IOSR Journal of Biotechnology and Biochemistry (IOSR-JBB)
ISSN: 2455-264X, Volume 12, Issue 5 (Sept. – Oct. 2026), PP 01-13
www.iosrjournals.org

Artificial Intelligence-Driven Multi-Omics and Molecular Docking Approaches for Therapeutic Target Identification in Huntington's Disease

Vineeta Johri[1], Uma Kumari[2]
[1]*Research Scholar, NIMS Institute of Allied Medical Science and Technology, NIMS University, Jaipur, India*
[2] *Senior Scientist, Department of Bioinformatics, Bioinformatics Project and Research Institute, Noida, India*
Corresponding Author Uma Kumari

Abstract
Huntington's Disease (HD) is a rare, autosomal dominant neurodegenerative disorder marked by progressive motor problems, cognitive decline, and psychiatric symptoms, and the cause of this disease is an irregular expansion of CAG trinucleotide repeats, which are present in the huntingtin (HTT) gene. This gene encodes a mutant huntingtin protein, mHTT, with an extended polyglutamine segment. This defective and abnormal protein misfolds and aggregates, leading to neuronal dysfunction and selective neurodegeneration, primarily in the striatum and cerebral cortex. Even though considerable progress has been made in understanding the genetic basis of HD, no effective disease-modifying treatments are available, underscoring the urgent need for new strategies to identify potential therapeutic targets. Current advances in artificial intelligence (AI) and high-throughput omics technologies have transformed neurodegenerative disease research. Multi-omics approaches provide a detailed perception into the molecular description of HD. Combined with AI techniques such as machine learning and deep learning, these datasets enable precise identification of biomarkers, molecular pathways, and potential drug targets. These AI-based models also elevate research for predictions of disease progression and help classify different disease subtypes. They support personalised treatment strategies. Meanwhile, molecular docking and virtual screening methods have become essential in computational drug discovery. They facilitate quick and accurate assessment of protein–ligand interactions and also aid the identification of potential drugs targeting crucial proteins involved in HD, such as mutant huntingtin and related pathways. Combining AI-driven multi-omics data with molecular docking creates a strong foundation for accelerating therapeutic discovery and enhancing drug development. Although many challenges remain, such as data heterogeneity, a lack of high-quality datasets, and concerns about model interpretability, accuracy, and reproducibility. Moreover, translating computational discoveries into clinically effective treatments requires rigorous experimental validation. Overall, the combination of AI technologies, multi-omics technologies, and molecular docking offers a significant, promising, and transformative approach to exploring the complex biology of HD and discovering new therapeutic options. Current ongoing progress in these areas is likely to boost precision medicine and expedite the creation of effective treatments for Huntington's Disease.

Keywords: *Huntington's disease, Artificial intelligence, multi-omics integration, Molecular docking, Neurodegeneration, biomarker discovery, machine learning, drug discovery, systems biology. Precision medicine*

Date of Submission: 13-09-2026 Date of Acceptance: 24-09-2026

I. Introduction

Huntington's Disease is a developing genetic neurodegenerative disorder. It is showing notable clinical and societal challenges. First identified in the 19th century, HD is now understood as a monogenic disorder caused by an expanded CAG trinucleotide repeat in the HTT gene on chromosome 4. Individuals who have more than 36 CAG repeats develop the disease. These longer CAG repeats are associated with earlier onset and greater severity. **[1,2]** The important pathological feature of HD is the aggregation of mutant huntingtin protein, which has an abnormally long polyglutamine (polyQ) tract, making it prone to misfolding and aggregation. Clinically, HD presents a triad of motor dysfunction, cognitive decline, and psychiatric symptoms. Motor signs of the body, such as chorea, dystonia, and coordination issues, as well as cognitive impairments, affect executive function, memory, and attention. Psychiatric symptoms like depression, anxiety, and irritability are common and often appear before motor issues. The disease's progressive nature results in severe disability and death, typically within 15–20 years of onset.**[3]** HD involves multiple interconnected molecular pathways. The production of mHTT protein disrupts cellular function through mechanisms including transcriptional dysregulation, mitochondrial dysfunction, impaired protein degradation, and neuroinflammation. These processes lead to selective neuronal loss, especially

in the striatum and cortex. Despite extensive research, the exact mechanisms underlying neuronal vulnerability remain incompletely understood.**[4]**

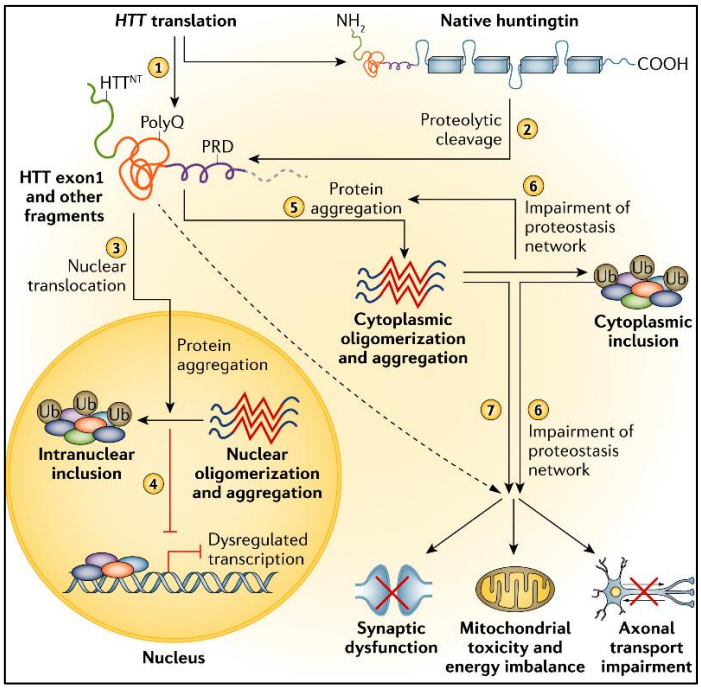

Figure -1: Pathogenetic cellular mechanisms in Huntington disease. (1) HTT is translated to produce the full-length huntingtin protein, as well as an amino-terminal HTT exon 1 fragment (the result of aberrant splicing). The length of the polyglutamine (polyQ) tract in these proteins depends on the extent of somatic instability. (2) Full-length native huntingtin is cleaved by proteolysis to generate additional protein fragments. (3) Protein fragments enter the nucleus. (4) Fragments are retained in the nucleus through self-association, oligomerisation and aggregation, leading to the formation of inclusions, a process that causes transcriptional dysregulation through the sequestration of other proteins and through other incompletely defined mechanisms. (5) Huntingtin fragments oligomerise and aggregate in the cytoplasm. (6) The aggregation of huntingtin is exacerbated by disease-related impairment of the proteostasis network, which also leads to global cellular impairments. (7) The aberrant forms of huntingtin result in additional global cellular impairments, including synaptic dysfunction, mitochondrial toxicity and a decreased rate of axonal transport. PRD, proline-rich domain; Ub, ubiquitin. Reproduced with permission from [7].**[54]**

