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Chrysanthus Chukwuma Sr*

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Review Article

Characterization of the Clinical and Molecular Perspectives of Epigenetics

Chrysanthus Chukwuma Sr

Executive Director the Chrysanthus Centre for Future-Oriented Studies Abakaliki, Ebonyi State, Nigeria.

Corresponding Author: Chrysanthus Chukwuma Sr, Executive Director the Chrysanthus Centre for Future-Oriented Studies Abakaliki, Ebonyi State, Nigeria.

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Abstract

This review provides the latitude to examine the extant information in the univeral characterizations of epigenetic formulations. Epigenetics encompasses the interaction of behaviours and environment culminating in changes which influence gene activity. In contrast to genetic modifications, epigenetic modifications are reversible; and do not alter the DNA sequence but are capable of interferring in the way the DNA sequence is read. Epigenetic alterations involve genetic changes which effect gene functionality without modifying the underlying DNA sequence. DNA methylation depicts the covalent superimposed methyl group to cytosine in CpG dinucleotides. DNA methylation presents as a veritable epigenetic modification; and it governs gene expression by changing chromosome structure, DNA conformation and stability as well as the function trajectory between DNA and protein. DNA methylation regulates gene expression via the conscription of proteins associated with gene expression or by the inhibition of the binding of transcription factor(s) to DNA. Whereas genetic alterations do modify protein formation, it is clear that epigenetic alterations impact on gene expression to put genes "on" and "off", as appropriate. The resultant impact of environmental and anthropogenic idiosyncracies, such as diet and physical activity are liable to induce epigenetic modifications in behaviours and gene-environment interactions. Genes are not always in functional mode. DNA methylation constitutes a select epigenetic process applied by cells for the control of gene expression. within the genome. Alterations in gene activity and epigenetic errors can result in varying genetic, metabolic and degenerative disorders which may disparately or in comorbid presentaions influence inter alia health, gene activity or expression, protein production and functionality. This entry exemplifies the reading and understanding of epigenetics in relation to inter alia beneficial developmental theories within the human race.

Keywords: epigenesis; preformation; philosophy; epigenome; gwas; ewas; ageing; senescence; Covid-19; diabetes; obesity; therapy

Introduction

Diverse disciplines have inculcated epigenetics in the evaluation of organism-environment or gene-environment interactions with particular reference to the application of genetic information within the life span of a person and transgenerational inheritance. Epigenetics is a science discipline engulfed in the genetic and non-genetic spheres correlated to heritable phenotypic modifications, DNA methylation and regulation of gene expression. Epigenetic modifications are DNA alterations which regulate the turning "on" and "off" regarding genes. These changes are attached to genes, and do not lead to the alteration of the building blocks of the DNA [1]. In the genome that constitutes the complete set of cellular DNA, the epigenome regulates gene expression. Epigenetic changes aid in the determination of the turning "on" or "off" regarding genes by influencing cell protein production. The regulation correlates to specificity and uniqueness of protein production by cells appropriate to its functionality, such that proteins which promote muscle growth and development are not produced in hepatic cells. There are differences or variations in epigenetic modifications between persons, tissues, and disparate cells within the same tissue. Epigenetic modifications can be sustained from one cell to the other during cell division. The environment, such as diet [1, 2], pollutant or irritant exposure or vulnerability can impact the epigenome; and in certain instances be inherited within generations or gene-environment interactions [3]. Instances of mechanisms which enact such changes are DNA methylation and histone modification; and as may be implicated or evident in coronavirus infection [4-6] The principal epigenetic processes involve DNA methylation, histone alterations and non-coding RNA. These mechanisms are established in

patterned regulation of tissue-specific gene expression, cell differentiation and imprinting of the genome.

