Review paper

Epigenetic mechanisms and their significance in livestock species

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ABSTRACT

Epigenetics refers to possible causal mechanisms acting on the genes that govern the phenotype. It plays a crucial role in many biological processes, such as gene imprinting, gene silencing, X chromosome inactivation, cell reprogramming etc. Epigenetic marks such as DNA methylation, histone tail modifications, chromatin remodelling, and other molecules which can transmit epigenetic information like noncoding RNA species constitute the "epigenome". For years, animal selection in livestock species has been performed by selecting animals using genetic inheritance. However, genomic information alone explains only a section of the phenotypic variance in traits. It is likely that some of the unaccounted variance is embedded within the "epigenome". Evolutionary studies have reported that non-genetic information derived from epigenetic, microbiota, environmental influences that drive natural selection can also be inherited across generations. Epigenetic factors respond to external or internal environmental factors like nutrition, microorganisms and climate have the ability to change gene expression leading to the emergence of specific phenotypes, which can be given consideration in livestock improvement programs. These diverse sources of inheritance can be utilized for the better prediction of the transmissable ability of the animal and thus can improve the methodologies of selection. Currently, high-throughput sequencing techniques and microarray-based techniques are intensively used in epigenomics profiling. The advances in next-generation sequencing technologies allow genome-wide profiling of methyl marks on DNA, which ultimately aims to find novel biomarkers for better understanding of complex polygenic traits. They can also be used along with genome-wide association study (GWAS), selection signature analysis and comparative epigenomics to shed light on potential adaptive evolution. However, epigenetic research on farm animal species is presently inadequate due to a lack of recognition, funding, and a worldwide integrated network of researchers.

Key words: Epigenetic mechanisms, Epigenomics, Missing heritability, Variation, Inheritance

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INTRODUCTION

The term epigenetics was coined by Conard Waddington in 1942 after experimenting effects of ether vapour on Drosophila melanogaster, which referred to probable mechanisms which influence the genes that controls phenotypic expression. Epigenetics are often defined as alterations within the gene expression profile of a cell that are not caused by changes within the DNA sequence (Peschansky and Wahlestedt, 2014). It supports Lamarckisms concept that organism can pass on to its offsprings, physical characteristics that they acquired through use or disuse during their lifetime (soft inheritance). Although an individual has one genome, but it's made up of as many epigenomes as number of different cell types. The epigenome of a cell is the complete collection of epigenetic marks, like DNA methylation, histone tail modifications, chromatin remodelling and non-coding RNA species (Rakyan et al., 2011). These mechanisms are known to be involved in various molecular mechanisms like gene silencing, Imprinting, paramutation, transposon silencing, position effect, cell reprogramming, maternal effects, and transvection (Triantaphyllopoulos et al., 2016) (fig 1). Today, variations within the genome are gaining increasing importance in livestock improvement strategies. Genomic information alone, however, explains only a part of the phenotypic variance in traits. Therefore, it is likely that some of the unaccounted variance is embedded within the epigenome. Ibeagha-Awemu and Zhao, 2015 and Triantaphyllopoulos et al., 2016 have made efforts to delineate importance of epigenetic inheritance in livestock species but till date only a few detailed reports are available on modelling epigenetic variation and their importance (David et al., 2020). Thus, here we attempted to review notable research work related to quantification of epigenetic variation in animal breeding along with recent developments in epigenomics.

Epigenetic mechanisms and their significance in central dogma

DNA methylation

DNA methylation occurs at CpG dinucleotides and involves the addition of a methyl group to the 5′ position of the cytosine to generate 5-methylcytosine (5mC). Cytosine methylation also occurs but to a lesser extent in non-CpG regions (Ziller et al., 2011). It is responsible for heterochromatin formation and maintenance causing transposon silencing, X chromosome inactivation, and gene imprinting (Bird, 2002; Mattick et al., 2009). Though CpG methylation in promoters prevents genes from their expression, methylation within the genes leads to transcriptional activation (Langevin and Kelsey, 2013).

