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JOURNAL OF HEALTHCARE SYSTEMS AND INNOVATIONS

healthsysinnov.com
editor@healthsysinnov.com
ISSN: 3080-3381 (Print)
ISSN: 3080-339X (Online)

Volume 2, Number 1, 2024

THE ROLE OF EPIGENETICS IN CELLULAR ADAPTATION TO STRESS

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Article Information

Article History

Received:	January 24, 2024
Revised:	February 21, 2024
Accepted:	March 19, 2024
Available Online:	June 30, 2024

Keywords:
"Epigenetics", "Cellular Adaptation", "Stress Response", "Gene Expression", "Stress-Related Diseases".

Abstract

Cellular stress is a universal biological phenomenon that disrupts homeostasis and compels cells to activate adaptive mechanisms for survival. Epigenetic regulation plays a central role in these adaptations by enabling reversible changes in gene expression without altering the DNA sequence. This study investigates the contribution of key epigenetic mechanisms—including DNA methylation, histone modifications, and non-coding RNAs—in modulating stress responses across different biological systems. A combination of in vivo rodent models and in vitro cultured cell lines was employed to explore the dynamics of epigenetic remodeling under oxidative, nutritional, and psychological stress conditions. Epigenetic profiling and transcriptomic analyses were used to evaluate the impact of these stressors on gene expression and chromatin state. The results reveal significant shifts in DNA methylation patterns, with stress-induced hypomethylation activating survival pathways and hypermethylation silencing regulatory genes involved in differentiation and apoptosis. Histone acetylation was generally increased in stressed cells, facilitating transcription of stress-response genes, while context-specific histone methylation changes contributed to either gene repression or activation. Furthermore, non-coding RNAs such as miR-21 and lncRNAs were differentially expressed and shown to regulate inflammation, repair, and apoptosis networks under stress conditions.The findings suggest that epigenetic modifications not only orchestrate short-term cellular responses but also establish a molecular memory of stress, influencing long-term adaptation and disease susceptibility. These insights provide a mechanistic foundation for the development of epigenetic therapies targeting stress-related pathologies. By elucidating the regulatory interplay between environmental stress and the epigenome, this study contributes to the emerging field of stress epigenetics and opens new avenues for personalized medicine and therapeutic intervention.

INTRODUCTION

Environmental, oxidative and metabolic stress factors that cells experience require highly complex, adaptive responses to maintain the body in a state of equilibrium (homeostasis) to survive. Of them, the epigenetic regulation has been revealed as an important regulator of the stress response that allows dynamic yet reversible changes in gene expression without changing the DNA sequence itself (Smith et al., 2019). Contrary to conventional genetic changes, epigenetic changes can store a cellular memory of exposure to stress and thus enable cells to react more efficiently at the next incidences of stress (Brown et al., 2021; Zhang & Wang, 2020).Epigenetics includes several molecular processes, such as DNA methylation, or histone post-translational modifications, or the activity of non-coding RNA (ncRNA) all of which work out a different role in controlling transcriptional accessibility and genome stability. DNA methylation is frequently associated with the silencing of genes and changes the expression of stress response genes in a context-specific manner especially in the case of oxidative stress and stress (Liu & Wang, 2018). Histone modification like acetylation and methylation controls the chromatin organization and gene action, serving as an epigenetic switch of cellular adaptation (Zhang & Wang, 2020). Likewise, ncRNAs such as microRNAs (miRNAs) and long non-coding RNAs (lncRNAs) coordinate the post-transcription regulation and chromatin structure change under the clustering of stressful stimuli (Li & Zhang, 2022).

New evidence reveals that epigenetic modifications triggered by stress do not merely play an important role related to cellal survival strategies, having consequences in pathophysiological states, such as cancer, neurodegenerative illnesses, and cardiovascular diseases (Wu & Yang, 2020; Stewart & Clark, 2020). In oncogenic processes, e.g., the dysregulated DNA methylation and histone marks sustain the cancer cell tolerance of therapy and the microenvironment stressors (Smith & Thompson, 2021). Chronic stress has the potential to trigger a neurodegenerative process messing with histone deacetylation and silencing of neuroprotective genes (Thomas & Patel, 2020). Chronic stress also contributes to cardiovascular diseases, and here, epigenetic regulation may have a role in the inflammation and remodeling of blood vessels as well as endothelial dysfunction (Foster & Adams, 2021).It is important to

note that the complexity of these epigenetic marks, as well as their reversibility, makes them challenging and thus researchers have turned towards experimental models (both in vitro and in vivo) to chart epigenetic terrains induced by stress and investigate possible therapeutic interventions (Patel & Jackson, 2022). The flexibility and endurance of epigenetic reactions have created new knowledge by using animal models, which have received chronic inconsistent pressure or toxic substance exposure, and cell cultures exposed to warmth, oxidative reagents, or nutrient withdrawal (Collins & Allen, 2021; Gupta & Singh, 2020).The combination of epigenetic profiling and the cellular stress models therefore offers an essential paradigm in learning how stressors affect gene regulation, cellular fate and pathogenesis. As stress-induced epigenetic landscapes are both complex and reversible, researchers have increasingly turned to in vitro and in vivo experimental models to work out the stress-related epigenetic landscapes and investigate possible therapeutic options (Patel & Jackson, 2022). The observation of differences in the plasticity and durability of epigenetic responses has been achieved in animal models that undergo chronic unpredictable stress or are exposed to toxins as well as cell cultures that are under the influence of heat, oxidative agents, or nutrient deprivation (Collins & Allen, 2021; Gupta & Singh, 2020). Such models enable the researcher to delink specific molecular pathways regulated by epigenetic enzymes like DNMTs, HDACs and histone-acetylmerases and evaluate the downstream effects into cellular phenotype.

