Review

Intergenerational and transgenerational epigenetic mechanisms shaping livestock production and reproduction

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Abstract. Epigenetic reprogramming during gametogenesis and early embryogenesis involves genome-wide erasure and re-establishment of DNA methylation, ensuring developmental plasticity. However, specific genomic regions, such as imprinted loci and transposable elements, can escape this reprogramming, allowing environmentally induced epigenetic marks to persist and potentially transmit across generations. This review summarizes current advances in intergenerational and transgenerational epigenetic inheritance in mammals, with emphasis on nutritional influences. Seminal studies from the Dutch famine cohorts and the *viable yellow agouti* (*Avy*) mouse model established that maternal diet could remodel the epigenome and induce long-term phenotypic effects. Extending these findings to livestock, our recent studies demonstrate that both maternal and paternal methionine supplementation alter DNA methylation and influence growth and fertility traits in sheep. Notably, some epigenetic marks and phenotypic effects persist through the F4 generation, providing rare evidence of stable transgenerational epigenetic inheritance in a mammalian livestock model. These findings highlight nutrition as a powerful modulator of the germline and embryonic epigenome. Understanding how dietary factors shape heritable epigenetic variation offers new opportunities to improve animal health, fertility, and productivity, while providing fundamental insights into the mechanisms and evolutionary relevance of epigenetic inheritance in mammals.
Key words: Epigenetic reprogramming, Parental nutrition, Transgenerational epigenetic inheritance

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Epigenetic mechanisms

The concept of epigenetics was first introduced by C.H. Waddington in the 1940s to describe how gene–environment interactions shape inherited traits beyond traditional Mendelian patterns [1]. He defined it as the study of interactions between genes and their products that give rise to the phenotype [2]. Today, his ideas are often associated with phenotypic plasticity, the ability of genes to produce different phenotypes under varying environments [3]. Later definitions describe epigenetics as heritable changes in gene function or expression that occur without altering the underlying DNA sequence. These changes are typically stable through cell divisions (mitotic and/or meiotic) and are governed by molecular mechanisms that regulate genome activity.

In recent years, the field of epigenetics has attracted considerable attention, particularly for how various environmental insults appear to be inherited across generations and manifest in diverse health and disease outcomes. Increasing evidence from both animal and human studies suggests that factors such as nutrition, stress, exposure to toxins, and reproductive or developmental environments can induce epigenetic modifications that persist beyond the directly exposed individuals. These environmentally-induced epigenetic alterations include DNA methylation changes, histone modifications, and non-coding RNAs, which can influence gene activity in offspring and contribute to traits or disorders.

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DNA methylation

DNA methylation, the most extensively studied epigenetic modification, involves adding a methyl group to cytosine residues, typically at CpG sites, leading to transcriptional repression [4, 5]. It is essential for genomic imprinting, X chromosome inactivation, and genome stability. Methylation is established by DNMT3A and DNMT3B, maintained by DNMT1, and enhanced by DNMT3L in the germline [6, 7]. Stable methylation marks maintain silencing of imprinted, X-linked, and germline-specific genes [8]. In females, *XIST*-driven X-chromosome inactivation depends on DNMT3B-mediated methylation, while imprinting involves parent-specific methylation at imprinting control regions established during gametogenesis [9]. DNA methylation also represses transposable elements, preserving genome integrity; loss of this control is linked to infertility, cancer, and metabolic disorders [10].

Histone modifications

Another central mechanism of epigenetic regulation involves post-translational modification of histone proteins, which are wrapped around DNA to form nucleosomes. These modifications include lysine acetylation, lysine and arginine methylation, arginine citrullination, ubiquitination, sumoylation, ADP-ribosylation, proline isomerization, and phosphorylation of serine, threonine, or tyrosine residues [11]. Collectively, these chemical alterations influence chromatin architecture and the recruitment of transcriptional cofactors, thereby modulating gene expression. Generally, histone acetylation promotes chromatin relaxation and transcriptional activation, whereas histone methylation is more often associated with chromatin condensation and transcriptional repression [12].

