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Paternal Diet and Epigenetic Inheritance: Unveiling Nutritional Influences on Offspring Metabolic Programming

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ABSTRACT

Emerging evidence highlights the critical role of paternal nutrition in shaping the metabolic health of offspring through epigenetic inheritance mechanisms. This review synthesizes recent advances (2015 to 2025) in understanding how paternal dietary patterns before conception modulate the sperm epigenome and influence transgenerational metabolic programming. Central to this process are dynamic alterations in DNA methylation, histone modifications, and Noncoding RNAs (ncRNAs), which serve as molecular carriers of environmental information from father to offspring. High-fat or protein-restricted paternal diets have been consistently associated with aberrant methylation of key metabolic genes, shifts in histone acetylation and methylation, and changes in sperm-borne miRNAs, collectively predisposing offspring to obesity, insulin resistance, and glucose intolerance. Advanced molecular tools, including bisulfite sequencing, ChIP-seq, and RNA-seq, have enabled precise profiling of these heritable epigenetic signatures. The review also examines experimental and human epidemiological studies that confirm the persistence of these effects into adulthood, reinforcing the long-term implications of paternal nutritional status. Importantly, emerging strategies such as nutritional supplementation, CRISPR-based epigenome editing, and personalized preconception dietary interventions offer promising avenues to mitigate adverse transgenerational outcomes. Furthermore, the review explores novel biochemical mediators, microplastics, gut-derived metabolites, circadian disruptions, and phytochemicals that interact with sperm epigenetics and highlights the future potential of artificial intelligence in predicting epigenetic inheritance patterns. By integrating molecular, epidemiological, and computational insights, this review underscores the underrecognized yet profound influence of paternal diet on offspring health and advocates for the inclusion of paternal nutrition in public health discourse and preventive strategies. Addressing this gap is imperative for curbing the intergenerational transmission of metabolic disorders and promoting lifelong health across generations.

KEYWORDS

Paternal nutrition, epigenetic inheritance, sperm epigenome, metabolic programming, DNA methylation, histone modifications, Noncoding RNAs (ncRNAs), transgenerational effects, offspring metabolic health

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INTRODUCTION

Epigenetics has emerged as a transformative paradigm in biomedical science, offering profound insights into how environmental cues can modulate gene expression without altering the DNA sequence[1]. Traditionally, the maternal environment has been the primary focus of studies examining developmental origins of health and disease. However, recent advances have revealed the significant and often underestimated role of paternal factors, particularly nutritional status before conception, in influencing offspring phenotype and long-term metabolic health[2]. This expanding body of evidence suggests that paternal dietary patterns can exert enduring biological effects through epigenetic modifications transmitted via the male germline[2,3]. The male gamete is now recognized as a dynamic vector of environmental information, carrying molecular signatures such as DNA methylation marks, histone posttranslational modifications, and diverse noncoding RNAs[2,3]. These epigenetic features can influence early embryonic development, reprogram metabolic pathways, and increase susceptibility to chronic diseases such as obesity, cardiovascular dysfunction, and type 2 diabetes[3]. Animal studies have demonstrated that high fat or protein restricted paternal diets induce specific epigenetic alterations in sperm, which are retained post fertilization and contribute to adverse metabolic phenotypes in offspring[3]. Complementary epidemiological evidence in humans reinforces the association between paternal nutritional status and intergenerational health outcomes[3]. Recent advances in epigenomic profiling techniques, including bisulfite sequencing, Chromatin Immunoprecipitation Sequencing (ChIP-seq), and RNA Sequencing (RNA-seq), have enabled high-resolution mapping of these heritable modifications[2,3]. Additionally, unconventional biochemical and environmental factors such as phytochemicals, microplastics, gut-derived metabolites, and circadian disruption have been proposed to modulate the paternal epigenome[4]. These findings not only expand our understanding of paternal contributions to developmental programming but also highlight opportunities for targeted preconception interventions[4]. This review critically examines the molecular mechanisms by which paternal nutrition modifies the sperm epigenome and explores the resulting implications for offspring metabolic health. By integrating current findings from molecular, epidemiological, and computational studies, the paper emphasizes the need to reposition paternal nutrition as a core focus in transgenerational disease prevention strategies.

