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Alterations in tp53 Gene, Telomere Length and Mitochondrial DNA in Patients with Benign Prostatic Hyperplasia

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Introduction

Benign Prostatic Hyperplasia (BPH) is a common, non-cancerous enlargement of the prostate gland affecting aging men. Although BPH is typically considered benign, recent studies have suggested molecular alterations that could provide insights into its pathogenesis. Among the key factors under investigation are the TP53 gene, telomere length, and mitochondrial DNA which are critical in cell cycle regulation, aging, and mitochondrial function, respectively. In this communication, we review the current evidence on alterations in these factors in BPH patients, shedding light on how such changes may contribute to the development of BPH and its progression. Understanding these molecular changes could open new avenues for targeted diagnostics and therapeutic strategies. Benign Prostatic Hyperplasia (BPH) is one of the most prevalent conditions in aging men, characterized by the non-cancerous enlargement of the prostate gland. This condition leads to lower urinary tract symptoms, such as urinary retention, frequency, and incomplete bladder emptying, significantly impacting the quality of life. While BPH is not directly life-threatening, its high prevalence, particularly in men over the age of 50, makes it a significant health concern globally. Despite its benign nature, the molecular underpinnings of BPH remain poorly understood. The role of genomic instability, telomere biology, and mitochondrial dysfunction in aging and cell proliferation has been well documented in cancer, but their roles in benign conditions like BPH are less clear. Key molecular components such as the TP53 tumor suppressor gene, telomere length, and mitochondrial DNA are being increasingly studied to determine their influence on prostatic tissue alterations associated with BPH. The purpose of this communication is to examine these molecular alterations in BPH patients and discuss their potential roles in the pathogenesis of this condition [1].

Description

The TP53 gene, commonly referred to as the "guardian of the genome," encodes the p53 protein, a key regulator of the cell cycle and apoptosis. TP53 mutations are well known for their roles in cancer development, particularly in prostate cancer. However, their role in benign conditions such as BPH is less understood. p53 plays a crucial role in maintaining genomic stability by activating DNA repair pathways or inducing apoptosis in response to DNA damage. In normal tissues, p53 helps prevent the accumulation of mutations by halting cell cycle progression in the presence of DNA damage, thereby reducing the risk of uncontrolled proliferation. In BPH, studies have shown varying degrees of p53 expression and TP53 mutations. Some research indicates an overexpression of p53 in hyperplastic prostate tissues compared to normal prostate tissues, suggesting a potential response to increased cellular stress or DNA damage in the enlarged prostate. Overexpression of p53 in BPH may serve as a compensatory mechanism to control cell proliferation and prevent the transformation of benign hyperplastic tissue into malignant cancer [2].

However, the significance of TP53 mutations in BPH is still debated. Unlike prostate cancer, where TP53 mutations are common and associated with poor prognosis, BPH generally exhibits fewer TP53 mutations. Instead, alterations in p53 signaling pathways, rather than direct mutations, may play a more critical role in BPH pathogenesis. Further research is needed to clarify whether TP53 mutations are a causative factor in BPH or merely a secondary response to cellular stress. Certain polymorphisms in TP53 have been associated with an increased risk of BPH development. For instance, the TP53 Arg72Pro polymorphism has been linked to altered p53 functionality, influencing susceptibility to hyperplasia in the prostate. Although these polymorphisms may not cause BPH directly, they may increase the likelihood of developing BPH in genetically predisposed individuals, particularly in the context of age-related decline in DNA repair mechanisms [3].

Telomeres are repetitive nucleotide sequences at the ends of chromosomes that protect them from degradation and fusion during cell division. Telomere shortening is a hallmark of aging and cellular senescence, and it has been implicated in a variety of age-related diseases, including cancer and cardiovascular diseases. Telomere dysfunction can lead to genomic instability, which might promote hyperplastic growth in tissues like the prostate. Several studies have investigated the relationship between telomere length and prostate conditions. In cancer, telomere shortening is linked to increased genomic instability, tumorigenesis, and progression. In BPH, telomere shortening has also been observed, though its role is less clear. Prostate epithelial cells in BPH patients exhibit significantly shorter telomeres compared to those in healthy individuals. This shortening may result from the increased proliferation of prostate cells due to hormonal stimuli, such as the action of androgens. As the prostate cells replicate more frequently, their telomeres shorten progressively, leading to cellular senescence or apoptosis. However, in BPH, this shortening does not appear to induce malignant transformation as seen in prostate cancer. Instead, it might contribute to the benign overgrowth characteristic of hyperplasia [4].