Non-coding RNAs

Non-coding RNAs (ncRNAs), including long non-coding RNAs (lncRNAs), Piwi-interacting RNAs (piRNAs), small interfering RNAs (siRNAs), and microRNAs (miRNAs), regulate gene expression epigenetically without encoding proteins [13]. lncRNAs (> 200 nucleotides) act through diverse mechanisms in both the nucleus and cytoplasm. The maternally expressed *H19* and paternally expressed *IGF2* form a classic imprinted locus, where aberrant methylation disrupts imprinting and promotes tumorigenesis [14]. Another well-characterized lncRNA, *Xist*, initiates X-chromosome inactivation by coating the chromosome and recruiting Polycomb repressive complexes to establish H3K27 trimethylation [15]. More broadly, lncRNAs interact with chromatin modifiers, methyltransferases, and acetyltransferases to modulate transcription [16].

piRNAs (26–31 nt) associate with Piwi proteins to silence transposable elements and guide DNA methylation in germ cells. In mice, Piwi proteins MILI and MIWI2 direct methylation of LINE-1 and IAP elements via DNMT3 enzymes, maintaining genome stability [17]. siRNAs, derived from long double-stranded RNAs, are processed by Dicer and act through Argonaute-containing complexes to silence genes and transposons. Endogenous siRNAs can also direct DNA methylation and histone modifications at specific loci [18]. miRNAs (19–24 nt) are generated from primary transcripts via Drosha and Dicer processing and incorporated into RNA-induced silencing complexes (RISCs) to guide post-transcriptional repression [19]. While generally associated with mRNA degradation or translational inhibition, some miRNAs also modulate transcription. For example, miR-205 and miR-24-1 can activate tumor suppressor genes or enhancers by recruiting histone-modifying enzymes [20].

Epigenetic reprogramming and epigenetic inheritance across generations

Epigenetic reprogramming

During mammalian development, DNMT3A and DNMT3B are highly expressed, particularly at the blastocyst stage and during primordial germ cell (PGC) development, two key windows of extensive epigenetic reprogramming [21] (Fig. 1). This reprogramming begins shortly after fertilization, when the epigenetic signatures of the gametes are erased from both parental genomes, thereby establishing the pluripotent state of the early embryo [22]. At fertilization, the paternal and maternal genomes are epigenetically distinct. The paternal genome is highly compacted with protamines instead of histones, and approximately 80–90% of CpG sites are methylated [23, 24]. In contrast, the maternal genome retains canonical histones and exhibits about 40% CpG methylation, resulting in distinct chromatin landscapes for each pronucleus [25]. After fertilization, the paternal genome undergoes rapid, active demethylation mediated by TET3-catalyzed oxidation of 5mC to 5hmC [26]. The maternal genome, in contrast, is demethylated more gradually through passive loss of methylation during replication in the absence of maintenance methylation [27].

This asymmetry in demethylation reflects intrinsic differences between the two pronuclei and the presence of protective mechanisms [22]. One such mechanism involves DPPA3 (also known as Stella/PGC7), which binds to H3K9me2-enriched regions of the maternal genome and protects them from TET3-mediated oxidation [28]. This function preserves DNA methylation at imprinted loci, ensuring the proper parent-of-origin–specific expression of genes in the embryo. Interestingly, loci marked by H3K9me2 in mature sperm are also protected by DPPA3 during early embryogenesis [29]. Moreover, the limited histones retained in sperm carry activating marks, such as H3K4me3, which may help maintain imprinting and regulate early paternal gene activation [30].