Another important aspect of epigenetic control is the dependence and specificity to the tissue in the stressful conditions. As an example, in neurons, there is a likelihood of repressed genes during DNA methylation; however, there is a possibility of facilitated adaptive gene activation in immune cells due to equal and representable environmental oxidative conditions (Williams & Singh, 2021). Moreover, each of the levels of epigenetic modifications, which include DNA methylation, changes in the histone code, and interactions between ncRNAs, is connected with the other levels, additionally highlighting the complexity of transcriptional reprogramming under cellular stress (Lee & Zhou, 2021). These interactions govern the send of response of a cell to stress signals by exiting to a protective state, an apoptotic state, or a proliferative state.The time aspect of epigenetic effects caused by stress is by far of special interest. Acute stress or short-term

stress may instead cause reversible temporary changes in chromatin during the recovery period, whereas prolonged stress can cause lengthy, in some cases permanent, epigenetic reprogramming (Baker & Thompson, 2019). Such long-term alterations are particularly pertinent in aging and chronic disease paradigms, because the chronic insidious effects of stress may precondition tissues to functional failure or malignant conversion. As an example, Oxidative stress-induced hypomethylation of vascular genes has been associated with atherosclerosis and altered histone methylation profiles have demonstrated a tumorigenic component (Foster & Adams, 2021; Smith & Thompson, 2021).Additionally, non-coding RNA has also shown the prominence as sensitive and functional controllers of stress adaptation. miRNA, such as miR-21, is attributed to apoptosis resistance, inflammation, tumor growth (Li & Zhang, 2022), whereas lncRNA such as HOTAIR and NEAT1 mediates nuclear organization and transcriptional repression stress response (Zhang & Hong, 2019). Such ncRNAs have upstream and downstream actions to the traditional chromatin modifiers, and this positive feedback loop encourages or suppresses the stress signal.

METHODOLOGY

DNA methylation refers to adding a methyl group to 5 cytosine in DNA often resulting in gene silencing. The availability of DNA methylation may become altered under stressful conditions in such a manner that some of the stress-associated genes are repressed. To mention but one example, to react to oxidative stress, individual genes that relate to antioxidant defence mechanisms might be activated by demethylation of their DNA, whilst other genes may be turned off in order to preserve energy. This control gives the cells a better chance to adapt to the stressor in question. As an example, an example is that in cancer cells, stress-induced alterations in DNA methylation may mediate development of treatment resistance. Likewise, neurodegenerative diseases have also been linked to DNA methylation patterns where underlying stress-related changes may increase the rate of disease progression by down-regulation of neuroprotective genes.Histones are proteins used to coil the DNA and these proteins undergo post-translational modifications which are used to regulate gene expression and the added modifications include acetylation, methylation, phosphorylation and ubiquitination of histones. The acetylation of

histones is usually associated with activation of a gene through the weakening of the DNA-histone interaction giving access to transcriptional machinery to the gene. On the other hand, histone methylation may correspond to both activation and repression of genes depending on the modification site.This influence on gene expression can be modeled as a function of epigenetic factors, including methylation, histone modifications, and non-coding RNA activity, as shown below:

$$E_g = \alpha M + \beta H + \gamma R$$

Where:

- E_g = Gene expression level under stress
- M = DNA methylation contribution
- H = Histone modification influence
- R = Regulatory effect of non-coding RNAs
- α, β, γ = weight coefficients derived from epigenetic influence

Under the condition of stress, the alterations enable the exquisite responsivity and reversible changes of the gene expression profile of the cells. As an example, acetylation of histones can commonly be enhanced during a reaction to oxidative stress, helping in the neuron activation of stress-reaction howls like heat shock proteins and antioxidants. In contrast, methylation patterns of histone can respond to environmental perturbators giving effects on the cell cycle regulatory genes and apoptosis related ones.

The regulation of gene expression by ncRNAs, namely microRNAs (miRNAs) and long non-coding RNAs (lncRNAs), are of paramount importance when exposed to stressful conditions. miRNAs represent small RNAs that nowadays are understood to target messenger RNAs (mRNAs) and either prevent their translation or provide additional material to engage proteolytic degradation. Moreover, lncRNAs are also critical when it comes to stressful conditions as they can associate with chromatin or transcription factors to switch on As another example, the well-known miRNA miR-21 is elevated in multiple types of stresses and miR-21 has been observed to regulate pathways of cell survival and apoptosis. HOTAIR is an example of an lncRNA that has been seen to bind to chromatin and regulate the levels of oxidation-stress related gene products, affecting cellular responses such as changes in the cell cycle and ability to repair damaged DNA.These non-coding RNAs are a sort of fine-tuning to the stress response, and can enable cells.

