



Epigenetic Inheritance Study Challenges Conventional Mendelian Patterns and Expands Understanding of Heritable Biological Information

Published On: 12-08-2026

Recent Developments:

- A study published in **Nature Genetics** identified widespread patterns of **non-Mendelian inheritance of DNA methylation** in mice, demonstrating that some epigenetic information can persist across generations without altering the underlying DNA sequence.
- Researchers used **long-read nanopore sequencing** to analyse allele-specific DNA methylation across generations in mouse **liver and muscle tissues**, allowing genetic sequence and methylation information to be examined on the same DNA molecules.
- The study identified approximately **7,600 autosomal genomic regions** showing distinct epigenetic inheritance patterns, of which **7,081 followed Mendelian inheritance**, while **at least 522 showed non-Mendelian inheritance**.
- Approximately **7% of the identified autosomal epigenetic inheritance patterns were non-Mendelian**, indicating that heritable epigenetic information may be more widespread than previously recognised.
- The researchers identified **five seemingly new imprinted genes**, including an **X-linked gene**, and observed widespread **sex-specific DNA methylation patterns** concentrated particularly in the liver.
- The study provided evidence for naturally occurring **intergenerational paramutation** at the **Capn11** locus and identified highly likely additional examples involving **intracisternal A particle transposable elements** at **Vps37c** and another genomic region.
- The findings do not establish that epigenetic inheritance operates in humans to the same extent, because comprehensive human studies remain difficult due to **environmental exposures, age, genetic variation and other confounding factors**.

Understanding Epigenetics:

Meaning and Core Concept:

- **Epigenetics** refers to heritable or persistent changes in **gene activity and regulation** that occur without changing the underlying **DNA sequence**.
- The **DNA sequence** provides the genetic information, whereas the **epigenome** consists of molecular modifications that influence which genes are accessible and expressed within a cell.
- Although most cells of an organism contain essentially the same DNA, different epigenetic states allow **liver, brain and muscle cells** to express different sets of genes and perform specialised functions.
- Epigenetic marks can respond to **diet, stress, ageing, physical activity, environmental exposures and toxins**, thereby providing a molecular mechanism through which environmental conditions can influence gene regulation.

Major Epigenetic Mechanisms:

Kamaraj IAS Academy

Plot A P.127, AF block, 6 th street, 11th Main Rd, Shanthi Colony, Anna Nagar, Chennai, Tamil Nadu 600040

Phone: **044 4353 9988 / 98403 94477** / Whatsapp : **09710729833**

DNA Methylation:

- **DNA methylation** involves the addition of a **methyl group** to DNA, most commonly at cytosine bases in **CpG sites**, and methylation at gene regulatory regions is often associated with reduced gene transcription.
- DNA methylation is central to processes such as **genomic imprinting, X-chromosome inactivation, transposon silencing and cellular differentiation**.

Histone Modification:

- DNA is wrapped around proteins called **histones** to form **chromatin**, and chemical modifications of histones influence how tightly DNA is packaged.
- **Tightly packed chromatin** generally reduces access to transcriptional machinery and promotes gene silencing, whereas **loosely packed chromatin** generally permits greater transcriptional activity.

Non-Coding RNA:

- **Non-coding RNAs** are RNA molecules that generally do not serve as templates for protein synthesis but can regulate gene expression through mechanisms involving RNA degradation, translation control and chromatin regulation.

Epigenetic Inheritance:

Meaning:

- **Epigenetic inheritance** occurs when epigenetic information influencing gene regulation is transmitted from one generation to another without requiring a change in the underlying DNA sequence.
- Most epigenetic marks are normally **reset or substantially erased during germ-cell formation and early embryonic development**, which acts as an important barrier to transgenerational inheritance.
- Some epigenetic information can nevertheless escape this resetting process or be re-established in a manner that produces parent-to-offspring or intergenerational effects.

Mendelian and Non-Mendelian Components:

- The study showed that most observed DNA methylation inheritance patterns were **Mendelian**, primarily because methylation differences were associated with **cis-acting methylation quantitative trait loci**, meaning that nearby genetic variants influenced methylation.
- At least **522 autosomal examples** displayed non-Mendelian patterns, including **emergent epigenetic inheritance, trans-acting methylation effects, genomic imprinting and paramutation**.
- Therefore, the study does not overturn Mendelian genetics; rather, it demonstrates that **inheritance of molecular regulatory information can contain additional layers beyond DNA sequence transmission**.

Major Findings of the Study:

Non-Mendelian Epigenetic Inheritance:

- Researchers identified at least **522 autosomal examples of non-Mendelian inheritance**, demonstrating that some DNA methylation patterns did not follow conventional allele-based inheritance.
- The findings suggest that **epigenetic information can contribute to inherited biological variation**, although the relative importance of this mechanism in naturally occurring human inheritance remains uncertain.

