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# ANALYSIS OF EPIGENETIC VARIATION BY SMALL MOLECULE COMPOUNDS FOR DIFFERENT NEURODEGENERATIVE DISORDERS

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**Abstract:**

*Epigenetics and epigenomic medicine encompass a new science of brain and behavior that are already providing unique insights into the mechanisms underlying brain development, evolution, neuronal and network plasticity and homeostasis, senescence, the etiology of diverse neurological diseases and neural regenerative processes. The basic aim of the study is to explore the epigenetic variation by small molecule compounds for different neurodegenerative disorders. The accumulation of somatic and genetic mutations which altered the structure and coding information of the DNA are the major cause of neurological disorders. However, our recent understanding of molecular mechanisms of 'epigenetic' phenomenon reveals that the modifications of chromatin play a significant role in the development and severity of neurological disorders. Neurodegenerative disorders are among the major difficulties and among the most medical issues that should be with standed by the world, particularly in light of expanding population age. They cause the degeneration and death of nerve cells as they form incurable conditions for treatment. Regardless of that specific set of semantic conventions, it also seems clear that the term neuroepigenetic is emerging due to the discoveries of a wide variety of roles for epigenetic molecular mechanisms in the CNS regarding acquired behaviors, CNS disorders, neural plasticity, neurotoxicity, and drug addiction . Thus, we have the emerging sub discipline now being called neuroepigenetics.*

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## INTRODUCTION:

Epigenetics and epigenomic medicine encompass a new science of brain and behavior that are already providing unique insights into the mechanisms underlying brain development, evolution, neuronal and network plasticity and homeostasis, senescence, the etiology of diverse neurological diseases and neural regenerative processes [1]. Epigenetic mechanisms include DNA methylation, histone modifications, nucleosome repositioning, higher order chromatin remodeling, non-coding RNAs, and RNA and DNA editing. RNA is centrally involved in directing these processes, implying that the transcriptional state of the cell is the primary determinant of epigenetic memory. This transcriptional state can be modified not only by internal and external cues affecting gene expression and post-transcriptional processing, but also by RNA and DNA editing through activity-dependent intracellular transport and modulation of RNAs and RNA regulatory supercomplexes, and through trans-neuronal and systemic trafficking of functional RNA subclasses [2]. These integrated processes promote dynamic reorganization of nuclear architecture and the genomic landscape to modulate functional gene and neural networks with complex temporal and spatial trajectories. Epigenetics represents the long sought after molecular interface mediating gene–environmental interactions during critical periods throughout the lifecycle. Histone acetyltransferases (HATs) are epigenetic drivers that catalyze the acetyl transfer from acetyl-CoA to lysines of both histone and non-histone substrates and thereby induce transcription either by chromatin remodeling or direct transcription factor activation. Histone deacetylases (HDACs) conduct the reverse reaction to counter HAT activity [3]. Physiological processes such as cell cycle progression or apoptosis require a thoroughly balanced equilibrium of the interplay between acetylation and deacetylation processes to maintain or, if required, alter the global acetylome status. Aberrant HAT activity has recently been demonstrated to play a crucial role in the progression of various diseases such as prostate, lung, and colon cancers as well as glioblastomas and neurodegenerative diseases [4].

### Epigenetic changes

Many fundamental cellular processes are affected by epigenetic modulation, and in recent years it has become evident that chromatin-based epigenetic mechanisms underlie important aspects of the aging process. However, despite the fact that age is a prominent risk factor in neurodegenerative disease (ND), there is remarkably little information on the role of epigenetic alterations in mechanisms of ND such as Alzheimer's disease (AD), Parkinson's dementia (PD), frontotemporal degeneration (FTLD) or amyotrophic lateral sclerosis (ALS). We believe that a detailed biological, mechanistic and molecular understanding of the epigenetic factors that are altered in human ND holds promise for an improved understanding of disease pathogenesis and for the development of novel therapeutic interventions [5]. The goals of this Project are to: (1) investigate whether major epigenetic modifications (histone post-translational modifications) change in the context of different NDs using an extensive bank of human samples available from the Penn Center for Neurodegenerative Disease Research (CNDR), (2) use our model systems to discover new epigenetic modifications that underlie ND disease, and (3) test the relevance of novel changes seen in human ND using models of ND [6].

