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MicroRNAs: An Important Signature Molecule to Improve Health and Welfare in Livestock: A Review

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ABSTRACT

Adverse conditions negatively impact livestock productivity, leading to significant financial losses for livestock businesses. Maintaining healthy and disease-free farm animals is crucial for producing high-quality food. MicroRNAs (miRNAs) have been discovered in domestic livestock, with their expression profiles revealing tissue-specific and temporal patterns. Their potential use in genomic selection systems is highlighted by breed-dependent expression patterns and single nucleotide polymorphisms in the target mRNA binding site, which have connections with economic value. Studies carried out in 2022-2023, a variety of reviews and research publications were evaluated and then extracted to enlist congestive data for quick detection of miRNA and their role as biomarkers for the assessment of the health status in livestock species. Study concluded that miRNA influences developmental decisions, like apoptosis, adipocyte differentiation, cell fate, cell cycle progression and muscle development and growth, by altering post-transcriptional regulation. Despite the significant interest in miRNA's role in animal biology, most existing literature primarily uses livestock models. Consequently, a review of the mechanisms by which miRNA alters gene translation as well as the most recent studies evaluating miRNA in livestock used for production is required. This systematic review summarizes and integrates previous findings to provide an overview of microRNAs are being investigated as potential biomarkers of disease, susceptibility and dietary exposure.

Key words: Animal health, Biomarker, Livestock diseases, MicroRNAs, Regulatory networks.

MicroRNAs (miRNAs), defined as short non-coding RNA (ncRNA) molecules of about 22 nucleotides in length, regulate a variety of biological processes through the post-transcriptional regulation of gene expression. miRNAs or microRNAs are essential for controlling gene expression in a variety of organisms, including livestock. By attaching to messenger RNA (mRNA) and either destroying it or preventing its translation, they play a role in post-transcriptional control. The function of miRNAs in a variety of biological processes, such as immune response, growth, development and reproduction, has been investigated in livestock.

Recent data has shown that various miRNAs go through different processing routes. Tumorigenesis and miRNA processing dysregulation are tightly connected (Jiang and Yan, 2016). More recently, the function of miRNA in a variety of inflammatory and immune illnesses, including allergic inflammation, has also been identified (Rebane and Akdis, 2014). miRNA regulates gene expression post-transcriptionally, either by targeting the 3'untranslated region (UTR) or coding region of mRNA. One cell type can have multiple genes targeted by a single miRNA and vice versa; the impact of a single miRNA on a target gene may be modest (Lu and Rothenberg, 2013). Consequently, the relationship between miRNAs and gene expression becomes extremely complex. A number of miRNAs exhibit tumor-suppressive or oncogenic properties and are crucial for the initiation, growth and spread of cancer (Romano *et al*., 2017). MicroRNA-140-5 p suppresses hypoxia induced nephrotoxicity and renal fibrogenesis in *in vitro* conditions (Wu *et al*., 2022). High stability in the biofluids (serum, plasma, milk) of livestock, active secretion from cells, cell-to-cell communication and ease of extraction confer the potential for circulating miRNA to act as a novel biomarker for the identification and tracking of disease progression in animals (Correia *et al*., 2017).

MicroRNAs (miRNAs) play a crucial role in regulating gene expression and their involvement in stress responses in livestock has been a subject of research. Stress unleashes negative impacts on cattle productivity and culminates in significant financial losses for livestock firms (Gupta *et al*., 2018). Producing safe and high-quality food requires keeping farm animals in perfect physical condition, free from

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illness or misery. Unpredictable and uncontrollable circumstances include metabolic stress, immunological stress, stress brought on by regrouping/splitting of livestock's during their productive life, stress related to weaning, stress resulting from dietary changes, transport stress, environmental stress and rough handling (Muroya *et al*., 2016). MiRNAs are part of the molecular mechanisms that help animals adapt to stress.

Expression profiling in domestic livestock has shown that miRNA exhibits unique temporal (at cellular and tissue level) and geographic expression patterns (Kuosmanen *et al*., 2017). The dysregulated expression of miRNA would result in improper regulation of several cellular processes and genetic networks. Research suggested that circulating miRNAs are significantly involved in metabolic disorders (Gupta *et al*., 2018), foot and mouth diseases (Basagoudanavar *et al*., 2018) and in paratuberculosis in livestock (Deiuliis *et al*., 2016). This article provides a comprehensive overview of the regulatory importance of miRNA in livestock stress.

miRNAs associated with immune system and diseases of livestock

Animal illnesses are a major source of financial losses for the livestock sector and serious problems for animal welfare (Bishop and Woolliams, 2014). Furthermore, a variety of diseases that affect livestock can spread to human, potentially leading to serious health problems or even death. For the livestock industry, effectively managing diseases is a global concern that calls for several layers of control and intervention. For the treatment of diseases in livestock, miRNA can be employed as biomarkers with diagnostic, prognostic, or therapeutic capabilities. Acute and chronic events exhibit distinct effects on the metabolic pathways of bovines, which can alter animal's quality of life and production. MicroRNAs influence immune function, mammary gland health, milk composition and quality, as well as other metabolic factors.

Small ruminant species have been found to contain hundreds of microRNAs; many of these microRNAs' functions in the various regulatory systems are still unknown. Economic factors like milk, meat and wool production have frequently been the focus of studies on sheep and goats (Zhai *et al*., 2019), but only a small number of studies have examined how their health status relates to their overall well-being.

Immunity

In large ruminants

Diseases, illnesses and certain environmental alterations related stresses can decrease the immune response through stimulating the Hypothalamic-Pituitary-Adrenal (HPA) axis and the SAM (Sympathetic-Adrenal-Medullary) system (Minton 1994). Recently studies have suggested that miRNAs regulate many immune cell activities and are essential for bovine immunity (Dong *et al*., 2017).

According to a recent experimentation, miRNAs are significant controllers of the host's gene expression and immunological responses and also performs as potential biomarkers to identify mycobacterial infection susceptibility (Wright *et al*., 2020). During mycobacterial infections in cattle, numerous miRNAs have been shown to be modified (Gupta *et al*., 2018; Iannaccone *et al*., 2018). When infected with *M. avium* subspecies *paratuberculosis* and *M. bovis*, the c-miRNAs miR-19b, miR-196b and miR-146 undergo changes associated to the immune system and inflammation (Iannaccone *et al*., 2018).

