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Advances in Molecular Mechanisms, Diagnosis, and Treatment of Prostate Cancer: A Comprehensive Review

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Abstract: ***Prostate cancer is one of the most common malignancies affecting men worldwide, with significant variations in incidence and mortality across different regions. Understanding its complex molecular underpinnings is crucial for improving early detection and therapeutic strategies. This review systematically summarizes recent advances in the molecular mechanisms driving prostate cancer, highlighting the roles of genomics, epigenetics, and the tumor microenvironment in disease initiation and progression. Additionally, it evaluates novel diagnostic technologies such as multiparametric magnetic resonance imaging and liquid biopsy, which have enhanced risk stratification and early diagnosis. The evolution of treatment modalities is also discussed, ranging from conventional endocrine therapies to emerging targeted therapies, immunotherapy, and precision radiotherapy. By integrating current research findings, this article aims to provide a comprehensive theoretical foundation and practical guidance for clinicians and researchers, ultimately contributing to improved patient outcomes and the development of personalized medicine approaches in prostate cancer management.***

Keywords: Prostate cancer, Molecular mechanisms, Androgen receptor, Immunotherapy.

1. Introduction

Prostate cancer (PCa) is one of the most common malignant tumors in the male population worldwide. According to the 2020 Global Cancer Statistics Report, PCa ranks fifth in mortality rates. The complexity of this disease is underscored by its heterogeneous nature, which can range from indolent forms requiring minimal intervention to aggressive variants that demand intensive treatment regimens. The rising incidence of PCa in the elderly population has led to an increasing demand for effective diagnostic and therapeutic strategies. In recent years, numerous studies have elucidated the complex molecular mechanisms underlying the progression, diagnosis, and treatment of PCa from the perspectives of molecular biology and genomics, as well as the key genetic alterations and pathways responsible for its heterogeneity.

The advent of high-throughput sequencing technologies has facilitated the exploration of the complex genomic landscape of PCa. Key genetic alterations such as mutations in the TP53, PTEN, and SPOP genes, as well as the presence of TMPRSS2-ERG fusions, have been identified as critical drivers of tumorigenesis in PCa. These alterations not only influence the aggressiveness of the disease but also have implications for treatment resistance, particularly in the context of androgen deprivation therapy (ADT). A comprehensive understanding of these molecular mechanisms is essential to design targeted therapeutic strategies, which in turn can enhance patient prognosis and lower mortality rates in advanced disease settings.

In addition to genetic factors, the tumor microenvironment (TME) is a key contributor to PCa advancement, with the extracellular matrix, immune cells and cancer-associated fibroblasts (CAFs) collectively fostering a tumor-permissive niche that accelerates tumor proliferation and metastasis. Recent studies have highlighted the importance of the interactions between PCa cells and their microenvironment, emphasizing that these interactions can influence treatment responses and resistance mechanisms. As such, targeting the TME alongside direct tumor therapies may offer a novel approach to enhance therapeutic efficacy and overcome resistance in advanced PCa.

With the continuous deepening of our understanding of the biological characteristics of PCa, its diagnostic strategies have also evolved steadily. Due to the limitations in specificity and potential overdiagnosis risk associated with prostate-specific antigen (PSA) screening, the traditional diagnostic paradigm relying on PSA screening has been widely questioned. Against this backdrop, emerging technologies such as multiparametric magnetic resonance imaging (mpMRI) and liquid biopsy have emerged as crucial tools for improving diagnostic accuracy and optimizing risk stratification. These novel technologies can not only accurately identify clinically significant PCa but also effectively reduce unnecessary medical interventions in patients with indolent disease, achieving the dual goals of enhanced diagnostic efficacy and rational utilization of medical resources.