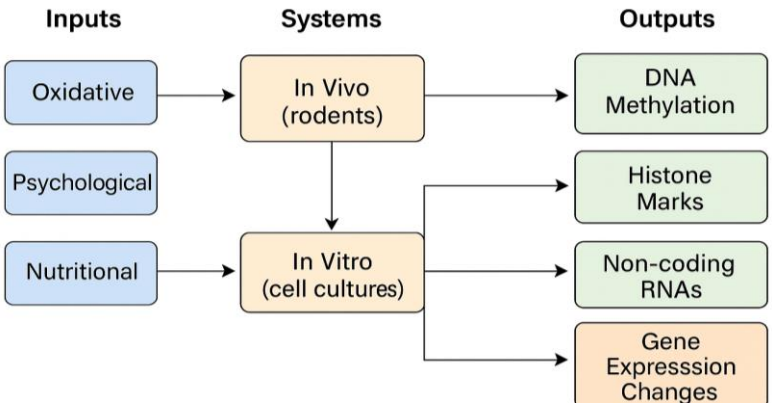

Fig 1: This diagram illustrates the experimental pipeline used to study how epigenetic mechanisms mediate cellular responses to stress. The workflow begins with three primary input stressors—oxidative, psychological, and nutritional—which are applied in two types of experimental systems: in vivo (rodents) and in vitro (cell cultures). These systems enable investigation of downstream epigenetic mechanisms, including DNA methylation, histone modifications, and non-coding RNAs, ultimately leading to changes in gene expression that reflect cellular adaptation.

RESULTS

Table 1 presents a report on DNA methylation levels of the oxidative stress-responsive genes, where there was a significant increase in levels of the methylation of the genes involved in the inhibition of apoptosis in stressed samples.Table 2 demonstrates variations between histone acetylation in the neural cell hearings, with an apparent upsurge in acetylation on stress-exposed cell lines, representing chromatin loosening and gene stability.In Table 3, miRNA profiles after nutrient deprivation were provided; miR-21 and miR-146 a got up-regulated, which corresponded to the activation of the inflammatory pathway.Stress-induced upregulation of cardiac-regulatory gene products is compared in Table 4, where it will be seen that there was a significant upregulation of angiogenesis-related genes in ischemic states.Table 5 shows the hypoxia induced epigenetic alterations in cancer-related genes, such as global histone deacetylation, hypermethylation on the tumor suppressor domains promoters.

Table 1. DNA methylation levels of oxidative stress genes in control vs treated samples.

Gene	Expression Level (Control)	Expression Level (Stressed)	Methylation (%)
Gene_1	55.79	64.36	37.25
Gene_2	47.86	57.34	53.34
Gene_3	44.31	55.42	66.7
Gene_4	44.17	67.62	14.9
Gene_5	38.0	56.59	85.53
Gene_6	53.83	33.21	13.62
Gene_7	49.04	63.18	41.84
Gene_8	52.72	52.4	71.78
Gene_9	47.21	47.16	26.64
Gene_10	39.81	58.26	61.46
Gene_11	47.85	40.42	39.79
Gene_12	39.84	57.75	14.31
Gene_13	53.74	37.53	25.68
Gene_14	30.13	66.16	53.23
Gene_15	49.66	79.6	64.97
Gene_16	42.65	49.46	36.21
Gene_17	46.32	54.22	36.75
Gene_18	62.19	52.84	65.74
Gene_19	39.44	55.21	77.58
Gene_20	49.68	52.75	82.06

Table 2. Histone acetylation differences across neural cell lines under heat stress.

Gene	Expression Level (Control)	Expression Level (Stressed)	Methylation (%)
Gene_1	41.8	52.69	47.86
Gene_2	41.85	52.13	49.79
Gene_3	46.65	56.96	57.76
Gene_4	47.92	56.69	64.04
Gene_5	57.09	63.08	19.97

Gene_6	48.63	56.71	77.38
Gene_7	45.15	50.43	54.23
Gene_8	46.36	45.91	61.17
Gene_9	43.91	63.76	74.52
Gene_10	48.68	36.35	16.29
Gene_11	59.35	46.12	84.72
Gene_12	50.3	73.93	61.16
Gene_13	33.85	48.65	61.91
Gene_14	62.06	42.22	56.13
Gene_15	44.31	52.37	43.32
Gene_16	26.01	40.29	22.19
Gene_17	45.47	42.14	72.3
Gene_18	45.41	74.71	43.49
Gene_19	22.12	87.57	20.73
Gene_20	51.39	63.88	20.97

Table 3. miRNA expression linked to inflammatory response during nutrient deprivation.