Current therapies for HD primarily treat symptoms and do not target the disease's root cause. Drugs like dopamine-depleting agents and antipsychotics are used to control motor and psychiatric symptoms, but they have limited success in halting disease progression. Advancements in high-throughput technologies have led to the creation of large biological datasets and to the rise of multi-omics. This approach combines data from genomics, transcriptomics, proteomics, and metabolomics, offering a detailed understanding of biological systems. **[5,6]** In HD research, multi-omics has helped identify disease-related genes, disrupted pathways, and possible biomarkers. Even so, the complexity and high dimensionality of these datasets pose substantial analytical challenges; however, Artificial Intelligence (AI), particularly machine learning and deep learning, has become an important tool for examining complex biological datasets. **[7]** AI algorithms can detect patterns and relationships within large datasets that traditional statistical methods might miss. In this research, AI has been used for gene expression analysis, biomarker discovery, disease classification, and disease progression prediction, and explainable AI techniques are increasingly utilised to interpret model results and gain biological insights. Another key development in computational biology is molecular docking and virtual screening for drug discovery. For the prediction of interactions between proteins and small molecules, helping to identify potential therapeutic compounds.**[8]** In HD, docking studies have targeted compounds that inhibit mHTT aggregation, modulate oxidative stress pathways, or improve cellular proteostasis. Combined with AI-based target identification, molecular docking offers a powerful approach to accelerate drug discovery. Combining AI, multi-omics analysis, and molecular docking has strong potential for discovering new therapeutic targets in HD. This integrative approach systematically identifies crucial molecular players involved in disease development and supports the creation of targeted treatments. It also aligns with the shift toward precision medicine, where therapies are customized based on individual molecular profiles. Despite progress, challenges remain. Data heterogeneity, batch

effects, and limited access to high-quality datasets can impact the accuracy of multi-omics analyses. Moreover, AI models often lack interpretability, making it hard to translate computational results into biological understanding. **[9,10]** Validating these predictions experimentally and clinically is essential but can be resource-intensive. This review offers an overview of AI-driven multi-omics and molecular docking methods in HD research. We explore the molecular mechanisms of HD, AI's role in analyzing multi-omics data, and the use of molecular docking in drug discovery. Finally, we address current challenges and future prospects, highlighting the potential of integrative computational strategies to advance therapeutic development for Huntington's Disease.

II. Molecular Mechanisms of Huntington's Disease

HD is a multifaceted combination of genetic, molecular, and cellular factors that together drive progressive neurodegeneration. The main cause is the expansion of CAG trinucleotide repeats in the HTT gene, which leads to the production of mHTT protein with a polyQ tract. This structural change significantly affects protein folding, leading to aggregation and toxicity. An important part of HD pathology is the formation of intracellular aggregates composed of misfolded mHTT. **[11]** These aggregates accumulate in neuronal cells and disrupt essential cellular functions, including transcription, protein degradation, and intracellular transport. The precise role of these aggregates remains debated, and they are used as indicators of disease progression and neuronal dysfunction. Transcriptional dysregulation is an essential mechanism in HD. In this dysregulation, mHTT interacts with transcription factors and co-regulators, disrupting gene expression.**[12]** This reduces the expression of genes critical for neuronal survival, synaptic function, and energy metabolism, including brain-derived neurotrophic factor (BDNF), which has been linked to neuronal degeneration in HD. Mitochondrial dysfunction also markedly contributes to HD because, in this dysregulation, mHTT hampers mitochondrial function by impairing the electron transport chain, leading to reduced ATP levels and increased reactive oxygen species (ROS). Oxidative stress from ROS damages lipids, proteins, and DNA, exacerbating neuronal injury. In addition to defective protein degradation pathways, such as the ubiquitin–proteasome system (UPS) and autophagy, lead to the accumulation of toxic proteins. When these systems fail to clear misfolded mHTT efficiently, cellular stress and apoptosis occur. Boosting these degradation mechanisms is considered a promising therapeutic approach. **[13,14]**

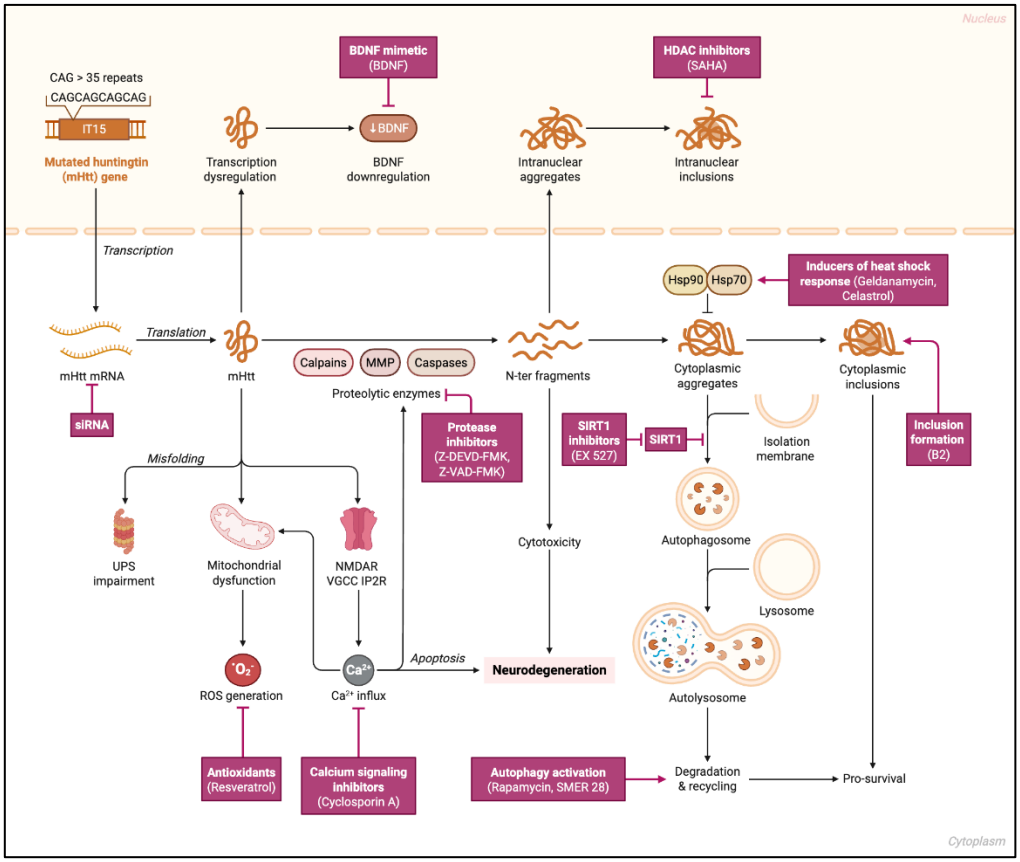

Figure -2: This template traces the molecular mechanisms of Huntington's disease from the CAG-repeat-expanded huntingtin gene through mHtt protein misfolding, transcriptional dysregulation, mitochondrial dysfunction, and the formation of intranuclear and cytoplasmic aggregates and inclusions. It also marks candidate therapies,

including siRNA, BDNF mimetics, HDAC inhibitors, protease inhibitors, antioxidants, and autophagy activators, at each step they target. **[image taken from bio reader site]**

Neuroinflammation also plays a significant role in HD progression by activating microglia and astrocytes and releasing pro-inflammatory cytokines that create a harmful environment, accelerating neuronal damage. Persistent inflammation further disrupts neuronal homeostasis and drives disease advancement. In addition, HD shows signs of synaptic dysfunction and impaired axonal transport. Mutant huntingtin protein disrupts vesicle trafficking and neurotransmitter release.**[15]** IN this process, deficits in synaptic communication are present. These changes contribute to the cognitive and motor symptoms seen in the disease. A newly identified mechanism involves somatic instability of CAG repeats, where repeat lengths in certain tissues continue to lengthen over time. This expansion of the repeat phenomenon relates to disease severity and progression, elaborating the dynamic nature of the HD mutation. In summary, HD's molecular mechanisms are complex and interconnected, including protein aggregation, transcriptional dysregulation, mitochondrial dysfunction, proteostasis impairment, oxidative stress, and neuroinflammation. Gaining a deeper understanding of these processes is vital for pinpointing therapeutic targets and creating effective treatments.**[16]**