MATERIALS AND METHODS

This comprehensive review synthesizes findings from rigorous, peer-reviewed studies investigating the intricate influence of paternal diet on offspring metabolism. The systematic data collection process involved an exhaustive search across prominent biomedical databases, including PubMed, Scopus, and Web of Science. The search strategy employed a combination of keywords and Medical Subject Headings (MeSH) terms, such as "Paternal diet", "Epigenetic inheritance", "Offspring metabolism", "DNA methylation", "Histone modifications", "Non-coding RNA", "Transgenerational effects", "Sperm epigenetics", and "Metabolic programming"[5]. Inclusion criteria for selecting studies were stringent, focusing exclusively on mammalian models (e.g., mice, rats, humans) that provided detailed evidence of changes in specific epigenetic markers in response to variations in paternal nutritional intake[5]. Prioritized studies published between 2015 and 2025 to ensure the inclusion of the most current and relevant research, thereby reflecting the latest advancements in the field. Furthermore, studies were selected based on methodological rigor, emphasizing those that employed robust molecular techniques for analyzing epigenetic changes. These techniques included bisulfite sequencing for comprehensive DNA methylation profiling, ChIP-seq for mapping histone modifications, and RNA-seq for quantifying ncRNA expression profiles, particularly miRNAs[6]. Data extraction involved meticulous collection of information regarding experimental design, dietary interventions, specific epigenetic marks analyzed, and observed metabolic outcomes in offspring. The synthesis of these findings aimed to identify consistent patterns and key mechanistic insights into the transgenerational effects of paternal diet on metabolic programming[6].

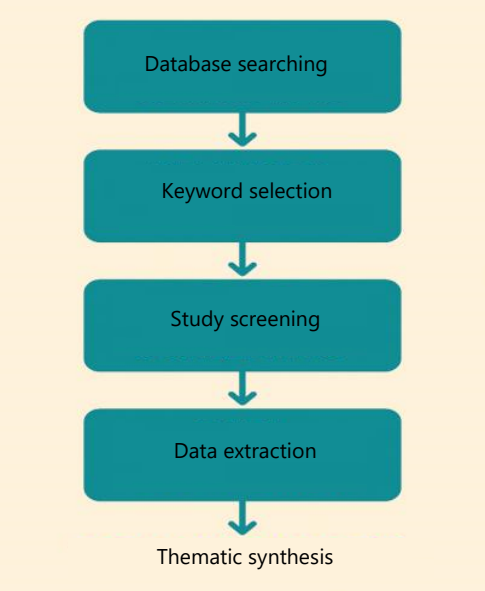

Fig. 1: Systematic review methodology: Data collection and analysis framework (self-generated, using Canvas and DALL.E)
This flowchart details key stages: Database searching, keyword selection, study screening, data extraction, and thematic synthesis and advanced molecular techniques (bisulfite sequencing, ChIP-seq, RNA-seq) were utilized

Figure 1 illustrates the systematic review methodology used in this study. The process begins with database searches in PubMed, Scopus, and Web of Science, utilizing targeted keywords and MeSH terms[18]. Inclusion criteria emphasized mammalian models with documented epigenetic alterations due to paternal nutritional intake[7]. After initial screening and eligibility assessment, relevant studies were selected for data extraction, focusing on experimental design, dietary interventions, epigenetic modifications, and metabolic outcomes[7,8]. Thematic synthesis involved analyzing patterns in DNA methylation, histone modifications, and ncRNA changes, ensuring methodological rigor in identifying transgenerational effects[8].

RESULTS AND DISCUSSION

This section outlines key findings derived from empirical studies, systematically categorized based on distinct epigenetic mechanisms through which paternal diet influences offspring metabolism.

DNA methylation modifications: The DNA methylation, a fundamental epigenetic mark, plays a pivotal role in regulating gene silencing and expression, particularly at CpG islands within gene promoter regions. Numerous studies elucidate that paternal dietary exposures can induce specific alterations in sperm DNA methylation patterns, which are subsequently transmitted to offspring, influencing their metabolic phenotype. For instance, a seminal study demonstrated that paternal high-fat diets in mice led to significant hypermethylation of genes involved in lipid metabolism and insulin signaling in offspring's liver, contributing to impaired glucose tolerance and increased adiposity[9]. Similarly, another study revealed that chronic paternal exposure to a Western-style diet in rodents resulted in altered DNA methylation profiles in sperm for genes associated with metabolic pathways, correlating with increased susceptibility to obesity and metabolic dysfunction in progeny[10]. Furthermore, paternal protein restriction caused distinct hypomethylation patterns in promoter regions of gluconeogenesis-related genes in offspring pancreas, leading to altered glucose homeostasis[11]. These findings collectively highlight DNA methylation as a critical epigenetic conduit for paternal diet to program offspring metabolic health.

As depicted in Fig. 2, comparative methylation profiles show differential CpG methylation levels in key gene regions among offspring of fathers consuming control, high-fat, or protein-restricted diets. Paternal high-fat diets result in hypermethylation of genes involved in lipid metabolism and insulin signaling[11], while paternal protein restriction induces hypomethylation at loci linked to gluconeogenesis[12]. The stability of these methylation marks suggests a robust mechanism for transgenerational metabolic programming[12].