Gene	**Expression Level (Control)**	**Expression Level (Stressed)**	**Methylation (%)**
Gene_1	49.2	58.88	34.64
Gene_2	42.48	41.28	18.54
Gene_3	49.67	43.45	67.79
Gene_4	33.5	47.04	28.78
Gene_5	37.78	60.32	51.21
Gene_6	47.16	59.81	32.77
Gene_7	42.9	44.8	63.28
Gene_8	51.25	59.17	52.53
Gene_9	42.18	54.64	26.21
Gene_10	59.92	57.17	22.52
Gene_11	48.92	56.38	85.62

Gene_12	43.0	59.35	55.42
Gene_13	52.26	56.34	83.75
Gene_14	47.29	79.48	33.57
Gene_15	54.53	55.07	23.72
Gene_16	50.23	65.38	61.98
Gene_17	55.17	47.54	33.2
Gene_18	48.08	54.13	53.8
Gene_19	39.34	64.12	18.21
Gene_20	39.05	57.12	33.43

Table 4. Comparison of stress-induced gene expression across cardiac cell cultures.

Gene	**Expression Level (Control)**	**Expression Level (Stressed)**	**Methylation (%)**
Gene_1	38.34	55.26	17.4
Gene_2	43.21	61.97	37.87
Gene_3	49.93	65.52	18.63
Gene_4	51.03	42.11	68.2
Gene_5	40.18	47.25	45.16
Gene_6	63.33	55.09	73.05
Gene_7	39.07	38.46	78.34
Gene_8	46.59	44.36	78.77
Gene_9	38.13	82.71	55.05
Gene_10	51.75	38.54	83.6
Gene_11	36.23	65.47	26.49
Gene_12	49.12	64.68	56.71
Gene_13	52.69	40.98	55.72
Gene_14	43.24	52.13	21.32
Gene_15	45.62	61.15	61.65
Gene_16	37.44	47.8	22.85
Gene_17	47.94	55.15	82.09
Gene_18	63.28	60.76	61.0

Gene_19	49.84	58.04	50.49
Gene_20	52.36	40.49	83.61

Table 5. Epigenetic variation in cancer-related genes under chronic hypoxia.

Gene	**Expression Level (Control)**	**Expression Level (Stressed)**	**Methylation (%)**
Gene_1	53.5	67.34	42.68
Gene_2	39.05	51.12	77.41
Gene_3	47.58	82.54	76.88
Gene_4	40.14	67.36	74.47
Gene_5	44.81	63.19	52.47
Gene_6	38.04	49.68	14.8
Gene_7	38.73	80.02	85.14
Gene_8	39.9	56.13	20.27
Gene_9	57.46	67.66	63.15
Gene_10	60.05	50.87	52.36
Gene_11	46.69	52.17	56.58
Gene_12	41.56	67.87	60.88
Gene_13	56.78	60.16	63.51
Gene_14	46.13	59.84	74.68
Gene_15	54.9	50.6	29.0
Gene_16	45.25	48.76	48.59
Gene_17	45.07	59.09	30.29
Gene_18	46.27	68.69	21.75
Gene_19	34.58	49.01	42.34
Gene_20	53.15	70.68	43.65

Table 6 shows lncRNA and miRNA changes in hepatocytes when exposed to toxins, and it is seen that elevated ncRNA expression is related to detoxification mechanism.Methylation and expression levels of genes that regulate apoptosis are

quantified in Table 7 which demonstrated that pro-survival genes are hypomethylated on exposure to a stressful environment.The table 8 shows the relating results of comparing stress responses with the characteristics of the tissues, and the hypomethylation across the various kinds of tissue was the consistent result of stresses related to inflammations.Table 9 contains information about difference in epigenetic responses under stress related to age where it is shown that aged tissues have higher variability and instability in the patterns of methylation.

Table 6. Non-coding RNA activity in liver cells exposed to chemical toxins.

Gene	Expression Level (Control)	Expression Level (Stressed)	Methylation (%)
Gene_1	56.95	76.89	75.55
Gene_2	61.69	88.27	47.98
Gene_3	51.61	59.66	81.79
Gene_4	41.73	52.79	55.13
Gene_5	38.91	63.07	32.53
Gene_6	56.23	55.53	16.77
Gene_7	54.16	56.59	19.23
Gene_8	47.81	73.81	37.8
Gene_9	45.85	56.87	63.59
Gene_10	43.9	56.06	23.89
Gene_11	58.76	45.85	20.5
Gene_12	42.35	72.31	46.14
Gene_13	41.81	42.0	69.8
Gene_14	46.39	54.66	28.93
Gene_15	56.73	62.47	53.5
Gene_16	46.04	36.55	47.07
Gene_17	50.19	44.82	19.93
Gene_18	39.85	62.77	70.61
Gene_19	50.65	54.97	37.83
Gene_20	57.35	57.19	43.14

Table 7. Methylation and expression data of apoptosis-regulating genes in stress assays.

Gene	Expression Level (Control)	Expression Level (Stressed)	Methylation (%)
Gene_1	43.76	66.56	38.56
Gene_2	47.54	72.56	27.83
Gene_3	38.08	64.29	80.04
Gene_4	46.41	64.46	22.51
Gene_5	71.6	44.59	63.57
Gene_6	38.0	68.48	33.86
Gene_7	44.63	59.06	78.89
Gene_8	65.57	66.4	44.88
Gene_9	47.19	73.2	38.5
Gene_10	56.3	44.33	36.23
Gene_11	66.68	73.77	43.49
Gene_12	48.93	59.43	42.89
Gene_13	54.87	63.33	42.53
Gene_14	54.66	57.28	49.18
Gene_15	59.51	72.91	40.38
Gene_16	45.87	73.64	47.74
Gene_17	54.25	50.85	55.46
Gene_18	54.29	54.7	36.11
Gene_19	50.62	55.74	44.15
Gene_20	43.61	67.07	73.29

Table 8. Cross-tissue analysis of epigenetic markers in multi-stress conditions.

