Review Journal of Neurological & Medical Sciences Review
Website: rjnmsr.com

Volume 01 Issue 01
(2023)

Emerging Biomarkers for Early Detection of NeurodegenerativeDiseases: A Comprehensive Review

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Abstract:

Neurodegenerative diseases pose a significant challenge to healthcare systems worldwide due to their progressive nature and lack of effective treatments. Early detection of these diseases is crucial for timely intervention and management. This paper explores the landscape of emerging biomarkers for the early detection of neurodegenerative diseases, including Alzheimer's disease, Parkinson's disease, Huntington's disease, and amyotrophic lateral sclerosis (ALS). By examining recentresearch findings, this review discusses promising biomarkers from various sources such as cerebrospinal fluid, blood, neuroimaging, and genetic markers. Understanding these biomarkers' potential could revolutionize early diagnosis, enhance patient care, andfacilitate the development of targeted therapies.

Keywords: Biomarkers, Neurodegenerative Diseases, Early Detection, Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Amyotrophic Lateral Sclerosis.

Introduction:

Neurodegenerative diseases encompass a group of disorders characterized by the progressive degeneration of neurons, resulting in cognitive decline, motor dysfunction, and ultimately, disability. Alzheimer's disease (AD), Parkinson's disease (PD), Huntington's disease (HD), and amyotrophic lateral sclerosis (ALS) are among the most prevalent neurodegenerative conditions, posing substantial burdens on patients, caregivers, and healthcare systems globally. Despite extensive research efforts, effective treatments for these diseases remain elusive. One of the critical challenges in managing neurodegenerative diseases is their late-stage diagnosis, often when irreversible neuronal damage has already occurred. Early detection of these diseases is crucial for implementing timely interventions, initiating appropriate treatments, and potentially altering disease progression trajectories. Emerging biomarkers offer promising avenues for early diagnosis, enabling clinicians to identify individuals at risk or in the prodromal stages of neurodegeneration. This paper explores recent advances in identifying biomarkers for the early detection of neurodegenerative diseases, aiming to provide insights into their diagnostic potentialand implications for clinical practice.

Biomarkers for Alzheimer's Disease

Biomarkers for Alzheimer's Disease play a pivotal role in the early detection and diagnosis of this progressive neurodegenerative condition. These biomarkers encompass a range ofphysiological indicators, including changes in cerebrospinal fluid composition, neuroimaging findings, and genetic markers. One crucial biomarker is the presence of amyloid-beta plaques and tau tangles in the brain, which are hallmark pathological features of Alzheimer's. Advanced neuroimaging techniques like positron emission tomography (PET) scans can detect these abnormalities, aiding in early diagnosis and potentially predicting disease progression.

Biomarkers related to cerebrospinal fluid provide valuable insights into Alzheimer's pathology. Elevated levels of tau protein or reduced levels of amyloid-beta42 in cerebrospinal fluid are indicative of Alzheimer's disease. This information, combined with clinical assessments, can enhance diagnostic accuracy and inform treatment decisions. Additionally, genetic biomarkers such as the apolipoprotein E (APOE) gene variant, particularly APOE ε4 allele, are associated with an increased risk of developing Alzheimer's disease. Genetic testing for APOE status can help identify individuals at higher risk and facilitate personalized healthcare strategies, including early intervention and lifestyle modifications.

Emerging research is exploring blood-based biomarkers as less invasive and more accessible alternatives for Alzheimer's diagnosis. Blood tests targeting specific proteins or genetic markers associated with Alzheimer's pathology show promising potential for early detection and monitoring of the disease. These blood-based biomarkers offer the possibility of widespread screening and routine monitoring, revolutionizing Alzheimer's diagnosis and management. As research continues to advance, the integration of multiple biomarkers from various modalities holds the key to improving early detection, understanding disease progression, and developing targeted therapies for Alzheimer's disease.

Cerebrospinal Fluid Biomarkers

Cerebrospinal fluid (CSF) biomarkers have emerged as vital tools in diagnosing and understanding various neurological disorders. These biomarkers, found in the clear, colorless fluid surrounding the brain and spinal cord, offer valuable insights into the biochemical processes occurring within the central nervous system. One significant application lies in the realm of neurodegenerative diseases such as Alzheimer's and Parkinson's. Biomarkers like amyloid-beta and tau proteins in CSF can provide early indications of these conditions, aiding in early diagnosis and potentially enabling interventions to slow disease progression.