DNA methylation and histones in epigenetic essence

Thus, a univerally acknowledged form of epigenetic change is DNA methylation that involves the attachment of the methyl group of one carbon and three hydrogen atoms to DNA building blocks. The occurrence of methyl groups in a gene, results in the gene being turned off or suppressed, leading to non-production of protein. A significant epigenetic feature realizable in the genome of higher eukaryotes is DNA methylation in the C-5 position of the cytosine ring. Depending on the DNA methylation locus, it may function as a suppressive or activation site for gene expression. Thus, DNA methylation is a prime control programne in gene expression modulation within numerous organisms. Gene silencing results from methylation due to DNA methyltransferases which transfer a methyl group from S-adenosyl-L-methionine to the cytosine carbon 5 position [7]. As developmental stages progress, DNA methylation presentation in the genome vary due to regulated compliance between de novo DNA methylation and demethylation. Consequently, a unique DNA formation that drives tissue-specific gene expression is inculcated and acquired by differentiated cells. Inasmuch as, DNA methylation ostensibly poses as a stable epigenetic mark, it is perspicuously fragile, with an intricate complexity in the interaction of epigenome, genome and other pertinent environmental factors during life progression antecedent to delivery. The characteristic of DNA methylation in an individual dynamically varies due to environmental factors during germ cell production, embryogenesis and post-delivery exposure. During development phases, the dissipation of balances in DNA methylation may culminate in imprinting health aberrations, with nonspecified loci to increased susceptibility to diverse disorders. The epigenome uniquely drives lifetime experiences ab initio en utero and present future opportunities in the improvisation of clinical applications [8].

Histones are structural proteins present in the cell nucleus. DNA encloses histones with resultant configuration of their forms. Histone modification is due to either the introduction or excision of methyl or acethyl groups, each made up of two carbon, three hydrogen and one oxygen atoms. These chemical groups determine the wrapped fortification of DNA on histones that impacts gene suppression or not. DNA methylation may either inhibit binding of the transcription machinery or formulate a platform appropriate for transcription, as evident in a crosstalk with histone modifiers [8]. Definable errors in the epigenetic process due to modification of the inappropriate gene or neglect to attach a chemical group to a specific gene or histone may culminate in aberrant gene functionality or outright nonfunctionality. Unequivocally, histone modification is an additional ubiquitous aetiology of epigenetic alteration. Alteration in gene activity, in addition to that engendered via epigenetic errors, constitutes a common aetiology of genetic disorders, with tumors, metabolic and degenerative diseases implicated in epigenetic untoward presentations. Exploration to explicate and elucidate the interrelatedness between the genome and the chemical moieties which contribute to its modification are being intensified, especially, to unravel the impacts of epigenetic changes and aberrations in ageing, gene functionality, protein production, environment and health [9].

Epigenetics constitutes the reversible heritable mechanisms which result in the absence of any modification of the underlying DNA sequence. Even though, chromosomes in the human genome convey genetic information, the epigenome has the task for the functional utlization and stabilization of that veritable or vital information that correlates the genotype with the phenotype [1]. These epigenetic alterations may occur spontaneously or governed by extraneous or inate forces.

Epigenetics and ageing

The rate of aging is morw or less governed by evolutionarily conserved genetic pathways, enviromental facyors and biological mechanisms. Ageing in epigenetics relates to the functional and biological importance of the epigenetic changes which accumulate as ageing progresses, and are critical in tumorigenesis. Paradigmatic instances are extant due to the global dissipation of DNA methylation in ageing and cancer as

well as via the promoter hypermethylation of genes with dual functionality in tumor suppression and progeria, such as the Werner syndrome (WRN) and lamin A/C genes [10]. Also sirtuins, a family of NAD-dependent deacetylases act on Lys16 of histone H4 as a link between cellular transformation and lifespan.