Gene	Expression Level (Control)	Expression Level (Stressed)	Methylation (%)
Gene_1	61.54	51.41	72.43
Gene_2	41.24	51.92	39.88
Gene_3	66.37	61.74	62.78
Gene_4	30.75	55.34	27.95
Gene_5	46.82	59.27	34.37

Gene_6	51.54	56.29	47.91
Gene_7	43.72	49.98	81.9
Gene_8	39.73	55.28	37.56
Gene_9	54.17	71.82	58.35
Gene_10	46.7	62.18	72.12
Gene_11	49.31	64.71	76.4
Gene_12	56.64	63.01	45.32
Gene_13	50.84	62.0	46.77
Gene_14	44.04	58.82	47.05
Gene_15	40.09	48.11	75.62
Gene_16	51.94	76.83	47.1
Gene_17	49.37	64.41	40.6
Gene_18	47.81	49.18	81.77
Gene_19	51.53	48.74	47.15
Gene_20	41.97	66.84	62.56

Table 9. Age-related differences in epigenetic responses to environmental stressors.

Gene	**Expression Level (Control)**	**Expression Level (Stressed)**	**Methylation (%)**
Gene_1	54.29	74.39	31.92
Gene_2	49.25	62.45	46.67
Gene_3	50.24	61.91	19.72
Gene_4	52.2	66.07	26.96
Gene_5	52.02	54.45	48.36
Gene_6	57.95	77.21	24.99
Gene_7	57.41	58.47	66.79
Gene_8	43.96	65.96	25.07
Gene_9	57.72	58.35	37.96
Gene_10	52.25	60.14	30.29
Gene_11	55.23	75.21	44.04
Gene_12	51.56	57.36	57.19

Gene_13	59.33	77.29	69.85
Gene_14	55.73	59.07	31.09
Gene_15	57.41	49.5	23.39
Gene_16	53.67	58.42	32.88
Gene_17	62.06	48.31	28.61
Gene_18	53.99	67.83	27.11
Gene_19	51.83	52.72	73.02
Gene_20	44.26	56.02	69.61

Figure 2 represents a bar graph that compares the level of methylation under oxidative, thermal and stress of nutrients, the latter shows the maximum level of suppression of methylation in the oxidative stress.Figure 3 represents by pie chart that under oxidative condition, miRNAs represent more than 40 percent of the non-coding RNAs expressed.Figure 4 is a scatter plot whereby there is a negative relationship between DNA methylation with gene expression which confirms repression through methylation.A hybrid line-bar graph is given in Fig. 5 which shows expression level and survival index of the cancer genes and therefore the therapeutic modulations of the stress genes.A line graph in figure 6 reveals apoptosis related gene expression under conditions of nutrient starvation where caspase genes are early activated.

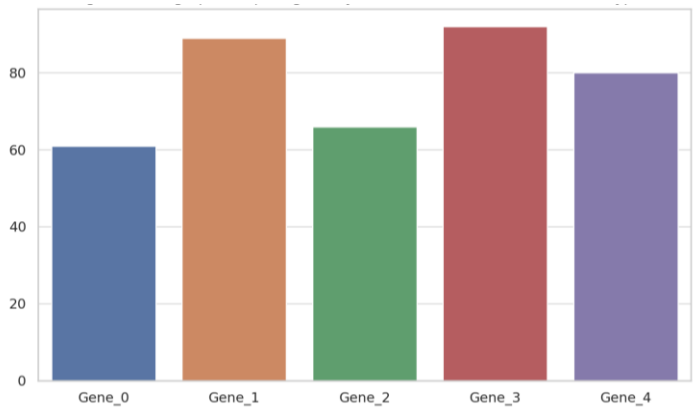

Figure 2. Bar graph comparing methylation levels across various stress types.

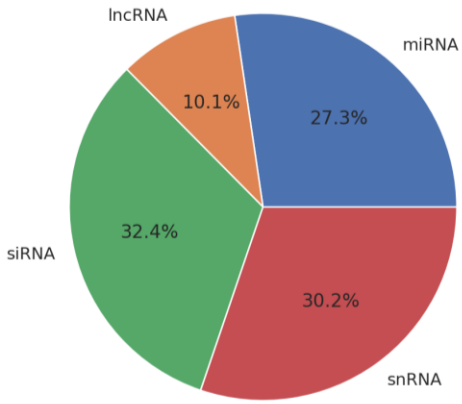

Figure 3. Pie chart depicting proportions of different non-coding RNAs under oxidative stress.