Post-translational histone modifications (PTMs)

DNA in eukaryotic cells is compacted and packaged into chromatin. Nucleosome is the fundamental unit of chromatin. It consists of a histone protein octamer (2 each of histones H3, H4, H2A and H2B) around which roughly1.75 turns of DNA are wrapped. Histones are subject to numerous PTMs that have the capability to encode epigenetic information. Common modifications include acetylation, methylation, phosphorylation and ubiquitylation which are deposited or removed from histones, by specific enzymes (Aravin et al., 2003). Histone modifications impact all DNA processes including transcription, DNA repair, replication and recombination (Bannister and Kouzarides, 2011).

Chromatin remodelling

Restructuring or repositioning of nucleosomes within chromatin to permit or inhibit access to the nearby DNA is termed as "Chromatin remodelling". It is majorly performed by ATP-dependent chromatin remodelling complexes (Martin, 2012). This dynamic epigenetic mechanism has regulatory role in several key biological processes, like egg cell DNA replication and repair, apoptosis, development and pluripotency (Ho and Crabtree, 2010).

Non-coding RNA

Small interfering RNAs and other non-coding RNAs such as piwi RNAs (piRNAs) and microRNAs (miRNAs) mediates regulation of gene expression and chromatin remodelling (Mattick et al., 2009). miRNAs are known to involve in pathways underlying disease manifestation, milk production and adipogenesis (Triantaphyllopoulos et al., 2016). Other group of non-coding RNA includes long ncRNAs (length > 200 nts) regulate DNA processes, via cis-acting and trans-acting mechanisms and also act as molecular guides, scaffolds, decoys and allosteric modulators of gene expression (Bassett et al., 2014).

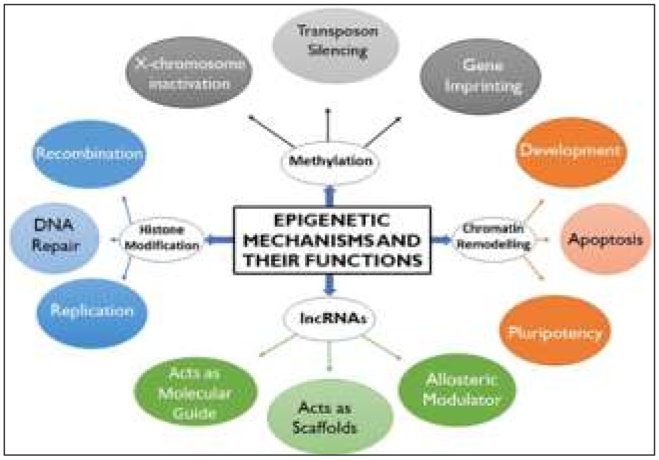

Figure 1. *Different epigenetic mechanisms and their role in various biological processes*

EPIGENETIC INHERITANCE

Epigenetic inheritance refers to the transmission of epigenetic marks to offspring (vanOtterdijk and Michels, 2016; Pang et al., 2017). It includes two independent phenomena environmental sensing (exposure to an event) in the parents, and phenotypic response or adaption in the offspring (Babenko et al., 2015). The epigenetic alteration of certain genes, produced by an environmental trigger, could lead to significant changes in an individual's body that could persist over time and in turn signal the epigenetic reorganization of the subsequent generation. Lacal and Ventura (2018) used three concepts, 1) a direct form of epigenetics (DE) and two indirect epigenetic processes - 2) within (WIE) and 3) across (AIE) (Fig 2).

DE refers to changes that can be seen in the lifespan of an individual, due to direct exposure to environment. This phenomenon implies dynamic and short-term regulation of gene expression, mediated by the action of regulatory proteins, called transcription factors, like c-fos, c-jun, ZENK and CREB. The genes that encode for such necessary functional elements are called immediate-early genes, due to change in their expression and is the first event that introduces series of adaptive changes, including the transcriptional regulations of other genes (Johnson, 2010), ultimately producing long-lasting effects. Epigenetic modifications can be triggered by many environmental factors, such as diet (Mathers et al., 2010), pollution (Christensen and Marsit, 2011), stressors (Talikka et al., 2012). For instance, epigenetic regulation of BDNF gene was found to be involved in fear extinction in mice following behaviour training which influenced changes in H3 acetylation near the p1-promoter of the BDNF gene (Bredy et al., 2007). In concordance with this, stress in rats, induced by their brief immobilization, which provokes a glucocorticoid-dependent down regulation in the expression of the BDNF gene, associated with histone acetylation changes around the promoter region (Fuchikami et al., 2009).