Studies sought to identify possible genes and miRNAs beneficial for developing mastitis prevention, diagnosis and treatment methods as well as to confirm the importance of miRNAs during innate immune responses (Chen *et al*., 2019; Srikok *et al*., 2020) and concluded that bovine serum of mammary tissue infected with *Streptococcus uberis* faces downregulation of miR-181a, 16 and miR-31 as compared to healthy tissue, whereas miR-223 was highly upregulated (Naeem *et al*., 2012). miRNAome and transcriptome of milk along with blood CD14+ monocytes were described using *S. uberis* to infect Holstein Friesians cows through next-generation sequencing done by Lawless *et al.* (2014). Interestingly, the majority of miRNAs found to be downregulated in milk monocytes recovered from mastitis infected animals and were anticipated to exclusively target genes associated in innate immunity, such as those implicated in the TLR, NOD and RIG-I-like receptor signaling pathways. MiR-26a was anticipated to target a bridging molecule (FGA) important in host defensive mechanisms against *S. aureus* (Ju *et al*., 2018). Due to the fact that miR-144 and miR-451 were markedly upregulated in mammary glands infected with *E. coli* and significantly downregulated in those infected with *S. aureus*, researchers determined that these two miRNAs could be useful for differentiating between the two pathogens (Luoreng *et al*., 2018). When compared to healthy animals, the serum of calves with mastitis caused by *S. aureus* has been shown to have a number of miRNAs that are differentially expressed (DE). Among these, miR-144 and miR-125 were discovered to be upregulated. DE-miRNAs play a significant role in innate immunity and inflammatory responses, as confirmed through KEGG pathway analysis as noted by Luoreng *et al.* (2018). Further research must be conducted on these DE-miRNAs as possible biomarkers for mastitis brought on by *E. coli*. Numerous studies have suggested that miRNAs may be used as MAP prognostic and diagnostic tools. In the blood of MAP-positive animals compared to unexposed animals, Malvisi *et al.* (2016) found two downregulated (miR-6517 and miR-7857) and seven upregulated (miR-19b, miR-19b-2, miR-1271, miR-100, miR-301a, miR-32 and one novel miRNA) miRNAs. Four miRNAs (miR-1976, miR-873-3p, miR-520f-3p and miR-126-3p) were combined by Gupta *et al.* (2018) to create a prediction model that could distinguish between animals with moderate to severe JD infection and healthy animals. Wang *et al.* (2019) reported the participation of a different group of miRNAs in the regulation of MAP response in the ileum and ileal lymph as well as the possible engagement of miR-100, miR-330 and miR-2447 in the Th17 cell differentiation pathway during MAP infection in the ileal lymph node. Additionally, as certain other prominent infectious diseases of cattle progress, such as tuberculosis, foot and mouth disease (FMD) and BVD, miRNA expression is altered (Iannaccone *et al*., 2018; Taxis *et al*., 2017).

In small ruminants

Globally, sheep and goats are among the small ruminants that provide a significant amount of meat, milk and wool. Mammary gland development (Galio *et al.,* 2013), muscle (Lie *et al.,* 2014), embryo/ovary (Chang *et al.,* 2018), milk-related phenotypes (yield and composition) (Lin *et al.,* 2013) and hair/skin related phenotypes (Wu *et al.,* 2014) have all been the focus of miRNA studies in small ruminants. Stress-activated immune responses and the HPA axis have been connected and C-miRNAs have been suggested as potential biomarkers in this connection (Naylor *et al*., 2020). MiR-145, miR-233 and miR-1246 expression levels rise in correlation with the inflammatory response, as determined by the assessment of immunological and stress markers (Naylor *et al*., 2020). Additionally, it has been demonstrated that miRNAs influence the immunological response of small ruminants to infectious illnesses. Peste des petits ruminants virus (PPRV) is a Morbilli virus that is extremely infectious and lethal to domestic and wild small ruminants (Kumar *et al*., 2014). However, miR-21-5p, which inhibits interferons (IFNs) antiviral activity and miR-30b, which limits initial macrophages ability to process and present antigen, were shown to be downregulated in PPRV infection (Khanduri *et al*., 2018). PPRV affected the levels of miRNA expression in the lungs and spleen of sick sheep and goats (Pandey *et al*., 2017). Comparing the two species, the spleen and lungs exhibited 20 and 11 DE-miRNAs, respectively. Du *et al.* (2017) identified 25 known and 240 novel DE miRNA candidates in primary sheep testicular cells infected with bluetongue virus as well as the significant enrichment of target genes in MAPK, PI3K-Akt, endocytosis, Hippo, NF-κB viral carcinogenesis, FoxO and JAK-STAT signaling pathways in an effort to investigate the mechanisms of bluetongue virus infection.

miRNAs as biomarker found in milk

In large ruminants

At birth, calves are devoid of circulating antibodies. Newborns' potential to resist infections in the early days of life is entirely dependent on the passive immunity conferred by ingested colostrums (Chase *et al*., 2008). Colostrum is rich in nutrients, bioactive compounds and microRNAs than milk. Recently, the potential consequences of colostrum ingestion on calves were evaluated (Van *et al*., 2020). Using a systematic sequencing-based investigation of milk and colostrum at different stages of lactation, miR-181a, miR-155 and miR-223, were considerably more abundant in colostrum than in milk (Chen *et al*., 2010). miRNA related to immune system were also discovered in microvesicles derived from milk. Several microRNAs (miRNAs) were discovered to be DE among the two breeds after sequencing and secondary confirmation by RT-qPCR (Özdemir *et al*., 2020). These included miR-21-5p, miR-142-3p, miR-222, miR-340, miR-1248, miR-29c, miR-101and let-7a-5p. Functional enrichment assessment found that the overall amount of microRNAs in the colostrum of DAK cows was significantly closely associated with immune pathways than in milk (Özdemir *et al*., 2020). The concentration and distribution of microRNAs in milk and colostrum may also be affected by management-related parameters, such as nutrition (Jacometo *et al*., 2018) and subclinical diseases (Cai *et al*., 2018). Milk exosomal microRNAs found to balance nutrition between buffalo breeds with low and high milk production (Pang *et al*., 2022).