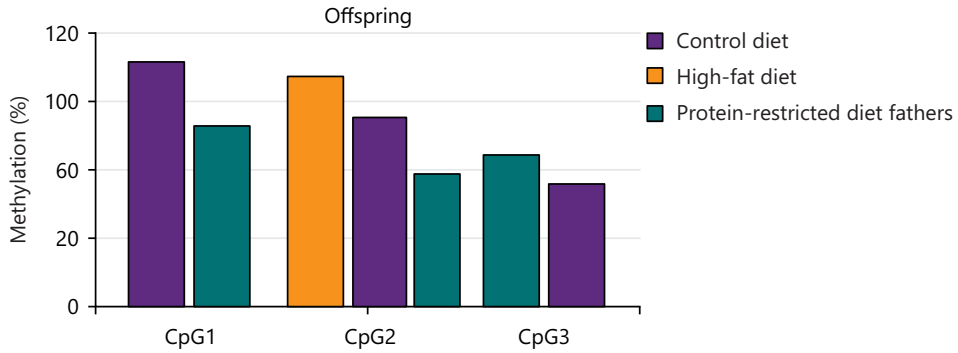

Fig. 2: Comparative methylation profiles in offspring of fathers with distinct diets (self-generated, using canvas and DALL.E)

Heatmaps and bar graphs contrast CpG methylation levels across key metabolic genes. Elevated methylation (high-fat diet fathers) correlates with increased adiposity and impaired glucose tolerance. Hypomethylation (protein-restricted fathers) potentially affects glucose homeostasis

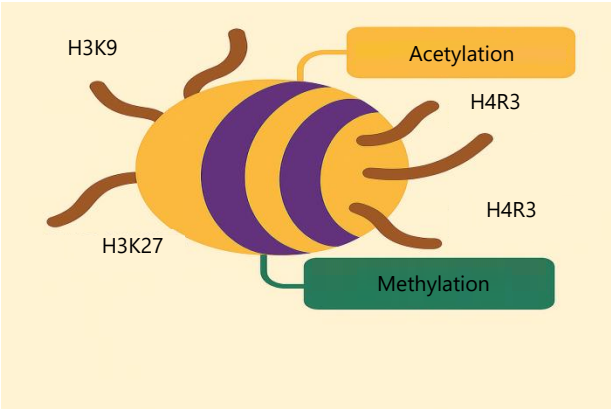

Fig. 3: Graphical representation of histone modification sites affected by paternal nutrition (self-generated, using canvas and DALL.E)

Nucleosomes depict key histone marks (acetylation: H3K9ac, H3K27ac; methylation: H3K4me3) regulating chromatin accessibility and gene expression

Histone modifications and chromatin remodeling: Beyond DNA methylation, dietary components exert profound effects on histone modifications, altering chromatin accessibility and gene transcription. Histone acetylation, methylation, phosphorylation, and ubiquitination are dynamic processes regulating gene expression. Emerging experimental evidence suggests paternal nutritional status can induce specific histone modifications in sperm, transmitted to the zygote, and influence offspring development. For example, Wei et al. found paternal folate deficiency in mice led to widespread histone hypoacetylation (particularly H3K9ac and H3K27ac) in sperm, associated with altered gene expression in offspring liver and impaired glucose homeostasis[13]. Paternal high-fat diet exposure increased H3K4me3 (active chromatin mark) at specific metabolic gene promoters in sperm, correlating with offspring metabolic dysregulation[14]. These findings suggest that alterations in paternal germline histone marks profoundly impact offspring metabolic programming by influencing the accessibility of crucial metabolic genes. The dynamic nature of histone modifications provides a flexible mechanism for integrating environmental signals into the epigenetic landscape[14]. It is important to note that while these marks can be inherited, extensive epigenetic reprogramming occurs during early embryogenesis, which can potentially erase or modify some paternal marks; however, evidence indicates certain environmentally-induced modifications escape this reprogramming[15].

Figure 3 highlights specific lysine and arginine residues on histone tails undergoing epigenetic modifications in response to paternal diet. Paternal folate deficiency leads to widespread histone hypoacetylation, while paternal high-fat diet exposure enhances H3K4me3 at metabolic gene promoters[16].

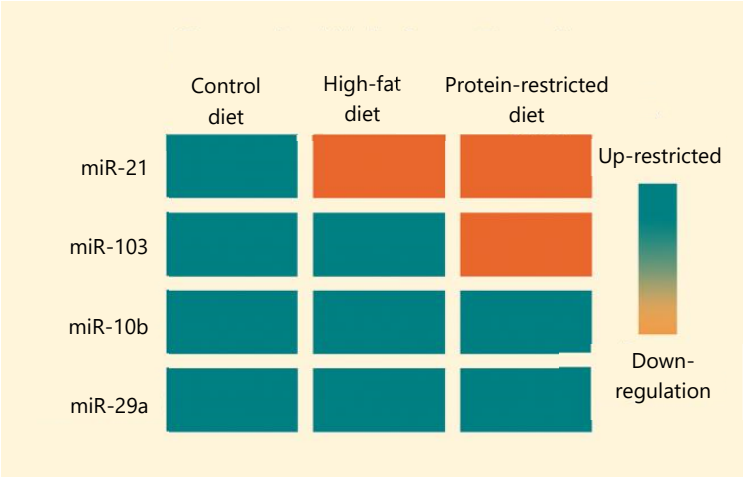

Fig. 4: miRNA expression differences in offspring under varied paternal diets (self-generated, using canvas and DALL.E)
Heatmaps and plots highlight upregulation/downregulation of specific miRNAs (e.g., miR-21, miR-103, miR-107) in sperm and offspring tissues

