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## **Epigenetic Markers for Animal Health and Productivity in Livestock**

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**Abstract:** Epigenetic markers are molecular modifications that affect gene expression without altering the DNA sequence. They are influenced by genetic and environmental factors and play crucial roles in animal health and productivity. Epigenetic processes include DNA methylation, histone modification, and chromatin remodeling. This review supports the recent discoveries on the impacts of epigenetic processes on livestock production and health traits, such as growth, development, disease resistance, and stress response. It also discusses the potential applications of epigenetic biomarkers in livestock management and improvement, as well as the challenges and gaps in livestock epigenetics research.

**Keywords:** DNA methylation; Histone modification; Chromatin remodeling; Gene expression; Phenotypic variation; Livestock productivity.

### **Introduction**

Epigenetics is a fascinating and rapidly evolving field of research that can help us understand how our genes interact with our environment. It is the study of how the environment and other factors can change the way that genes are expressed. While epigenetic changes do not alter the sequence of a species's genetic code, they play an important role in development, health, and disease. Scientists who work in epigenetics explore the mechanisms that affect the activity of genes, such as DNA methylation, histone modification, and non-coding RNA. Epigenetic changes are influenced by various factors, such as nutrition, stress, age, and exposure to chemicals. Epigenetic changes are also inherited from one generation to the next (Ibeagha Awemu et al.,2015; Ieagha Awemu et al.,2021).

Epigenetic markers are measurable changes in the epigenome that reflect the status of epigenetic processes. They are used to assess the effects of epigenetic processes on livestock traits, such as productivity, disease resistance, stress response, and reproduction. They are also used to identify the genes and pathways involved in epigenetic regulation of livestock phenotypes (Ibeagha Awemu et al.,2015; Ieagha Awemu et al.,2021).

Epigenetic profiling is the analysis of epigenetic markers across the genome or at specific genomic regions. It is performed using various techniques, such as bisulfite sequencing, chromatin immunoprecipitation, or methylated DNA immunoprecipitation. They reveal the patterns of epigenetic variation among individuals, tissues, or conditions (Ibeagha Awemu et al.,2015; Ieagha Awemu et al.,2021).

Epigenetic applications are the potential uses of epigenetic information in livestock production and health management. Therefore, these epigenetic markers are involved improving animal breeding by incorporating epigenetic data into genomic selection, enhancing animal welfare by modulating epigenetic processes through

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nutrition or environmental interventions, and developing epigenetic biomarkers for disease diagnosis or prognosis.

## **The Importance of Epigenetic Markers in Animal Productivity**

Epigenetic markers are chemical modifications or molecules that can affect gene expression without altering the DNA sequence. They include DNA methylation, histone modifications, chromatin remodeling, and non-coding RNAs. Epigenetic markers can respond to environmental factors such as nutrition, pathogens, climate, and management practices, and influence animal phenotypes such as health, reproduction, growth, and production (Ibeagha Awemu & Zhao, 2015; Ieagha Awemu & Yu, 2021).

Epigenetic markers are important for animal productivity because they can modulate the expression of genes involved in various biological processes that affect animal performance. For example, DNA methylation and histone modifications can regulate genes related to milk production, meat quality, feed efficiency, and disease resistance in livestock species<sup>12</sup>. Epigenetic markers can also mediate the effects of maternal nutrition, fetal programming, and early-life experiences on animal development and health (Ibeagha Awemu & Zhao, 2015; Ieagha Awemu & Yu, 2021).

Epigenetic markers can be used as tools to improve animal productivity through various strategies. For instance, epigenetic markers can be used to identify animals with desirable traits or to predict their breeding values based on their epigenetic profiles (Ibeagha Awemu & Zhao, 2015; Ieagha Awemu & Yu, 2021). Epigenetic markers can also be used to manipulate gene expression by using epigenetic drugs, dietary supplements, or gene editing techniques (Ibeagha Awemu & Zhao, 2015; Ieagha Awemu & Yu, 2021). Epigenetic markers can also be used to monitor animal health and welfare by detecting epigenetic changes associated with stress, inflammation, or infection (Ibeagha Awemu & Zhao, 2015; Ieagha Awemu & Yu, 2021).

## **Mechanisms of Epigenetic Markers in Animals**

The mechanism of epigenetic markers in animals is the regulation of gene expression by modifying the accessibility and activity of the DNA without changing its sequence. Epigenetic markers are elicited by environmental cues or inherited from parents, and affect the metabolic function, behavior, and performance of animals and their offspring. Some of the main types of epigenetic mechanisms are:

- DNA methylation: This is the addition of a methyl group to a cytosine base, usually in a CpG dinucleotide context, which silences gene expression by preventing transcription factor binding or recruiting methyl-binding proteins that alter chromatin structure (Jin et al., 2011).
- Histone modifications: These are the addition or removal of various chemical groups (such as acetyl, methyl, or phosphate) to the amino-terminal tails of histone proteins, which activate or repress gene expression by changing the affinity between histones and DNA or by recruiting chromatin-modifying enzymes or transcriptional regulators. (Li et al., 2020).
- Non-coding RNAs: These are RNA molecules that do not encode proteins, but regulate gene expression at various levels, such as transcription, splicing, translation, or degradation. Examples of non-coding RNAs include microRNAs, long non-coding RNAs, circular RNAs, and small interfering RNAs (Li et al., 2020).
- Chromatin remodeling: This is the alteration of the nucleosome position or composition by ATP-dependent complexes, which enhance or inhibit gene expression by exposing or occluding regulatory elements or by exchanging histone variants with different properties (Li et al., 2020).