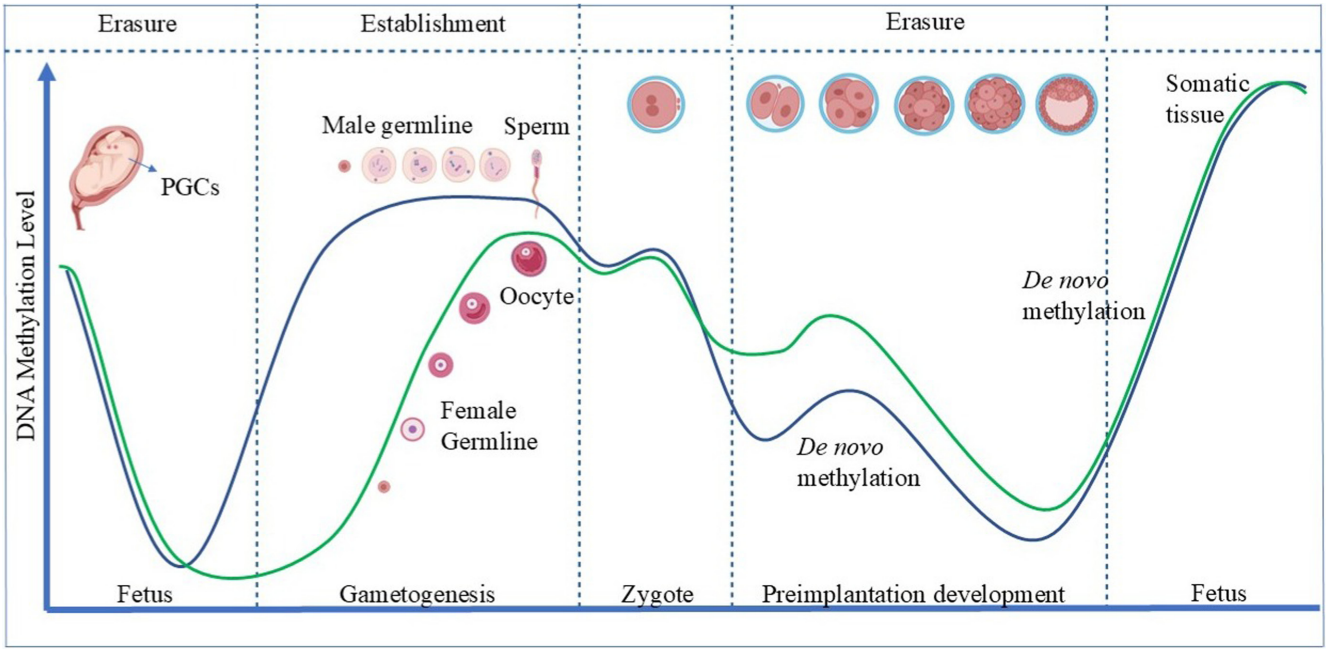

Fig. 1. Global DNA methylation dynamics during the two waves of epigenetic reprogramming. The first wave of DNA methylation erasure occurs in primordial germ cells (PGCs), followed by de novo methylation during gametogenesis. In this phase, the sperm genome is highly methylated, whereas the oocyte genome exhibits relatively lower methylation levels. The second wave of demethylation takes place after fertilization, reducing global methylation to approximately 20% at the blastocyst stage. Subsequently, methylation is progressively re-established from the blastocyst to the gastrula stage through the activity of DNA methyltransferase enzymes.