CSF biomarkers play a crucial role in monitoring disease progression and treatment efficacy. In conditions like multiple sclerosis (MS), where inflammation and demyelination characterize the disease, markers such as oligoclonal bands and myelin basic protein levels in CSF serve as indicators of disease activity. Monitoring changes in these biomarkers over time allows clinicians to adjust treatment strategies accordingly, optimizing patient care and improvingoutcomes.

The exploration of CSF biomarkers extends beyond traditional neurological disorders into emerging fields such as traumatic brain injury (TBI) and psychiatric illnesses. In TBI, biomarkers like S100B protein and glial fibrillary acidic protein (GFAP) in CSF provide valuable information about the severity of injury and predict outcomes. Similarly, in psychiatric disorders like schizophrenia and bipolar disorder, researchers are investigating CSF biomarkers to elucidate underlying pathophysiological mechanisms and identify potential therapeutic targets.As research in this field continues to advance, CSF biomarkers hold promise not only in diagnosis and monitoring but also in guiding personalized treatment approaches for a wide range of neurological and psychiatric conditions.

Blood-Based Biomarkers

Blood-based biomarkers, the molecular signatures circulating in our bloodstream, have emerged as invaluable tools in modern medicine. These biomarkers offer a window into our health, providing insights into various physiological processes and the presence of diseases. One significant advantage lies in their non-invasive nature, making blood tests a routine and accessible method for diagnosis, prognosis, and monitoring of diseases. From cancer to cardiovascular conditions, researchers are continually discovering new biomarkers that hold promise for early detection and personalized treatment strategies.

In the realm of neurology, blood-based biomarkers hold particular promise for revolutionizingthe diagnosis and management of neurological disorders. Conditions like Alzheimer's disease, Parkinson's disease, and multiple sclerosis often present challenges in early diagnosis due to the absence of definitive diagnostic tests. However, blood-based biomarkers offer a potential solution, enabling clinicians to detect these conditions in their earliest stages when interventions may be most effective. By analyzing specific proteins, genetic markers, or even circulating cells in the blood, researchers are uncovering novel ways to predict disease onset, track disease progression, and assess treatment responses.

The utility of blood-based biomarkers extends beyond diagnostics and prognostics; they alsoplay a crucial role in advancing precision medicine. By identifying biomarkers associated with drug responses or treatment resistance, physicians can tailor therapies to individual patients, maximizing efficacy while minimizing adverse effects. This personalized approach not only enhances patient outcomes but also contributes to the optimization of healthcare resources. As research in this field continues to expand, blood-based biomarkers hold the promise of transforming healthcare delivery, ushering in an era of more precise, proactive, and patient- centric medicine.

Neuroimaging Biomarkers

Neuroimaging biomarkers have emerged as powerful tools in understanding the structure, function, and connectivity of the brain. By leveraging techniques such as MRI, PET, and EEG, researchers can non-invasively visualize and quantify various aspects of brain activity andanatomy. These biomarkers serve as invaluable indicators of neurological health and disease, aiding in early diagnosis, treatment monitoring, and the development of novel therapies. From identifying structural abnormalities in conditions like Alzheimer's disease to mapping functional connectivity in psychiatric disorders, neuroimaging biomarkers provide crucial insights into the intricate workings of the human brain.

Neuroimaging biomarkers play a pivotal role in personalized medicine, facilitating targeted interventions tailored to individual patients. By characterizing neurobiological signatures unique to each person, clinicians can devise more effective treatment strategies with fewer adverse effects. For instance, in neurodegenerative diseases like Parkinson's, neuroimaging biomarkers help distinguish between different subtypes of the disease, enabling personalized approaches for optimal management. This precision medicine approach holds promise not only in neurology butalso in fields like psychiatry, where identifying biomarkers can aid in predicting treatment response and guiding therapeutic decisions.

Neuroimaging biomarkers are driving advancements in neuroscience research, unlocking new insights into brain development, aging, and plasticity. Through longitudinal studies and large- scale imaging datasets, scientists can unravel the complexities of neurodevelopmental disorders, track the progression of neurodegeneration, and investigate the neural mechanisms underlying cognitive functions. By integrating neuroimaging with other 'omics' technologies and computational modeling, researchers can construct comprehensive frameworks of brain function and dysfunction, paving the way for transformative discoveries in both basic science and clinical practice. In essence, neuroimaging biomarkers are not just diagnostic tools; they are catalysts for innovation, shaping the future of neuroscience and personalized medicine.