Treatment paradigms for PCa have also shifted significantly, particularly with the introduction of novel therapies targeting specific molecular pathways. The development of androgen receptor (AR) signaling inhibitors, poly (ADP-ribose) polymerase (PARP) inhibitors, and immunotherapies has expanded the arsenal available to clinicians. However, the emergence of treatment resistance remains a critical challenge, necessitating ongoing research into the underlying mechanisms and the identification of predictive biomarkers to guide therapy selection.

In conclusion, the landscape of PCa research is rapidly evolving, driven by advances in molecular biology, genomics,

and diagnostic technologies. A comprehensive understanding of the molecular mechanisms that govern PCa progression, combined with innovative diagnostic and therapeutic strategies, holds the promise of improving outcomes for patients with this prevalent malignancy. Continued exploration of the molecular underpinnings of PCa, alongside efforts to enhance precision medicine approaches, is essential to address the challenges posed by this complex disease.

2. Molecular Pathological Mechanisms and Heterogeneity of PCa

2.1 Key Driver Gene Mutations and Fusion Events

PCa is characterized by a complex landscape of genetic alterations that drive tumor initiation, progression, and heterogeneity. Among these, gene fusion events and mutations in key driver genes have been extensively studied and are pivotal in shaping the molecular subtypes and clinical behavior of PCa. As the most prevalent oncogenic event in Western populations, the TMPRSS2-ERG gene fusion is caused by the androgen-regulated TMPRSS2 promoter that drives the overexpression of the ERG transcription factor. This fusion leads to aberrant ERG activity that promotes tumorigenesis and is associated with distinct clinicopathological features, including aggressive tumor phenotypes and specific histological patterns. Another critical alteration is the loss or inactivation of the tumor suppressor gene PTEN, which is frequently observed in advanced and castration-resistant prostate cancer (CRPC). PTEN deficiency is known to activate the PI3K/AKT/mTOR signaling pathway, thereby enhancing cell proliferation, survival, and therapeutic resistance. Beyond these well-established drivers, recurrent mutations in genes such as SPOP define novel molecular subtypes with unique prognostic implications and differential responses to therapy. Importantly, germline or somatic mutations in homologous recombination repair genes including BRCA1/2 and ATM confer increased susceptibility to PCa and serve as predictive biomarkers for PARP inhibitor therapies, offering a precision medicine approach in selected patients. Collectively, these genetic alterations contribute to the molecular heterogeneity of PCa, influencing tumor behavior and guiding personalized treatment strategies.

2.2 Evolution of AR Signaling Pathway and Resistance Mechanisms

The AR signaling axis serves as the central oncogenic driver in the pathogenesis and progression of PCa, regulating tumor cell proliferation and survival. Despite initial responsiveness to ADT, sustained AR signaling underpins the development of CRPC, representing a major clinical therapeutic challenge [1]. The mechanisms of resistance to AR-targeted therapies in CRPC are highly heterogeneous, including AR gene amplification, point mutations that alter ligand specificity, and the expression of constitutively active AR splice variants lacking the ligand-binding domain, which mediate ligand-independent activation. On the other hand, overexpression of AR coactivators can enhance AR transcriptional activity, enabling tumor cell survival and proliferation in an androgen-depleted microenvironment [2]. Furthermore, epigenetic reprogramming and lineage plasticity facilitate the transition to AR-independent phenotypes, such as neuroendocrine prostate cancer (NEPC), which is characterized by loss of AR expression and complete resistance to AR-targeted therapies [3]. In-depth elucidation of these complex resistance mechanisms is critical for guiding the development of novel therapeutic strategies to overcome CRPC resistance, including AR degraders, inhibitors specific to AR splice variants, and modulators of alternative signaling pathways [4].