Ageing involves intricately complex multifactorial biological, chemical and physical processes, gene-environment interactions [3] or disparately by genes or environment exhibited by all biota. Spatiotemporally, it is depicted by premature, gradual or accelerated decline in structural-functional perspectives. Organismal aging is significant in human health in correlation to vulnerability and susceptibility to diverse diseases, such as diabetes, metabolic and other endocrine disorders as well as cancer, cardiovascular and neurodegenerative debilities [11]. Conversely, cellular or replicative senescence is a specialized and potential endogenous anticancer mechanism whereby there is irreversible growth obliteration due to response of potential oncogenic stimuli [12]. It is a potential driver in tissue remodelling in embryonic development and in the aftermath of tissue derangement that necessitates proliferation arrest [13]. Cellular senescence shares several similarities as ageing but with contrasting characteristics. Ageing and diabetes result in identical organ and system perturbations which are supported concurrently by molecular processes and cellular senescence. Cellular is basically an ageing mechanism implicated in numerous ageing-related diseases, and is significantly involved in the aetiology of tissue degradation, Senescent cells agggregation occurs during the ageing process: It is not clear how senescence contributes to diabetes pathogenesis [14].

Epigenetic change depicts a critical underlying mechanism in perspicuous in impaired cellular activities during ageing and age-related diseases. Patterns of DNA methylation are determined by the de novo DNA methyltransferases DNMTs being DNMT3A and DNMT3B, which are eventually sustained by DNMY1 [7]. Ageing and age-associated aberrations involve unique alterations in 5-methylcytosine concentration with usual characterization of genome-wide hypomethylation and promoter-defined hypermethylation. These modifications in the epigenetic domain reflect potential disease biomarkers and contribute to age-linked disorders. Certain diseases, such as a hereditary type of sensory neuropathy with concomitant dementia are incontrovertibly due to methylomic modifications. Epigenetic information and alterations are reversible since they are determined by enzymes; and thus, epigenetics is a potential target for therapeutic interventions in contrast to genetic alterations which are irreversible in humans. Drugs which target-specific for DNMTs included 5-azacytidine for rejuvenation [7]. The repercussions of epigenetic alterations in ageing are modified locus access to the genetic material with resultant untoward gene expression, reactivation of transposable elements as well as genomic instability [15]. A transposable element (TE, transposon, or jumping gene) is a DNA nucleic acid sequence in DNA capable of changing its position within a genome, and periodically creating or reversing mutations and modifying the genetic identity and genome size of the cell. Transposition frequently occurs in the duplication of the same genetic material.

These epigenetic progressive alterations to epigenetic information run concurrently with ageing in both dividing and nondividing cells as epigenetic changes have expansive influence in the ageing process, with occurrence at diverse levels, including decreased bulk levels of core histones, modified arrangements of histone posttranslational changes and methylation of DNA, canonical histone substitution with histone variants, and modified noncoding RNA expression in both organismal chronological ageing and replicative or cellular senescence [15]. Certain varieties of epigenetic information may influence the

lifespan of the offspring in a transgenerational way [15]. it is sugggested that lifespan is more epigenetically predetermined

than genetically predetermined. Also, that diet and other environmental factors influence lifespan through epigenetic information alterations; and epigenetic enzyme inhibitors may drive the lifespan of model organisms. Epigenetics studies tend to postulate that it is not nature versus nurture rather nature plus nurture, enforcing the obliteration of genetic determinism. Irrespective of the epigenome stance, it ostensibly does not translate across generations in essence. Researchers are exploiting the sphere of the epigenome in order to explicate the manner in which lifestyle factors including alcohol, obesity and smoking dictate cancer risk.

