Clinical Oncology: Case Reports

Mini Review

A SCITECHNOL JOURNAL

Glycolytic Enzyme Enolase-1 (ENO-1) as a Novel Target for Neuroendocrine-Like Prostate Cancer: A Review of Up-to-date Research and Future Prospects

Carlos A. Cardenas*

Abstract

Prostate Cancer (PCa) remains a significant health burden, with advanced cases presenting significant challenges for treatment. Taxane-based chemotherapy has been the last line of defense for men with advanced PCa, but chemoresistance often leads to treatment failure. Targeted therapy using the Protein-Specific Membrane Antigen (PSMA) has shown promise; however, neuroendocrine-like PCa (NEPC) poses a hurdle due to its limited response to PSMA-RLT, attributed to the absence of PSMA expression. This review explores a promising alternative target, the glycolytic enzyme enolase-1 (ENO-1), which displays differential expression patterns in African American (AA) and European American (EA) men with PCa and could potentially serve as a novel therapeutic target for NEPC. Neuroendocrine-Like Prostate Cancer (NEPC) is a rare and aggressive subtype of prostate cancer, accounting for less than 1% of all cases, but its incidence has been reported to be increasing. NEPC is characterized by the loss of androgen receptor signaling and activation of neuroendocrine pathways, contributing to an adverse clinical outcome. Patients diagnosed with NEPC have a higher chance of metastasis and lower overall survival rates compared to those diagnosed with conventional prostate cancer. Furthermore, NEPC is more commonly diagnosed in African American patients, indicating potential ethnic disparities.

Despite recent progress in understanding the genomic and molecular basis of NEPC, there is still no standard treatment for this aggressive form of prostate cancer. Chemotherapy, radiation therapy, and androgen deprivation therapy are commonly used but with limited effectiveness. Therefore, more research is needed to better understand the underlying mechanisms of NEPC, discover new therapeutic targets, and develop more effective treatments.

The identification of alternative therapeutic targets, such as ENO-1, offers a promising avenue for addressing the challenges posed by NEPC. ENO-1's differential expression patterns in AA and EA men with PCa present an opportunity to personalize treatment approaches and address potential ethnic disparities in NEPC incidence. However, further research is essential to validate ENO-1's efficacy as a targeted therapy for NEPC and to develop novel treatment strategies to improve clinical outcomes for patients with this aggressive prostate cancer subtype. The review emphasizes the urgent need for ongoing research efforts in this area to pave the way for more effective and personalized treatments for NEPC patients.

Keywords: Neuroendocrine-like Prostate cancer; Novel targets; ENO-1; Targeted therapy; Chemoresistance.

Introduction

Prostate Cancer (PCa) is a prevalent malignancy among men worldwide and remains an ongoing public health concern [1]. Recent estimates suggest that in 2023, there were over 288,300 newly diagnosed PCa cases in the United States, making it the second most common cancer in American men [2]. Furthermore, PCa incidence rates are expected to rise significantly over the next few years, with projections of over 248,000 new cases by the year 2025 [1, 2].

Notably, PCa disproportionately affects men of African Ancestry (AA), who experience twice the mortality rate compared to men of European Ancestry (EA) [1]. Despite accounting for only 13% of the US population, AA men comprise nearly 25% of all PCa cases in the country. The factors contributing to these disparities are not well understood, although genetic, environmental, and socioeconomic factors have been proposed as potential culprits.

Given that advanced PCa is often refractory to conventional therapies, developing effective therapeutic targets has become an urgent priority in oncology research. In this context, the glycolytic enzyme enolase-1 (ENO-1) has emerged as a promising target for Neuroendocrine-like PCa (NEPC) in both AA and EA patients [3]. NEPC is a highly aggressive subtype of PCa that tends to respond poorly to traditional treatments.

This review aims to summarize recent findings on the role of ENO-1 in PCa, including its molecular mechanisms of action, and to explore its potential as a novel therapeutic target. Moreover, we aim to discuss the implications of ENO-1-based therapies in the context of NEPC and their disproportionate impact on AA patients [3]. By illuminating the underlying mechanisms that link ENO-1 to PCa and its potential clinical implications, this review could provide important insights to enhance the development of more effective treatment modalities for patients with advanced PCa.