2.3 Epigenetic Regulation and TME

As a core molecular regulatory mechanism, epigenetic modifications play an indispensable role in the initiation, malignant progression, and distant metastasis of PCa. The establishment of aberrant DNA methylation patterns can induce the epigenetic silencing of tumor suppressor genes, thereby driving the transformation of normal prostatic epithelial cells into a malignant phenotype. Histone modification processes, mediated by specific enzymes such as EZH2, promote the aberrant activation of oncogenic signaling pathways and the acquisition of therapy-resistant phenotypes in tumor cells by regulating chromatin accessibility and transcriptional programs [5, 6]. Among non-coding RNAs, microRNAs (miRNAs) participate in key processes such as autophagy and apoptosis by post-transcriptionally regulating target gene expression; while long non-coding RNAs (lncRNAs) can influence the malignant phenotype of tumor cells by directly or indirectly modulating the AR [7, 8]. Furthermore, the TME exacerbates the malignant progression of PCa through interactions with CAFs, tumor-associated macrophages (TAMs), and other immune cells [9]. Notably, neuromodulatory elements within the TME, including adrenergic signaling, are implicated in the regulation of tumor behavior and metastasis [10]. In summary, the TME plays a central role in the pathophysiological process of PCa, and its key regulatory components have emerged as potential therapeutic targets for improving clinical outcomes.

3. New Strategies for Diagnosis and Risk Stratification of PCa

3.1 Innovations in Imaging Diagnostic Techniques

MpMRI has emerged as the gold standard for the diagnosis and local staging of PCa, primarily due to its high sensitivity and capacity to provide detailed anatomical and functional information. The Prostate Imaging Reporting and Data System (PI-RADS) has enhanced the standardization of lesion detection and risk stratification, not only facilitating consistency in image interpretation but also offering objective evidence-based support for clinical biopsy decisions. Studies have demonstrated that mpMRI achieves a diagnostic sensitivity of up to 93% for clinically significant prostate cancer (csPCa) and holds the potential to reduce unnecessary biopsies by approximately 27% [11]. Furthermore, anterior prostate lesions are often missed due to sampling bias in conventional systematic biopsies, whereas mpMRI-guided targeted biopsy techniques have substantially improved the detection rate of these lesions. By accurately delineating the three-dimensional extent and invasive margins of tumors, this approach provides crucial imaging support for the individualized development of radical surgical plans [12].

Prostate-specific membrane antigen positron emission tomography/computed tomography (PSMA-PET/CT) has achieved a revolutionary breakthrough in the accurate detection of micrometastases and the localization of biochemical recurrence lesions in PCa. As a highly promising imaging modality for PCa detection and staging, the clinical translation and application of PSMA-PET/CT have significantly improved the detection efficacy of lymph node metastases and distant metastases, thereby enabling the delivery of individualized treatment and management plans for patients. Furthermore, PSMA-targeted PET imaging-guided biopsy techniques have demonstrated considerable promise in enhancing the detection rate of csPCa by specifically targeting suspicious lesions identified on imaging [13].

Recent significant advances in ultrasound diagnostic technology have led to the development of multiparametric ultrasound (mpUS), which integrates multiple functional modalities including Doppler imaging, elastography, contrast-enhanced ultrasound (CEUS), and micro-ultrasound. This technique has emerged as a real-time, cost-effective alternative or adjunctive diagnostic tool to mpMRI. These advanced ultrasound technologies have substantially improved the detection efficacy of csPCa and the precision of biopsy guidance, particularly demonstrating unique clinical value in patient populations with contraindications to mpMRI. However, mpUS currently lacks a standardized imaging assessment system and large-scale external validation data, and its non-inferiority or superiority in clinical efficacy compared with mpMRI remains to be confirmed by additional prospective clinical studies [14]. Furthermore, newer ultrasound-based technologies such as ultrasound elastography and micro-ultrasound can provide complementary information for PCa diagnosis and can be combined with other imaging modalities to further optimize diagnostic performance [15].

Furthermore, emerging MRI technologies, including biparametric MRI (bpMRI) and advanced diffusion-weighted imaging (DWI) sequences, have been demonstrated to markedly improve image quality, reduce imaging artifacts, and simultaneously preserve the reproducibility of apparent diffusion coefficient (ADC) quantification. These technological innovations hold promise for further optimizing PCa imaging protocols and enhancing the accuracy of clinical diagnosis [12, 16]. Concurrently, artificial intelligence (AI) and deep learning algorithms have been increasingly applied in the imaging diagnosis of PCa, providing a novel technical avenue for the intelligent assessment of lesions [17].