Epigenetic markers, clocks and ageing

Epigenetic clocks depend on algorithms in calculating biological age, basically on the read-out of the magnitude in which various loci traversing the genome of an individual are bound by methyl groups, an instance of epigenetic alteration. DNA hypomethylation, the decrement in universal DNA methylation is probably due to methyl- deficiency from diverse environmental factors which have been postulated as a molecular marker in cancer and other biological processes [17]. The determination of the 5-mC concentration or global methylation in deteriorated or environmentally affected cells may provide the latitude for veritable data for disease detection and analysis. The detection of DNA demethylation intermediate, 5-fC in diverse cells and tissues is applicable as a marker for indication of active DNA demethylation. Direct 5-fC excision by thymine DNA glycosylase, TDG for subsequent base excision repair, BER processing that reverts altered cytosine to its unaltered form. Differentially methylated regions, DMRs are DNA spheres which present critically different methylation status among numerous samples. Genome-wide methylation profiling is frequently conducted for the identification of DMRs among treated and untreated samples to unravel active areas which are associated with regulation of gene transcription due to inter alia DMRs specificity to cells, tissues and individuals. DMRs are feasible as biomarkers or potential targets for epigenetic therapy [17].

Epigenetic clocks encompass a set of CpG sites with determined DNA methylation concentrations correlate to individual age [18]. The clocks are recognisably esteemed accurate molecular correlate with chronological age in humans and other vertebrates, and quantification potential in rates of biological ageing as well as longevity tests and rejuvenating interventions. These unravel issues and opportunities to elucidate clock mechanisms and biochemical utility which necessitate exploiting or exploring nonhuman models, epigenomic marks, population studies, drivers and regulators of age-associated modifications in single-cell, tissue- and disease- specific models, as well as ethical issues in forensic age determination and prediction of chronological aging trajectory in a person [18]. Research suggested evidence, particularly, epigenetics for genome-wide DNA methylation changes in ageing and age-related disorders [19]. Epigenetic clocks which determine alterations in a limited hundred specific CpG loci can predict chronological age accurately in an expansive range of species; and credible biomarkers for mortality prediction in humans. The impacts of ageing across the methylome in an expansive array of human and mice tissues exhibited age-related hyper- or hypo-methylation alterations. There is the tendency for the DNA methylation age-related changes to be enriched and deficient in specific genomic contexts, with certain similarities among tissues and species necessitating further research [19]. The indefatigable proof that the age-related changes in DNA methylation contribute to ageing emanates from anti-ageing interventions, such as caloric restriction [3, 20], dwarfism and rapamycin application in mice [20]. The anti-ageing interventions retard the epigenetic clocks with reversal and/or obliteration of reasonable age-related modifications in DNA methylation. Genome-wide maps [21] of DNA methylation can be generated to track biological ageing, that is distinct from chronological ageing. The initial epigenetic clocks were determined regarding blood which depicted significant relationships with blood pressure and lipid concentrations, which are other variables of blood ageing. However, the epigenetic ageing signature differs in disparate tissues [22], and thus, these observations cannot be extrapolated to the kidney, for instance. It will be interesting to configure tissue-specific epigenetic clocks which may correlate with other ageing indicators. These may expose robust divergence regarding the aetiology, expanse, mechanisms, consequence, and genes disrupted in the pathological process for the development of novel diagnostic tools and clinical applications. These technologies may generate expansive data concerning the modification of genetic material in the present and in the future.

Epigenetics is observed to be divergent to genetics but they are both inextricably-linked, with incessant research to elucidate the relationship per Jonathan Mill [23]. The environmental role in shaping the genome may have been exaggerated because cells have the self-preservation to self- insulate from environmental assault per Adrian Bird [23]. Transgenerational epigenetic inheritance prevails in the mention of epigenetics in terms of the nuances and complexities of human health and disorders. The accumulated marks in somatic cells provide expansive information regarding these spheres of influence and mechanisms as modeled for the environment or lifestyle. Epigenetics has been defined as chromatin alterations with inclusion of RNA alterations. Besides DNA methylation, DNA can undergo hydroxymethylation, while modification can also be exerted on proteins in the chromatin complex. It has been postulated that the ageing process is reversible. Despite the lifestyle, the internal clock causes certain individuals to age rapidly and die early. Also, it is suggested via epigenome study that the biological scars of traumatic experiences are passed on to their children [23], thus suggesting that DNA is not merely the mode of biological inheritance in organisms, and that acquired traits are inheritable, however, researchers are more interested in its potential to determine disease risk. As the full complement of genes are received in conception without modification until death, the information is conceivably transmitted through "epigenetic marks" as chemical tags on genes which dial gene output up or down [23]. The transgenerational epigenetic inheritance phenomenon does not provide compelling evidence by any realisable physiological phenomenon for it to function, excepting in rare genetic disorders, definable genetic marks are deleted from the genetic material of the ovum and sperm of humans in fertilization following nuclei fusion. The nascent epigenetic configurations are determined in every generation. It has been well-nigh impossible to estrange the genetic, epigenetic and environmental spheres to traits inherited. Neuroepigenetics depicted critical impact in the spheres of learned behaviour, addiction, cognition neurotoxicology and psychopathology with tendency towards fascinating indictments rather than established or veritable findings [24].