Non-coding rna and transgenerational effects: Non-coding RNAs, particularly miRNAs, are crucial regulators of gene expression stability and play a significant role in mediating transgenerational epigenetic effects. These small RNA molecules modulate gene expression by binding to target mRNAs, leading to degradation or translational repression. Research indicates paternal nutritional status significantly alters the miRNA cargo of sperm, delivered to the oocyte upon fertilization, influencing early embryonic development and offspring metabolic programming. Paternal undernutrition in mice significantly increased sperm miR-21 expression, linked to altered fatty acid oxidation pathways and increased lipid accumulation in offspring liver[17]. Paternal obesity changed sperm miRNA profiles, including elevated miR-103 and miR-107, associated with impaired insulin signaling and glucose intolerance in offspring[18]. These findings highlight the critical role of sperm ncRNAs as carriers of epigenetic information, providing a rapid mechanism for transmitting environmental signals. The unique packaging and delivery of miRNAs during fertilization suggest direct involvement in shaping offspring metabolic landscape[19].

Figure 4 illustrates differential miRNA expression in offspring based on paternal dietary exposures. Paternal undernutrition increases miR-21 expression, while paternal obesity elevates miR-103 and miR-107 levels[20].

Experimental models and longitudinal observations: The transgenerational effects of paternal diet on offspring metabolism have been extensively studied using various experimental models, predominantly rodents, alongside emerging human epidemiological investigations. Rodent models provide a controlled environment to systematically analyze underlying molecular mechanisms. Preconception paternal exposure to high-fat or protein-restricted diets significantly alters hepatic gene expression in offspring, influencing glucose and lipid metabolism[21]. These metabolic disruptions often manifest as increased adiposity, insulin resistance, and impaired glucose tolerance, mimicking metabolic syndrome features. Longitudinal studies confirm these metabolic phenotypes persist into adulthood, reinforcing the lasting impact of paternal nutritional exposures[22].

Figure 5 demonstrates the pathway through which paternal diet influences sperm epigenetics (DNA methylation, histone modifications, ncRNAs). These alterations are transmitted to the zygote, affecting offspring gene expression and metabolic phenotype. Rodent model studies confirm persistent metabolic consequences from high-fat or protein-restricted paternal diets. Epidemiological studies support correlations between paternal dietary habits and metabolic health outcomes in human offspring[23].

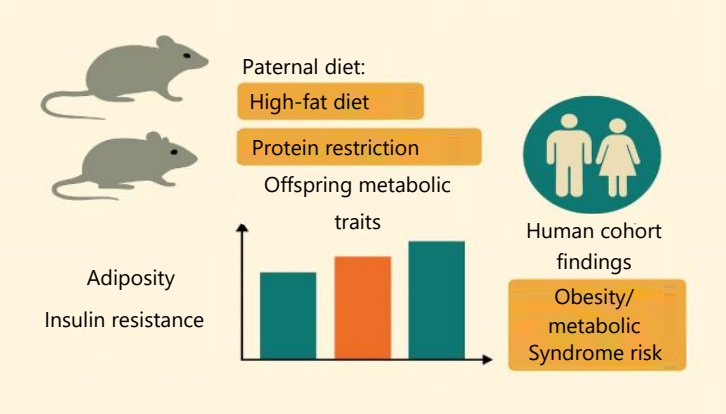

Fig. 5: Trans generational impact of paternal diet on offspring metabolism (self-generated, using canvas and DALL.E)
Schematic showing paternal diet affecting sperm epigenetics, transmission to the zygote, and resulting offspring gene expression/metabolic phenotype

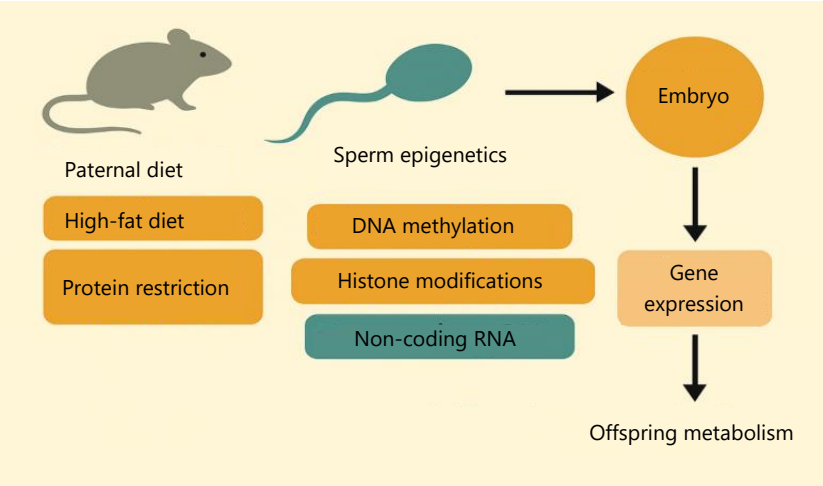

Fig. 6: Impact of paternal diet on offspring metabolism through epigenetic mechanisms (self-generated, using canvas and DALL.E)
Schematic showing paternal diet influencing sperm epigenetics and subsequent effects on zygote and offspring metabolism