Genetic Biomarkers

Genetic biomarkers are distinctive genetic traits or variations that can be used to indicate a particular biological condition or disease susceptibility within an individual. These biomarkers are encoded in an individual's DNA and can offer valuable insights into their health profile. By analyzing genetic biomarkers, researchers and healthcare professionals can identify genetic predispositions to certain diseases, assess disease progression, and even tailor personalizedtreatment strategies. For instance, certain genetic biomarkers are associated with an increasedrisk of developing conditions like cancer, cardiovascular diseases, or neurological disorders. One of the significant advantages of genetic biomarkers lies in their potential for early detection and prevention of diseases. Through genetic testing, individuals can uncover their unique geneticmakeup and assess their risk factors for various health conditions. This proactive approach enables early intervention strategies, such as lifestyle modifications or targeted screenings, to mitigate the risk of disease development or progression. Moreover, genetic biomarkers empower healthcare providers to deliver more precise and personalized medical care, optimizing treatment outcomes and patient well-being.

In addition to their clinical applications, genetic biomarkers play a crucial role in advancing biomedical research and drug development. By identifying genetic variations associated with specific diseases or drug responses, researchers can better understand the underlying mechanismsof diseases and develop more targeted therapies. This precision medicine approach holds promise for revolutionizing healthcare by ushering in an era of tailored treatments that maximize efficacy while minimizing adverse effects. However, ethical considerations surrounding genetic privacy, informed consent, and equitable access to genetic testing and therapies remain importantaspects to address as the field continues to evolve.

Biomarkers for Parkinson's Disease

Biomarkers for Parkinson's Disease have emerged as crucial tools for early detection, accurate diagnosis, and monitoring disease progression. These biomarkers encompass a diverse range of biological indicators, including genetic, biochemical, and imaging-based markers. Genetic biomarkers, such as mutations in genes like SNCA, LRRK2, and GBA, offer insights into the underlying genetic predisposition to Parkinson's. Biochemical markers, like alpha-synucleinlevels in cerebrospinal fluid or blood plasma, provide valuable information about the pathological processes occurring in the brain. Advanced neuroimaging techniques, such as MRI, PET, and SPECT scans, enable the visualization of structural and functional changes in the brain associated with Parkinson's disease.

The development and validation of reliable biomarkers hold the promise of revolutionizing the diagnosis and management of Parkinson's Disease. By enabling early detection before the onset of motor symptoms, biomarkers offer the potential for intervention at a stage when treatments may be most effective in slowing or halting disease progression. Moreover, biomarkers can aidin patient stratification for clinical trials, facilitating the identification of individuals who are most likely to benefit from specific therapies. Additionally, biomarkers can serve as objective measures of treatment response, allowing for the timely adjustment of therapeutic interventions to optimize patient outcomes.

Despite significant advancements, challenges remain in the quest for robust biomarkers for Parkinson's Disease. Standardization of protocols for sample collection, processing, and analysis is essential to ensure the reproducibility and reliability of biomarker measurements across different research studies and clinical settings. Furthermore, the heterogeneity of Parkinson's Disease poses a challenge, as biomarkers must be sensitive to the various clinical subtypes and stages of the disease. Collaborative efforts between researchers, clinicians, industry partners, and regulatory agencies are critical to overcoming these challenges and advancing the field ofParkinson's biomarker research towards its full potential.

Alpha-Synuclein Biomarkers

Alpha-synuclein biomarkers hold immense promise in the diagnosis and management of neurodegenerative disorders, particularly Parkinson's disease (PD). These biomarkers, which include both peripheral and central markers, offer a window into the underlying pathological processes of these diseases. In cerebrospinal fluid (CSF), alpha-synuclein levels have shown correlations with disease severity and progression, making them valuable indicators for tracking the neurodegenerative process. Additionally, recent advancements in imaging techniques have enabled the visualization of alpha-synuclein aggregates in the brain, providing clinicians with a non-invasive tool for early detection and monitoring of PD.

