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Role of Epigenetics in Early Childhood Development

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***Abstract*: Ayurveda places great emphasis on prevention and encourages the maintenance of health through close attention to balance in one's life, right thinking, diet, lifestyle and the use of herbs. "Epigenetics" is an emerging area of scientific research that shows how environmental influences—children's experiences—actually affect the expression of their genes. The term *epigenetics* came into general use in the early 1940s, when British embryologist Conrad Waddington used it to describe the interactions between genes and gene products, which direct development and give rise to an organism's phenotype. Epigenetic changes are modifications to DNA that regulate whether genes are turned on or off. These modifications are attached to DNA and do not change the sequence of DNA building blocks. Recent research demonstrates there may be ways to reverse certain negative changes and restore healthy functioning. This paper thoroughly discusses how Ayurveda defines the science of epigenetics in its own terms and how we can regulate gene expression by following suggestions stated in Ayurvedic literature for healthy living.**

***Keywords*: Epigenetics, Early childhood, Prakruthi.**

1. Introduction

The term epigenetics was first introduced in 1942 by Conrad Waddington and was defined as the causal interactions between genes and their products that allow for the phenotypic expression [1]. This term has now been somewhat redefined, and although there are many variants of the definition of this term today, a consensus definition is that epigenetics is the collective heritable changes in phenotype due to processes that arise independent of the primary DNA sequence [2], [3].

A. Molecular Mechanisms of Epigenetics

1. Mechanisms of DNA Methylation and Demethylation
2. Mechanisms of Histone Modifications
3. The Epigenetics of Noncoding RNA

1) Mechanisms of DNA Methylation and Demethylation

DNA methylation is the process of the addition of methyl groups to the 5' carbon of the cytosine rings in the DNA molecule. This addition mostly occurs at the CpG islands, meaning, at the cytosine bases that precede the guanine bases. DNA methylation is essential for mammalian development and plays key roles in multiple biological processes, such as gene expression, genomic imprinting, X-chromosome inactivation, and transposon silencing [4]. DNA methylation patterns are altered in pathological conditions. For example, cancer cells usually exhibit global hypomethylation and local hypermethylation, which contribute to genomic instability and tumour suppressor silencing, respectively. The process of methylation is assisted by the enzyme DNA methyltransferases (DNMT).

It is generally believed that DNA methylation functions cooperatively and collaboratively with other epigenetic mechanisms, such as posttranslational modifications of histones, to stably maintain gene silencing and chromatin structure.

DNA methylation is generally associated with gene silencing [5], and DNA demethylation is usually connected with gene activation [5], [6].

2) Histone modification [7]

Similarly to DNA methylation, posttranslational histone modifications do not affect DNA nucleotide sequence but can modify its availability to the transcriptional machinery. Several types of histone modifications are known, amongst which acetylation, methylation, phosphorylation, and ubiquitination are the best studied and most important in terms of the regulation of chromatin structure and transcriptional activity. In general, histone modifications are catalysed by specific enzymes that act, predominantly, but not exclusively. Histone methylation in turn has either transcriptionally permissive or repressive character, depending on the location of targeted amino acid residues in the histone tail and/or the number of modifying (e.g. methyl) groups added.

Histone acetylation is an epigenetic modification in the lysine residues of the nucleosomes. The enzyme histone acetyltransferases (HAT) catalyse the reaction. Acetylation is the process of transfer of an acetyl group from acetyl coenzyme A to the N terminal of the lysine residues.

3) Non-Coding RNA

Non-coding RNAs (ncRNAs) are small RNA molecules that do not encode any protein. Non-encoding RNAs (non-coding RNAs) that are not translated into proteins can be divided into housekeeping non-coding RNAs and regulatory non-coding RNAs. RNA that has a regulatory role is mainly divided into two categories based on size; short chain non-coding RNAs (including siRNAs, miRNAs, and piRNAs) and long non-coding RNA (lncRNAs). In recent years, a large number of studies have shown that non-encoding RNAs play a significant

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role in epigenetic modification and can regulate expression at the level of the gene and the level of chromosome to control cell differentiation [8].