Complementing animal studies, human epidemiological research provides compelling evidence linking paternal diet quality to offspring metabolic health. A prospective cohort study found poor paternal preconception dietary quality, characterized by high processed food consumption and low fruit/vegetable intake, as associated with elevated risk of childhood obesity and type 2 diabetes[23,24]. A systematic review synthesizing human cohort data identified consistent correlations between paternal metabolic status and offspring health outcomes, emphasizing paternal diet as a determinant of long-term metabolic trajectories[24].

Nutritional interventions to mitigate epigenetic effects: The role of paternal diet in shaping offspring metabolism through epigenetic inheritance has gained significant attention. Epigenetic modifications serve as molecular mediators transmitting environmental influences across generations. Sperm epigenetics is a crucial mechanism through which paternal nutritional status affects offspring phenotypes[25].

As illustrated in Fig. 6, paternal diet affects sperm epigenetics through DNA methylation, histone modifications, and ncRNAs, impacting zygote and offspring metabolism. Altered nutritional environments modify sperm epigenetic markers, leading to metabolic reprogramming in offspring[26]. Histone modifications regulate chromatin structure and gene accessibility[26]. ncRNAs, particularly miRNAs, facilitate transmission of epigenetic information[27].

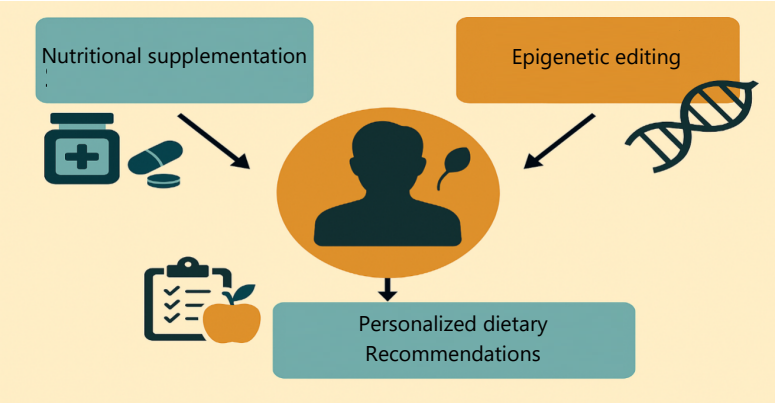

Fig. 7: Conceptual diagram of future interventions targeting paternal dietary effects (self-generated, using canvas and DALL.E)
Framework integrating nutritional supplementation, epigenetic editing, and personalized dietary interventions

Studies reveal paternal dietary interventions directly influence sperm DNA methylation and histone modifications, altering offspring gene expression. Differential CpG methylation in sperm from fathers exposed to altered nutritional environments contributes to offspring metabolic programming[27,28]. Modifications to histone tails regulate chromatin accessibility and transcriptional activity[28]. These mechanisms underscore the transgenerational impact.

Additionally, ncRNAs, particularly miRNAs, are key factors in paternal epigenetic inheritance. miRNAs in sperm modulate gene expression post-fertilization, shaping offspring metabolic traits. Dietary-induced variations in sperm miRNA content correlate with offspring susceptibility to metabolic disorders[28].

Integrating molecular epigenetic insights highlights the importance of paternal preconception health in determining offspring metabolic trajectories. A deeper understanding may pave the way for targeted interventions.

Future directions in epigenetic research: The field of paternal epigenetic inheritance is rapidly evolving. One crucial focus is the reversibility of paternal diet-induced epigenetic modifications, holding significant therapeutic potential. Advanced genome-wide methylation techniques provide deeper insights, while CRISPR-based epigenetic editing tools may enable precise modifications[29].

Figure 7 presents an integrative framework for interventions: nutritional supplementation modulating sperm epigenetics[29], CRISPR-based editing reversing germline changes[30], and personalized dietary recommendations tailored to paternal metabolic profiles. Validation through large-scale human cohort studies is essential[30].

Further efforts are needed to elucidate molecular mechanisms governing dietary impact on epigenetic inheritance. Identifying key nutrient sensors and signaling pathways that translate dietary inputs into epigenetic modifications is crucial. Emerging research emphasizes the need for human-centric studies validating animal model findings[31]. Novel in vitro models, such as three-dimensional (3D) testicular organoids, enhance understanding of human spermatogenesis and offer new epigenetic research platforms[31,32].

Translating epigenetic research into policy and public health initiatives is paramount. The World Health Organization's (WHO) global action plan highlights addressing non-communicable disease (NCD) risk factors, including epigenetic inheritance[32]. Integrating epigenetic insights into nutritional guidelines could enable evidence-based paternal interventions. Findings will inform strategies optimizing paternal diet to mitigate long-term health risks for future generations.