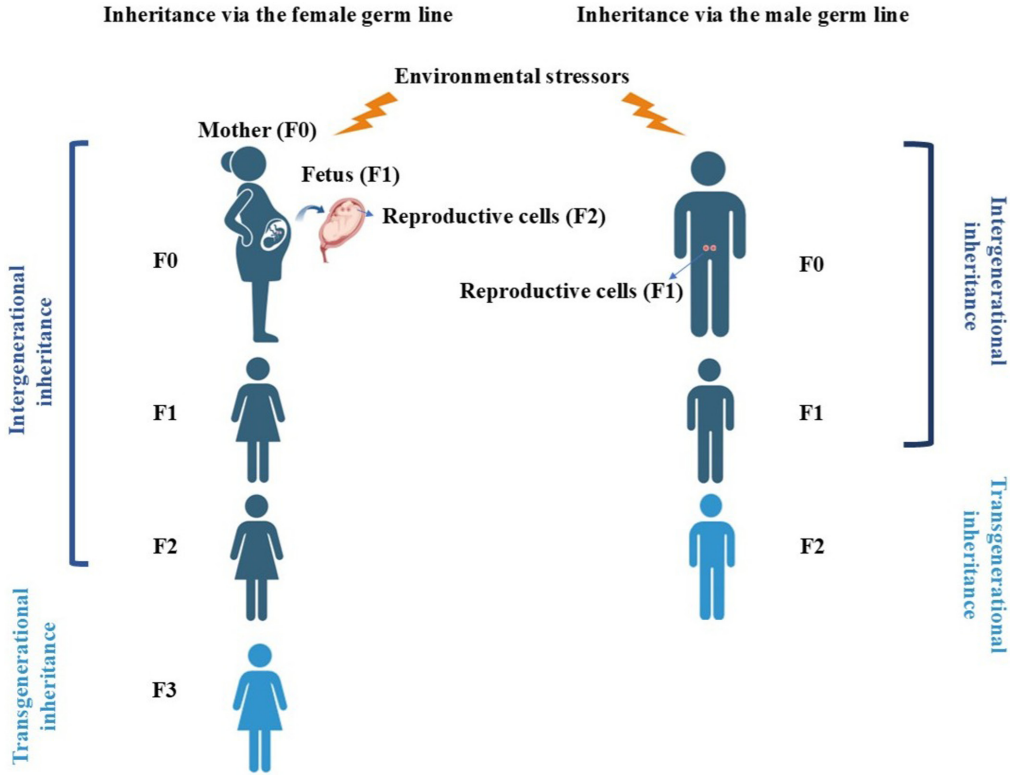

Fig. 2. Intergenerational and transgenerational epigenetic inheritance through the female and male germ lines. In intergenerational epigenetic inheritance, exposure of a gestating mother (F0) to environmental factors directly affects both the developing fetus (F1) and the germ cells within that fetus (F2). Consequently, the F2 generation is also considered directly exposed. In contrast, transmission of phenotypes or epigenetic marks to the F3 generation, which has not been directly exposed, is classified as transgenerational epigenetic inheritance. When a male or a non-pregnant female (F0) is exposed, only the individual and their germ cells (F1) are directly affected, and inheritance to the F2 generation represents transgenerational epigenetic inheritance.

Following fertilization, global DNA methylation levels in the embryo continue to decline through successive cleavage divisions, reaching a minimum at the blastocyst stage [31]. During gastrulation, de novo methylation re-establishes epigenetic landscapes via DNMT activity, guiding cellular differentiation and conceptus development [22].

The first wave of global demethylation and remethylation thus supports somatic lineage commitment around implantation in mice and humans. A second wave of epigenetic reprogramming occurs during PGC specification and migration. PGCs, derived from epiblast cells, are specified around embryonic day 6.25 in mice [32] and migrate from the posterior primitive streak to the genital ridge [33]. During this migration, PGCs undergo extensive genome-wide demethylation, erasing methylation marks across nearly all genomic regions, including imprinted loci, CpG islands of the inactive X chromosome in females, and germline-specific and meiosis-related genes [34, 35]. By embryonic day 13.5, PGCs exhibit the lowest global DNA methylation levels of the mammalian life cycle [36].

After this widespread erasure, sex-specific re-establishment of DNA methylation occurs during gametogenesis. In the male germline, de novo methylation begins around embryonic day 14.5, is completed mainly by birth, and is stably maintained during spermatogenesis [36, 37]. In contrast, the female germline remains hypomethylated until after birth. Primary oocytes, arrested in prophase I, initiate methylation postnatally during oocyte growth, continuing until ovulation [36, 37]. It is noteworthy that key aspects of epigenetic reprogramming, particularly global DNA demethylation and imprint resetting, are conserved across mammals. However, substantial species-specific differences exist in their timing, kinetics, and histone modification patterns, reflecting both shared fundamental mechanisms and species-specific evolutionary adaptations [38].