III. Artificial Intelligence in Huntington's Disease

Artificial intelligence (AI) has become an important tool in biomedical research, especially for studying complex neurodegenerative diseases like Huntington's Disease (HD). Due to the multifaceted nature of HD, genetic mutations, protein aggregation, and widespread molecular disruption, analytical methods capable of managing large, high-dimensional datasets are necessary.**[17]** AI, including machine learning (ML) and deep learning (DL), offers robust computational frameworks for extracting valuable insights from such data. In HD research, researchers widely use machine learning algorithms for classification, prediction, and biomarker identification. Supervised learning methods such as support vector machines (SVMs), random forests, and logistic regression are often used to distinguish disease from control samples using gene expression or imaging data. **[18]** These techniques have shown high accuracy in identifying disease-specific molecular signatures, aiding early diagnosis. Unsupervised learning methods, such as clustering and principal component analysis (PCA), are used to uncover hidden patterns and classify subgroups within HD populations, thereby improving understanding of disease heterogeneity. Deep learning models, especially artificial neural networks (ANNs) and convolutional neural networks (CNNs), have become prominent because they can capture complex nonlinear relationships. In HD, researchers have used deep learning on neuroimaging data to detect structural and functional brain changes associated with disease progression. **[19]** For instance, CNN models can analyse magnetic resonance imaging (MRI) scans to detect early neurodegenerative alterations in the striatum and cortex, often before clinical symptoms appear. This is vital for early diagnosis and tracking disease progression. AI also plays a vital role in biomarker discovery. By combining transcriptomic, proteomic, and metabolomic data, machine learning algorithms can identify biomarkers that predict disease onset, severity, and progression. Feature selection helps identify the most relevant genes or proteins associated with HD, simplifying the data and boosting model accuracy. Moreover, AI-driven biomarker discovery advances precision medicine, enabling treatments tailored to individual molecular profiles. Another key area for AI in HD research is drug discovery. **[20]** Machine learning models can predict drug–target interactions, screen large chemical libraries, and identify promising therapeutic compounds. These methods greatly reduce time and costs compared to conventional drug development. Additionally, AI facilitates drug repurposing by identifying existing drugs with potential therapeutic effects in HD based on molecular similarities and pathway insights. Explainable artificial intelligence (XAI) has gained increasing importance in addressing the opacity of AI models, often referred to as the 'black box.' Techniques like SHAP (Shapley Additive Explanations) and LIME (Local Interpretable Model-Agnostic Explanations) shed light on model predictions by emphasizing the role of individual features. **[21]** In Huntington's disease (HD), XAI allows researchers to pinpoint key genes, pathways, and molecular interactions that influence disease progression, thereby improving the biological interpretability of AI models. However, applying AI in HD research presents several challenges. Data heterogeneity, batch effects, and a scarcity of high-quality datasets can hinder model performance and generalisation. Concerns like overfitting and reproducibility are particularly relevant in studies with small sample sizes. Ethical issues, such as data privacy and algorithmic bias, also need careful consideration. In summary, AI has greatly contributed to the understanding of HD by analysing complex datasets, identifying biomarkers, and accelerating drug discovery. Ongoing efforts to develop robust, interpretable, and scalable AI models, along with the integration of diverse data sources, are expected to further enhance its role in HD research and therapy development.**[22]**

IV. Multi-Omics Approaches

The rise of multi-omics technologies has transformed the research of complex diseases like Huntington's Disease (HD) by allowing detailed analysis across various levels of biological data. Multi-omics involves

combining different datasets—such as genomics, transcriptomics, proteomics, and metabolomics—to gain a comprehensive understanding of disease mechanisms. **[23]** In HD, these methods have greatly helped uncover molecular pathways involved in neurodegeneration and identify new therapeutic targets. Genomics underpins multi-omics research in HD, as the disease results from a specific genetic mutation in the HTT gene. Techniques such as genome-wide association studies (GWAS) and next-generation sequencing (NGS) have identified genetic factors that influence when the disease begins and how it progresses. These factors may affect processes such as DNA repair, protein balance, and neuronal health, helping explain the differences observed among patients.**[23]** Transcriptomics, which studies RNA expression, offers insights into gene regulation and activity. RNA sequencing (RNA-seq) in HD has revealed widespread transcriptional disruptions, including changes in genes involved in synaptic function, energy metabolism, and stress responses. Analysing gene expression differences helps pinpoint key pathways affected by mutant huntingtin, thereby providing potential therapeutic targets. Proteomics complements transcriptomics by offering insights into protein levels, post-translational modifications, and protein interactions. Mass spectrometry-based studies have identified changes in proteins related to mitochondrial function, cytoskeletal structure, and cellular signalling in HD. Since proteins are the primary effectors of cellular function, proteomics is vital for understanding disease mechanisms at the functional level.**[24]** Metabolomics focuses on small molecules that reflect the biochemical state of a cell or organism. In HD, metabolomic research has uncovered disturbances in energy, lipid, and neurotransmitter metabolism. These metabolic alterations help explain disease progression and could serve as early diagnostic biomarkers or for monitoring treatment. Integrating these omics layers offers a system-wide view of HD. Combining genomic, transcriptomic, proteomic, and metabolomic data enables the creation of detailed molecular networks that capture the complexity of disease processes. Network-based methods, such as gene co-expression and protein interaction networks, help identify crucial regulatory hubs and pathways that drive HD development. One of the key benefits of multi-omics strategies is their ability to identify biomarkers for early diagnosis and to track disease progression.**[25]** For instance, combining transcriptomic and proteomic data enhances the accuracy of biomarker discovery by cross-validating findings across different biological layers. Likewise, adding metabolomic data can shed light on the biochemical effects of gene and protein changes. However, multi-omics research also faces several hurdles. Data integration is challenging due to disparities in data types, scales, and formats. Technical variability and batch effects may introduce noise and bias into results. Standardising experimental protocols and data processing techniques is crucial for reproducibility and comparability among studies. The high costs and substantial computational demands are additional limitations. Producing and analysing large datasets requires advanced infrastructure and expertise in bioinformatics and computational biology. Still, ongoing technological and methodological improvements are gradually making multi-omics more accessible and efficient. In conclusion, multi-omics approaches offer a robust framework to explore the intricate molecular landscape of HD. By synthesising data from various biological levels, these methods facilitate the discovery of vital pathways, biomarkers, and therapeutic targets. Continued innovation in integrative analysis and collaboration will further enhance the role of multi-omics in HD research.**[26]**

V. AI-Driven Multi-Omics Integration

The use of artificial intelligence (AI) in multi-omics data analysis marks a significant shift in the study of complex diseases such as Huntington's Disease (HD). While individual omics technologies offer insights into specific biological layers, integrating them is crucial to understanding the full complexity of disease mechanisms.**[27]** AI-driven multi-omics integration leverages advanced computational algorithms and high-dimensional biological data to facilitate comprehensive analysis and identify new therapeutic targets. A key challenge in multi-omics research is combining heterogeneous datasets from various platforms that differ in scale, dimensionality, and noise levels, making traditional statistical methods inadequate. AI techniques, especially machine learning and deep learning, are particularly effective at managing this complexity by detecting patterns and relationships across different omics layers to pinpoint important molecular interactions and regulatory networks.**[28]** Different strategies have been developed for AI-based multi-omics integration. Early integration merges data from multiple omics layers into a single dataset before analysis. Intermediate integration analyses each layer separately before combining the results. Late integration involves analysing datasets independently and then integrating findings during interpretation. Each method has its own benefits and limitations, and the choice depends on the research goals and the specifics of the data.**[29]**