Within indirect epigenetics (WIE) comprise all of the epigenetic changes that act on the developing individual. Initially, it begins at the very moment when zygote is formed and the environment begins acting upon it. This class includes all the factors that can affect the developing individual, from formation of zygote to end of gestation. Kovalchuk (2012) supported the idea of function of the intrauterine environment in epigenetic transmission. The underlying concept is that environmental changes occur when the (proto)-individual actually exists, synchronously. One such study, involving ruminants, investigated the effects of restricted methyl donor dietary vitamins, *i.e*., vitamin B6, vitamin B12, methionine and folate in pregnant ewes of Scottish blackface breed. The offspring of these ewes exhibited higher blood pressure greater tendency to obesity and insulin resistance when compared with the controls (Sinclair et al., 2007).

Across indirect epigenetics (AIE) describes what happens in offsprings (F2) due to environmental sensing in parents (F0) (and even grandparents), which asynchronously modify the composition of germ cells (intrauterine environment can also act upon germ cells). WIE and AIE resemble the concept of epimutations: all epigenetic changes that appear to be transmitted across generations as a result of RNA-based trans homologous epigenetic modulation of gene expression (Bennett-Baker et al., 2003; Tomar and Teperino, 2020). As a matter of fact, environmental exposure of mice to methoxychlor, an endocrine disruptor that is commonly used as an agricultural fungicide, increases sensitivity to stress, anxious behaviour in the F3 generation (Crews et al., 2012) reflects significance of AIE. Across generations, epigenetically mediated changes in behaviour pattern through DNA methylation occur in chickens because of both chronic stress and brief periods of early social isolation from their flock (Goerlich et al., 2012). For detailed understanding of molecular mechanisms behind epigenetic inheritance one can refer (Skvortsova et al., 2018).