Intergenerational versus transgenerational epigenetic inheritance

Intergenerational epigenetic inheritance refers to the transmission of epigenetic modifications from parents to offspring when all generations have been directly exposed to the inducing environmental factor. For example, when a pregnant female (F0) is exposed, both the fetus (F1) and its developing germ cells (F2) are directly exposed, making it challenging to distinguish inherited epigenetic effects from those arising from direct environmental influences [39] (Fig. 2). In contrast, transgenerational epigenetic inheritance (TEI) is defined as the transmission of epigenetic modifications across generations that were not directly exposed [39] (Fig. 2). In mammals, TEI is considered to be confirmed only when these modifications persist to the F3 generation following exposure of pregnant females, or to the F2 generation following paternal exposure or exposure of non-pregnant females [39].

Although the existence of TEI in mammals remains a subject of debate due to the extensive epigenetic reprogramming that typically erases acquired marks during germ cell development and early embryogenesis, specific genomic regions, such as imprinted genes [40] and transposable elements [41], are known to escape this reprogramming and retain their methylation status. The maintenance

of DNA methylation in transposable elements is crucial for preserving genomic stability, as its loss can lead to aberrant gene expression [10]. Beyond these well-established exceptions, accumulating evidence suggests that environmentally induced epigenetic modifications can occasionally evade reprogramming and influence phenotypic traits in subsequent generations. This emerging evidence has intensified interest in mammalian TEI and fueled ongoing debate over whether such findings truly represent transgenerational inheritance [42].

One of the first studies to investigate TEI examined the effects of exposing pregnant rats to the agricultural fungicide vinclozolin. Anway *et al*. [43] reported that treatment with this endocrine disruptor during the period of sex determination induced reproductive abnormalities, such as increased testicular germ cell apoptosis and reduced sperm motility, in the F3 generation. These phenotypes were also associated with altered DNA methylation patterns in F3 sperm [43]. Subsequent rodent studies have explored TEI in response to other environmental toxicants. For example, exposure of mice to the phthalate di(2-ethylhexyl) phthalate (DEHP) has been linked to transgenerational alterations in stress hormone levels and behavior [44] and to disrupted ovarian function [45]. Similarly, Manikkam *et al*. [46] demonstrated that exposure to a mixture of phthalates and bisphenol A (BPA) increased the incidence of pubertal abnormalities, testicular disease, and ovarian dysfunction across multiple generations.

Although these and numerous other studies claim evidence of TEI, their validity has been questioned. Some researchers argue that true TEI is unlikely in mammals because extensive epigenetic reprogramming during germ cell development and early embryogenesis should theoretically erase environmentally induced marks [47]. Concerns about reproducibility have also been raised, as several studies have failed to replicate previously reported transgenerational effects [48].

Given these challenges, our laboratory recently proposed consensus criteria for defining TEI in mammals. These criteria require not only inheritance of phenotypes in the first unexposed generation, but also evidence of heritable epigenetic marks, persistence of the same epimutations, associated gene expression changes in subsequent generations, and evaluation of germ cells in each generation [42]. Applying these criteria, the studies discussed above, while valuable, would not fulfill the stringent definition of true TEI, as they primarily demonstrate phenotypic inheritance without direct confirmation of persistent epigenetic modifications across generations. Nonetheless, these pioneering studies provide crucial insights into how environmental factors can shape reproductive and developmental outcomes and underscore the importance of continued research in this emerging field.

Epigenetic memory: how parental diet influences subsequent generations

Nutritional epigenomics

Although the existence of TEI in mammals remains debated, one of the most firmly established mechanisms through which the environment shapes the epigenome is via dietary factors. The field of nutritional epigenomics investigates how diet and nutrition influence the epigenome, thereby affecting health outcomes and disease susceptibility across the lifespan and potentially across generations.

