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ATP-induced Cell Death Mechanism

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Abstract: "ATP-induced cell death" is a novel form of cellular demise identified since 1991, typically characterized by a substantial accumulation of adenosine triphosphate (ATP) and the activation of ATP membrane receptors during the cell death process. The perturbation of ATP homeostasis is intricately linked to mitochondrial function. In recent years, ATP-induced cell death (AICD) has emerged as a discernible pattern of cell demise attributed to heightened levels of extracellular ATP (eATP). This phenomenon is intimately associated with the pathophysiological mechanisms underpinning a plethora of maladies, including malignancies, neurodegenerative disorders, ischemia-reperfusion injury, renal impairment, and hematological conditions. The strategic modulation of ATP-induced cell death to mitigate the onset and progression of these related diseases has garnered significant attention and stands as a focal point in etiological research and therapeutic interventions. Nevertheless, the functional alterations and precise molecular mechanisms governing ATP-induced cell death demand further comprehensive exploration. This paper comprehensively synthesizes the most recent advancements in the understanding of ATP-induced cell death mechanisms, with the overarching objective of serving as a reference for a deeper comprehension of its pathogenesis and the proposition of novel therapeutic targets for the management of associated diseases.

Keywords: ATP Induced Cell Death; Mechanism; Unsolved Mysteries.

1. Introduction

"ATP-induced cell death," also known as "AICD" represents a mode of cellular demise triggered when cells are subjected to ATP stimulation, either from extracellular or intracellular sources. This intricate process entails the influence of ATP, which can, when present in adequate quantities or excess, elicit a cascade of intricate biological responses culminating in cellular demise. It is imperative to note that this modality of cell death distinguishes itself from the more conventional mechanisms of cell death, such as apoptosis or necrosis. In light of these considerations, we have elucidated the intricacies of AICD mechanisms with the aim of furnishing a comprehensive resource for a deeper comprehension of its pathogenesis and the formulation of novel therapeutic targets for the management of associated diseases.

2. The Abbreviation of ATP-induced Cell Death

AICD (Adenosine Triphosphate-Induced Cell Death): In the realm of scientific literature and the medical domain, abbreviations serve as a means to concisely reference complex terminologies. In the context of "ATP-induced cell death," "A" signifies "ATP," "I" represents "induced," and "CD" denotes "cell death." This adoption of abbreviations is a prevailing practice in scientific and medical discourse as it aptly preserves the essential components of the original terminology.

3. ATP-induced Cell Death Mechanism

We have categorized the mechanisms underlying ATP-induced cell death into four distinct types. The initial category pertains to an ATP-mediated elevation in intracellular calcium concentrations upon interaction with P2X7Rs, thereby instigating caspase activation and culminating in cellular demise. The second category encompasses ATP's capacity to induce the release of HMGB1/TLR4 (High Mobility Group Box 1/ Toll-like Receptor 4), which subsequently activates caspase-1 and initiates cell death by triggering the NLRP3 (Nucleotide-binding Oligomerization Domain, Leucine Rich Repeat and Pyrin Domain-containing Protein 3) inflammasome. The third classification involves ATP's interaction with P2X7Rs, prompting the activation of the NF-κB (Nuclear Factor-κB) and PI3K-AKT/HIF (Phosphoinositide 3-Kinase-Akt/Hypoxia-Inducible Factor) pathways, leading to DNA damage and cellular demise. The fourth category concerns the persistent accumulation of calcium ions (Ca2+), which can trigger the opening of the mitochondrial permeability transition pore (mPTP), resulting in DNA damage and eventual cell death. Additionally, calcium ions can induce the release of cytochrome c from the mitochondria [1-10].

4. Whether ATP-induced Cell Death Constitutes the Fundamental Mechanistic Basis for All Forms of Cellular Demise

Cell death represents a multifaceted domain encompassing diverse modes of cellular demise, such as apoptosis, necrosis,

isostatic death, and autophagy, each characterized by distinct molecular mechanisms and triggering pathways. Among these, ATP-induced cell death constitutes a relatively recent addition, frequently entailing the participation and impact of adenosine triphosphate (ATP). Varied cell death modalities are orchestrated by discrete molecular mechanisms and pathways. For instance, apoptosis is an intricately regulated form of cell demise typically involving the activation of cysteine proteases (caspases) and a sequence of intracellular molecular cascades. Necrosis, in contrast, is an informal and often deemed an emergency mode of cell death, frequently marked by cellular membrane rupture and the efflux of cellular contents.

ATP-induced cell death, being a newcomer, intricately associates with ATP's presence and influence, but it is not universally applicable to all cellular demise scenarios. As a result, it does not constitute the fundamental rationale governing cell death; rather, it serves as one of numerous cell death pathways, pertinent to specific physiological and pathological contexts. Research within the realm of cell death remains in continual evolution as we endeavor to elucidate the mechanisms and pathways governing the heterogeneous facets of cellular demise.

Currently, there exists insufficient scientific substantiation or theoretical underpinning to posit that "ATP-induced cell death" serves as the overarching logic underpinning all forms of cell death. The tenets of scientific inquiry necessitate grounding in empirical verifiability and robust evidentiary foundations. Present investigations are better directed towards elucidating the diverse cell death modalities and their interrelationships, eschewing endeavors to simplify all cell death modalities into a singular underlying logic.

A correlation exists between ATP-induced cell death and other modes of cell demise, and further investigation is warranted to ascertain whether the initiation of alternative cell death modalities leads to a concurrent surge in extracellular ATP levels or expedites the onset of ATP-induced cell death. In instances where ATP-induced cell death co-occurs with other modes of cell demise, the overarching question arises as to whether ATP-induced cell death serves as the fundamental paradigm underlying the majority of cell death scenarios.

5. Conclusion

While ATP-induced cell death has not yet achieved worldwide consensus, it persists as a promising domain of research that has piqued the curiosity of investigators. Diverse interpretations of the definition and attributes of ATP-induced cell death within the scientific community and literature have engendered a measure of perplexity and incongruity. ATP-induced cell death, being a relatively recent conceptualization, continues to evolve in its investigation and comprehension. Emerging paradigms typically necessitate the accumulation of substantial empirical evidence and robust scientific endorsement over time to secure ubiquitous recognition.

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