024a, b). Exposure to elevated environmental temperatures disrupts physiological homeostasis and leads to reduced feed intake, impaired

growth performance, oxidative stress, immune dysfunction, reduced reproductive efficiency, and increased mortality (Rostagno, 2020; Uyanga et al., 2022; Eletu et al., 2026).

Traditionally, heat stress research in poultry has focused primarily on organ-specific alterations, including intestinal damage, endocrine dysfunction, and metabolic disturbances (Hai et al., 2000; Mahmoud et al., 2014). However, accumulating evidence suggests that heat stress induces coordinated systemic responses involving neuroendocrine, immune, metabolic, and microbial pathways (Smith & Vale, 2006; Quinteiro-Filho et al., 2010). Activation of stress-responsive pathways, particularly the hypothalamic–pituitary–adrenal (HPA) axis, stimulates corticosterone release and contributes

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to immune suppression, oxidative imbalance, and metabolic dysregulation (Renaudeau *et al.*, 2012; Bohler *et al.*, 2020). These observations highlight the limitations of isolated organ-level models and support the view that heat stress should be considered as a whole-organism disturbance involving complex physiological cross-talk (Nawaz *et al.*, 2021).

Recent advances in microbiome research, neuroendocrine physiology, and stress biology have further strengthened interest in integrative frameworks linking gut health, brain signalling, and cellular metabolism (Cryan *et al.*, 2019). In poultry, heat stress compromises intestinal epithelial integrity, increases gut permeability, and promotes microbial dysbiosis, often characterised by reductions in beneficial microbial populations (Quinteiro-Filho *et al.*, 2017; Oke *et al.*, 2025b). These alterations may influence systemic physiology through the microbiota–gut–brain axis, a bidirectional communication network involving microbial metabolites, vagal pathways, enteric signalling, and neuroendocrine responses (Cryan & Dinan, 2012). Under heat stress conditions, elevated corticosterone concentrations, inflammatory cytokines, and oxidative stress collectively exacerbate intestinal dysfunction and systemic inflammatory responses (Quinteiro-Filho *et al.*, 2010; Scanes, 2016).

Within this integrative framework, mitochondrial function has emerged as a critical mediator linking gut integrity, neuroendocrine regulation, and cellular energy metabolism during thermal stress. Heat stress impairs mitochondrial oxidative phosphorylation, increases reactive oxygen species (ROS) production, and disrupts ATP synthesis, thereby contributing to oxidative damage and reduced cellular efficiency (Zaboli *et al.*, 2019). Because mitochondria play essential roles in epithelial barrier maintenance, immune regulation, and neuronal signalling, mitochondrial dysfunction may represent an important mechanistic link connecting gut and brain responses during heat exposure (Oke *et al.*, 2025a). Collectively, these interactions support the emerging concept of a gut–brain–mitochondria axis (GBMA) that regulates physiological resilience and thermotolerance in poultry. Therefore, this review critically examines current evidence regarding the role of the GBMA in the physiological and metabolic responses of poultry to heat stress. Particular emphasis is placed on mechanistic interactions among gut microbiota, neuroendocrine signalling, mitochondrial dysfunction, oxidative stress, and systemic inflammation, as well as emerging directions for improving resilience under heat stress conditions.

2. Gut–brain–mitochondria axis

2.1 Conceptual basis of the gut–brain–mitochondria axis

The GBMA represents an integrated communication network linking the gastrointestinal tract, enteric nervous system, central nervous system (CNS), immune system, and mitochondrial metabolism through neural, endocrine, immune, and metabolic pathways (Forsythe & Kunze, 2013; Cryan *et al.*, 2019; Yassin *et al.*, 2025). Rather than functioning as isolated systems, these components interact dynamically to coordinate energy metabolism, stress adaptation, immune regulation, and physiological homeostasis. Growing evidence suggests that stressors such as heat exposure simultaneously disrupt these interconnected pathways, leading to intestinal dysfunction, neuroendocrine imbalance, oxidative stress, and impaired mitochondrial bioenergetics (Zhang *et al.*, 2024).

Within this framework, the gut microbiota functions as a major regulatory interface by producing metabolites, neuroactive compounds, and signalling molecules that influence host physiology locally and systemically. Alterations in microbial composition and metabolite production during dysbiosis have been associated with impaired intestinal barrier integrity, neuroinflammation, altered blood–brain barrier permeability, and behavioural disturbances in both humans and animals (Braniste *et al.*, 2014; Yassin *et al.*, 2025). Bidirectional signalling between the gut and brain occurs through vagal pathways, neuroendocrine responses, immune mediators, and microbial metabolites that collectively influence stress responsiveness, appetite regulation, immune activity, and metabolic function (Rhee *et al.*, 2009; Carabotti *et al.*, 2015).

Although mitochondria are not traditionally considered a structural component of the microbiota–gut–brain axis, mitochondrial metabolism is increasingly recognised as a critical downstream integrator of gut-derived and neuroendocrine signals (Picard *et al.*, 2018; Margineanu *et al.*, 2020). Mitochondria regulate ATP production, oxidative phosphorylation, ROS generation, redox signalling, and apoptosis, all of which are highly sensitive to inflammatory and metabolic disturbances induced during heat stress. Consequently, mitochondrial dysfunction may represent a mechanistic link connecting gut dysbiosis, systemic inflammation, oxidative stress, and neuroendocrine dysregulation within the GBMA framework.

Figure 1 presents a conceptual overview of the GBMA in poultry and illustrates the bidirectional communication among intestinal, neuroendocrine, and mitochondrial

systems under heat stress conditions. The figure highlights how heat stress alters gut microbiota composition, intestinal barrier integrity, neuroendocrine signalling, and mitochondrial function through immune, metabolic, and hormonal pathways. It further demonstrates the role of microbial metabolites, cytokines, neurotransmitters, and oxidative stress in mediating cross-talk among these systems, ultimately contributing to impaired growth performance, immune dysfunction, metabolic disturbances, and reduced poultry productivity.

2.2 Major communication pathways within the GBMA

2.2.1 Neural pathways

Neural communication between the gut and the brain is primarily mediated by the vagus nerve and the enteric nervous system. Approximately 80% of vagal fibres are afferent, transmitting sensory information from the gastrointestinal tract to the brain, including signals derived from microbial metabolites, inflammatory mediators, and

gut hormones (Lyte et al., 1998). Experimental evidence demonstrating that vagotomy abolishes microbiota-associated behavioural effects further supports the importance of vagal signalling in gut–brain communication. Through these neural pathways, alterations in intestinal microbial activity can influence central stress responses, appetite regulation, and behavioural adaptation during thermal stress.

2.2.2 Endocrine pathways

Endocrine signalling represents another major component of GBMA communication. Heat stress activates both the sympatho–adrenal–medullary system and the HPA axis, resulting in the rapid release of catecholamines followed by glucocorticoids such as corticosterone (Burokas et al., 2017; Cryan et al., 2019; Cao et al., 2021). Elevated stress hormone concentrations influence gut permeability, immune activity, microbial composition, and nutrient metabolism. In parallel, enteroendocrine cells release signalling peptides such as serotonin and glucagon-like peptide-1, which regulate gastrointestinal motility, appetite, and CNS activity (Holzer (2002); Aresti Sanz & El Aidy,

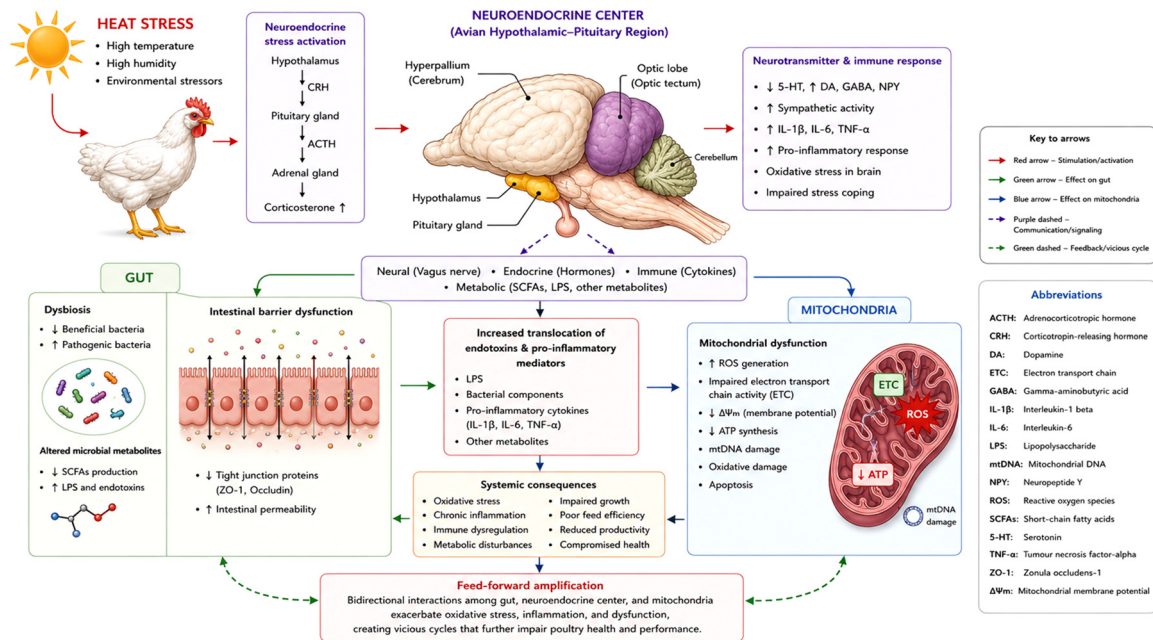


Figure 1. Schematic representation of the gut–brain–mitochondria axis in poultry under heat stress conditions. Heat stress disrupts intestinal homeostasis by altering gut microbiota composition, increasing intestinal permeability, and modifying microbial metabolite production. These alterations stimulate neuroendocrine and immune signalling pathways involving the hypothalamic–pituitary–adrenal axis, neurotransmitters, cytokines, and circulating hormones. Concurrently, mitochondrial dysfunction, characterised by impaired electron transport activity, oxidative stress, reduced ATP production, and cellular damage, further amplifies systemic stress responses. Bidirectional communication among the gut, brain, and mitochondria occurs through neural, endocrine, immune, and metabolic pathways, creating feed-forward loops that contribute to impaired growth performance, immune suppression, metabolic disturbances, and reduced productivity in poultry.

2019). These endocrine pathways therefore provide an important mechanistic link between thermal stress, gut function, and neuroendocrine regulation.

2.2.3 Immune pathways

Immune signalling plays a central role in coordinating communication between intestinal and neural systems. Microbial products, such as lipopolysaccharides (LPS), stimulate immune cells to release pro-inflammatory cytokines that can influence brain function and blood–brain barrier integrity (Cryan & Dinan, 2012; Hsiao *et al.*, 2013). Sustained systemic inflammation has been associated with altered neuroendocrine regulation, oxidative stress, and behavioural disturbances, indicating that immune activation may contribute substantially to stress-induced dysfunction within the GBMA network (Dowlati *et al.*, 2010).

2.2.4 Metabolic and redox signalling

Microbial metabolites, including short-chain fatty acids (SCFAs), catecholamines, and neurotransmitter precursors, also contribute to GBMA communication by regulating cellular metabolism and redox balance (Kraimi *et al.*, 2019; Margineanu *et al.*, 2020). These metabolites influence mitochondrial function, oxidative stress responses, epithelial barrier integrity, and neuronal activity. Disruption of these signalling pathways during heat stress may impair neuroplasticity, immune regulation, and cellular energy metabolism, thereby contributing to systemic physiological dysfunction (Yassin *et al.*, 2025).

2.3 Gastrointestinal alterations within the GBMA during heat stress

The gastrointestinal tract constitutes a major functional component of the GBMA because it integrates microbial, immune, metabolic, and neuroendocrine signals. The avian gut microbiota consists primarily of bacteria belonging to Firmicutes, Bacteroidota, Proteobacteria, and Actinobacteria, with regional variation across the gastrointestinal tract (Videnska *et al.*, 2014; Ducatelle *et al.*, 2023). Beneficial microbial metabolites, particularly SCFAs such as acetate, propionate, and butyrate, contribute to epithelial integrity, immune regulation, and intestinal homeostasis through receptor-mediated signalling pathways (Sommer & Bäckhed, 2013).

Heat stress profoundly disrupts gastrointestinal structure and function. Reduced splanchnic blood flow,

oxidative stress, and hypoxia impair epithelial integrity and promote villus atrophy, epithelial erosion, and reduced crypt development (Fouad *et al.*, 2016; Nanto-Hara *et al.*, 2020). These structural alterations compromise nutrient absorption and intestinal barrier function. Concurrently, heat stress disrupts tight junction proteins, including occludin, claudins, and ZO-1, thereby increasing intestinal permeability and promoting the development of a “leaky gut” phenotype (Wu *et al.*, 2018; Hu *et al.*, 2022). Although multiple studies consistently report heat stress-induced dysbiosis and barrier dysfunction, most evidence remains associative, and relatively few studies have simultaneously evaluated microbial, neuroendocrine, and mitochondrial endpoints *in vivo* (Oke *et al.*, 2025b).

Microbial dysbiosis is another consistent consequence of heat stress exposure. Beneficial bacterial populations such as *Lactobacillus* and *Bifidobacterium* decline, whereas opportunistic pathogens, including *Escherichia coli*, *Clostridium perfringens* (Sohail *et al.*, 2010), and *Salmonella* (Shi *et al.*, 2019), increase in abundance. These alterations may further amplify intestinal inflammation, impair epithelial repair, and reduce SCFA production, thereby perpetuating barrier dysfunction and systemic inflammatory activation (Kamada *et al.*, 2013). Shi *et al.* (2019) demonstrated increased Enterobacteriaceae abundance during chronic heat exposure, whereas Ahmad *et al.* (2022) linked these microbial shifts to impaired immune function.

Barrier disruption facilitates the translocation of endotoxins, such as LPS, into the systemic circulation, thereby activating Toll-like receptor 4 (TLR4)-mediated inflammatory pathways and increasing circulating concentrations of pro-inflammatory cytokines, including tumor necrosis factor- α (TNF- α) and Interleukin (IL)-6 (Quinteiro-Filho *et al.*, 2012; Alhenaky *et al.*, 2017). These inflammatory responses contribute to oxidative stress, metabolic reprogramming, muscle proteolysis, and impaired growth performance (Frost & Lang, 2008).

At the cellular level, intestinal heat stress is closely associated with mitochondrial dysfunction and redox imbalance. Excessive ROS production, impaired ATP synthesis, and activation of nuclear factor (NF)- κ B and mitogen-activated protein kinase (MAPK) signalling pathways exacerbate epithelial injury and inflammatory responses (Kikusato & Toyomizu, 2013; Wang *et al.*, 2019; Liu *et al.*, 2021). Although heat shock proteins such as HSP70 and HSP90 are upregulated as protective responses, prolonged heat exposure may overwhelm these adaptive mechanisms, leading to persistent mitochondrial and epithelial dysfunction (Zayani *et al.*, 2025).

2.4 Neuroendocrine responses and brain alterations during heat stress

The brain coordinates thermal adaptation through hypothalamic thermosensory pathways, autonomic regulation, and activation of the HPA axis. Heat exposure stimulates behavioural and physiological responses, including panting, vasodilation, reduced locomotion, and decreased feed intake, in order to facilitate heat dissipation (Yahav et al., 2004; Lara & Rostagno, 2013). However, these adaptive responses also reduce intestinal perfusion and alter nutrient availability, thereby linking central thermoregulation with gastrointestinal dysfunction (Lambert, 2009; Gonzalez-Rivas et al., 2020; Mazzoni et al., 2022).