## **Measurement of Epigenetic Profile of Farm Animals**

The epigenetic profile of animals can be measured by various methods that detect and quantify different types of epigenetic marks across the genome. Some of the common methods are:

- Bisulfite sequencing: This method converts unmethylated cytosines to uracils, while leaving methylated cytosines unchanged, and then sequences the DNA to identify the methylation status of each cytosine (Li et al., 2011).

- Chromatin immunoprecipitation (ChIP): This method uses antibodies to pull down DNA fragments that are bound by specific histone modifications or other chromatin-associated proteins, and then sequences or hybridizes the DNA to identify the genomic regions enriched for those modifications or proteins (Gade & Kalvakolanu, 2012).
- Non-coding RNA sequencing: This method isolates and sequences different classes of non-coding RNAs, such as microRNAs, long non-coding RNAs, or circular RNAs, and then maps them to the genome or transcriptome to identify their expression levels and targets (Cable et al., 2021).
- Single-cell epigenetic profiling: This method combines single-cell isolation techniques with epigenetic assays to measure the epigenetic marks of individual cells, and then uses computational methods to infer the epigenetic age or cell type identity of each cell (Clark et al., 2016).

## **Current Studies on Epigenetic Markers in Livestock**

Current research on epigenetic markers in livestock has also demonstrated that epigenetic markers is used as tools to improve animal productivity and health through various strategies. For instance, epigenetic markers can be used to identify animals with desirable traits or to predict their breeding values based on their epigenetic profiles (Ibeagha Awem & Wang, 2020; Whelan et al., 2023). Epigenetic markers are also used to manipulate gene expression by using epigenetic drugs, dietary supplements, or gene editing techniques(Ibeagha Awem & Wang, 2020; Whelan et al., 2023). Epigenetic markers are also be used to monitor animal health and welfare by detecting epigenetic changes associated with stress, inflammation, or infection (Ibeagha Awem & Wang, 2020; Whelan et al., 2023).

However, current research on epigenetic markers in livestock faces several challenges and limitations that need to be addressed. Some of the challenges include the complexity and diversity of epigenetic mechanisms, the lack of standardized methods and protocols for epigenetic analysis, the ethical and social implications of epigenetic interventions, and the need for more funding and collaboration among researchers (Ibeagha Awem & Wang 2020; Whelan et al.,2023).Some of the limitations include the scarcity of epigenetic data and resources for livestock species, the difficulty of integrating epigenetic information with genomic and phenotypic data, the uncertainty of the stability and heritability of epigenetic marks, and the lack of causal evidence for the effects of epigenetic marks on animal traits (Ibeagha Awem & Wang, 2020; Whelan et al., 2023).

## **The Potential of Epigenetic Markers for Improving Animal Breeding Programs**

The potential of epigenetic markers for improving animal breeding programs lies in their ability to provide additional information and control over gene expression and animal performance. Epigenetic markers can modulate the expression of genes involved in various biological processes that affect animal traits of economic importance. Epigenetic markers can also mediate the effects of maternal nutrition, fetal programming, and early-life experiences on animal development and health (Ibeagha Awemu & Zhao,2015; Wang & Ibeagha Awemu, 2020).

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## **Challenges and Limitations in the Use of Epigenetic Markers**

Epigenetic biomarkers are molecular features that can reflect the influence of environmental factors on gene expression, without altering the DNA sequence. They can provide valuable information about the function and regulation of genes, as well as the risk and progression of diseases. Epigenetic biomarkers can be measured using various technologies, such as PCR, sequencing, and pyrosequencing, on different types of biological samples, such as blood, tissue, urine, and saliva. However, there are several challenges and limitations in the use

of epigenetic biomarkers in the clinical laboratory, such as the lack of standardization, validation, and interpretation of epigenetic data, as well as the ethical and social implications of epigenetic testing (Rozek et al., 2014).

Epigenetics is the study of how environmental factors can affect gene expression without changing the DNA sequence. Epigenetics encompasses four main research subfields: gene expression, molecular epigenetics, clinical epigenetics, and epigenetic epidemiology. Each subfield has a different focus and perspective on what constitutes the environment and how it interacts with genes and epigenetics. Epigenetics researchers use various discursive strategies to describe the relationships between genes, epigenetics, and environment, such as metaphors, analogies, and models (Pinel et al., 2019).