Epigenetics and certain diseases

Numerous human diseases are connected with complex gene regulations and functions. These are integrated in environmental signals for cell modulation in the functional output of the genome. Diabetes is inextricably-linked with premature .ageing. There is palpable variation in the progression rate of ageing in humans. A simplistic biological paradigm is well-nigh impossible to determine both the clinicopathological and theoretical modalities in gene-environment interaction processes [3]. The potential epigenetic, gerontological and clinicopathplogical correlates and implications are to configure the population at risk for developing premature ageing and senescence within diabetic and obese individuals [25, 26] for early development of therapeutic regimen in order to stem pecuniary nurden and aberrant sequelae.

The extant understanding of the relationships between genetics, epigenetics, and environment in diabetes and evidence for the role of epigenetic factors in metabolism regulation and diabetes and its risks and complications highlight how the complex interactions between genes and environment or gene-environment interactions [3] may partly be mediated via epigenetic alterations and how information

regarding nutritional and other environmental stimuli are transmitted to the next generation. There is convergence in knowledge lacunae, research, recommendations and expansive interest in the epigenome, defined broadly as modifications to chromatin morphological functionality which exclude the modification of DNA sequence. Epigenetic control is crucial to both normal homeostasis and the disease state or process. Since diabetes risk complications are inextricably-linked to both genetic and environmental influences, numerous studies have perspicuously addressed the intersection of diabetes and epigenetics or epigenomics. Multiple layers of epigenetic regulation, such as direct methylation of cytosine or adenine residues, covalent changes to histone proteins, higher-order chromatin morphology, and noncoding RNA pertain [27]. These have severally been indicted in cellular mechanisms pertinent to diabetes; with sustained erstwhile inextricably-linked associations between epigenetics, diabetes, obesity, and a litany of metabolic aberrations. For instance, the agouti Ay mouse is an inbred strain that demonstrates profound obesity due to epigenomic changes of a gene that affects food consumption [28]. Incontrovertibly, obesity observed in Prader-Willi syndrome results due to impaired imprinting, a specialized epigenomic alteration [29]. Depending on the experimental paradigm, data have demonstrated that epigenome alterations by manipulating defined chromatin-modifying enzymes are associated with metabolic repercussions, with resultant obesity or mitigating obesity and hyperglycemia [30]. A vast majority of extant data associate epigenetic processes [31-33] in the risk of inherited or acquired diabetes and obesity [34, 35], as in infamy of human experiments documented regarding the Dutch Hunger Winter, for instance [31], in conjunction with inordinate rodent research. It is purposeful to enact data relating epigenomics to diabetes and metabolism in advances toward therapeutic intervention for the future.