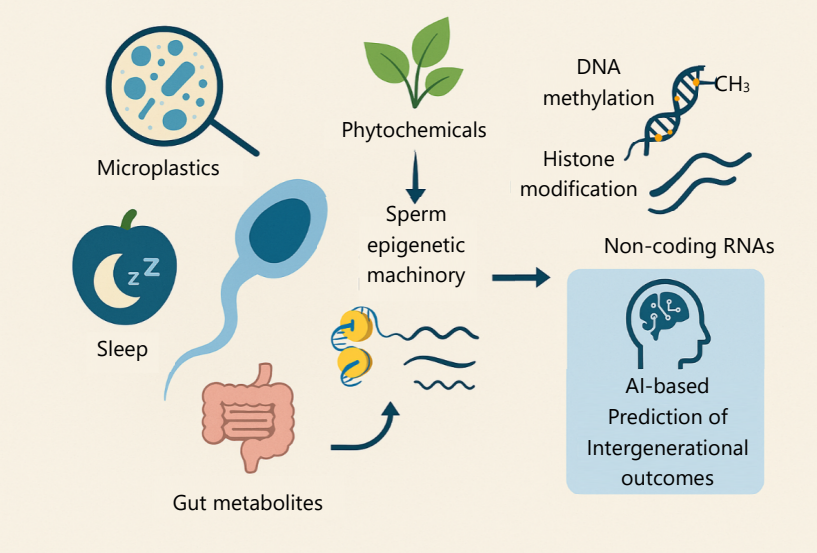

Fig. 8: Systems level diagram of paternal biochemical influences on epigenetic inheritance (self-generated, using canvas and DALL.E)

This diagram illustrates how paternal exposures such as microplastics, phytochemicals, sleep patterns, and gut metabolites modulate sperm epigenetic markers. Artificial intelligence platforms interpret these biochemical signals to predict transgenerational health risks

Emerging biochemical horizons in paternal epigenetic inheritance: Recent advances in biochemical and molecular biology have uncovered unconventional systems that may influence epigenetic inheritance from fathers to their offspring. Notably, environmental particles such as microplastics have been shown to disrupt endocrine and immune function through oxidative stress pathways, which may indirectly alter sperm epigenetic markers and downstream transcriptional programs in embryos[33]. Additionally, disturbances in sleep regulation, a function increasingly linked to the epigenome, may mediate transgenerational metabolic imbalances, particularly when paternal circadian rhythms are chronically disrupted[34].

Biologically active metabolites derived from the gut microbiota also represent a novel biochemical interface with potential for cross-generational communication. These metabolites can regulate neurotransmission and immunity and are suspected to influence germline epigenetic status through histone modification and DNA methylation[35]. Furthermore, natural plant compounds traditionally used for their therapeutic effects may possess specific molecular targets that interact with chromatin remodeling complexes in sperm cells, suggesting a previously underexplored dimension of phytochemical influence in inherited disease predisposition[36].

Of particular future relevance is the integration of artificial intelligence in mapping these biochemical interactions. AI-driven bioinformatics platforms can decode complex biological data and predict multigenerational epigenetic trajectories from paternal biochemical inputs[37]. This convergence of computational and biochemical sciences holds promise for identifying predictive biomarkers of offspring health rooted in paternal exposures.

Figure 8 presents a systems-level schematic illustration of paternal influences such as microplastics, phytochemicals, sleep, and gut metabolites on sperm epigenetic machinery. These factors modulate DNA methylation, histone modification, and noncoding RNAs. AI based tools are shown as downstream predictors of intergenerational health outcomes[33-37].

CONCLUSION

Paternal nutrition plays a pivotal role in shaping offspring's metabolic health through epigenetic mechanisms that include DNA methylation, histone remodeling, and noncoding RNA dynamics. Evidence from animal models and human studies underscores that dietary exposures before conception can reprogram the sperm epigenome and contribute to transgenerational disease susceptibility. These heritable molecular imprints influence embryonic development and persist into later life, altering metabolic trajectories. Advances in high-throughput epigenomic profiling and emerging intervention strategies offer promising avenues to counteract adverse paternal influences. Recognizing the male germline as a conduit of nutritional memory redefines preventive medicine, advocating for the inclusion of paternal dietary assessment in reproductive health policies. Strategic focus on preconception paternal health holds immense potential to reduce the burden of metabolic disorders across generations.

SIGNIFICANCE STATEMENT

This review highlights the emerging role of paternal diet as a determinant of offspring metabolic health via epigenetic inheritance. It reveals how preconception nutritional exposures modulate the sperm epigenome, influencing gene regulation in the next generation. Mechanistic insights into DNA methylation, histone modifications, and noncoding RNAs underscore the molecular basis of this transmission. Animal and human studies demonstrate consistent links between poor paternal nutrition and metabolic disorders in progeny. The findings advocate for a paradigm shift in reproductive health that includes paternal dietary evaluation and intervention. Incorporating these insights into public health strategies may reduce the intergenerational burden of metabolic diseases.