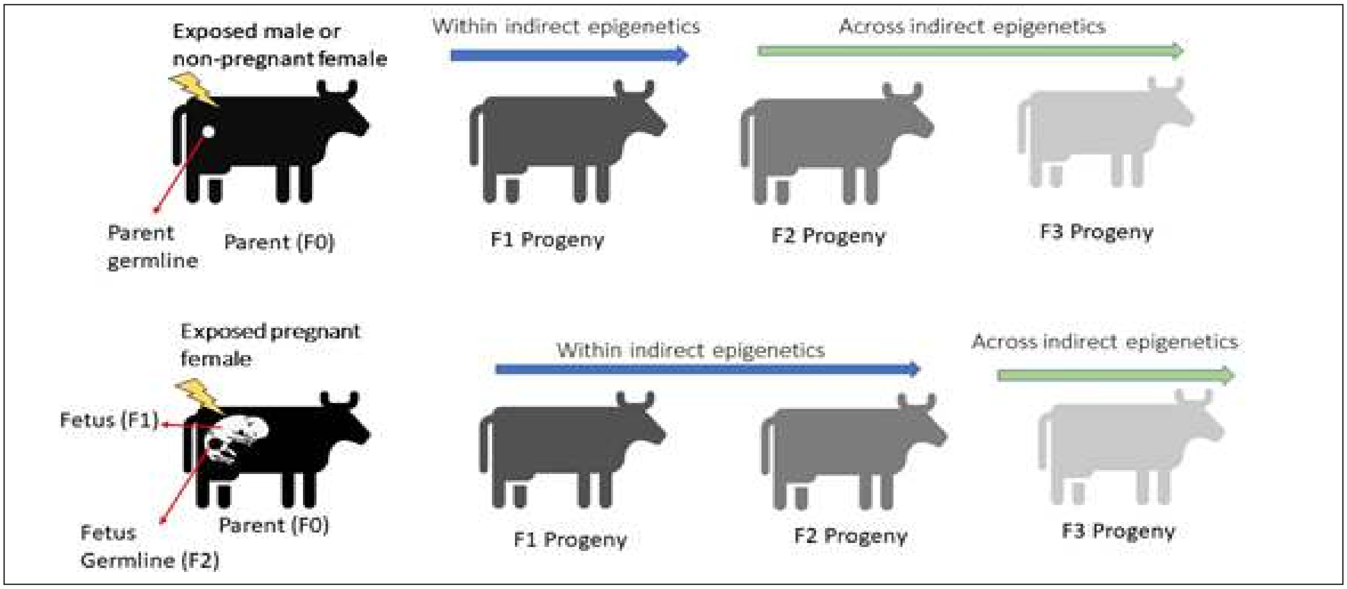

Fig 2*: Environmental sensing and epigenetic inheritance from generations to generations.*

Concept of missing heritability and modelling epigenetic variation

While genome wide association studies have identified more than one lakh strong trait-variant associations (Buniello et al., 2019), many of these variants can only explain a portion of the observed heritability (Manolio et al., 2009). Many indeed failed to predict manifestation of complex traits. This is regarded as the “Missing Heritability” problem and this phenomenon highlights a gap in our knowledge of the basic mechanisms of phenotypic variation, ontogeny, and inheritance. The missing heritability is contributed by both genetic and non-genetic factors (Bonduriansky and Day, 2018). The majority of economic traits are polygenic in nature. Therefore, complex network of genetic interactions between genes and their variants associated with the traits and contribute to the phenotype, thereby might explain specific "missing heritability". Epigenetic variations and epistasis (gene–gene interactions result in masked or altered genotype–phenotype relationships) are known to explain missing heritability. Some authors also considered it as "phantom heritability" (Zuk et al., 2012).

For years, animal selection has been performed by exploiting additive genetic inheritance. However, evolutionary biologists have reported that non-genetic factors (epigenetic, microbiota, environmental inheritance etc) which drive natural selection can also be inherited to offsprings. Significant numbers of inheritance studies have suggested inclusive or general heritability which combines all sources of information that inherits across generations (Danchin et al., 2011). The missing heritability is contributed by both genetic and non-genetic factors (Bonduriansky and Day, 2018). It bridges a gap in our knowledge of the basic mechanisms of phenotypic variation, ontogeny, and inheritance.

Tal et al. (2010) developed a model for the estimation of the covariance between relatives for both asexual and sexual reproduction as a function of epigenetic heritability, the reset coefficient (v) which can be defined as unknown probability of changing the epigenetic state during gametogenesis and/or early development, and its complement, the epigenetic transmission coefficient (1- v). According to their model, the covariance between relatives is reduced as there is many ways to dissipate (or reset) the epigenetic marks. Therefore, for sexual diploid organisms, the covariance between parent and its offspring is greater than the covariance between sibs, even though the additive numerator relationship between them is identical. The ideology of this model is that, during the vertical transmission of epigenetic marks from dam to offspring and from sire to offspring, an unknown portion of them is lost thus not transmitted to the subsequent generation.

Varona et al. (2015) proposed a Bayesian mixed model methodology that allows the calculation of epigenetic variance from a genealogical and phenotypic database. The methodology is based on the establishment of a matrix of epigenetic relationships that depends on the reset coefficient. David and Ricard 2019 came up with transmissibility model to estimate general heritability. Similar to the animal model, their model uses pedigree and phenotypic records to calculate variance components and predict the transmissible ability of an individual, but differs by estimating the path coefficients of inherited variance from parent to offspring instead of using a presumed value of 0.5 for both the sire and the dam (as in additive genetic relationship matrix). Using this model in a simulated study it is found heritability corresponding to epigenetic inheritance as 0.05 to 0.1 (David and Ricard, 2019).