Activation of the HPA axis increases circulating corticosterone concentrations, which influence metabolism, immune competence, intestinal permeability, and microbial composition (Star et al., 2008; Quinteiro-Filho et al., 2012). Chronic corticosterone elevation promotes muscle catabolism, suppresses lymphoid tissue development, alters leukocyte profiles, and exacerbates oxidative stress and intestinal dysfunction (Shini et al., 2008; Patra & Kar, 2021).

Heat stress has also been associated with neuroinflammation and oxidative damage in hypothalamic and mid-brain regions involved in appetite regulation and stress responsiveness (Beckford et al., 2020). Altered concentrations of neurotransmitters such as serotonin, dopamine, norepinephrine, and epinephrine may further impair neuroplasticity and behavioural adaptation during prolonged heat exposure (Calefi et al., 2019). These neuroendocrine disturbances contribute to suppression of appetite-regulating neuropeptides, including NPY and AGRP, while promoting anorexigenic signalling pathways involving corticotropin-releasing hormone (CRH), GLP-1, and leptin (Beckford et al., 2020; Nanto-Hara et al., 2020).

2.5 Mitochondrial dysfunction as a central integrator of heat stress responses

Mitochondria function as major downstream mediators of GBMA signalling because they integrate metabolic, inflammatory, and oxidative inputs from both gut and neuroendocrine pathways (Picard et al., 2018; Margineanu et al., 2020). Heat stress increases mitochondrial ROS production through electron leakage from electron transport chain complexes I and III, particularly in skeletal muscle and intestinal tissues (Mujahid et al., 2006, 2007; Yang et al., 2010; Akbarian et al., 2016). Excessive ROS generation overwhelms endogenous antioxidant systems, leading to lipid peroxidation, protein oxidation, DNA damage, and

impaired cellular homeostasis (Huang et al., 2015; Surai et al., 2019).

Oxidative damage to electron transport chain components decreases oxidative phosphorylation efficiency, reduces ATP synthesis, and increases proton leakage across the mitochondrial membrane (Yang et al., 2010; Liao et al., 2022). Simultaneously, chronic heat exposure disrupts mitochondrial biogenesis, fusion-fission dynamics, and mitophagy, thereby promoting the accumulation of dysfunctional mitochondria and persistent oxidative stress (de Oliveira et al., 2015; Zhang et al., 2016; Ouyang et al., 2022).

Mitochondrial DNA is particularly susceptible to oxidative injury due to its proximity to the electron transport chain and the limited protective histone structures (Surai et al., 2019; Zhang et al., 2022). Combined effects of oxidative stress, inflammatory cytokines, dysbiosis, and corticosterone further amplify mitochondrial dysfunction and contribute to metabolic inefficiency, impaired neurogenesis, and tissue injury during chronic heat stress.

2.6 Integrated interactions within the GBMA during heat stress

Current evidence suggests that heat stress disrupts the GBMA through interconnected feedback mechanisms involving gut dysbiosis, systemic inflammation, neuroendocrine activation, and mitochondrial dysfunction. Heat-induced microbial dysbiosis reduces beneficial SCFA-producing bacteria while increasing pathogenic taxa, thereby promoting inflammatory cytokine production and impairing mitochondrial energy metabolism (Shi et al., 2019). Simultaneously, disruption of intestinal tight junctions increases endotoxin translocation into circulation, activating innate immune pathways and stimulating the HPA axis (Alhenaky et al., 2017). Elevated corticosterone concentrations then exacerbate oxidative stress, impair immune function, and further compromise intestinal integrity, thereby reinforcing gut–brain dysfunction. The major microbiome, neuroendocrine, and mitochondrial pathways affected by heat stress, together with their underlying mechanisms and physiological consequences, are summarised in Table 1.

Mitochondrial ROS production also activates redox-sensitive inflammatory pathways, including NF- κ B and MAPK, contributing to neuroinflammation, impaired neurogenesis, and reduced stress resilience (Prince et al., 2004; Ganesan et al., 2017; Chen et al., 2023). These processes collectively impair feed intake, nutrient utilisation, immune competence, growth performance, meat quality, and overall welfare in poultry exposed to prolonged heat stress (Lara & Rostagno, 2013; Hillerer and Gimsa, 2024).

Table 1. Microbiome, neuroendocrine, and mitochondrial pathways affected by heat stress

Component	Pathway/subcategory	Effects of heat stress	Mechanisms	Consequences	References
Microbiome (gut)	Morphological alterations	Villus atrophy, crypt depth changes, epithelial erosion, reduced goblet cells	Hypoxia, oxidative injury, reduced blood flow	↓ Absorptive surface, impaired renewal	Santos et al. (2015)
	Tight junction disruption	Occludin, claudins, ZO-1, JAM-A disruption	Hypoxia, oxidative stress, and corticosterone elevation	Leaky gut, ↑ permeability (FITC-dextran confirmed)	Lambert (2009); Song et al. (2014); Ruff et al. (2020)
	Dysbiosis	↓ <i>Lactobacillus</i> , <i>Bifidobacterium</i> ; ↑ <i>E. coli</i> , <i>Clostridium</i> , <i>Salmonella</i>	Altered motility, mucus, immunity, nutrients	Inflammation, delayed repair, self-amplifying damage	Lan et al. (2004); Shi et al. (2019)
	Endotoxin translocation	↑ Plasma LPS (24–72 h), TLR4/NF-κB activation	Barrier failure	↑ TNF-α, IL-2; pathogen dissemination to organs	Quinteiro-Filho et al. (2010, 2012); Nanto-Hara et al. (2020)
	Nutrient absorption	↓ Enzyme activity (trypsin, amylase), ↓ transporters	Villus atrophy, inflammation, dysbiosis	↓ Feed efficiency, body weight gain	Mitchell and Carlisle (1992); Enami et al. (2021)
	Gut redox/mitochondrial	↑ ROS, lipid peroxidation, ↓ ATP	Hypoperfusion, hypoxia	NF-κB/MAPK activation, barrier failure	Kikusato and Toyomizu (2013); Liu et al. (2021)
Neuroendocrine (brain)	Hypothalamic sensing	Panting, vasodilation, ↓ and feed intake	Thermosensitive neurons	Splanchnic hypoxia, gut disturbances	Yahav et al. (2004); Lambert (2009)
	HPA axis activation	↑ CRH, ACTH, corticosterone	Chronic stress response	Gut permeability ↑, immune suppression, dysbiosis	Star et al. (2008); Quinteiro-Filho et al. (2012)
	Stress hormones	Muscle proteolysis, gluconeogenesis	Corticosterone-mediated catabolism	↓ Growth, immune resilience, carcass yield	Geraert et al. (1996); Shini et al. (2008)
	Neuroinflammation	↑ Cytokines to the brain, monoamine disruption	LPS translocation	Appetite dysregulation, impaired neuroplasticity	Calefi et al. (2019); Beckford et al. (2020)
	Feed intake regulation	↓ NPV/AGRP, ↑ POMC/CRH	Neuropeptide imbalance	Anorexia, negative energy balance	Nanto-Hara et al. (2020)
	Gut–brain signalling	↓ Vagal tone, sympathetic imbalance	Autonomic dysregulation	↓ Motility/secretion, dysbiosis feedback	Rostagno (2020)
Mitochondrial	ROS generation	↑ ETC leakage (complexes I/III)	Substrate-independent surge	Lipid/protein/DNA damage	Mujahid et al. (2006); Akbarian et al. (2016)
	OXPPOS/ATP disruption	↓ MMP, proton leak, avUCP downregulation	ROS damage to ETC	Glycolysis reliance, energy deficits	Yang et al. (2010); Liao et al. (2022)
	Biogenesis/fusion/fission	↓ PGC-1α, mitophagy impairment	SCFA deficits from dysbiosis	Mitochondrial fragmentation, apoptosis	Zhang et al. (2016); Hu et al. (2020)
	mtDNA damage	↑ 8-OHdG lesions	ROS proximity, no histones		Surai et al. (2019)

Table 1: Continued

Component	Pathway/subcategory	Effects of heat stress	Mechanisms	Consequences	References
Interconnections	Proteotoxicity/UPR	Protein denaturation, HSP60/70 activation	Oxidation/carbonylation	Respiratory gene failure, ROS vicious cycle	Saracila et al. (2023)
	Tissue specific	Gut: barrier ROSBrain: neuroinflammationLiver: lipid peroxidationMuscle: protein catabolism	Tissue metabolic demands	Chronic apoptosis, ATP synthesis failure	Mujahid et al. (2007); Ouyang et al. (2022)
	Dysbiosis → Inflammation → Mitochondria	↓ SCFA, ↑ pathogens/cytokines	Barrier dysfunction	Performance/welfare decline	Song et al. (2014)
	Leaky Gut → LPS → HPA	TJ protein loss	Circulating LPS	Systemic ROS, energy failure	Alhenaky et al. (2017)
	Brain → Gut motility	Neuropeptide/autonomic changes	Vagal tone reduction	Corticosterone surge, immune suppression	Cryan and Dinan (2012); Bohler et al. (2020)
	ROS → Neuroimmune	NF-κB/MAPK activation	Redox signalling	Dysbiosis amplification	Ganesan et al. (2017); Chen et al. (2023)
	Feedback loops	Dysbiosis–LPS–HPA–ROS cycles	Self-reinforcing	Neuroinflammation, apoptosis	Akbarian et al. (2016); Kikusato and Toyomizu (2013)
	Performance impacts	Anorexia, malabsorption, immunosuppression	Axis breakdown	Metabolic inefficiency, catabolism	Lara and Rostagno (2013); Wen et al. (2021)
				↓ Growth, welfare, disease resistance	

Figure 2 illustrates the mechanistic disruption of the GBMA in poultry during heat stress. The figure demonstrates how thermal stress activates neuroendocrine pathways, induces intestinal barrier dysfunction and dysbiosis, and impairs mitochondrial function through oxidative and inflammatory processes. It further highlights the bidirectional signalling and feed-forward interactions among the gut, brain, and mitochondria mediated by microbial metabolites, cytokines, neuropeptides, and ROS, ultimately contributing to compromised poultry health and performance.

3. Nutritional interventions targeting the gut-brain-mitochondria axis

Nutritional strategies that modulate the gut microbiota, oxidative balance, neuroendocrine responses, and mitochondrial function have attracted increasing attention as

supportive approaches for alleviating heat stress in poultry. Rather than acting independently, many of these interventions exert interconnected effects across the GBMA by preserving intestinal barrier integrity, reducing systemic inflammation, attenuating oxidative stress, and supporting cellular energy metabolism. Major nutritional and early-life interventions targeting the GBMA during heat stress are summarised in Table 2.

3.1 Microbiota-targeted nutritional strategies

Among the most extensively investigated interventions are probiotics, prebiotics, and synbiotics, primarily because heat stress consistently induces intestinal dysbiosis, barrier dysfunction, and endotoxin translocation (Quinteiro-Filho *et al.*, 2012). Supplementation with probiotic organisms, particularly *Lactobacillus* and *Bifidobacterium* species, has been associated with improved intestinal morphology, reduced pathogenic bacterial

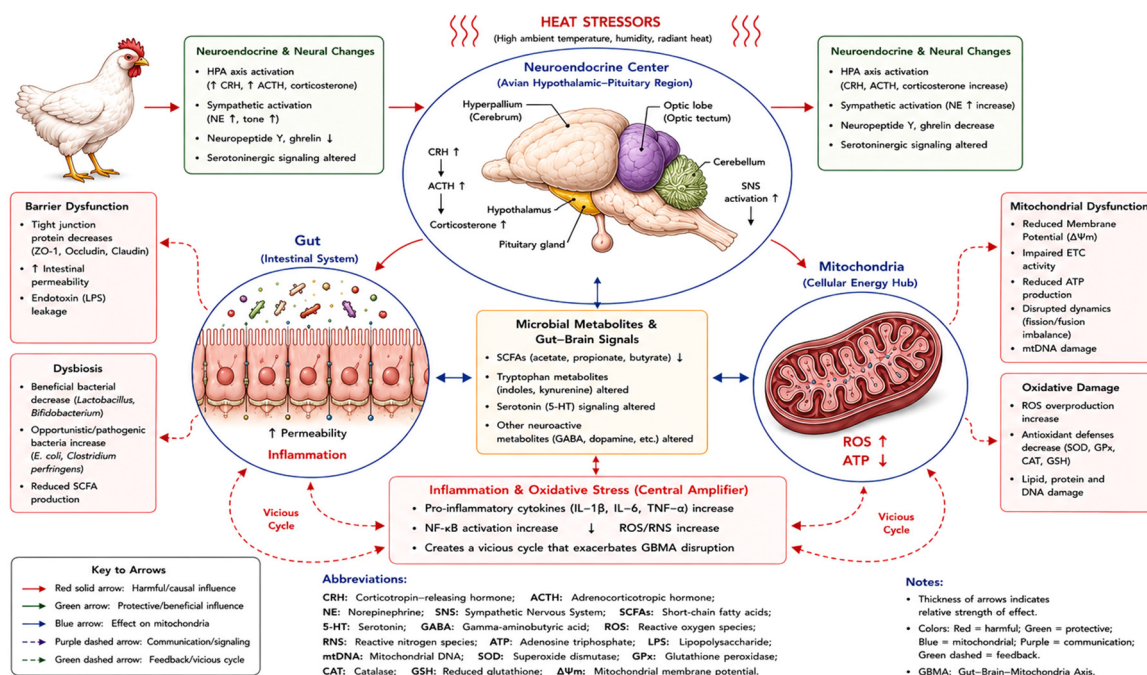


Figure 2. Mechanistic illustration of heat stress-induced disruption of the gut-brain-mitochondria axis in poultry. Heat stress activates neuroendocrine stress pathways, including the hypothalamic-pituitary-adrenal axis and sympathetic nervous system, leading to altered neurotransmitter release, corticosterone secretion, and inflammatory responses. Simultaneously, intestinal barrier dysfunction and dysbiosis increase gut permeability and modify microbial metabolite production, resulting in elevated translocation of endotoxins and pro-inflammatory mediators. These alterations contribute to mitochondrial dysfunction through excessive reactive oxygen species (ROS) generation, impaired electron transport chain activity, reduced ATP synthesis, and oxidative cellular damage. Bidirectional interactions among the gut, brain, and mitochondria are mediated through neural, endocrine, immune, and metabolic signalling pathways, generating feed-forward cycles that exacerbate oxidative stress, inflammation, and physiological dysfunction, ultimately compromising poultry health and performance.

