RELATIONSHIP BETWEEN PURINERGIC SIGNALLING AND OXIDATIVE STRESS IN PROSTATE CANCER: PERSPECTIVES FOR FUTURE THERAPY

Rafael Zatti Rossetto[1-3] ; Andréia M. Cardoso[1]; Sarah F.V.O. Maciel[1]
[1]Federal University of Fronteira Sul, Graduate Program in Biomedical Sciences, Chapecó (SC)

INTRODUCTION

Prostate cancer (PCa) is a complex and lethal disease in men, influenced by risk factors such as age, heredity, and lifestyle. This article aims to review the roles of purinergic signaling and reactive species in PCa progression. The purinergic system, involving signaling molecules like ATP and adenosine, specific receptors (P1 and P2), and catalytic enzymes (e.g., CD39 and CD73), plays a significant role in cell proliferation, angiogenesis, and immune evasion. Similarly, reactive oxygen species (ROS) and reactive nitrogen species (RNS) contribute to genetic instability and uncontrolled cell proliferation. Understanding the interplay between these systems is crucial for developing effective PCa treatments.

METHODOLOGY

A systematic review was conducted to explore the relationship between purinergic signaling and oxidative stress in prostate cancer. PubMed, Scopus, and Web of Science databases were used with specific search terms and Boolean operators. Peer-reviewed articles were selected based on inclusion and exclusion criteria, focusing on clinical and preclinical studies. Titles and abstracts were screened, followed by full-text review, data extraction, and quality assessment. The synthesized findings highlighted key themes, mechanisms, and potential therapeutic targets, identifying knowledge gaps and future research areas. PRISMA guidelines were followed to ensure transparent reporting, providing a comprehensive overview of the interplay between purinergic signaling and oxidative stress in Pca.

DISCUSSION

In PCa, extracellular ATP activates P2 receptors, which connect to other signaling pathways such as MAPK and HIF-1. This modulates transcription factors like VEGF and creates an inflammatory environ ment by releasing pro-inflammatory cytokines, such as IL-1β, through the NLRP3 inflammasome. Additionally, there are changes in bio energetics and mtDNA, with the activation of NADPH oxidase, which increases the production of ROS. ADO has anti-inflammatory effects, impacting the anti-cancer response mainly through T cells. The outcome of this system can have both pro-tumor and anti-tumor effects, depending on specific factors in the TME and surrounding healthy cells.

Furthermore, the presence of CD39 and CD73 enzymes in the purinergic signaling cascade also in f luences ROS production and the inflammatory profile. When there is greater ATP degradation, generating more ADO, the TME becomes immunosuppressive and anti-inflammatory. On the other hand, this ef fect can reduce oxidative damage caused by ROS, which is produced when more ATP is present. In PCa, mitochondrial energy depletion oc curs, and when ATP is degraded, cellular apoptosis mechanisms are reduced due to the immunosuppressive environment. There is a presence of a pro-inflammatory cellular TME, primarily due to the presence of ATP and ROS with the entire derived signaling cascade. However, this mechanism may lead to pro-tumor collateral damage, such as uncontrolled cellular proliferation, and other conditions like angiogenesis, leading to tumor progression. Purinergic signaling and oxidative stress represent interconnected pathways influencing PCa progression and treatment resistance. Ther apeutic interventions targeting these mechanisms hold promise for improving outcomes in PCa patients. Advancing our understanding of these pathways and their interplay within the TME will be crucial in developing innovative, effective therapies.

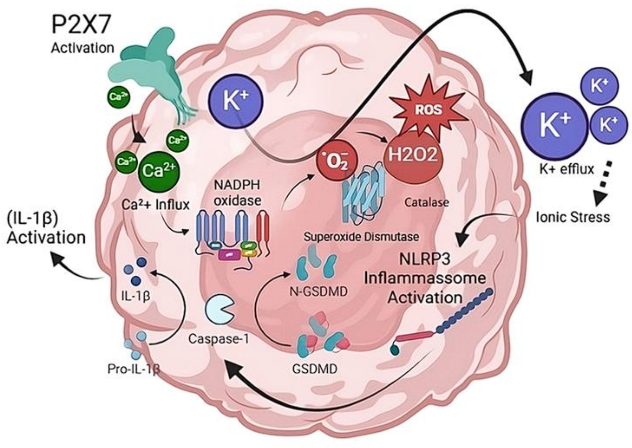

Fig. 2. Ionic change mechanism by P2X7.

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