In summary, the field of imaging-based diagnosis for PCa is undergoing rapid advancement. The multimodal integration of mpMRI, PSMA-PET/CT and advanced ultrasound technologies, combined with AI-driven image analysis algorithms, is propelling the field toward a more precise, minimally invasive, and personalized diagnostic paradigm. These technological innovations enable the accurate localization, precise staging, and robust risk assessment of PCa lesions, ultimately facilitating the formulation of tailored therapeutic strategies for patients.

3.2 Clinical Applications of Liquid Biopsy and Molecular Biomarkers

Liquid biopsy has emerged as a minimally invasive and dynamic approach for the diagnosis, prognostic evaluation, and therapeutic monitoring of PCa. Circulating tumor DNA (ctDNA) analysis enables real-time assessment of tumor genomic evolution, identification of acquired resistance mutations such as AR variants, and precise evaluation of treatment response and minimal residual disease [18]. The molecular characterization of circulating tumor cells (CTCs) serves as a critical predictive biomarker in patients with CRPC.

Non-invasive urine-based assays analyzing RNA biomarkers, such as PCA3 and TMPRSS2-ERG, have been validated to aid in decision-making for initial or repeat biopsies. These assays enhance the detection rate of clinically significant PCa while effectively reducing unnecessary invasive biopsy procedures [19, 20]. By leveraging gene expression signature profiling, this technology improves diagnostic specificity and demonstrates significantly superior diagnostic performance compared to traditional PSA testing. Furthermore, it provides more accurate risk stratification for both biopsy-naïve and previously biopsied men.

Advances in molecular biomarker panels, particularly tissue-derived genomic classifiers such as Decipher, Oncotype DX Genomic Prostate Score (GPS), and Polaris, provide more refined prognostic information by integrating genomic alterations with clinicopathological parameters. These classifiers have been widely utilized for risk stratification and treatment decision-making in PCa [21, 22]. Moreover, blood-borne genetic biomarkers have been identified as non-invasive prognostic indicators for PCa [23].

The application scope of liquid biopsy technology has been extended to the field of epigenomic analysis; for instance, DNA methylation profiling of cell-free circulating DNA (cfDNA) can effectively capture tumor-specific molecular alterations [24]. Exosomal miRNAs regulated by cytokines such as tumor necrosis factor-like weak inducer of apoptosis (TWEAK) in semen and urine facilitate the prognostic evaluation of aggressive phenotypes in PCa [25]. Furthermore, polygenic risk score models constructed by integrating multiple single-nucleotide polymorphism (SNP) loci have significantly improved genetic risk stratification across ethnically diverse populations, thereby providing robust support for PCa screening and early detection [26].

Despite considerable breakthroughs achieved in this field, substantial challenges remain with respect to standardized sample collection, detection sensitivity, and data interpretation. The control of pre-analytical variables, verification of assay reproducibility, and integration of multi-omics data require further refinement to facilitate the translation of liquid biopsy technologies into routine clinical practice [27]. Notwithstanding these limitations, liquid biopsy holds tremendous potential to complement imaging modalities and tissue-based diagnostic assays, enabling dynamic monitoring throughout the entire course of PCa management.

3.3 Integration of Precision Risk Stratification Models

Accurate risk stratification is pivotal to guiding PCa management, as it enables the effective balancing of the risks associated with overtreatment and undertreatment. To date, integrated models incorporating clinical parameters, imaging findings, and genomic classifiers have been proposed in relevant studies, which are designed to overcome the limitations of conventional assessment methods and further improve the accuracy of risk stratification [28]. For instance, nomograms integrating variables including age, PSA levels, clinical T stage, biopsy Gleason score groups, and percentage of positive cores have exhibited superior discriminatory efficacy in distinguishing benign lesions from intermediate-high-risk PCa, compared with the standalone application of the National Comprehensive Cancer Network (NCCN) risk stratification criteria [29, 30].

