Universal Journal of Pharmaceutical Research

Available online at ***www.ujpronline.com***

Universal Journal of Pharmaceutical Research

An International Peer Reviewed Journal

ISSN: 2831-5235 (Print); 2456-8058 (Electronic)

REVIEW ARTICLE

INTERGENERATIONAL EPIGENETIC INHERITANCE: A MINIREVIEW OF MECHANISMS AND IMPLICATIONS FOR HUMAN HEALTH AND DISEASE

Mostafa Essam Eissa

Independent Researcher and Consultant, Cairo, Egypt.

Article Info:

Article History:
Received: 6 April 2025
Reviewed: 12 May 2025
Accepted: 27 June 2025
Published: 15 July 2025

Cite this article:
Eissa ME. Intergenerational epigenetic inheritance: A minireview of mechanisms and implications for human health and disease. Universal Journal of Pharmaceutical Research 2025; 10(3): 59-62.
http://doi.org/10.22270/ujpr.v10i3.1354

***Address for Correspondence:**
Dr. Mostafa Essam Eissa, Independent Researcher and Consultant, Cairo, Egypt;
Tel: +20100615485;
E-mail: *mostafaessameissa@yahoo.com*

Abstract

The concept of inherited memories, where experiences from one generation can influence the traits and behaviors of subsequent generations, has long captivated scientific curiosity. Recent advancements in epigenetics have provided compelling evidence for the potential mechanisms underlying this phenomenon. This focused brief review article outlines the current state of knowledge on inherited memories, examining the transgenerational effects observed in animal models, the epigenetic mechanisms involved, and the environmental influences that shape these heritable traits. Additionally, Highlights about emerging areas of inquiry were explored, including the cross-generational transmission of social behaviors, the evolutionary implications of inherited memories, and the ethical considerations surrounding research in humans. Thus, a unique perspective could be deduced from this rapidly evolving field and accordingly, further research could be stimulated into the implication of inherited memories.

Keywords: DNA methylation, epigenetic inheritance, histone modifications, transgenerational effects, transgenerational inheritance.

INTRODUCTION

The notion that experiences acquired during an individual's lifetime can be transmitted to subsequent generations has intrigued scientists and philosophers for centuries[1]. While the concept has often been relegated to the realm of folklore and cultural beliefs, recent advancements in the field of epigenetics have provided compelling evidence for the potential mechanisms underlying such transgenerational inheritance[2]. Epigenetics, the study of heritable changes in gene expression that do not involve alterations to the DNA sequence, offers a plausible framework for understanding how environmental factors can influence the development and behavior of future generations[3,4]. Table 1 provides a chronological overview of key studies in the field of intergenerational epigenetic inheritance, highlighting their contributions and findings[5-20]. Specifically, this brief paper aimed to summarize the current state of knowledge, pinpoint to the epigenetic mechanisms, highlight the influence of environmental factors, examine the ethical considerations and recommend future research directions.

Key findings in intergenerational epigenetic inheritance

Recent research has significantly advanced our understanding of intergenerational epigenetic inheritance, demonstrating how environmental factors and experiences can influence gene expression and traits across generations without altering the underlying DNA sequence. A non-exhaustive list of such studies highlights several key findings. Early investigations revealed that exposure to endocrine disruptors in rats led to transgenerational effects on male fertility. Concurrently, studies in mice confirmed that epigenetic modifications can be inherited and affect gene expression. The impact of environmental toxins was further underscored by research on zebrafish, which showed that environmental toxins can cause transgenerational epigenetic changes. The role of maternal factors was also explored, with findings indicating that maternal diet can alter DNA methylation and affect gene expression in offspring. In a compelling demonstration of behavioral inheritance, mice conditioned to fear a specific odor were found to pass this fear to their offspring, suggesting transgenerational epigenetic inheritance. Expanding on parental influence, research showed that paternal diet influences offspring metabolism through sperm RNA.