Sex-Specific DNA Methylation:

- Researchers identified widespread **sex-specific DNA methylation patterns**, particularly in the mouse liver, indicating that epigenetic regulation can differ substantially between males and females.
- Such sex-dependent epigenetic variation may contribute to differences in **gene expression, metabolism and disease susceptibility**, although the biological consequences require further investigation.

Genomic Imprinting:

- The study identified **at least five seemingly new imprinted genes**, including one located on the **X chromosome**.
- **Genomic imprinting** is an established epigenetic phenomenon in which gene expression depends on whether a particular allele was inherited from the **mother or father**.
- In an imprinted gene, one parental copy may be epigenetically silenced, resulting in preferential expression of the other parental copy.

Paramutation at Capn11:

- The researchers identified naturally occurring **intergenerational paramutation** at the **Capn11** locus, providing evidence of a non-Mendelian epigenetic inheritance mechanism in a naturally occurring mammalian genome.
- **Paramutation** occurs when the epigenetic state of one allele influences the epigenetic state of its homologous allele, with the altered state potentially persisting into subsequent generations.
- The **Capn11** gene encodes a calcium-dependent protease that is predominantly expressed in the testis during later stages of meiosis and has been associated with male reproductive biology.

Role of Intracisternal A Particles:

- Researchers identified highly likely additional examples of paramutation involving **intracisternal A particles**, which are **endogenous retroviral transposable elements** present within the mouse genome.
- These elements are important because they can resist genome-wide demethylation processes occurring during **gametogenesis and embryogenesis**, potentially allowing certain epigenetic states to persist between generations.

Tissue-Specific Epigenetic Inheritance:

- The researchers examined DNA methylation in both **liver and muscle**, demonstrating that epigenetic inheritance can be strongly influenced by tissue type because DNA methylation is itself tissue-specific.
- The study therefore highlights that inheritance cannot always be understood solely by examining DNA sequence because **tissue-specific regulatory information** may also influence gene activity.

Important Concepts for UPSC:

Genomic Imprinting:

- **Genomic imprinting** is a form of epigenetic regulation in which expression of an allele depends on its **parental origin**.
- Unlike conventional Mendelian inheritance, where maternal and paternal alleles are generally treated according to their genetic identity, imprinting can cause one parental allele to remain active while the other is epigenetically silenced.

Paramutation:

- **Paramutation** is an epigenetic interaction in which one allele induces a heritable change in the epigenetic state of its homologous allele.

- It differs from an ordinary DNA mutation because the **DNA sequence itself does not necessarily change**, while the altered regulatory state can persist across generations.

Epialleles:

- **Epialleles** are alleles that have identical or essentially identical DNA sequences but differ in their epigenetic states and consequently may differ in gene expression.
- Epialleles provide an important conceptual link between **genetic variation, epigenetic regulation and phenotype**.

Methylation Quantitative Trait Loci:

- **Methylation quantitative trait loci** are genomic variants associated with differences in DNA methylation levels.
- **Cis-acting methylation quantitative trait loci** influence methylation near the genetic variant, whereas **trans-acting methylation quantitative trait loci** can influence methylation at more distant genomic locations.

Epigenetic Inheritance and Mendelian Inheritance:

Feature

Conventional Mendelian Inheritance

Epigenetic Inheritance

Basis

Involves the transfer of **DNA sequence variants, including alleles**, from parents to their offspring.

Involves the transmission of **epigenetic regulatory states** that may persist without altering the underlying DNA sequence.

Key Principle

Usually operates according to **Mendelian principles**, particularly the laws of segregation and independent assortment.

May result in **inheritance patterns that differ from classical Mendelian expectations** under certain conditions.

Gene Expression

Gene activity is largely determined by the **inherited DNA sequence**, together with other regulatory processes.

Gene activity may be modified by **epigenetic marks**, which can either promote or suppress the expression of particular genes.

Stability

The nucleotide sequence is generally **highly stable between generations**, although mutations can introduce changes.

Epigenetic modifications are generally **more flexible and reversible** than alterations to the DNA sequence.

Reproductive Resetting

Kamaraj IAS Academy

Plot A P.127, AF block, 6 th street, 11th Main Rd, Shanthi Colony, Anna Nagar, Chennai, Tamil Nadu 600040

Phone: **044 4353 9988 / 98403 94477** / Whatsapp : **09710729833**

Genetic information is passed to the next generation through **sperm and egg cells**.

Many epigenetic modifications undergo **erasure or reprogramming during germ-cell development and early embryogenesis**.