2. Factors Influencing Epigenetic Changes

A. Environmental Factors

Children are susceptible to environmental contaminants and are at risk of developing diseases, more so if the exposure begins at an early age. Prenatal and early life environmental factors, from diet to exposure to pollutants, have been associated with epigenetic changes, specifically DNA-methylation. Thus, maternal nutrition and smoking and exposure to air particulate matter, polycyclic aromatic hydrocarbons, arsenic, heavy metals, persistent organic pollutants, and some endocrine disrupters during pregnancy have been associated with genomic and gene-specific newborns' DNA-methylation changes that have shown in some cases sex-specific patterns. In addition, these maternal factors may deregulate the placental DNA-methylation balance and could induce a fetal reprogramming and later-in-life diseases [5].

B. Nutrition

The nutrients we extract from food enter metabolic pathways where they are manipulated, modified, and moulded into molecules the body can use. One such pathway is responsible for making methyl groups - important epigenetic tags that silence genes.

Familiar nutrients like folic acid, B vitamins, and SAM-e (S-Adenosyl methionine, a popular over-the-counter supplement) are key components of this methyl-making pathway. Diets high in these methyl-donating nutrients can rapidly alter gene expression, especially during early development when the epigenome is first being established [9].

C. Psychological

Stress and stimulant exposure can predispose similar behaviours, including impaired decision-making, cognitive inflexibility, and resilience to updating information; these are governed in part by the dorsal striatum.

Epigenetic changes – such as DNA methylation, transposable element activity, and histone post-translational modifications – accumulate as stress or stimulant exposure is maintained from an acute to a chronic condition.

Stress or stimulant-induced accumulation of epigenetic changes can potentiate differential gene regulation, altering immediate and future neuronal functions that include exposure-induced synaptic plasticity.

Chronic epigenetic dysregulation of regulatory genes in the dorsal striatum may contribute to compulsivity and cognitive inflexibility phenotypes, which are among the hallmarks of anxiety and addiction [10].

Accumulating evidence indicates that early childhood adversity might modify epigenetic patterns, particularly for DNA methylation. In *The Lancet Child & Adolescent Health*, Alexandre Lussier and colleagues investigated the relationship between childhood adversity and DNA methylation across different developmental stages. They found that adversity experienced between the ages of 3 and 5 years was more strongly associated with differences in DNA methylation patterns at age 15 years, compared with adversity experienced at other periods between birth and age 11 years.

These findings not only support the well documented role of childhood adversity in behavioural and epigenetic regulation,

but also unveil how the timing of environmental exposure can influence the effect of early-life adversity on epigenetic regulation [11].

"स्वस्थस्य स्वास्थ्यरक्षणम्
आतुरस्य विकारा प्रशमनं च " [12]

The main aim of Ayurveda is to maintain a healthy state of life and to remain free from the burden of diseases and sufferings so as to accomplish the ultimate goal of human life. To achieve this objective, ayurveda has advocated certain percepts and rules which can ensure the normal functioning of human body without any hindrance.

Ayurveda has suggested schedules of s*wasthvritt*a including *dinacharya, ratricharya*, *ritucharya, rasayana,* and *sadvritta* as some of the practices.

Life starts from ovulation/spermatogenesis. Thus, guidelines for diet and conduct also starts from menstrual care i.e., *ritucharya*, so that healthy ovum is produced in that cycle. If the woman conceives in that cycle after following preconception rituals mentioned in Ayurveda, she has to follow antenatal guidelines regarding diet and conduct for proper formation and development of fetus in womb. After delivery post-delivery guidelines in the form of *sutika paricharya* are there. That is epigenetics in today's term. By improving our own genetic expression, we are improving our next generations too.

D. Concept of Garbhini Ahara

In Ayurveda, *Garbhini Ahara* is one of the most impactful factors on child health and development. Systemic supervision and care including diet, code and conducts of daily living along with perfect advice is known as *Garbhini paricharya* in Ayurveda. It is a unique concept in Ayurveda designed to fulfil four main intentions i.e, *Anupghataya* (delivery without complication), *Paripuranatavaya* (for optimum fetal growth and development), *Sukhprasavaya* (for easy and safe delivery) and *Arogya balavarna samhanan sampat apatya jannaya* (for getting progeny with excellence in health, immunity, complexion and constitution) [13].