In small ruminants

The development of the mammary gland throughout various stages of pregnancy, lactogenesis and colostrogenesis in small ruminant species has been linked to the presence of numerous miRNAs (Galio *et al*., 2013). The enhanced expression of both microRNAs towards the end of lactation and pregnancy had a significant influence in mammary gland development (Galio *et al*., 2013). For dairy goats, profiles of miRNA expression throughout milk lactation and during the dry periods have been observed. During breastfeeding, miR-7, miR-423- 5p and miR-378 have been recognized as serving crucial regulatory roles in milk component transport and ingredient synthesis (Dong *et al*., 2013). MiR-574 may be connected to the development of the mammary gland and milk production in goats through oxytocin, estrogen, adipocytokine, endocrine and MAPK signaling pathways (Hou *et al*., 2017). The mammary gland of a dairy goat and the raw milk it produced were both discovered to contain high concentrations of 13 microRNAs, proving that the miRNAs in the milk came from the mammary gland's cells (Li *et al*., 2012).

miRNAs and genetic background

Cattle's genetic make-up has an effect on microRNAs that are related to stressor stimuli. Ioannidis *et al*. (2018) studied the potential use of c-miRNAs as genetic performance indicators in age, fertility and welfare traits in dairy cattle. Certain miRNAs, such as miR-127 or 140, were related to immunological responses, inflammation and health attributes (mastitis, fertility, lameness). Perinatal mortality and dystocia are quantifiable features that profoundly influence animal welfare and productivity. Using genome-wide association studies and quantitative trait loci mapping, researchers discovered many significant genomic sites in Holstein dairy cows that are associated with perinatal mortality and dystocia. MiRNA expression in livestock genetic selection is in its infancy; further research is needed to assess their functional significance and potential use in selective breeding programs.

MicroRNAs as biomarkers in livestock stress

A biomarker is a measurable indicator of a certain biological state, such as health and disease. Growing body of research is supporting the important role of miRNAs in stress reactions as well as in several diseases where they can be used as potential biomarkers for both illnesses and stressors, indicating their significance in diagnostic and monitoring applications. The identification of particular miRNAs in cow blood is an extremely useful approach for determining how the animals react to thermal alterations. Animal health and productivity might suffer from high ambient temperatures. Cow blood samples were obtained in experimentation by Lee *et al.* (2020), to examine the mRNA expression under various environmental situations. Different types of miRNAs as signature biomarkers with functions addressing various livestock diseases are listed in Table 1.

miRNAs and management induced stress

In large ruminants

Diverse factors associated to housing and management can induce stress in cattle and severely alter physiological and productive metrics. Stress alters miRNA synthesis, mRNA target expression and the functionalities of miRNA-protein complexes (Olejniczak *et al*., 2018). As a stress model, Colitti *et al*. (2019) investigated the reformation of the hierarchy in social group in lactating cows by concentrating on composition of milk exosome and discovered that a number of miRNAs were differently expressed. Genes associated with glucocorticoid receptor signaling and neurotrophic factor-mediated TRK receptor signaling was discovered by functional pathway investigation of potential target genes of DE microRNAs (Jeanneteau *et al*., 2012).

In small ruminants

Inability to adapt to a different diet causes inexperienced stress in small ruminants, which is characterized by growth stagnation (Magistrelli *et al*., 2013). Weaning stress is able to adversely affect the growth in the animals by reducing cell proliferation, the researchers suggested that drastically changed miRNAs may be effective biomarkers to assess the degree of weaning stress in goat production (Liao *et al*., 2019). Yang *et al*, (2018) evaluated the levels of estrus rate, body state score and hypothalamus–ovary–nutrition-related microRNAs in sheep fed with or without concentrate. A substantial number of DE miRNAs were discovered, in which 113 were released in the ovary and 148 in the hypothalamus, respectively. MiR-200b, miR-200c and miR-200a were considerably DE-miRNAs that were expressed in both ovary and hypothalamus. The scientists discovered that food deprivation had the greatest impact on the production of miR-204-5p and miR-223-3p. Since the welfare of livestock is a pressing concern, researchers have been attempting for many years to determine the optimal housing system for small ruminants considering their geographical climate in order to maximize productivity and welfare. The researchers concluded that housing systems for small ruminants needed to be economical, well-ventilated, hygienic and constructed from materials that could be found nearby. Materials for flooring and roofing should be chosen with consideration for the climate, animal preferences and parasite burden. Similar to this, when building a shed for small ruminants in the age of climate change and global warming, consideration must be given to behavioral and physiological changes, ventilation rate, wind speed and direction (Wadhwani *et al*., 2016).

miRNAs and environmental stress

Heat stress

In large ruminants

One of the most influential environmental elements effecting cattle productivity, welfare and health is high temperature. In dairy and feedlot farms, cooling methods (such as shade, fans and sprinklers) are utilized to counteract the harmful effects of thermal stress. miRNAs perform a crucial contribution in the transcriptional control of genes encoding proteins implicated in heat stress response pathways (Li *et al*., 2018). Heat stress has a detrimental impact on dairy cow homeostasis. Heat stress, in particular, appears to impact lipolysis and lipogenesis-related enzymes in bovine adipocytes (Faylon *et al*., 2015).

A bovine mammary epithelial cell line exhibited significant variations in miRNA expression in response to thermal stressed conditions relative to thermal neutral conditions (Salama *et al*., 2019). Mutations or SNPs (Single Nucleotide Polymorphisms) in the 3'-untranslated regions (UTRs) of genes might change expression of protein by introducing misleading miRNA binding sites (Clop *et al*., 2006).

In small ruminants

Using miRNA-mRNA linkages in hypoxia-related pathways, such as the one linked with HIF-1 (Hypoxia Inducible Factor 1), a comparative study of miRNA transcriptome of two goat populations at differing elevations generated convincing evidence for acclimatization. The research concluded that miRNA-509-3p, miR-3069-1-3p, miR-208-3p and miR-409-5p, were downregulated, while miR-106a-5p was upregulated, in hypoxia-sensitive tissues such as the liver, heart, kidney, spleen and muscle encouraging that miRNAs play a central role in the regulation in mechanisms attributed to high adaptation (Feng *et al*., 2020). These DE-miRNAs have genes engaged in a variety of processes as possible targets, including energy metabolism, erythropoiesis, DNA repair and apoptosis (Feng *et al*., 2020). Furthermore, it was reported that miR-106a-5p targeted the VEGFR1 (or FLT1) gene, exerting an adverse regulatory impact on angiogenesis and paving the way for enhanced use of genetic resources in plateau areas.