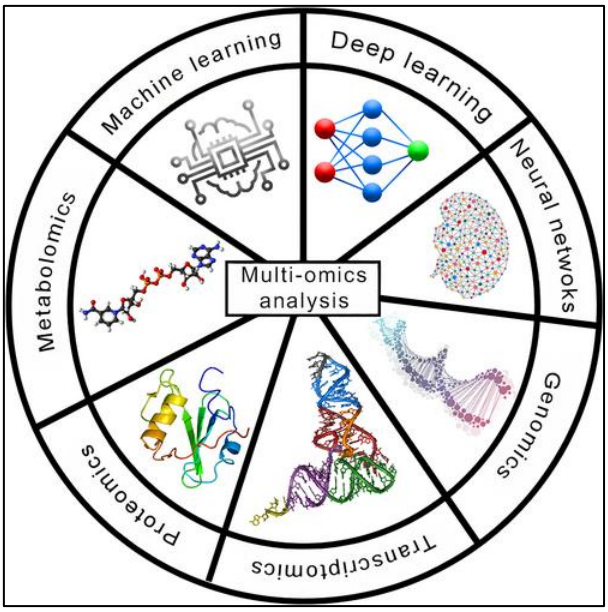

Figure 3: AI-Derived Multi-Omics Approaches in Huntington Disease **[55]**

Deep learning models like autoencoders and graph neural networks (GNNs) have demonstrated significant potential in multi-omics integration. Autoencoders are effective at reducing data dimensionality while maintaining key features, making them suitable for high-dimensional omics data.**[30]** GNNs can model intricate relationships between genes, proteins, and metabolites by representing these elements as interconnected networks. These models facilitate the identification of crucial regulatory nodes and pathways involved in HD development. AI-based multi-omics integration has vital applications in HD research, particularly in identifying disease subtypes. Analysing multi-omics data enables AI models to classify patients into distinct subgroups based on molecular profiles, which is critical for understanding disease heterogeneity and advancing personalised treatment approaches. Another important application is biomarker discovery, where AI models can identify markers predictive of disease onset, progression, and treatment response.**[31]** These biomarkers aid early diagnosis, monitor disease development, and assess treatment effectiveness. Combining multiple omics layers improves the accuracy and robustness of biomarker detection. AI-driven integration is also essential for finding therapeutic targets; analysing multi-omics data helps pinpoint key genes, proteins, and pathways involved in disease mechanisms. These potential targets can then be validated through molecular docking and experimental methods, thereby accelerating drug discovery and increasing the likelihood of finding effective therapies. However, challenges remain for AI-based multi-omics integration. Data quality and availability are major hurdles since large, well-annotated datasets are necessary to train reliable AI models. Furthermore, the complexity of AI models can hinder their interpretability, limiting clinical application.**[32]** Developing explainable AI techniques is vital to address this issue. Another challenge involves integrating multi-omics data with clinical and phenotypic information. Combining molecular and patient data enhances AI models' predictive power and supports personalised medicine, but requires standardised formats and robust data-sharing frameworks. In summary, AI-driven multi-omics integration is a powerful approach to understand HD's complex biology. Merging diverse datasets with advanced computational methods facilitates the discovery of new biomarkers and therapeutic targets. Ongoing advancements in AI and multi-omics are poised to significantly advance HD research and enable personalised treatments and more effective therapies. **[33,34]**

VI. Molecular Docking and Drug Discovery

Molecular docking has become a fundamental method in computational drug discovery, especially for complex neurodegenerative diseases like Huntington's Disease (HD). Given HD's multifactorial nature and the lack of effective disease-modifying treatments, computational strategies offer a rapid, cost-effective means to identify potential therapeutic agents. Molecular docking predicts how a small molecule (ligand) prefers to orient itself when bound to a target protein, enabling estimation of binding strength and interaction stability. In HD, identifying the right target is an essential first step. The mutant huntingtin (mHTT) protein is the main cause of the disease and a key therapeutic target. However, because of its large size and disordered structure, directly targeting mHTT is difficult. As a result, other targets are being investigated, including proteins involved in protein folding (molecular chaperones), oxidative stress, mitochondrial function, and the regulation of autophagy. Enzymes and signalling molecules in these pathways are promising drug targets. **[35]** Molecular docking enables testing of large compound libraries against selected targets. Structure-based drug design (SBDD) relies on high-

resolution protein structures, often from databases such as the Protein Data Bank (PDB). Docking algorithms evaluate different conformations of ligands within the binding site and rank them by the estimated binding energy using scoring functions. Popular docking tools include AutoDock, Glide, and GOLD, each with their own algorithms and scoring methods. Virtual screening extends molecular docking by enabling high-throughput testing of thousands to millions of compounds. It is especially useful for finding new lead compounds and repurposing existing drugs.**[36,37]** In Huntington's disease research, virtual screening helps identify small molecules that can inhibit mHTT aggregation, boost autophagy, or lower oxidative stress. Drug repurposing is beneficial because it uses existing pharmacokinetic and safety data, reducing development time and costs. Molecular dynamics (MD) simulations complement docking by providing insights into how protein–ligand complexes behave over time, showing their stability and dynamics. While docking captures a static view of binding, MD simulations reflect how molecules move under physiological conditions. Metrics such as RMSD, RMSF, and binding free energy (like MM-PBSA) help assess the stability and interaction strength of complexes. **[38]**