Transmissibility model: $y = X\beta + Zt + Wp + Sm + Rl + e$

where, y is phenotype β is the vector of fixed effects; t is the vector of transmissible values; p is the vector of permanent environmental effects; m is the vector of maternal genetic effects; l is the vector of random effects; e is the vector of residuals; X, Z, W, S, and R are the corresponding known incidence matrices. In recent study using this model, to determine whether non-genetic inherited effects play a role in the inheritance of residual feed intake, the two path coefficients of transmission (sire or dam) estimated by the transmissibility model differed from 0.5 (David et al., 2020) (Fig 3). This model did not consider microbial and cultural inheritance from sire side as progeny never comes in contact with sire in animal husbandry because of advancement and practice of artificial insemination. Trejo and Coworkers in 2020, developed a statistical approach based on Bayesian inference, to infer the epigenetic architecture of complex disease, determine the variation captured by epigenetic effects, and estimate phenotype-epigenetic probe associations jointly.

However, quantifying the proportion of variance explained by different sources of non-genetic inherited effects including epigenetic effects is challenging without additional information than pedigree and phenotypes (David and Ricard, 2019), which may explain the relatively low number of reports of significant epigenetic variance in the literature (Paiva et al., 2018). This objective can be only achieved by considering additional information in the model such as measurement of the shared microbiota, methylation patterns reflecting epigenetic transmission, etc. (David et al., 2020).

Expanding horizons: epigenetics to epigenomics

Earlier pyrosequencing, methylation-specific polymerase chain reaction (PCR), and direct Sanger sequencing have been the commonly used methods for

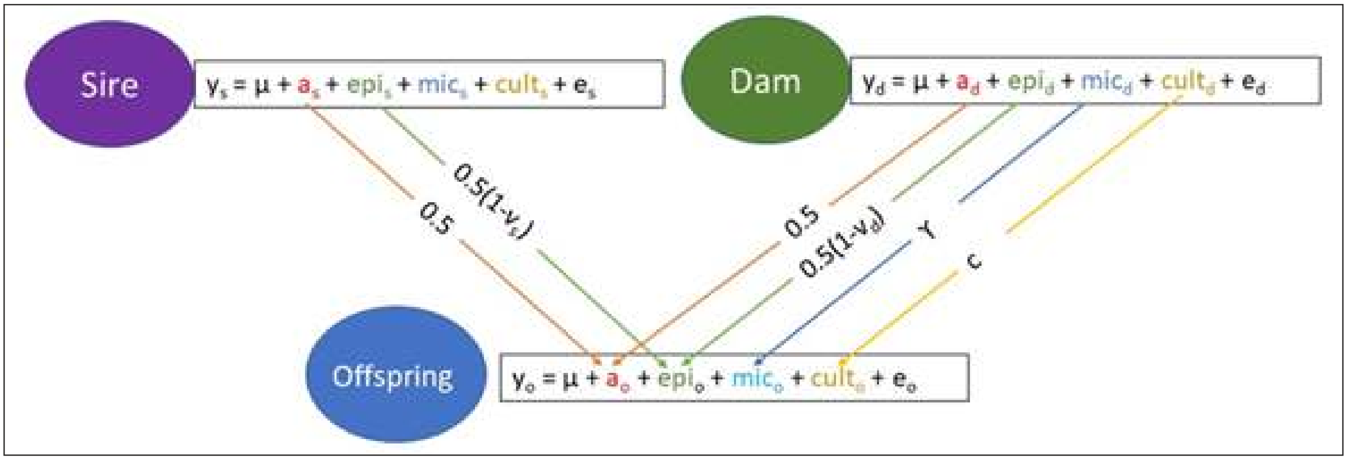

Fig 3: *Path coefficient diagram describing the transmission of the different inherited factors in livestock species. Here a: genetic effects; epi: epigenetic effect; mic: microbiota effect; cult: cultural effect; y: phenotype; e: residual. Indices s, d and o refer to sire, dam and offspring,*

