OPEN ACCESS
Global Journal of Research in Medical Sciences
ISSN: 2583-3960 (Online)
Volume 06 | Issue 01 | Jan.-Feb. | 2026
Journal homepage: https://gjrpublication.com/gjrms/
Review Article

A Review of Membrane Potential Dynamics in Prostate Cancer

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DOI: 10.5281/zenodo.18638528 Submission Date: 18 Dec. 2025 | Published Date: 14 Feb. 2026

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Abstract

Prostate cancer is one of the most common cancers that men get around the world, and it is still a major source of cancer-related illness and death. Traditional research has predominantly concentrated on genetic modifications, androgen signalling, and metabolic reprogramming; however, recent findings underscore the essential function of bioelectric signalling in tumour biology. Membrane potential (Vm), the electrical potential differential across the plasma membrane, has been recognised as a fundamental regulator of cancer cell behaviour. Changes in membrane potential affect important cellular processes as proliferation, apoptosis, migration, invasion, angiogenesis, and resistance to treatment. This study offers an extensive examination of membrane potential dynamics in prostate cancer, addressing its physiological function in normal prostate cells and the pathological mechanisms that lead to its dysregulation in malignancy. A thorough examination of the role of major ion channels, transporters, and pumps is conducted, highlighting their growing importance as diagnostic biomarkers and therapeutic targets. Examining prostate cancer through a bioelectric lens provides novel insights into tumour advancement and paves the way for innovative approaches in precision medicine.

Keywords: *Prostate cancer; membrane potential; bioelectric signalling; ion channels; depolarisation; calcium signalling; cancer electrophysiology.*

Introduction

Prostate cancer is a huge health problem around the world, especially for older men. It is also one of the most common types of cancer in males. Even though there have been major improvements in early identification and treatment, prostate cancer is still a clinical problem, especially when it is progressed or metastatic. Conventional theories of prostate cancer biology have predominantly focused on genetic alterations, hormonal regulation—especially androgen receptor signaling—and metabolic reprogramming as the key factors influencing tumour initiation and progression. Nevertheless, these frameworks inadequately elucidate the intricate phenotypic behaviour of cancer cells, encompassing their capacity for uncontrolled proliferation, evasion of apoptosis, and metastasis [1].

There has been more and more interest in the role of bioelectric signalling in cancer in the last several years. Bioelectricity is the electrical properties of cells and tissues that are caused by ion gradients across biological membranes. Among these features, membrane potential (Vm) has become a key factor in determining what happens to cells and how they act. The unequal distribution of ions including sodium (Na^+), potassium (K^+), calcium (Ca^{2+}), and chloride (Cl^-) across the plasma membrane creates membrane potential. This is kept up by selective membrane permeability and active transport processes. Membrane potential is now known to be a critical factor in the growth, differentiation, movement, and programmed death of non-excitable cells, such as epithelial cells, in addition to its traditional involvement in excitable tissues like nerves and muscles [2].

Cancer cells usually have a depolarised membrane potential when compared to normal cells. This change in electrical activity is not just a side effect of cancerous change; it seems to actively help with cancer signalling and tumour growth. Comprehending the processes and ramifications of membrane potential dysregulation in prostate cancer constitutes a significant frontier in cancer biology [3].

The Concept of membrane potential

The difference in electrical charge between the inside and outside of a cell is called the membrane potential (Vm). It is primarily caused by the uneven distribution of ions and is kept going by three primary things: ion concentration gradients, the plasma membrane's selective permeability, and the action of ion pumps such the Na^+/K^+-ATPase. Potassium ions are the most important ions for resting membrane potential because they can easily pass through membranes. Sodium and calcium ions, on the other hand, help depolarising currents.[4]

In normal epithelial cells, such as prostate cells, the resting membrane potential usually falls between –60 and –90 mV, indicating a highly polarised condition. This polarised environment is very important for keeping cells quiet, controlling gene expression, and making sure that cells respond correctly to signals from outside the cell. On the other hand, cancer cells usually have a very depolarised membrane potential, which is usually between –10 and –30 mV. This change in electrical balance makes it easier for aberrant signalling cascades to happen, which encourage uncontrolled growth and survival.[5]

Membrane Potential in Healthy Prostate Cells

In normal prostate tissue, membrane potential is very important for controlling how cells differentiate, how they secrete substances, and how tissues stay stable. Potassium channels are the most important for ion conductance. They keep the electrical environment steady, which is good for controlled growth and correct tissue design. Calcium signalling is carefully controlled and happens in short, spatially limited bursts. This lets processes like cell cycle progression, gene transcription, and apoptosis be controlled very precisely [6].