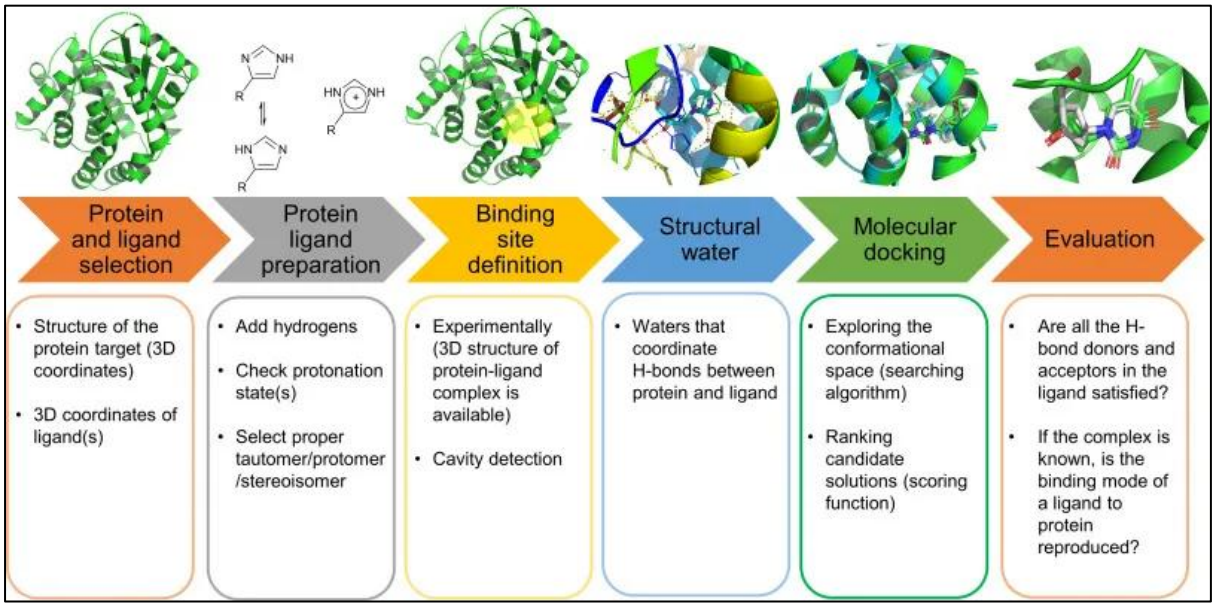

Figure 4: Molecular Docking and Drug Discovery workflow

Another vital element in computational drug discovery is ligand-based methods like QSAR modelling. QSAR links chemical structure to biological activity, helping predict how effective compounds will be and improving lead optimization. When combined with docking, QSAR improves the accuracy of drug candidate selection. Despite its strengths, molecular docking has limits. Its accuracy depends on the quality of protein structures and scoring functions. Docking often assumes proteins are rigid, which may not fully capture their true flexibility. Recent advances in flexible and ensemble docking aim to overcome this issue. In summary, molecular docking and related computational techniques are essential to accelerate drug discovery for HD. They enable quick screening, detailed interaction analysis, and lead optimization. Their power increases when integrated with AI and multi-omics data, opening new possibilities for more precise and effective treatments for Huntington's Disease.**[39]**

VII. Integrated Computational Pipeline

The integration of computational methods into a single pipeline has transformed the way researchers identify therapeutic targets and discover drugs for complex diseases such as Huntington's Disease (HD). This pipeline combines multi-omics data analysis, artificial intelligence (AI), and molecular docking in a systematic workflow, improving efficiency, accuracy, and scalability. The process begins with data collection and preprocessing. Multi-omics data—such as genomics, transcriptomics, proteomics, and metabolomics—are sourced from public repositories like GEO, TCGA, and PDB. These datasets often require normalisation, noise reduction, and batch effect correction to ensure quality and comparability, which is crucial for reliable modelling. After preprocessing, feature selection and dimensionality reduction are performed to identify the most relevant features for disease pathology. Methods like principal component analysis (PCA), t-SNE, and autoencoders help reduce data complexity while retaining essential information. The next phase involves AI-based analysis, where machine learning models trained on the processed data detect patterns, classify disease states, and predict outcomes. Supervised learning handles classification and regression, while unsupervised learning uncovers hidden

structures. Deep learning models, including neural networks and graph-based approaches, are especially effective at capturing complex relationships across multi-omics layers.**[40]**

Figure 5: Integrated Computational Pipeline for Huntington Disease**[56]**

Target identification is a crucial outcome of AI analysis. By combining data from various sources, AI models can pinpoint genes, proteins, and pathways central to HD development. Network analysis techniques, such as protein–protein interaction (PPI) and gene co-expression networks, help identify hub genes and key regulatory nodes. These potential targets are then candidates for further validation and drug discovery. Once potential targets are identified, molecular docking assesses their interaction with candidate compounds. Researchers screen ligand libraries—including natural compounds, synthetic molecules, and approved drugs—against these targets. Researchers evaluate docking results based on binding affinity, interaction energy, and structural fit. The most promising compounds proceed to further analysis.**[41]** Next, molecular dynamics simulations validate docking results and examine the stability of protein–ligand complexes. These simulations provide insights into molecular behaviour and help refine candidate selection. Binding free energy calculations further increase prediction accuracy. The final step involves prioritising and validating candidates. Selected compounds are assessed for pharmacokinetic and pharmacodynamic properties—such as absorption, distribution, metabolism, excretion, and toxicity (ADMET)—using tools like SwissADME and pkCSM. Promising candidates then undergo experimental validation in vitro and in vivo. An integrated computational pipeline has multiple benefits. It enables systematic analysis of complex datasets, minimises trial-and-error, and accelerates drug discovery. It also supports personalised therapeutic strategies by integrating patient-specific data. However, implementing such pipelines requires expertise across bioinformatics, computational biology, and data science. Challenges such as data integration, computational demands, and model interpretability must be addressed to ensure effective use. In summary, integrated computational pipelines are powerful tools for advancing HD research and therapy

development. Combining multi-omics, AI, and molecular docking offers a comprehensive framework for discovering new targets and accelerating drug development.**[42]**

VIII. Recent Advances

In recent years, considerable progress has been made in using computational and experimental methods to study Huntington's Disease (HD). Advances in artificial intelligence (AI), multi-omics technologies, and molecular modelling have collectively deepened our understanding of the disease mechanisms and helped identify new therapeutic strategies. A key breakthrough in HD research is the development of gene-targeting therapies to lower mutant huntingtin (mHTT) protein levels. **[43]**Techniques such as antisense oligonucleotides (ASOs) and RNA interference (RNAi) have shown promising results in both preclinical and clinical trials. These methods specifically target HTT mRNA, reducing the production of toxic mHTT protein. Though challenges like delivery and long-term effectiveness remain, these approaches mark a significant step toward disease-modifying treatments. In AI, deep learning models increasingly analyse complex data and forecast disease progression. For example, convolutional neural networks (CNNs) are used to analyse neuroimaging data, enabling early detection of brain structural changes associated with HD. Similarly, machine learning applied to transcriptomic and proteomic data helps identify biomarkers and therapeutic targets. The adoption of explainable AI techniques has improved the interpretability of these models, encouraging their use in biomedical research. Multi-omics research has shed light on HD's molecular landscape. Recent studies emphasize the importance of DNA repair pathways in controlling CAG repeat expansion, pointing to new therapeutic targets. Furthermore, single-cell RNA sequencing (scRNA-seq) has revealed cell-type-specific changes in gene expression, highlighting the diversity of neuronal and glial cell populations in HD.**[44]** These discoveries enhance our understanding of disease progression and open new paths for targeted therapies. Recent progress in molecular docking and virtual screening has accelerated the identification of potential drug candidates. High-throughput screening of compound libraries has resulted in molecules that can inhibit mHTT aggregation and influence key signaling pathways. Incorporating AI has boosted these efforts by helping prioritize compounds with high therapeutic potential. Another key development is network pharmacology, which examines multi-target drug interactions. Unlike traditional single-target methods, it accounts for the complex interplay among multiple pathways involved in disease development. This approach is especially relevant for HD, given its multifactorial characteristics. By targeting several pathways simultaneously, network pharmacology offers the promise of more effective therapies. Drug repurposing has also become popular as a cost-efficient way to treat HD. Studies have identified existing drugs that may have therapeutic effects by influencing relevant molecular pathways.**[45]** Computational tools, including docking and AI prediction models, have been essential in discovering these candidates. However, challenges still exist. Transforming computational insights into clinical therapies requires extensive testing and trials. Variability among patients and differences in disease progression also make developing universal treatments difficult. In summary, recent advances in AI, multi-omics, and molecular docking have greatly improved our understanding of HD and sped up discovering potential treatments. Continued combining of these approaches, along with progress in validation and clinical research, should drive further breakthroughs and bring us closer to effective therapies for Huntington's Disease.**[46]**