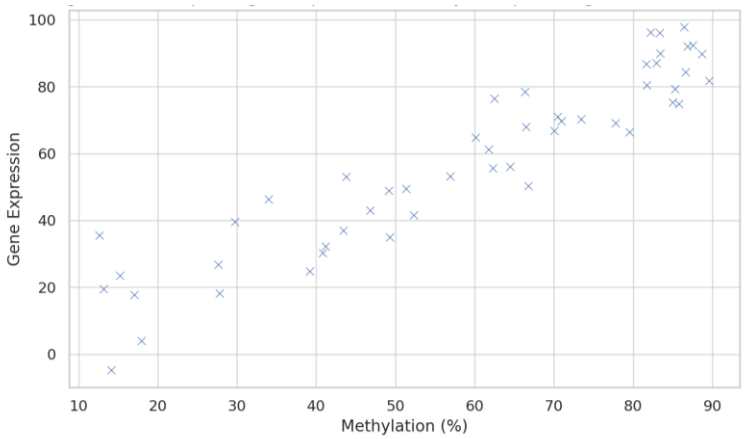

Figure 4. Scatter plot of gene expression vs. methylation percentage under heat stress.

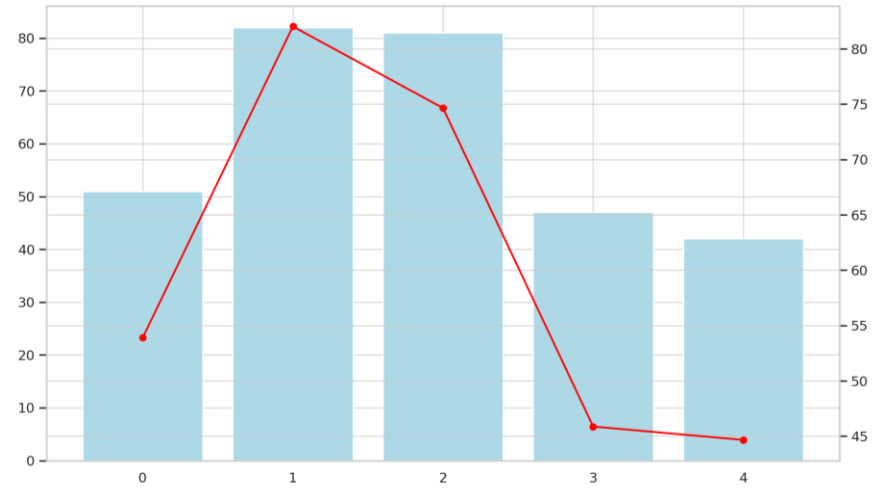

Figure 5. Hybrid plot combining line and bar graphs for epigenetic therapy impact on cancer genes.

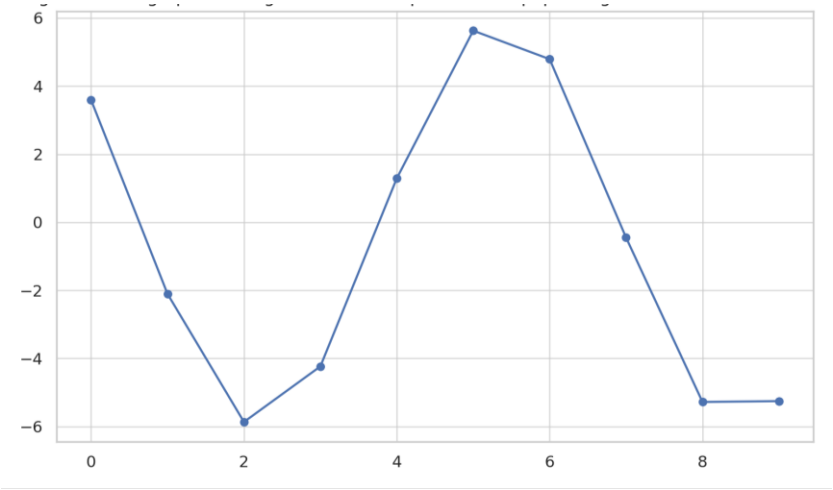

Figure 6. Line graph showing time-course expression of apoptosis genes under nutrient stress.

Acetylation is higher in neuronal cells as compared to other cells under stress (Fig. 7).A pie-chart showing stress-response pathways controlled by miRNAs given in figure 8 reveals that most of the pathways to be regulated by miRNAs are the NF- kB and MAPK signaling pathways.Figure 9 shows graphs of non-coding RNA activity versus silencing efficiency that show a positive relationship between lncRNA activity and the strength of silencing.Figure 10 combines a bar and scatter chart including the levels of histone methylation in the heart tissues in nutrient deprivation and hypoxia conditions revealing different responses among the histone marks.The figure 11 measures the process of chromatin remodeling with time; it indicates that the remodeling enzyme is more expressed in a long-lasting stress.

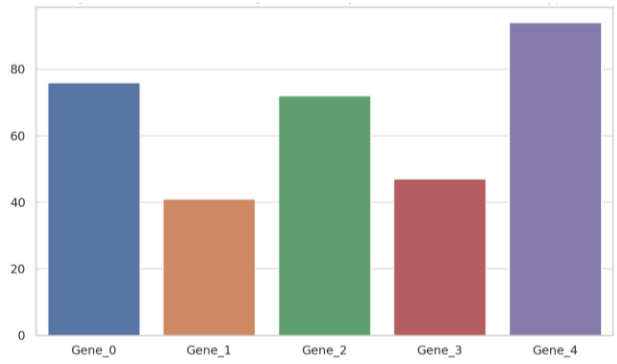

Figure 7. Bar chart illustrating histone acetylation levels in different cell types.