A central framework guiding this research is the Developmental Origins of Health and Disease (DOHaD) hypothesis, which posits that environmental conditions encountered during critical periods of early development exert lasting effects on health and disease risk throughout life [49]. The DOHaD concept emerged from landmark epidemiological studies, notably those examining individuals exposed to the Dutch famine during World War II [50]. These findings, together with early experimental work using the agouti mouse model, laid the foundation for nutritional epigenomics by demonstrating that dietary factors can remodel the epigenetic landscape with enduring consequences for health and disease.

The Dutch famine

The Dutch famine, which occurred during the winter of 1944–1945 in the western Netherlands, resulted from a German-imposed food embargo near the end of World War II [51]. At the height of famine, official daily rations for adults ranged from 400 to 800 calories. Despite severe undernutrition, many women conceived and carried pregnancies to term, creating a natural experiment to investigate the long-term health consequences of maternal undernutrition at different gestational stages [52].

Early studies revealed striking stage-specific effects of prenatal famine exposure. Men exposed to famine in early gestation were more likely to develop obesity later in life, whereas those exposed in late gestation were less likely to be obese [53]. Individuals conceived during the famine, particularly those exposed during early gestation, showed a twofold increase in the risk of schizophrenia and antisocial personality disorder [54]. Exposure at any gestational stage was associated with elevated glucose levels and impaired insulin secretion in adulthood [55]. Evidence for transgenerational effects has also emerged. Grandmaternal exposure to famine did not influence birth weight or the incidence of cardiovascular and metabolic diseases, but was associated with increased neonatal adiposity and poorer health outcomes in the next generation [56].

Importantly, the Dutch famine studies provided some of the first direct evidence linking prenatal nutritional stress to epigenetic changes. Individuals exposed periconceptionally exhibited reduced methylation of the *IGF2* gene compared with their unexposed siblings [51]. These findings suggest that maternal undernutrition during critical developmental windows can induce stable epigenetic modifications with lasting consequences, underscoring how transient environmental insults in one generation can shape health and disease risk in subsequent generations.

The agouti mouse

Building on insights from the Dutch famine studies, the viable yellow agouti (*Avy*) mouse model has been instrumental in advancing the field of nutritional epigenomics. In this model, variation in coat color reflects epigenetic marks established early in development, providing a robust system to study how nutrition and environmental exposures influence the fetal epigenome.

The wild-type murine *Agouti* gene encodes a paracrine signaling molecule that regulates the production of black eumelanin and yellow phaeomelanin [57]. In *Avy* mice, a metastable epiallele is created by the insertion of an intracisternal A particle (IAP) retrotransposon upstream of the *Agouti* transcription start site [58]. This insertion activates a cryptic promoter within the IAP, leading to constitutive ectopic *Agouti* expression across all tissues, resulting in a yellow coat color along with adult-onset obesity, diabetes, and tumorigenesis [59].

In *Avy* mice, DNA methylation levels at the IAP locus inversely correlate with ectopic Agouti expression—higher methylation yields the brown "pseudoagouti" phenotype, while lower methylation yields a yellow coat [57]. Using this model, Dolinoy *et al*. [60] demonstrated that maternal dietary supplementation with genistein, a phytoestrogen found in soy, shifted offspring coat color toward brown by increasing DNA methylation at CpG sites within the *Avy* IAP. This effect was observed in tissues derived from all three germ layers and persisted

into adulthood, protecting offspring from obesity. Similarly, Waterland and Jirtle [58] showed that maternal supplementation with dietary methyl donors—folic acid, vitamin B12, choline, and betaine—also shifted the offspring phenotype toward pseudoagouti by increasing CpG methylation at the *Avy* locus.

Together, these studies established the *Avy* mouse as a foundational model for understanding how maternal diet influences the establishment and maintenance of epigenetic marks, linking early nutritional environments to long-term phenotypic outcomes.