Table 2. Interventions targeting the gut–brain–mitochondria axis in heat-stressed poultry

Interventions	Types	Key interventions	Mechanisms and benefits	References
Nutritional interventions	Probiotics, prebiotics, synbiotics	<i>Lactobacillus</i> , <i>Bifidobacterium</i> , galactooligosaccharides, synbiotics	Enhance intestinal morphology, tight junctions, SCFA production, and reduce pathogens/oxidative stress/corticosterone	Quinteiro-Filho et al. (2012); Cao et al. (2021); Hu et al. (2020)
	Phytogenics and essential oils	Peppermint, fenugreek, thymol, carvacrol, cinnamaldehyde	Antimicrobial, antioxidant, anti-inflammatory; improve barrier function, HPA axis regulation	Abbass and Abid (2023); Akbarian et al. (2016); Madkour et al. (2025)
	BSFL	Antimicrobial peptides, bioactive lipids	Favourable microbiota shifts, antioxidant defences, mitochondrial redox balance	Giller et al. (2021); Beldowska et al. (2023); Sjöfjan et al. (2025)
	Functional amino acids	Glutamine, tryptophan, methionine, taurine, arginine	Gut barrier maintenance, serotonin/melatonin synthesis, glutathione production, osmoprotection	Chalvon Demersay et al. (2021); Wang et al. (2015); Yue et al. (2017)
	Antioxidants	Vitamins E/C, selenium, zinc, polyphenols	Preserve mitochondrial integrity, activate Nrf2, reduce ROS/malondialdehyde	Surai et al. (2019); Olayiwola and Adedokun (2025)
Environmental and management	Cooling and ventilation	Tunnel ventilation, evaporative cooling, fogging, and reduced stocking density	Lower thermal load, HPA axis attenuation, preserve gut/mitochondrial function	Bhadoria (2017); Cuadrado and Dridi (2024); Renaudeau et al. (2012)
	Early-life thermal conditioning	Mild heat exposure during development	Long-term thermotolerance, antioxidant capacity, gut–brain stability	Yahav et al. (2004); Saeed et al. (2019)
	Stocking density, lighting, enrichment	Optimised density, low-intensity lighting, perches/pecking substrates	Reduce HPA activation, improve ventilation/feed intake, and behavioural thermoregulation	Parvin et al. (2014); Bilal et al. (2021)
Precision livestock farming	Wearable sensors and microclimate	Body temperature, respiration, activity monitoring	Early heat stress detection to prevent gut/mitochondrial damage	Bohler et al. (2020); Kennedy et al. (2022);
	Predictive modelling	Climate + physiology integration	Proactive nutritional/environmental management	Ma et al. (2021); St-Pierre et al. (2003); Karl et al. (2018)
Targeted therapies	Real-time biomarkers	Corticosterone, cytokines, SCFAs, H/L ratio	Precision intervention targeting axis health	Zaytsoff et al. (2020)
	SCFA-enhancing strategies	Fibre enrichment, butyrate producers (Ruminococcaceae)	Tight junctions, anti-inflammation, mitochondrial ATP synthesis	Wong et al. (2006); Hu et al. (2020)
	Emerging mitochondrial stabilisers	Nrf2 activators, uncoupling protein regulators	Reduce ROS, preserve oxidative phosphorylation	Mishra and Jha (2019); Uyanga et al. (2022)
	Postbiotics and metabolites	Organic acids, peptides, bacteriocins, and indole derivatives	Gut barrier, neuroimmune signalling, metabolic stability	Arnal and Lallès (2016); Ahmad et al. (2022)

colonisation, and enhanced immune stability during thermal stress. Prebiotics and synbiotics further support these responses by selectively stimulating beneficial microbial populations and increasing the production of SCFAs, particularly butyrate, which supports epithelial integrity and mitochondrial ATP production (Cryan & Dinan, 2012; Hu *et al.*, 2020).

Experimental studies have shown that synbiotic supplementation promotes microbial communities enriched with *Lactobacillus* and Ruminococcaceae while reducing opportunistic taxa such as *Escherichia* and *Clostridium* under heat stress conditions (Heida *et al.*, 2016). These microbial shifts are associated with reduced intestinal inflammation and improved gut barrier function, suggesting that microbiota modulation may indirectly attenuate HPA-axis activation and systemic oxidative stress. Similarly, early-life interventions such as *in ovo* administration of galactooligosaccharides have been reported to enhance mucosal defence through increased goblet cell density and mucin expression, thereby improving intestinal resilience later in life (Alemka *et al.*, 2012; Calefi *et al.*, 2016). Collectively, these findings support the concept that microbiota-directed nutritional strategies contribute to GBMA stability by limiting endotoxin leakage, preserving immune homeostasis, and maintaining metabolic balance during heat exposure (Abdelqader *et al.*, 2017; Alhenaky *et al.*, 2017).

3.2 Phytochemicals and functional bioactive compounds

Phytochemical feed additives and essential oils have also received attention because of their antioxidant, anti-inflammatory, and antimicrobial properties (Oyelola *et al.*, 2024). Several phytochemical compounds, including black seed, peppermint, fenugreek, and curcumin, have demonstrated protective effects against heat stress by reducing oxidative injury and improving gut health and mitochondrial function (Oke *et al.*, 2021; Abbass & Abid, 2023). Polyphenol-rich compounds may additionally modulate cytokine production and microbial diversity, thereby influencing neuroimmune signalling and mitochondrial redox balance (Akbarian *et al.*, 2016; Chen & Vitetta, 2020).

Essential oils containing thymol, carvacrol, and cinnamaldehyde have similarly been associated with improved intestinal barrier integrity and reduced pathogenic bacterial load in heat-stressed poultry (Madkour *et al.*, 2025). Although evidence directly linking phytochemicals to GBMA regulation remains limited, available studies suggest that these compounds may indirectly modulate neuroendocrine stress responses by reducing systemic inflammation and oxidative

stress, thereby supporting mitochondrial function during thermal challenge (Zaboli *et al.*, 2019; Saracila *et al.*, 2023).

Black soldier fly larvae (BSFL) meal has emerged as another promising functional ingredient because of its antimicrobial peptides, bioactive lipids, and immunomodulatory compounds (Giller *et al.*, 2021; Aruwa *et al.*, 2021). Studies indicate that BSFL supplementation can improve antioxidant status, immune responses, and microbial composition under stressful conditions (Beldowska *et al.*, 2023; Sjöfjan *et al.*, 2025). However, mechanistic evidence specifically connecting BSFL supplementation to integrated GBMA regulation remains scarce, highlighting an important area for future investigation.

3.3 Functional amino acids and mitochondrial regulation

Functional amino acids play important roles beyond protein synthesis by participating in antioxidant defence, intestinal integrity, immune modulation, and neuroendocrine regulation during heat stress (Chalvon-Demersay *et al.*, 2021; Lee *et al.*, 2022; Ajayi *et al.*, 2024). Among these, L-citrulline has attracted considerable interest because of its thermoregulatory and antioxidant properties. Experimental evidence demonstrates that L-citrulline supplementation improves thermotolerance, attenuates oxidative stress, enhances antioxidant enzyme activity, and supports mitochondrial energetics during heat exposure (Uyanga *et al.*, 2022). In addition, its role in maintaining intestinal integrity and modulating gut microbial composition suggests potential relevance within the GBMA framework (Ma *et al.*, 2025).

Glutamine has similarly been shown to preserve intestinal barrier function by enhancing tight junction integrity, supporting villus morphology, and contributing to glutathione synthesis under heat stress conditions (Wang *et al.*, 2015; Rao & Samak, 2012). Tryptophan, as a precursor of serotonin and melatonin, may influence appetite regulation, stress responsiveness, and neuroendocrine signalling while also modulating gut microbial balance and mitochondrial homeostasis (Cryan & Dinan, 2012; Yue *et al.*, 2017; Beldowska *et al.*, 2023).

Methionine, betaine, and taurine further contribute to antioxidant protection and mitochondrial stability through their involvement in methylation reactions, glutathione synthesis, osmoregulation, and membrane stabilisation (Yang *et al.*, 2010; Mishra & Jha, 2019; Abd El-Ghany & Babazadeh, 2022). Nevertheless, excessive dietary protein or imbalanced amino acid supplementation may increase microbial fermentation of undigested substrates and generate harmful metabolites, indicating that

nutritional interventions targeting the GBMA require careful dietary formulation (Smith & Macfarlane, 1998).

3.4 Antioxidant strategies and redox homeostasis

Oxidative stress represents one of the central mechanisms linking heat stress to mitochondrial dysfunction and GBMA disruption. Consequently, antioxidant supplementation has been widely investigated as a strategy to preserve mitochondrial integrity and cellular homeostasis. Vitamins E and C, selenium, zinc, and related micronutrients have been shown to improve antioxidant enzyme activity, growth performance, and survivability in heat-stressed poultry (Oke et al., 2017; Oke, 2018; Olayiwola & Adedokun, 2025). These compounds help stabilise mitochondrial membranes and reduce lipid and protein oxidation by supporting endogenous antioxidant systems, including superoxide dismutase, catalase, and glutathione peroxidase (Akbarian et al., 2016; Oni et al., 2024a, Oni & Oke, 2025).

Additional evidence suggests that phytochemical antioxidants and dietary polyphenols may also contribute to gut microbial stability and modulation of inflammatory signalling pathways, thereby indirectly supporting gut–brain communication and mitochondrial function (Surai et al., 2019; Chen et al., 2023; Oni et al., 2025). Despite promising experimental findings, many antioxidant studies remain focused on isolated physiological outcomes, and relatively few have comprehensively evaluated integrated GBMA responses under heat stress conditions.

4. Environmental and management interventions relevant to GBMA stability

Although environmental and management interventions are not direct modulators of the GBMA, they substantially influence the physiological pathways involved in GBMA disruption during heat stress. By reducing thermal load and limiting neuroendocrine activation, these strategies indirectly preserve intestinal integrity, mitochondrial function, immune stability, and metabolic homeostasis.

4.1 Environmental cooling and ventilation

Environmental cooling remains one of the most effective approaches for reducing the physiological burden of heat

stress in poultry production systems. Tunnel ventilation, evaporative cooling systems, exhaust fans, fogging devices, and climate-controlled housing reduce ambient temperature and humidity while improving evaporative heat dissipation (Bhadauria, 2017; Cuadrado & Dridi, 2024). These interventions reduce excessive HPA-axis activation and corticosterone secretion, thereby limiting oxidative stress and inflammatory responses that contribute to gut barrier dysfunction and mitochondrial injury (Lin et al., 2006).

In tropical and subtropical production systems, housing designs that maximise natural ventilation and airflow are particularly important where mechanical cooling is economically limited (Oloyo & Ojerinde, 2020; Gitau Gicheha, 2021). Improved airflow reduces heat-induced hypoxia and endotoxemia, thereby indirectly supporting intestinal integrity and microbial homeostasis (Rostagno, 2020). Additional management practices, including reduced stocking density and optimisation of drinking water temperature, further help lower thermal load and preserve physiological stability during periods of elevated environmental temperature (Renaudeau et al., 2012).

4.2 Early-life thermal conditioning

Early-life thermal conditioning has been proposed as a developmental strategy for improving thermotolerance later in life. Exposure of chicks to controlled thermal challenges during early developmental stages may induce adaptive responses involving thermoregulation, neuroendocrine signalling, and mitochondrial metabolism (Yahav et al., 2004). Experimental studies indicate that thermally conditioned birds exhibit reduced physiological stress responses and improved tolerance to subsequent heat exposure (Saeed et al., 2019).

Although the precise mechanisms remain incompletely understood, these adaptive responses may involve long-term modulation of stress signalling pathways, mitochondrial efficiency, and gut integrity. However, the extent to which early-life thermal conditioning directly alters GBMA function remains insufficiently characterised and requires further mechanistic investigation.

4.3 Stocking density, lighting, and environmental enrichment

Management conditions influencing bird behaviour and stress responsiveness can also affect physiological pathways associated with GBMA stability. Reduced stocking density improves airflow, decreases competition and

aggression, and lowers physiological stress under high ambient temperatures (Parvin *et al.*, 2014; Abbas *et al.*, 2021). These improvements may indirectly attenuate HPA-axis activation, oxidative stress, and intestinal dysfunction during thermal challenge (Quinteiro-Filho *et al.*, 2010).

Lighting programmes additionally influence feeding behaviour, activity patterns, and stress physiology. Manipulation of photoperiod and light intensity may improve feed intake and reduce stress-associated heterophil-to-lymphocyte ratios during hot periods by encouraging feeding during cooler hours of the day (Wu *et al.*, 2022). Environmental enrichment strategies, including perches and pecking substrates, may also improve behavioural adaptation and reduce stress-related behaviours, although direct evidence linking enrichment practices to modulation of GBMA remains limited (Bilal *et al.*, 2021; Beldowska *et al.*, 2023).

4.4 Precision livestock farming and predictive technologies

Precision livestock farming technologies offer opportunities for earlier detection and management of heat stress before severe physiological disruption occurs. Continuous monitoring systems capable of assessing body temperature, respiration rate, activity, and environmental conditions provide real-time indicators of thermal stress and associated physiological disturbances (Bohler *et al.*, 2020; Kennedy *et al.*, 2022). These technologies may help identify early alterations associated with oxidative stress, behavioural dysfunction, or intestinal disturbance before irreversible damage develops (Pollock *et al.*, 2021).

Predictive modelling approaches integrating climatic, behavioural, and physiological data may further improve preparedness for heat stress events and facilitate targeted nutritional or environmental interventions (St-Pierre *et al.*, 2003; Kennedy *et al.*, 2022; Oke *et al.*, 2025c). Nevertheless, current applications remain largely focused on production and welfare monitoring rather than direct assessment of GBMA function.

Recent advances in biosensing technologies may enable real-time evaluation of biomarkers associated with oxidative stress, immune activation, and intestinal integrity, including corticosterone, inflammatory cytokines, antioxidant enzyme activity, and microbial metabolites (Quinteiro-Filho *et al.*, 2012; Santos *et al.*, 2015; Zaytsoff *et al.*, 2020). However, the integration of these biomarkers into practical predictive systems for monitoring GBMA disruption in poultry is still at an early stage and requires substantial validation under commercial production conditions.

5. Insights from omics and systems biology targeting the gut–brain–mitochondria axis

5.1 Microbiome shifts and metabolomics

The gastrointestinal tract of chickens harbours a complex microbial community, including Firmicutes, Bacteroidetes, and Proteobacteria, while the ceca are the primary sites of microbial fermentation and SCFA production (Józeffiak *et al.*, 2004; Choi *et al.*, 2015). Metagenomic analyses have shown that a large proportion of microbial genes are involved in carbohydrate metabolism, thereby underscoring the importance of the microbiome in energy harvesting and nitrogen utilisation (Danzeisen *et al.*, 2011).

Microbial homeostasis is affected by thermal stress, which reduces beneficial taxa and alters SCFA profiles, thereby impairing nutrient absorption, feed efficiency, and immune competence (Alhenaky *et al.*, 2017; Ahmad *et al.*, 2022). Metabolomic studies consistently show that thermal stress shifts carbohydrate, protein, and lipid metabolism toward increased fat deposition and reduced protein synthesis, accompanied by elevated ROS and oxidative damage in intestinal and muscle tissues (Kikusato & Toyomizu, 2023). Conversely, diets enriched with fermentable fibres and polyphenols restore SCFA production and limit the production of toxic metabolites such as ammonia and indole derivatives, thereby reinforcing gut and metabolic homeostasis (Agus *et al.*, 2021; Whitman *et al.*, 2024).

5.2 Neurotransmitter-related transcriptomic changes

Microbial metabolites play a major role in regulating host neuroendocrine and immune signalling. SCFAs serve as energy sources while regulating epithelial proliferation and villus architecture. The butyrate produced improves intestinal integrity through its anti-inflammatory properties and stimulation of glucagon-like peptide-2 (Panda *et al.*, 2009; Eeckhaut *et al.*, 2011; Liu *et al.*, 2021). SCFAs influence central appetite regulation by stimulating the secretion of GLP-1 and peptide YY, as well as acetate, which can cross the blood–brain barrier to alter hypothalamic neuropeptide expression (Frost *et al.*, 2014; Zhang *et al.*, 2022). The inflammatory response induced by dysbiosis, mediated by LPS and pro-inflammatory cytokines, obstructs signalling pathways and impairs gut–brain communication (Abd El-Hack *et al.*, 2022; Salahi *et al.*, 2025).