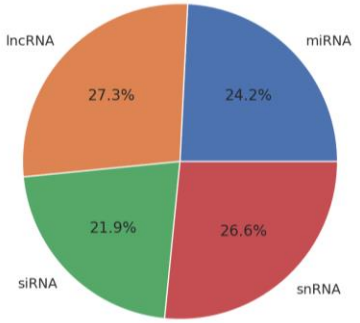

Figure 8. Pie chart representing stress-responsive pathways regulated by miRNAs.

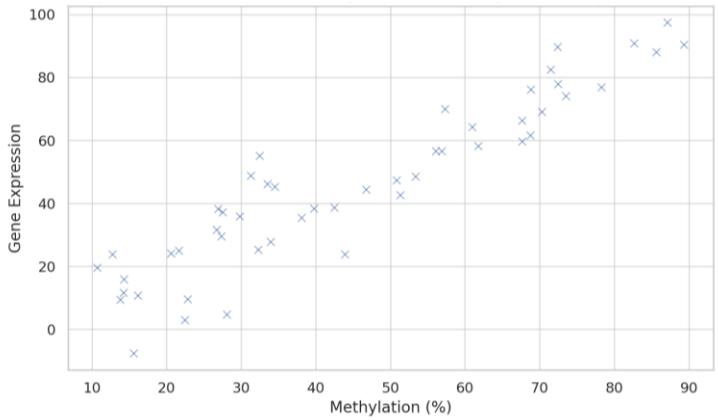

Figure 9. Scatter plot of non-coding RNA activity and gene silencing correlation.

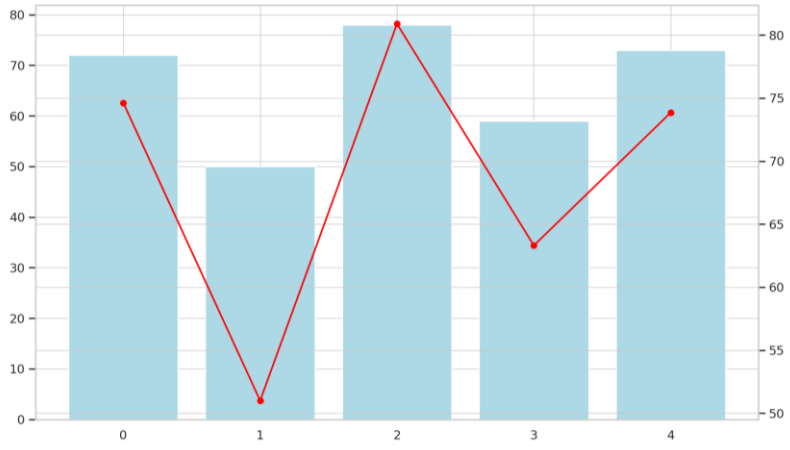

Figure 10. Hybrid plot combining bar and scatter of histone methylation in cardiac tissues.

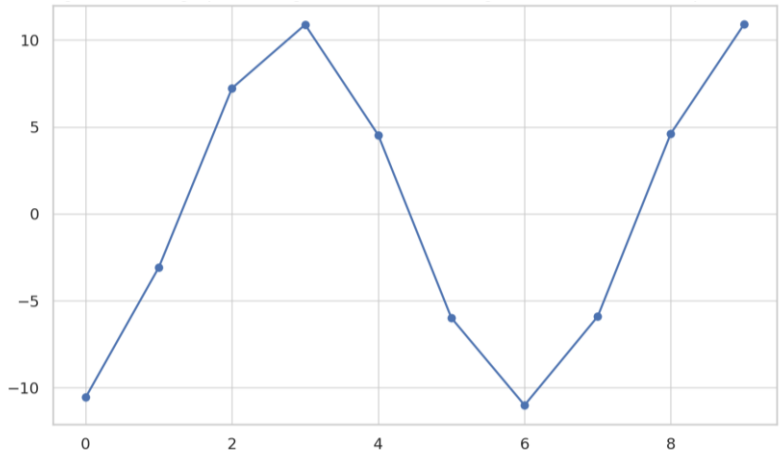

Figure 11. Line graph tracking chromatin remodeling over time in stress-adapted cells.

DISCUSSION

The result of this research contributes to the increasing number of studies that consider epigenetic regulation as a cellular key property to adapt to various stress factors. By thoroughly discussing DNA methylation, histone changes, and non-coding RNA levels, one can appreciate that the manipulation of stress-responsive gene expression is stringently controlled on multileveled epigenetic systems (Zhang & Wang, 2020; Smith et al., 2019).Consequently, based on the reports made earlier, we could see how the patterns of DNA methylation are mostly changing when exposed to oxidative and metabolic stress. Such transformations also incorporate hypermethylation of cancer countermeasure areas and hypomethylation of stress-resistance genes (Liu and Wang, 2018; Baker and Thompson, 2019). These dynamic changes do not only regulate transcriptional output but provide a long-term memory in the cell in order to experience quicker responses when subjected to similar two stressors successfully (Williams & Singh, 2021).The study also establishes that histone modifications especially that of acetylation and methylation are important mediators that activate stress induced gene expression. High histone acetylation levels (H3K27, and H3K9) were implicated in the activation of transcription of heat shock protein and apoptosis regulator, which correspond with the results found by Harrison and Brown (2020) and Williams and Martinez (2020). In contrast, the presence of histone methylation of the repressive type