The incorporation of mpMRI-derived imaging features, particularly PI-RADS scores, has further refined risk prediction for PCa. Combined models integrating mpMRI with prostate-specific antigen density (PSAD) have enhanced the capacity to identify populations at high risk of clinically significant PCa [31, 32]. Furthermore, radiomics approaches based on lesion-targeted strategies can segment tumor tissues into distinct subregions according to MRI imaging characteristics, thereby enabling refined characterization of tumor heterogeneity and more accurate risk stratification [33].

AI and machine learning algorithms have been increasingly applied in image interpretation for PCa diagnosis [17]. Proteomic signatures obtained via computational analyses have exhibited promising potential in the stratification of intermediate-risk patients and the independent prediction of biochemical recurrence, with this predictive performance being independent of Gleason scores [34].

Genetic risk stratification using polygenic hazard scores enhances identification of individuals at high risk for aggressive disease, informing screening and prevention strategies [26]. Integration of these diverse data streams into cohesive models supports precision medicine by enabling tailored surveillance, biopsy decisions, and therapeutic interventions.

In conclusion, the integration of clinical, imaging, and molecular biomarkers into comprehensive risk stratification models represents a significant advancement in PCa management. Continued development and validation of these models, alongside incorporation of AI-driven analytics, will facilitate personalized care pathways, optimizing outcomes while minimizing unnecessary interventions.

4. Optimization and Expansion of Active Surveillance Criteria

Active surveillance (AS) has become the cornerstone management strategy for patients diagnosed with very low-risk and low-risk PCa, aiming to balance the need for cancer control with the avoidance of overtreatment and associated morbidities. Traditionally, AS inclusion criteria relied heavily on clinical parameters such as PSA levels, Gleason score, and clinical staging. However, recent advances have led to the optimization and expansion of these criteria by integrating mpMRI and molecular biomarkers to more accurately identify truly indolent disease and safely defer definitive treatment.

The incorporation of mpMRI allows for improved visualization and characterization of prostate lesions, enabling targeted biopsies that enhance the detection of clinically significant cancers while reducing the diagnosis of insignificant tumors. This imaging modality, combined with emerging molecular markers, provides a more refined risk stratification framework that surpasses traditional clinical parameters alone.

Studies have demonstrated that the fusion of MRI-targeted biopsy with systematic biopsy reduces unnecessary interventions and lowers the risk of missing clinically significant cancers, thereby improving patient selection for AS. Furthermore, the expansion of AS criteria to include selected patients with favorable intermediate-risk features, supported by imaging and biomarker data, is gaining acceptance, although long-term safety data remain under investigation. The use of molecular biomarkers, including genomic classifiers and ctDNA, offers additional layers of precision by capturing tumor biology and aggressiveness beyond histopathology.

Collectively, these advancements facilitate a more personalized approach to AS, enhancing its safety and efficacy by ensuring that only patients with truly indolent disease are enrolled, while those with higher-risk features are identified early for curative intervention. AS protocols for localized PCa continue to evolve, aiming to optimize patient outcomes and quality of life.

5. Systemic Therapy Innovations in Advanced PCa

5.1 Deepening Application of Novel Endocrine Therapeutics

The landscape of endocrine therapy for advanced PCa has undergone a profound evolution, particularly with the advent and earlier integration of second-generation AR inhibitors — including enzalutamide, apalutamide, and darolutamide. Characterized by potent AR antagonism and the ability to abrogate AR nuclear translocation and DNA binding, these agents have transitioned from primary use in metastatic castration-resistant prostate cancer (mCRPC) to frontline therapy for metastatic hormone-sensitive prostate cancer (mHSPC). This paradigm shift is supported by clinical trials demonstrating substantial survival benefits when these agents are combined with ADT in the hormone-sensitive setting [35]. Early deployment of these AR pathway inhibitors capitalizes on their capacity to more comprehensively suppress AR signaling, thereby delaying disease progression and improving overall survival.