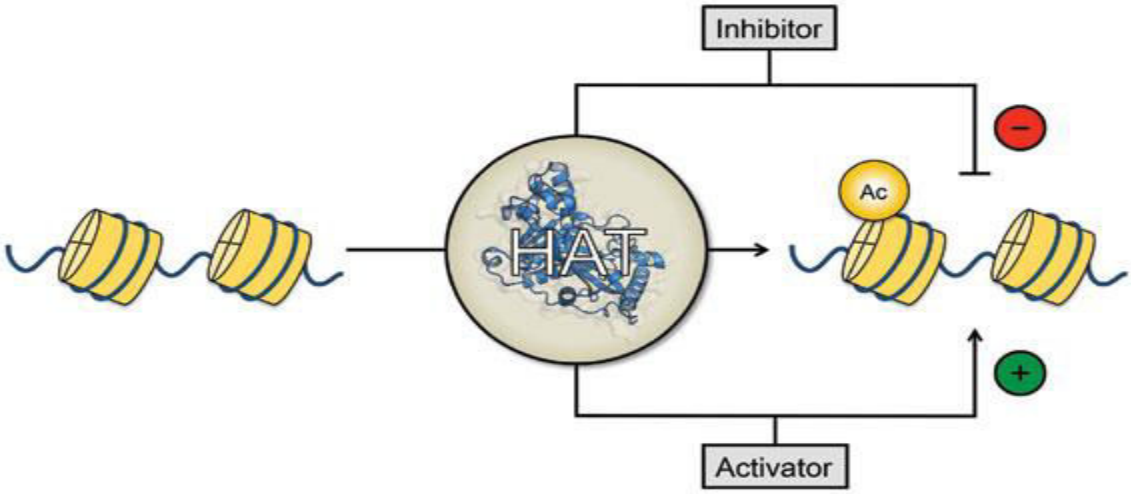


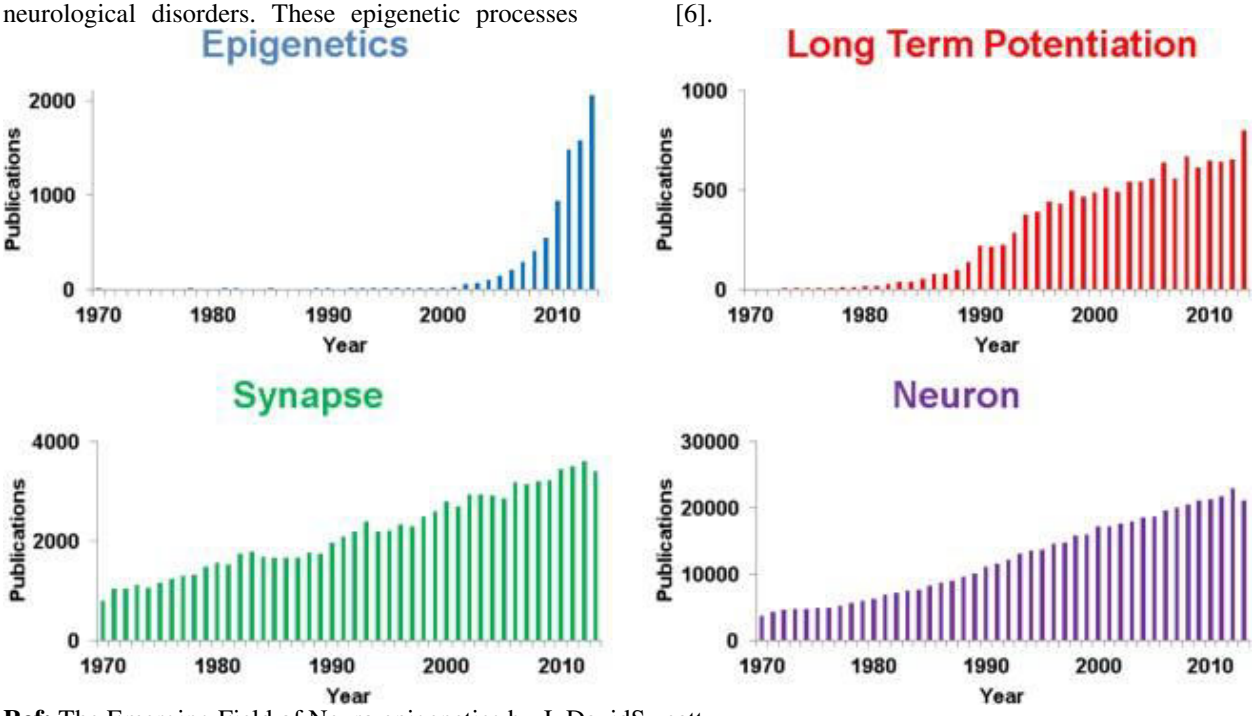

**Figure 01:** Graphical explanation of epigenetic modulation

**Objectives of the study**

The basic aim of the study is to explore the epigenetic variation by small molecule compounds for different neurodegenerative disorders.