Table 1: Role of microRNAs as signature biomarkers in livestock.

Livestock disease/Stress/ Events	Sampling source	Type of miRNA as a potential biomarker	Role of miRNA	Reference
Endometritis (Inflammation of uterine lining)	Epithelial cells of the bovine mammary gland	miR-21-3p	Performs a significant function in encouraging the vitality and the development of epithelial cells in the mammary glands of dairy cows.	Zhang *et al.* (2019)
Liver function and post-partum retained fetal membrane syndrome	Plasma, blood cells	miR-802	Sensitivity to insulin and lipogenesis	Ioannidis and Donadeu, 2018)
	serum	miR-185	Control vascular endothelial growth factor A (VEGFA) signalling cascades in dairy cows with retained fetal membrane	Zheng *et al.* (2018)
Pregnancy and heat stress	Serum	Group 1. miRNAs bta-miR-19a bta-miR-19b bta-miR-30a-5p bta-miR-2284	Show differential expression in both pregnant and non-pregnant cows	Lee *et al.* (2020)
		Group 2. miRNAs bta-miR-20b bta-miR-29-d-3p bta-miR-146b bta-miR-1246	Target progesterone synthesis (StAR) and the activity of corpus luteum-associated genes (CCL 11, XCL)	
Pregnancy and lactation in Holstein cows	Serum, mammary gland tissues	miRNAs miR-10a miR-15b miR-16 miR-31 miR-33b miR-145 miR-146b miR-181a miR-205 miR-221 miR-223	Except for miR-31, all miRNAs displayed upregulated expression between 30 days before delivery and 7 days after delivery. miRNA-31 prevents cyclin gene expression. The expression of miR-221 was observed to further rise 30 days after delivery, which correlated with the onset of early lactation. miR-221 also influences regulation of angiogenesis and/or endothelial cell proliferation	Wang *et al.* (2012)
Paratuberculosis	Serum	1. Upregulated miR-24-1 miR-24-2 miR-378c miR-6517 miR-7857 2. Downregulated miR-19b miR-19b-2 miR-32a miR-100	Differentiate moderate to severely infected animals from non-infected ones	Gupta *et al.* (2018)

Table 1: Continue...

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		miR-301a miR-1271		
Foot and mouth disease	Serum	Group 1. miR-21-5p bta-miR-10 bta-miR-126-3p bta-miR-145 bta-miR-197 bta-miR-223	Group 1. on day 2 post infection, 119 miRNAs show higher expression in comparison to day 0 post-infection, of which 39 were significantly. elevated. These c-miRNAs are produced from cells in a paracrine manner or discharged by lysed cells.	Basagoudanavar *et al.*, 2018; Stenfeldt *et al.*, 2017
		Group 2. bta-miR-17-5p bta-miR-22-5p bta-miR-23b-5p bta-miR-26b bta-miR-31 bta-miR-144 bta-miR-146a bta-miR-154a bta-miR-205 bta-miR-369-3p bta-miR-455-3p bta-miR-1224	Group 2. performs cellular proliferation and regulates apoptosis.	
		Group 3. bta-miR-26b bta-miR-17-5p bta-miR-34a bta-miR-146a bta-miR-147 bta-miR-150 bta-miR-205	Group 3. regulates immune function	
		Group 4. bta-miR-17-5p bta-miR-31 miR-1281	Group 4. suppresses tumor	
Bovine mastitis (inflammation of breast tissue)	Milk isolated monocytes	bta-miR-146b miR-149 bta-miR-411a bta-miR-451 bta-miR-615	Upregulated miRNAs primarily target genes involved in metabolism, while significantly more downregulated miRNAs are linked to innate immunity	Lawless *et al.* (2014)
Bovine viral diarrhea virus	Serum	bta-miR-151-3p bta-miR-423-5p	Elicit immune responses	Taxis and Casas, 2017
Staphylococcus aureus	Bovine exosomes (milk)	bta-miR-142-5p bta-miR-223	Indicators of mammary gland bacterial infection	Sun *et al.*, 2015
Mycoplasma bovis	Serum	1. bta-let-7b bta-miR-24-3p bta-miR-92a bta-miR-423-5p 2. Increase miR-146a miR-146b-5p miR-155	Elicit immune response against bacterial infection	Casas *et al.*, 2016

Table 1: Continue...

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		miR-886-5p 3. Decrease miR-18 miR-20a miR-30c miR-185 miR-191 miR-374a miR-378 miR-423-5p miR-768-5p		
Aujeszky's disease virus (ADV)	Tissues samples (olfactory bulb "OB" and trigeminal ganglia "TG" Saliva	miR-37 miR-133a miR-133b miR-206	Regulates metabolic pathways associated with immune response and viral infection	Timoneda *et al.* (2014)
Acute pain, 4-days old piglets		miR-27b-3p miR-215 miR-22-3p miR-155-5p hsa-miR-365-5p hsa-miR-204 miR-19b	Regulates expression profile of cytokines release and monitor focal adhesion pathways	Lecchi *et al.* (2020)
Respiratory diseases	Serum, milk	bta-miR-423-5p bta-miR-151-3p	Helps in escaping from host immune system	Taxis and Casas, 2017
Skeletal muscle development	Biceps femoris muscle	miR-206 miR-208b	Expression of muscle gene is changed as the skeletal muscles adjust to grazing	Muroya *et al.*, 2016

High-altitude stress

Animals' immune systems are impacted by high-altitude hypoxia, which reduces cytokine release and modifies immunoglobulin secretion (Mishra *et al.*, 2015). These occurrences are consistent with persistent stress having an impact on an animal's physical health and making them more susceptible to diseases and infection (Kong *et al.*, 2019).