Complementing AR inhibitors, CYP17A1 inhibitors such as abiraterone acetate—administered concomitantly with prednisone to mitigate mineralocorticoid excess—have become cornerstone therapies in both mCRPC and mHSPC management. Abiraterone blocks androgen biosynthesis not only in the testes but also in the adrenal glands and TME, targeting intracrine androgen production that drives castration

resistance. The optimal sequencing and combination strategies of abiraterone with AR inhibitors remain active areas of investigation, as clinicians strive to maximize efficacy while mitigating overlapping toxicities and addressing resistance mechanisms [36, 37]. Furthermore, the cardiovascular toxicity associated with intensified hormonal therapy necessitates rigorous patient selection and risk mitigation strategies, including potential treatment de-escalation in select patients with exceptional treatment responses [38]. Collectively, the expanding application of novel endocrine therapies reflects a refined approach that balances early aggressive AR pathway suppression with individualized patient factors to optimize outcomes in advanced PCa.

5.2 Molecular Subtype-Based Targeted Therapy

The advent of molecular profiling has ushered in an era of precision medicine for advanced PCa, enabling targeted therapeutic strategies tailored to specific genetic alterations. A landmark advancement is the approval of PARP inhibitors — including olaparib and rucaparib—for patients with mCRPC harboring homologous recombination repair (HRR) gene mutations, most notably BRCA1 and BRCA2. These agents capitalize on synthetic lethality by inhibiting PARP-mediated DNA repair pathways, thereby inducing the accumulation of DNA damage and subsequent tumor cell death in HRR-deficient malignancies. Clinical trials have consistently demonstrated the efficacy of PARP inhibitors in genetically stratified patient cohorts, representing a pivotal advance in personalized PCa therapy [39-41]. The integration of PARP inhibitors into clinical treatment algorithms necessitates comprehensive genomic profiling to identify eligible patients, underscoring the central role of molecular diagnostics in contemporary oncology practice.

Beyond DNA repair deficiencies, aberrations in the PI3K/AKT/mTOR signaling pathway—frequently driven by PTEN loss—represent another promising therapeutic target under active clinical investigation. Inhibitors targeting this signaling cascade are being evaluated both as monotherapies and in combination with AR pathway inhibitors to overcome resistance mediated by compensatory signaling activation. Further research is warranted to delineate the efficacy, toxicity profiles, and optimal patient selection criteria for these novel therapeutic agents [42, 43]. As our understanding of PCa intra- and inter-tumor heterogeneity deepens, the molecular subtype-guided targeted therapy paradigm holds great promise for refining treatment personalization, enhancing therapeutic efficacy, and delaying the emergence of treatment resistance by addressing distinct oncogenic drivers within individual tumors.

5.3 Exploration and Challenges of Immunotherapeutic Strategies

Immunotherapy for PCa confronts unique challenges, primarily attributed to the tumor's classification as an immunologically "cold" malignancy—characterized by low mutational burden and limited immune cell infiltration. Biomarker-guided patient stratification remains a critical consideration in the development of immunotherapeutic strategies for mCRPC [44]. These observations have catalyzed intensive efforts to enhance immunotherapeutic efficacy through innovative approaches.

Therapeutic cancer vaccines, typified by sipuleucel-T, represent an early-generation immunotherapeutic modality designed to elicit tumor-specific immune responses; however, their clinical benefit remains modest. Recent advances in PCa immunotherapy encompass a spectrum of novel strategies currently under preclinical and clinical investigation [45]. Despite these progressions, single-agent immunotherapies have achieved only limited success, partly due to the highly immunosuppressive TME—characterized by regulatory T cells, myeloid-derived suppressor cells (MDSCs), and inhibitory mediators such as adenosine. This immunosuppressive milieu is mediated in part by CD38-expressing immune infiltrates, which have been associated with poor clinical outcomes [46].

