Commentary
Volume 18:03, 2024

Journal of Molecular and Genetic Medicine

ISSN: 1747-0862

Open Access

Dyskerin Downregulation Through AKT-mTOR Signaling Dysregulation Can Cause ER Stress and Encourage Autophagy

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Introduction

Dyskerin, a vital component of the H/ACA ribonucleoprotein complex, plays a crucial role in the biogenesis of small nucleolar RNAs (snoRNAs) and the maintenance of telomeres. Its functional importance is underscored by its involvement in the post-transcriptional modification of ribosomal RNA and its association with diseases such as dyskeratosis congenita and various cancers. Dysregulation of dyskerin expression or activity has profound cellular consequences, particularly in the context of signaling pathways such as AKT-mTOR, which are pivotal for cell growth, survival, and metabolism. The AKT-mTOR signaling pathway is a key regulator of cellular processes, including protein synthesis, cell proliferation, and survival. Dysregulation of this pathway is often linked to cancer and other diseases characterized by uncontrolled cell growth and proliferation [1].

AKT (also known as protein kinase B) is activated by various growth factors and subsequently phosphorylates a range of substrates involved in metabolism, cell cycle progression, and apoptosis. One of its primary downstream targets is the mechanistic target of rapamycin (mTOR), a central regulator of cell growth and metabolism. mTOR exists in two distinct complexes: mTORC1 and mTORC2. mTORC1 is sensitive to rapamycin and regulates protein synthesis, autophagy, and metabolism in response to nutrients, growth factors, and cellular energy status. mTORC2, on the other hand, regulates cytoskeletal organization and cell survival. Dysregulation of mTOR signaling can lead to various pathological conditions, including cancer, metabolic disorders, and neurodegenerative diseases [2].

Description

The interplay between dyskerin, the AKT-mTOR signaling pathway, ER stress, and autophagy is complex and multifaceted. Dyskerin downregulation can influence cellular processes through the dysregulation of AKT-mTOR signaling, leading to ER stress and the activation of autophagy. This article aims to explore the intricate relationship between these molecular pathways and their implications for cellular homeostasis and disease. Autophagy, a cellular degradation process, is closely linked to the UPR and ER stress. It is a catabolic pathway that involves the lysosomal degradation of cytoplasmic components, including damaged organelles, misfolded proteins, and pathogens. Autophagy serves as a survival mechanism under stress conditions, allowing cells to recycle nutrients and maintain energy homeostasis. Dysregulation of autophagy is implicated in various diseases, including cancer, neurodegeneration, and infectious diseases [3].

Dyskerin downregulation can disrupt the normal functioning of the AKT-mTOR signaling pathway, leading to aberrant cellular responses. Dyskerin is essential for the proper functioning of ribosomes and telomeres, and its downregulation can impair ribosome biogenesis and telomere maintenance. This impairment can trigger a cascade of cellular stress responses, including ER stress. ER stress is a condition characterized by the accumulation of misfolded or unfolded proteins in the ER lumen. This accumulation activates the UPR, a signaling pathway aimed at restoring normal ER function. The UPR consists of three main branches: the PERK pathway, the IRE1 pathway, and the ATF6 pathway. Each of these branches has distinct but overlapping functions in mitigating ER stress [4].

The PERK pathway involves the phosphorylation of the eukaryotic translation initiation factor 2α (eIF2α), leading to a temporary reduction in global protein synthesis. This reduction helps alleviate the burden of misfolded proteins in the ER. However, selective translation of specific mRNAs, such as ATF4, is enhanced, leading to the expression of genes involved in amino acid metabolism, antioxidant responses, and autophagy. The IRE1 pathway involves the activation of inositol-requiring enzyme 1 (IRE1), which has endoribonuclease activity. IRE1 splices X-box binding protein 1 (XBP1) mRNA, producing a potent transcription factor that upregulates genes involved in protein folding, ER-Associated Degradation (ERAD), and lipid biosynthesis. Additionally, IRE1 can degrade certain mRNAs to reduce the protein load in the ER [5].

Conclusion

In metabolic disorders, dysregulation of these pathways can contribute to insulin resistance and metabolic dysfunction. Dyskerin downregulation can impair ribosome biogenesis and telomere maintenance, leading to cellular stress responses, including ER stress. The activation of the UPR can inhibit mTORC1 activity and promote autophagy, which can help maintain cellular energy homeostasis under conditions of nutrient deprivation. However, chronic activation of these stress responses can contribute to metabolic dysfunction and insulin resistance.

In conclusion, dyskerin downregulation through AKT-mTOR signaling dysregulation can cause ER stress and encourage autophagy. The intricate interplay between these molecular pathways has significant implications for cellular homeostasis and disease. Dyskerin downregulation can impair ribosome biogenesis and telomere maintenance, leading to cellular stress responses, including ER stress. The activation of the UPR can inhibit mTORC1 activity and promote autophagy, which serves as a survival mechanism under stress conditions. Dysregulation of these pathways can contribute to the pathogenesis of various diseases, including cancer, neurodegenerative diseases, and metabolic disorders. Understanding the molecular mechanisms underlying this interplay is crucial for developing targeted therapies to modulate these pathways and improve cellular homeostasis and disease outcomes.

Acknowledgement

None.

Conflict of Interest

None.

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Received: 19 April, 2024, Manuscript No. jmgm-24-137738; **Editor assigned:** 22 April, 2024, PreQC No. P-137738; **Reviewed:** 04 May, 2024, QC No. Q-137738; **Revised:** 16 May, 2024, Manuscript No. R-137738; **Published:** 23 May, 2024, DOI: 10.37421/1747-0862.2024.18.667

References

1. Montanaro, Lorenzo, Maurizio Brigotti, J. Clohessy and Stefania Barbieri, et al. "Dyskerin expression influences the level of ribosomal RNA pseudo-uridylation and telomerase RNA component in human breast cancer." *The J Pathol: J Pathologic Soc Great Britain and Ireland* 210 (2006): 10-18.
2. Vicidomini, Rosario, Annamaria Di Giovanni, Arianna Petrizzo and L. F. Iannucci, et al. "Loss of Drosophila pseudouridine synthase triggers apoptosis-induced proliferation and promotes cell-nonautonomous EMT." *Cell Death Dis* 6 (2015): e1705-e1705.
3. Angrisani, Alberto, Mimmo Turano, Lorella Paparo and Concetta Di Mauro, et al. "A new human dyskerin isoform with cytoplasmic localization." *Biochimica et Biophysica Acta (BBA)-General Subjects* 1810 (2011): 1361-1368.
4. Ron, David and Peter Walter. "Signal integration in the endoplasmic reticulum unfolded protein response." *Nat Rev Mol Cell Biol* 8 (2007): 519-529.
5. Wang, Peng, Jingzhi Li and Bingdong Sha. "The ER stress sensor PERK luminal domain functions as a molecular chaperone to interact with misfolded proteins." *Acta Crystallographica Section D: Structur Biol* 72 (2016): 1290-1297.

How to cite this article: Müller, Jenifer. "Dyskerin Downregulation Through AKT-mTOR Signaling Dysregulation Can Cause ER Stress and Encourage Autophagy." *J Mol Genet Med* 18 (2024): 667.