**Epigenetic modulation by small molecules**

The accumulation of somatic and genetic mutations which altered the structure and coding information of the DNA are the major cause of neurological disorders. However, our recent understanding of molecular mechanisms of 'epigenetic' phenomenon reveals that the modifications of chromatin play a significant role in the development and severity of neurological disorders. These epigenetic processes are dynamic and reversible as compared to genetic ablations which are stable and irreversible. Therefore, targeting these epigenetic processes through small molecule modulators are of great therapeutic potential. To date, large number of small molecule modulators have been discovered which are capable of altering the brain pathology by targeting epigenetic enzymes. The field of epigenetics has undergone an exponential expansion as of late. A quick check of the PubMed publication database reveals that about 98% of all the research published in the broad area of epigenetics was published within the last 15 years [6].




**Ref:** The Emerging Field of Neuro epigenetics by J. DavidSweatt

**Epigenetics-neurodevelopmental and neurodegenerative disease**

Neurodegenerative disorders are among the major difficulties and among the most medical issues that should be with standed by the world, particularly in light of expanding population age. They cause the degeneration and death of nerve cells as they form incurable conditions for treatment. According to a collaborative study of the WHO, the World Bank and the Harvard School of Public Health by 2020 neurodegenerative diseases, dementia will be the eighth cause of disease among developed regions. It is also estimated that they will occupy the world's second leading cause of death by 2050, overtaking cancer [7]. During embryogenesis and for differentiation of neural cells Epigenetic mechanisms are essential required. Thus, precise understanding of Epigenetic mechanisms, including DNA methylation and histone modification, is important to elucidate the pathogenic pathways in neurodevelopmental disorders [8].

Most common neurodegenerative diseases

- Parkinson's disease
- Alzheimer disease.
- Huntington disease

Neurodegenerative disorders are among the real challenges and among the most therapeutic issues that ought to be withstanded by the world, especially in light of extending populace age. They cause the degeneration and passing of nerve cells as they shape hopeless conditions for treatment. As indicated by a synergistic investigation of the WHO, the World Bank and the Harvard School of Public Health by 2020 neurodegenerative infections, dementia will be the eighth reason for sickness among created regions. It is additionally assessed that they will possess the

world's second driving reason for death by 2050, surpassing growth. Amid embryogenesis and for separation of neural cells Epigenetic instruments are fundamental required. Accordingly, exact comprehension of epigenetic components, including DNA methylation and histone adjustment, is vital to explain the pathogenic pathways in neurodevelopmental issue [9].

**Table 01:** Areas Where Epigenetic Mechanisms in Human Nervous System Function

| Function or Disorder | Mechanism(s) Implicated |
|---|---|
| learning and memory | histone modifications, DNA methylation, piRNAs, miRNAs |
| maternal nurturing | histone modifications, DNA methylation |
| adult neurogenesis | histone modifications, DNA methylation |
| stress responses | histone modifications, DNA methylation |
| Alzheimer's disease | histone modifications, DNA methylation |
| Rett syndrome | MeCP2 methylcytosine binding |
| fragile X mental retardation | DNA methylation, miRNAs |
| schizophrenia | DNA and histone methylation, miRNAs |
| Rubinstein-Taybi syndrome | histone acetyltransferase deficiency |
| Angelman syndrome | genomic imprinting (DNA methylation) |
| depression and/or suicide | DNA methylation |
| bipolar disorder | histone modifications, DNA methylation, miRNAs |
| addiction and reward behavior | histone modifications, DNA methylation, miRNAs |
| PTSD | histone modifications, DNA methylation |
| ATR-X syndrome (α-thalassemia mental retardation) | SNF2 chromatin remodeling, H3.3 |
| cognitive aging | histone modifications, DNA methylation |
| Coffin-Lowry syndrome | histone phosphorylation |
| Kleefstra syndrome | histone methylation |
| epilepsy | histone modifications, DNA methylation, miRNAs |

## DISCUSSION:

Over the last decade, there has been a great expansion of the number of research papers and reviews published concerning epigenetic mechanisms in the nervous system, especially as related to adult CNS function. These burgeoning neuroscience discoveries have necessitated a redefinition of epigenetics, at least in regard to epigenetic mechanisms in adult neurons. As mentioned already, epigenetic mechanisms were originally defined as heritable either in a procreative organismal sense or at the cellular level across cell division [6]. An epigenetic molecular mark in an adult neuron can be long-lasting, permanent, and self-regenerating but cannot be inherited by a daughter cell since the neuron does not divide. This sets the roles of epigenetic mechanisms in adult neurons apart from their roles in developmental biology, such as perpetuation of cell fate determination, heritability, genomic imprinting, etc [10,11].

## CONCLUSION:

Regardless of that specific set of semantic conventions, it also seems clear that the term neuroepigenetic is emerging due to the discoveries of a wide variety of roles for epigenetic molecular mechanisms in the CNS regarding acquired behaviors, CNS disorders, neural plasticity, neurotoxicity, and drug addiction . Thus, we have the emerging subdiscipline now being called neuroepigenetics. A few small molecule modulators which have been shown to possess promising results in the animal model system of neurological disorders will also be discussed with future perspectives.

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