Inheritance Pattern

Usually gives rise to relatively predictable **genetic transmission patterns between parents and offspring**.

Certain epigenetic states may **persist despite reproductive reprogramming**, show parent-of-origin effects, or affect the expression of another allele through mechanisms such as **paramutation**.

Why the Study Matters:

Understanding Heritability:

- Traditional genetic studies cannot explain every heritable phenotype because some biological variation may arise from **gene regulation, environmental interactions and epigenetic states** rather than DNA sequence differences alone.
- Epigenetic mechanisms may therefore contribute to the broader problem of **missing heritability**, although they do not provide a universal explanation for it.

Environment and Inheritance:

- Epigenetic mechanisms provide a plausible molecular pathway through which **environmental conditions can influence gene regulation**, but evidence for stable transgenerational inheritance in humans remains limited.
- Therefore, environmental effects on parents should not automatically be interpreted as permanently inherited epigenetic traits in their descendants.

Precision Medicine:

- Because many epigenetic modifications are **potentially reversible**, enzymes and molecular pathways controlling DNA methylation, histone modification and chromatin structure represent potential therapeutic targets.
- Epigenetic therapies are already relevant to the treatment of certain diseases, particularly some **cancers**, although their clinical use requires careful control because epigenetic pathways regulate many genes simultaneously.

Disease Research:

- Abnormal epigenetic regulation is associated with **cancer, metabolic disorders, developmental abnormalities and other complex diseases**.
- Understanding epigenetic inheritance may improve the interpretation of disease susceptibility where genetic sequence alone cannot fully explain observed patterns.

Evolution:

- Epigenetic changes can sometimes arise and change more rapidly than DNA sequence mutations, creating a potential mechanism for short-term responses to environmental conditions.
- However, whether such changes become stable evolutionary adaptations depends on their **persistence, inheritance, effects on fitness and interaction with genetic evolution**.

Epigenetic Inheritance and Lamarckism:

Similarity:

- The possibility that environmentally influenced epigenetic states may persist across generations has a conceptual resemblance to **Lamarckian inheritance**, because acquired biological states could potentially influence descendants.

Critical Difference:

- Modern epigenetic inheritance does **not validate classical Lamarckism**, because inheritance remains governed primarily by genetic mechanisms and most environmentally induced epigenetic changes are not permanently transmitted across generations.
- Epigenetic inheritance should therefore be understood as an **additional regulatory layer of heredity**, rather than as a replacement for Mendelian genetics or the modern theory of evolution.

Limitations of the Study:

Mouse Model:

- The study was conducted in **mice**, and its findings cannot be directly extrapolated to humans because mammalian species differ in developmental processes, epigenetic regulation and environmental exposure patterns.

Germline Reprogramming:

- Extensive **epigenetic reprogramming during gametogenesis and early embryonic development** normally removes many parental epigenetic marks, limiting the persistence of acquired epigenetic states.

Human Evidence:

- Comprehensive genome-wide studies of epigenetic inheritance in human families have not yet established that the patterns observed in mice occur in humans with comparable frequency or biological significance.

Environmental Confounding:

- Human populations experience highly variable **diet, age, lifestyle, environmental exposure and socioeconomic conditions**, making it difficult to distinguish inherited epigenetic effects from shared environmental effects.

Broader Scientific Significance:

Beyond the DNA Sequence:

- The study strengthens the concept that biological inheritance involves more than the transmission of DNA sequence alone because **DNA methylation and other regulatory states can influence gene activity**.
- Nevertheless, DNA sequence remains the fundamental hereditary information system, while epigenetic mechanisms primarily determine how that information is regulated and expressed.

Integration of Genetics and Epigenetics:

- Modern biology increasingly treats phenotype as the outcome of interactions among **DNA sequence, epigenetic regulation, environment, development and cellular context**.

- The study therefore contributes to a more comprehensive understanding of heredity rather than overturning the foundations of classical genetics.

Value Addition for UPSC:

- **Conceptual distinction:** Genetic mutation changes DNA sequence, whereas **epigenetic modification** generally changes gene regulation without altering the DNA sequence.
- **Inheritance distinction:** **Mendelian inheritance** primarily tracks transmission of alleles, whereas **epigenetic inheritance** concerns transmission or persistence of regulatory states that can influence gene expression.
- **Evolutionary perspective:** Epigenetic mechanisms demonstrate that phenotype can be shaped by interactions among **genes, regulatory states and environment**, while natural selection continues to operate on heritable variation.
- **Scientific caution:** Evidence from mice demonstrates a biological possibility but does not establish equivalent **transgenerational epigenetic inheritance in humans**.