In another spectrum, SARS-CoV-2, the pathological aetiologic agent of COVID-19 [36-41], an increasingly transmittable and pathogenic viral infection relies on the age and health status of an individual to exert its severity and untoward consequences. It provides ample latitude to comparatively analyze viral host epigenome regulation. Epigenetic changes may be conceivably involved in the initiation of coronavirus complications necessitating epigenetic drugs to stem viral outbreak as well as configure pre- and post-exposure prophylaxis per COVID-19 [42]

DNA Methylation Analysis

In the epigenetic field, there are extant plethora of procedures in the determination of the status of DNA methylation. These are categorized into (a) the discovery of unknown epigenetic modifications; and (b) DNA methylation assessment within defined regulatory genes and/or regions. [43]. These tools are selected based on feasibility and cost-benefit analysis. These epigenetic technologies involve nascent strategies with latitude to single-cell level, elevated- throughput genomic and epigenomic profiling with augmented high resolution having beneficial progress in epigenetics [44].

Notwithstanding the rewarding outcome of genome-wide association studies (GWAS) in the identification of loci connected to ubiquitous disorders, a vast majority of the aetiologies have not been explicated. Progress in genomic technologies has provided the latitude to commence large-scale research in human disease-related epigenetic disparity, specifically in DNA methylation [45]. These Epigenome-Wide Association Studies, EWAS provide ample and novel challenges and opportunities [46] which are not available in GWAS. Integrating EWAS and GWAS is a potential to analyse and elucidate the functionalities of complex GWAS haplotypes Explicating and unravelling the genetic and non- genetic determinants of human complex disorders constitute a prime challenge in biomedical studies which exposed an excess of 800 single nucleotide polymorphism, SNP relationships for over 150 disorders and multiple traits. Despite the lacunae in the knowledge of complete genetic basis for human complex disorder, resequencing of exomes, and whole genomes make provision for the identification of the unelucidated causal genetic disparities. Interests persist to explore the influence of non-genetic and epigenetic factors in intricately complex disease aetiology.

Asthma is a ubiquitous chronic respiratory airway disorder elicited by environmental factors, and ostensibly via interaction with human genome culminating in epigenetic alterations. EWAS principally examined DNA methylation and its relationship with disease or traits thereof, exposure variables or gene expression [47]. A method that is precise, specific and efficient for the detection of the exact DNA methylation levels is pertient for the elucidation of the prime functionalities of DNA methylation in biological processes or mechanisms with the objectives to augment research and development of novel optimum diagnostic and therapeutic trends and targets.

Epigenesis vs epigenetics

The application of the terminologies epigenesis and epigenetics has remarkably increased concurrently with confusing and conflating disparate issues prevailing in contextual biological and philosophical literature. Due to the extant confusion encompassing these two terms, it has become pertinent to explicate the disparities within their conceptual and historical evolutionary perspectives. The term "epigenesis" evolved from primordial embryological studies [48]. In contradistinction to Aristotelian natural philosophy, it was determined that epigenesis received fluctuating prominence since the 17th century, with its entry into neo- classical embryology and relevance in divergence to the preformationist stance. Whereas preformation relates that the germ cells of any organism contains preformed minute adults which unfold during the developmental process. epigenesis propounds that the embryo is formed in progressive consecutive exchanges within an amorphous zygote. Both stances tend to explicate developmental organization, religious and metaphysical polemics within the context of embryonic matter exclusively as active or passive. The proponents of these two norms perspicuously underlie the application of gene-centric metaphors in 20th century molecular revolution.

On that score, development constitutes the central biological mechanism, and postulations about its modalities have influenced biological reasoning. Regarding “epigenesis vs.preformation", epigenesis states that any developing organism arises from an unformed material and, over time, the gradual emergence of form during the development process. Conversely, preformation postulates that development starts with an entity as either in a preformed, predelineated, predetermined [49], preestablished or predefined manner. The debate of “epigenesis or preformation”is partly metaphysical about what is in existence. Whether it is form or also the unformed that culminates in the formed. In part, it is epistemological whther it is determined and established by observation or inference. Polemics in these inextricably-linked questions have persisted since eternity but genetic determinists currently rely on the already “formed”via genetic inheritance, whereas others depend on the efficacy of environmental plasticity. There are major development theories