analysis of targeted regions, such as a regulatory region of a single gene or a CpG (Cytosine-phosphate-Guanine) island. Although useful, the short comes of these techniques include low quantification accuracy, short read length, and low throughput. Over the last years, several methods were developed to profile 5mC providing a genome-wide spread of DNA methylation change. Next-generation sequencing technology has brought significant advancement to epigenomic research, particularly in DNA methylation profiling (Lister and Ecker, 2009). A detailed characterization of the most commonly used genome-wide techniques for capturing DNA methylation is depicted in Table 1 (adopted from Barros-Silva et al., 2018). Affinity enrichment-based methods uses antibodies and methylated CpG binding proteins to capture the methylated genomic regions for sequencing (Serre et al., 2009). Restriction enzyme-based methods utilise restriction enzymes like *Msp*I which cleave the recognition sequence near DNA methylation (CCCG motifs) allowing identification of 5-methylcytosine in selected sequences (Maunakea et al., 2010). Whereas in bisulfite conversion-based sequencing, bisulfite treatment is carried after denaturating DNA during which the unmodified cytosine is converted to uracil, but a methylated cytosine remains unchanged. This allows base resolution detection of cytosine methylation (Hayatsu et al., 2008).

Epigenome wide association studies (EWAS) have markedly replaced targeted approaches focusing on particular candidate genes, and they offer promising results for systematically decrypting the role of epigenetic variation in inheritance of complex polygenic traits. Genome-wide association studies (GWAS) developed from trait association similarly EWAS also harnessed the association studies intended to understand the molecular basis of complex inheritance. Epigenome-wide association studies hold promise for the identification of new regulatory mechanisms that may be influenced by modification in environmental and husbandry factors (Michels et al., 2013). *Table 1: Key features of genome-wide approaches for DNA methylation profiling. CpGs: Cytosine-phosphate-Guanine; bp: base pair.*Through EWAS differential methylation regions have been identified in rats exposed to a pesticide methoxychlor that are known to involved in prostate disease, kidney disease, obesity, and the presence of multiple diseases (Nilsson et al., 2020). In another EWAS study related to severity of COVID -19, DNA methylation status of 44 CpG sites were associated with the clinical severity of the disease. Of these loci, 23 (52.3%) were located in 20 annotated coding genes. These genes, like the inflammasome component Absent in Melanoma 2 (AIM2) and the Major Histocompatibility Complex, class I C (HLA-C) mainly participated in the production of interferon to viral infections (de Moura et al., 2021). Liu et al., 2019 identified 2214 differentially methylated genes known to involve in different biological functions by enrichment analysis in seven types of cancer. Liu et al., 2020 using comparative epigenomic approach, cross-mapped 8 histone marks of 1300 samples from human to cattle, covering 178 unique tissues/cell types. By analyzing 723 RNA-seq and 40 whole genome bisulfite sequencing (WGBS) datasets in cattle, validated that cross-mapped histone marks captured tissue-specific expression and methylation, reflecting tissue-relevant biological function. They also estimated 2610 trait correlations by using their tissue-trait associations. For instance, the age-at-menopause in human was significantly (r = 0.69) correlated with stillbirth in cattle. Further, epigenomic variation could also explain manifestation of morphological traits like coat colour, stature, horn pattern etc. Significant differential methylation patterns for coat colour were observed between Nili Ravi black and white skin tissues for pigmentation related genes (Annual Report, ICAR-NBAGR, 2020).

APPLICATION IN LIVESTOCK SPECIES

Production

Attributes	**Affinity Enrich-Based Methods**	**Restriction Enzymes-Based Methods**	**Bisulfite Conversion-Methods**
Resolution	~150 bp	Single-base	Single-base Reads/
Sample	~30-50 million reads	~ 10 millon reads	>500 million reads
CpGs covered	~23 million CpGs	~2 million CpGs	>28 million CpGs
Pros	Cost-effective method No mutations introduced	High sensitivity with lower costs	Evaluate methy lationstatus of every CpG sites
Cons	Biased towards hypermethylated regions	CpG regions without restriction sites are not covered	High cost Requires high DNA input
Application	Suitable for rapid, large scale and low-resolution studies	Suitable for site-specific/ targeted studies	Suitable for resolution studies