Transcriptomic studies reveal downregulation of thyroid hormone (T3 and T4) levels and changes in the expression of stress-responsive genes, which may reflect adaptive reductions in metabolic heat production, protein synthesis, and reproductive performance (Del Vesco et al., 2016; Juiputta et al., 2023). Transcript profiling also identifies functional pathways enriched during heat stress, such as corticosteroid release, feeding behaviour, and the inflammatory response, along with their associated candidate genes, providing deeper insights into the molecular regulation of thermoregulation in poultry (Uyanga et al., 2023; Majekodunmi et al., 2025).

5.3 Mitochondrial proteomics and metabolic fingerprints

Through proteomic analysis, chronic heat stress has been shown to consistently cause oxidative damage to all the major mitochondrial components, such as proteins, lipids, and DNA, with a decrease in the activity of the antioxidant enzymes like superoxide dismutase, catalase, and glutathione peroxidase (Akbarian et al., 2016; Song et al., 2018). In addition, reduced thyroid hormone activity decreases metabolic heat production, whereas elevated corticosterone levels facilitate fat storage, both of which contribute to alterations in mitochondrial energy balance (Del Vesco et al., 2016; Kikusato & Toyomizu, 2023).

The composition of gut microbiota has a significant impact on mitochondrial metabolism. Comparative analyses of fat and lean chicken lines found that higher abundances of Fusobacteria and Proteobacteria characterise fatty chicken lines. In contrast, lean chicken lines are dominated by Bacteroidetes (Ding et al., 2016). The relative scarcity of butyrate- and propionate-producing bacteria among the birds makes them more susceptible to inflammation, oxidative stress, and metabolic dysfunction, while, on the contrary, the presence of SCFAs strengthens mitochondrial antioxidant capacity and the oxidative phosphorylation process (Tong et al., 2016; Costa et al., 2017; Cheng et al., 2018; Chen & Vitetta, 2020).

5.4 Multi-omics integration for gut–brain–mitochondria axis mapping

By integrating metagenomic, transcriptomic, proteomic, and metabolomic data, researchers can develop a comprehensive picture of the interactions between the gut microbiota and the host. Functional characterisations of these metatranscriptome, metagenome, proteome, and

metabolome datasets, as well as dietary manipulation and antibiotics used for growth promotion, have changed the composition of the gut microbiota and improved how effectively energy is gained through harvesting biomass and utilisation of nutrients through the host animal (Danzeisen et al., 2011; Costa et al., 2017).

Multi-omics strategies also support the genetic selection of birds for thermotolerance and feed efficiency. The merging of SNP data with the profiles of genes expression and proteins abundance shows the presence of signalling pathways like IGF/PI3K/Akt, ribosomal biogenesis, and mitochondrial oxidative phosphorylation that help to segregate the resilient and high-efficiency birds from those with a susceptible phenotype (Zhou et al., 2015; Juiputta et al., 2023). Collectively, these findings reveal coordinated interactions among the gut microbiota, neuroendocrine regulation, and mitochondrial metabolism in the GBMA.

5.5 Emerging biomarkers and therapies for understanding the gut–brain–mitochondria axis

Biomarkers, whether physiological or molecular, provide insights into overall stress and gut health. This includes heterophil-to-lymphocyte ratios, corticosterone concentrations, thyroid hormones, stress-responsive genes, and tight junction proteins, which provide insights into systemic stress and gut integrity (Du et al., 2016; Juiputta et al., 2023).

Research based on omics technologies has identified some biomarkers that could be used to monitor the GBMA function and stress resilience. Microbiome indicators include a high proportion of SCFA-producing taxa such as Lachnospiraceae, Ruminococcaceae, Faecalibacterium, and Ruminococcus, and the related increase in Enterobacteriaceae that occurs during dysbiosis (Torok et al., 2008; Stanley et al., 2014). Using different methods, the metabolic markers such as SCFA ratios, bile acid profiles, ROS levels, and antioxidant enzyme activity were identified (Li et al., 2018; Cheng et al., 2018). Also, neuroendocrine signals such as GLP-1, PYY, and serotonin link appetite control, energy expenditure, and microbial metabolism (Frost et al., 2014; Yu et al., 2024). The synergistic action of these biomarkers provides effective methods for assessing GBMA interactions and improving resilience in poultry production systems. Some GBMA targeted therapies include the following.

5.5.1 SCFA-enhancing strategies

Beneficial gut bacteria that produce SCFAs help maintain intestinal integrity, modulate the immune system, and

manage energy metabolism. There are several ways to increase SCFA production, especially butyrate, to help maintain the intestinal barrier, reduce inflammation, and support mitochondrial ATP production (the energy source in our cells) under heat stress (Wong *et al.*, 2006). The abundance of butyrate-producing bacteria such as Ruminococcaceae, Lachnospiraceae, *Faecalibacterium prausnitzii*, and particular *Clostridium* species has been shown to improve the intestinal barrier, reduce inflammatory signals, and regulate appetite through GLP-1 and leptin pathways (Eckhaut *et al.*, 2011; Abdelqader *et al.*, 2017; Beldowska *et al.*, 2023).

Enriching the diet with fibres and manipulating intestinal microbes are both effective methods to increase the production of SCFA, which can strengthen gut-mitochondrial communication and improve metabolic resilience during thermal stress (Hu *et al.*, 2020; Wu *et al.*, 2014). The use of complementary strategies that focus on the production of mitochondrial ROS and the enhancement of antioxidant defences would preserve oxidative phosphorylation and maintain cellular energy balance (Mujahid *et al.*, 2006; Akbarian *et al.*, 2016).

5.5.2 Emerging mitochondrial stabilisers

Nutritional and phytochemical interventions aimed at stabilising mitochondrial membranes and improving electron transport chain function are becoming major strategies for managing heat-induced cellular dysfunction. For instance, compounds that mitigate ROS production, activate the Nrf2 pathway, and modulate mitochondrial uncoupling proteins can maintain energy production and minimise oxidative damage during thermal stress (Mishra & Jha, 2019; Surai *et al.*, 2019). Newly emerging mitochondrial-directed agents are likely to protect the redox balance and preserve mitochondrial bioenergetics under high ambient temperatures (Uyanga *et al.*, 2022).

5.5.3 Postbiotics and functional metabolites

The use of postbiotics, such as organic acids, peptides, indole derivatives, bacteriocins, and neurotransmitters produced by bacteria, represents a novel approach to modulating immune and metabolic pathways without requiring microorganisms. These metabolic products have direct effects on gut barrier integrity, appetite control, neuroimmune communication, and mitochondrial energy metabolism, thereby eliminating inconsistencies in probiotic viability (Cryan & Dinan, 2012; El Aidy *et al.*, 2016; Zhu *et al.*, 2019). The inclusion of bioactive microbial metabolites will improve epithelial cell integrity, increase

the stability of gut–brain–liver communication, and enhance the body's overall ability to withstand heat stress (Arnal & Lallès, 2016; Wang *et al.*, 2020).

5.6 Artificial intelligence, systems biology, and predictive modelling in GBMA research

The increasing complexity of heat stress biology in poultry has highlighted the need for integrative analytical approaches that can simultaneously evaluate microbiome dynamics, neuroendocrine responses, immune regulation, and mitochondrial function. Because the GBMA involves highly interconnected pathways operating across multiple biological scales, conventional single-variable analyses are often insufficient to explain the systemic responses associated with thermal stress. Consequently, systems biology, multi-omics integration, and artificial intelligence (AI)-driven modelling are emerging as valuable tools for advancing GBMA research.

Recent advances in transcriptomics, metabolomics, proteomics, metagenomics, and epigenomics now permit simultaneous characterisation of microbial composition, host gene expression, mitochondrial activity, inflammatory signalling, and metabolic adaptation during heat stress (Bohler *et al.*, 2020; Beldowska *et al.*, 2023). Integrating these datasets through systems biology approaches may facilitate the identification of coordinated molecular pathways linking intestinal dysbiosis, neuroendocrine activation, oxidative stress, and mitochondrial dysfunction. Such approaches may also help distinguish adaptive from maladaptive responses during acute and chronic heat exposure.

Artificial intelligence and machine learning approaches offer additional opportunities for analysing these large and multidimensional datasets. For example, machine learning algorithms can be trained to identify microbial dysbiosis signatures associated with reduced thermotolerance, impaired feed efficiency, or elevated inflammatory responses. Predictive models integrating microbiome composition, cytokine profiles, corticosterone levels, antioxidant status, and mitochondrial biomarkers may help classify birds into heat stress susceptibility or resilience categories (Karl *et al.*, 2018; Kennedy *et al.*, 2022).

AI-assisted modelling may also improve the prediction of mitochondrial dysfunction during heat stress by integrating physiological and molecular indicators, including ROS generation, ATP depletion, mitochondrial membrane potential, and expression of oxidative stress-related genes. These predictive frameworks could support earlier

detection of subclinical thermal injury before severe declines in productivity or welfare occur. In addition, network-based modelling approaches may help identify key regulatory nodes within the GBMA, thereby improving understanding of how alterations in gut microbial metabolites, neuroendocrine signalling, and mitochondrial energetics interact under heat stress conditions.

Another promising application involves integrating environmental and physiological datasets into thermal resilience models. Combining climatic variables, behavioural indicators, gut microbiota profiles, and metabolic biomarkers using AI-driven platforms may improve heat stress response forecasting under commercial production conditions. Such predictive systems could facilitate precision nutrition and targeted management interventions designed to preserve intestinal integrity, mitochondrial function, and neuroendocrine stability during thermal challenge.

Despite these promising developments, the application of AI and predictive modelling in GBMA research remains in its early stages. Many current studies rely on relatively small experimental datasets, limiting the robustness and generalisability of predictive algorithms. Furthermore, the lack of standardised biomarkers and harmonised experimental protocols complicates cross-study comparisons and model validation. Future studies should therefore prioritise large-scale longitudinal datasets, standardised phenotyping approaches, and integrative multi-omics platforms to improve the reliability and practical applicability of AI-driven GBMA research in poultry production systems.

6. Research gaps and future directions

Despite significant advances in omics technologies, nutritional interventions, and genetic approaches, several gaps remain in our understanding and management of GBMA under poultry heat stress. Addressing these gaps will be critical for developing sustainable strategies that enhance resilience, productivity, and welfare.

6.1 Need for integrative *in vivo* studies on the gut–brain–mitochondria axis

Most studies to date have investigated alterations in the gut microbiota, neuroendocrine responses, or mitochondrial dysfunction under heat stress as independent processes. Although the association between intestinal

dysbiosis and increased intestinal permeability has been linked to the development of systemic inflammation and HPA dysregulation (Quinteiro-Filho et al., 2012; He et al., 2019), mitochondrial oxidative stress has been demonstrated to decrease the efficiency and viability of cells' metabolism (Rhoads et al., 2013; Surai et al., 2019). These types of experimental analyses are typically evaluated separately and therefore do not provide sufficient data to determine how the microbial, neuroendocrine, and mitochondrial systems function concurrently when animals are subjected to heat stress.

Hence, there is a need for integrative *in vivo* experimental designs that simultaneously evaluate gut microbial composition and metabolites, central and peripheral neuroendocrine signals, and mitochondrial bioenergetics. Comprehensive studies of the GBMA in poultry remain limited, particularly under heat stress, although the possibility that microbial metabolites might influence hypothalamic signalling and mitochondrial dynamics through this triad communication pathway is attracting increasing attention (Picard et al., 2018; Dalile et al., 2019). Innovative experimental approaches, such as gnotobiotic or microbiota-manipulated chickens subjected to controlled heat stress, can elucidate these interactions and provide means to overcome the limitations of *ex vivo* or single-component studies (Stanley et al., 2014; Diaz Carrasco et al., 2019). Future studies can develop a mechanistically informed understanding of the regulation of this axis by using microbiome profiling, transcriptomics of neurotransmitter-related genes, and proteomics of mitochondrial proteins under defined stress or pathogen challenges. These approaches will allow researchers to better capture the dynamic nature of heat stress-related physiology at the systems level and identify key regulatory points that contribute to the development of resilience in poultry (Wen et al., 2021; Salahi et al., 2025).

6.2 Biomarker standardisation for monitoring the gut–brain–mitochondria axis

One major hindrance to meaningful comparisons across studies is the lack of standardised biomarkers to evaluate GBMA function under heat stress. Researchers use various indicators in their studies, including plasma corticosterone, tight junction proteins, heat shock proteins (HSP70, HSP90), antioxidant enzymes, mitochondrial DNA copy number, and inflammatory mediators. However, they also differ in several aspects, including the types of tissues sampled, the time range, and the

thresholds used for analysis (Rhoads et al., 2013; Surai et al., 2019). Differences in methods thus lead to low reproducibility and ultimately weaken conclusions regarding the severity of stress or the effectiveness of the intervention. While emerging biomarkers like SCFAs, brain-derived neurotrophic factor, cytokine profiles (IL-6, IL-17, TNF- α), intestinal barrier proteins, and mitochondrial ROS levels are promising as integrated indicators of axis health, no consensus has been reached on their use in poultry systems (Cao et al., 2021; Beldowska et al., 2023).

Omics-based methods such as metabolomics and transcriptomics are particularly effective for uncovering conserved, functionally relevant biomarkers, but their effectiveness depends on coordinated protocols and cross-validation across breeds, ages, stressors, and production environments (Wen et al., 2021; An et al., 2025). Creating standardised biomarker panels, with agreed sampling strategies and assay validation, will be important for reliable monitoring of axis perturbations and resilience in commercial flocks (Quinteiro-Filho et al., 2012; Lavelle & Sokol, 2020).

6.3 Genomic selection for gut–brain–mitochondria resilience

Genomic selection has become a common tool for improving traits such as growth, feed efficiency, and thermotolerance in poultry. However, breeding methods that focus on resilient GBMA functionality are yet to be developed. There is growing evidence that host genetics determines the composition of the gut microbiota, the stress response, and mitochondrial activity. Moreover, specific genomic regions related to heat tolerance and cellular energetics have been identified (Van Goor et al., 2016). On the other hand, the selection indices currently used rarely account for characteristics associated with microbiome stability, neuroendocrine control, or mitochondrial efficiency.

Future breeding programmes could use SNP markers associated with SCFA-producing taxa, stress hormone regulation, mitochondrial oxidative phosphorylation pathways, or uncoupling protein variants to redirect selection toward physiological robustness under heat stress (Mignon-Grasteau et al., 2015; Xu et al., 2025). Implementing microbiome heritability and axis-related quantitative trait loci into multi-trait genomic models would enable increases in thermotolerance without a decline in productivity (Mignon-Grasteau et al., 2015; Juiputta et al., 2023). These methods would complement nutritional and management interventions to mitigate heat stress in poultry.

6.4 Early-life programming

The application of early-life interventions provides an opportunity to enhance the GBMA's resistance to heat stress. The practices of *in ovo* feeding, thermal conditioning, and early probiotic administration have been shown to have a long-lasting impact on the gut, immune system, and temperature tolerance in chickens (Uni and Ferket, 2004; Saeed et al., 2019; Eletu et al., 2025). Nevertheless, how these practices affect neuroendocrine regulation and the ability of cells to produce energy via respiration under heat stress remains unexplored.

There is evidence that early microbial colonisation and nutritional signals can epigenetically influence axis development; however, linking neonatal microbiota profiles to adult mitochondrial efficiency and stress resilience in longitudinal poultry studies remains rare (Romano et al., 2021). It is necessary to conduct controlled growth-based experiments that monitor birds from embryo development through production cycles to determine whether early-life programming results in stable bacterial configurations, enduring epigenetic changes, and persistent mitochondrial adaptations. The ability to reveal such developmental plasticity will be an important factor in the development of preventive, rather than reactive, approaches to heat stress and enteric disease (Wen et al., 2021; Salahi et al., 2025).

