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Perspective

Role of Nucleosomes in Gene Regulation and Chromatin Dynamics

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DESCRIPTION

Neurodegenerative diseases represent a significant and growing challenge in healthcare, affecting millions worldwide with devastating consequences for quality of life. Understanding the intricate biochemical mechanisms underlying these diseases is important for developing effective therapeutic interventions. This article discusses about the current state of knowledge regarding the biochemistry of neurodegenerative diseases, focusing on key mechanisms, pathological features, and emerging therapeutic strategies.

Biochemical basis of neurodegenerative diseases

Neurodegenerative diseases, such as Alzheimer's Disease (AD), Parkinson's Disease (PD), Huntington's Disease (HD), and Amyotrophic Lateral Sclerosis (ALS), share common biochemical pathways that contribute to progressive neuronal dysfunction and death. Central to many of these diseases is the aggregation of misfolded proteins, which disrupts cellular homeostasis and leads to neurotoxicity.

Protein misfiling and aggregation

The attribute pathology of neurodegenerative diseases involves the misfiling and aggregation of specific proteins within neurons. In AD, beta-amyloid peptides and tau protein aggregates form plaques and neurofibrillary tangles, respectively, disrupting synaptic function. In PD, alpha-syncline aggregates into Lowy bodies, compromising protein degradation pathways and inducing oxidative stress. Similar protein aggregation phenomena occur in HD and ALS (misfolded *SOD1* or *TDP-43* proteins), contributing to neuronal toxicity and dysfunction.

Deciphering the biochemistry of alzheimer's and parkinson's diseases

Alzheimer's Disease (AD) and Parkinson's Disease (PD) are two of the most prevalent neurodegenerative disorders worldwide, each characterized by distinct clinical manifestations and underlying biochemical mechanisms. Understanding the intricate biochemistry of these diseases is important for developing effective treatments to alleviate their extreme impact on patients' lives. Biochemistry of Alzheimer's Disease (AD).

Alzheimer's disease is characterized by the progressive accumulation of beta-amyloid plaques and Neuro Fibrillary Tangles (NFTs) in the brain. Amyloid beta peptides (Aβ) are derived from the Amyloid Precursor Protein (APP) through sequential cleavage by β-secretase and γ-secretase enzymes. Aberrant processing leads to the accumulation of neurotoxic Aβ42 aggregates, which disrupt synaptic function and trigger neuroinflammation. Concurrently, hyper phosphorylation of tau protein causes it to aggregate into NFTs, compromising neuronal integrity and function. These pathological changes culminate in synaptic dysfunction, neuronal loss, and cognitive decline in AD patients.

Biochemistry of Parkinson's Disease (PD)

Parkinson's disease is characterized by the progressive degeneration of dopaminergic neurons in the substantia nigari region of the brain. The pathological attribute of PD is the accumulation of misfolded alpha-syncline protein into insoluble aggregates known as Lowy bodies. Alpha-syncline aggregation disrupts cellular homeostasis, impairs protein clearance mechanisms (e.g., autophagy and ubiquitin-proteasome system), and induces oxidative stress and mitochondrial dysfunction. These processes contribute to the progressive loss of dopaminergic neurons, leading to motor symptoms such as bradykinesia, rigidity, and tremors.

Common biochemical pathways and mechanisms

Despite their distinct clinical presentations, AD and PD share several common biochemical pathways contributing to neurodegeneration. Oxidative stress plays a pivotal role in both diseases, exacerbated by mitochondrial dysfunction and the accumulation of misfolded proteins. Oxidative damage leads to lipid peroxidation, protein oxidation, and DNA damage, further compromising neuronal viability. Neuroinflammation, mediated by activated microglia and astrocytes, amplifies neurodegeneration through the release of pro-inflammatory cytokines and reactive oxygen/nitrogen species, exacerbating synaptic dysfunction and neuronal loss in AD and PD.

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Therapeutic strategies and future directions

Current therapeutic strategies for AD and PD aim to target these underlying biochemical mechanisms to slow disease progression and improve patient outcomes. In AD, approaches include the development of BACE1 inhibitors, γ-secretase modulators, and anti-Aβ antibodies to reduce Aβ production and aggregation. Therapies targeting tau pathology, such as tau aggregation inhibitors and tau immunotherapy, hold potential for preserving neuronal function. In PD, therapeutic strategies focus on enhancing mitochondrial function, promoting alpha-syncline clearance through autophagy, and modulating neuroinflammation with anti-inflammatory agents or immunomodulatory therapies.

Emerging therapeutic avenues, including gene therapy, stem cell transplantation, and neuroprotective agents, offer potential disease-modifying strategies that may revolutionize AD and PD treatment paradigms. Biomarker research continues to advance, enabling early detection and monitoring of disease progression, which is important for evaluating treatment efficacy and developing personalized therapeutic interventions.

The biochemistry of Alzheimer's and Parkinson's diseases is complex, involving multiple interconnected pathways that contribute to neurodegeneration and clinical symptomatology. Advances in understanding these biochemical mechanisms have paved the way for innovative therapeutic approaches aimed at modifying disease progression and improving patient outcomes. Continued interdisciplinary research efforts are essential to unravelling the full complexity of AD and PD pathogenesis, translating discoveries into effective treatments, and ultimately alleviating the burden of these devastating neurodegenerative disorders on individuals, families, and healthcare systems globally.