IX. Challenges and Limitations

Despite notable progress in artificial intelligence (AI), multi-omics technologies, and molecular docking techniques, several obstacles limit their effective use in Huntington's Disease (HD) research and therapy development. A major issue is data heterogeneity. Multi-omics data are generated using various platforms such as next-generation sequencing, mass spectrometry, and metabolomics, each with distinct formats, scales, and noise levels. Combining these diverse datasets is inherently difficult and can cause inconsistencies in analysis. Variations in experimental procedures, sample handling, and data preprocessing worsen this, leading to batch effects that hinder reproducibility. **[47]** Another challenge is the limited availability of high-quality, large-scale HD-specific datasets. Despite HD being a well-understood genetic disorder, its low prevalence restricts the number of large patient cohorts, making it hard to train reliable AI models that need extensive data for accuracy and generalization. Small datasets can cause overfitting, where models excel on the training data but perform poorly on new data. Model interpretability is also a significant concern. Many advanced machine learning and deep learning models act as "black boxes," offering predictions without transparent explanations. This opacity reduces biological interpretability and slows clinical adoption. Although explainable AI (XAI) methods exist, their use in HD research is still developing. **[48]** The multifaceted nature of HD pathogenesis, involving pathways like transcriptional dysregulation, mitochondrial dysfunction, and neuroinflammation (MDPI), adds complexity. Modeling these interconnected processes, especially when integrating data across different biological levels, remains challenging. In molecular docking, several limitations remain. Docking algorithms usually depend on static protein structures, which may not accurately reflect the proteins' dynamic conformational changes in vivo. Also, scoring functions that estimate binding affinity may lack precision, leading to false positives or false

negatives. Although molecular dynamics simulations can mitigate some of these issues, they are computationally demanding and time-consuming. Another challenge involves translating computational results into clinical practice. While AI and multi-omics techniques can identify potential therapeutic targets and drug candidates, experimental validation is necessary to verify their safety and effectiveness. This process requires considerable time, resources, and interdisciplinary cooperation. Many promising candidates also fail during clinical trials due to unforeseen toxicity or insufficient efficacy.**[49]** Data integration with clinical and phenotypic information remains limited. Combining molecular data with patient-specific clinical information could improve predictive accuracy and facilitate personalized treatment. However, differences in data formats, lack of standardization, and privacy concerns hinder effective integration. Ethical issues—such as data privacy, consent, and algorithmic bias—must also be considered. AI models trained on biased datasets can produce skewed outcomes, potentially causing disparities in diagnosis and treatment. Moreover, the high computational costs and infrastructure needed for multi-omics analysis and AI modeling can be restrictive. Access is often limited to those with high-performance computing resources and specialized expertise. In conclusion, although AI-driven multi-omics and molecular docking approaches offer significant promise for HD research, overcoming challenges related to data quality, model transparency, validIn molecular docking, several limitations remain. Docking algorithms usually depend on static protein structures, which may not accurately reflect the proteins' dynamic conformational changes in vivo. Also, scoring functions that estimate binding affinity may lack precision, leading to false positives or false negatives. Although molecular dynamics simulations can mitigate some of these issues, they are computationally demanding and time-consuming. Another challenge involves translating computational results into clinical practice. While AI and multi-omics techniques can identify potential therapeutic targets and drug candidates, experimental validation is necessary to verify their safety and effectiveness. This process requires considerable time, resources, and interdisciplinary cooperation. Many promising candidates also fail during clinical trials due to unforeseen toxicity or insufficient efficacy. Data integration with clinical and phenotypic information remains limited. Combining molecular data with patient-specific clinical information could improve predictive accuracy and facilitate personalized treatment. **[50,51]**

X. Future Perspectives

The integration of artificial intelligence (AI), multi-omics technologies, and molecular docking is set to transform research and treatment for Huntington's Disease (HD). Future studies will likely focus on better data integration, increased model accuracy, and smoother clinical application. One promising area is the advancement of single-cell multi-omics technologies. Unlike bulk approaches, single-cell analysis reveals cellular heterogeneity, offering insights into cell-type-specific molecular changes in HD. This is crucial because of the selective vulnerability of certain neuronal populations. Combining single-cell transcriptomics, proteomics, and epigenomics with AI models will allow for more precise identification of disease mechanisms and targets. The development of digital twin models is another exciting area. These computational models simulate individual patients' biological processes using their molecular and clinical data, helping predict disease progression, assess treatment responses, and create personalized therapies. AI-powered digital twins could revolutionize precision medicine in HD. Additionally, progress in explainable AI (XAI) will improve the interpretability of complex models. By clarifying how predictions are made, XAI will boost trust in AI systems and support their use in clinical practice. Enhanced interpretability will also help researchers pinpoint key molecular drivers of HD more effectively. The combination of gene-editing tools like CRISPR-Cas9 with AI-based target discovery holds great promise for therapy development. CRISPR can directly fix genetic mutations or influence gene activity, targeting the fundamental cause of HD. Meanwhile, AI can help pinpoint the best target sites and anticipate possible off-target effects. An important future direction involves integrating various data types, including imaging, clinical, and wearable device data, with multi-omics datasets for a deeper understanding of HD and better predictive models. For example, combining neuroimaging with transcriptomic data can improve early diagnosis and disease tracking. AI and computational modeling are also enhancing drug discovery, with generative AI aiding in designing new compounds alongside molecular docking and simulations to speed up finding effective drugs.**[50]** Drug repurposing remains vital for identifying existing medications that may work for HD. Collaborative efforts and open data sharing will be critical to overcoming current challenges. Standardized datasets and analytical tools will boost reproducibility and large-scale research, while international partnerships can address the issue of small sample sizes. Incorporating patient-specific data into models will enable personalized treatments by tailoring therapies to individual genetic, molecular, and clinical profiles, aiming to improve outcomes and minimize side effects. In summary, advances in AI-driven multi-omics and molecular modeling are poised to deepen our understanding of HD and hasten therapeutic development. Ongoing innovation, cross-disciplinary teamwork, and clinical testing are key to turning this scientific progress into real-world benefits.**[51]**

XI. Conclusion

Huntington's Disease remains a challenging neurodegenerative disorder because of its complex molecular mechanisms and the absence of effective treatments. In the past decade, substantial progress has been made in understanding its genetic and molecular basis. However, turning this knowledge into practical therapies has been difficult. The rise of artificial intelligence (AI) and multi-omics technologies offers new opportunities to tackle these issues. AI enables the analysis of large, complex datasets, helping identify disease biomarkers, molecular pathways, and potential treatment targets. Multi-omics approaches—such as genomics, transcriptomics, proteomics, and metabolomics—provide a detailed view of HD's molecular landscape, uncovering insights inaccessible through single-omics studies. Combining AI with multi-omics data creates a powerful strategy for revealing the complex interactions underlying HD development. These integrated methods help identify key regulatory networks and hub genes vital for disease progression. AI-based models can also predict disease progression and classify patients based on their molecular profiles, aiding precision medicine efforts. Additionally, molecular docking and computational drug discovery techniques support these strategies by validating targets and screening new therapeutic compounds. These methods predict protein–ligand interactions and binding strengths, accelerating drug discovery and reducing reliance on trial and error. When combined with AI-driven target identification, these approaches improve the speed and accuracy of developing new treatments. Recent advancements in AI, multi-omics, and molecular modeling have greatly expanded our understanding of HD and opened new possibilities for treatment. For instance, AI-based transcriptomic analysis has uncovered new druggable targets, while multi-omics research has shown how DNA repair pathways influence disease progression (MDPI). These discoveries demonstrate the value of computational methods in tackling the complexity of HD. However, challenges remain, such as data heterogeneity, limited dataset availability, and the need for experimental validation. Overcoming these will require ongoing innovation, interdisciplinary teamwork, and standardized protocols. In the future, integrating emerging technologies like single-cell omics, explainable AI, and gene editing is expected to boost the role of computational methods in HD research. These innovations will allow for more accurate targeting and support personalized therapies. In summary, combining AI, multi-omics, and molecular docking offers a transformative approach to understanding and treating Huntington's Disease. Despite existing challenges, progress in these areas provides hope for developing effective therapies that can enhance patients' quality of life.