6.5 Opportunities for AI-driven modelling

The nonlinear interactions among the microbiota, neuroendocrine pathways, and mitochondrial metabolism are beyond the scope of conventional analytical frameworks. Recently, artificial intelligence and machine learning have become powerful means for integrating high-dimensional datasets from genomics, microbiomics, metabolomics, physiological measurements, and environmental sensors. For instance, AI-derived models have demonstrated utility in predicting animal performance and stress responses in precision livestock systems (Karl et al., 2018; Naeem et al., 2025).

In heat stress physiology, such methods could be used to theoretically model dysregulation of the GBMA, identify central regulatory nodes, and test nutritional or genetic interventions *in silico* before on-farm implementation (Karl et al., 2018; Kennedy et al., 2022). Recent methods, such as graph neural networks, may be beneficial for unravelling the complex, rapid interactions among microbe–neuron–mitochondria and for predicting thermal tolerance or heat stress resilience under different

heat conditions (Zampiga et al., 2018; Videla Rodriguez et al., 2024). To achieve high-quality, standards-based datasets, animal scientists, physiologists, and data scientists will work closely together, with AI becoming climate-smart and precision poultry production being installed (Pollock et al., 2021).

7. Conclusions

With rising global temperatures, heat stress imposes a significant burden on poultry producers, particularly in tropical and subtropical climates. Heat stress in poultry does not affect birds' physiology through a single pathway. On the contrary, heat stress operates through a highly interconnected GBMA, in which intestinal dysbiosis, neuroendocrine activation, and mitochondrial dysfunction reinforce one another through forward signalling and feedback mechanisms. Mitochondrial dysfunction appears to represent an important integrative mechanism linking intestinal, neuroendocrine, and metabolic responses during heat stress. When heat stress induces mitochondrial dysfunction, a hallmark is the overproduction of ROS and reduced ATP levels. Changes within mitochondria disrupt cellular signalling mechanisms that normally maintain intestinal barrier function and immune homeostasis. The central positioning of mitochondria underscores the crucial role of mitochondrial resilience in determining the whole-animal system's response to thermal stress.

Using a gut–brain–mitochondria framework to understand heat stress broadens the scope for interventions beyond conventional management strategies. Nutritional modulation of the gut microbiota, early-life programming strategies, and genomic selection for thermotolerance and mitochondrial efficiency are novel, complementary, and thus promising ways of enhancing resilience, productivity, and disease resistance in poultry. These strategies are becoming increasingly relevant as climate change intensifies heat stress. Moving forward, climate-smart research should adopt a systems-biology perspective. *In vivo* experiments, combined with multi-omics technologies, standardised biomarkers, and AI models, will play a significant role in understanding heat stress physiology and in generating mechanistic insights that could lead to the development of scalable solutions. This comprehensive framework would facilitate the poultry industry's transition to sustainable production systems that protect the health and performance of birds.

Heat stress disrupts gut, brain, and mitochondrial function in poultry, with immune, hormonal, and metabolic signals reinforcing systemic dysfunction.

Heat stress triggers gut barrier failure, dysbiosis, neuroendocrine changes, and mitochondrial damage, creating feedback loops that impair poultry health.

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References

- Abbas, G., Arshad, M., Tanveer, A. J., Jabbar, M. A., Arshad, M., Al-Taey, D. K. A., Mahmood, A., Khan, M. A., Konca, Y., Sultan, Z., & Qureshi, R. A. (2021). Combating heat stress in laying hens: A review. *Pakistan Journal of Science*, 73(4), 633–655. <http://pjosr.com/index.php/pjs/article/view/365>
- Abbass, G., & Abid, A. R. (2023). Effect of peppermint, fenugreek and their mixture on production traits of heat-stressed broiler chickens. *Journal of Survey in Fisheries Sciences*, 10(3S), 2704–2716.
- Abd El-Ghany, W. A., & Babazadeh, D. (2022). Betaine: A potential nutritional metabolite in the poultry industry. *Animals*, 12(19), Article 2624. doi: 10.3390/ani12192624
- Abd El-Hack, M. E., El-Saadony, M. T., Alqhtani, A. H., Swelum, A. A., Salem, H. M., Elbestawy, A. R., Noreldin, A. E., Babalghith, A. O., Khafaga, A. F., Hassan, M. I., & El-Tarabily, K. A. (2022). The relationship among avian influenza, gut microbiota and chicken immunity: An updated overview. *Poultry Science*, 101(9), Article 102021. doi: 10.1016/j.psj.2022.102021

- Abdelqader, A. M., Abuajamieh, M., Hammad, H. M., & Al-Fataftah, A.-R. A. (2017). Effects of dietary butyrate supplementation on intestinal integrity of heat-stressed cockerels. *Journal of Animal Physiology and Animal Nutrition*, 101(6), 1115–1121. doi: 10.1111/jpn.12622
- Agus, A., Clément, K., & Sokol, H. (2021). Gut microbiota-derived metabolites as central regulators in metabolic disorders. *Gut*, 70(6), 1174–1182. doi: 10.1136/gutjnl-2020-323071
- Ahmad, R., Yu, Y. H., Hsiao, F. S., Su, C. H., Liu, H. C., Tobin, I., Zhang, G., & Cheng, Y. H. (2022). Influence of heat stress on poultry growth performance, intestinal inflammation, and immune function and potential mitigation by probiotics. *Animals*, 12(17), Article 2297. doi: 10.3390/ani12172297
- Ajayi, O., Akosile, O. A., Oso, A. O., & Oke, O. E. (2024). Thermotolerance in broiler chickens: Evaluating the influence of embryonic thermal manipulation and *in ovo* feeding of lysine and cysteine in a hot tropical environment. *The Journal of Agricultural Sciences*, 19(3), 517–529. doi: 10.4038/jas.v19i3.10245.
- Akbarian, A., Michiels, J., Degroote, J., Majdeddin, M., Golian, A., & De Smet, S. (2016). Association between heat stress and oxidative stress in poultry; mitochondrial dysfunction and dietary interventions with phytochemicals. *Journal of Animal Science and Biotechnology*, 7, Article 37.
- Alemka, A., Corcionivoschi, N., & Bourke, B. (2012). Defense and adaptation: The complex inter-relationship between *Campylobacter jejuni* and mucus. *Frontiers in Cellular and Infection Microbiology*, 2, Article 15. doi: 10.3389/fcimb.2012.00015
- Alhenaky, A., Abdelqader, A., Abuajamieh, M., & Al-Fataftah, A.-R. (2017). The effect of heat stress on intestinal integrity and *Salmonella* invasion in broiler birds. *Journal of Thermal Biology*, 70, 9–14. doi: 10.1016/j.jtherbio.2017.10.015
- An, B., Liu, P., Yang, Z., Ying, F., Liu, D., Wen, J., & Zhao, G. (2025). Integrative transcriptomics and metabolomics reveal neuroendocrine-lipid crosstalk and adenosine signaling in broiler under heat stress. *BMC Genomics*, 26(1), Article 699. doi: 10.1186/s12864-025-11881-7
- Aresti Sanz, J., & El Aidy, S. (2019). Microbiota and gut neuropeptides: A dual action of antimicrobial activity and neuroimmune response. *Psychopharmacology*, 236(5), 1597–1609. doi: 10.1007/s00213-019-05224-0
- Arnal, M.-E., & Lallès, J.-P. (2016). Gut epithelial inducible heat-shock proteins and their modulation by diet and the microbiota. *Nutrition Reviews*, 74(3), 181–197. doi: 10.1093/nutrit/nuv104
- Aruwa, C. E., Pillay, C., Nyaga, M. M., & Sabiu, S. (2021). Poultry gut health – microbiome functions, environmental impacts, microbiome engineering and advancements in characterization technologies. *Journal of Animal Science and Biotechnology*, 12(1), Article 119. doi: 10.1186/s40104-021-00640-9
- Beckford, R. C., Ellestad, L. E., Proszkowiec-Weglarz, M., Farley, L., Brady, K., Angel, R., Liu, H. C., & Porter, T. E. (2020). Effects of heat stress on performance, blood chemistry, and hypothalamic and pituitary mRNA expression in broiler chickens. *Poultry Science*, 99(12), 6317–6325. doi: 10.1016/j.psj.2020.09.052
- Beldowska, A., Barszcz, M., & Dunislawska, A. (2023). State of the art in research on the gut-liver and gut-brain axis in poultry. *Journal of Animal Science and Biotechnology*, 14(1), Article 53. doi: 10.1186/s40104-023-00853-0
- Bhadauria, P. (2017). Different types of poultry housing system for tropical climate. *Indian Council of Agricultural Research*, 1-68
- Bilal, R. M., Hassan, F., Farag, M. R., Nasir, T. A., Ragni, M., Mahgoub, H. A. M., & Alagawany, M. (2021). Thermal stress and high stocking densities in poultry farms: Potential effects and mitigation strategies. *Journal of Thermal Biology*, 99, Article 102944. doi: 10.1016/j.jtherbio.2021.102944
- Bohler, M., Gilbert, E. R., Cline, M. A. (2020). Reduced food intake during exposure to high ambient temperatures is associated with molecular changes in the nucleus of the hippocampal commissure and the paraventricular and arcuate hypothalamic nuclei. *General and Comparative Endocrinology*, 298, Article 113576.
- Braniste, V., Al-Asmakh, M., Kowal, C., Anuar, F., Abbaspour, A., Tóth, M., Korecka, A., Bakocovic, N., Ng, L. G., Kundu, P., & Gulyás, B. (2014). The gut microbiota influences blood-brain barrier permeability in mice. *Science Translational Medicine*, 6(263), Article 263ra158.
- Burokas, A., Arbolea, S., Moloney, R. D., Peterson, V. L., Murphy, K., Clarke, G., Stanton, C., Dinan, T. G., & Cryan, J. F. (2017). Targeting the Microbiota-Gut-Brain Axis: Prebiotics Have Anxiolytic and Antidepressant-like Effects and Reverse the Impact of Chronic Stress in Mice. *Biological Psychiatry*, 82(7), 472–487. doi: 10.1016/j.biopsych.2016.12.031
- Calefi, A. S., de Siqueira, A., Namazu, L. B., Costola-de-Souza, C., Honda, B. B. T., Ferreira, A. J. P., Quinteiro-Filho, W. M., da Silva Fonseca, J. G., & Palermo-Neto, J. (2016). Effects of heat stress on the formation of splenic germinal centres and immunoglobulins in broilers infected by *Clostridium*

- perfringens type A. *Veterinary Immunology and Immunopathology*, 171, 38–46. doi: 10.1016/j.vetimm.2016.02.004
- Calefi, A. S., Fonseca, J. G. D. S., Nunes, C. A. Q., Lima, A. P. N., Quinteiro-Filho, W. M., Flório, J. C., Zager, A., Ferreira, A. J. P., & Palermo-Neto, J. (2019). Heat stress modulates brain monoamines and their metabolites production in broiler chickens co-infected with *Clostridium perfringens* Type A and *Eimeria* spp. *Veterinary Sciences*, 6(1), Article 4. doi: 10.3390/vetsci6010004
- Cao, C., Chowdhury, V. S., Cline, M. A., & Gilbert, E. R. (2021). The microbiota-gut-brain axis during heat stress in chickens: A review. *Frontiers in Physiology*, 12, Article 752265. doi: 10.3389/fphys.2021.752265
- Carabotti, M., Scirocco, A., Maselli, M. A., & Severi, C. (2015). The gut-brain axis: Interactions between enteric microbiota, central and enteric nervous systems. *Annals of Gastroenterology*, 28(2), 203–209.
- Chalvon-Demersay, T., Yamphet, T., Srinongkote, S., Ohara, H., & Lambert, W. (2021). Supplementing functional amino acids and polyphenols at low dose can restore performance and amino acid digestibility in broilers challenged with coccidiosis. *Livestock Science*, 254, Article 104769. doi: 10.1016/j.livsci.2021.104769
- Chen, J., & Vitetta, L. (2020). The role of butyrate in attenuating pathobiont-induced hyperinflammation. *Immune Network*, 20(2), Article e15. doi: 10.4110/in.2020.20.e15
- Chen, S., Liu, H., Zhang, J., Zhou, B., He, X., Wang, T., & Wang, C. (2023). Dietary rutin improves breast meat quality in heat-stressed broilers and protects mitochondria from oxidative attack via the AMPK/PINK1-Parkin pathway. *Journal of the Science of Food and Agriculture*, 103(5), 2367–2377. doi: 10.1002/jsfa.12431
- Cheng, C. Y., Tu, W. L., Chen, C. J., Chan, H. L., Chen, C. F., Chen, H. H., Tang, P. C., Lee, Y. P., Chen, S. E., & Huang, S. Y. (2018). Functional genomics study of acute heat stress response in the small yellow follicles of layer-type chickens. *Scientific Reports*, 8(1), Article 872. doi: 10.1038/s41598-017-18335-5
- Choi, D.W., Lim, M.S., Lee, J.W., Chun, W., Lee, S.H., Nam, Y.H., Park, J.M., Choi, D.H., Kang, C.D., Lee, S.J., & Park, S.C. (2015). The cytotoxicity of kahweol in HT-29 human colorectal cancer cells is mediated by apoptosis and suppression of heat shock protein 70 expression. *Biomolecules & Therapeutics*, 23(2), 128–133.
- Costa, M. C., Bessegatto, J. A., Alfieri, A. A., Weese, J. S., Filho, J. A. B., & Oba, A. (2017). Different antibiotic growth promoters induce specific changes in the cecal microbiota membership of broiler chicken. *PLoS One*, 12(2), e0171642. doi: 10.1371/journal.pone.0171642
- Cryan, J. F., & Dinan, T. G. (2012). Mind-altering microorganisms: The impact of the gut microbiota on brain and behaviour. *Nature Reviews Neuroscience*, 13(10), 701–712. doi: 10.1038/nrn3346
- Cryan, J. F., O’Riordan, K. J., Cowan, C. S., Sandhu, K. V., Bastiaanssen, T. F., Boehme, M., Codagnone, M.G., Cusotto, S., Fulling, C., Golubeva, A.V., & Guzzetta, K.E. (2019). The microbiota–gut–brain axis. *Physiological Reviews*, 99(4), 1877–2013. doi: 10.1152/physrev.00018.2018
- Cuadrado, M., & Dridi, S. (2024). Impact of heat stress on poultry production: Feed intake, water homeostasis, gut integrity, and meat quality. *German Journal of Veterinary Research*, 4(4), 43–51. doi: 10.51585/gjvr.2024.4.0108
- Dalile, B., Van Oudenhove, L., Vervliet, B., & Verbeke, K. (2019). The role of short-chain fatty acids in microbiota–gut–brain communication. *Nature Reviews Gastroenterology & Hepatology*, 16(8), 461–478.
- Danzeisen, J. L., Kim, H. B., Isaacson, R. E., Tu, Z. J., & Johnson, T. J. (2011). Modulations of the chicken cecal microbiome and metagenome in response to anticoccidial and growth promoter treatment. *PLoS One*, 6(11), e27949. doi: 10.1371/journal.pone.0027949
- de Oliveira, M. R., Nabavi, S. F., Habtemariam, S., Erdogan Orhan, I., Daglia, M., & Nabavi, S. M. (2015). The effects of baicalin and baicalin on mitochondrial function and dynamics: A review. *Pharmacological Research*, 100, 296–308. doi: 10.1016/j.phrs.2015.08.021
- Del Vesco, A. P., Gasparino, E., Zancanela, V., Grieser, D. O., Stanquevis, C. E., Pozza, P. C., & Oliveira Neto, A. R. (2016). Effects of selenium supplementation on the oxidative state of acute heat stress-exposed quails. *Journal of Animal Physiology and Animal Nutrition*, 101(1), 170–179. doi: 10.1111/jpn.12437
- Díaz Carrasco, J. M., Casanova, N. A., & Fernández Miyakawa, M. E. (2019). Microbiota, gut health and chicken productivity: *What is the connection?* *Microorganisms*, 7(10), 374. doi: 10.3390/microorganisms7100374
- Ding, J., Zhao, L., Wang, L., Zhao, W., Zhai, Z., Leng, L., Wang, Y., He, C., Zhang, Y., Zhang, H., Li, H., & Meng, H. (2016). Divergent selection-induced obesity alters the composition and functional pathways of chicken gut microbiota. *Genetics Selection Evolution*, 48(1), 93. doi: 10.1186/s12711-016-0270-5
- Dowlati, Y., Herrmann, N., Swardfager, W., Liu, H., Sham, L., Reim, E. K., & Lanctôt, K. L. (2010). A meta-