Ayurveda is far advanced as the concept of *Garbhini paricharya* particularly concept of month wise dietary regime is highly scientific and practical in terms of modern scientific knowledge

On screening the dietary articles mentioned for pregnant lady, it was found that every single fact pertaining to maternal diet mentioned in Ayurvedic text is scientific and has potential to modify the phenotypic expression [14].

Nowadays, intrauterine fetal reprogramming is major area of concern to prevent the onset of fetal origin of diseases.

Thus, it can be concluded that this fetal programming

paradigm provides good opportunity for Ayurveda practitioners to prioritize the *Garbhini paricharya* regimen to bring healthy epigenetic changes in upcoming offspring and ensure favorable health outcome for future generation.

E. Concept of Shadgharbhakara Bhavas

These are six essential factors are responsible for physical and psychological development of fetus in utero.

At the time of embryogenesis six essential factors are required

1. *Matrija* (Maternal)
2. *Pitrija* (Paternal)
3. *Atmaja* (Soul)
4. *Satmyaja* (Palatability)
5. *Rasaja* (Nutrition)
6. *Satvaja* (Psyche)

Here *Matruja* and *Pitruja Bhava* are responsible for genetic constitution of the fetus whereas *Atmaja, Satvaja, Satmyaja* and *Rasaja Bhava* probably can be understood to play role in epigenetics.

F. Samskaras

The Sanskrit term Samskara is derived from the root word 'Kri' with 'Sam' *Upasarga* which is being used for different meanings according to reference to context.

Samskara means '*Gunantaradhanam'* which is used to transform the qualities. Any process which brings continuous positive change in a given material (Dravya), physical body (Shareera), intellectual capacity (*Mana*) and the personality (*Aatma*) is called *Sanskara*. Different meaning of the word Sanskar can be applicable in medical science - Addition of new qualities, skilful activities, bringing fitness, self-productive and impression creating quality etc. *Sanskara* are highly individualistic and got its impact on producing qualitative society.

That may be in the form of addition of certain new qualities, deletion of unwanted qualities or modification/refinement of existing quality.

G. Kreedabhumi and Kreedanaka

Play is essential to development because it contributes to the cognitive, physical, social and emotional well-being of children's.

Ayurveda was 1st among the medical sciences to emphasis on these important aspects of child development i.e., *Kreedanaka* and *Kreedabhumi*

The number and the variety of toys mentioned by Kashyapa Samhita hints towards the concept of providing extensive learning opportunity and the role of toys in the physical and mental development of child and importance given towards the upbringing of the child.

3. Discussion

The augmenting field of epigenetic has perception that environment and individual lifestyle can directly interact with genome to influence epigenetic transformation. The epigenetic factors in life affect the phenotype in a positive or negative way, and indirectly affect the genetic expression in a positive or negative way, which can be transmitted to the progeny.

The genotype is the set of genes in the DNA that is responsible for the unique trait or characteristics. Phenotype is responsible for organisms' observable characteristics. A key difference between them is genotype is inherited from parents whereas phenotype is not. Also, phenotype is influenced by the genotype and many other factors like epigenetic modifications.

Fetal and early life presents a period where the human epigenome has a high degree of plasticity and is susceptible to external exposures It can also be initiated or disrupted by external factors.

According to ayurvedic science, it can be inferred from the following information:

A. Determining Factors of Prakriti

Individuals from all ethnic groups are classified as belonging to one of the seven types of prakriti. It is influenced by genetic and environmental variables. Many other variables influence an individual's prakriti at the time of birth [15].

1. *Shukra-shonitaprakriti* (sperm and ovum)
2. *Kala-prakriti* is a type of kala-prakriti (time of conception or season)
3. *Garbhashayaprakriti* (health status of uterus)
4. *Maturahar-viharprakriti* (diet and lifestyle habits of mother)
5. *Panchamahabhuta vikara prakriti*

Prakriti is derived by both genetic (sperm and ovum) and epigenetic (uterus state, period of conception, availability of food, and mother's behaviours) variables throughout its formation.

Factors such as *Jati prasakta, Kula prasakta, Deshanupatini, Kalanupatini, Balanupatini* influence the development of *Prakruthi* [16].

Hence it is necessary to provide supportive and positive nurturing environment from the earliest years.