Effects of parental nutrition on the epigenome and offspring phenotypes in livestock

While studies such as the Dutch famine cohort and the *Agouti* mouse model have provided foundational insights into how early-life environmental and nutritional exposures shape the epigenome, they represent only a fraction of the growing body of research on the importance of parental nutrition. Although nutritional epigenomics has been extensively explored in rodent models, corresponding studies in livestock remain comparatively limited.

In sheep, a study using Scottish Blackface ewes demonstrated that maternal restriction of vitamin B12, folate, and methionine led to offspring with increased body weight, greater fat accumulation, insulin resistance, and altered immune responses following antigenic challenge. DNA methylation alterations accompanied these phenotypic changes at approximately 4% of the 1,400 CpG sites analyzed in offspring liver tissue [61]. In pigs, maternal betaine supplementation, an important methyl donor in one-carbon metabolism, resulted in increased serum and hepatic betaine concentrations and upregulated expression of methionine metabolism enzymes in the liver. Methylation changes were also observed at CpG sites and histone marks on the promoters of key gluconeogenic genes, suggesting that maternal betaine modulates metabolic programming through epigenetic mechanisms [62].

Paternal nutritional effects have also been investigated, though to a lesser extent. In Swiss Large White pigs, a methyl donor–enriched paternal diet was associated with altered body composition in F2 offspring, including reduced backfat percentage and increased shoulder mass, despite these traits not being measured in the F0 or F1 generations. Transcriptomic analyses further revealed twofold differences in mRNA abundance across 79 muscle, 64 liver, and 53 kidney genes between offspring of control and supplemented sires [63].

Given the limited evidence for true transgenerational epigenetic inheritance (TEI) in mammals, particularly in livestock, our laboratory investigated the effects of paternal methionine supplementation in Polypay sheep. Gross *et al*. [64] reported that methionine supplementation in prepubertal rams advanced the age at puberty in F0 animals and influenced scrotal circumference and body weight in their F1 offspring. Analysis of sperm DNA identified 824 differentially methylated cytosines (DMCs) in supplemented rams. Expanding on this work, Braz *et al*. [65] identified over 100 cytosines whose methylation patterns were altered in F0 sperm and inherited by both the F1 and F2 generations. Phenotypically, F0 paternal diet influenced scrotal circumference across both generations; while weaning and post-weaning weights were affected in F2 females, and loin muscle depth was altered exclusively in F2 males.

Recent work has begun to explore whether paternal nutritional interventions can exert effects beyond the F2 generation in livestock. Building upon the findings of Braz *et al*. [65], Kizilaslan *et al*. [66] investigated the persistence of paternal methionine supplementation effects across multiple generations in sheep. Using whole-genome bisulfite sequencing of F3 and F4 descendants derived from control and methionine-supplemented F0 twin-pair rams, the study identified 41 differentially methylated genes (DMGs) showing evidence of transgenerational epigenetic inheritance (TEI-DMGs) across four generations and 11 TEI-DMGs maintained across five generations. Moreover, analysis of growth and fertility-related traits revealed significant associations between F0 diet group and F3–F4 phenotypes, supporting the phenotypic manifestation of inherited epigenetic alterations. Collectively, these findings provide the first gene-level and phenotypic evidence in livestock that a moderate paternal dietary intervention can induce stable, long-lasting epigenetic and phenotypic effects extending beyond the F2 generation [66]. For epigenetic inheritance to be considered transgenerational, phenotypic and epigenetic changes induced by an environmental insult must be transmitted to generations that were not directly exposed [42]. In males, if exposure of the F0 generation to environmental factors such as diet leads to phenotypic and epigenetic effects that persist beyond the F1 generation, extending into the F2 or F3 generations, this inheritance is classified as transgenerational epigenetic inheritance. Accordingly, the detection of consistent phenotypes, DMCs, and DMGs in the F3 and F4 generations [65, 66] constitutes strong evidence of true TEI.