- analysis of cytokines in major depression. *Biological Psychiatry*, 67(5), 446–457. doi: 10.1016/j.biopsych.2009.09.033
- Du, E., Wang, W., Gan, L., Li, Z., Guo, S., & Guo, Y. (2016). Effects of thymol and carvacrol supplementation on intestinal integrity and immune responses of broiler chickens challenged with *Clostridium perfringens*. *Journal of Animal Science and Biotechnology*, 7, 19. doi: 10.1186/s40104-016-0079-7
- Ducatelle, R., Goossens, E., Eeckhaut, V., & Van Immerseel, F. (2023). Poultry gut health and beyond. *Animal Nutrition*, 13, 240–248. doi: 10.1016/j.aninu.2023.03.005
- Eeckhaut, V., Van Immerseel, F., Croubels, S., De Baere, S., Haesebrouck, F., Ducatelle, R., Louis, P., & Vandamme, P. (2011). Butyrate production in phylogenetically diverse Firmicutes isolated from the chicken caecum. *Microbial Biotechnology*, 4(4), 503–512. doi: 10.1111/j.1751-7915.2010.00244.x
- El Aidy, S., Stilling, R., Dinan, T. G., & Cryan, J. F. (2016). Microbiome to brain: Unravelling the multidirectional axes of communication. In T. G. Lyte, & J. F. Cryan (Eds.), *Microbial Endocrinology: Interkingdom Signaling in Infectious Disease and Health* (pp. 301–336). Springer. doi: 10.1007/978-3-319-20215-0_15
- Eletu, T. A., Anjola, I. A., Fasasi, L. O., Fadipe, D. P., Afuye, A. T., Fasanya, F. O., & Oke, O. E. (2026). Heat stress in quail: Impacts on health and productivity, and strategies for mitigation. *Animal Research and One Health*, 1–19. doi: 10.1002/aro2.70061
- Eletu, T. A., Idowu, O. P. A., Adeyeye, E. A., Olatunbosun, O., & Adesope, A. I. (2025, October 27). *In ovo* vitamin B6 supplementation at different embryonic days influences duodenal morphology in guinea fowls. *Proceedings of the 30th Annual Conference of the Animal Science Association of Nigeria (ASAN)*, (pp. 580–583).
- Emami, N. K., Greene, E. S., Kogut, M. H., & Dridi, S. (2021). Heat stress and feed restriction distinctly affect performance, carcass and meat yield, intestinal integrity, and inflammatory (chemo)cytokines in broiler chickens. *Frontiers in Physiology*, 12, 707757. doi: 10.3389/fphys.2021.707757
- Forsythe, P., & Kunze, W. A. (2013). Voices from within: Gut microbes and the CNS. *Cellular and Molecular Life Sciences*, 70(1), 55–69. doi: 10.1007/s00018-012-1028-z
- Fouad, A. M., Chen, W., Ruan, D., Wang, S., Xia, W. G., & Zheng, C. T. (2016). Impact of heat stress on meat, egg quality, immunity and fertility in poultry and nutritional factors that overcome these effects: A review. *International Journal of Poultry Science*, 15(3), 81–95. doi: 10.3923/ijps.2016.81.95
- Frost, G., Sleeth, M. L., Sahuri-Arisoylu, M., Lizarbe, B., Cerdan, S., Brody, L., Anastasovska, J., Ghourab, S., Hankir, M., Zhang, S., Carling, D., Swann, J. R., Gibson, G., Viardot, A., Morrison, D., Thomas, E. L., & Bell, J. D. (2014). The short-chain fatty acid acetate reduces appetite via a central homeostatic mechanism. *Nature Communications*, 5, 3611. doi: 10.1038/ncomms4611
- Frost, R. A., & Lang, C. H. (2008). Regulation of muscle growth by pathogen-associated molecules. *Journal of Animal Science*, 86(Suppl. 14), E84–E93. doi: 10.2527/jas.2007-0483
- Ganesan, S., Volodina, O., Pearce, S. C., Gabler, N. K., Baumgard, L. H., Rhoads, R. P., & Selsby, J. T. (2017). Acute heat stress activated inflammatory signaling in porcine oxidative skeletal muscle. *Physiological Reports*, 5(16), e13397. doi: 10.14814/phy2.13397
- Geraert, P. A., Padilha, J. C. F., Guillaumin, S. (1996). Metabolic and endocrine changes induced by chronic heat exposure in broiler chickens: Biological and endocrinological variables. *British Journal of Nutrition*, 75(2), 205–216. doi: 10.1017/S0007114596001250
- Giller, K. E., Hijbeek, R., Andersson, J. A., & Sumberg, J. (2021). Regenerative agriculture: An agronomic perspective. *Outlook on Agriculture*, 50(1), 13–25. doi: 10.1177/0030727021998063
- Gitau Gicheha, M. (2021). The effects of heat stress on production, reproduction, health in chicken and its dietary amelioration. In: *Advances in Poultry Nutrition Research*. IntechOpen. doi: 10.5772/intechopen.97284
- Gonzalez-Rivas, P. A., Chauhan, S. S., Ha, M., Fegan, N., Dunshea, F. R., & Warner, R. D. (2020). Effects of heat stress on animal physiology, metabolism, and meat quality: A review. *Meat Science*, 162, 108025. doi: 10.1016/j.meatsci.2019.108025
- Hai, L., Rong, D., & Zhang, Z. Y. (2000). The effect of thermal environment on the digestion of broilers. *Journal of Animal Physiology and Animal Nutrition*, 83(2), 57–64. doi: 10.1046/j.1439-0396.2000.00223.x
- He, X., Lu, Z., Ma, B., Zhang, L., Li, J., Jiang, Y., Zhou, G., & Gao, F. (2019). Chronic heat stress alters hypothalamus integrity, serum indices, and attenuates the expression of hypothalamic appetite genes in broilers. *Journal of Thermal Biology*, 81, 110–117. doi: 10.1016/j.jtherbio.2019.02.025
- Heida, F. H., van Zoonen, A. G., Hulscher, J. B., Te Kieft, B. J., Wessels, R., Kooi, E. M., Bos, A. F., Harmsen, H. J., &

- de Goffau, M. C. (2016). A necrotizing enterocolitis-associated gut microbiota is present in the meconium: Results of a prospective study. *Clinical Infectious Diseases*, 62(7), 863–870. doi: 10.1093/cid/ciw016
- Hillner, K. M., & Gimsa, U. (2024). Adult neurogenesis and the microbiota–gut–brain axis in farm animals: Underestimated and understudied parameters for improving welfare in livestock farming. *Frontiers in Neuroscience*, 18, 1493605. doi: 10.3389/fnins.2024.1493605
- Holzer, P. (2002). Sensory neurone responses to mucosal noxae in the upper gut: Relevance to mucosal integrity and gastrointestinal pain. *Neurogastroenterology & Motility*, 14(5), 459–475. doi: 10.1046/j.1365-2982.2002.00353.x
- Hsiao, E. Y., McBride, S. W., Hsien, S., Sharon, G., Hyde, E. R., McCue, T., Codelli, J. A., Chow, J., Reisman, S. E., Petrosino, J. F., Patterson, P. H., & Mazmanian, S. K. (2013). Microbiota modulate behavioral and physiological abnormalities associated with neurodevelopmental disorders. *Cell*, 155(7), 1451–1463. doi: 10.1016/j.cell.2013.11.024
- Hu, C., Yadnyavalkya, P., Gong, D., Yu, T., Li, J., Wu, L., Liu, X., Yu, Z., Ma, X., Chen, J., Gooneratne, R., Yong, Y., & Ju, X. (2020). Heat stress induced gut microbiota changes activate the TLR4/NF- κ B signaling pathway contributing to inflammatory bowel disease in pigs. *Research Square (Preprint)*. doi: 10.21203/rs.2.21626/v1
- Hu, J. Y., Mohammed, A. A., Murugesan, G. R., & Cheng, H. W. (2022). Effect of a synbiotic supplement as an antibiotic alternative on broiler skeletal, physiological, and oxidative parameters under heat stress. *Poultry Science*, 101(4), 101769. doi: 10.1016/j.psj.2022.101769
- Huang, C., Jiao, H., Song, Z., Zhao, J., Wang, X., & Lin, H. (2015). Heat stress impairs mitochondrial functions and induces oxidative injury in broiler chickens. *Journal of Animal Science*, 93(5), 2144–2153. doi: 10.2527/jas.2014-8739
- Józefiak, D., Rutkowski, A., & Martin, S. A. (2004). Carbohydrate fermentation in the avian ceca: A review. *Animal Feed Science and Technology*, 113(1–4), 1–15. doi: 10.1016/j.anifeeds.2003.09.007
- Juiputta, J., Chankitisakul, V., & Boonkum, W. (2023). Appropriate genetic approaches for heat tolerance and maintaining good productivity in tropical poultry production: A review. *Veterinary Sciences*, 10(10), 591. doi: 10.3390/vetsci10100591
- Kamada, N., Seo, S. U., Chen, G. Y., & Núñez, G. (2013). Role of the gut microbiota in immunity and inflammatory disease. *Nature Reviews Immunology*, 13(5), 321–335. doi: 10.1038/nri3430
- Karl, J. P., Hatch, A. M., Arcidiacono, S. M., Pearce, S. C., Pantoja-Feliciano, I. G., Doherty, L. A., & Soares, J. W. (2018). Effects of psychological, environmental and physical stressors on the gut microbiota. *Frontiers in Microbiology*, 9, 2013. doi: 10.3389/fmicb.2018.02013
- Kennedy, G. M., Lichoti, J. K., & Ommeh, S. C. (2022). Heat stress and poultry: Adaptation to climate change, challenges and opportunities for genetic breeding in Kenya. *Journal of Agriculture, Science and Technology*, 21(1), 49–61. doi: 10.4314/jagst.v21i1.6
- Kikusato, M., & Toyomizu, M. (2013). Crucial role of membrane potential in heat stress-induced overproduction of reactive oxygen species in avian skeletal muscle mitochondria. *PLoS One*, 8(5), e64412. doi: 10.1371/journal.pone.0064412
- Kikusato, M., & Toyomizu, M. (2023). Mechanisms underlying the effects of heat stress on intestinal integrity, inflammation, and microbiota in chickens. *The Journal of Poultry Science*, 60(2), 2023021. doi: 10.2141/jpsa.2023021
- Kraimi, N., Dawkins, M., Gebhardt-Henrich, S. G., Velge, P., Rychlik, I., Volf, J., Creach, P., Smith, A., Colles, F., & Leterrier, C. (2019). Influence of the microbiota–gut–brain axis on behavior and welfare in farm animals: A review. *Physiology & Behavior*, 210, 112658. doi: 10.1016/j.physbeh.2019.112658
- Lambert, G. P. (2009). Stress-induced gastrointestinal barrier dysfunction and its inflammatory effects. *Journal of Animal Science*, 87(14 Suppl), E101–E108. doi: 10.2527/jas.2008-1339
- Lan, P. T. N., Sakamoto, M., & Benno, Y. (2004). Effects of two probiotic Lactobacillus strains on jejunal and cecal microbiota of broiler chicken under acute heat stress condition as revealed by molecular analysis of 16S rRNA genes. *Microbiology and Immunology*, 48(12), 917–929. doi: 10.1111/j.1348-0421.2004.tb03620.x
- Lara, L. J., & Rostagno, M. H. (2013). Impact of heat stress on poultry production. *Animals*, 3(2), 356–369. doi: 10.3390/ani3020356
- Lavelle, A., & Sokol, H. (2020). Gut microbiota-derived metabolites as key actors in inflammatory bowel disease. *Nature Reviews Gastroenterology & Hepatology*, 17(4), 223–237. doi: 10.1038/s41575-019-0258-z
- Lee, C., Kim, J. H., & Kil, D. Y. (2022). Comparison of stress biomarkers in laying hens raised under a long-term multiple stress condition. *Poultry Science*, 101(6), 101868. doi: 10.1016/j.psj.2022.101868
- Li, Z., Quan, G., Jiang, X., Yang, Y., Ding, X., Zhang, D., Wang, X., Hardwidge, P. R., Ren, W., & Zhu, G. (2018). Effects of metabolites derived from gut microbiota and