Nutrition is one of the most important environmental factors affecting phenotype. For example, feeding diet rich in corn straw to milking cows led to changes in the methylation state of genes involved in fat and protein biosynthesis in the mammary tissues (Dong et al., 2014). Similarly, supplementing the diets of dairy cows with diet rich in unsaturated fatty acids showed significant alterations in the expression of two histone acetyltransferases (HAT1 and KAT2) which revealed that epigenetic mechanisms might participate in the metabolism of nutrient effect on milk fat synthesis (Li et al., 2013). Nutrients are also known to have influence on miRNA expression in livestock species. A high/low fat diet modified the miRNA expression in subcutaneous and visceral adipose tissues in cattle. Moreover, a higher number of miRNAs were identified in the animals fed with high fat diet when compared to the low-fat diet (Romao et al., 2012). High lactating cows fed diets rich in unsaturated fatty acids shown a differentially regulated pattern of miRNAs in comparison to same cows on control diets (Li et al., 2014).

It is evident that the nutritional contents of diets, fed in different proportions influence how epigenetic mechanisms drive gene regulation and corresponding phenotypes. Nutritional impact could be temporary or long lasting and more research is needed to find out when and how it can be specifically utilized in animal improvement programs. Harvesting the nutritional effect on epigenetic regulation of gene expression may positively impact livestock production. However, limited present knowledge impedes its applicability thus signifying the need to progressively generate knowledge regarding exploitation of the impact of nutrition on epigenetic marks.

Reproduction

miRNAs perform important regulatory roles in animal reproductive processes such as, follicular development, ovarian function, estrous cycle, spermatogenesis, and embryonic and fetal development (Salilew-Wondim et al., 2014). miRNA expression patterns of granulosa cells in graffian follicles play their role in follicular recruitment, selection, and dominance in early luteal phase of estrous cycle in bovines. Further functions of miRNAs in reproduction include control of granulosa cell differentiation (Lei et al., 2010), mediation of granulosa cell responses to transforming growth factor b1 in pre-antral follicles and oestradiol production; and helps in granulosa cell survival at the time of ovulation (McBride et al., 2012). It was observed that when the pregnant cows were fed with a protein rich diet during last trimester, their daughters had higher conception rate with reduced age at first calving and manifested changes in miRNA level in mammary tissues (Martin et al., 2007).

Calorie-overfed female rabbits experience significant changes in the expression levels of the deacetylase Sirtuin 1 (silent mating type information regulation 2 homologue 1; SIRT1) deliver male offspring with significantly reduced SIRT1 protein expression in their livers (Triantaphyllopoulos et al., 2016). In cattle, dietary enrichment with a rumen protected B- complex vitamin along with folate led to higher conception rate at first service indicating a link between DNA methylation and conception rate in bovines (Juchem et al., 2012). In swine, the effect of restricting dietary protein and excess during pregnancy stage was shown to change epigenetic marks and the expression of important metabolic genes in piglets (Altmann et al., 2013). Epigenetic marks reprogramming is believed to influence gene expression in imprinted genes in cloned animals born through somatic cell nuclear transfer, explaining its low rate of success (0.5 to 3) in cloning (Khosla et al., 2001). For instance, H19, a paternally imprinted gene, was observed to be hypomethylated in reprogrammed fibroblast cells of goats (Lal et al., 2012). Elucidation of the function of epigenetic mechanisms on observed effects following utilization of assisted reproductive technologies show that these technologies perturb usual developmental processes of the progeny. Such kind of information is necessary as it will determine the situations under which these technologies can be used.