Epigenetic markers are molecular elements that mediate the communication between genes and environment. They can be understood as signals that enable a cell to remember past events and respond to current stimuli. Epigenetic markers can modulate gene expression by adding or removing chemical groups to DNA or histones, which are proteins that wrap around DNA. The most common epigenetic markers are DNA methylation and histone modifications. Epigenetic markers can be influenced by various environmental factors, such as diet, stress, infection, pollution, and drugs (Zovkic et al., 2013).

Epigenetic biomarkers have potential applications in various clinical settings, such as diagnosis, prognosis, classification, and treatment of diseases. For example, epigenetic biomarkers can be used to detect cancer at an early stage, predict the response and resistance to therapy, identify subtypes of cancer with different outcomes and therapeutic options, and monitor the recurrence and progression of cancer. Epigenetic biomarkers can also be used to assess the risk and susceptibility to complex diseases, such as cardiovascular disease, diabetes, obesity, and neurodegenerative disorders (Kamińska et al., 2019).

Machine learning is a branch of artificial intelligence that can analyze large and complex data sets using algorithms that learn from data. Machine learning can be applied to epigenetic data to identify patterns, associations, and predictions that are not easily detectable by conventional statistical methods. Machine learning can also help to integrate epigenetic data with other types of data, such as genomic, transcriptomic, proteomic, metabolomic, and phenotypic data. Machine learning can facilitate the discovery and validation of novel epigenetic biomarkers for clinical purposes (Rauschert et al., 2020).

Machine learning also faces some challenges and limitations in the analysis of epigenetic data. One challenge is the high dimensionality and sparsity of epigenetic data, which means that there are many more features (such as CpG sites) than samples (such as patients), and that many features have missing or zero values. Another challenge is the heterogeneity and variability of epigenetic data across different tissues, cells, individuals, populations, and environments. A third challenge is the causality and interpretability of machine learning models, which means that it is not always clear how machine learning models make predictions or what they imply for biological mechanisms or clinical implications (Brasil et al., 2021).

## **Future Directions for Research on Epigenetic Markers in Animal Health and Productivity**

- a. Epigenetic variation is the diversity of epigenetic states among individuals or populations, which can result from genetic variation, environmental variation, or stochastic variation. Epigenetic variation can contribute to phenotypic variation and plasticity, as well as evolutionary potential and adaptation. Epigenetic variation can be measured using various techniques, such as bisulfite sequencing, chromatin immunoprecipitation, and RNA sequencing, which can reveal the patterns and levels of epigenetic modifications across the genome.
- b. Epigenetic biomarkers are epigenetic features that can be used to diagnose, predict, or monitor diseases or traits in animals. Epigenetic biomarkers can reflect the effects of environmental factors on gene expression and disease susceptibility or resistance. Epigenetic biomarkers can also provide information about the function and regulation of genes, as well as the interactions between genes and environment. Epigenetic biomarkers can be detected in various biological samples, such as blood, tissue, milk, hair, and saliva.
- c. Epigenetic processes can respond to environmental factors and underlying genotypes to influence animal health and productivity. For example, epigenetic processes can affect animal growth and development, milk yield and quality, wool quality and quantity, meat quality and quantity, reproduction and fertility, disease resistance and immunity, behavior and welfare, and adaptation and resilience. Epigenetic processes can also be manipulated by various interventions, such as nutrition, stress management, breeding strategies, and gene editing.

- d. Epigenetic processes can also have transgenerational effects on animal health and productivity. For example, epigenetic processes can mediate the effects of maternal nutrition, stress, infection, or exposure to toxins on offspring development and performance. Epigenetic processes can also transmit the effects of paternal nutrition, stress, infection, or exposure to toxins on offspring health and fertility. Epigenetic processes can also influence the inheritance of acquired traits or adaptations across generations.
- e. Epigenetic research faces some challenges and limitations in animal health and productivity. One challenge is the complexity and variability of epigenetic processes across different tissues, cells, individuals, species, and environments. Another challenge is the lack of standardization and validation of epigenetic methods and data analysis. A third challenge is the ethical and social implications of epigenetic research and applications, such as animal welfare, consumer acceptance, regulatory issues, and intellectual property rights.

## **Conclusion**

Epigenetic markers are molecular features that reflect and modulate the effects of environmental factors on gene expression and phenotypic traits in animals. They have various implications for animal health and productivity, such as influencing stress response, immune function, metabolism, behavior, and adaptation. They can also be used as biomarkers for disease diagnosis, prognosis, classification, and treatment. In addition, they can be inherited across generations, mediating the effects of parental experiences on offspring performance. Moreover, they provide novel insights and opportunities for improving animal health and productivity. However, they face some challenges and limitations, such as the complexity and variability of epigenetic processes, the lack of standardization and validation of epigenetic methods and data analysis, and the ethical and social implications of epigenetic research and applications. Therefore, epigenetic research requires interdisciplinary collaboration, rigorous methodology, and careful consideration of its potential benefits and risks for animals and humans.

## **Scientific Ethics Declaration**

The authors declare that the scientific ethical and legal responsibility of this article published in EPHELS journal belongs to the authors.

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