Abbreviations

HD – Huntington's Disease
AI – Artificial Intelligence
ML – Machine Learning
DL – Deep Learning
mHTT – Mutant Huntingtin
GWAS – Genome-Wide Association Study
RNA-seq – RNA Sequencing
PPI – Protein–Protein Interaction
MD – Molecular Dynamics
QSAR – Quantitative Structure–Activity Relationship
XAI – Explainable Artificial Intelligence
ROS – Reactive Oxygen Species
UPS – Ubiquitin–Proteasome System
ADMET – Absorption, Distribution, Metabolism, Excretion, Toxicity
CNS – Central Nervous System

Reference

[1]. Barker, R. A., & Priller, J. (2013). Huntington's Disease. Oxford University Press EBooks. https://doi.org/10.1093/med/9780199609536.003.0020
[2]. Bates, G. P., Dorsey, R., Gusella, J. F., Hayden, M. R., Kay, C., Leavitt, B. R., ... & Tabrizi, S. J. (2015). Huntington disease. *Nature Reviews Disease Primers, 1*, 15005. https://doi.org/10.1038/nrdp.2015.5
[3]. Peng, Q., Wu, B., Jiang, M., Jin, J., Hou, Z., Zheng, J., Zhang, J., & Duan, W. (2016). Characterization of Behavioral, Neuropathological, Brain Metabolic and Key Molecular Changes in zQ175 Knock-In Mouse Model of Huntington's Disease. PLoS One, 11(2), e0148839.
[4]. Ross, C. A., & Tabrizi, S. J. (2019). Huntington's disease: From molecular pathogenesis to clinical treatment. *The Lancet Neurology, 18*(1), 83–98. https://doi.org/10.1016/S1474-4422(18)30475-3
[5]. Tabrizi, S. J., Ghosh, R., & Leavitt, B. R. (2019). Huntingtin lowering strategies for disease modification in Huntington's disease. *Neuron, 101*(5), 801–819. https://doi.org/10.1016/j.neuron.2019.01.039
[6]. Wild, E. J., & Tabrizi, S. J. (2020). Therapies targeting DNA and RNA in Huntington's disease. *The Lancet Neurology, 19*(10), 837–847. https://doi.org/10.1016/S1474-4422(20)30280-6
[7]. Sukhwal, P. C., Cui, W., & Kankanhalli, A. (2023). Knowledge Transfer between Humans and Conversational Agents: A Review, Organizing Framework, and Future Directions. https://core.ac.uk/download/552657936.pdf

[8]. Bhimavarapu, U. (2025). Artificial Intelligence and the 2024 US Presidential Election. IGI Global EBooks. https://doi.org/10.4018/979-8-3693-8749-8.ch005

[9]. Dorsey, E. R., et al. (2020). Emerging therapies for Huntington disease. *Nature Reviews Neurology, 16*(6), 347–361. https://doi.org/10.1038/s41582-020-0362-0

[10]. Di Pardo, A., Amico, E., Scalabri, F., Pepe, G., & Maglione, V. (2020). Mitochondrial dysfunction in Huntington's disease. *Cells, 9*(12), 2631. https://doi.org/10.3390/cells9122631

[11]. Chanda, P. (2025). Optimization Techniques in Smart Grids: A Review of Machine Learning and Artificial Intelligence Approaches. IISE Annual Conference. Proceedings, (), 1-6.

[12]. Zhu, X., Lyu, C., Ji, D., Liao, H., & Li, F. (2020). Deep neural model with self-training for scientific keyphrase extraction. PLoS One, 15(5), e0232547.

[13]. Teletin, M., Czibula, G., Albert, S. I., & Bocicor, M. I. (2018). Using unsupervised learning methods for enhancing protein structure insight. Procedia Computer Science. https://doi.org/10.1016/j.procs.2018.07.205

[14]. Agrafiotis, D., Yang, E., Littman, G., Byttebier, G., Dipietro, L., DiBernardo, A., Chavez, J., Rykman, A., McArthur, K., Hajjar, K., Lees, K., Volpe, B., Krams, M., & Krebs, H. (2021). Accurate prediction of clinical stroke scales and improved biomarkers of motor impairment from robotic measurements. PLoS One, 16(1), e0245874.

[15]. Nasseri, M., Brandtner, P., Brandtner, P., & Darbanian, F. (2023). Applying Machine Learning in Retail Demand Prediction—A Comparison of Tree-Based Ensembles and Long Short-Term Memory-Based Deep Learning. Applied Sciences, 13(19), 11112.

[16]. Joshi, S. (2025). Comprehensive Review of Gen Agentic AI in Marketing: Tools, Theories and Applications. International Journa1 of Innovative Research in Engineering & Management. https://doi.org/10.55524/ijirem.2025.12.5.1

[17]. Tella, A., Osunkeye, O. J., Dandara, G. B., & Agbetuyi, O. A. (2025). Immunogenomics for disease resistance in farm animals: A review. https://doi.org/10.21303/2504-5695.2025.003725

[18]. Du, Y., & Mohan, J. (2026). Applications of AI for the Optimal Operations of Power Systems Under Extreme Weather Events: A Task-Driven and Methodological Review. Energies, 19(2), 506.

[19]. Juan, C., & Peng, Y. (2025). The Molecular Landscape and Utility of Multiomic Analyses in Triple Negative Breast Cancer: Further Subtyping and Exploring Novel Biomarkers and Therapeutic Targets. https://doi.org/10.20944/preprints202510.0714.v1

[20]. (2023). Drug Discovery in the 21st Century. Toxicology and Applied Pharmacology Insights. https://doi.org/10.33140/tapi.06.01.09

[21]. Hammad, M., Hammad, M., Pławiak, P., Pławiak, P., ElAffendi, M., Abd El-Latif, A., & Abdel Latif, A. (2023). Enhanced Deep Learning Approach for Accurate Eczema and Psoriasis Skin Detection. Sensors, 23(16), 7295.

[22]. Wali, A., Ali, S., Naseer, A., Karim, S., & Alamgir, Z. (2023). Computer-aided COVID-19 diagnosis: A possibility? Journal of Experimental and Theoretical Artificial Intelligence. https://doi.org/10.1080/0952813x.2023.2165722

[23]. Bandbe, T., Johri, V., Kumari, U. (2025). Structure-guided Genome-wide Association Analysis of ALK Variants with GWAS Data Using R. *Computational Biology and Bioinformatics*, *13*(2), 72-85. https://doi.org/10.11648/j.cbb.20251302.13

[24]. Johri, V., & Kumari, U. (2026). Sustainable neuroprotection via proteomics and integrative NGS-CADD analysis of 6CVP variant to improve future neurodegenerative health outcomes. IOSR Journal of Pharmacy and Biological Sciences, 21(3), 1–10. https://doi.org/10.9790/3008-2103010110, IOSR Journals

[25]. Vineeta Johri, Uma Kumari, 2025, NGS-Based Polyglutamine Expansion Pattern Detection Using Machine Learning Models to Predict the Conformation States of Huntingtin, IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS) e-ISSN:2278-3008, p-ISSN:2319-7676. Volume 20, Issue 5, Ser. 3 (Sept. – Oct. 2025), pp. 19- 27, DOI: 10.9790/ 3008-2005031927

[26]. Kumari, U., Gunjan, & Basak, S. (2023). NGS contribution in genetic diagnosis for brain disorder. Journal of Clinical Otorhinolaryngology, Head, and Neck Surgery, 27(1), 5525–5536

[27]. Kumari, U., Mukherjee, S., Pradhan, M., & Chakrabarti, S. (2023). NGS analysis approach for neurodegenerative disease with Biopython. Journal of Emerging Technologies and Innovative Research, 10(9), 1–? . https://doi.org/10.1729/Journal.36043

[28]. Kumari, U., & Pacholee, K. (2023). In-silico drug discovery-based approach to treat impairments in patients of Alzheimer's disease. Journal of Emerging Technologies and Innovative Research, 10(12), B236–B245. https://doi.org/10.1729/Journal.37001

[29]. Kumari, U., Gunjan, & Basak, S. (2023). NGS contribution in genetic diagnosis for brain disorder. Journal of Clinical Otorhinolaryngology, Head, and Neck Surgery, 27(1), 5525–5536

[30]. Nagpal, G., & Kumari, U. (2025). Next generation sequence analysis of amyloid precursor-like protein 2 (APLP2) E2 domain in Alzheimer's disease. Journal of Emerging Technologies and Innovative Research, 12(1), ppd72–ppd79.