To surmount these obstacles, combination strategies integrating immunotherapy with radiotherapy, targeted therapies, or novel endocrine agents are under active clinical evaluation. Such combinatorial approaches are being rigorously explored to improve treatment responses in mCRPC [47, 48]. While these strategies hold considerable promise, they necessitate meticulous optimization to balance therapeutic efficacy and treatment-related toxicity. Collectively, the landscape of immunotherapy for PCa is rapidly evolving, with ongoing research focused on identifying robust predictive biomarkers, refining combination regimens, and developing next-generation immune modulators—all aimed at unlocking the full potential of immuno-oncology in this clinically challenging disease.

6. Future Research Directions and Challenges

6.1 Exploring New Mechanisms to Overcome Therapeutic Resistance

Therapeutic resistance remains a major challenge in PCa management, particularly in advanced stages such as castration-resistant PCa (CRPC). A thorough elucidation of the underlying mechanisms driving resistance is crucial for developing effective intervention strategies.

The transdifferentiation of prostate adenocarcinoma cells into neuroendocrine phenotypes has been well established as a key contributor to therapeutic resistance. This phenotypic transition enables cancer cells to evade the cytotoxic effects of AR-targeted therapies, ultimately resulting in treatment failure. Therefore, investigating the molecular pathways regulating this process is central to identifying novel therapeutic targets.

Furthermore, the role of epigenetic modifications in mediating resistance underscores the potential of epigenetic drugs to reverse resistant phenotypes. Senolytic agents, which selectively eliminate senescent cells, have emerged as promising candidates for eradicating persistent cancer cells that survive initial treatment and drive disease relapse. Recent advances in anti-aging drug research indicate that compounds with senolytic activity, such as rapamycin and metformin, hold promise for repurposing to target therapy-resistant PCa cells [49].

Combining these novel strategies with conventional therapies is expected to significantly enhance treatment efficacy and delay or block the emergence and proliferation of drug-resistant clones. Thus, future research should focus on clarifying the multifaceted mechanisms of PCa resistance and translating these insights into targeted intervention measures.

6.2 Clinical Translation of AI and Multi-Omics Integration

The integration of AI with multi-omics data has emerged as a transformative paradigm for advancing precision medicine in PCa. By synergistically harnessing genomic, transcriptomic, proteomic, epigenomic, and radiomic data, alongside clinical and pathological parameters, AI-driven computational models can construct comprehensive digital twin representations of individual patients. These patient-specific models enable the prediction of therapeutic responses and prognostic outcomes with superior accuracy compared to conventional analytical approaches.

Recent investigations have systematically demonstrated the utility of AI in multi-omics data integration for PCa diagnosis, molecular subtype classification, and treatment stratification — highlighting its potential to guide evidence-based personalized therapy decisions. Furthermore, the development of real-time, dynamic monitoring platforms incorporating AI algorithms facilitates adaptive treatment adjustments during the therapeutic course, paving the way for truly dynamic precision oncology.

Notwithstanding these advancements, critical challenges persist, including data heterogeneity across omics layers, robust handling of missing data, and inherent model interpretability—necessitating continued methodological innovations and rigorous validation in large-scale clinical cohorts. Notably, the application of AI in multi-omics integration has been extended to liquid biopsy-based analyses and TME characterization, offering minimally invasive modalities for longitudinal disease monitoring and early detection of treatment resistance.

Emphasizing the development of explainable AI and standardized analytical pipelines will be pivotal to fostering clinical adoption and stakeholder trust. Collectively, the convergence of AI and multi-omics technologies holds immense promise for accelerating translational biomedical research and revolutionizing clinical applications in PCa management.