4. Conclusion

- Epigenetics is an emerging science which shows how external influences affect the expression of genes, in other words, how a child's experiences modify their inherited genetic DNA makeup.
- Ayurveda describes the science of epigenetics in its own terms and how we can modify the gene expression by following guidelines mentioned in Ayurvedic texts for healthy living.
- Evidences has thrown up insights about the universality of the Ayurvedic concepts as well as their apparent association with concepts in current science.
- By the implementation of various dietary, lifestyle and habitual changes as required from early age we can optimize the expression of our genes in a way that supports evolution and growth both individually and collectively.
- This implementation of preventive practices from early age may result in such children leading healthy, disease free and more productive life.

- Further research is needed for better understanding of the interplay between genetic and epigenetic interaction in critical time windows of development and its effect on susceptibility of individual to a wide range of diseases.

References

[1] Waddington CH. The epigenotype. Endeavour 1942;1:18–20.

[2] Li Y, Saldanha SN, Tollefsbol TO. Impact of epigenetic dietary compounds on transgenerational prevention of human diseases. AAPS J. 2014; 16:27–36.

[3] Tollefsbol TO, (editor). Transgenerational epigenetics: evidence and debate. London: Academic Press; 2014.

[4] Smith ZD, Meissner A. DNA methylation: roles in mammalian development. Nat Rev Genet 2013;14(3):204–20.

[5] Alvarado-Cruz I, Alegría-Torres JA, Montes-Castro N, Jiménez-Garza O, Quintanilla-Vega B. Environmental Epigenetic Changes, as Risk Factors for the Development of Diseases in Children: A Systematic Review. Ann Glob Health. 2018 Jul 27;84(2):212-224.

[6] Michael D. Murphy, Elizabeth A. Heller, "Convergent actions of stress and stimulants via epigenetic regulation of neural circuitry," Trends in neuro sciences, vol. 45, no. 12, pp. 955-967, 2022.

[7] Alaskhar Alhamwe, B., Khalaila, R., Wolf, J. et al. Histone modifications and their role in epigenetics of atopy and allergic diseases. Allergy Asthma Clin Immunol., 14, 39, 2018.

[8] Wei, J., Huang, K., Yang, C., & Kang, C. (2017). Non-coding RNAs as regulators in epigenetics (Review). Oncology Reports, 37, 3-9.

[9] Bhardwaj, Priyanka; Sabharwal, Pooja. Changing the Phenotypes − Epigenetics in Ayurveda. Journal of Ayurveda, 17(1): pp. 54-57, Jan–Mar 2023.

[10] Murphy MD, Heller EA. Convergent actions of stress and stimulants via epigenetic regulation of neural circuitry. Trends Neurosci. 2022 Dec;45(12):955-967.

[11] Lin PI, Eapen V. New insights into the link between childhood adversity and epigenetic changes. Lancet Child Adolesc Health. 2023 Aug;7(8):520-521.

[12] Agnivesha, Charaka Samhita, revised by Charaka and Dridabala with Shri Chakrapanidatta Ayurveda Dipika Commentary in Sanskrit edited by Vaidya Yadavji Trikamji Acharya. Choukamba Sanskrit Sansthan, Varanasi, 5th edition, Sutra Stana, Chapter 30/26-P. No-187.

[13] Shastri Kasinath, Vidyotini Vyakhya, Charak Samhita, Chaukhamba Bharati Academy Varanasi. 2005, Sharira Sthana 8/32.

[14] Thakur Jyotsna, Masand Sameet. Scientific Analysis of Garbhini Ahar as Epigenetics Modifier of Offspring Genetics - A Critical Review. Ayushdhara. 2022 Dec.3;9(Suppl2):29-33.

[15] Agnivesha, Charaka Samhita, revised by Charaka and Dridabala with Shri Chakrapanidatta Ayurveda Dipika Commentary in Sanskrit edited by Vaidya Yadavji Trikamji Acharya. Choukamba Sanskrit Sansthan, Varanasi, 5th edition, Vimana Stana, Chapter 8/95-P. No-277

[16] Agnivesha, Charaka Samhita, revised by Charaka and Dridabala with Shri Chakrapanidatta Ayurveda Dipika Commentary in Sanskrit edited by Vaidya Yadavji Trikamji Acharya. Choukamba Sanskrit Sansthan, Varanasi, 5th edition, Indriya Stana, Chapter 1/5-P. No-354.