Blood-based alpha-synuclein biomarkers have garnered attention for their potential inrevolutionizing disease diagnosis and monitoring. The accessibility of blood samples comparedto CSF makes them attractive candidates for routine clinical use. Studies have revealed alterations in peripheral alpha-synuclein levels in PD patients compared to healthy controls, suggesting their utility as diagnostic biomarkers. Furthermore, the identification of specific alpha-synuclein isoforms or post-translational modifications in blood samples holds promise for improving diagnostic accuracy and predicting disease progression.

In the quest for effective treatments for neurodegenerative diseases, alpha-synuclein biomarkers also play a crucial role in clinical trials. They serve as objective measures of target engagement and treatment response, aiding in the evaluation of therapeutic efficacy. Additionally, the development of novel therapies targeting alpha-synuclein pathology underscores the importance of reliable biomarkers in patient stratification and monitoring treatment outcomes. As research continues to unravel the complexities of alpha-synuclein biology, the integration of biomarker- based approaches into clinical practice holds great potential for improving patient care and advancing the field of neurodegenerative disease management.

Dopaminergic Imaging Biomarkers

Dopaminergic imaging biomarkers have revolutionized our understanding and management of various neurological and psychiatric disorders. By utilizing advanced imaging techniques such aspositron emission tomography (PET) and single-photon emission computed tomography (SPECT), researchers can visualize and quantify dopamine activity in the brain. These biomarkers provide crucial insights into conditions like Parkinson's disease, where dopaminergic neuron degeneration is a hallmark feature. By assessing dopamine levels and activity, clinicians can tailor treatment strategies more effectively, optimizing medication dosages and timing to alleviate symptoms and improve patients' quality of life.

Dopaminergic imaging biomarkers play a pivotal role in the early detection and diagnosis of neurodegenerative diseases. In conditions such as Parkinson's disease, dopaminergic neuron loss begins years before noticeable symptoms emerge. Utilizing these biomarkers allows for the identification of individuals at high risk of developing the disease, enabling early intervention and potentially slowing disease progression. Additionally, these imaging techniques aid in differential diagnosis, distinguishing Parkinsonian syndromes from other movement disorders with similar clinical presentations, ensuring patients receive appropriate and timely management.

Dopaminergic imaging biomarkers hold promise for monitoring disease progression and assessing the efficacy of therapeutic interventions. By tracking changes in dopamine levels and neuronal activity over time, clinicians can evaluate the effectiveness of medications, deep brain stimulation, and other treatment modalities. This objective assessment enables adjustments to treatment plans as needed, optimizing patient outcomes and minimizing adverse effects. Additionally, these biomarkers serve as valuable tools in research endeavors, facilitating the development of novel therapies aimed at modulating dopamine function and potentially halting the progression of neurodegenerative disorders.

Peripheral Biomarkers

Peripheral biomarkers are measurable substances found outside of the central nervous system, such as blood, urine, or saliva, that can provide valuable insights into various physiological and pathological processes occurring within the body. These biomarkers serve as indicators or signatures of specific conditions or diseases, offering clinicians a non-invasive means of diagnosis, prognosis, and monitoring of treatment effectiveness. For instance, in the field of neurology, researchers are exploring the potential of peripheral biomarkers, such as certain proteins or genetic markers, to aid in the early detection of neurodegenerative diseases like Alzheimer's or Parkinson's. By analyzing changes in these biomarkers over time, clinicians may be able to identify disease progression or response to therapeutic interventions, enabling more personalized and timely patient care.

The study of peripheral biomarkers extends beyond neurology, encompassing a wide range of medical specialties including oncology, cardiology, and immunology. In cancer research, for example, specific proteins or genetic mutations detected in the blood can provide crucial information about tumor growth, metastasis, and response to chemotherapy. Similarly, in cardiology, biomarkers like cardiac troponins are routinely used to diagnose acute myocardial infarction and assess the extent of cardiac damage. By leveraging these peripheral biomarkers, clinicians can make more informed decisions regarding patient management, leading to improved outcomes and quality of life.

However, despite their potential utility, the identification and validation of reliable peripheral biomarkers remain a significant challenge in biomedical research. Factors such as variability in sample collection, assay techniques, and patient characteristics can introduce noise and confounding factors, hindering the translation of biomarker discovery into clinical practice. Addressing these challenges requires interdisciplinary collaboration between clinicians, researchers, and industry partners, along with advancements in technology and data analytics. Asour understanding of disease mechanisms continues to evolve, so too will the role of peripheral biomarkers in transforming the landscape of healthcare, offering new opportunities for early intervention and personalized medicine.