from Aristotle on generation to current systems-theoretic and stem cell-based perspectives. Indubitably, “epigenesis vs preformation”does not represent the exclusive enduring theoretical divergence on development. However, this is an inclusive trajectory to inculcate patterns of transformation and consistency in arguments in biological development. Nature or nurture, epigenesis or preformation, genetic determinism or developmental free will, or whether a certain version of convergence are plausible remain the issues for determination. The terms of the never-ending discourse, and the undergirding hypothesis incessantly sustain arguments on the temporal beginning of life, with resultant indepth implications for bioethics and policy. Recently, molecular biology has rapidly evolved to incorporate epigenetic research for the evaluation of organism-environment interactions which are liable to present chronic resultant impacts. These sort of responses are likely to emanate from stress in early life stage, the usage of genetic information within the life span of an individual and transgenerational inheritance. Elucidation of epigenetic mechanisms potentiates the evaluation of

multigenerational and heritable impacts due to environmental stressors, such as contaminants [50] and pollutants, as are driven by epigenetic modifiers for the identification of prime heritable marks with concomitant results at the levels of the organism and population.

Discussion

Epigenetics is defined as the molecular DNA changes which regulate gene activity and are independent of DNA sequence, and are stable mitotically. Epigenetics studies have attained exponential growth recently, in progressive trajectories resulting in groundbreaking findings. These demand stringent methodologies and superior technologies to promote epigenetics to the apex of molecular biology. The prime epigenetic regulations include DNA methylation, histone modifications, and non-coding RNAs (ncRNAs) [44].

Genes are susceptible to diverse fluctuations. The stem cell epigenome simulates a fragile balance of chromatin (de-) alteration mechanisms. A model [51] demonstrated that modifications in DNA methylation were due to dynamics of histone alterations. This model may create a mechanistic explanation in the origin of tissue, age and cancer-specific DNA methylation profiles. DNA methylation is a critical ingredient in epigenetic change that is inextricably-linked in gene expression regulation. A key DNA methylation pathway diminishes the potential of transcription factors to bind to gene promoter regions [52]. Although several investigations have been conducted have to measure genome-wide DNA methylation levels at high resolution, the significance of these varied DNA methylation levels on transcription/factor binding potentials has not been clearly explicated.

The stem cell epigenome conveys a sensitive mechanistic balance of chromatin (de-)modification mechanisms. An introduction of a computational model of stem cell populations whereby each cell has an artificial genome, depicted that transcription of the genes encoded by the genome was influenced by DNA methylation, histone alteration and a cis- regulatory network [51]. Model dynamics were investigated using molecular crosstalk between the disparate mechanisms. The epigenetic states of the genes were vulnerable to disparate magnitudes of variations. It was exhibited that the timescales of these fluctuations effect if the condition or form connected with a defined gene will drift during cell replication. The model suggests that modifications in DNA methylation states are determined due to the dynamics of histone modification. It is suggested that the model demonstrates a mechanistic explication of the profiles pertaining to the origin of tissue, age and cancer-specific DNA methylation [51].

Conclusion

This article argues that epigenetic changes mediate environmental influences in gene expression, and modulate disease risk inextricably-linked with genetic spatiotemporal variation and transmissability. Analytical epigenetic paradigm presents substainable objectives and advancements for identifying, explicating and elucidating mechanisms wherein genetic and environmental influences are combinatorial contributary factors to disease risks and sequelae. The unravelling of spatiotemporal disparities in epigenetic profiling is of pertinence for the research in aging,the variables associated with diverse diseases, such as cancer, respiratory diseases, SARS-CoV-2/COVID-19, diabetes, metabolic and endocrine disorders. Thus, the article reviews epigenetic mechanisms on DNA methylation; genetic and environmental as they influence ageing, cellular senescence and certain confounding diseases, and philosophical development theories as they relate to humans. A conspectus of methodological analysis for epigenetic profiling is considered for cost-benefit of tools and techniques as well as advancement in disease treatment.

Conflict of Interest

There is no extant conflict of/competing interest regarding this entry.

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