Regulation and control of livestock's thermal stress responses by microRNA19a/b

miRNA-19a/b regulates innate immunity in response to temperature stress by directly targeting the TLR2 gene (Zheng *et al.*, 2014). Stress related to temperature is detrimental to animal health, since it suppresses the immune system and increases susceptibility to illness (Abdelnour *et al.*, 2019). TLRs play a crucial role in detection of pathogens and protection (O'Neill, 2006) and through modulating anti-inflammatory responses to pristine tissue wounds, they serve as guards of tissue deterioration (Ju *et al.*, 2014). miRNA-19a/b is hypothesized to adversely influence cytokine secretion, notably interleukin-6 (IL-6) (Ju *et al.*, 2014). In both murine and human cells, miRNA-19b was discovered to influence the activities of nuclear factor-B (NF-B) (Gantier *et al.*, 2012). The ability to quickly respond to any unfavorable ecological factors and pro-inflammatory stimuli depends on the NF-B transcription dysfunction (Gantier *et al.*, 2012). However, additional research is needed to establish the relationship between heat stress effects and the protective function of NF-B (Liu *et al.*, 2018) postulated a distinct role for an NF-B signaling pathway comprising, reactive oxygen species (ROS), heat shock protein 27 (HSP27) and mitogen-activated protein kinases (MAPKs) in preventing heat stress-induced cell death.

CONCLUSION

Enhancing the perception of consumer and acceptance of product as well as improving the cattle industry depend on improving animal health and wellbeing. In this situation, there is still a need for easily measurable, objective laboratory markers that may be used to assess an animal's quality of life and general wellbeing. Numerous research that has been done up to this point have mostly centered to resiliency biomarkers/stress and miRNAs which provide data on the regulation of numerous processes activities across the tissue-biofluid channel. Traditional biomarkers play important role as indicators of injury/stress, but they don't provide noticeable acquaintance about the molecular mechanisms driving an animal's reaction to difficulty. Extracellular miRNAs can be employed in concert with other phenotypic metrics to more precisely follow the stress reactions of particular animals or groups. Here, we have discussed the function of miRNAs in the stress of livestock brought on by management factors (such as housing, transportation by road and disease), environmental difficulties (such as thermal stress) and productive performance. But there are still a number of difficulties in detecting c-miRNAs. In contrast with miRNA expression profiles across various laboratories is hampered by the absence of a standardized protocol for the quantification of c-miRNAs. Clarifying c-miRNAs' cellular origins, connection to their tissues and connection to stressors will help establish them as novel biomarkers. The expression of miRNAs in various livestock species under stressed situations of different duration and severity must be compared in larger-scale investigations in order to verify the viability of miRNAs as biomarkers.

Conflict of interest

No conflict of interest to declare.

REFERENCES

Abdelnour, S.A., Abd El-Hack, M.E., Khafaga, A.F., Arif, M., Taha, A.E., Noreldin, A.E. (2019). Stress biomarkers and proteomics alteration to thermal stress in ruminants: A review. Journal of Thermal Biology. 79: 120-134.

Basagoudanavar, S.H., Hosamani, M., Tamil Selvan, R.P., Sreenivasa, B.P., Sanyal, A., Venkataramanan, R. (2018). Host serum microRNA profiling during the early stage of foot-and-mouth disease virus infection. Archives of Virology. 163(8): 2055-2063.

Bishop, S.C. and Woolliams, J.A. (2014). Genomics and disease resistance studies in livestock. Livestock Science. 166: 190-198.

Cai, M., He, H., Jia, X., Chen, S., Wang, J., Shi, Liu, B., Xiao, W., Lai, S. (2018). Genome-wide microRNA profiling of bovine milk-derived exosomes infected with *Staphylococcus aureus*. Cell Stress and Chaperones. 23: 663-672.

Casas, E., Cai, G., Kuehn, L.A., Register, K.B., McDaneld, T.G., Neill, J.D. (2016). Association of microRNAs with antibody response to *Mycoplasma bovis* in beef cattle. PloS One. 11(8): e0161651. https://doi.org/10.1371/journal.pone.0161651.

Chang, W., Juanhong, W., Yong, Z., Junyuan, W. (2018). Discovery of two novel miRNAs from the Ovis aries by a combinatorial approach of experiments and bioinformatics. Indian Journal of Animal Research. 52(8): 1155-1161. Doi: 10.18805/ijar.B-721.

Chase, C.C.L., Hurley, D.J., Reber, A.J. (2008). Neonatal immune development in the calf and its impact on vaccine response. The Veterinary clinics of North America. Food Animal Practice. 24(1): 87-104.

Chen, X., Gao, C., Li, H., Huang, L., Sun, Q., Dong, Y., Tian, C., Gao, S., Dong, H., Guan, D., Hu, X., Zhao, S., Li, L., Zhu, L., Yan, Q., Zhang, J., Zen, K., Zhang, C.Y. (2010). Identification and characterization of microRNAs in raw milk during different periods of lactation, commercial fluid and powdered milk products. Cell Research. 20(10): 1128-37.

Chen, Z., Zhou, J., Wang, X., Zhang, Y., Lu, X., Fan, Y., Mao, Y., Loor, J.J., Yang, Z. (2019). Screening candidate microR-15a- IRAK2 regulatory pairs for predicting the response to *Staphylococcus aureus*-induced mastitis in dairy cows. Journal of Dairy Research. 86(4): 425-31. doi: 10.1017/S0022029919000785.

Clop, A., Marcq, F., Takeda, H., Pirottin, D., Tordoir, X., Bibé, B., Bouix, J., Caiment, F., Elsen, J.M. *et al.* (2006). A mutation creating a potential illegitimate microRNA target site in the myostatin gene affects muscularity in sheep. Nature Genetics. 38(7): 813-818.

Colitti, M., Sgorlon, S., Licastro, D., Stefanon, B. (2019). Differential expression of miRNAs in milk exosomes of cows subjected to group relocation. Research in Veterinary Science. 122: 148-155.

Correia, C.N., Nalpas, N.C., McLoughlin, K.E., Browne, J.A., Gordon, S.V., MacHugh, D.E., Shaughnessy, R.G. (2017). Circulating microRNAs as Potential Biomarkers of Infectious Disease. Frontiers in Immunology. 16(8): 118. doi: 10.3389/fimmu.2017.00118.

Deiuliis, J.A. (2016). MicroRNAs as regulators of metabolic disease: Pathophysiologic significance and emerging role as biomarkers and therapeutics. International Journal of Obesity. 40(1): 88-101.

Dong, F., Ji, Z.B., Chen, C.X., Wang, G.Z., Wang, J.M. (2013). Target gene and function prediction of differentially expressed microRNAs in lactating mammary glands of dairy goats. International Journal of Genomics. 2013: 917342. doi: 10.1155/2013/917342.