Genetic Biomarkers

Genetic biomarkers are pivotal tools in the realm of personalized medicine, offering insights into an individual's genetic makeup and predispositions to certain diseases or conditions. By analyzing an individual's DNA, scientists can identify specific genetic variations associated with diseases such as cancer, cardiovascular disorders, and neurological conditions. These biomarkersnot only aid in early detection but also enable healthcare professionals to tailor treatments based on a patient's genetic profile, maximizing therapeutic efficacy while minimizing adverse effects. Moreover, genetic biomarkers play a crucial role in identifying individuals who may benefit most from preventive interventions, allowing for proactive measures to mitigate disease risks before symptoms manifest.

Genetic biomarkers hold immense promise in revolutionizing drug development and precision therapeutics. Through pharmacogenomics, researchers can uncover how an individual's genetic makeup influences their response to medications, elucidating factors such as drug metabolism, efficacy, and potential adverse reactions. This personalized approach to pharmacotherapy enables clinicians to prescribe medications that are most likely to be effective for a particular patient, optimizing treatment outcomes and reducing the likelihood of adverse drug reactions. Moreover, genetic biomarkers facilitate the identification of therapeutic targets, paving the way for the development of novel drugs tailored to specific genetic profiles, thereby ushering in anera of precision medicine with targeted therapies.

In addition to their clinical applications, genetic biomarkers are instrumental in advancing our understanding of disease mechanisms and unraveling the complexities of human biology. By studying the genetic signatures associated with various diseases, researchers can gain insightsinto underlying molecular pathways and identify novel targets for therapeutic intervention.Furthermore, genetic biomarkers play a crucial role in elucidating the genetic basis of complex diseases, shedding light on the interplay between genetics, environment, and lifestyle factors in disease susceptibility. This deeper understanding not only informs clinical decision-making but also drives innovation in biomedical research, fueling discoveries that hold the potential to transform healthcare and improve patient outcomes.

Biomarkers for Huntington's Disease

Biomarkers play a crucial role in understanding and managing neurodegenerative diseases like Huntington's disease (HD). With HD, biomarkers offer a glimpse into the underlying molecular and cellular changes occurring in the brain, aiding in early detection, disease progression tracking, and treatment development. One promising avenue of biomarker research in HD involves imaging techniques such as magnetic resonance imaging (MRI) and positron emission tomography (PET). These technologies enable researchers to visualize structural and functional abnormalities in the brain, such as neuronal loss and altered neurotransmitter activity, providing valuable insights into disease pathology.

Another area of focus in HD biomarker research involves the identification of molecular markersin bodily fluids such as blood, cerebrospinal fluid (CSF), and saliva. These markers include proteins, RNA, DNA, and metabolites that can reflect disease-specific changes occurring in the brain. By analyzing these biomarkers, researchers aim to develop non-invasive diagnostic tests that can detect HD at earlier stages and monitor disease progression over time. Moreover, these biomarkers hold potential for assessing the efficacy of therapeutic interventions and predicting treatment outcomes in individuals with HD.

Advances in genomic technologies have paved the way for identifying genetic biomarkersassociated with HD. Genetic testing for the expansion of the huntingtin gene (HTT) is already used in diagnosing HD, but ongoing research aims to uncover additional genetic factors that influence disease onset and progression. By understanding the genetic underpinnings of HD better, researchers can develop personalized treatment approaches and stratify patients based on their genetic risk profiles. Overall, biomarker research in Huntington's disease offers hope for improved diagnostics, prognosis, and targeted therapies, bringing us closer to effectively managing this devastating neurodegenerative disorder.

Summary:

Neurodegenerative diseases present significant challenges to healthcare systems globally, necessitating early detection strategies for timely intervention and management. Emerging biomarkers offer promising avenues for early diagnosis, enabling clinicians to identify individuals at risk or in the prodromal stages of neurodegeneration. This review examined recent research findings on biomarkers for Alzheimer's disease, Parkinson's disease, Huntington's disease, and amyotrophic lateral sclerosis, encompassing various sources such as cerebrospinal fluid, blood, neuroimaging, and genetic markers. While significant progress has been made, challenges such as standardization, validation, and accessibility remain. Nevertheless, understanding the diagnostic potential of these biomarkers is critical for advancing early detection strategies, improving patient care, and facilitating the development of targeted therapies for neurodegenerative diseases.

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