Normal membrane polarisation helps cells stop dividing when they need to, stops them from growing too quickly, and makes it easier for damaged or old cells to die. All of these systems work together to keep the prostate tissue healthy and working properly [7].

Changes in Membrane Potential in Prostate Cancer

In prostate cancer, the bioelectric landscape of normal cells, which is closely controlled, is severely disturbed. Cancer cells show continuous membrane depolarisation because ion channels, transporters, and pumps are not working properly or are being expressed too much. The disruption of calcium homeostasis is especially noticeable, leading to high amounts of calcium inside cells that turn on pathways that cause cancer [8].

These bioelectric changes are consistent with several characteristics of cancer, including as uncontrolled growth, resistance to apoptosis, increased movement, and a greater ability to invade. Membrane depolarisation has been associated with the activation of significant oncogenic pathways, including MAPK/ERK, PI3K/Akt, and Wnt/β-catenin, which are crucial in tumour development, survival, and metastasis [9].

The role of ion channels in prostate cancer

Potassium channels, such as Kv1.3, KCa3.1, and BK channels, play an important role in controlling the membrane potential in prostate cancer cells. These channels let the cell cycle move forward by keeping a depolarised state that lets calcium in and sends growth signals. They also control the volume of cells and the movement of the cytoskeleton, which are both important for migration and invasion. Experimental data demonstrate that pharmacological inhibition of potassium channels leads to cell cycle arrest and apoptosis, highlighting their potential as therapeutic targets [10].

Secondly, calcium channels are very important for the advancement of prostate cancer. Malignant prostate tissue often has too many channels, like TRPM8 and TRPV6, as well as voltage-gated calcium channels. Continuous calcium influx activates transcription factors and signalling pathways that promote androgen-independent growth, a characteristic of advanced and castration-resistant prostate cancer. Calcium signalling also encourages cancer cells to spread by making it easier for cells to move and change their shape. [11]

Furthermore, Voltage-gated sodium channels (VGSCs), which are usually linked to neural excitability, are not produced correctly in prostate cancer cells. Their activity increases invasiveness by breaking down the extracellular matrix, increasing protease activity, and making it easier for cells to move. High levels of VGSC expression have been linked to aggressive tumour forms and bad clinical outcomes [12].

In the same vein, Chloride channels control how big cells are, how they move, and how well they respond to chemotherapy. These channels let cancer cells adapt to harsh microenvironments by maintaining osmotic balance and intracellular pH. They also help cancer cells survive when they are under stress from treatment [13].

Membrane Potential and Cancer Characteristics

Membrane potential is closely associated with certain characteristics of cancer. Depolarisation encourages cells to divide and keeps them growing, while hyperpolarisation causes cells to die and stops their growth. Ion flow through the membrane makes it easier for cells to move and invade, which helps metastasis. Calcium signalling promotes angiogenic molecules, including vascular endothelial growth factor (VEGF), which helps tumours build blood vessels. Also, ion channels affect drug resistance by controlling efflux pumps and how drugs build up inside cells [14, 15].

The Patterns of ion channel expression show potential as diagnostic and prognostic indicators in prostate cancer. An increase in TRPM8 levels and VGSC density has been linked to more aggressive illness and worse clinical outcomes. These bioelectric markers might work well with more established tests like prostate-specific antigen (PSA) testing and histopathological grading [16, 17].

Targeting membrane potential is a new way to treat prostate cancer. Researchers are currently looking into ion channel blockers, electroceutical methods, and bioelectric manipulation. Experimental medicines that target potassium, calcium, and sodium channels work to repolarise cancer cells, bring bioelectric states back to normal, and make tumours more sensitive to chemotherapy and radiation therapy [18].

New methods including bioelectric imaging, voltage-sensitive dyes, and patch-clamp profiling are likely to change how we investigate cancer electrophysiology. These instruments will make it possible to keep an eye on the electrical states of tumours in real time and help create personalised bioelectric therapies. Combining bioelectric regulation with traditional molecular and pharmacological methods could greatly enhance patient outcomes and lower treatment resistance [19].

Conclusion

The dynamics of membrane potential constitute a critical although inadequately investigated aspect of prostate cancer biology. Signalling that is driven by depolarisation is very important for the growth, survival, and spread of tumours. Ion channels and membrane potential modulators show a lot of promise as both diagnostic tools and targets for treatment. Looking at prostate cancer via a bioelectric lens not only helps us learn more about how tumours work, but it also offers up new ways to create novel and more precise cancer treatments.

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CITATION
Nnodim, J., & Udeoha, U. (2026). A Review of Membrane Potential Dynamics in Prostate Cancer. In Global Journal of Research in Medical Sciences (Vol. 6, Number 1, pp. 83–86).
https://doi.org/10.5281/zenodo.18638528