The mechanisms by which DNA methylation changes induced by parental nutrition are maintained across generations through TEI remain largely unknown. However, despite two waves of genome-wide DNA methylation erasure and re-establishment, certain genomic regions, such as imprinted genes and transposable elements, retain their methylation marks across generations. DNA methylation at imprinted control regions is preserved during early embryonic development despite global demethylation. This protection is mediated by specific factors, including PGC7/Stella, which binds H3K9me2 and blocks Tet3-mediated demethylation, and the DNA-binding factor Zfp57 in complex with Kap1/Trim28, which maintains methylation imprints after fertilization [47]. Whether these factors contribute to the maintenance of sperm DNA methylation marks induced by paternal nutrition remains to be determined.

Maternal nutrition, particularly methionine supplementation, is known to affect offspring traits by influencing DNA methylation. However, its direct impact on the oocyte and early embryo epigenome remains poorly understood. Our recent study in Polypay sheep showed that supplementing the mother's diet with methionine remodels both nuclear and mitochondrial DNA methylation in oocytes and embryos [67]. Using whole-genome bisulfite sequencing (WGBS), we identified 2,056 DMCs in oocytes and 113 in embryos, including some shared mitochondrial DMCs. Functional analyses through siRNA-mediated knockdown of two embryo DMC-associated genes, *SCRIB* and *CERS3*, reduced blastocyst formation rates by 16.4% and 9.5%, respectively, indicating their roles in early embryonic development. These results confirm that maternal methionine intake directly alters the oocyte and embryonic epigenome, suggesting a mechanism for how fetal development is programmed through changes in nuclear and mitochondrial methylation.

Conclusion and future directions

Epigenetic mechanisms serve as key mediators linking environmental inputs to heritable changes in gene regulation, influencing reproductive performance, offspring development, and long-term health. Although substantial progress has been made in characterizing epigenetic reprogramming and inheritance in model organisms, the extent and biological relevance of true TEI in mammals remain

unresolved. Recent evidence from livestock, including studies demonstrating that paternal diet induces DNA methylation changes that are inherited across multiple generations, highlights the potential of agricultural species as translational models for investigating epigenetic inheritance in natural populations. Future studies should prioritize high-resolution analyses of germline and early embryonic epigenomes to identify loci that resist reprogramming and contribute to reproductive and developmental variation. Integrating epigenomics with transcriptomics, proteomics, and phenotypic data across generations will be essential to link molecular mechanisms with functional outcomes. Several challenges limit the effective use of epigenetic data to improve production and reproductive traits in livestock species. A significant challenge is distinguishing epigenetic changes induced by environmental factors from those driven by underlying genetic variation. Integrating epigenetic information, such as DNA methylation and gene expression, with genetic data, including single-nucleotide polymorphisms, can help disentangle genetic and epigenetic contributions to complex traits. For example, a recent cattle study employed a multi-omics approach that integrated histone modifications, DNA methylation, gene expression, chromatin accessibility, and CTCF binding to map regulatory elements in response to butyrate supplementation [68]. Such integrative analyses improve resolution and facilitate the identification of environmentally responsive epigenetic regulation. Another challenge is tracking epigenetic information that changes across generations at the cellular level [69]. Unlike DNA sequence, DNA methylation is dynamic rather than stable over an individual's lifetime and is continuously shaped by environmental influences over time. However, it is still possible to track many environmentally induced DNA methylation changes even after five generations, as we recently demonstrated [65, 66]. Another major limitation is the high cost of comprehensive epigenetic profiling, particularly whole-genome DNA methylation and histone modification analyses, which currently restrict large-scale and routine implementation in livestock populations. However, these costs are expected to decrease as sequencing technologies advance, library preparation costs decline, and targeted and low-coverage approaches develop. As analytical methods become more efficient and scalable, epigenetic data are likely to become increasingly accessible, enabling their broader integration into breeding and selection programs.

Understanding how environmental and nutritional factors shape the reproductive epigenome across generations will not only refine breeding strategies but also enhance animal health, fertility, and productivity through targeted nutritional and management interventions.

Conflict of interests: The author declares no conflicts of interest.

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