Dong, H., Gao, Q., Peng, X., Sun, Y., Han, T., Zhao, B., Liu, Y., Wang, C., Song, X., Wu, J. and Yang, L. (2017). Circulating microRNAs as potential biomarkers for veterinary infectious diseases. Frontiers in Veterinary Science. 4: 186. https://doi.org/10.3389/fvets.2017.00186.

Du J., Gao S., Tian Z., Xing S., Huang D., Zhang G., Zheng Y., Liu G., Luo J., Chang H. *et al.* (2017). MicroRNA expression profiling of primary sheep testicular cells in response to bluetongue virus infection. Infection, Genetics and Evolution. 49: 256-267.

Faylon, M.P., Baumgard, L.H., Rhoads, R.P., Spurlock, D.M. (2015). Effects of acute heat stress on lipid metabolism of bovine primary adipocytes. Journal of Dairy Science. 98(12): 8732-8740.

Feng, S., Ma, J., Long, K., Zhang, J., Qiu, W., Li, Y., Jin, L., Wang, X., Jiang, A., Liu, L., Xiao, W., Li, X., Tang, Q., and Li, M. (2020). Comparative microRNA transcriptomes in domestic goats reveal acclimatization to high altitude. Frontiers in Genetics. 11: 809. https://doi.org/10.3389/fgene.2020.00809.

Galio, L., Droineau, S., Yeboah, P., Boudiaf, H., Bouet, S., Truchet, S., Devinoy, E. (2013). MicroRNA in the ovine mammary gland during early pregnancy: spatial and temporal expression of miR-21, miR-205 and miR-200. Physiological Genomics. 45(4): 151-161.

Gantier, M.P., Stunden, H.J., McCoy, C.E., Behlke, M.A., Wang, D., Kaparakis-Liaskos, M.and Williams, B.R. (2012). A miR-19 regulon that controls NF-κB signaling. Nucleic Acids Research. 40(16): 8048-8058.

Gupta, S.K., Maclean, P.H., Ganesh, S., Shu, D., Buddle, B.M., Wedlock, D.N., Heiser, A. (2018). Detection of microRNA in cattle serum and their potential use to diagnose severity of Johne's disease. Journal of Dairy Science. 101(11): 10259-10270.

Hou, J., An, X., Song, Y., Cao, B., Yang, H., Zhang, Z., Shen, W., Li, Y. (2017). Detection and comparison of microRNAs in the caprine mammary gland tissues of colostrum and common milk stages. BMC Genetics. 18(1): 1-8.

Iannaccone, M., Cosenza, G., Pauciullo, A., Garofalo, F., Proroga, Y.T., Capuano, F., Capparelli, R. (2018). Milk microRNA-146a as a potential biomarker in bovine tuberculosis. Journal of Dairy Research. 85(2): 178-180. doi: 10.1017/S0022029918000122.

Ioannidis, J. and Donadeu, F. (2018). Comprehensive analysis of blood cells and plasma identifies tissue-specific miRNAs as potential novel circulating biomarkers in cattle. BMC Genomics. 19(1): 243. doi: 10.1186/s12864-018-4646-5.

Ioannidis, J., Sánchez-Molano, E., Psifidi, A., Donadeu, F.X., Banos, G. (2018). Association of plasma microRNA expression with age, genetic background and functional traits in dairy cattle. Scientific Reports. 8(1): 12955. https://doi.org/10.1038/s41598-018-31099-w.

Jacometo, C.B., Alharthi, A.S., Zhou, Z., Luchini, D., Loor, J.J. (2018). Maternal supply of methionine during late pregnancy is associated with changes in immune function and abundance of microRNA and mRNA in holstein calf polymorphonuclear leukocytes. Journal of Dairy Science. 101(9): 8146-8158.

Jeanneteau, F.D., Lambert, W.M., Ismaili, N., Bath, K.G., Lee, F.S., Garabedian, M.J., Chao, M.V. (2012). BDNF and glucocorticoids regulate corticotrophin-releasing hormone (CRH) homeostasis in the hypothalamus. Proceedings of the National Academy of Sciences. 109(4): 1305-1310.

Jiang, S. and Yan, W. (2016). Current View of microRNA Processing. Signal Transduction Insights. 5: 9-13.

Ju, X.H., Xu, H.J., Yong, Y.H., An, L.L., Jiao, P.R., Liao, M. (2014). Heat stress upregulation of Toll-like receptors 2/4 and acute inflammatory cytokines in peripheral blood mononuclear cell (PBMC) of bama miniature pigs: An *in vivo* and *in vitro* study. Animal. 8(9): 1462-1468.

Ju, Z., Jiang, Q., Liu, G., Wang, X., Luo, G., Zhang, Y., Zhang, J., and Huang, J. (2018). Solexa sequencing and custom micro RNA chip reveal repertoire of micro RNA s in mammary gland of bovine suffering from natural infectious mastitis. Animal Genetics. 49(1): 3-18.

Khanduri, A., Sahu, A.R., Wani, S.A., Khan, R.I.N., Pandey, A., Saxena, S., Malla, W.A., Mondal, P. *et al.* (2018). Dysregulated miRNAome and proteome of PPRV infected goat PBMCs reveal a coordinated immune response. Frontiers in Immunology. 9: 2631. https://doi.org/10.3389/fimmu.2018.02631.

Kong, Z., Zhou, C., Chen, L., Ren, A., Zhang, D., Basang, Z., Tan, Z., Kang, J. and Li, B. (2019). Multi-omics analysis reveals up-regulation of APR signaling, LXR/RXR and FXR/RXR activation pathways in holstein dairy cows exposed to high-altitude hypoxia. Animals. 9(7): 406. doi: 10.3390/ani9070406.

Kumar, N., Maherchandani, S., Kashyap, S.K., Singh, S.V., Sharma, S., Chaubey, K.K., Ly, H. (2014). Peste des petits ruminants virus infection of small ruminants: A comprehensive review. Viruses. 6(6): 2287-2327.

Kuosmanen, S.M., Kansanen, E., Sihvola, V., Levonen, A.L. (2017). MicroRNA profiling reveals distinct profiles for tissue-derived and cultured endothelial cells. Scientific Reports. 7(1): 10943. DOI: 10.1038/s41598-017-11487-4.