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REFERENCES

1. Jahan-Mihan, A., J. Leftwich, K. Berg, C. Labyak, R.R. Nodarse, S. Allen and J. Griggs, 2024. The impact of parental preconception nutrition, body weight, and exercise habits on offspring health outcomes: A narrative review. Nutrients, Vol. 16. 10.3390/nu16244276.
2. Bird, A., 2024. Transgenerational epigenetic inheritance: A critical perspective. Front. Epigenet. Epigenomics, Vol. 2. 10.3389/freae.2024.1434253.
3. Tian, Z., B. Zhang, Z. Xie, Y. Yuan and X. Li *et al*., 2025. From fathers to offspring: Epigenetic impacts of diet and lifestyle on fetal development. Epigenet. Insights, Vol. 18. 10.48130/epi-0025-0004.
4. Camilleri, T.L., 2025. Clarifying the public misrepresentation of transgenerational epigenetic inheritance. Theor. Med. Bioethics, 10.1007/s11017-025-09717-2.
5. Fernando, K.K., J.M. Craig and S.L. Dawson, 2023. Relationships between the maternal prenatal diet and epigenetic state in infants: A systematic review of human studies. J. Dev. Origins Health Dis., 14: 540-555.
6. Nakato, R. and K. Shirahige, 2017. Recent advances in ChIP-seq analysis: From quality management to whole-genome annotation. Briefings Bioinf., 18: 279-290.
7. Gross, N., T. Taylor, T. Crenshaw and H. Khatib, 2020. The intergenerational impacts of paternal diet on DNA methylation and offspring phenotypes in sheep. Front. Genet., Vol. 11. 10.3389/fgene.2020.597943.
8. Donkin, I., S. Versteyhe, L.R. Ingerslev, K. Qian and M. Mechta *et al*., 2016. Obesity and bariatric surgery drive epigenetic variation of spermatozoa in humans. Cell Metab., 23: 369-378.
9. Haberman, M., T. Menashe, N. Cohen, T. Kisliouk and T. Yadid *et al*., 2024. Paternal high-fat diet affects weight and DNA methylation of their offspring. Sci. Rep., Vol. 14. 10.1038/s41598-024-70438-y.

10. Akhatova, A., C. Jones, K. Coward and M. Yeste, 2025. How do lifestyle and environmental factors influence the sperm epigenome? Effects on sperm fertilising ability, embryo development, and offspring health. Clin. Epigenet., Vol. 17. 10.1186/s13148-025-01815-1.
11. Guo, Y., P. Zhou, L. Qiao, H. Guan, J. Gou and X. Liu, 2023. Maternal protein deficiency impairs peroxisome biogenesis and leads to oxidative stress and ferroptosis in liver of fetal growth restriction offspring. J. Nutr. Biochem., Vol. 121. 10.1016/j.jnutbio.2023.109432.
12. Kizilaslan, M., C.U. Braz, J. Townsend, T. Taylor, T.D. Crenshaw and H. Khatib, 2025. Transgenerational epigenetic and phenotypic inheritance across five generations in sheep. Int. J. Mol. Sci., Vol. 26. 10.3390/ijms26136412.
13. Wei, S., S. Luo, H. Zhang, Y. Li and J. Zhao, 2023. Paternal high-fat diet altered SETD2 gene methylation in sperm of F0 and F1 mice. Genes Nutr., Vol. 18. 10.1186/s12263-023-00731-4.
14. Morgan, H.L., S. Furse, I.H.K. Dias, K. Shabir and M. Castellanos *et al*., 2022. Paternal low protein diet perturbs inter-generational metabolic homeostasis in a tissue-specific manner in mice. Commun. Biol., Vol. 5. 10.1038/s42003-022-03914-8.
15. Zhang, L., W. Zou, S. Zhang, H. Wu, Y. Gao, J. Zhang and J. Zheng, 2024. Maternal high-fat diet orchestrates offspring hepatic cholesterol metabolism via MEF2A hypermethylation-mediated CYP7A1 suppression. Cell. Mol. Biol. Lett., Vol. 29. 10.1186/s11658-024-00673-8.
16. Tomar, A., M. Gomez-Velazquez, R. Gerlini, G. Comas-Armangué and L. Makharadze *et al*., 2024. Epigenetic inheritance of diet-induced and sperm-borne mitochondrial RNAs. Nature, 630: 720-727.
17. Morgan, H.L., N. Eid, N. Holmes, S. Henson and V. Wright *et al*., 2024. Paternal undernutrition and overnutrition modify semen composition and preimplantation embryo developmental kinetics in mice. BMC Biol., Vol. 22. 10.1186/s12915-024-01992-0.
18. Fullston, T., E.M.C. Ohlsson-Teague, C.G. Print, L.Y. Sandeman and M. Lane, 2016. Sperm microRNA content is altered in a mouse model of male obesity, but the same suite of microRNAs are not altered in offspring's sperm. PLoS ONE, Vol. 11. 10.1371/journal.pone.0166076.
19. Rodgers, A.B., C.P. Morgan, N.A. Leu and T.L. Bale, 2015. Transgenerational epigenetic programming via sperm microRNA recapitulates effects of paternal stress. Proc. Natl. Acad. Sci. U.S.A., 112: 13699-13704.
20. Yang, C., Q.X. Zeng, J.C. Liu, W.S.B. Yeung, J.V. Zhang and Y.G. Duan, 2023. Role of small RNAs harbored by sperm in embryonic development and offspring phenotype. Andrology, 11: 770-782.
21. Fullston, T., N.O. McPherson, J.A. Owens, W.X. Kang, L.Y. Sandeman and M. Lane, 2015. Paternal obesity induces metabolic and sperm disturbances in male offspring that are exacerbated by their exposure to an "obesogenic" diet. Physiol. Rep., Vol. 3. 10.14814/phy2.12336.
22. McPherson, N.O., T. Fullston, W.X. Kang, L.Y. Sandeman, M.A. Corbett, J.A. Owens and M. Lane, 2016. Paternal under-nutrition programs metabolic syndrome in offspring which can be reversed by antioxidant/vitamin food fortification in fathers. Sci. Rep., Vol. 6. 10.1038/srep27010.
23. Dupont, C., L. Kappeler, S. Saget, V. Grandjean and R. Lévy, 2019. Role of miRNA in the transmission of metabolic diseases associated with paternal diet-induced obesity. Front. Genet., Vol. 10. 10.3389/fgene.2019.00337.
24. Champroux, A., M. Sadat-Shirazi, X. Chen, J. Hacker, Y. Yang and L.A. Feig, 2025. Astrocyte-derived exosomes regulate sperm miR-34c levels to mediate the transgenerational effects of paternal chronic social instability stress. Epigenetics, Vol. 20. 10.1080/15592294.2025.2457176.
25. Isacson, S., K. Karlsson, S. Zalavary, A. Asratian, U. Kugelberg, S. Liffner and A. Öst, 2025. Small RNA in sperm-paternal contributions to human embryo development. Nat. Commun., Vol. 16. 10.1038/s41467-025-62015-2.
26. Naveed, M., Z. Shen and J. Bao, 2025. Sperm-borne small non-coding RNAs: Potential functions and mechanisms as epigenetic carriers. Cell Biosci., Vol. 15. 10.1186/s13578-025-01347-4.
27. Liu, X., T. Peng, M. Xu, S. Lin and B. Hu *et al*., 2024. Spatial multi-omics: Deciphering technological landscape of integration of multi-omics and its applications. J. Hematol. Oncol., Vol. 17. 10.1186/s13045-024-01596-9.