- hosts on pathogens. *Frontiers in Cellular and Infection Microbiology*, 8, 314. doi: 10.3389/fcimb.2018.00314
- Liao, H., Zhang, L., Li, J., Xing, T., & Gao, F. (2022). Acute stress deteriorates breast meat quality of Ross 308 broiler chickens by inducing redox imbalance and mitochondrial dysfunction. *Journal of Animal Science*, 100(9), skac221. doi: 10.1093/jas/skac221
- Lin, H., Sui, S. J., Jiao, H. C., Buyse, J., & Decuyper, E. (2006). Impaired development of broiler chickens by stress mimicked by corticosterone exposure. *Comparative Biochemistry and Physiology Part A: Molecular & Integrative Physiology*, 143(3), 400–405. doi: 10.1016/j.cbpa.2005.12.030
- Liu, W. C., Zhu, Y. R., Zhao, Z. H., Jiang, P., & Yin, F. Q. (2021). Effects of dietary supplementation of algae-derived polysaccharides on morphology, tight junctions, antioxidant capacity and immune response of duodenum in broilers under heat stress. *Animals*, 11(8), 2279. doi: 10.3390/ani11082279
- Lyte, M., Varcoe, J. J., & Bailey, M. T. (1998). Anxiogenic effect of subclinical bacterial infection in mice in the absence of overt immune activation. *Physiology & Behavior*, 65(1), 63–68. doi: 10.1016/S0031-9384(98)00145-0
- Ma, B., Zhang, L., Li, J., Xing, T., Jiang, Y., & Gao, F. (2021). Heat stress alters muscle protein and amino acid metabolism and accelerates liver gluconeogenesis for energy supply in broilers. *Poultry Science*, 100(1), 215–223. doi: 10.1016/j.psj.2020.09.090
- Ma, Y., Liu, T., Chen, S., Shen, H., & Wang, J. (2025). Dietary supplementation with L-citrulline improves amino acid composition and broiler performance, and modulates gut microbiota. *Frontiers in Microbiology*, 16, 1551012. doi: 10.3389/fmicb.2025.1551012
- Madkour, M., Hosny, M., Aboelazab, O., Fahmy, S., Rayan, G. N., Ali, A. H. H., Abdel Moati, Y. A., Elolimy, A. A., & Fathi, M. M. (2025). Dietary encapsulated essential oils improve growth performance and regulate stress-responsive genes in heat-stressed broilers. *Journal of Animal Science*, 103, skaf417. doi: 10.1093/jas/skaf417
- Mahmoud, U. T., Abdel-Rahman, M. A., & Darwish, M. H. (2014). Effects of propolis, ascorbic acid and vitamin E on thyroid and corticosterone hormones in heat-stressed broilers. *Journal of Advanced Veterinary Research*, 4(1), 18–27.
- Majekodunmi, B. C., Wheto, M., Oke, O. E., Akinjute, O. F., Ojoawo, H. T., Chika, C. R., Adekunle, O. M., Adeyeri, Y. O., & Abioja, M. O. (2025). Thermoregulatory response, growth performance and organ weights of FUNAAB-Alpha chicken genotypes administered sweet citrus peel powder. *Journal of Animal Physiology and Animal Nutrition*, 109(4), 916–925. doi: 10.1111/jpn.14106
- Margineanu, M. B., Sherwin, E., Golubeva, A., Peterson, V., Hoban, A., Fiumelli, H., Rea, K., Cryan, J. F., & Magistretti, P. J. (2020). Gut microbiota modulates expression of genes involved in the astrocyte-neuron lactate shuttle in the hippocampus. *European Neuropsychopharmacology*, 41, 152–159. doi: 10.1016/j.euroneuro.2020.11.006
- Mazzoni, M., Zampiga, M., Clavenzani, P., Lattanzio, G., Tagliavia, C., & Sirri, F. (2022). Effect of chronic heat stress on gastrointestinal histology and expression of feed intake-regulatory hormones in broiler chickens. *Animal*, 16(8), 100600. doi: 10.1016/j.animal.2022.100600
- Mignon-Grasteau, S., Moreri, U., Narcy, A., Rousseau, X., Rodenburg, T. B., Tixier-Boichard, M., & Zerjal, T. (2015). Robustness to chronic heat stress in laying hens: A meta-analysis. *Poultry Science*, 94(4), 586–600. doi: 10.3382/ps/pev028
- Mishra, B., & Jha, R. (2019). Oxidative stress in the poultry gut: Potential challenges and interventions. *Frontiers in Veterinary Science*, 6, 60. doi: 10.3389/fvets.2019.00060
- Mitchell, M. A., & Carlisle, A. J. (1992). The effects of chronic exposure to elevated environmental temperature on intestinal morphology and nutrient absorption in the domestic fowl (*Gallus domesticus*). *Comparative Biochemistry and Physiology Part A: Comparative Physiology*, 101(1), 137–142. doi: 10.1016/0300-9629(92)90641-3
- Mujahid, A., Akiba, Y., & Toyomizu, M. (2007). Acute heat stress induces oxidative stress and decreases adaptation in young White Leghorn cockerels by downregulation of avian uncoupling protein. *Poultry Science*, 86(2), 364–371. doi: 10.1093/ps/86.2.364
- Mujahid, A., Sato, K., Akiba, Y., & Toyomizu, M. (2006). Acute heat stress stimulates mitochondrial superoxide production in broiler skeletal muscle, possibly via downregulation of uncoupling protein content. *Poultry Science*, 85(7), 1259–1265. doi: 10.1093/ps/85.7.1259
- Naeem, M., Jia, Z., Wang, J., Poudel, S., Manjankattil, S., Adhikari, Y., Bailey, M., & Bourassa, D. (2025). Advancements in machine learning applications in poultry farming: A literature review. *Journal of Applied Poultry Research*, 34(4), 100602. doi: 10.1016/j.japr.2025.100602
- Nanto-Hara, F., Kikusato, M., Ohwada, S., & Toyomizu, M. (2020). Heat stress directly affects intestinal integrity

- in broiler chickens. *The Journal of Poultry Science*, 57(4), 284–290. doi: 10.2141/jpsa.0190004
- Nawaz, A. H., Amoah, K., Leng, Q. Y., Zheng, J. H., Zhang, W. L., & Zhang, L. (2021). Poultry response to heat stress: Its physiological, metabolic, and genetic implications on meat production and quality. *World's Poultry Science Journal*, 77(3), 491–508.
- Oke, O. E. (2018). Evaluation of physiological response and performance by supplementation of *Curcuma longa* in broiler feed under hot humid tropical climate. *Tropical Animal Health and Production*, 50, 1071–1077. doi: 10.1007/s11250-018-1532-8
- Oke, O. E., Akosile, O. A., Oni, A. I., Opopwoye, I. O., Ishola, C. A., Adebisi, J. O., Odeyemi, A. J., Adjei-Mensah, B., Uyanga, V. A., & Abioja, M. O. (2024a). Oxidative stress in poultry production. *Poultry Science*, 103(9), 104003. doi: 10.1016/j.psj.2024.104003
- Oke, O. E., Akosile, O. A., Uyanga, V. A., Oke, F. O., Oni, A. I., Tona, K., & Onagbesan, O. M. (2024b). Climate change and broiler production. *Veterinary Medicine and Science*, 10, e1416. doi: 10.1002/vms3.1416
- Oke, O. E., Emeshili, U. K., Iyasere, O. S., Abioja, M. O., Daramola, J. O., Ladokun, A. O., Abiona, J. A., Williams, T. J., Rahman, S. A., Rotimi, S. O., Balogun, S. I., & Adejuyigbe, A. E. (2017). Physiological responses and performance of broiler chickens offered olive leaf extract under hot humid tropical climate. *Journal of Applied Poultry Research*, 26(3), 376–382. doi: 10.3382/japr/pfx005
- Oke, O. E., Fasasi, L. O., Opopwoye, I. O., & Akosile, O. A. (2025a). The role of gut microbiota-derived metabolites in modulating poultry immunometabolism. *Frontiers in Physiology*, 16, 1700406. doi: 10.3389/fphys.2025.1700406
- Oke, O. E., Oni, A. I., Akosile, O. A., Oliyide, K. M., Ishola, C. A., Logunleko, M. O., Jimoh, O. A., Njoku, C. P., Fasasi, L. O., & Uyanga, V. A. (2025b). Heat stress and gut microbiome dynamics in poultry: Interplay, consequences, and mitigation strategies. *Animal Research and One Health*, 3, 1–20. doi: 10.1002/aro2.70046
- Oke, O. E., Oyelola, O. B., Iyasere, O. S., Njoku, C. P., Oso, A. O., Oso, O. M., Fatoki, S. T., Bankole, K. O., Jimoh, I. O., Sybill, N. I., Awodipe, H. O., Adegbite, H. O., Rahman, S. A., & Daramola, J. O. (2021). *In ovo* injection of black cumin (*Nigella sativa*) extract on hatching and post-hatch performance of thermally challenged broiler chickens during incubation. *Poultry Science*, 100, 100831. doi: 10.1016/j.psj.2020.10.072
- Oke, O. E., Uyanga, V. A., Oretomiloye, F., & Abioja, M. O. (2025c). Editorial: Climate-smart livestock production: Strategies for enhanced sustainability and resilience. *Frontiers in Veterinary Science*, 12, 1638289. doi: 10.3389/fvets.2025.1638289
- Olayiwola, S. F., & Adedokun, S. A. (2025). Heat stress in poultry: The role of nutritional supplements in alleviating heat stress and enhancing gut health in poultry. *Frontiers in Veterinary Science*, 12, 1691532. doi: 10.3389/fvets.2025.1691532
- Oloyo, A., & Ojerinde, A. (2020). Poultry housing and management. In *Poultry – An Advanced Learning*. IntechOpen. doi: 10.5772/intechopen.83811
- Onagbesan, O. M., Uyanga, V. A., Oso, O., Tona, K., & Oke, O. E. (2023). Alleviating heat stress effects in poultry: Updates on methods and mechanisms of actions. *Frontiers in Veterinary Science*, 10, 1255520. doi: 10.3389/fvets.2023.1255520
- Oni, A. I., & Oke, O. E. (2025). Gut health modulation through phytochemicals in poultry: Mechanisms, benefits, and applications. *Frontiers in Veterinary Science*, 12, 1616734. doi: 10.3389/fvets.2025.1616734
- Oni, A. I., Abiona, J. A., Fafiolu, A. O., & Oke, O. E. (2024a). Early-age thermal manipulation and supplemental antioxidants on physiological, biochemical and productive performance of broiler chickens in hot-tropical environments. *Stress*, 27, 2319803. doi: 10.1080/10253890.2024.2319803
- Oni, A. I., Adeleye, O. O., Adebawale, T. O., & Oke, O. E. (2024b). The roles of phytochemical feed additives in stress mitigation in broiler chickens. *Journal of Animal Physiology and Animal Nutrition*, 108(1), 81–98. doi: 10.1111/jpn.13869
- Oni, A. I., Bello, Y. O., Ibhigami, D. J., Ishola, C. A., Adesanya, S. O., Adeniran, D. A., & Oke, O. E. (2025). Effects of early-age feed restriction and thermal conditioning on the physiological and performance responses of broiler chickens under heat stress. *Scientific Reports*, 15, 28653. doi: 10.1038/s41598-025-01048-5
- Ouyang, J., Zhou, H., Li, Q., Zheng, J., Chen, C., Guo, S., You, J., & Li, G. (2022). Tryptophan alleviates acute heat stress-induced impairment of antioxidant status and mitochondrial function in broilers. *Frontiers in Veterinary Science*, 9, 863156. doi: 10.3389/fvets.2022.863156
- Oyelola, O. B., Iyasere, O. S., Adeleye, O. O., & Oke, O. E. (2024). The influence of *in ovo* black cumin extract on the physiological responses of broilers under hot tropical environments. *Acta Scientiarum. Animal Sciences*, 46, e62653. doi: 10.4025/actascianimsci.v46i1.62653
- Panda, A. K., Rao, S. V. R., Raju, M. V. L. N., & Sunder, G. S. (2009). Effect of butyric acid on performance, gastrointestinal tract health and carcass characteristics in

- broiler chickens. *Asian-Australasian Journal of Animal Sciences*, 22(7), 1026–1031. doi: 10.5713/ajas.2009.80298
- Parvin, R., Mushtaq, M. M. H., Kim, M. J., & Choi, H. C. (2014). Light emitting diode (LED) as a source of monochromatic light: A novel lighting approach for immunity and meat quality of poultry. *World's Poultry Science Journal*, 70(3), 557–562. doi: 10.1017/S0043933914000609
- Patra, A. K., & Kar, I. (2021). Heat stress on microbiota composition, barrier integrity, and nutrient transport in gut, production performance, and its amelioration in farm animals. *Journal of Animal Science and Technology*, 63(2), 211–247. doi: 10.5187/jast.2021.e48
- Picard, M., McEwen, B. S., Epel, E. S., & Sandi, C. (2018). An energetic view of stress: Focus on mitochondria. *Frontiers in Neuroendocrinology*, 49, 72–85. doi: 10.1016/j.yfrne.2018.01.001
- Pollock, H. S., Brawn, J. D., & Cheviron, Z. A. (2021). Heat tolerances of temperate and tropical birds and their implications for susceptibility to climate warming. *Functional Ecology*, 35(1), 93–104. doi: 10.1111/1365-2435.13693
- Prince, L. R., Allen, L., Jones, E. C., Hellewell, P. G., Dower, S. K., Whyte, M. K. B., & Sabroe, I. (2004). The role of interleukin-1 β in direct and Toll-like receptor 4-mediated neutrophil activation and survival. *The American Journal of Pathology*, 165(5), 1819–1826. doi: 10.1016/S0002-9440(10)63437-2
- Quinteiro-Filho, W. M., Calefi, A. S., Cruz, D. S. G., Aloia, T. P. A., Zager, A., Astolfi-Ferreira, C. S., ..., Palermo-Neto, J. (2017). Heat stress decreases expression of the cytokines, avian β -defensins 4 and 6 and Toll-like receptor 2 in broiler chickens infected with *Salmonella* Enteritidis. *Veterinary Immunology and Immunopathology*, 186, 19–28. doi: 10.1016/j.vetimm.2017.02.006
- Quinteiro-Filho, W. M., Gomes, A. V. S., Pinheiro, M. L., Ribeiro, A., Ferraz-de-Paula, V., Astolfi-Ferreira, C. S., ..., Palermo-Neto, J. (2012). Heat stress impairs performance and induces intestinal inflammation in broiler chickens infected with *Salmonella* Enteritidis. *Avian Pathology*, 41(5), 421–427. doi: 10.1080/03079457.2012.709315
- Quinteiro-Filho, W. M., Ribeiro, A., Ferraz-de-Paula, V., Pinheiro, M. L., Sakai, M., Sá, L. R. M. D., ..., Palermo-Neto, J. (2010). Heat stress impairs performance parameters, induces intestinal injury, and decreases macrophage activity in broiler chickens. *Poultry Science*, 89(9), 1905–1914. doi: 10.3382/ps.2010.00812
- Rao, R., & Samak, G. (2012). Role of glutamine in protection of intestinal epithelial tight junctions. *Journal of Epithelial Biology and Pharmacology*, 5(Suppl. 1-M7), 47–54. doi: 10.2174/1875044301205010047
- Renaudeau, D., Collin, A., Yahav, S., De Babilio, V., Gourdiere, J. L., & Collier, R. J. (2012). Adaptation to hot climate and strategies to alleviate heat stress in livestock production. *Animal*, 6(5), 707–728. doi: 10.1017/S1751731111002448
- Rhee, S. H., Pothoulakis, C., & Mayer, E. A. (2009). Principles and clinical implications of the brain–gut–enteric microbiota axis. *Nature Reviews Gastroenterology & Hepatology*, 6(5), 306–314. doi: 10.1038/nrgastro.2009.35
- Rhoads, R. P., Baumgard, L. H., & Suagee, J. K. (2013). 2011 and 2012 early careers achievement awards: Metabolic priorities during heat stress with an emphasis on skeletal muscle. *Journal of Animal Science*, 91(6), 2492–2503. doi: 10.2527/jas.2012-6120
- Romano, A., Possenti, C. D., Caprioli, M., De Felice, B., Rubolini, D., & Parolini, M. (2021). Prenatal yolk corticosterone exposure promotes skeletal growth and induces oxidative imbalance in yellow-legged gull embryos. *Journal of Experimental Biology*, 224(22). doi: 10.1242/jeb.242943
- Rostagno, M. H. (2020). Effects of heat stress on the gut health of poultry. *Journal of Animal Science*, 98(4), skaa090. doi: 10.1093/jas/skaa090
- Ruff, J., Barros, T. L., Tellez, G., Jr., Blankenship, J., Lester, H., Graham, B. D., Selby, C. A. M., Vuong, C. N., Dridi, S., Greene, E. S., Hernandez-Velasco, X., Hargis, B. M., & Tellez-Isaias, G. (2020). Research note: Evaluation of a heat stress model to induce gastrointestinal leakage in broiler chickens. *Poultry Science*, 99(3), 1687–1692. doi: 10.1016/j.psj.2019.10.075
- Saeed, M., Abbas, G., Alagawany, M., Kamboh, A. A., Abd El-Hack, M. E., Khafaga, A. F., & Chao, S. (2019). Heat stress management in poultry farms: A comprehensive overview. *Journal of Thermal Biology*, 84, 414–425. doi: 10.1016/j.jtherbio.2019.07.025
- Salahi, A., Abd El-Ghany, W. A., Attia, Y. A., Zabermaawi, N. M., Bovera, F., & Tufarelli, V. (2025). Gut dysbiosis: Nutritional causes and risk prevention in poultry, with reference to other animals. *South African Journal of Animal Science*, 55(2), 32–63. doi: 10.4314/sajas.v55i2.01
- Santos, R. R., Awati, A., Roubos-van den Hil, P. J., Tersteeg-Zijderfeld, M. H., Koolmees, P. A., & Fink-Gremmels, J. (2015). Quantitative histomorphometric analysis of heat stress-related damage in the small intestines of