[31]. Uniyal, U., & Kumari, U. (2025). Next generation sequencing data analysis of A25T transthyretin structure associated with Parkinson's disease. Journal of Emerging Technologies and Innovative Research, 12(3), B612–B622. https://doi.org/10.1729/Journal.44079

[32]. Kokad, M., & Kumari, U. (2025). Next-generation sequencing data analysis in DYRK1A associated with neurodegenerative disease. IOSR Journal of Biotechnology and Biochemistry, 11(6), 40–48. https://doi.org/10.9790/264X-1106014048, IOSR Journals

[33]. Mehrotra, K., Kumari, U., & Pande, S. (2025).Integrative workflow of Biopython and molecular docking to explore novel therapeutics targeting PARK7-DJ1. IOSR Journal of Biotechnology and Biochemistry, 11(6), 1–10. https://doi.org/10.9790/264X-1106010110, IOSR Journals

[34]. Singh, N., & Kumari, U. (2026). Multi-omics-based drug discovery pipelines incorporating machine learning, AI, and BioPython in Parkinson's disease: A case study of 5A polymorph of alpha-synuclein. Journal of Emerging Technologies and Innovative Research, 13(2). https://doi.org/10.56975/jetir.v13i2.575492, Science Publishing Group

[35]. Mandra, D., Kumari, U., Singh, N., & Marouthu, A. (2026). Integrated multi-omics and Biopython approaches for target identification of α-synuclein polymorph in Parkinson's disease. IOSR Journal of Biotechnology and Biochemistry, 12(2), 12–21. , IOSR Journals

[36]. Singh, N., Kumari, U., Mandra, D., & Marouthu, A. (2026). Integrated machine learning-based toxicity prediction with molecular docking for safer drug candidate screening in Parkinson's disease. Computational Biology and Bioinformatics, 14(1), 41–53. https://doi.org/10.11648/j.cbb.20261401.14

[37]. Johri V, Ramakrishnan S, Tripathi A, Kumari U, Jayaraman A. Structural Insights into the Interaction of TAP01 Antibody with Amyloid Beta Peptide (Aβ pE3-14) for Alzheimer's Disease Therapeutics. Int J Drug Deliv Technol. 2026;16(50s): 1007-1017. DOI: 10.25258/ijddt.16.50s.105

[38]. Uma Kumari, Vineeta Johri, Tijil Jha, Swarali Dhopate (2024). Structure-Based Drug Designing for the prediction of epitope for targeting Malignant brain Tumor, Journal of Emerging Technologies and Innovative Research (JETIR)

[39]. Perino, A., & Schoonjans, K. (2015). TGR5 and Immunometabolism: Insights from Physiology and Pharmacology. Trends in Pharmacological Sciences. https://doi.org/10.1016/j.tips.2015.08.002

[40]. Araldi, R. P., et al. (2025). Artificial intelligence-enhanced transcriptomic analysis in Huntington's disease. *Brain Sciences, 15*(8), 865. https://doi.org/10.3390/brainsci15080865

[41]. Li, T., et al. (2025). Multi-omics integration using machine learning: Applications in disease research. *Frontiers in Immunology, 16*, 1561544. https://doi.org/10.3389/fimmu.2025.1561544

[42]. Yildirim, Z., et al. (2025). Artificial intelligence in drug discovery. *Annual Review of Pharmacology and Toxicology, 65*, 123–145. https://doi.org/10.1146/annurev-pharmtox-022724-095035
[43]. Alam, P., et al. (2026). Multi-omics approaches in neurodegenerative diseases. *Trends in Biotechnology*. https://doi.org/10.1016/j.tibtech.2026.01.005
[44]. Paulsen, J. S. (2019). Cognitive impairment in Huntington disease: Diagnosis and treatment. *The Lancet Neurology, 18*(1), 19–21. https://doi.org/10.1016/S1474-4422(18)30394-2
[45]. Mestre, T. A., et al. (2021). Clinical management of Huntington's disease. *Movement Disorders, 36*(5), 1037–1050. https://doi.org/10.1002/mds.28449
[46]. Tabrizi, S. J., et al. (2022). A biological classification of Huntington's disease. *The Lancet Neurology, 21*(7), 632–644. https://doi.org/10.1016/S1474-4422(22)00120-X
[47]. McColgan, P., & Tabrizi, S. J. (2018). Huntington's disease biomarkers. *The Lancet Neurology, 17*(7), 684–695. https://doi.org/10.1016/S1474-4422(18)30159-6
[48]. Jimenez-Sanchez, M., Licitra, F., Underwood, B. R., & Rubinsztein, D. C. (2017). Huntington's disease: Mechanisms of pathogenesis and therapeutic strategies. *Nature Reviews Neuroscience, 18*(6), 341–357. https://doi.org/10.1038/nrn.2017.48
[49]. Saudou, F., & Humbert, S. (2016). The biology of huntingtin. *Neuron, 89*(5), 910–926. https://doi.org/10.1016/j.neuron.2016.02.003
[50]. Hensman Moss, D. J., et al. (2017). Genetic modifiers of Huntington's disease. *Lancet Neurology, 16*(10), 837–847. https://doi.org/10.1016/S1474-4422(17)30275-5
[51]. Keum, J. W., et al. (2016). CAG repeat instability in Huntington's disease. *Nature Genetics, 48*(4), 407–411. https://doi.org/10.1038/ng.3513
[52]. Evers, M. M., et al. (2018). Gene therapy for Huntington's disease. *Molecular Therapy, 26*(9), 2139–2150. https://doi.org/10.1016/j.ymthe.2018.06.008
[53]. Schobel, S. A., et al. (2017). Imaging biomarkers in Huntington disease. *Neuron, 95*(4), 678–692. https://doi.org/10.1016/j.neuron.2017.07.016
[54]. McColgan, P. and Tabrizi, S.J. (2018), Huntington's disease: a clinical review. Eur J Neurol, 25: 24-34. https://doi.org/10.1111/ene.13413
[55]. Yetgin A. *Revolutionizing multi-omics analysis with artificial intelligence and data processing*. *Quantitative Biology*. 2025;e70002. https://doi.org/10.1002/qub2.70002
[56]. Johri, V., & Kumari, U. (2025). NGS-based polyglutamine expansion pattern detection using machine learning models to predict the conformation states of huntingtin. IOSR Journal of Pharmacy and Biological Sciences, 20(5, Ser. 3), 19–27,https://doi.org/10.9790/3008-2005031927