Mechanistic insights into this phenomenon were provided by studies on *C. elegans*, which found that transgenerational epigenetic inheritance is mediated by histone modifications. Subsequent research in mice linked early life stress to depressive-like behaviors in offspring, mediated by sperm microRNAs, further supported by findings that paternal stress affects offspring behavior and stress response through sperm microRNA. The broader impact of environmental stressors was reinforced by a study demonstrating that environmental stress can lead to transgenerational epigenetic changes in sperm. More recent comprehensive reviews and studies have identified that DNA methylation changes in animals can be inherited across generations, affecting gene expression[5-20]. This body of work provides robust evidence that epigenetic instructions contribute to gene regulation in offspring, highlighting the biological consequences of inherited epigenetic information.

Transgenerational effects in animal models

A growing body of research in animal models has provided compelling evidence for the existence of transgenerational effects. Studies in rodents have demonstrated that parental experiences, such as prenatal stress or exposure to specific environmental toxins, can have lasting effects on the offspring's physiology, behavior and susceptibility to disease. For instance, prenatal stress in mice has been shown to lead to altered stress responses and anxiety-like behavior in subsequent generations[21]. Similarly, paternal exposure to a high-fat diet has been linked to an increased risk of obesity and metabolic disorders in offspring[22]. Beyond mammals, studies in simpler organisms like *Caenorhabditis elegans* - a model organism for developmental biology and behavior - have shed light on the potential for transgenerational inheritance of learned behaviors. Research has shown that *C. elegans* can transmit learned aversions to specific odors across generations[23], suggesting the existence of underlying epigenetic mechanisms that allow for the inheritance of acquired information.

Epigenetic mechanisms: The language of transgenerational inheritance

Epigenetic modifications, including DNA methylation, histone modifications, and non-coding RNAs, are believed to play a crucial role in mediating transgenerational effects. DNA methylation, the addition of a methyl group to cytosine residues in DNA, can silence gene expression and has been implicated in various transgenerational phenomena. For example, studies have shown that parental exposure to environmental stressors can lead to altered DNA methylation patterns in the germline, which are then transmitted to offspring[24]. Histone modifications, such as acetylation and methylation, can also influence gene expression by altering chromatin structure. These modifications can be inherited across generations, leading to long-lasting changes in gene activity. Non-coding RNAs, particularly microRNAs, have emerged as important players in epigenetic regulation. They can target specific mRNAs for degradation or translational repression, thereby influencing gene expression and potentially contributing to transgenerational effects[25].

Environmental influences on epigenetic inheritance

Environmental factors play a critical role in shaping the epigenetic landscape of an organism. Parental diet, exposure to toxins and social stress can all leave a lasting mark on the epigenome, which can be transmitted to subsequent generations. For instance, studies have shown that a high-fat diet in male mice can lead to altered sperm DNA methylation patterns and increased obesity risk in offspring[26]. Exposure to air pollution during pregnancy has been linked to altered gene expression and increased susceptibility to respiratory diseases in offspring[27]. Moreover, social stressors, such as chronic stress or social isolation, can have profound effects on the epigenetic programming of the brain and behavior, which can be transmitted across generations[28].

Emerging areas of inquiry

The field of inherited memories is rapidly evolving, with new areas of research emerging. One exciting area of investigation is the cross-generational transmission of social behaviors. Studies have shown that parental social experiences can influence the social behavior of offspring, suggesting a potential role for epigenetic mechanisms in shaping social interactions across generations[29]. Another intriguing area explores the evolutionary implications of inherited memories. Some researchers propose that transgenerational epigenetic inheritance might contribute to the rapid adaptation of populations to changing environmental conditions[30]. However, the extent to which inherited memories contribute to evolutionary processes remains a subject of debate.

Intervention strategies

Developing strategies to mitigate adverse transgenerational effects is a critical area of research[31-34]. This could involve nutritional interventions, stress management programs, or pharmacological approaches aimed at reversing harmful epigenetic modifications. Personalized medicine, which tailors medical treatment to the individual characteristics of each patient, offers a promising avenue in this context. By leveraging detailed genetic, epigenetic, and environmental information, personalized medicine can provide targeted interventions that address specific epigenetic changes inherited from previous generations. This approach not only enhances the efficacy of treatments but also minimizes potential side effects, paving the way for more precise and effective healthcare solutions. For instance, personalized dietary plans or stress reduction programs could be designed based on an individual's unique epigenetic profile, thereby improving health outcomes and reducing the risk of transgenerational transmission of adverse traits.