- broiler chickens. *Avian Pathology*, 44(1), 19–22. doi: 10.1080/03079457.2014.988122
- Saracila, M., Panaite, T. D., Predescu, N. C., Untea, A. E., & Vlaicu, P. A. (2023). Effect of dietary salicin standardized extract from *Salix alba* bark on oxidative stress biomarkers and intestinal microflora of broiler chickens exposed to heat stress. *Agriculture*, 13(3), 698. doi: 10.3390/agriculture13030698
- Scanes, C. G. (2016). Biology of stress in poultry with emphasis on glucocorticoids and the heterophil to lymphocyte ratio. *Poultry Science*, 95(9), 2208–2215. doi: 10.3382/ps/pew137
- Shi, D., Bai, L., Qu, Q., Zhou, S., Yang, M., Guo, S., Li, Q., & Liu, C. (2019). Impact of gut microbiota structure in heat-stressed broilers. *Poultry Science*, 98(6), 2405–2413. doi: 10.3382/ps/pez026
- Shini, S., Kaiser, P., Shini, A., & Bryden, W. L. (2008). Differential alterations in ultrastructural morphology of chicken heterophils and lymphocytes induced by corticosterone and lipopolysaccharide. *Veterinary Immunology and Immunopathology*, 122(1–2), 83–93. doi: 10.1016/j.vetimm.2007.10.009
- Sjofjan, O., Ardiantoro, A., Cahyawati, I. N., Jihana, A. I., Natsir, M. H., Nuningtyas, Y. F., & Adli, D. N. (2025). Microwave-dried black soldier fly larvae enhance growth, intestinal health, and humoral immunity in broiler chickens: A functional feed approach. *Veterinary World*, 1840–1849. doi: 10.14202/vetworld.2025.1840-1849
- Smith, E. A., & Macfarlane, G. T. (1998). Enumeration of amino acid fermenting bacteria in the human large intestine: Effects of pH and starch on peptide metabolism and dissimilation of amino acids. *FEMS Microbiology Ecology*, 25(4), 355–368. doi: 10.1111/j.1574-6941.1998.tb00487.x
- Smith, S. M., & Vale, W. W. (2006). The role of the hypothalamic–pituitary–adrenal axis in neuroendocrine responses to stress. *Dialogues in Clinical Neuroscience*, 8(4), 383–395. doi: 10.31887/DCNS.2006.8.4/ssmith
- Sohail, M. U., Ijaz, A., Yousaf, M. S., Ashraf, K., Zaneb, H., Aleem, M., & Rehman, H. (2010). Alleviation of cyclic heat stress in broilers by dietary supplementation of mannan-oligosaccharide and *Lactobacillus*-based probiotic: Dynamics of cortisol, thyroid hormones, cholesterol, C-reactive protein, and humoral immunity. *Poultry Science*, 89(9), 1934–1938. doi: 10.3382/ps.2010-00751
- Sommer, F., & Bäckhed, F. (2013). The gut microbiota—masters of host development and physiology. *Nature Reviews Microbiology*, 11(4), 227–238. doi: 10.1038/nrmicro2974
- Song, J., Xiao, K., Ke, Y. L., Jiao, L. F., Hu, C. H., Diao, Q. Y., Shi, B., & Zou, X. T. (2014). Effect of a probiotic mixture on intestinal microflora, morphology, and barrier integrity of broilers subjected to heat stress. *Poultry Science*, 93(3), 581–588. doi: 10.3382/ps.2013-03455
- Song, Z. H., Cheng, K., Zheng, X. C., Ahmad, H., Zhang, L. L., & Wang, T. (2018). Effects of dietary supplementation with enzymatically treated *Artemisia annua* on growth performance, intestinal morphology, digestive enzyme activities, immunity, and antioxidant capacity of heat-stressed broilers. *Poultry Science*, 97(2), 430–437. doi: 10.3382/ps/pex312
- Stanley, D., Hughes, R. J., & Moore, R. J. (2014). Microbiota of the chicken gastrointestinal tract: Influence on health, productivity and disease. *Applied Microbiology and Biotechnology*, 98(10), 4301–4310. doi: 10.1007/s00253-014-5646-2
- Star, L., Kemp, B., van den Anker, I., & Parmentier, H. K. (2008). Effect of single or combined climatic and hygienic stress in four layer lines: 1. Performance. *Poultry Science*, 87(6), 1022–1030. doi: 10.3382/ps.2007-00142
- St-Pierre, N. R., Cobanov, B., & Schnitkey, G. (2003). Economic losses from heat stress by U.S. livestock industries. *Journal of Dairy Science*, 86(Supplement), E52–E77. doi: 10.3168/jds.S0022-0302(03)74040-5
- Surai, P. F., Kochish, I. I., Fisinin, V. I., & Kidd, M. T. (2019). Antioxidant defence systems and oxidative stress in poultry biology: An update. *Antioxidants*, 8(7), 235. doi: 10.3390/antiox8070235
- Tong, L. C., Wang, Y., Wang, Z. B., Liu, W. Y., Sun, S., Li, L., Su, D. F., & Zhang, L. C. (2016). Propionate ameliorates dextran sodium sulfate-induced colitis by improving intestinal barrier function and reducing inflammation and oxidative stress. *Frontiers in Pharmacology*, 7, 253. doi: 10.3389/fphar.2016.00253
- Torok, V. A., Ophel-Keller, K., Loo, M., & Hughes, R. J. (2008). Application of methods for identifying broiler chicken gut bacterial species linked with increased energy metabolism. *Applied and Environmental Microbiology*, 74(3), 783–791. doi: 10.1128/AEM.01384-07
- Uni, Z., & Ferket, R. P. (2004). Methods for early nutrition and their potential. *World's Poultry Science Journal*, 60(1), 101–111. doi: 10.1079/WPS20038
- Uyanga, V. A., Liu, L., Zhao, J., Wang, X., Jiao, H., & Lin, H. (2022). Central and peripheral effects of L-citrulline on thermal physiology and nitric oxide regeneration in broilers. *Poultry Science*, 101, 101669. doi: 10.1016/j.psj.2021.101669

- Uyanga, V. A., Musa, T. H., Oke, O. E., Zhao, J., Wang, X., Jiao, H., ..., Lin, H. (2023). Global trends and research frontiers on heat stress in poultry from 2000 to 2021: A bibliometric analysis. *Frontiers in Physiology*, 14, 1123582. doi: 10.3389/fphys.2023.1123582
- Van Goor, A., Slawinska, A., Schmidt, C. J., & Lamont, S. J. (2016). Distinct functional responses to stressors of bone marrow-derived dendritic cells from diverse inbred chicken lines. *Developmental and Comparative Immunology*, 63, 96–110. doi: 10.1016/j.dci.2016.05.016
- Videla Rodriguez, E. A., Mitchell, J. B. O., & Smith, V. A. (2024). Robust identification of interactions between heat-stress responsive genes in the chicken brain using Bayesian networks and augmented expression data. *Scientific Reports*, 14(1), 9019. doi: 10.1038/s41598-024-58679-3
- Videnska, P., Sedlar, K., Lukac, M., Faldynova, M., Gerzova, L., Cejkova, D., ..., Rychlik, I. (2014). Succession and replacement of bacterial populations in the caecum of egg-laying hens over their whole life. *PLoS One*, 9(12), e115142. doi: 10.1371/journal.pone.0115142
- Wang, L., Ren, B., Zhang, Q., Chu, C., Zhao, Z., Wu, J., Zhao, W., Liu, Z., & Liu, X. (2020). Methionine restriction alleviates high-fat diet-induced obesity: Involvement of diurnal metabolism of lipids and bile acids. *Biochimica et Biophysica Acta (BBA) – Molecular Basis of Disease*, 1866(11), 165908. doi: 10.1016/j.bbadis.2020.165908
- Wang, S. H., Cheng, C. Y., Chen, C. J., Chan, H. L., Chen, H. H., Tang, P. C., Chen, C. F., Lee, Y. P., & Huang, S. Y. (2019). Acute heat stress changes protein expression in the testes of a broiler-type strain of Taiwan country chickens. *Animal Biotechnology*, 30(2), 129–145. doi: 10.1080/10495398.2018.1446972
- Wang, T., Hu, X., Liang, S., Li, W., Wu, X., Wang, L., & Jin, F. (2015). *Lactobacillus fermentum* NS9 restores the antibiotic-induced physiological and psychological abnormalities in rats. *Beneficial Microbes*, 6(5), 707–718. doi: 10.3920/BM2014.0177
- Wen, C., Wei, S., Zong, X., Wang, Y., & Jin, M. (2021). Microbiota-gut-brain axis and nutritional strategy under heat stress. *Animal Nutrition*, 7(4), 1329–1336. doi: 10.1016/j.aninu.2021.09.008
- Whitman, J. A., Doherty, L. A., Pantoja-Feliciano de Goodfellow, I. G., Racicot, K., Anderson, D. J., Kensil, K., Karl, J. P., Gibson, G. R., & Soares, J. W. (2024). *In vitro* fermentation shows polyphenol and fiber blends have an additive beneficial effect on gut microbiota states. *Nutrients*, 16(8), 1159. doi: 10.3390/nu16081159
- Wong, J. M. W., de Souza, R., Kendall, C. W. C., Emam, A., & Jenkins, D. J. A. (2006). Colonic health: Fermentation and short-chain fatty acids. *Journal of Clinical Gastroenterology*, 40(3), 235–243. doi: 10.1097/00004836-200603000-00015
- Wu, Q. J., Liu, N., Wu, X. H., Wang, G. Y., & Lin, L. (2018). Glutamine alleviates heat stress-induced impairment of intestinal morphology, intestinal inflammatory response, and barrier integrity in broilers. *Poultry Science*, 97(8), 2675–2683. doi: 10.3382/ps/pey123
- Wu, S.-B., Stanley, D., Rodgers, N., Swick, R. A., & Moore, R. J. (2014). Two necrotic enteritis predisposing factors, dietary fishmeal and *Eimeria* infection, induce large changes in the caecal microbiota of broiler chickens. *Veterinary Microbiology*, 169(3–4), 188–197. doi: 10.1016/j.vetmic.2014.01.007
- Wu, Y., Huang, J., Quan, S., & Yang, Y. (2022). Light regimen on health and growth of broilers: An updated review. *Poultry Science*, 101(1), 101545. doi: 10.1016/j.psj.2021.101545
- Xu, J., Hu, L., Ning, J., Zhang, F., Xu, Q., & Wang, Y. (2025). Identification of single nucleotide polymorphisms (SNPs) associated with heat stress and milk production traits in Chinese Holstein cows. *BMC Genomics*, 26(1), 534. https://rdcu.be/fzrSU
- Yahav, S., Straschnow, A., Luger, D., Shinder, D., Tanny, J., & Cohen, S. (2004). Ventilation, sensible heat loss, broiler energy, and water balance under harsh environmental conditions. *Poultry Science*, 83(2), 253–258. doi: 10.1093/ps/83.2.253
- Yang, L., Tan, G. Y., Fu, Y. Q., Feng, J. H., & Zhang, M. H. (2010). Effects of acute heat stress and subsequent stress removal on function of hepatic mitochondrial respiration, reactive oxygen species production and lipid peroxidation in broiler chickens. *Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology*, 151(2), 204–208. doi: 10.1016/j.cbpc.2009.10.010
- Yassin, L. K., Nakhal, M. M., Alderei, A., Almehairbi, A., Mydeen, A. B., Akour, A., & Hamad, M. I. K. (2025). Exploring the microbiota-gut-brain axis: Impact on brain structure and function. *Frontiers in Neuroanatomy*, 19, 1504065. doi: 10.3389/fnana.2025.1504065
- Yu, M., Yu, B., & Chen, D. (2024). The effects of gut microbiota on appetite regulation and the underlying mechanisms. *Gut Microbes*, 16(1), 2414796. doi: 10.1080/19490976.2024.2414796
- Yue, Y., Guo, Y., & Yang, Y. (2017). Effects of dietary L-tryptophan supplementation on intestinal response to

- chronic unpredictable stress in broilers. *Amino Acids*, 49(7), 1227–1236. doi: 10.1007/s00726-017-2424-3
- Zaboli, G., Huang, X., Feng, X., & Ahn, D. U. (2019). How can heat stress affect chicken meat quality? A review. *Poultry Science*, 98(3), 1551–1556. doi: 10.3382/ps/pey399
- Zampiga, M., Flees, J., Meluzzi, A., Dridi, S., & Sirri, F. (2018). Application of omics technologies for a deeper insight into quali-quantitative production traits in broiler chickens: A review. *Journal of Animal Science and Biotechnology*, 9, 61. doi: 10.1186/s40104-018-0278-5
- Zayani, Z., Matinahmadi, A., Tavakolpournegari, A., & Bidooki, S. H. (2025). Exploring Stressors: Impact on Cellular Organelles and Implications for Cellular Functions. *Stresses*, 5(2), 26. doi: 10.3390/stresses5020026
- Zaytsoff, S. J. M., Uwiera, R. R. E., & Inglis, G. D. (2020). Physiological stress mediated by corticosterone administration alters intestinal bacterial communities and increases the relative abundance of *Clostridium perfringens* in the small intestine of chickens. *Microorganisms*, 8(10), 1518. doi: 10.3390/microorganisms8101518
- Zhang, S., Su, H., Zhou, Y., Li, X., Feng, J., Zhang, M. (2016). Effects of sustained cold and heat stress on energy intake, growth and mitochondrial function of broiler chickens. *Journal of Integrative Agriculture*, 15(10), 2336–2342. doi: 10.1016/S2095-3119(15)61314-4
- Zhang, Y., Li, X., Lu, S., Guo, H., Zhang, Z., Zheng, H., Zhang, C., Zhang, J., Wang, K., Pei, F., & Duan, L. (2024). Stress triggers gut dysbiosis via CRH–CRHR1–mitochondria pathway. *npj Biofilms and Microbiomes*, 10, 93. doi: 10.1038/s41522-024-00571-z
- Zhang, Y., Xie, L., Ding, X., Wang, Y., Xu, Y., Li, D., Liang, S., Wang, Y., Zhang, L., Fu, A., & Zhan, X. (2022). Mechanisms underlying the protective effect of maternal zinc (ZnSO₄ or Zn-Gly) against heat stress-induced oxidative stress in chicken embryo. *Antioxidants*, 11(9), 1699. doi: 10.3390/antiox11091699
- Zhou, N., Lee, W. R., & Abasht, B. (2015). Messenger RNA sequencing and pathway analysis provide novel insights into the biological basis of chickens' feed efficiency. *BMC Genomics*, 16(1), 195. doi: 10.1186/s12864-015-1364-0
- Zhu, Z., Kawai, T., Umehara, T., Hoque, S. A. M., Zeng, W., & Shimada, M. (2019). Negative effects of reactive oxygen species (ROS) generated during linear sperm motility on gene expression and adenosine triphosphate (ATP) generation in boar sperm mitochondria. *Free Radical Biology and Medicine*, 141, 159–171. doi: 10.1016/j.freeradbiomed.2019.06.018