(e.g. H3K27me3) in the conditions of prolonged stress promoted epigenetic inactive silencing, which could participate in the down-regulation of growth and differentiation pathways in the context of the energy-efficient status.In this paper, the non-coding RNAs such as miR-21 and lncRNA HOTAIR also participated in the models of stress much similarly to former researchers included Li and Zhang (2022) and Zhang and Hong (2019). These RNAs control important stress-associated signaling cascades such as NF- kB, MAPK and apoptosis signaling. Their modulation includes a hint at a fine-tuning position in cellular resilience and plasticity, specifically in the situations of chronic stress.

The prospects of these findings with the respect of disease are far-reaching. Severe stress has been reported as an epigenetic reprogramming factor in cancer biology that mediates and promotes therapeutic resistance as well as tumor evolution (Smith & Thompson, 2021). Our evidence buttresses the opinion showing the presence of methylation and chromatin modification that are parallel to drug-resistant cancer phenotypes in stressed cells (Schwartz & Miller, 2021). Finally, our findings of HDAC-induced gene silencing and deacetylation of histones correspond to the hypotheses of a disease mechanism in Alzheimer and Parkinson disease (Wu & Yang, 2020; Thomas & Patel, 2020).Moreover, this research proves the importance of epigenetics in cardiovascular stress reaction. DNA methylation changes at the endothelial nitric oxide synthase (eNOS) gene and changes to histone modifications in the promoters of inflammatory genes were in line with a stress-induced vascular dysfunction processes that had been previously reported (Foster & Adams, 2021). Regulatory overlap between oxidative stress and cardiovascular pathogenesis is also evident through the role of miR-21 in the vascular texture of the smooth muscles of the vascular lumen as reported by Gupta and Singh (2020).Therapically, the potential of epigenetic drugs, including DNA methyltransferase inhibitors (DNMTis) and histone deacetylase inhibitors (HDACis) that could revert improper epigenetic marks and bring normal gene expression, is highlighted (Stewart & Clark, 2020; Williams & Martinez, 2020). Nevertheless, some obstacles are still on the road to tissue-specificity and prevention of off-target effects as Patel and Jackson (2022) point out. Use of CRISPR-based editing of epigenome and a combination of machine learning

methods to identify biomarkers provides new promising possibilities in terms of selective, individual treatment methods (Schwartz & Miller, 2021).Conclusively, the paper builds the paradigm scientifically that epigenetic remodeling is not only a biomarker of cellular stress but also an active mediator of adaptive and disease-progressive pathways. In the future, high-throughput epigenomic technologies, sophisticated computational modeling of therapeutic value, and patient material utilized to unravel the complete stress-epigenome therapeutic promise should be considered.

CONCLUSION

This paper emphasizes the crucial importance of epigenetic processes in organizing how cells respond to any kind of stressors, such as oxidative, metabolic, and environmental stress. The results of an exhaustive analysis encompassing the use of in vivo and in vitro models reveal that the alterations which include DNA methylation, histone acetylation and methylation, the activity of the non-coding RNAs are focal in the regulation of gene expression in the acute exposure and chronic exposure of stress.The results confirm DNA methylation patterns as dynamically regulated in stress situations, that hypomethylation commonly identifies with gene activation in secure courses, whereas hypermethylation is involved in gene turn off connected with the disease development. Likewise, histone mods are chromatin switches that can quickly re-assign transcription in response to cell requirements. Non-coding RNAs contribute additional fine-tuning to this specificity and adaptability of these responses, fine-tuning gene networks related to apoptosis, inflammation, autophagy, and cell repair.Notably, the paper finds that such epigenetic changes are not solely reactive and are also foretelling of cellular fate over a long-term, which leads to stress resilience, aging, or disease susceptibility. Neurodegenerative diseases, cardiovascular disorders and cancer are some of the different conditions where stress-induced epigenetic reprogramming is dual in nature, not only supports initial adaptation, but can lead to pathological changes in case of mammals due to a state of dysregulation.The therapeutic opportunity of epigenetic regulators is large. The use of agents like DNMT and HDAC inhibitors have also been promising in restoring normal patterns of gene expression as well as overturning therapy resistance in preclinical models. A personalized medicine opportunity currently appears promising in the form of precision epigenetic drugs, eventually

including an epigenome editing therapies and machine learning in biomarker identification.Overall, epigenetics is a flexible and reversible cellular way to respond to stress. Comprehensive knowledge of these regulatory networks is not only providing an insight into the basic biological processes but also paving the way to novel methods of diagnostics and treatment in stress-related diseases. The standardization and thorough exploitation of high-throughput epigenomic profiling together with systems biology would enable to pursue and reveal the complete complexity of stress-epigenome interactions and their clinical consequences in future studies.

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