Enzyme telomerase is responsible for maintaining telomere length by adding nucleotide repeats to the ends of chromosomes. While telomerase activity is typically low in normal somatic cells, its expression is elevated in cancer cells, enabling them to bypass senescence. Interestingly, elevated telomerase activity has also been reported in BPH tissue, suggesting that telomerase may help maintain telomere length in hyperplastic cells, allowing them to continue dividing without undergoing senescence. This may partly explain why BPH results in enlarged prostate tissue without progressing to cancer. The balance between telomere shortening and telomerase activity in BPH appears to be a critical factor in determining the fate of prostate cells. Dysregulation of this balance could contribute to the excessive cell proliferation seen in BPH, while still maintaining the benign nature of the condition. Mitochondria are the powerhouses of the cell, responsible for producing ATP through oxidative phosphorylation. Apart from energy production, mitochondria also play a pivotal role in apoptosis, ROS production, and cellular metabolism. Mitochondria have their own circular DNA which is more prone to mutations than nuclear DNA due to limited repair mechanisms and constant exposure to oxidative stress.

Mitochondrial dysfunction has been implicated in various age-related conditions, including BPH. In aging tissues, such as the prostate, an increase in mtDNA mutations has been observed, leading to impaired mitochondrial function. These mutations may accumulate due to oxidative stress generated during mitochondrial respiration, resulting in reduced ATP production and increased ROS. In BPH patients, mtDNA alterations have been reported

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in hyperplastic prostate tissues. These alterations may lead to defective oxidative phosphorylation, causing increased ROS production and cellular damage. The resulting oxidative stress could trigger chronic inflammation, a known contributor to BPH pathogenesis. Chronic inflammation in the prostate promotes the proliferation of prostate cells, further contributing to hyperplasia. Mitochondrial biogenesis, the process by which new mitochondria are formed in the cell, is essential for maintaining mitochondrial function, particularly in proliferating cells. In BPH, studies suggest that mitochondrial biogenesis may be dysregulated, leading to a compensatory increase in the number of dysfunctional mitochondria in hyperplastic prostate cells. This may allow cells to meet the high energy demands associated with hyperplasia, but at the cost of increased oxidative stress and mtDNA mutations [5].

Conclusion

Given the importance of mitochondrial function in BPH pathogenesis, targeting mitochondria could offer novel therapeutic opportunities. Strategies aimed at reducing oxidative stress, promoting mitochondrial biogenesis, or correcting mtDNA mutations may help alleviate the cellular damage that drives prostate hyperplasia. Additionally, mitochondrial-targeted antioxidants could mitigate the effects of ROS in hyperplastic prostate tissues. The alterations in TP53, telomere length, and mitochondrial DNA in BPH are not isolated events but are likely interconnected. p53 is known to influence both telomere biology and mitochondrial function, highlighting the potential for cross-talk between these pathways in BPH pathogenesis. The p53 protein regulates the cell cycle and can induce senescence in response to telomere shortening. In BPH, elevated p53 expression in response to telomere shortening may act as a safeguard against malignant transformation, promoting a benign hyperplastic state rather than cancer. TP53 and Mitochondria: p53 also plays a role in mitochondrial apoptosis by interacting with pro-apoptotic proteins like BAX and PUMA. In BPH, p53 may help maintain a balance between cell proliferation and apoptosis, preventing excessive cell death in response to mitochondrial dysfunction.

Acknowledgement

None.

Conflict of Interest

None.

References

1. Chughtai, Bilal, James C. Forde, Dominique Dana Marie Thomas and Leanna Laor, et al. "Benign prostatic hyperplasia." *Nat Rev Dis Primers* 2 (2016): 1-15.
2. Chin, Lynda, Steven E. Artandi, Qiong Shen and Alice Tam et al. "p53 deficiency rescues the adverse effects of telomere loss and cooperates with telomere dysfunction to accelerate carcinogenesis." *Cell* 97 (1999): 527-538.
3. Flores, Ignacio and Maria A. Blasco. "A p53-dependent response limits epidermal stem cell functionality and organismal size in mice with short telomeres." *PloS One* 4 (2009): e4934.
4. Sahin, Ergün and Ronald A. DePinho. "Linking functional decline of telomeres, mitochondria and stem cells during ageing." *Nature* 464 (2010): 520-528.
5. Sahin, Ergün, Simona Colla, Marc Liesa and Javid Moslehi et al. "Telomere dysfunction induces metabolic and mitochondrial compromise." *Nature* 470 (2011): 359-365.

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