Lawless, N., Reinhardt, T.A., Bryan, K., Baker, M., Pesch, B., Zimmerman, D., Zuelke, K., Sonstegard, T., Farrelly, C.O., Lippolis, J.D., Lynn, D.J. (2014). MicroRNA regulation of bovine monocyte inflammatory and metabolic networks in an *in vivo* infection model. G3: Genes, Genomes, Genetics. 4(6): 957-971.

Lecchi, C., Zamarian, V., Gini, C., Avanzini, C., Polloni, A., Nodari, S.R., Ceciliani, F. (2020). Salivary microRNAs are potential biomarkers for the accurate and precise identification of inflammatory response after tail docking and castration in piglets. Journal of Animal Science. 98(5): skaa153. doi: 10.1093/jas/skaa153.

Lee, J., Lee, S., Son, J., Lim, H., Kim, E., Kim, D., Ha, S., Hur, T., Lee, S., Choi, I. (2020). Analysis of circulating-microRNA expression in lactating holstein cows under summer heat stress. PLoS One. 15(8): e0231125. https://doi.org/10.1371/journal.pone.0231125.

Li, Q., Yang, C., Du, J., Zhang, B., He, Y., Hu, Q., Li, M., Zhang, Y., Wang, C., Zhong, J. (2018). Characterization of miRNA profiles in the mammary tissue of dairy cattle in response to heat stress. BMC Genomics. 19: 1-11.

Li, Z., Lan, X., Guo, W., Sun, J., Huang, Y., Wang, J., Huang, T., Lei, C., Fang, X., Chen, H. (2012). Comparative transcriptome profiling of dairy goat microRNAs from dry period and peak lactation mammary gland tissues. Plos One. 7(12): e52388. doi: 10.1371/journal.pone.0052388.

Li, Z., Wang, H., Chen, L., Wang, L., Liu, X., Ru, C., Song, A. (2014). Identification and characterization of novel and differentially expressed microRNAs in peripheral blood from healthy and mastitis holstein cattle by deep sequencing. Animal Genetics. 45(1): 20-7.

Liao, R., Lv, Y., Zhu, L., Lin, Y. (2019). Altered expression of miRNAs and mRNAs reveals the potential regulatory role of miRNAs in the developmental process of early weaned goats. PLoS One. 14(8): e0220907. https://doi.org/10.1371/journal.pone.0220907.

Lie, S., Morrison, J.L., Williams-Wyss, O., Suter, C.M., Humphreys, D.T., Ozanne, S.E., Zhang, S., Maclaughlin, S.M., Kleemann, D.O., Walker, S.K., Roberts, C.T., McMillen, I.C. (2014). Periconceptional undernutrition programs changes in insulin-signaling molecules and microRNAs in skeletal muscle in singleton and twin fetal sheep. Biology of Reproduction. 90(1): 5. doi: 10.1095/biolreprod.113.109751.

Lin, X., Luo, J., Zhang, L., Zhu, J. (2013). MicroRNAs synergistically regulate milk fat synthesis in mammary gland epithelial cells of dairy goats. Gene Expression The Journal of Liver Research. 16: 1-13.

Liu, H., Lei, C., He, Q., Pan, Z., Xiao, D., Tao, Y. (2018). Nuclear functions of mammalian MicroRNAs in gene regulation, immunity and cancer. Molecular Cancer. 17(1): 1-14.

Lu, T.X. and Rothenberg, M.E. (2013). Diagnostic, functional and therapeutic roles of microRNA in allergic diseases. Journal of Allergy and Clinical Immunology. 132(1): 3-13.

Luoreng, Z.M., Wang, X.P., Mei, C.G., Zan, L.S. (2018). Comparison of microRNA profiles between bovine mammary glands infected with *Staphylococcus aureus* and *Escherichia coli*. International Journal of Biological Sciences. 14(1): 87-99.

Magistrelli, D., Aufy, A.A., Pinotti, L., Rosi, F. (2013). Analysis of weaning induced stress in saanen goat kids. Journal of Animal Physiology and Animal Nutrition. 97(4): 732-739.

Malvisi, M., Palazzo, F., Morandi, N., Lazzari, B., Williams, J.L., Pagnacco, G., Minozzi, G. (2016). Responses of bovine innate immunity to *Mycobacterium avium* subsp. paratuberculosis infection revealed by changes in gene expression and levels of microRNA. Plos One. 11: e0164461. https://doi.org/10.1371/journal.pone.0164461

Minton, J.E. (1994). Function of the hypothalamic-pituitary-adrenal axis and the sympathetic nervous system in models of acute stress in domestic farm animals. Journal of Animal Science. 72(7): 1891-1898.

Mishra, K.P., Ganju, L., Singh, S.B. (2015). Hypoxia modulates innate immune factors: A review. International Immunopharmacology. 28(1): 425-428.

Muroya, S., Shibata, M., Hayashi, M., Oe, M., Ojima, K. (2016). Differences in circulating microRNAs between grazing and grain-fed wagyu cattle are associated with altered expression of intramuscular microRNA, the potential target PTEN and lipogenic genes. PLoS One. 11(9): e0162496. https://doi.org/10.1371/journal.pone.0162496.

Naeem, A., Zhong, K., Moisá, S.J., Drackley, J.K., Moyes, K.M., Loor, J.J. (2012). Bioinformatics analysis of microRNA and putative target genes in bovine mammary tissue infected with *Streptococcus uberis*. Journal of Dairy Science. 95(11): 6397-6408.

Naylor, D., Sharma, A., Li, Z., Monteith, G., Sullivan, T., Canovas, A., Mallard, B.A., Baes, C. and Karrow, N.A. (2020). Characterizing ovine serum stress biomarkers during endotoxemia. Journal of Dairy Science. 103(6): 5501-5508.

O'Neill, L.A. (2006). How Toll-like receptors signal: what we know and what we don't know. Current Opinion in Immunology. 18(1): 3-9.

Olejniczak, M., Kotowska-Zimmer, A., Krzyzosiak, W. (2018). Stress-induced changes in miRNA biogenesis and functioning. Cellular and Molecular Life Sciences. 75: 177-191.

Özdemir, S. (2020). Identification and comparison of exosomal microRNAs in the milk and colostrum of two different cow breeds. Gene. 743: 144609. doi: 10.1016/j.gene.2020.144609.