28. Dyer, S.C., O. Austine-Orimoloye, A.G. Azov, M. Barba and I. Barnes *et al*., 2025. Ensembl 2025. Nucleic Acids Res., 53: D948-D957.
29. Bhadsavle, S.S. and M.C. Golding, 2022. Paternal epigenetic influences on placental health and their impacts on offspring development and disease. Front. Genet., Vol. 13. 10.3389/fgene.2022.1068408.
30. Wu, D., K. Zhang, K. Guan, F.A. Khan and N.S. Pandupuspitasari *et al*., 2024. Future in the past: Paternal reprogramming of offspring phenotype and the epigenetic mechanisms. Arch. Toxicol., 98: 1685-1703.
31. Kaltsas, A., A. Zikopoulos, V. Kojovic, F. Dimitriadis, N. Sofikitis, M. Chrisofos and A. Zachariou, 2024. Paternal contributions to recurrent pregnancy loss: Mechanisms, biomarkers, and therapeutic approaches. Medicina, Vol. 60. 10.3390/medicina60121920.
32. Ren, H., Y. Zhou and J. Liu, 2025. Nutrition in early life and its impact through the life course. Nutrients, Vol. 17. 10.3390/nu17040632.
33. Anih, D.C., A.K. Arowora, M.A. Abah and K.C. Ugwuoke, 2025. Biochemical effects of microplastics on human health: A comprehensive review. Sci. Int., 13: 27-34.
34. Anih, D.C., O.E. Yakubu, A.K. Arowora, M.A. Abah and U.K. Chinekwu, 2025. Biochemical mechanisms of sleep regulation. Sci. Int., 13: 35-45.
35. Anih, D.C., A.K, Arowora, M.A. Abah and K.C. Ugwuoke, 2025. Biochemically active metabolites of gut bacteria: Their influence on host metabolism, neurotransmission, and immunity. Sci. Int., 13: 46-57.
36. Chinonso, A.D., A.A. Kayode, M.A. Adondua and U.K. Chinekwu, 2025. Biochemistry of traditional herbal compounds and their molecular targets. Pharmacogn. Rev., 19: 83-90.
37. Arowora, A.K., I. Chinedu, D.C. Anih, A.A. Moses and K.C. Ugwuoke, 2022. Application of artificial intelligence in biochemistry and biomedical sciences: A review. Asian Res. J. Curr. Sci., 4: 302-312.