Immunotherapy

Protein-Specific Membrane Antigen (PSMA) has emerged as a promising target for the diagnosis and treatment of advanced Prostate Cancer (PCa). In recent years, PSMA-targeted imaging and therapy have gained considerable attention due to their excellent specificity and sensitivity. Specifically, PSMA Radioligand Therapy (PSMA-RLT) has emerged as a novel option for men with advanced PCa [3]. Nevertheless, a significant proportion of patients with advanced PCa do not respond adequately to PSMA-RLT due to the emergence of Neuroendocrine Prostate Cancer (NEPC), a phenomenon characterized by loss of PSMA expression. Reports indicate that approximately 30% of patients fall into this category. As of 2023, research efforts are underway to develop treatments that are effective

***Corresponding author:** Carlos A. Cardenas, Department of Oncology, Foundation for Research and Sciences (FORESC), USA. E-mail: Karmed@live.com

Received: July 16, 2023; Manuscript No: COCR-23-108190; **Editor Assigned:** July 18, 2023; PreQC Id: COCR-23-108190 (PQ); **Reviewed:** July 24, 2023; QC No: COCR-23-108190 (Q); **Revised:** July 27, 2023; Manuscript No: COCR-23-108190 (R); **Published:** July 29, 2023; DOI: 10.4172/cocr.6(7).303

SciTechnol International Publisher of Science, Technology and Medicine

All articles published in Clinical Oncology: Case Reports are the property of SciTechnol, and is protected by copyright laws. Copyright © 2023, SciTechnol, All Rights Reserved.

against both PSMA-expressing and NEPC forms of advanced PCa. Prostate-Specific Membrane Antigen (PSMA) is a protein that is commonly targeted in prostate cancer treatment. However, recent research has also explored targeting this protein in sarcomas[4-6], a type of cancer [7, 8] that affects connective tissue such as muscles and bone [5, 9, 10].

Glycolytic Enzyme Enolase-1 (ENO-1) as an Alternative Target

ENO-1, a glycolytic enzyme, has gained attention as a potential alternative target for NEPC. Recent research has shown that AA and EA men with PCa exhibit differential serum antibody reactivity to ENO-1. While circulating serum antibodies from EA-PCa patients recognized ENO in both docetaxel (DTX)-sensitive and -resistant PCa cell lines, sera from AA-PCa men only recognized ENO in DTX-sensitive cells [3], with loss of immunoreactivity in the resistant cells. This suggests that AA-PCa patients may generate a preferential antibody response to ENO-1, while EA-PCa patients preferentially target ENO-2.

ENO-1 Expression in Chemosensitive and Chemoresistant NEPC Cells

Recent research studies analyzing ENO-1 expression in chemosensitive and Chemoresistant NEPC cells with immunoblotting and monoclonal antibodies have yielded compelling results. ENO-1 and ENO-2 were found to be expressed in chemosensitive cells, while DTX-resistant cells had only ENO-1 expression and a clear loss of ENO-2. The e xpression p attern in t he cells was found t o match the differential immunoreactivity observed in AA-PCa serum antibodies, signifying that targeting ENO-1 could be an efficacious treatment for NEPC [3]. Utilizing advanced techniques, such as immunofluorescence microscopy, membrane fractionation analysis, and flow cytometry, provides an opportunity to examine ENO-1 expression more comprehensively and gain further insights into NEPC. Accessing this information could pave the way toward the development of more efficacious treatments for NEPC in the future.

Targeting ENO-1 with Small Molecule Inhibitors (SMIs)

Recent research studies involving the targeting of ENO-2 in Chemoresistant Prostate Cancer (PCa) cells have highlighted the metabolic vulnerability caused by the loss of ENO redundancy.

As of the year 2023, there is a significant emphasis on the exploration of potential therapeutic interventions that are directed toward targeting ENO-1. The current research efforts are primarily focused on investigating the level of surface expression of ENO-1 in patient-derived Neuroendocrine Prostate Cancer (NEPC) cell lines. These research endeavors have the potential to uncover effective treatment options and can significantly augment our knowledge and understanding of the underlying complexities of the NEPC [3]. Advanced techniques such as monoclonal antibodies, immuno fluorescence microscopy, membrane fractionation analysis, and flow cytometry are employed to conduct this investigation. Researchers are further evaluating the efficacy of Small Molecule Inhibitors (SMIs) that target ENO-1 in Chemoresistant NEPC cells, with promising initial results indicating the potential of such inhibitors as a viable treatment option.

Collectively, these investigations offer an encouraging avenue for the development of effective treatment strategies for the NEPC [3], with significant clinical implications.