Pandey, A., Sahu, A.R., Wani, S.A., Saxena, S., Kanchan, S., Sah, V., Rajak, K.K., Khanduri, A. *et al*. (2017). Modulation of host miRNAs transcriptome in lung and spleen of peste des petits ruminants virus infected sheep and goats. Frontiers in Microbiology. 8: 1146. https://doi.org/10.3389/fmicb.2017.01146.

Pang, C., Liang, S., Zhong, W., Feng, L., Wei, K., Wen, C. and Liang, X. (2022). The role of milk exosomal micrornas in balancing the nutrition between buffalo breeds with low and high milk production. Indian Journal of Animal Research. 56: 1228-1234.

Rebane, A. and Akdis, C.A. (2014). MicroRNAs in allergy and asthma. Current Allergy and Asthma Reports. 14(4): 1-9.

Romano, G., Veneziano, D., Acunzo, M., Croce, C.M. (2017). Small non-coding RNA and cancer. Carcinogenesis. 38(5): 485-491.

Salama, A.A.K., Duque, M., Wang, L., Shahzad, K., Olivera, M., Loor, J. J. (2019). Enhanced supply of methionine or arginine alters mechanistic target of rapamycin signaling proteins, messenger RNA and microRNA abundance in heat-stressed bovine mammary epithelial cells *in vitro*. Journal of Dairy Science. 102(3): 2469-2480.

Srikok, S., Patchanee, P., Boonyayatra, S., Chuammitri, P. (2020). Potential role of MicroRNA as a diagnostic tool in the detection of bovine mastitis. Preventive Veterinary Medicine. 182: 105101. doi: 10.1016/j.prevetmed.2020.105101.

Stenfeldt, C., Arzt, J., Smoliga, G., LaRocco, M., Gutkoska, J. Lawrence, P. (2017). Proof-of-concept study: Profile of circulating microRNAs in bovine serum harvested during acute and persistent FMDV infection. Virology Journal. 14(1): 1-18.

Sun, J., Aswath, K., Schroeder, S.G., Lippolis, J.D., Reinhardt, T.A., Sonstegard, T.S. (2015). MicroRNA expression profiles of bovine milk exosomes in response to *Staphylococcus aureus* infection. BMC Genomics. 16(1): 1-10.

Taxis, T.M. and Casas, E. (2017). MicroRNA expression and implications for infectious diseases in livestock. CAB Reviews. 12(26): 1-20.

Taxis, T.M., Bauermann, F.V., Ridpath, J.F., Casas, E. (2017). Circulating MicroRNAs in serum from cattle challenged with bovine viral diarrhea virus. Frontiers in Genetics. 8: 91. https://doi.org/10.3389/fgene.2017.00091.

Timoneda, O., Nunez-Hernandez, F., Balcells, I., Muñoz, M., Castello, A., Vera, G., Perez, L.J., Egea, R. *et al*. (2014). The role of viral and host microRNAs in the Aujeszky's disease virus during the infection process. PloS One. 9(1): e86965. https://doi.org/10.1371/journal.pone.0086965.

Van Hese, I., Goossens, K., Vandaele, L., Opsomer, G. (2020). Invited review: MicroRNAs in bovine colostrum-focus on their origin and potential health benefits for the calf. Journal of Dairy Science. 103(1): 1-15.

Wadhwani, K.N., Modi, R.J., Islam, M.M., Patel, Y. G. (2016). Role of housing in welfare of small ruminants. Indian Journal of Animal Production and Management. 32(3-4): 130-139.

Wang, M., Moisa, S., Khan, M.J., Wang, J., Bu, D., Loor, J.J. (2012). MicroRNA expression patterns in the bovine mammary gland are affected by stage of lactation. Journal of Dairy Science. 95(11): 6529-6535.

Wang, M., Bissonnette, N., Griebel, P., Dudemaine, P.L., Do, D.N., Ibeagha-Awemu, E.M. (2019). PSVI-15 Transcriptome analysis of ileal lymph nodes identifies key microRNAs affecting disease progression in Holstein cows with subclinical Johne's disease. Journal of Animal Science. 97: 207-208.

Wright, K., Plain, K., Purdie, A., Saunders, B.M., Silva, K.D. (2020). Biomarkers for detecting resilience against mycobacterial disease in animals. Infection and Immunity. 88(1): e00401-19.

Wu, M., Yi, Z., Shanshan, M., Congbo, M., Lingxia, O. (2022). MicroRNA-140-5p suppresses hypoxia-induced nephrotoxicity and renal fibrogenesis in *in vitro* conditions. Indian Journal of Animal Research. 56(11): 1338-1344. Doi: 10.18805/IJAR.BF-1488.

Wu Z., Fu Y., Cao J., Yu M., Tang X., Zhao S. (2014). Identification of differentially expressed miRNAs between white and black hair follicles by RNA-sequencing in the goat (*Capra hircus*). International Journal of Molecular Sciences. 15: 9531-9545.

Yang, H., Liu, X., Hu, G., Xie, Y., Lin, S., Zhao, Z., Chen, J. (2018). Identification and analysis of microRNAs-mRNAs pairs associated with nutritional status in seasonal sheep. Biochemical and Biophysical Research Communications. 499(2): 321-327.

Zhai, B., Zhang, L., Wang, C., Zhao, Z., Zhang, M., Li, X. (2019). Identification of microRNA-21 target genes associated with hair follicle development in sheep. Peer J. 7: e7167. doi: 10.7717/peerj.7167.

Zhang, X., Cheng, Z., Wang, L., Jiao, B., Yang, H., Wang, X. (2019). MiR-21-3p centric regulatory network in dairy cow mammary epithelial cell proliferation. Journal of Agricultural and Food Chemistry. 67(40): 11137-11147.

Zheng, C.Y., Zou, X., Lin, H.J., Zhao, B.C., Zhang, M.L., Luo, C.H., Fu, S.X. (2018). miRNA-185 regulates the VEGFA signaling pathway in dairy cows with retained fetal membranes. Theriogenology. 110: 116-121.

Zheng, Y., Chen, K.L., Zheng, X.M., Li, H.X., Wang, G.L. (2014). Identification and bioinformatics analysis of microRNAs associated with stress and immune response in serum of heat-stressed and normal Holstein cows. Cell Stress and Chaperones. 19: 973-981.