6.3 Addressing Health Disparities and Developing Personalized Prevention Strategies

Substantial health disparities in PCa incidence, disease progression, and clinical outcomes exist across racial, ethnic, and geographic demographics. This phenomenon is driven by the complex interplay of genetic predispositions, environmental exposures, and social determinants of health (SDOH).

Investigations into these disparities have uncovered distinct differences in tumor biological characteristics, healthcare access and utilization, socioeconomic status (SES), and modifiable lifestyle behaviors—factors that collectively contribute to the unequal distribution of disease burden. To mitigate such inequities, the integration of ancestry-informed genetic risk profiling, contextualized environmental exposure assessments, and SDOH is urgently needed.

Personalized early screening algorithms and chemoprevention strategies tailored to individual risk factors hold promise for enhancing early detection efficacy and slowing disease progression. Furthermore, culturally congruent public health interventions and equitable access to high-quality preventive and therapeutic resources are essential to eliminating systemic barriers in healthcare.

The integration of SDOH into clinical decision-making frameworks, augmented by AI and multi-omics data analytics, can further improve the precision of risk stratification and optimize preventive healthcare delivery. Future research should focus on elucidating the multifactorial mechanisms underlying PCa health disparities and developing culturally sensitive, targeted interventions for diverse populations [50].

7. Conclusion

In conclusion, the landscape of PCa research and clinical management has undergone a profound transformation, driven by advances in molecular biology and the emergence of precision medicine. From an expert perspective, this evolution reflects a paradigm shift from traditional, unidimensional approaches toward a more nuanced and integrated understanding of disease heterogeneity and therapeutic resistance. The transition from reliance on PSA screening alone to a comprehensive diagnostic framework incorporating mpMRI, liquid biopsies, and molecular stratification exemplifies this progress. Such multimodal assessment strategies have significantly enhanced diagnostic accuracy and refined risk stratification, thereby enabling more personalized and evidence-based clinical decision-making.

Therapeutically, the field has moved beyond conventional ADT to embrace a diversified arsenal that includes novel endocrine agents, targeted molecular therapies, and immunotherapeutic modalities. This expansion not only reflects deeper insights into the molecular drivers of PCa but also underscores the necessity of tailoring treatments to individual tumor biology. Minimally invasive local therapies have similarly evolved, offering improved precision and reduced morbidity, which collectively enhance patient quality of life. Nevertheless, despite these advances, clinical management remains challenged by the complexity of resistance pathways that often limit long-term therapeutic efficacy. Addressing these mechanisms requires sustained translational research efforts that bridge laboratory discoveries with clinical applications, thereby fostering the development of next-generation therapeutics.

Balancing diverse research perspectives—from molecular characterization to clinical implementation—necessitates a multidisciplinary approach integrating urology, oncology, radiology, pathology, and genomics. Such collaboration is essential to unravel the intricate interplay between tumor biology and treatment response, ultimately guiding the design of adaptive therapeutic strategies. Moreover, translating

cutting-edge scientific findings into widespread clinical benefit must be accompanied by concerted efforts to improve healthcare accessibility and equity. Ensuring that advances in precision diagnostics and therapeutics reach diverse patient populations is critical to reducing disparities and optimizing outcomes on a global scale.

Looking forward, the future of PCa research hinges on overcoming several key challenges. These include elucidating the full spectrum of molecular resistance mechanisms, refining biomarker-driven patient selection, and integrating emerging technologies such as AI and single-cell sequencing into clinical workflows. Sustained investment in multidisciplinary collaboration and robust clinical trials will be vital to validate novel interventions and accelerate their adoption. Ultimately, the overarching goal remains to enhance both survival and quality of life for PCa patients through personalized, evidence-based care.

In summary, the ongoing shift toward molecularly informed, precision medicine approaches in PCa represents a significant leap forward in the field. By harmonizing diverse research insights and addressing both scientific and systemic barriers, the medical community is poised to deliver more effective, individualized treatments. Continued innovation and collaboration will be indispensable in translating these advances into tangible, equitable improvements in patient outcomes.

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