Future Prospects and Implications for AA-PCa Patients

The identification of ENO-1 as a promising therapeutic target for Neuroendocrine Prostate Cancer (NEPC) represents a significant advancement in the quest for effective treatment options [1]. This development is particularly relevant for African American (AA) patients with Prostate Cancer (PCa), who experience disproportionately higher morbidity and mortality rates than their European American (EA) counterparts [3]. Given the reduced immune response against ENO-1 in AA-PCa patients, targeted therapy against this antigen may offer a promising avenue for improved outcomes. As of the year 2023, current ongoing endeavors are directed toward appraising the practicality of creating targeted therapies against ENO-1, which could have the potential to significantly reduce the health disparities observed in PCa between AA and EA men [3]. If successful, such therapies could offer a much-needed solution for patients with NEPC and could have an enormous impact on the future of PCa treatment. In addition to the challenges posed by cancer treatments, patient burnout has also become an increasingly concerning issue [11]. Patients with NEPC and other types of cancer often experience a great deal of physical and emotional exhaustion, causing a decline in overall quality of life and impacting cancer treatment outcomes [11]. Therefore, it is essential that future treatment options, such as targeted therapies against ENO-1 [3], are accompanied by robust patient support systems to manage these side effects, reducing the risk of patient burnout and leading to better treatment outcomes [11].

Conclusion

In conclusion, the identification of glycolytic enzyme ENO-1 as a potential therapeutic target for Neuroendocrine-Like Prostate Cancer (NEPC) represents a promising avenue for addressing the challenges posed by this aggressive form of prostate cancer. Additionally, the differential expression of ENO-1 in African American and European American men provides the opportunity to personalize treatment approaches and address potential ethnic disparities in NEPC incidence. While ENO-1-targeted therapies have shown promise in preclinical studies, further research is needed to validate their efficacy and develop effective treatment strategies for NEPC patients.

Research efforts are underway using advanced techniques such as immunofluorescence microscopy, membrane fractionation analysis, monoclonal antibodies, and flow cytometry to investigate the level of surface expression of ENO-1 in patient-derived NEPC cell lines and identify effective therapeutic interventions. Moreover, researchers are evaluating Small Molecule Inhibitors (SMIs) that target ENO-1 in Chemoresistant NEPC cells with promising initial results, highlighting the potential of SMIs as a viable treatment option. The discovery of such therapies has significant clinical implications in addressing the health disparities observed between African American and European American men with prostate cancer, offering a much-needed solution for patients with NEPC and paving the way for personalized and effective treatment strategies for patients with advanced prostate cancer.

References

1. Cardenas CA (2023) The State of Prostate Cancer Around the World - Advances in Prostate Cancer. Clin Oncol Case Rep 6: 1-4.
2. Jain MA, Leslie SW, Sapra A (2022) Prostate cancer screening. StatPearls Pub.
3. Santiago KR, Duran AM, Casiano CA, Almaguel FG, Das B (2023) Abstract C063: Enolase-1 as a candidate theranostics target for neuroendocrine prostate cancer. Cancer Epidemiol Biomarkers Prev 32: 63.
4. Cardenas CA (2023) Sarcomas: A Comprehensive Review of Classification, Diagnosis, Treatment, and Psychosocial Aspects. Clin Oncol Case Rep 6: 1-4.
5. Donoso PC, Perez MPS, Aguirre CC, Barbosa AO, Gomez CMG, et al. (2022) Angiosarcoma suprarrenal primario. Reporte de caso. Archivos Patologia 3: 96-103.
6. Ferrer NR, Romero MB, Ochenduszko S, Perpina LG, Malagon SP, et al. (2022) Solitary fibrous tumor of the thyroid. Report of a case with unusual clinical and morphological findings. Arch Pathol 3 : 104-109.
7. Cardenas CA, Abrishami S (2023) Heartbound Invaders: Reviewing Rare Malignant Carcinomas with Metastatic Fervor to the Heart. Clin Oncol Case Rep 6: 1-4.
8. Cardenas CA, Abrishami S (2023) Colorectal Carcinoma: Review and Novelties in 2023. Clin Oncol Case Rep 6: 1-4.
9. Nodar SR, Salazar S, Cardenas C, Yllan VG (2022) Testicular tumor in children: A rare case report. Curr Prac Med Sci 9:25-34.
10. Nodar SR, Barbosa APO, Garcia BE, Aguirre CC, Gomez JTC (2022) Primary angiosarcoma of the spleen with spontaneous rupture: A case report. Clin Oncol Case Rep 5: 1-4.
11. Cardenas C (2022) Extinguising the unknown from Burnout. Archivos Patologia 3: 87-87.

Author Affiliations Top

Department of Oncology, Foundation for Research and Sciences (FORESC), USA.