Ethical considerations and future directions

The study of inherited memories raises significant ethical considerations, particularly when considering potential interventions that could manipulate epigenetic mechanisms[30,35-37]. It is crucial to establish ethical guidelines for research involving human subjects, especially those that might impact future generations. Moreover, it is important to consider the potential social and psychological implications of such interventions. Future research in the field of inherited memories should focus on mechanistic studies. Further elucidation of the molecular mechanisms underlying transgenerational epigenetic inheritance is essential. This includes identifying specific epigenetic marks and understanding how they are maintained and transmitted across generations.

Human Studies: While much of the current evidence comes from animal models, it is important to investigate whether similar mechanisms operate in humans. Longitudinal studies and advanced genomic technologies could provide insights into the transgenerational effects of environmental exposures in human populations.

Intervention Strategies: Developing strategies to mitigate adverse transgenerational effects is a critical area of research. This could involve nutritional interventions, stress management programs or pharmacological approaches aimed at reversing harmful epigenetic modifications.

Evolutionary Perspectives: Understanding the role of epigenetic inheritance in evolution could provide new insights into how species adapt to changing environments. Comparative studies across different species and ecological contexts could shed light on the evolutionary significance of inherited memories.

Ethical Frameworks: Establishing robust ethical frameworks for research and potential clinical applications is paramount. This includes addressing issues related to consent, privacy, and the long-term implications of manipulating epigenetic mechanisms.

Epigenetic inheritance: A new path to understand heath and disease

The study of intergenerational epigenetic inheritance has revealed a complex biological dimension, demonstrating how one generation's experiences can influence the health and behavior of those that follow. This developing field not only questions conventional understandings of heredity but also creates new paths for comprehending human health and illness. An innovative strategy involves integrating multi-omics technologies, which merge genomics, epigenomics, transcriptomics, and proteomics, to offer a complete picture of how environmental elements impact epigenetic inheritance. This comprehensive viewpoint can expose intricate interactions and pinpoint biomarkers for transgenerational effects, facilitating more accurate interventions.

Another promising avenue is the application of advanced CRISPR-based epigenome editing tools. These technologies enable precise alterations to epigenetic marks, providing potential therapeutic approaches to reverse detrimental epigenetic changes passed down from prior generations. Such advancements could transform the treatment of diseases with an epigenetic component, including certain cancers, metabolic disorders, and neuro-psychiatric conditions.

CONCLUSIONS

Research into intergenerational epigenetic inheritance has highlighted the crucial role of early-life environments in determining long-term health outcomes. It emphasizes the necessity for public health policies that reduce exposure to harmful environmental factors, such as pollutants and stressors, especially during crucial developmental stages. Furthermore, this field has stressed the interconnectedness of physical and mental health across generations. Understanding how stress, diet, and social environments influence epigenetic programming can inform interventions designed to disrupt cycles of disadvantage and foster resilience in susceptible populations. Future research should prioritize conducting long-term studies to monitor epigenetic changes over several human generations, investigating epigenetic inheritance in diverse species to identify conserved mechanisms and evolutionary patterns, designing and executing trials to evaluate the effectiveness of interventions aimed at modifying epigenetic marks, addressing ethical concerns related to manipulating the epigenome particularly regarding heritable changes and enhancing public understanding of epigenetics and its health implications. By embracing these innovative approaches and insights, the field of intergenerational epigenetic inheritance possesses the potential to redefine our understanding of heredity and clear the way for novel strategies to enhance human health and well-being.

ACKNOWLEDGEMENTS

None to declare.

AUTHOR'S CONTRIBUTIONS

Eissa ME: conceived the idea, writing the manuscript, literature survey, formal analysis, critical review.

DATA AVAILABILITY

Data will be made available on request.

CONFLICT OF INTEREST

None to declare.

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