Growth and Development

The mechanism of gene imprinting, a process controlled by epigenetic processes has been shown to modulate a wide range of biological functions including fetal growth and development, behavior and metabolism (Lambertini et al., 2012). In goats, it has been found that 10 CpG sites were differentially methylated in *Xist* (X-chromosome inactive specific transcript) gene in fibroblast and cumulus cells, which is known to play a crucial role in dosage compensation during embryogenesis (Prusty et al., 2014). DNA methylation profile of fetal and adult longissimus dorsi muscles of Qinchuan cattle of China depicted a negative correlation between methylation and regulation patterns of genes from nine different tissues at several developmental stages (Huang et al., 2014). Epigenome-wide DNA methylation patterns have been demostrated in sheep muscles and skeletal muscles of young pigs (Jin et al., 2014). A role for epigenetic mechanisms in the growth and differentiation of several organs including lipid metabolism and adipogenesis has been revealed. The miRNA expression patterns in bovine adipose tissues were characterized by Jin et al., 2010 and about 20% were reported for being correlated with back fat thickness. In concordance, functional analysis revealed that fat enriched miRNAs targeted genes with regulatory functions in fatty acid and lipid metabolism while skeletal muscle enriched miRNAs targeted cysteine and glycine-rich protein 3, a gene with function in muscular system development (Sun et al., 2014). Further studies revealed that DNA methylation status influenced tissue specific expression of lipogenic and adipogenic genes in the longissimus dorsi muscle and intramuscular fat tissue in a cattle breed of Korea (Baik et al., 2014).

Health

Diseases are caused due to multiple entities including bacteria, viruses, parasites, and fungi and pose a major threat to animal husbandry globally and a primary cause to production losses. Although much effort has been made in understanding the mechanisms of animal disease pathogenesis, medicine and immunology, but still some major challenges exist. Thus understanding the role of epigenetic marks to disease onset may aid further advancement in control.

Investigating the involvement of epigenetic factors in bovine mastitis, the most common and costliest disease of dairy cattle, a hypomethylated region of the upstream promoter region of alpha S1 casein gene becomes remethylated (followed by stop in alpha S1 casein biosynthesis) following experimental challenge of the mammary tissues with pathogenic *Escherichia coli* strain. This cues that infection-related remethylation of this region reorganised the chromatin and physically restricted regulatory mechanisms that protected the promoter against high concentration of circulating prolactin and thus acts as an acute regulatory role in CpG methylation (Vanselow et al., 2006).

DNA methylation status is potentially linked with tumourigenesis for example, the DNA methylation status of several genes has been linked to the resistance to Marek's disease (MD), a chicken lymphoma (Luo et al., 2011). Feeding diet with low folate and methionine led to altered genomic DNA methylation associated with cancer in mammals. DNA methylation and histone acetylation to the regulation of bovine innate immunity related gene expression in response to lipopolysaccharide (LPS) was worked out by Doherty et al., 2013. Similarly, treatment with AZA-TSA modifies expression of genes, such as tumour necrosis factor alpha (TNF), interleukin (IL)-8, IL-6 and serum amyloid A3 indicating an epigenetic control of LPS inducted responses and constitutive cytokine gene expression (Green and Kerr, 2014). Vorinostat, a potent HDAC inhibitor, which mediates acetylation of histones, has been passed by the FDA for clinical use in patients with cutaneous T cell lymphoma in humans. It supports concept of 'epigenetic' drug design and offers promising future in therapeutic aspect, not only in humans but livestock as well (Triantaphyllopoulos et al., 2016). A high zinc (micromineral) maternal diet causes an anti-inflammatory effect via epigenetic modifications of the A20 gene promoter in offspring chicks (Li et al., 2015).

CONCLUSION

The wealth of epigenetic profile data progressively being generated in livestock has the potential to scale up livestock productivity and health. A thorough understanding of epigenetic processes, such as DNA methylation, is hopefully expected to leverage information on genome processes, such as biological, molecular, cellular, and immune responses, and provide clear insights on how they interact to express phenotype. Even though many technological advances are made in the field of epigenetics and epigenomics like genome-wide next-generation sequencing, dynamic imaging of genomic loci, quantitative proteomics and computational analyses, but there are some potential challenges which need to be addressed, most importantly, 1) tracking epigenetic information that changes from one generation to another, 2) Imprinted gene is in effect heterozygotic, making it more vulnerable to negative mutational effects that are often connected to disease, 3) Needs to bring changes in the current standard breeding programs, 4) Insufficient recognition and limited tools, 5) Shortage of funding and 6) Lack of a global network of researchers. More studies are therefore needed to get a better understanding of the epigenetic mechanisms underlying phenotypic variation in livestock production and breeding.

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